COMMONWEALTH OF MASSACHUSETTS

SUFFOLK, ss SUPERIOR COURT

COMMONWEALTH OF MASSACHUSETTS,	)	
	)	
v.	)	
	)	
PURDUE PHARMA L.P., PURDUE PHARMA INC., RICHARD SACKLER, THERESA SACKLER, KATHE SACKLER, JONATHAN SACKLER, MORTIMER D.A. SACKLER, BEVERLY SACKLER, DAVID SACKLER, ILENE SACKLER LEFCOURT, PETER BOER, PAULO COSTA, CECIL PICKETT, RALPH SNYDERMAN, JUDY LEWENT, CRAIG LANDAU, JOHN STEWART, MARK TIMNEY, and RUSSELL J. GASDIA.	)	CIVIL ACTION NO. 1884-CV-01808 (BLS2)

AFFIDAVIT OF TIMOTHY C. BLANK

I am a Partner at Dechert LLP, located at One International Place, 40th Floor, 100 Oliver Street Boston, MA 02110, counsel for Purdue Pharma L.P. and Purdue Pharma Inc. (collectively, "Purdue") in the above-captioned action. I make this affidavit under pains and penalty of perjury in support of Purdue's accompanying Motion to Dismiss the First Amended Complaint filed by the Commonwealth of Massachusetts as follows:

1. Attached hereto as Exhibit A is a 2007 Consent Judgment entered into between the Commonwealth of Massachusetts and Purdue dated May 3, 2007.

2. Attached hereto as Exhibit B is the FDA-approved labeling for OxyContin.

3. Attached hereto as Exhibit C is a 2013 FDA denial of a "Citizen's Petition" submitted by Physicians for Responsible Opioid Prescribing ("PROP").

4. Attached hereto as Exhibit D is the Commonwealth's 2016 Chapter 55 report entitled, "An Assessment of Opioid Related Deaths (2013-2014)." It is publicly available at https://www.mass.gov/media/971976/download.

5. Attached hereto as Exhibit E is the Commonwealth's 2017 Chapter 55 Report entitled, "An Assessment of Fatal and Nonfatal Opioid Overdoses in Massachusetts (2011-2015)." It is publicly available at https://www.mass.gov/media/1573931/download.

6. Attached hereto as Exhibit F is the home page of the Commonwealth's Chapter 55 website, which is publicly available at https://chapter55.digital.mass.gov/.

7. Attached hereto as Exhibit G is a publication from the Commonwealth entitled, "Data Brief: Opioid-Related Overdose Deaths among Massachusetts Residents." It is publicly available at https://www.mass.gov/lists/current-opioid-statistics#updated-data---q4-2018---as-of-february-2019-.

8. Attached hereto as Exhibit H is the "Final Report" of the Massachusetts OxyContin and Other Drug Abuse Commission. It is publicly available at https://archives.lib.state.ma.us/bitstream/handle/2452/265674/ocm70914663.pdf?sequence=1&isAllowed=y.

9. Attached hereto as Exhibit I is a presentation by Dr. Douglas C. Throckmorton entitled, "FDA Perspective on Abuse-Deterrent Opioid Development." It is publicly available at https://www. fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM545923.pdf.

10. Attached hereto as Exhibit J is a presentation by Dr. Douglas C. Throckmorton entitled, "FDA's Actions to Address the Opioid Epidemic." It is publicly available at https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM601178.pdf.

11. Attached hereto as Exhibit K is an FDA publication entitled, "Abuse-Deterrent Opioid Analgesics." It is publicly available at https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm600788.htm.

12. Attached hereto as Exhibit L is an FDA publication entitled, "FDA Analysis of Long-Term Trends in Prescription Opioid Analgesic Products: Quantity, Sales, and Price Trends." It is publicly available at https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM598899.pdf

13. Attached hereto as Exhibit M is a report entitled, "Recommendations of the OxyContin and Heroin Commission of the Commonwealth of Massachusetts," dated November 2009. It is publicly available at https://archives.lib.state.ma.us/bitstream/ handle/2452/46748/ocn466141823.pdf?sequence=1.

14. Attached hereto as Exhibit N is a 2015 report entitled, "Recommendations of the Governor's Opioid Working Group." It is publicly available at https://www.mass.gov/files/2017-08/recommendations-of-the-governors-opioid-working-group.pdf.

15. Attached hereto as Exhibit O is Table 8 of the MassHealth (the Commonwealth's Medicaid Provider) Covered Drug List. It is publicly available at https://masshealthdruglist.ehs.state.ma.us/MHDL/pubtheradetail.do?id=8.

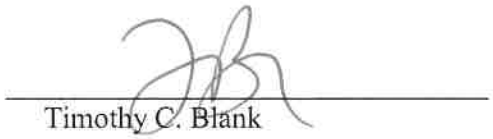
16. Attached hereto as Exhibit P is a 2014 report from the Massachusetts Department of Public Health entitled, "Findings of the Opioid Task Force and Department of Public Health Recommendations on Priorities for Investments in Prevention, Intervention, Treatment and Recovery." It is publicly available at https://www.mass.gov/files/documents/2016/07/tp/report-of-the-opioid-task-force-6-10-14.pdf.

17. Attached hereto as Exhibit Q is the 2012 "Citizen's Petition" submitted by Physicians for Responsible Opioid Prescribing ("PROP"). It is publicly available at https://www.regulations.gov/document?D=FDA-2012-P-0818-0001.

18. Exhibit A is referred to in the First Amended Complaint (¶¶ 193, 859) and the Commonwealth is a party to this Judgment.

19. Exhibits B through Q are all publicly available, either on federal government websites (Exs. B, C, I, J, K, L, and Q) or on the Commonwealth's own websites (Exs. D, E, F, G, H, M, N, O, and P).

Signed under the pains and penalties of perjury this 1st day of March 2019.



Timothy C. Blank

Exhibit A

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COMMONWEALTH OF MASSACHUSETTS
SUPERIOR COURT

COMMONWEALTH OF MASSACHUSETTS, Plaintiff, v. PURDUE PHARMA L.P., PURDUE PHARMA INC.; and THE PURDUE FREDERICK COMPANY, INC., Defendants	)	Civil Action No. 07-1967 (B)

CONSENT JUDGMENT

This Consent Judgment (hereinafter referred to as "Judgment") is entered into between the Massachusetts Attorney General and the defendants, Purdue Pharma, L.P., Purdue Pharma, Inc. and The Purdue Frederick Company, Inc. (collectively referred to as "Purdue"), and is part of a multistate settlement between Purdue and the Attorneys General of the States and Commonwealths of Arizona, Arkansas, California, Connecticut, District of Columbia, Idaho, Illinois, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Montana, Nebraska, Nevada, New Mexico, North Carolina, Ohio, Oregon, Pennsylvania, South Carolina, Tennessee, Texas, Vermont, Virginia, Washington, and Wisconsin (hereinafter referred to as "Signatory Attorneys General"), acting on behalf of their respective states, and pursuant to their respective consumer protection statutes. Upon the consent of the parties hereto, IT IS HEREBY ORDERED, ADJUDGED AND DECREED AS FOLLOWS:

I. DEFINITIONS

1. The following definitions shall be used in construing this Consent Judgment (hereinafter "Judgment"):

A. "Covered Persons" shall mean all officers, employees and all contract or third-party sales representatives, including Medical Liaisons, of Purdue or retained by Purdue having direct responsibility for marketing and promoting OxyContin to Health Care Professionals.

B. "Effective Date" shall mean the date on which Purdue receives a copy of this Judgment, duly executed by Purdue and by the Signatory Attorney General and filed with the Court.

C. "FDA Guidances for Industry" shall mean documents published by the United States Department of Health and Human Services, Food and Drug Administration ("FDA") that represent the FDA's current recommendations on a topic.

D. "Health Care Professional" or "Health Care Professionals" shall mean any person or persons duly licensed by relevant federal and/or state law to prescribe Schedule II pharmaceutical products, as well as duly licensed pharmacists, nurses and other licensed health professionals.

E. "Off-Label Promotion" shall mean the marketing and promotion of an Off-Label Use. Off-Label Promotion shall not mean discussion of the abuse and diversion of OxyContin that is not inconsistent with the Package Insert.

F. "Off-Label Use" shall mean any use inconsistent with the "Indications and Usage" section of the Package Insert.

G. "OxyContin" shall mean any controlled-release drug distributed by Purdue which contains oxycodone as an active pharmaceutical ingredient.

H. "Package Insert" shall mean the FDA approved label (as described in 21 C.F.R. §§ 201.56 and 57) for OxyContin, including all modifications to the label theretofore approved by the FDA.

I. "Parties" shall mean Purdue and the Signatory Attorneys General.

J. "Purdue" shall mean Purdue Pharma Inc., Purdue Pharma L.P., The Purdue Frederick Company, Inc. (d/b/a The Purdue Frederick Company), and all of their United States affiliates, subsidiaries, predecessors, successors, parents and assigns, who manufacture, sell, distribute and/or promote OxyContin.

K. "Remuneration" shall mean any gift, fee, or payment, exceeding twenty-five dollars ($25.00) in value, provided by Purdue directly or indirectly in connection with marketing or promotion of OxyContin.

L. "Signatory Attorney General" shall mean the Attorney General, or his or her designee, who has agreed to this Judgment.

M. "Subject Matter of this Judgment" shall mean the investigation under the State Consumer Protection Laws[1] of Purdue's promotional and marketing practices regarding OxyContin.

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[1] ARIZONA Consumer Fraud Act, Ariz. Rev. Stat. §44-1521, *et. seq.*; ARKANSAS - Deceptive Trade Practices Act, Ark. Code Ann. § 4-88-101 *et seq.*; CALIFORNIA Business and Professions Code § 17200 *et seq* 17500 *et seq* ; CONNECTICUT – Connecticut Unfair Trade Practices Act, Conn. Gen. Stat. §42-110 *et seq.*; DISTRICT OF COLUMBIA – District of Columbia Consumer Protection Procedures Act, D.C. Code § 28-3901 *et seq.*; IDAHO - Consumer Protection Act, Idaho Code § 48-601 *et seq.*; ILLINOIS - Consumer Fraud and Deceptive Business Practices Act, 815 ILCS § 505/1 *et seq.* (2002); KENTUCKY - Consumer Protection Statute, KRS 367.170; LOUISIANA – Unfair Trade Practices and Consumer Protection Law, LSA-R.S. 51:1401 *et seq.*; MAINE – Unfair Trade Practices Act, 5 M.R.S.A. section 205-A *et.* seq; MARYLAND - Consumer Protection Act, Maryland Commercial Law Code Annotated § 13-101 *et seq.*; MASSACHUSETTS - Consumer Protection Act, M.G.L. c. 93A *et seq.*; MONTANA - Mont. Code Ann. § 30-14-101 *et seq.*; NEBRASKA – Consumer Protection Act:

II. COMPLIANCE PROVISIONS

2. In the promotion and marketing of OxyContin, Purdue shall not make any written or oral claim that is false, misleading or deceptive.

3. In the promotion and marketing of OxyContin, Purdue shall not market or promote OxyContin in a manner that is, directly or indirectly, inconsistent with the "Indication and Usage" section of the Package Insert for OxyContin. Further, Purdue shall, consistent with the Package Insert, or as otherwise permitted by the FDA, not promote or market OxyContin in a manner that: (a) avoids or minimizes the fact that OxyContin is indicated for moderate to severe pain when a continuous around-the-clock analgesic is needed for an extended period of time; or (b) avoids, minimizes, or is inconsistent with individualizing treatment using a plan of pain management, such as outlined by the World Health Organization, the Agency for Healthcare Research and Quality (formerly known as the Agency for HealthCare Policy and Research), the Federation of State Medical Boards Model Guidelines or the American Pain Society, as referenced in the Package Insert.

Neb.Rev.Stat. 59-1601, *et seq.* (Reissue 2004 & RS Supp. 2006), Uniform Deceptive Trade Practices Act: Neb.Rev.Stat. 87-301 *et seq.* (Reissue 1999 & RS Supp. 2006); NEVADA - Deceptive Trade Practices Act, Nevada Revised Statutes 598.0903 *et seq.*; NEW MEXICO – Unfair Practices Act" NMSA 1978, S 57-12-1 *et seq.* (1967); NORTH CAROLINA - Unfair and Deceptive Trade Practices Act, N.C.G.S. § 75-1.1 *et seq.*; OHIO - Consumer Sales Practices Act, R.C. § 1345.01 *et seq.*; OREGON - Unlawful Trade Practices Act, ORS 646.605 to 646.656; PENNSYLVANIA - Unfair Trade Practices and Consumer Protection Law, 73 P.S. § 201-1 *et seq.*; SOUTH CAROLINA - Unfair Trade Practices Act, Sections 39-5-10 *et seq.*; TENNESSEE - Consumer Protection Act, Tenn. Code Ann. § 47-18-101 *et seq.*, (1977); TEXAS - Deceptive Trade Practices and Consumer Protection Act, Tex. Bus. And Com. Code § 17.41 *et seq.*, (Vernon 2002); VERMONT - Consumer Fraud Act, 9 V.S.A. § 2451 *et seq.*; VIRGINIA - Virginia Consumer Protection Act, Va. Code Ann. § 59.1 -196 *et seq.*; WASHINGTON - Washington Consumer Protection Act – R.C.W. 1986 *et seq*; WISCONSIN - Wis. Stat. § 100.18 (Fraudulent Representations).

4. In the promotion and marketing of OxyContin, Purdue shall provide "fair balance" statements, as defined in 21 C.F.R. §202.1 as may be amended or supplemented, or as appearing in FDA Guidances for Industry from time to time, regarding contraindications and adverse events, including but not limited to statements regarding OxyContin's potential for abuse, addiction, or physical dependence as set forth in the Package Insert.

5. In the promotion and marketing of OxyContin, Purdue shall not make misrepresentations with respect to OxyContin's potential for abuse, addiction, or physical dependence as set forth in the Package Insert. Further to this general prohibition on misrepresentations, Purdue, in the promotion and marketing of OxyContin, shall not represent, except as may be set forth in the Package Insert, that: a) OxyContin is "nonaddictive" or "virtually nonaddictive"; b) addiction to OxyContin occurs in "less than 1%" of patients being treated with OxyContin; or c) OxyContin's potential for abuse, addiction or physical dependence differs from any other Schedule II opioid analgesic.

6. In the promotion and marketing of OxyContin, Purdue shall not make any written or oral promotional claim of safety or effectiveness for Off-Label Uses of OxyContin in a manner that violates the Food, Drug and Cosmetic Act, 21 U.S.C. § 301 *et seq.* ("FDCA"), and accompanying regulations as may be amended or supplemented, or as appearing in FDA Guidances for Industry from time to time.

7. Except upon a request for such information without solicitation by Purdue to make the request, Purdue shall not provide to Health Care Professionals written materials describing the Off-Label Use of OxyContin that have not appeared in a

scientific or medical journal or reference publication or any portion thereof. Purdue shall maintain records for three (3) years of the identity of all Health Care Professionals to whom such materials relating to the Off-Label Use of OxyContin have been provided. "Scientific or medical journal" is a publication whose articles are published in accordance with regular peer-reviewed procedures; that uses experts to review or provide comment on proposed articles; and that is not in the form of a special supplement that has been funded in whole or in part by one or more manufacturers. "Reference publication" is a publication that has no common ownership or other corporate affiliation with a pharmaceutical or medical device manufacturer; that has not been written, edited, excerpted, or published specifically for, or at the request of, such a manufacturer; and that has not been edited or significantly influenced by such a manufacturer.

8. A. When Purdue provides an individual or entity with any educational grant, research grant, or other similar Remuneration relating to OxyContin, Purdue shall obtain the recipient's agreement: (i) to clearly and conspicuously disclose the existence of said funding or Remuneration to the readers of any resulting letter, study, research or other materials which was supported by said funding or Remuneration, and (ii) to refund said funding or Remuneration if such disclosure is not made.

B. Purdue shall require that a recipient of any Remuneration from Purdue for the promotion of OxyContin agree: (i) to clearly and conspicuously disclose the existence, nature and purpose of the Remuneration to the participants in any educational event at which the recipient discusses an Off-Label Use of OxyContin, and (ii) to refund said Remuneration if such disclosure is not made.

C. Purdue shall itself clearly and conspicuously disclose the existence of any grant or other form of Remuneration that it has provided for the publication of a letter, study, research or other material relating to OxyContin when Purdue disseminates or refers to said letter, study, research or other material in communications with Health Care Professionals.

9. Purdue shall comply with all applicable Accreditation Council for Continuing Medical Education ("ACCME") Guidelines.

10. Purdue shall comply with paragraphs 2, 3, 4, 5, 7 and 8 of the Pharmaceutical Research and Manufacturers of America Code (effective on July 1, 2002) with respect to payments, gifts and other compensation to Health Care Professionals regarding OxyContin.

11. In the promotion and marketing of OxyContin, Purdue shall not misrepresent the existence, non-existence, or findings of any medical or scientific evidence, including anecdotal evidence, relating to Off-Label Uses of OxyContin. Purdue shall not provide any information that is misleading or lacking in fair balance, as defined in 21.C.F.R. 202.1, as may be amended or supplemented, or as appearing in FDA Guidances for Industry from time to time, in any discussion of the Off-Label Uses of OxyContin.

12. Purdue shall not sponsor or fund any educational events where Purdue has knowledge at the time the decision for sponsorship or funding is made that a speaker will recommend the Off-Label Use of OxyContin. Further, Purdue shall not promote or fund Health Care Professionals' attendance at educational events where Purdue has

knowledge, at the time of said promotion, that Off-Label Use of OxyContin will be recommended or encouraged.

13. Purdue shall, no later than thirty (30) business days after the Effective Date of this Judgment, establish, implement and follow an OxyContin abuse and diversion detection program consisting of internal procedures designed to identify potential abuse or diversion of OxyContin in certain settings (the "OxyContin Abuse and Diversion Detection Program"). The OxyContin Abuse and Diversion Detection Program will apply to Purdue employees and contract or third-party sales representatives, including Medical Liaisons, who contact practicing Health Care Professionals in person or by telephone for the purpose of promoting OxyContin. That Program directs those persons to report to the Office of the General Counsel situations, including, but not limited to the following examples, to the extent that such information or activities are observed or learned of by them: a) an apparent pattern of an excessive number of patients for the practice type, such as long lines of patients waiting to be seen, waiting rooms filled to standing-room-only capacity, or patient-prescriber interactions that are exceedingly brief or non-existent; b) an atypical pattern of prescribing techniques or locations, such as repeated prescribing from an automobile, or repeated prescribing at atypical times, such as after usual office hours when the Health Care Professional is not on call; c) information from a highly credible source or several sources (e.g., pharmacists, law enforcement, other health care workers) that a Health Care Professional or their patients are abusing or diverting medications; d) sudden, unexplained changes in prescribing or dispensing patterns that are not accounted for by changes in patient numbers or practice type; e) a Health Care Professional who has a disproportionate number of patients who

pay for office visits and dispensed medications with cash; f) multiple allegations that individuals from a particular practice have overdosed; or g) unauthorized individuals signing prescriptions or dispensing controlled substances. Upon identification of potential abuse or diversion involving a Health Care Professional with whom Purdue employees or its contract or third-party sales representatives, including Medical Liaisons, interact, Purdue will conduct an internal inquiry which will include but not be limited to a review of the Health Care Professional's prescribing history, to the extent such history is available and relevant, and shall take such further steps as may be appropriate based on the facts and circumstances, which may include ceasing to promote Purdue products to the particular Health Care Professional, providing further education to the Health Care Professional about appropriate use of opioids, or providing notice of such potential abuse or diversion to appropriate medical, regulatory or law enforcement authorities. Purdue's obligations under this Section shall expire ten (10) years following the Effective Date of this Judgment or three months from the date on which the last of Purdue's patents covering OxyContin expires, whichever is earlier, but in no event shall be earlier than seven (7) years following the Effective Date of this Judgment.

14. Purdue shall implement and maintain a training and education program with respect to the OxyContin Abuse and Diversion Detection Program, and shall require all Purdue employees and contract or third-party sales representatives, including Medical Liaisons, who contact practicing Health Care Professionals in person or by telephone for the purpose of promoting OxyContin to complete the training and education program no later than thirty (30) business days after the Effective Date of this Judgment. Further, Purdue shall require those Purdue employees and contract or third-party sales

representatives, including Medical Liaisons, who contact practicing Health Care Professionals in person or by telephone for the purpose of promoting OxyContin to complete the training and education program before being allowed to market or promote OxyContin. Purdue's obligations under this Section shall expire ten (10) years following the Effective Date of this Judgment or three months from the date on which the last of Purdue's patents covering OxyContin expires, whichever is earlier, but in no event shall be earlier than seven (7) years following the Effective Date of this Judgment.

15. Within 90 days of the Effective Date of this Judgment, Purdue shall provide to each Health Care Professional whom Covered Persons contact, written, non-branded educational information related to detecting and preventing abuse and diversion of opioid analgesics. To the extent that Purdue concludes that a specific Health Care Professional needs repeated exposure to such non-branded educational materials, Purdue will provide those materials. Purdue's obligations under this Section will remain in effect for ten (10) years following the Effective Date of this Judgment.

16. Purdue shall continue to review news media stories addressing the abuse or diversion of OxyContin and undertake appropriate measures as reasonable under the circumstances to address abuse and diversion so identified, including but not limited to, (i) correcting misinformation, (ii) offering non-branded educational materials to local substance abuse prevention and treatment initiatives, or (iii) directing Health Care Professionals to Purdue's Medical Services group for fair and balanced information on appropriate use of opioid analgesics, prevention and detection of abuse and diversion. Purdue's obligations under this Section shall expire ten (10) years following the Effective Date of this Judgment or three months from the date on which the last of Purdue's patents

covering OxyContin expires, whichever is earlier, but in no event shall be earlier than seven (7) years following the Effective Date of this Judgment.

17. No sales incentive (bonus) program for sales of OxyContin shall allow incentive credit to be earned for a Health Care Professional who has been identified through the OxyContin Abuse and Diversion Detection Program as one upon whom sales representatives shall not call. In addition, Purdue shall not employ a compensation structure for persons involved in marketing or promoting OxyContin that is based exclusively on the volume of OxyContin sales.

18. For a period of ten (10) years following the Effective Date of this Judgment, Purdue's performance evaluation of persons involved in marketing or promoting OxyContin shall meaningfully take into account that sales persons inform Health Care Professionals to whom the sales persons promote OxyContin about its potential for abuse and diversion, and how to minimize those risks; failure to do so shall be considered as a basis for disciplinary action, including, but not limited to censure, probation and termination.

19. In its promotion and marketing of OxyContin, Purdue shall not misrepresent, in any written or oral claim relating to OxyContin, that its sales, medical or research personnel have experience or credentials or are engaging in research activities if they do not in fact possess such credentials or experience, or are not engaging in such activities.

20. All material used in promoting OxyContin, regardless of format (audio, internet, video, print) and whether directed primarily to patients or to Health Care Professionals, shall, not inconsistent with the Package Insert, contain only information

that is truthful, balanced, accurately communicated, and not minimize the risk of abuse, addiction or physical dependence associated with the use of OxyContin.

21. Purdue shall not provide samples of OxyContin to Health Care Professionals.

22. The obligations of Purdue under this Judgment shall be prospective only. No Signatory Attorney General shall institute any proceeding or take any action against Purdue under its State Consumer Protection Laws or any similar state authority, or under this Judgment, based on Purdue's prior promotional or marketing practices for OxyContin.

23. Nothing in this Judgment shall require Purdue to:

(a) take an action that is prohibited by the FDCA, the Controlled Substances Act or any regulation promulgated thereunder, or by FDA or the Drug Enforcement Administration;

(b) fail to take an action that is required by the FDCA, the Controlled Substances Act or any regulation promulgated thereunder, or by FDA or the Drug Enforcement Administration;

(c) refrain from dissemination of safety information concerning OxyContin; or

(d) refrain from making any written or oral promotional claim which is the same or substantially the same as the language permitted by FDA under the OxyContin Package Insert and which accurately portrays the data or other information referenced in the OxyContin Package Insert.

24. Purdue shall:

(a) to the extent necessary for compliance with this Judgment, no later than ninety (90) days after the Effective Date of this Judgment, institute compliance procedures which are designed to begin training currently employed Covered Persons on the contents of this Judgment, and about how to comply with this Judgment;

(b) submit to the Attorney General (per the Notice below), no later than one hundred and twenty (120) days after the Effective Date of this Judgment, a written description of such training;

(c) submit to the Attorney General (per the Notice below), one (1) year after the Effective Date of this Judgment, a written affirmation setting forth Purdue's compliance with this paragraph;

(d) for a period of three (3) years from the Effective Date of this Judgment, Purdue shall advise in writing all Covered Persons of the requirements of Paragraphs 2 through 23 of this Judgment;

(e) beginning one (1) year after the Effective Date of this Judgment, for a period of three (3) years, produce and provide on an annual basis to the Attorney General on the anniversary of the Effective Date of this Consent Judgment a report containing basic statistics on Purdue's Abuse and Diversion Detection Program including, but not limited to, statistics on the number of reports, the number of investigations, and a summary of the results, including the number of "Do Not Call" determinations, but shall not include the names of any specific Health Care Professionals; and

(f) upon written request, the Attorney General may obtain state-specific information as described in subsection (e). In addition, Purdue agrees to accept service of a civil investigative demand or similar process by the Attorney General requesting the

names of any specific Health Care Professionals described in subsection (e). The Attorney General in receipt of such information shall not disclose it except as provided by law.

III. PAYMENT TO THE STATES

25. No later than thirty (30) days after the Effective Date of this Judgment, Purdue shall pay nineteen million and five hundred thousand U.S. dollars ($19,500,000.00, to be paid by Purdue to the States by electronic fund transfer made payable to the Oregon Department of Justice (as instructed by that Office) which shall divide and distribute these funds as designated by and in the sole discretion of the Signatory Attorneys General as part of the consideration for the termination of their respective investigations under the State Consumer Protection Laws regarding the Subject Matter of this Judgment. Said payment shall be used by the Massachusetts Attorney General to fund or assist in funding programs directed at combating prescription drug abuse, addiction and/or diversion, including, but not limited to, education, outreach, prevention or monitoring programs, or for other uses permitted by state law, at the sole discretion of the Attorney General.

IV. GENERAL PROVISIONS

26. This Judgment shall be governed by the laws of the Commonwealth of Massachusetts.

27. This Judgment is entered into by the Parties as their own free and voluntary act and with full knowledge and understanding of the nature of the proceedings and the obligations and duties imposed by this Judgment.

28. Nothing in this Judgment constitutes any agreement by the Parties concerning the characterization of the amounts paid pursuant to this Judgment for

purposes of the Internal Revenue Code or any state tax laws, or the resolution of any other matters.

29. This Judgment does not constitute an approval by the Attorney General of any of Purdue's business practices, including its promotional or marketing practices, and Purdue shall make no representation or claim to the contrary.

V. REPRESENTATIONS AND WARRANTIES

30. Purdue warrants and represents that it and its predecessors, successors and assigns manufactured, sold and promoted OxyContin. Purdue further acknowledges that it is a proper party to this Judgment. Purdue further warrants and represents that the individual(s) signing this Judgment on behalf of Purdue is doing so in his (or her) official capacity and is fully authorized by Purdue to enter into this Judgment and to legally bind Purdue to all of the terms and conditions of the Judgment.

31. Each of the Parties represents and warrants that it negotiated the terms of this Judgment in good faith.

32. Each of the Signatory Attorneys General warrants and represents that he or she is signing this Judgment in his or her official capacity, and that he or she is fully authorized by his or her state to enter into this Judgment, including but not limited to the authority to grant the release contained in Paragraphs 34 and 35 of this Judgment, and to legally bind the state to all of the terms and conditions of this Judgment.

33. Purdue acknowledges and agrees that the Attorney General has relied on all of the representations and warranties set forth in this Judgment and that, if any representation is proved false, unfair, deceptive, misleading, or inaccurate in any material respect, the Attorney General has the right to seek any relief or remedy afforded by law or equity in the state.

VI. RELEASE

34. Based on his or her inquiry into Purdue's promotion of OxyContin, the Attorney General has concluded that this Judgment is the appropriate resolution of any alleged violations of the State Consumer Protection Laws. The Attorney General acknowledges by consenting to entry of this Judgment that this Judgment terminates the Attorney General's inquiry under the State Consumer Protection Laws into Purdue's promotion of OxyContin prior to the Effective Date of this Judgment.

35. In consideration of the Compliance Provisions, payments, undertakings, and acknowledgments provided for in this Judgment, and conditioned on Purdue's making full payment of the amount specified in Paragraph 25, and subject to the limitations and exceptions set forth in Paragraph 36, the State releases and forever discharges, to the fullest extent permitted by law, Purdue and its past and present officers, directors, shareholders, employees, co-promoters, affiliates, parents, subsidiaries, predecessors, assigns, and successors (collectively, the "Releasees"), of and from any and all civil causes of action, claims, damages, costs, attorney's fees, or penalties that the Attorney General could have asserted against the Releasees under the State Consumer Protection Law by reason of any conduct that has occurred at any time up to and including the Effective Date of this Judgment relating to or based upon the Subject Matter of this Judgment ("Released Claims").

36. The Released Claims set forth in Paragraph 35 specifically do not include the following claims:

(a) private rights of action by consumers, provided, however, that this Judgment does not create or give rise to any such private right of action of any kind;

(b) claims relating to Best Price, Average Wholesale Price or Wholesale Acquisition Cost reporting practices or Medicaid fraud or Abuse;

(c) claims of antitrust, environmental or tax liability;

(d) claims for property damage;

(e) claims to enforce the terms and conditions of this Judgment; and

(f) any state or federal criminal liability that any person or entity, including Releasees, has or may have to the Commonwealth.

VII. NO ADMISSION OF LIABILITY

37. This Judgment does not constitute an admission by Purdue for any purpose, of any fact or of a violation of any state law, rule, or regulation, nor does this Judgment constitute evidence of any liability, fault, or wrongdoing, by Purdue nor does Purdue's agreement in this Judgment not to engage in certain conduct constitute an admission that Purdue has ever engaged in such conduct. Purdue enters into this Judgment for the purpose of resolving the concerns of the Attorney General regarding Purdue's promotional and marketing practices regarding OxyContin. Purdue does not admit any violation of the State Consumer Protection Laws, and does not admit any wrongdoing that could have been alleged by the Attorney General.

38. This Judgment shall not be construed or used as a waiver or any limitation of any defense otherwise available to Purdue. This Judgment is made without trial or adjudication of any issue of fact or law or finding of liability of any kind. Nothing in this Judgment, including this paragraph, shall be construed to limit or to restrict Purdue's right to use this Judgment to assert and maintain the defenses of res judicata, collateral estoppel, payment, compromise and settlement, accord and satisfaction, or any other legal

or equitable defenses in any pending or future legal or administrative action or proceeding.

VIII. DISPUTES REGARDING COMPLIANCE

39. For the purposes of resolving disputes with respect to compliance with this Judgment, should the Attorney General have legally sufficient cause (which shall include, at a minimum, a reasonable basis to believe that Purdue has violated a provision of this Judgment) to object to any promotional or marketing practices relating to OxyContin subsequent to the Effective Date of this Judgment, then the Attorney General shall notify Purdue in writing of the specific objection, identify with particularity the provisions of this Judgment and/or the State Consumer Protection Laws that the practice appears to violate, and give Purdue thirty (30) business days to respond to the notification; provided, however, that the Attorney General may take any action upon notice to Purdue where the Attorney General concludes that, because of the specific practice, a threat to the health or safety of the public requires immediate action.

40. Upon receipt of written notice and within the thirty (30) business-day period, Purdue shall provide a good faith written response to the Attorney General's objection. The response shall include an affidavit containing either:

a. A statement explaining why Purdue believes it is in compliance with the Judgment; or

b. A detailed explanation of how the alleged violation[s] occurred; and

i. A statement that the alleged breach has been cured and how it has been cured; or

ii. A statement that the alleged breach cannot be reasonably cured within thirty (30) business days from receipt of the notice, but (1) Purdue has

begun to take corrective action to cure the alleged breach; (2) Purdue is pursuing such corrective action with reasonable and due diligence; and (3) Purdue has provided the Attorney General with a detailed and reasonable time table for curing the alleged breach.

41. Nothing herein shall prevent the Attorney General from agreeing in writing to provide Purdue with additional time beyond the thirty (30) business-day period to respond to the notice.

42. Nothing herein shall be construed to exonerate any failure to comply with any provision of this Judgment after the date of entry or to compromise the authority of the Signatory Attorney General to initiate a proceeding for failure to comply. Further, nothing in this subsection shall be construed to limit the authority of the Signatory Attorney General to protect the interests of the State.

43. The Signatory Attorney General represents that he or she will seek enforcement of the provisions of this Judgment with due regard for fairness and, in so doing, shall take into account efforts that Purdue has taken to cure any claimed violation of this Judgment.

44. Upon giving Purdue thirty (30) business days to respond to the notification described in Paragraph 39 above, the Attorney General shall be permitted to request and Purdue shall produce relevant, non-privileged, non-work-product records and documents in the possession, custody or control of Purdue that relate to Purdue's compliance with each provision of this Judgment as to which legally sufficient cause has been shown.

XI. COMPLIANCE WITH ALL LAWS

47. Except as expressly provided in this Judgment, nothing in this Judgment shall be construed as:

(a) relieving Purdue of its obligation to comply with all state laws, regulations or rules, or granting permission to engage in any acts or practices prohibited by such law, regulation or rule; or

(b) limiting or expanding in any way any right the State may otherwise have to obtain information, documents or testimony from Purdue pursuant to any state law, regulation or rule, or any right Purdue may otherwise have to oppose any subpoena, civil investigative demand, motion, or other procedure issued, served, filed, or otherwise employed by the State pursuant to any such state law, regulation, or rule.

XII. NOTICES

48. Any notices required to be sent to the State or to Purdue by this Judgment shall be sent by overnight United States mail. The documents shall be sent to the following addresses:

For the State:

Christopher K. Barry-Smith
Assistant Attorney General
Consumer Protection Division
Office of the Attorney General
One Ashburton Place
Boston MA 02108

For Purdue:

Vice President, Associate General Counsel
Purdue Pharma L.P.
One Stamford Forum
Stamford, CT 06901-3431

APPROVED:

Judge

5-9-07
Date

XIII. SIGNATURES

CONSENT TO JUDGMENT

Purdue:

1. acknowledges that it has read the foregoing Consent Judgment, is aware of its right to a trial in this matter and has waived that right;

2. admits to the jurisdiction of the Court and consents to the entry of this Consent Order;

3. states that no promise of any kind or nature whatsoever (other than the written terms of this Consent Order)was made to it to induce it to enter this Consent Order, that it has entered into this Consent Order voluntarily, and that this Consent Order constitutes the entire agreement between Purdue and the Commonwealth.

4. represents that the undersigned is an officer of Purdue and that, as such, has been authorized by Purdue to enter into this Consent Order for and on behalf of all entities bound by this Consent Order.

Exhibit B

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use OXYCONTIN® safely and effectively. See full prescribing information for OXYCONTIN.

OXYCONTIN® (oxycodone hydrochloride) extended-release tablets, for oral use, CII
Initial U.S. Approval: 1950

WARNING: ADDICTION, ABUSE AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; CYTOCHROME P450 3A4 INTERACTION; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

See full prescribing information for complete boxed warning.

- **OXYCONTIN exposes users to risks of addiction, abuse and misuse, which can lead to overdose and death. Assess patient's risk before prescribing and monitor regularly for these behaviors and conditions. (5.1)**
- **To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) for these products. (5.2)**
- **Serious, life-threatening, or fatal respiratory depression may occur. Monitor closely, especially upon initiation or following a dose increase. Instruct patients to swallow OXYCONTIN tablets whole to avoid exposure to a potentially fatal dose of oxycodone. (5.3)**
- **Accidental ingestion of OXYCONTIN, especially by children, can result in a fatal overdose of oxycodone. (5.3)**
- **Prolonged use of OXYCONTIN during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated. If prolonged opioid use is required in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available. (5.4)**
- **Concomitant use with CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers) can result in a fatal overdose of oxycodone. (5.5, 7, 12.3)**
- **Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation. (5.6, 7)**

----------RECENT MAJOR CHANGES----------

Boxed Warning	09/2018
Warnings and Precautions (5.2)	09/2018

----------INDICATIONS AND USAGE----------

OXYCONTIN is an opioid agonist indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate in:

- Adults; and
- Opioid-tolerant pediatric patients 11 years of age and older who are already receiving and tolerate a minimum daily opioid dose of at least 20 mg oxycodone orally or its equivalent.

Limitations of Use

- Because of the risks of addiction, abuse and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve OXYCONTIN for use in patients for whom alternative treatment options (e.g. non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. (1)
- OXYCONTIN is not indicated as an as-needed (prn) analgesic. (1)

----------DOSAGE AND ADMINISTRATION----------

- To be prescribed only by healthcare providers knowledgeable in use of potent opioids for management of chronic pain. (2.1)
- OXYCONTIN 60 mg and 80 mg tablets, a single dose greater than 40 mg, or a total daily dose greater than 80 mg are only for use in patients in whom tolerance to an opioid of comparable potency has been established. (2.1)
- Patients considered opioid-tolerant are those taking, for one week or longer, at least 60 mg oral morphine per day, 25 mcg transdermal fentanyl per hour, 30 mg oral oxycodone per day, 8 mg oral hydromorphone per day, 25 mg oral oxymorphone per day, 60 mg oral hydrocodone per day, or an equianalgesic dose of another opioid. (2.1)
- Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals (2.1).
- Individualize dosing based on the severity of pain, patient response, prior analgesic experience, and risk factors for addiction, abuse, and misuse. (2.1)
- Instruct patients to swallow tablets intact and not to cut, break, chew, crush, or dissolve tablets (risk of potentially fatal dose). (2.1, 5.1)
- Instruct patients to take tablets one at a time, with enough water to ensure complete swallowing immediately after placing in mouth. (2.1, 5.10)
- Do not abruptly discontinue OXYCONTIN in a physically dependent patient. (2.9)

Adults: For opioid-naïve and opioid non-tolerant patients, initiate with 10 mg tablets orally every 12 hours. See full prescribing information for instructions on conversion from opioids to OXYCONTIN, titration and maintenance of therapy. (2.2, 2.3, 2.5)

Pediatric Patients 11 Years of Age and Older

- For use only in pediatric patients 11 years and older already receiving and tolerating opioids for at least 5 consecutive days with a minimum of 20 mg per day of oxycodone or its equivalent for at least two days immediately preceding dosing with OXYCONTIN. (2.4)
- See full prescribing information for instructions on conversion from opioids to OXYCONTIN, titration and maintenance of therapy. (2.4, 2.5)

Geriatric Patients: In debilitated, opioid non-tolerant geriatric patients, initiate dosing at one third to one half the recommended starting dosage and titrate carefully. (2.7, 8.5)

Patients with Hepatic Impairment: Initiate dosing at one third to one half the recommended starting dosage and titrate carefully. (2.8, 8.6)

----------DOSAGE FORMS AND STRENGTHS----------

Extended-release tablets: 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, and 80 mg. (3)

----------CONTRAINDICATIONS----------

- Significant respiratory depression (4)
- Acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment (4)
- Known or suspected gastrointestinal obstruction, including paralytic ileus (4)
- Hypersensitivity to oxycodone (4)

----------WARNINGS AND PRECAUTIONS----------

- Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients: Monitor closely, particularly during initiation and titration. (5.7)
- Adrenal Insufficiency: If diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid. (5.8)
- Severe Hypotension: Monitor during dosage initiation and titration. Avoid use of OXYCONTIN in patients with circulatory shock. (5.9)
- Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness: Monitor for sedation and respiratory depression. Avoid use of OXYCONTIN in patients with impaired consciousness or coma. (5.10)
- Risk of Obstruction in Patients who have Difficulty Swallowing or have Underlying GI Disorders that may Predispose them to Obstruction: Consider use of an alternative analgesic. (5.11)

----------ADVERSE REACTIONS----------

Most common adverse reactions (incidence >5%) were constipation, nausea, somnolence, dizziness, vomiting, pruritus, headache, dry mouth, asthenia, and sweating. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Purdue Pharma L.P. at 1-888-726-7535 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

----------DRUG INTERACTIONS----------

- CNS Depressants: Concomitant use may cause hypotension, profound sedation, respiratory depression, coma, and death. If co-administration is required and the decision to begin OXYCONTIN is made, start with 1/3 to 1/2 the recommended starting dosage, consider using a lower dosage of the concomitant CNS depressant, and monitor closely. (2.6, 5.6, 7)
- Serotonergic Drugs: Concomitant use may result in serotonin syndrome. Discontinue OXYCONTIN if serotonin syndrome is suspected. (7)
- Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics: Avoid use with OXYCONTIN because they may reduce analgesic effect of OXYCONTIN or precipitate withdrawal symptoms. (5.14, 7)
- Monoamine Oxidase Inhibitors (MAOIs): Can potentiate the effects of morphine. Avoid concomitant use in patients receiving MAOIs or within 14 days of stopping treatment with an MAOI. (7)

----------USE IN SPECIFIC POPULATIONS----------

Pregnancy: May cause fetal harm. (8.1)
Lactation: Not recommended. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 09/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

WARNING: ADDICTION, ABUSE AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; CYTOCHROME P450 3A4 INTERACTION; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse

OXYCONTIN® exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing OXYCONTIN and monitor all patients regularly for the development of these behaviors and conditions *[see Warnings and Precautions (5.1)]*.

Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS):

To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a REMS for these products *[see Warnings and Precautions (5.2)]*. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to

- **complete a REMS-compliant education program,**
- **counsel patients and/or their caregivers, with every prescription, on safe use, serious risks, storage, and disposal of these products,**
- **emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist, and**
- **consider other tools to improve patient, household, and community safety.**

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of OXYCONTIN. Monitor for respiratory depression, especially during initiation of OXYCONTIN or following a dose increase. Instruct patients to swallow OXYCONTIN tablets whole; crushing, chewing, or dissolving OXYCONTIN tablets can cause rapid release and absorption of a potentially fatal dose of oxycodone *[see Warnings and Precautions (5.3)]*.

Accidental Ingestion

Accidental ingestion of even one dose of OXYCONTIN, especially by children, can result in a fatal overdose of oxycodone *[see Warnings and Precautions (5.3)]*.

Neonatal Opioid Withdrawal Syndrome

Prolonged use of OXYCONTIN during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of

neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available *[see Warnings and Precautions (5.4)]*.

Cytochrome P450 3A4 Interaction
The concomitant use of OXYCONTIN with all cytochrome P450 3A4 inhibitors may result in an increase in oxycodone plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in oxycodone plasma concentration. Monitor patients receiving OXYCONTIN and any CYP3A4 inhibitor or inducer *[see Warnings and Precautions (5.5), Drug Interactions (7), Clinical Pharmacology (12.3)]*.

Risks From Concomitant Use With Benzodiazepines Or Other CNS Depressants
Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death *[see Warnings and Precautions (5.6), Drug Interactions (7)]*.

- **Reserve concomitant prescribing of OXYCONTIN and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.**
- **Limit dosages and durations to the minimum required.**
- **Follow patients for signs and symptoms of respiratory depression and sedation.**

1 INDICATIONS AND USAGE

OXYCONTIN is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate in:

- Adults; and
- Opioid-tolerant pediatric patients 11 years of age and older who are already receiving and tolerate a minimum daily opioid dose of at least 20 mg oxycodone orally or its equivalent.

Limitations of Use

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations *[see Warnings and Precautions (5.1)]*, reserve OXYCONTIN for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.

- OXYCONTIN is not indicated as an as-needed (prn) analgesic.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage and Administration Instructions

OXYCONTIN should be prescribed only by healthcare professionals who are knowledgeable in the use of potent opioids for the management of chronic pain.

OXYCONTIN 60 mg and 80 mg tablets, a single dose greater than 40 mg, or a total daily dose greater than 80 mg are only for use in patients in whom tolerance to an opioid of comparable potency has been established. Adult patients who are opioid tolerant are those receiving, for one week or longer, at least 60 mg oral morphine per day, 25 mcg transdermal fentanyl per hour, 30 mg oral oxycodone per day, 8 mg oral hydromorphone per day, 25 mg oral oxymorphone per day, 60 mg oral hydrocodone per day, or an equianalgesic dose of another opioid.

- Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals *[see Warnings and Precautions (5)]*.

- Initiate the dosing regimen for each patient individually; taking into account the patient's severity of pain, patient response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse *[see Warnings and Precautions (5.1)]*.

- Monitor patients closely for respiratory depression, especially within the first 24-72 hours of initiating therapy and following dosage increases with OXYCONTIN and adjust the dosage accordingly *[see Warnings and Precautions (5.3)]*.

Instruct patients to swallow OXYCONTIN tablets whole, one tablet at a time, with enough water to ensure complete swallowing immediately after placing in the mouth *[see Patient Counseling Information (17)]*. Instruct patients not to pre-soak, lick, or otherwise wet the tablet prior to placing in the mouth *[see Warnings and Precautions (5.11)]*. Cutting, breaking, crushing, chewing, or dissolving OXYCONTIN tablets will result in uncontrolled delivery of oxycodone and can lead to overdose or death *[see Warnings and Precautions (5.1)]*.

OXYCONTIN is administered orally every 12 hours.

2.2 Initial Dosage in Adults who are not Opioid-Tolerant

The starting dosage for patients who are not opioid tolerant is OXYCONTIN 10 mg orally every 12 hours.

Use of higher starting doses in patients who are not opioid tolerant may cause fatal respiratory depression *[see Warnings and Precautions (5.3)]*.

2.3 Conversion from Opioids to OXYCONTIN in Adults

Conversion from Other Oral Oxycodone Formulations to OXYCONTIN
If switching from other oral oxycodone formulations to OXYCONTIN, administer one half of the patient's total daily oral oxycodone dose as OXYCONTIN every 12 hours.

Conversion from Other Opioids to OXYCONTIN
Discontinue all other around-the-clock opioid drugs when OXYCONTIN therapy is initiated.

There are no established conversion ratios for conversion from other opioids to OXYCONTIN defined by clinical trials. Initiate dosing using OXYCONTIN 10 mg orally every 12 hours.

It is safer to underestimate a patient's 24-hour oral oxycodone requirements and provide rescue medication (e.g., immediate-release opioid) than to overestimate the 24-hour oral oxycodone dosage and manage an adverse reaction due to an overdose. While useful tables of opioid equivalents are readily available, there is substantial inter-patient variability in the relative potency of different opioids.

Close observation and frequent titration are warranted until pain management is stable on the new opioid. Monitor patients for signs and symptoms of opioid withdrawal and for signs of oversedation/toxicity after converting patients to OXYCONTIN.

Conversion from Methadone to OXYCONTIN
Close monitoring is of particular importance when converting from methadone to other opioid agonists. The ratio between methadone and other opioid agonists may vary widely as a function of previous dose exposure. Methadone has a long half-life and can accumulate in the plasma.

Conversion from Transdermal Fentanyl to OXYCONTIN
Treatment with OXYCONTIN can be initiated after the transdermal fentanyl patch has been removed for at least 18 hours. Although there has been no systematic assessment of such conversion, start with a conservative conversion: substitute 10 mg of OXYCONTIN every 12 hours for each 25 mcg per hour fentanyl transdermal patch. Follow the patient closely during conversion from transdermal fentanyl to OXYCONTIN, as there is limited documented experience with this conversion.

2.4 Initial Dosage in Pediatric Patients 11 Years and Older

The following dosing information is for use only in pediatric patients 11 years and older already receiving and tolerating opioids for at least five consecutive days. For the two days immediately preceding dosing with OXYCONTIN, patients must be taking a minimum of 20 mg per day of oxycodone or its equivalent. OXYCONTIN is not appropriate for use in pediatric patients requiring less than a 20 mg total daily dose. Table 1, based on clinical trial experience, displays the conversion factor when switching pediatric patients 11 years and older (under the conditions described above) from opioids to OXYCONTIN.

Discontinue all other around-the-clock opioid drugs when OXYCONTIN therapy is initiated.

There is substantial inter-patient variability in the relative potency of different opioid drugs and formulations. Therefore, a conservative approach is advised when determining the total daily dosage of OXYCONTIN. It is safer to underestimate a patient's 24-hour oral oxycodone requirements and provide rescue medication (e.g., immediate-release opioid) than to

overestimate the 24-hour oral oxycodone requirements and manage an adverse reaction due to an overdose.

Consider the following when using the information in Table 1.

- This is not a table of equianalgesic doses.
- The conversion factors in this table are only for the conversion from one of the listed oral opioid analgesics to OXYCONTIN.
- The table cannot be used to convert from OXYCONTIN to another opioid. Doing so will result in an over-estimation of the dose of the new opioid and may result in fatal overdose.
- The formula for conversion from prior opioids, including oral oxycodone, to the daily dose of OXYCONTIN is mg per day of prior opioid x factor = mg per day of OXYCONTIN. Divide the calculated total daily dose by 2 to get the every-12-hour OXYCONTIN dose. If rounding is necessary, always round the dose down to the nearest OXYCONTIN tablet strength available.

Table 1: Conversion Factors When Switching Pediatric Patients 11 Years and Older to OXYCONTIN

Prior Opioid	Conversion Factor	
	Oral	Parenteral*
Oxycodone	1	--
Hydrocodone	0.9	--
Hydromorphone	4	20
Morphine	0.5	3
Tramadol	0.17	0.2

*For patients receiving high-dose parenteral opioids, a more conservative conversion is warranted. For example, for high-dose parenteral morphine, use 1.5 instead of 3 as a multiplication factor.

Step #1: To calculate the estimated total OXYCONTIN daily dosage using Table 1:

- For pediatric patients taking a single opioid, sum the current total daily dosage of the opioid and then multiply the total daily dosage by the approximate conversion factor to calculate the approximate OXYCONTIN daily dosage.
- For pediatric patients on a regimen of more than one opioid, calculate the approximate oxycodone dose for each opioid and sum the totals to obtain the approximate OXYCONTIN daily dosage.

- For pediatric patients on a regimen of fixed-ratio opioid/non-opioid analgesic products, use only the opioid component of these products in the conversion.

Step #2: If rounding is necessary, always round the dosage down to the nearest OXYCONTIN tablet strength available and initiate OXYCONTIN therapy with that dose. If the calculated OXYCONTIN total daily dosage is less than 20 mg, there is no safe strength for conversion and do not initiate OXYCONTIN.

Example conversion from a single opioid (e.g., hydrocodone) to OXYCONTIN: Using the conversion factor of 0.9 for oral hydrocodone in Table 1, a total daily hydrocodone dosage of 50 mg is converted to 45 mg of oxycodone per day or 22.5 mg of OXYCONTIN every 12 hours. After rounding down to the nearest strength available, the recommended OXYCONTIN starting dosage is 20 mg every 12 hours.

Step #3: Close observation and titration are warranted until pain management is stable on the new opioid. Monitor patients for signs and symptoms of opioid withdrawal or for signs of over-sedation/toxicity after converting patients to OXYCONTIN. [*see Dosage and Administration (2.5)]* for important instructions on titration and maintenance of therapy.

There is limited experience with conversion from transdermal fentanyl to OXYCONTIN in pediatric patients 11 years and older. If switching from transdermal fentanyl patch to OXYCONTIN, ensure that the patch has been removed for at least 18 hours prior to starting OXYCONTIN. Although there has been no systematic assessment of such conversion, start with a conservative conversion: substitute 10 mg of OXYCONTIN every 12 hours for each 25 mcg per hour fentanyl transdermal patch. Follow the patient closely during conversion from transdermal fentanyl to OXYCONTIN.

If using asymmetric dosing, instruct patients to take the higher dose in the morning and the lower dose in the evening.

2.5 Titration and Maintenance of Therapy in Adults and Pediatric Patients 11 Years and Older

Individually titrate OXYCONTIN to a dosage that provides adequate analgesia and minimizes adverse reactions. Continually reevaluate patients receiving OXYCONTIN to assess the maintenance of pain control, signs and symptoms of opioid withdrawal, and adverse reactions, as well as monitoring for the development of addiction, abuse and misuse *[see Warnings and Precautions (5.1)]*. Frequent communication is important among the prescriber, other members of the healthcare team, the patient, and the caregiver/family during periods of changing analgesic requirements, including initial titration. During chronic therapy, periodically reassess the continued need for the use of opioid analgesics.

Patients who experience breakthrough pain may require a dosage adjustment of OXYCONTIN or may need rescue medication with an appropriate dose of an immediate-release analgesic. If the level of pain increases after dose stabilization, attempt to identify the source of increased pain

before increasing the OXYCONTIN dosage. Because steady-state plasma concentrations are approximated in 1 day, OXYCONTIN dosage may be adjusted every 1 to 2 days.

If unacceptable opioid-related adverse reactions are observed, consider reducing the dosage. Adjust the dosage to obtain an appropriate balance between management of pain and opioid-related adverse reactions.

There are no well-controlled clinical studies evaluating the safety and efficacy with dosing more frequently than every 12 hours. As a guideline for pediatric patients 11 years and older, the total aily oxycodone dosage usually can be increased by 25% of the current total daily dosage. As a guideline for adults, the total daily oxycodone dosage usually can be increased by 25% to 50% of the current total daily dosage, each time an increase is clinically indicated.

2.6 Dosage Modifications with Concomitant Use of Central Nervous System Depressants

If the patient is currently taking a central nervous system (CNS) depressant and the decision is made to begin OXYCONTIN, start with one-third to one-half the recommended starting dosage of OXYCONTIN, consider using a lower dosage of the concomitant CNS depressant, and monitor patients for signs of respiratory depression, sedation, and hypotension *[see Warnings and Precautions (5.6), Drug Interactions (7)]*.

2.7 Dosage Modifications in Geriatric Patients who are Debilitated and not Opioid-Tolerant

For geriatric patients who are debilitated and not opioid tolerant, start dosing patients at one-third to one-half the recommended starting dosage and titrate the dosage cautiously *[see Use in Specific Populations (8.5]*.

2.8 Dosage Modifications in Patients with Hepatic Impairment

For patients with hepatic impairment, start dosing patients at one-third to one-half the recommended starting dosage and titrate the dosage carefully. Monitor for signs of respiratory depression, sedation, and hypotension *[see Use in Specific Populations, (8.6), Clinical Pharmacology (12.3)]*.

2.9 Discontinuation of OXYCONTIN

When the patient no longer requires therapy with OXYCONTIN, taper the dosage gradually, by 25% to 50% every 2 to 4 days, while monitoring for signs and symptoms of withdrawal. If a patient develops these signs or symptoms, raise the dose to the previous level and taper more slowly, either by increasing the interval between decreases, decreasing the amount of change in dose, or both. Do not abruptly discontinue OXYCONTIN *[see Warnings and Precautions (5.14), Drug Abuse and Dependence (9.3)]*.

3 DOSAGE FORMS AND STRENGTHS

Extended-release tablets: 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, and 80 mg.

- 10 mg film-coated extended-release tablets (round, white-colored, bi-convex tablets debossed with OP on one side and 10 on the other)
- 15 mg film-coated extended-release tablets (round, gray-colored, bi-convex tablets debossed with OP on one side and 15 on the other)
- 20 mg film-coated extended-release tablets (round, pink-colored, bi-convex tablets debossed with OP on one side and 20 on the other)
- 30 mg film-coated extended-release tablets (round, brown-colored, bi-convex tablets debossed with OP on one side and 30 on the other)
- 40 mg film-coated extended-release tablets (round, yellow-colored, bi-convex tablets debossed with OP on one side and 40 on the other)
- 60 mg film-coated extended-release tablets (round, red-colored, bi-convex tablets debossed with OP on one side and 60 on the other)
- 80 mg film-coated extended-release tablets (round, green-colored, bi-convex tablets debossed with OP on one side and 80 on the other)

4 CONTRAINDICATIONS

OXYCONTIN is contraindicated in patients with:

- Significant respiratory depression *[see Warnings and Precautions (5.3)]*
- Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment *[see Warnings and Precautions (5.7)]*
- Known or suspected gastrointestinal obstruction, including paralytic ileus *[see Warnings and Precautions (5.12)]*
- Hypersensitivity (e.g., anaphylaxis) to oxycodone *[see Adverse Reactions (6.2)]*

5 WARNINGS AND PRECAUTIONS

5.1 Addiction, Abuse, and Misuse

OXYCONTIN contains oxycodone, a Schedule II controlled substance. As an opioid, OXYCONTIN exposes users to the risks of addiction, abuse, and misuse. Because extended-release products such as OXYCONTIN deliver the opioid over an extended period of time, there is a greater risk for overdose and death due to the larger amount of oxycodone present *[see Drug Abuse and Dependence (9)]*.

Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed OXYCONTIN. Addiction can occur at recommended doses and if the drug is misused or abused.

Assess each patient's risk for opioid addiction, abuse, or misuse prior to prescribing OXYCONTIN, and monitor all patients receiving OXYCONTIN for the development of these behaviors and conditions. Risks are increased in patients with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). The potential for these risks should not, however, prevent the proper management of pain in any given patient. Patients at increased risk may be prescribed opioids such as OXYCONTIN, but use in such patients necessitates intensive counseling about the risks and proper use of OXYCONTIN along with intensive monitoring for signs of addiction, abuse, and misuse.

Abuse or misuse of OXYCONTIN by crushing, chewing, snorting, or injecting the dissolved product will result in the uncontrolled delivery of oxycodone and can result in overdose and death *[see Overdosage (10)]*.

Opioids are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing OXYCONTIN. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on the proper disposal of unused drug *[see Patient Counseling Information (17)]*. Contact local state professional licensing board or state controlled substances authority for information on how to prevent and detect abuse or diversion of this product.

5.2 Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)

To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) for these products. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to do all of the following:

- Complete a REMS-compliant education program offered by an accredited provider of continuing education (CE) or another education program that includes all the elements of the FDA Education Blueprint for Health Care Providers Involved in the Management or Support of Patients with Pain.
- Discuss the safe use, serious risks, and proper storage and disposal of opioid analgesics with patients and/or their caregivers every time these medicines are prescribed. The Patient Counseling Guide (PCG) can be obtained at this link: www.fda.gov/OpioidAnalgesicREMSPCG .
- Emphasize to patients and their caregivers the importance of reading the Medication Guide that they will receive from their pharmacist every time an opioid analgesic is dispensed to them.
- Consider using other tools to improve patient, household, and community safety, such as patient-prescriber agreements that reinforce patient-prescriber responsibilities.

To obtain further information on the opioid analgesic REMS and for a list of accredited REMS CME/CE, call 1-800-503-0784, or log on to www.opioidanalgesicrems.com. The FDA Blueprint can be found at www.fda.gov/OpioidAnalgesicREMSBlueprint .

5.3 Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended. Respiratory depression, if not immediately recognized and treated, may lead to respiratory arrest and death. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status *[see Overdosage (10)]*. Carbon dioxide (CO_2) retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids.

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of OXYCONTIN, the risk is greatest during the initiation of therapy or following a dosage increase. Monitor patients closely for respiratory depression, especially within the first 24-72 hours of initiating therapy with and following dosage increases of OXYCONTIN.

To reduce the risk of respiratory depression, proper dosing and titration of OXYCONTIN are essential *[see Dosage and Administration (2)]*. Overestimating the OXYCONTIN dosage when converting patients from another opioid product can result in a fatal overdose with the first dose.

Accidental ingestion of even one dose of OXYCONTIN, especially by children, can result in respiratory depression and death due to an overdose of oxycodone.

5.4 Neonatal Opioid Withdrawal Syndrome

Prolonged use of OXYCONTIN during pregnancy can result in withdrawal in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. Observe newborns for signs of neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using opioids for a prolonged period of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available *[see Use in Specific Populations (8.1), Patient Counseling Information (17)]*.

5.5 Risks of Concomitant Use or Discontinuation of Cytochrome P450 3A4 Inhibitors and Inducers

Concomitant use of OXYCONTIN with a CYP3A4 inhibitor, such as macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g., ketoconazole), and protease inhibitors (e.g., ritonavir), may increase plasma concentrations of oxycodone and prolong opioid adverse reactions, which may cause potentially fatal respiratory depression *[see Warnings and Precautions (5.3)]*, particularly when an inhibitor is added after a stable dose of OXYCONTIN is achieved. Similarly, discontinuation of a CYP3A4 inducer, such as rifampin, carbamazepine, and phenytoin, in OXYCONTIN-treated patients may increase oxycodone plasma concentrations and prolong opioid adverse reactions. When using OXYCONTIN with CYP3A4 inhibitors or discontinuing CYP3A4 inducers in OXYCONTIN-treated patients, monitor patients closely at frequent intervals and consider dosage reduction of OXYCONTIN until stable drug effects are achieved *[see Drug Interactions (7)]*.

Concomitant use of OXYCONTIN with CYP3A4 inducers or discontinuation of a CYP3A4 inhibitor could decrease oxycodone plasma concentrations, decrease opioid efficacy or, possibly, lead to a withdrawal syndrome in a patient who had developed physical dependence to oxycodone. When using OXYCONTIN with CYP3A4 inducers or discontinuing CYP3A4 inhibitors, monitor patients closely at frequent intervals and consider increasing the opioid dosage if needed to maintain adequate analgesia or if symptoms of opioid withdrawal occur *[see Drug Interactions (7)]*.

5.6 Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants

Profound sedation, respiratory depression, coma, and death may result if OXYCONTIN is used concomitantly with alcohol or other central nervous system (CNS) depressants (e.g., non-benzodiazepines sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioid analgesics alone. Because of similar pharmacological properties, it is reasonable to expect similar risk with the concomitant use of other CNS depressant drugs with opioid analgesics *[see Drug Interactions (7)]*.

If the decision is made to prescribe a benzodiazepine or other CNS depressant concomitantly with an opioid analgesic, prescribe the lowest effective dosages and minimum durations of concomitant use. In patients already receiving an opioid analgesic, prescribe a lower initial dose of the benzodiazepine or other CNS depressant than indicated in the absence of an opioid, and titrate based on clinical response. If an opioid analgesic is initiated in a patient already taking a benzodiazepine or other CNS depressant, prescribe a lower initial dose of the opioid analgesic, and titrate based on clinical response. Follow patients closely for signs and symptoms of respiratory depression and sedation.

Advise both patients and caregivers about the risks of respiratory depression and sedation when OXYCONTIN is used with benzodiazepines or other CNS depressants (including alcohol and illicit drugs). Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the benzodiazepine or other CNS depressant have been determined. Screen patients for risk of substance use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of additional CNS depressants including alcohol and illicit drugs *[see Drug Interactions (7), Patient Counseling Information (17)]*.

5.7 Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients

The use of OXYCONTIN in patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment is contraindicated.

Patients with Chronic Pulmonary Disease: OXYCONTIN-treated patients with significant chronic obstructive pulmonary disease or cor pulmonale, and those with a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression are at increased risk of decreased respiratory drive including apnea, even at recommended dosages of OXYCONTIN *[see Warnings and Precautions (5.3)]*.

Elderly, Cachectic, or Debilitated Patients: Life-threatening respiratory depression is more likely to occur in elderly, cachectic, or debilitated patients because they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients *[see Warnings and Precautions (5.3)]*.

Monitor such patients closely, particularly when initiating and titrating OXYCONTIN and when OXYCONTIN is given concomitantly with other drugs that depress respiration *[see Warnings and Precautions (5.3, 5.6)]*. Alternatively, consider the use of non-opioid analgesics in these patients.

5.8 Adrenal Insufficiency

Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. Presentation of adrenal insufficiency may include non-specific symptoms and signs including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

5.9 Severe Hypotension

OXYCONTIN may cause severe hypotension, including orthostatic hypotension and syncope in ambulatory patients. There is an increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (e.g., phenothiazines or general anesthetics) *[see Drug Interactions (7)]*. Monitor these patients for signs of hypotension after initiating or titrating the dosage of OXYCONTIN. In patients with circulatory shock, OXYCONTIN may cause vasodilation that can further reduce cardiac output and blood pressure. Avoid the use of OXYCONTIN in patients with circulatory shock.

5.10 Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness

In patients who may be susceptible to the intracranial effects of CO_2 retention (e.g., those with evidence of increased intracranial pressure or brain tumors), OXYCONTIN may reduce respiratory drive, and the resultant CO_2 retention can further increase intracranial pressure.

Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy with OXYCONTIN.

Opioids may also obscure the clinical course in a patient with a head injury. Avoid the use of OXYCONTIN in patients with impaired consciousness or coma.

5.11 Difficulty in Swallowing and Risk for Obstruction in Patients at Risk for a Small Gastrointestinal Lumen

There have been post-marketing reports of difficulty in swallowing OXYCONTIN tablets. These reports included choking, gagging, regurgitation and tablets stuck in the throat. Instruct patients not to pre-soak, lick, or otherwise wet OXYCONTIN tablets prior to placing in the mouth, and to take one tablet at a time with enough water to ensure complete swallowing immediately after placing in the mouth.

There have been rare post-marketing reports of cases of intestinal obstruction, and exacerbation of diverticulitis, some of which have required medical intervention to remove the tablet. Patients with underlying GI disorders such as esophageal cancer or colon cancer with a small gastrointestinal lumen are at greater risk of developing these complications. Consider use of an alternative analgesic in patients who have difficulty swallowing and patients at risk for underlying GI disorders resulting in a small gastrointestinal lumen.

5.12 Risks of Use in Patients with Gastrointestinal Conditions

OXYCONTIN is contraindicated in patients with known or suspected gastrointestinal obstruction, including paralytic ileus.

The oxycodone in OXYCONTIN may cause spasm of the sphincter of Oddi. Opioids may cause increases in the serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis, for worsening symptoms.

5.13 Increased Risk of Seizures in Patients with Seizure Disorders

The oxycodone in OXYCONTIN may increase the frequency of seizures in patients with seizure disorders, and may increase the risk of seizures occurring in other clinical settings associated with seizures. Monitor patients with a history of seizure disorders for worsened seizure control during OXYCONTIN therapy.

5.14 Withdrawal

Avoid the use of mixed agonist/antagonist (e.g.., pentazocine, nalbuphine, and butorphanol) or partial agonist (e.g., buprenorphine) analgesics in patients who are receiving a full opioid agonist analgesic, including OXYCONTIN. In these patients, mixed agonist/antagonist and partial agonist analgesics may reduce the analgesic effect and/or may precipitate withdrawal symptoms.

When discontinuing OXYCONTIN, gradually taper the dosage *[see Dosage and Administration (2.9)]*. Do not abruptly discontinue OXYCONTIN *[see Drug Abuse and Dependence (9.3)]*.

5.15 Risks of Driving and Operating Machinery

OXYCONTIN may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery. Warn patients not to drive or operate dangerous machinery unless they are tolerant to the effects of OXYCONTIN and know how they will react to the medication *[see Patient Counseling Information (17)]*.

5.16 Laboratory Monitoring

Not every urine drug test for "opioids" or "opiates" detects oxycodone reliably, especially those designed for in-office use. Further, many laboratories will report urine drug concentrations below a specified "cut-off" value as "negative". Therefore, if urine testing for oxycodone is considered in the clinical management of an individual patient, ensure that the sensitivity and specificity of the assay is appropriate, and consider the limitations of the testing used when interpreting results.

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:

- Addiction, Abuse, and Misuse *[see Warnings and Precautions (5.1)]*
- Life-Threatening Respiratory Depression *[see Warnings and Precautions (5.3)]*
- Neonatal Opioid Withdrawal Syndrome *[see Warnings and Precautions (5.4)]*
- Interactions With Benzodiazepines and Other CNS Depressants *[see Warnings and Precautions (5.6)]*
- Adrenal Insufficiency *[see Warnings and Precautions (5.8)]*
- Severe Hypotension *[see Warnings and Precautions (5.9)]*
- Gastrointestinal Adverse Reactions *[see Warnings and Precautions (5.11, 5.12)]*
- Seizures *[see Warnings and Precautions (5.13)]*
- Withdrawal *[see Warnings and Precautions (5.14)]*

6.1 Clinical Trial Experience

Adult Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of OXYCONTIN was evaluated in double-blind clinical trials involving 713 patients with moderate to severe pain of various etiologies. In open-label studies of cancer pain, 187 patients received OXYCONTIN in total daily doses ranging from 20 mg to 640 mg per day. The average total daily dose was approximately 105 mg per day.

OXYCONTIN may increase the risk of serious adverse reactions such as those observed with other opioid analgesics, including respiratory depression, apnea, respiratory arrest, circulatory depression, hypotension, or shock *[see Overdosage (10)]*.

The most common adverse reactions (>5%) reported by patients in clinical trials comparing OXYCONTIN with placebo are shown in Table 2 below:

TABLE 2: Common Adverse Reactions (>5%)

Adverse Reaction	**OXYCONTIN (n=227) (%)**	**Placebo (n=45) (%)**
Constipation	(23)	(7)
Nausea	(23)	(11)
Somnolence	(23)	(4)
Dizziness	(13)	(9)
Pruritus	(13)	(2)
Vomiting	(12)	(7)
Headache	(7)	(7)
Dry Mouth	(6)	(2)
Asthenia	(6)	-
Sweating	(5)	(2)

In clinical trials, the following adverse reactions were reported in patients treated with OXYCONTIN with an incidence between 1% and 5%:

Gastrointestinal disorders: abdominal pain, diarrhea, dyspepsia, gastritis

General disorders and administration site conditions: chills, fever

Metabolism and nutrition disorders: anorexia

Musculoskeletal and connective tissue disorders: twitching

Psychiatric disorders: abnormal dreams, anxiety, confusion, dysphoria, euphoria, insomnia, nervousness, thought abnormalities

Respiratory, thoracic and mediastinal disorders: dyspnea, hiccups

Skin and subcutaneous tissue disorders: rash

Vascular disorders: postural hypotension

The following adverse reactions occurred in less than 1% of patients involved in clinical trials:

Blood and lymphatic system disorders: lymphadenopathy

Ear and labyrinth disorders: tinnitus

Eye disorders: abnormal vision

Gastrointestinal disorders: dysphagia, eructation, flatulence, gastrointestinal disorder, increased appetite, stomatitis

General disorders and administration site conditions: withdrawal syndrome (with and without seizures), edema, peripheral edema, thirst, malaise, chest pain, facial edema

Injury, poisoning and procedural complications: accidental injury

Investigations: ST depression

Metabolism and nutrition disorders: dehydration

Nervous system disorders: syncope, migraine, abnormal gait, amnesia, hyperkinesia, hypoesthesia, hypotonia, paresthesia, speech disorder, stupor, tremor, vertigo, taste perversion

Psychiatric disorders: depression, agitation, depersonalization, emotional lability, hallucination

Renal and urinary disorders: dysuria, hematuria, polyuria, urinary retention

Reproductive system and breast disorders: impotence

Respiratory, thoracic and mediastinal disorders: cough increased, voice alteration

Skin and subcutaneous tissue disorders: dry skin, exfoliative dermatitis

Clinical Trial Experience in Pediatric Patients 11 Years and Older

The safety of OXYCONTIN has been evaluated in one clinical trial with 140 patients 11 to 16 years of age. The median duration of treatment was approximately three weeks. The most frequently reported adverse events were vomiting, nausea, headache, pyrexia, and constipation.

Table 3 includes a summary of the incidence of treatment emergent adverse events reported in ≥5% of patients.

Table 3: Incidence of Adverse Reactions Reported in ≥ 5.0% Patients 11 to 16 Years

System Organ Class **Preferred Term**	**11 to 16 Years** **(N=140)** **n (%)**
Any Adverse Event >= 5%	71 (51)

GASTROINTESTINAL DISORDERS	56 (40)
Vomiting	30 (21)
Nausea	21 (15)
Constipation	13 (9)
Diarrhea	8 (6)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	32 (23)
Pyrexia	15 (11)
METABOLISM AND NUTRITION DISORDERS	9 (6)
Decreased appetite	7 (5)
NERVOUS SYSTEM DISORDERS	37 (26)
Headache	20 (14)
Dizziness	12 (9)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	23 (16)
Pruritus	8 (6)

The following adverse reactions occurred in a clinical trial of OXYCONTIN in patients 11 to 16 years of age with an incidence between ≥1.0% and < 5.0%. Events are listed within each System/Organ Class.

Blood and lymphatic system disorders: febrile neutropenia, neutropenia

Cardiac disorders: tachycardia

Gastrointestinal disorders: abdominal pain, gastroesophageal reflux disease

General disorders and administration site conditions: fatigue, pain, chills, asthenia

Injury, poisoning, and procedural complications: procedural pain, seroma

Investigations: oxygen saturation decreased, alanine aminotransferase increased, hemoglobin decreased, platelet count decreased, neutrophil count decreased, red blood cell count decreased, weight decreased

Metabolic and nutrition disorders: hypochloremia, hyponatremia

Musculoskeletal and connective tissue disorders: pain in extremity, musculoskeletal pain

Nervous system disorders: somnolence, hypoesthesia, lethargy, paresthesia

Psychiatric disorders: insomnia, anxiety, depression, agitation

Renal and urinary disorders: dysuria, urinary retention

Respiratory, thoracic, and mediastinal disorders: oropharyngeal pain

Skin and subcutaneous tissue disorders: hyperhidrosis, rash

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of extended-release oxycodone. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Abuse, addiction, aggression, amenorrhea, cholestasis, completed suicide, death, dental caries, increased hepatic enzymes, hyperalgesia, hypogonadism, hyponatremia, ileus, intentional overdose, mood altered, muscular hypertonia, overdose, palpitations (in the context of withdrawal), seizures, suicidal attempt, suicidal ideation, syndrome of inappropriate antidiuretic hormone secretion, and urticaria.

In addition to the events listed above, the following have also been reported, potentially due to the swelling and hydrogelling property of the tablet: choking, gagging, regurgitation, tablets stuck in the throat and difficulty swallowing the tablet.

Serotonin syndrome: Cases of serotonin syndrome, a potentially life-threatening condition, have been reported during concomitant use of opioids with serotonergic drugs.

Adrenal insufficiency: Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use.

Anaphylaxis: Anaphylaxis has been reported with ingredients contained in OXYCONTIN.

Androgen deficiency: Cases of androgen deficiency have occurred with chronic use of opioids *[see Clinical Pharmacology (12.2)]*.

7 DRUG INTERACTIONS

Table 4 includes clinically significant drug interactions with OXYCONTIN.

Table 4: Clinically Significant Drug Interactions with OXYCONTIN

Inhibitors of CYP3A4 and CYP2D6	
Clinical Impact:	The concomitant use of OXYCONTIN and CYP3A4 inhibitors can increase the plasma concentration of oxycodone, resulting in increased or prolonged opioid effects. These effects could be more pronounced with concomitant use of OXYCONTIN and CYP2D6 and CYP3A4 inhibitors, particularly when an inhibitor is added after a stable dose of OXYCONTIN is achieved *[see Warnings*

	and Precautions (5.5)]. After stopping a CYP3A4 inhibitor, as the effects of the inhibitor decline, the oxycodone plasma concentration will decrease *[see Clinical Pharmacology (12.3)]*, resulting in decreased opioid efficacy or a withdrawal syndrome in patients who had developed physical dependence to oxycodone.
Intervention:	If concomitant use is necessary, consider dosage reduction of OXYCONTIN until stable drug effects are achieved. Monitor patients for respiratory depression and sedation at frequent intervals. If a CYP3A4 inhibitor is discontinued, consider increasing the OXYCONTIN dosage until stable drug effects are achieved. Monitor for signs of opioid withdrawal.
Examples	Macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g. ketoconazole), protease inhibitors (e.g., ritonavir)
CYP3A4 Inducers	
Clinical Impact:	The concomitant use of OXYCONTIN and CYP3A4 inducers can decrease the plasma concentration of oxycodone *[see Clinical Pharmacology (12.3)]*, resulting in decreased efficacy or onset of a withdrawal syndrome in patients who have developed physical dependence to oxycodone *[see Warnings and Precautions (5.5)]*. After stopping a CYP3A4 inducer, as the effects of the inducer decline, the oxycodone plasma concentration will increase *[see Clinical Pharmacology (12.3)]*, which could increase or prolong both the therapeutic effects and adverse reactions, and may cause serious respiratory depression.
Intervention:	If concomitant use is necessary, consider increasing the OXYCONTIN dosage until stable drug effects are achieved. Monitor for signs of opioid withdrawal. If a CYP3A4 inducer is discontinued, consider OXYCONTIN dosage reduction and monitor for signs of respiratory depression.
Examples:	Rifampin, carbamazepine, phenytoin
Benzodiazepines and Other Central Nervous System (CNS) Depressants	
Clinical Impact:	Due to additive pharmacologic effect, the concomitant use of benzodiazepines or other CNS depressants, including alcohol, can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death.
Intervention:	Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients closely for signs of respiratory depression and sedation *[see Dosage and Administration (2.6), Warnings and Precautions (5.6)]*.
Examples:	Benzodiazepines and other sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol.
Serotonergic Drugs	
Clinical Impact:	The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Intervention:	If concomitant use is warranted, carefully observe the patient, particularly during treatment initiation and dose adjustment. Discontinue OXYCONTIN if serotonin syndrome is suspected.
Examples:	Selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine

	reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), triptans, 5-HT3 receptor antagonists, drugs that affect the serotonin neurotransmitter system (e.g., mirtazapine, trazodone, tramadol), monoamine oxidase (MAO) inhibitors (those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue).
Monoamine Oxidase Inhibitors (MAOIs)	
Clinical Impact:	MAOI interactions with opioids may manifest as serotonin syndrome or opioid toxicity (e.g., respiratory depression, coma) *[see Warnings and Precautions (5.3)]*.
Intervention:	The use of OXYCONTIN is not recommended for patients taking MAOIs or within 14 days of stopping such treatment.
Examples:	phenelzine, tranylcypromine, linezolid
Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics	
Clinical Impact:	May reduce the analgesic effect of OXYCONTIN and/or precipitate withdrawal symptoms.
Intervention:	Avoid concomitant use.
Examples:	butorphanol, nalbuphine, pentazocine, buprenorphine
Muscle Relaxants	
Clinical Impact:	Oxycodone may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.
Intervention:	Monitor patients for signs of respiratory depression that may be greater than otherwise expected and decrease the dosage of OXYCONTIN and/or the muscle relaxant as necessary.
Diuretics	
Clinical Impact:	Opioids can reduce the efficacy of diuretics by inducing the release of antidiuretic hormone.
Intervention:	Monitor patients for signs of diminished diuresis and/or effects on blood pressure and increase the dosage of the diuretic as needed.
Anticholinergic Drugs	
Clinical Impact:	The concomitant use of anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Intervention:	Monitor patients for signs of urinary retention or reduced gastric motility when OXYCONTIN is used concomitantly with anticholinergic drugs.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Prolonged use of opioid analgesics during pregnancy may cause neonatal opioid withdrawal syndrome *[see Warnings and Precautions (5.4)]*. There are no available data with OXYCONTIN in pregnant women to inform a drug-associated risk for major birth defects and miscarriage. In animal reproduction studies, there was no embryo-fetal toxicity when

oxycodone hydrochloride was orally administered to rats and rabbits, during the period of organogenesis, at doses 1.3 to 40 times the adult human dose of 60 mg/day, respectively. In a pre- and postnatal toxicity study, when oxycodone was orally administered to rats, there was transiently decreased pup body weight during lactation and the early post-weaning period at the dose equivalent to an adult dose of 60 mg/day. In several published studies, treatment of pregnant rats with oxycodone hydrochloride at clinically relevant doses and below resulted in neurobehavioral effects in offspring *[see Data]*. Based on animal data, advise pregnant women of the potential risk to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Prolonged use of opioid analgesics during pregnancy for medical or nonmedical purposes can result in physical dependence in the neonate and neonatal opioid withdrawal syndrome shortly after birth.

Neonatal opioid withdrawal syndrome presents as irritability, hyperactivity and abnormal sleep pattern, high pitched cry, tremor, vomiting, diarrhea, and failure to gain weight. The onset, duration, and severity of neonatal opioid withdrawal syndrome vary based on the specific opioid used, duration of use, timing and amount of last maternal use, and rate of elimination of the drug by the newborn. Observe newborns for symptoms of neonatal opioid withdrawal syndrome and manage accordingly *[see Warnings and Precautions (5.4)]*.

Labor or Delivery

Opioids cross the placenta and may produce respiratory depression and psycho-physiologic effects in neonates. An opioid antagonist, such as naloxone, must be available for reversal of opioid-induced respiratory depression in the neonate. OXYCONTIN is not recommended for use in women immediately prior to labor, when use of shorter-acting analgesics or other analgesic techniques are more appropriate. Opioid analgesics, including OXYCONTIN, can prolong labor through actions which temporarily reduce the strength, duration, and frequency of uterine contractions. However this effect is not consistent and may be offset by an increased rate of cervical dilatation, which tends to shorten labor. Monitor neonates exposed to opioid analgesics during labor for signs of excess sedation and respiratory depression.

Data

Animal Data

Pregnant rats were treated with 0.5, 2, 4, and 8 mg/kg oxycodone hydrochloride (0.08, 0.3, 0.7, and 1.3 times the human daily dose of 60 mg/day, respectively based on a mg/m^2 basis) during the period of organogenesis. Oxycodone did not cause adverse effects to the fetus at exposures up to 1.3 times the human dose of 60 mg/day. The high dose produced maternal toxicity characterized by excessive gnawing on forelimbs and decreased body weight gain.

Pregnant rabbits were treated with 1, 5, 25, and 125 mg/kg oxycodone hydrochloride (0.3, 2, 8, and 40 times the human daily dose of 60 mg/day, respectively, based on a mg/m^2 basis) during the period of organogenesis. Oxycodone did not cause adverse effects to the fetus at exposures up to 40 times the human dose of 60 mg/day. The 25 mg/kg and 125 mg/kg doses high doses produced maternal toxicity characterized by decreased food consumption and body weight gain.

Pregnant rats were treated with 0.5, 2, and 6 mg/kg oxycodone hydrochloride (0.08, 0.32, and 1 times the human daily dose of 60 mg/kg, respective, based on a mg/m^2 basis, during the period of organogenesis through lactation. Decreased body weight was found during lactation and the early post-weaning phase in pups nursed by mothers given the highest dose used (6 mg/kg/day, equivalent to an adult human dose of 60 mg/day, on a mg/m^2 basis). However, body weight of these pups recovered.

In published studies, offspring of pregnant rats administered oxycodone hydrochloride during gestation have been reported to exhibit neurobehavioral effects including altered stress responses and increased anxiety-like behavior (2 mg/kg/day IV from Gestation Day 8 to 21 and Postnatal Day 1, 3, and 5; 0.3 times an adult human oral dose of 60 mg/day on a mg/m^2 basis), and altered learning and memory (15 mg/kg/day orally from breeding through parturition; 2.4 times an adult human oral dose of 60 mg/day on a mg/m^2 basis).

8.2 Lactation

Oxycodone is present in breast milk. Published lactation studies report variable concentrations of oxycodone in breast milk with administration of immediate-release oxycodone to nursing mothers in the early postpartum period. The lactation studies did not assess breastfed infants for potential adverse reactions. Lactation studies have not been conducted with extended–release oxycodone, including OXYCONTIN, and no information is available on the effects of the drug on the breastfed infant or the effects of the drug on milk production. Because of the potential for serious adverse reactions, including excess sedation and respiratory depression in a breastfed infant, advise patients that breastfeeding is not recommended during treatment with OXYCONTIN.

Clinical Considerations

Infants exposed to OXYCONTIN through breast milk should be monitored for excess sedation and respiratory depression. Withdrawal symptoms can occur in breast-fed infants when maternal administration of an opioid analgesic is stopped, or when breast-feeding is stopped.

8.3 Females and Males of Reproductive Potential

Infertility

Chronic use of opioids may cause reduced fertility in females and males of reproductive potential. It is not known whether these effects on fertility are reversible *[see Adverse Reactions (6.2), Clinical Pharmacology (12.2)]*.

8.4 Pediatric Use

The safety and efficacy of OXYCONTIN have been established in pediatric patients ages 11 to 16 years. Use of OXYCONTIN is supported by evidence from adequate and well-controlled trials with OXYCONTIN in adults as well as an open-label study in pediatric patients ages 6 to 16 years. However, there were insufficient numbers of patients less than 11 years of age enrolled in this study to establish the safety of the product in this age group.

The safety of OXYCONTIN in pediatric patients was evaluated in 155 patients previously receiving and tolerating opioids for at least 5 consecutive days with a minimum of 20 mg per day of oxycodone or its equivalent on the two days immediately preceding dosing with OXYCONTIN. Patients were started on a total daily dose ranging between 20 mg and 100 mg depending on prior opioid dose.

The most frequent adverse events observed in pediatric patients were vomiting, nausea, headache, pyrexia, and constipation *[see Dosage and Administration (2.4), Adverse Reactions (6.1), Clinical Pharmacology (12.3) and Clinical Trials (14)]*.

8.5 Geriatric Use

In controlled pharmacokinetic studies in elderly subjects (greater than 65 years) the clearance of oxycodone was slightly reduced. Compared to young adults, the plasma concentrations of oxycodone were increased approximately 15% *[see Clinical Pharmacology (12.3)]*. Of the total number of subjects (445) in clinical studies of oxycodone hydrochloride controlled-release tablets, 148 (33.3%) were age 65 and older (including those age 75 and older) while 40 (9.0%) were age 75 and older. In clinical trials with appropriate initiation of therapy and dose titration, no untoward or unexpected adverse reactions were seen in the elderly patients who received oxycodone hydrochloride controlled-release tablets. Thus, the usual doses and dosing intervals may be appropriate for elderly patients. However, a dosage reduction in debilitated, non-opioid-tolerant patients is recommended *[see Dosage and Administration (2.7)]*.

Respiratory depression is the chief risk for elderly patients treated with opioids, and has occurred after large initial doses were administered to patients who are not opioid-tolerant or when opioids were co-administered with other agents that depress respiration. Titrate the dosage of OXYCONTIN slowly in these patients and monitor closely for signs of central nervous system and respiratory depression. *[see Warnings and Precautions (5.7)]*.

Oxycodone is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

8.6 Hepatic Impairment

A study of OXYCONTIN in patients with hepatic impairment demonstrated greater plasma concentrations than those seen at equivalent doses in persons with normal hepatic function *[see Clinical Pharmacology (12.3)]*. Therefore, a dosage reduction is recommended for these patients *[see Dosage and Administration (2.8)]*. Monitor closely for signs of respiratory depression, sedation, and hypotension.

8.7 Renal Impairment

In patients with renal impairment, as evidenced by decreased creatinine clearance (<60 mL/min), the concentrations of oxycodone in the plasma are approximately 50% higher than in subjects with normal renal function *[see Clinical Pharmacology (12.3)]*. Follow a conservative approach to dose initiation and adjust according to the clinical situation.

8.8 Sex Differences

In pharmacokinetic studies with OXYCONTIN, opioid-naïve females demonstrate up to 25% higher average plasma concentrations and greater frequency of typical opioid adverse events than males, even after adjustment for body weight. The clinical relevance of a difference of this magnitude is low for a drug intended for chronic usage at individualized dosages, and there was no male/female difference detected for efficacy or adverse events in clinical trials.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

OXYCONTIN contains oxycodone, a Schedule II controlled substance.

9.2 Abuse

OXYCONTIN contains oxycodone, a substance with a high potential for abuse similar to other opioids including fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxymorphone, and tapentadol. OXYCONTIN can be abused and is subject to misuse, addiction, and criminal diversion *[see Warnings and Precautions (5.1)]*.

The high drug content in extended-release formulations adds to the risk of adverse outcomes from abuse and misuse.

All patients treated with opioids require careful monitoring for signs of abuse and addiction, because use of opioid analgesic products carries the risk of addiction even under appropriate medical use.

Prescription drug abuse is the intentional non-therapeutic use of a prescription drug, even once, for its rewarding psychological or physiological effects. Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance use and includes: a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal.

"Drug-seeking" behavior is very common in persons with substance use disorders. Drug-seeking tactics include emergency calls or visits near the end of office hours, refusal to undergo appropriate examination, testing or referral, repeated “loss” of prescriptions, tampering with prescriptions, and reluctance to provide prior medical records or contact information for other treating healthcare provider(s). “Doctor shopping” (visiting multiple prescribers to obtain additional prescriptions) is common among drug abusers and people suffering from untreated addiction. Preoccupation with achieving adequate pain relief can be appropriate behavior in a patient with poor pain control.

Abuse and addiction are separate and distinct from physical dependence and tolerance. Healthcare providers should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of true addiction.

OXYCONTIN, like other opioids, can be diverted for non-medical use into illicit channels of distribution. Careful record-keeping of prescribing information, including quantity, frequency, and renewal requests, as required by state and federal law, is strongly advised.

Proper assessment of the patient, proper prescribing practices, periodic reevaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs.

Risks Specific to Abuse of OXYCONTIN

OXYCONTIN is for oral use only. Abuse of OXYCONTIN poses a risk of overdose and death. The risk is increased with concurrent use of OXYCONTIN with alcohol and other central nervous system depressants. Taking cut, broken, chewed, crushed, or dissolved OXYCONTIN enhances drug release and increases the risk of overdose and death.

With parenteral abuse, the inactive ingredients in OXYCONTIN can be expected to result in local tissue necrosis, infection, pulmonary granulomas, increased risk of endocarditis, valvular

heart injury, embolism, and death. Cases of thrombotic microangiopathy (a condition characterized clinically by thrombocytopenia and microangiopathic hemolytic anemia) associated with parenteral abuse have been reported.

Parenteral drug abuse is commonly associated with transmission of infectious diseases, such as hepatitis and HIV.

Abuse Deterrence Studies

OXYCONTIN is formulated with inactive ingredients intended to make the tablet more difficult to manipulate for misuse and abuse. For the purposes of describing the results of studies of the abuse-deterrent characteristics of OXYCONTIN resulting from a change in formulation, in this section, the original formulation of OXYCONTIN, which is no longer marketed, will be referred to as "original OxyContin" and the reformulated, currently marketed product will be referred to as "OXYCONTIN".

In Vitro Testing
In vitro physical and chemical tablet manipulation studies were performed to evaluate the success of different extraction methods in defeating the extended-release formulation. Results support that, relative to original OxyContin, there is an increase in the ability of OXYCONTIN to resist crushing, breaking, and dissolution using a variety of tools and solvents. The results of these studies also support this finding for OXYCONTIN relative to an immediate-release oxycodone. When subjected to an aqueous environment, OXYCONTIN gradually forms a viscous hydrogel (i.e., a gelatinous mass) that resists passage through a needle.

Clinical Studies
In a randomized, double-blind, placebo-controlled 5-period crossover pharmacodynamic study, 30 recreational opioid users with a history of intranasal drug abuse received intranasally administered active and placebo drug treatments. The five treatment arms were finely crushed OXYCONTIN 30 mg tablets, coarsely crushed OXYCONTIN 30 mg tablets, finely crushed original OxyContin 30 mg tablets, powdered oxycodone HCl 30 mg, and placebo. Data for finely crushed OXYCONTIN, finely crushed original OxyContin, and powdered oxycodone HCl are described below.

Drug liking was measured on a bipolar drug liking scale of 0 to 100 where 50 represents a neutral response of neither liking nor disliking, 0 represents maximum disliking and 100 represents maximum liking. Response to whether the subject would take the study drug again was also measured on a bipolar scale of 0 to 100 where 50 represents a neutral response, 0 represents the strongest negative response ("definitely would not take drug again") and 100 represents the strongest positive response ("definitely would take drug again").

Twenty-seven of the subjects completed the study. Incomplete dosing due to granules falling from the subjects' nostrils occurred in 34% (n = 10) of subjects with finely crushed OXYCONTIN, compared with 7% (n = 2) of subjects with finely crushed original OxyContin and no subjects with powdered oxycodone HCl.

The intranasal administration of finely crushed OXYCONTIN was associated with a numerically lower mean and median drug liking score and a lower mean and median score for take drug again, compared to finely crushed original OxyContin or powdered oxycodone HCl as summarized in Table 5.

Table 5: Summary of Maximum Drug Liking (E_{max}) Data Following Intranasal Administration

VAS Scale (100 mm)*		OXYCONTIN (finely crushed)	Original OxyContin (finely crushed)	Oxycodone HCl (powdered)
Drug Liking	Mean (SE)	80.4 (3.9)	94.0 (2.7)	89.3 (3.1)
	Median (Range)	88 (36-100)	100 (51-100)	100 (50-100)
Take Drug Again	Mean (SE)	64.0 (7.1)	89.6 (3.9)	86.6 (4.4)
	Median (Range)	78 (0-100)	100 (20-100)	100 (0-100)

* Bipolar scales (0 = maximum negative response, 50 = neutral response, 100 = maximum positive response)

Figure 1 demonstrates a comparison of drug liking for finely crushed OXYCONTIN compared to powdered oxycodone HCl in subjects who received both treatments. The Y-axis represents the percent of subjects attaining a percent reduction in drug liking for OXYCONTIN vs. oxycodone HCl powder greater than or equal to the value on the X-axis. Approximately 44% (n = 12) had no reduction in liking with OXYCONTIN relative to oxycodone HCl. Approximately 56% (n = 15) of subjects had some reduction in drug liking with OXYCONTIN relative to oxycodone HCl. Thirty-three percent (n = 9) of subjects had a reduction of at least 30% in drug liking with OXYCONTIN compared to oxycodone HCl, and approximately 22% (n = 6) of subjects had a reduction of at least 50% in drug liking with OXYCONTIN compared to oxycodone HCl.

Figure 1: Percent Reduction Profiles for E_{max} of Drug Liking VAS for OXYCONTIN vs. oxycodone HCl, N=27 Following Intranasal Administration

The results of a similar analysis of drug liking for finely crushed OXYCONTIN relative to finely crushed original OxyContin were comparable to the results of finely crushed OXYCONTIN relative to powdered oxycodone HCl. Approximately 43% (n = 12) of subjects had no reduction in liking with OXYCONTIN relative to original OxyContin. Approximately 57% (n = 16) of subjects had some reduction in drug liking, 36% (n = 10) of subjects had a reduction of at least 30% in drug liking, and approximately 29% (n = 8) of subjects had a reduction of at least 50% in drug liking with OXYCONTIN compared to original OxyContin.

Summary
The *in vitro* data demonstrate that OXYCONTIN has physicochemical properties expected to make abuse via injection difficult. The data from the clinical study, along with support from the *in vitro* data, also indicate that OXYCONTIN has physicochemical properties that are expected to reduce abuse via the intranasal route. However, abuse of OXYCONTIN by these routes, as well as by the oral route, is still possible.

Additional data, including epidemiological data, when available, may provide further information on the impact of the current formulation of OXYCONTIN on the abuse liability of the drug. Accordingly, this section may be updated in the future as appropriate.

OXYCONTIN contains oxycodone, an opioid agonist and Schedule II controlled substance with an abuse liability similar to other opioid agonists, legal or illicit, including fentanyl, hydromorphone, methadone, morphine, and oxymorphone. OXYCONTIN can be abused and is

subject to misuse, addiction, and criminal diversion *[see Warnings and Precautions (5.1) and Drug Abuse and Dependence (9.1)]*.

9.3 Dependence

Both tolerance and physical dependence can develop during chronic opioid therapy. Tolerance is the need for increasing doses of opioids to maintain a defined effect such as analgesia (in the absence of disease progression or other external factors). Tolerance may occur to both the desired and undesired effects of drugs, and may develop at different rates for different effects.

Physical dependence results in withdrawal symptoms after abrupt discontinuation or a significant dosage reduction of a drug. Withdrawal also may be precipitated through the administration of drugs with opioid antagonist activity (e.g., naloxone, nalmefene), mixed agonist/antagonist analgesics (e.g., pentazocine, butorphanol, nalbuphine), or partial agonists (e.g., buprenorphine). Physical dependence may not occur to a clinically significant degree until after several days to weeks of continued opioid usage.

OXYCONTIN should not be abruptly discontinued *[see Dosage and Administration (2.9)]*. If OXYCONTIN is abruptly discontinued in a physically-dependent patient, a withdrawal syndrome may occur. Some or all of the following can characterize this syndrome: restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, and mydriasis. Other signs and symptoms also may develop, including irritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhea, or increased blood pressure, respiratory rate, or heart rate.

Infants born to mothers physically dependent on opioids will also be physically dependent and may exhibit respiratory difficulties and withdrawal signs *[see Use in Specific Populations (8.1)]*.

10 OVERDOSAGE

Clinical Presentation

Acute overdose with OXYCONTIN can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, and in some cases, pulmonary edema, bradycardia, hypotension, partial or complete airway obstruction, atypical snoring, and death. Marked mydriasis rather than miosis may be seen with hypoxia in overdose situations.

Treatment of Overdose

In case of overdose, priorities are the reestablishment of a patent and protected airway and institution of assisted or controlled ventilation, if needed. Employ other supportive measures (including oxygen, vasopressors) in the management of circulatory shock and pulmonary edema as indicated. Cardiac arrest or arrhythmias will require advanced life support techniques.

The opioid antagonists, naloxone or nalmefene, are specific antidotes to respiratory depression resulting from opioid overdose. For clinically significant respiratory or circulatory depression

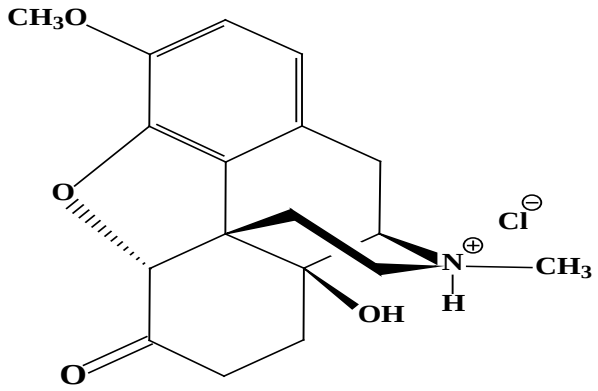
secondary to oxycodone overdose, administer an opioid antagonist. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overdose.

Because the duration of reversal is expected to be less than the duration of action of oxycodone in OXYCONTIN, carefully monitor the patient until spontaneous respiration is reliably reestablished. OXYCONTIN will continue to release oxycodone and add to the oxycodone load for 24 to 48 hours or longer following ingestion, necessitating prolonged monitoring. If the response to an opioid antagonist is suboptimal or only brief in nature, administer additional antagonist as directed by the product's prescribing information.

In an individual physically dependent on opioids, administration of the recommended usual dosage of the antagonist will precipitate an acute withdrawal syndrome. The severity of the withdrawal symptoms experienced will depend on the degree of physical dependence and the dose of the antagonist administered. If a decision is made to treat serious respiratory depression in the physically dependent patient, administration of the antagonist should be initiated with care and by titration with smaller than usual doses of the antagonist.

11 DESCRIPTION

OXYCONTIN® (oxycodone hydrochloride) extended-release tablets is an opioid agonist supplied in 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, and 80 mg tablets for oral administration. The tablet strengths describe the amount of oxycodone per tablet as the hydrochloride salt. The structural formula for oxycodone hydrochloride is as follows:



$C_{18}H_{21}NO_4 \bullet HCl$ MW 351.83

The chemical name is 4, 5α-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride.

Oxycodone is a white, odorless crystalline powder derived from the opium alkaloid, thebaine. Oxycodone hydrochloride dissolves in water (1 g in 6 to 7 mL). It is slightly soluble in alcohol (octanol water partition coefficient 0.7).

The 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg and 80 mg tablets contain the following inactive ingredients: butylated hydroxytoluene (BHT), hypromellose, polyethylene glycol 400, polyethylene oxide, magnesium stearate, titanium dioxide.

The 10 mg tablets also contain hydroxypropyl cellulose.

The 15 mg tablets also contain black iron oxide, yellow iron oxide, and red iron oxide.

The 20 mg tablets also contain polysorbate 80 and red iron oxide.

The 30 mg tablets also contain polysorbate 80, red iron oxide, yellow iron oxide, and black iron oxide.

The 40 mg tablets also contain polysorbate 80 and yellow iron oxide.

The 60 mg tablets also contain polysorbate 80, red iron oxide and black iron oxide.

The 80 mg tablets also contain hydroxypropyl cellulose, yellow iron oxide and FD&C Blue #2/Indigo Carmine Aluminum Lake.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Oxycodone is a full opioid agonist and is relatively selective for the mu receptor, although it can bind to other opioid receptors at higher doses. The principal therapeutic action of oxycodone is analgesia. Like all full opioid agonists, there is no ceiling effect to analgesia for oxycodone. Clinically, dosage is titrated to provide adequate analgesia and may be limited by adverse reactions, including respiratory and CNS depression.

The precise mechanism of the analgesic action is unknown. However, specific CNS opioid receptors for endogenous compounds with opioid-like activity have been identified throughout the brain and spinal cord and are thought to play a role in the analgesic effects of this drug.

12.2 Pharmacodynamics

Effects on the Central Nervous System

Oxycodone produces respiratory depression by direct action on brain stem respiratory centers. The respiratory depression involves a reduction in the responsiveness of the brain stem respiratory centers to both increases in CO_2 tension and electrical stimulation.

Oxycodone causes miosis, even in total darkness. Pinpoint pupils are a sign of opioid overdose but are not pathognomonic (e.g., pontine lesions of hemorrhagic or ischemic origin may produce similar findings). Marked mydriasis rather than miosis may be seen with hypoxia in overdose situations *[see Overdosage (10)]*.

Effects on the Gastrointestinal Tract and Other Smooth Muscle

Oxycodone causes a reduction in motility associated with an increase in smooth muscle tone in the antrum of the stomach and duodenum. Digestion of food in the small intestine is delayed and propulsive contractions are decreased. Propulsive peristaltic waves in the colon are decreased, while tone may be increased to the point of spasm, resulting in constipation. Other opioid-induced effects may include a reduction in biliary and pancreatic secretions, spasm of sphincter of Oddi, and transient elevations in serum amylase.

Effects on the Cardiovascular System

Oxycodone produces peripheral vasodilation which may result in orthostatic hypotension or syncope. Manifestations of histamine release and/or peripheral vasodilation may include pruritus, flushing, red eyes, sweating, and/or orthostatic hypotension.

Effects on the Endocrine System

Opioids inhibit the secretion of adrenocorticotropic hormone (ACTH), cortisol, and luteinizing hormone (LH) in humans *[see Adverse Reactions (6.2)]*. They also stimulate prolactin, growth hormone (GH) secretion, and pancreatic secretion of insulin and glucagon.

Chronic use of opioids may influence the hypothalamic-pituitary-gonadal axis, leading to androgen deficiency that may manifest as low libido, impotence, erectile dysfunction, amenorrhea, or infertility. The causal role of opioids in the clinical syndrome of hypogonadism is unknown because the various medical, physical, lifestyle, and psychological stressors that may influence gonadal hormone levels have not been adequately controlled for in studies conducted to date *[see Adverse Reactions (6.2)]*.

Effects on the Immune System

Opioids have been shown to have a variety of effects on components of the immune system in in vitro and animal models. The clinical significance of these findings is unknown. Overall, the effects of opioids appear to be modestly immunosuppressive.

Concentration –Efficacy Relationships

Studies in normal volunteers and patients reveal predictable relationships between oxycodone dosage and plasma oxycodone concentrations, as well as between concentration and certain expected opioid effects, such as pupillary constriction, sedation, overall subjective "drug effect", analgesia and feelings of relaxation.

The minimum effective analgesic concentration will vary widely among patients, especially among patients who have been previously treated with potent agonist opioids. The minimum effective analgesic concentration of oxycodone for any individual patient may increase over time due to an increase in pain, the development of a new pain syndrome, and/or the development of analgesic tolerance *[see Dosage and Administration (2.1, 2.5)]*.

Concentration –Adverse Reaction Relationships

There is a relationship between increasing oxycodone plasma concentration and increasing frequency of dose-related opioid adverse reactions such as nausea, vomiting, CNS effects, and respiratory depression. In opioid-tolerant patients, the situation may be altered by the development of tolerance to opioid-related adverse reactions *[see Dosage and Administration (2.1, 2.5)]*.

12.3 Pharmacokinetics

The activity of OXYCONTIN is primarily due to the parent drug oxycodone. OXYCONTIN is designed to provide delivery of oxycodone over 12 hours.

Cutting, breaking, chewing, crushing or dissolving OXYCONTIN impairs the controlled-release delivery mechanism and results in the rapid release and absorption of a potentially fatal dose of oxycodone.

Oxycodone release from OXYCONTIN is pH independent. The oral bioavailability of oxycodone is 60% to 87%. The relative oral bioavailability of oxycodone from OXYCONTIN to that from immediate-release oral dosage forms is 100%. Upon repeated dosing with OXYCONTIN in healthy subjects in pharmacokinetic studies, steady-state levels were achieved within 24-36 hours. Oxycodone is extensively metabolized and eliminated primarily in the urine as both conjugated and unconjugated metabolites. The apparent elimination half-life ($t_{½}$) of oxycodone following the administration of OXYCONTIN was 4.5 hours compared to 3.2 hours for immediate-release oxycodone.

Absorption

About 60% to 87% of an oral dose of oxycodone reaches the central compartment in comparison to a parenteral dose. This high oral bioavailability is due to low pre-systemic and/or first-pass metabolism.

Plasma Oxycodone Concentration over Time

Dose proportionality has been established for OXYCONTIN 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, and 80 mg tablet strengths for both peak plasma concentrations (C_{max}) and extent of absorption (AUC) *(see Table 6)*. Given the short elimination $t_{½}$ of oxycodone, steady-state plasma concentrations of oxycodone are achieved within 24-36 hours of initiation of dosing with OXYCONTIN. In a study comparing 10 mg of OXYCONTIN every 12 hours to 5 mg of immediate-release oxycodone every 6 hours, the two treatments were found to be equivalent for AUC and C_{max}, and similar for C_{min} (trough) concentrations.

TABLE 6

Mean [% coefficient of variation]

Regimen	Dosage Form	AUC (ng•hr/mL)*	C_{max} (ng/mL)	T_{max} (hr)
Single Dose†	10 mg	136 [27]	11.5 [27]	5.11 [21]
	15 mg	196 [28]	16.8 [29]	4.59 [19]
	20 mg	248 [25]	22.7 [25]	4.63 [22]
	30 mg	377 [24]	34.6 [21]	4.61 [19]
	40 mg	497 [27]	47.4 [30]	4.40 [22]
	60 mg	705 [22]	64.6 [24]	4.15 [26]
	80 mg	908 [21]	87.1 [29]	4.27 [26]

* for single-dose AUC = $AUC_{0\text{-}inf}$

†data obtained while subjects received naltrexone, which can enhance absorption

Food Effects

Food has no significant effect on the extent of absorption of oxycodone from OXYCONTIN.

Distribution

Following intravenous administration, the steady-state volume of distribution (V_{ss}) for oxycodone was 2.6 L/kg. Oxycodone binding to plasma protein at 37°C and a pH of 7.4 was about 45%. Once absorbed, oxycodone is distributed to skeletal muscle, liver, intestinal tract, lungs, spleen, and brain. Oxycodone has been found in breast milk *[see Use in Specific Populations (8.4)]*.

Elimination

Metabolism

Oxycodone is extensively metabolized by multiple metabolic pathways to produce noroxycodone, oxymorphone and noroxymorphone, which are subsequently glucuronidated. Noroxycodone and noroxymorphone are the major circulating metabolites. CYP3A mediated *N*-demethylation to noroxycodone is the primary metabolic pathway of oxycodone with a lower contribution from CYP2D6 mediated *O*-demethylation to oxymorphone. Therefore, the formation of these and related metabolites can, in theory, be affected by other drugs *[see Drug Interactions (7)]*.

Noroxycodone exhibits very weak anti-nociceptive potency compared to oxycodone, however, it undergoes further oxidation to produce noroxymorphone, which is active at opioid receptors. Although noroxymorphone is an active metabolite and present at relatively high concentrations in circulation, it does not appear to cross the blood-brain barrier to a significant extent. Oxymorphone is present in the plasma only at low concentrations and undergoes further metabolism to form its glucuronide and noroxymorphone. Oxymorphone has been shown to be active and possessing analgesic activity but its contribution to analgesia following oxycodone administration is thought to be clinically insignificant. Other metabolites (α- and ß-oxycodol, noroxycodol and oxymorphol) may be present at very low concentrations and demonstrate limited penetration into the brain as compared to oxycodone. The enzymes responsible for keto-reduction and glucuronidation pathways in oxycodone metabolism have not been established.

Excretion

Oxycodone and its metabolites are excreted primarily via the kidney. The amounts measured in the urine have been reported as follows: free and conjugated oxycodone 8.9%, free noroxycodone 23%, free oxymorphone less than 1%, conjugated oxymorphone 10%, free and conjugated noroxymorphone 14%, reduced free and conjugated metabolites up to 18%. The total plasma clearance was approximately 1.4 L/min in adults.

Specific Populations

Age: Geriatric Population

The plasma concentrations of oxycodone are only nominally affected by age, being 15% greater in elderly as compared to young subjects (age 21-45).

Age: Pediatric Population

In the pediatric age group of 11 years of age and older, systemic exposure of oxycodone is expected to be similar to adults at any given dose of OXYCONTIN.

Sex

Across individual pharmacokinetic studies, average plasma oxycodone concentrations for female subjects were up to 25% higher than for male subjects on a body weight-adjusted basis. The reason for this difference is unknown *[see Use in Specific Populations (8.9)]*.

Hepatic Impairment

Data from a study involving 24 patients with mild to moderate hepatic dysfunction show peak plasma oxycodone and noroxycodone concentrations 50% and 20% higher, respectively, than healthy subjects. AUC values are 95% and 65% higher, respectively. Oxymorphone peak plasma concentrations and AUC values are lower by 30% and 40%. These differences are accompanied by increases in some, but not other, drug effects. The mean elimination $t_{½}$ for oxycodone increased by 2.3 hours.

Renal Impairment

Data from a pharmacokinetic study involving 13 patients with mild to severe renal dysfunction (creatinine clearance <60 mL/min) showed peak plasma oxycodone and noroxycodone concentrations 50% and 20% higher, respectively, and AUC values for oxycodone, noroxycodone, and oxymorphone 60%, 50%, and 40% higher than normal subjects, respectively. This was accompanied by an increase in sedation but not by differences in respiratory rate, pupillary constriction, or several other measures of drug effect. There was an increase in mean elimination $t_{½}$ for oxycodone of 1 hour.

Drug Interaction Studies

CYP3A4 Inhibitors

CYP3A4 is the major isoenzyme involved in noroxycodone formation. Co-administration of OXYCONTIN (10 mg single dose) and the CYP3A4 inhibitor ketoconazole (200 mg BID) increased oxycodone AUC and C_{max} by 170% and 100%, respectively *[see Drug Interactions (7)]*.

CYP3A4 Inducers

A published study showed that the co-administration of rifampin, a drug metabolizing enzyme inducer, decreased oxycodone AUC and C_{max} values by 86% and 63%, respectively *[see Drug Interactions (7)]*.

CYP2D6 Inhibitors

Oxycodone is metabolized in part to oxymorphone via CYP2D6. While this pathway may be blocked by a variety of drugs such as certain cardiovascular drugs (e.g., quinidine) and antidepressants (e.g., fluoxetine), such blockade has not been shown to be of clinical significance with OXYCONTIN *[see Drug Interactions (7)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Long-term studies in animals to evaluate the carcinogenic potential of oxycodone have not been conducted.

Mutagenesis

Oxycodone was genotoxic in the in vitro mouse lymphoma assay. Oxycodone was negative when tested at appropriate concentrations in the in vitro chromosomal aberration assay, the in vitro bacterial reverse mutation assay (Ames test), and the in vivo bone marrow micronucleus assay in mice.

Impairment of Fertility

In a study of reproductive performance, rats were administered a once daily gavage dose of the vehicle or oxycodone hydrochloride (0.5, 2, and 8 mg/kg/day). Male rats were dosed for 28 days before cohabitation with females, during the cohabitation and until necropsy (2-3 weeks post-cohabitation). Females were dosed for 14 days before cohabitation with males, during cohabitation and up to Gestation Day 6. Oxycodone hydrochloride did not affect reproductive function in male or female rats at any dose tested (up to 8 mg/kg/day), up to 1.3 times a human dose of 60 mg/day.

14 CLINICAL STUDIES

Adult Clinical Study

A double-blind, placebo-controlled, fixed-dose, parallel group, two-week study was conducted in 133 patients with persistent, moderate to severe pain, who were judged as having inadequate pain control with their current therapy. In this study, OXYCONTIN 20 mg, but not 10 mg, was statistically significant in pain reduction compared with placebo.

Pediatric Clinical Study

OXYCONTIN has been evaluated in an open-label clinical trial of 155 opioid-tolerant pediatric patients with moderate to severe chronic pain. The mean duration of therapy was 20.7 days (range 1 to 43 days). The starting total daily doses ranged from 20 mg to 100 mg based on the patient's prior opioid dose. The mean daily dose was 33.30 mg (range 20 to 140 mg/day). In an extension study, 23 of the 155 patients were treated beyond four weeks, including 13 for 28 weeks. Too few patients less than 11 years were enrolled in the clinical trial to provide meaningful safety data in this age group.

16 HOW SUPPLIED/STORAGE AND HANDLING

OXYCONTIN (oxycodone hydrochloride) extended-release tablets 10 mg are film-coated, round, white-colored, bi-convex tablets debossed with OP on one side and 10 on the other and are supplied as child-resistant closure, opaque plastic bottles of 100 (**NDC 59011-410-10**) and unit dose packaging with 10 individually numbered tablets per card; two cards per glue end carton (**NDC 59011-410-20**).

OXYCONTIN (oxycodone hydrochloride) extended-release tablets 15 mg are film-coated, round, gray-colored, bi-convex tablets debossed with OP on one side and 15 on the other and are supplied as child-resistant closure, opaque plastic bottles of 100 (**NDC 59011-415-10**) and unit dose packaging with 10 individually numbered tablets per card; two cards per glue end carton (**NDC 59011-415-20**).

OXYCONTIN (oxycodone hydrochloride) extended-release tablets 20 mg are film-coated, round, pink-colored, bi-convex tablets debossed with OP on one side and 20 on the other and are supplied as child-resistant closure, opaque plastic bottles of 100 (**NDC 59011-420-10**) and unit dose packaging with 10 individually numbered tablets per card; two cards per glue end carton (**NDC 59011-420-20**).

OXYCONTIN (oxycodone hydrochloride) extended-release tablets 30 mg are film-coated, round, brown-colored, bi-convex tablets debossed with OP on one side and 30 on the other and are supplied as child-resistant closure, opaque plastic bottles of 100 (**NDC 59011-430-10**) and unit dose packaging with 10 individually numbered tablets per card; two cards per glue end carton (**NDC 59011-430-20**).

OXYCONTIN (oxycodone hydrochloride) extended-release tablets 40 mg are film-coated, round, yellow-colored, bi-convex tablets debossed with OP on one side and 40 on the other and are supplied as child-resistant closure, opaque plastic bottles of 100 (**NDC 59011-440-10**) and unit dose packaging with 10 individually numbered tablets per card; two cards per glue end carton (**NDC 59011-440-20**).

OXYCONTIN (oxycodone hydrochloride) extended-release tablets 60 mg are film-coated, round, red-colored, bi-convex tablets debossed with OP on one side and 60 on the other and are supplied as child-resistant closure, opaque plastic bottles of 100 (**NDC 59011-460-10**) and unit dose packaging with 10 individually numbered tablets per card; two cards per glue end carton (**NDC 59011-460-20**).

OXYCONTIN (oxycodone hydrochloride) extended-release tablets 80 mg are film-coated, round, green-colored, bi-convex tablets debossed with OP on one side and 80 on the other and are supplied as child-resistant closure, opaque plastic bottles of 100 (**NDC 59011-480-10**) and unit dose packaging with 10 individually numbered tablets per card; two cards per glue end carton (**NDC 59011-480-20**).

Store at 25°C (77°F); excursions permitted between 15°-30°C (59°-86°F) [see USP Controlled Room Temperature].

Dispense in tight, light-resistant container.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Addiction, Abuse and Misuse

Inform patients that the use of OXYCONTIN, even when taken as recommended, can result in addiction, abuse, and misuse, which can lead to overdose and death *[see Warnings and Precautions (5.1)]*. Instruct patients not to share OXYCONTIN with others and to take steps to protect OXYCONTIN from theft or misuse.

Life-Threatening Respiratory Depression

Inform patients of the risk of life-threatening respiratory depression, including information that the risk is greatest when starting OXYCONTIN or when the dosage is increased, and that it can occur even at recommended dosages *[see Warnings and Precautions (5.3)]*. Advise patients how to recognize respiratory depression and to seek medical attention if breathing difficulties develop.

To guard against excessive exposure to OXYCONTIN by young children, advise caregivers to strictly adhere to recommended OXYCONTIN dosing.

Accidental Ingestion

Inform patients that accidental ingestion, especially by children, may result in respiratory depression or death *[see Warnings and Precautions (5.3)]*. Instruct patients to take steps to store OXYCONTIN securely and to dispose of unused OXYCONTIN by flushing the tablets down the toilet.

Interactions with Benzodiazepines or Other CNS Depressants

Inform patients and caregivers that potentially fatal additive effects may occur if OXYCONTIN is used with benzodiazepines or other CNS depressants, including alcohol, and not to use these concomitantly unless supervised by a healthcare provider *[see Warnings and Precautions (5.6), Drug Interactions (7)]*.

Serotonin Syndrome

Inform patients that opioids could cause a rare but potentially life-threatening condition resulting from concomitant administration of serotonergic drugs. Warn patients of the symptoms of serotonin syndrome and to seek medical attention right away if symptoms develop. Instruct patients to inform their healthcare provider if they are taking, or plan to take serotonergic medications *[see Drug Interactions (7)]*.

MAOI Interaction

Inform patients to avoid taking OXYCONTIN while using any drugs that inhibit monoamine oxidase. Patients should not start MAOIs while taking OXYCONTIN *[see Drug Interactions (7)]*.

Adrenal Insufficiency

Inform patients that opioids could cause adrenal insufficiency, a potentially life-threatening condition. Adrenal insufficiency may present with non-specific symptoms and signs such as nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. Advise patients to seek medical attention if they experience a constellation of these symptoms *[see Warnings and Precautions (5.8)]*.

Important Administration Instructions

Instruct patients how to properly take OXYCONTIN, including the following:

- OXYCONTIN is designed to work properly only if swallowed intact. Taking cut, broken, chewed, crushed, or dissolved OXYCONTIN tablets can result in a fatal overdose *[see Dosage and Administration (2.1)]*.
- OXYCONTIN tablets should be taken one tablet at a time *[see Dosage and Administration (2.1)]*.
- Do not pre-soak, lick, or otherwise wet the tablet prior to placing in the mouth *[see Dosage and Administration (2.1)]*.
- Take each tablet with enough water to ensure complete swallowing immediately after placing in the mouth *[see Dosage and Administration (2.1)]*.
- Do not discontinue OXYCONTIN without first discussing the need for a tapering regimen with the prescriber *[see Dosage and Administration (2.9)]*.

Hypotension

Inform patients that OXYCONTIN may cause orthostatic hypotension and syncope. Instruct patients how to recognize symptoms of low blood pressure and how to reduce the risk of serious consequences should hypotension occur (e.g., sit or lie down, carefully rise from a sitting or lying position) *[see Warnings and Precautions (5.9)]*.

Anaphylaxis

Inform patients that anaphylaxis has been reported with ingredients contained in OXYCONTIN. Advise patients how to recognize such a reaction and when to seek medical attention *[see Contraindications (4), Adverse Reactions (6)]*.

Pregnancy

Neonatal Opioid Withdrawal Syndrome

Inform female patients of reproductive potential that prolonged use of OXYCONTIN during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated *[see Warnings and Precautions (5.4), Use in Specific Populations (8.1)]*.

Embryo-Fetal Toxicity
Inform female patients of reproductive potential that OXYCONTIN can cause fetal harm and to inform their healthcare provider of a known or suspected pregnancy *[see Use in Specific Populations (8.1)]*.

Lactation:

Advise patients that breastfeeding is not recommended during treatment with OXYCONTIN *[see Use in Specific Populations (8.2)]*

Infertility

Inform patients that chronic use of opioids may cause reduced fertility. It is not known whether these effects on fertility are reversible *[see Use in Specific Populations (8.3)]*.

Driving or Operating Heavy Machinery

Inform patients that OXYCONTIN may impair the ability to perform potentially hazardous activities such as driving a car or operating heavy machinery. Advise patients not to perform such tasks until they know how they will react to the medication *[see Warnings and Precautions (5.15)]*.

Constipation

Advise patients of the potential for severe constipation, including management instructions and when to seek medical attention *[see Adverse Reactions (6)]*.

Disposal of Unused OXYCONTIN

Advise patients to flush the unused tablets down the toilet when OXYCONTIN is no longer needed.
Healthcare professionals can telephone Purdue Pharma's Medical Services Department (1-888-726-7535) for information on this product.

Purdue Pharma L.P.
Stamford, CT 06901-3431

U.S. Patent Numbers 6,488,963; 7,129,248; 8,309,060; 8,808,741; 8,821,929; 8,894,987; 8,894,988; 9,060,976; 9,073,933; 9,492,389, 9,492,391, 9,492,392, 9,492,393, and 9,522,919

Medication Guide
OXYCONTIN® (ox-e-KON-tin) (oxycodone hydrochloride) extended-release tablets, CII

OXYCONTIN is:

- A strong prescription pain medicine that contains an opioid (narcotic) that is used to manage pain severe enough to require daily around-the-clock, long-term treatment with an opioid, when other pain treatments such as non-opioid pain medicines or immediate-release opioid medicines do not treat your pain well enough or you cannot tolerate them.
- A long-acting (extended-release) opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death.
- Not for use to treat pain that is not around-the-clock.
- Not for use in children less than 11 years of age and who are not already using opioid pain medicines regularly to manage pain severe enough to require daily around-the-clock long-term treatment of pain with an opioid.

Important information about OXYCONTIN:

- **Get emergency help right away if you take too much OXYCONTIN (overdose).** When you first start taking OXYCONTIN, when your dose is changed, or if you take too much (overdose), serious or life-threatening breathing problems that can lead to death may occur.
- Taking **OXYCONTIN** with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, decreased awareness, breathing problems, coma, and death.
- Never give anyone else your OXYCONTIN. They could die from taking it. Store OXYCONTIN away from children and in a safe place to prevent stealing or abuse. Selling or giving away OXYCONTIN is against the law.

Do not take OXYCONTIN if you have:

- severe asthma, trouble breathing, or other lung problems.
- a bowel blockage or have narrowing of the stomach or intestines.

Before taking OXYCONTIN, tell your healthcare provider if you have a history of:

- head injury, seizures
- problems urinating
- liver, kidney, thyroid problems
- pancreas or gallbladder problems
- abuse of street or prescription drugs, alcohol addiction, or mental health problems.

Tell your healthcare provider if you are:

- **pregnant or planning to become pregnant.** Prolonged use of OXYCONTIN during pregnancy can cause withdrawal symptoms in your newborn baby that could be life-threatening if not recognized and treated.
- **breastfeeding.** Not recommended during treatment with OXYCONTIN. It may harm your baby.
- taking prescription or over-the-counter medicines, vitamins, or herbal supplements. Taking OXYCONTIN with certain other medicines can cause serious side effects that could lead to death.

When taking OXYCONTIN:

- Do not change your dose. Take OXYCONTIN exactly as prescribed by your healthcare provider. Use the lowest dose possible for the shortest time needed.
- Take your prescribed dose every 12 hours at the same time every day. Do not take more than your prescribed dose in 12 hours. If you miss a dose, take your next dose at your usual time.
- Swallow OXYCONTIN whole. Do not cut, break, chew, crush, dissolve, snort, or inject OXYCONTIN because this may cause you to overdose and die.
- OXYCONTIN should be taken 1 tablet at a time. Do not pre-soak, lick, or wet the tablet before placing in your mouth to avoid choking on the tablet.
- **Call your healthcare provider if the dose you are taking does not control your pain.**
- **Do not stop taking OXYCONTIN without talking to your healthcare provider.**
- After you stop taking OXYCONTIN, flush any unused tablets down the toilet.

While taking OXYCONTIN DO NOT:

- Drive or operate heavy machinery until you know how OXYCONTIN affects you. OXYCONTIN can make you sleepy, dizzy, or lightheaded.
- Drink alcohol, or use prescription or over-the-counter medicines that contain alcohol. Using products containing alcohol during treatment with OXYCONTIN may cause you to overdose and die.

The possible side effects of OXYCONTIN are:

- constipation, nausea, sleepiness, vomiting, tiredness, headache, dizziness, abdominal pain. Call your healthcare provider if you have any of these symptoms and they are severe.

Get emergency medical help if you have:

- trouble breathing, shortness of breath, fast heartbeat, chest pain, swelling of your face, tongue, or throat, extreme drowsiness, light-headedness when changing positions, feeling faint, agitation, high body temperature, trouble walking, stiff muscles, or mental changes such as confusion.

These are not all the possible side effects of OXYCONTIN. Call your doctor for medical advice about side effects.
You may report side effects to FDA at 1-800-FDA-1088. **For more information go to dailymed.nlm.nih.gov**

Manufactured by: Purdue Pharma L.P., Stamford, CT 06901-3431, **www.purduepharma.com or call 1-888-726-7535**

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 12/2016

OXYCONTIN® (II)
(OXYCODONE HCl) EXTENDED-RELEASE TABLETS

Exhibit C

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Building #51
Silver Spring, MD 20993

SEP 10 2013

Andrew Kolodny, MD
President, Physicians for Responsible Opioid Prescribing
920 48th Street, Suite 1510
Brooklyn, NY 11219

Re: Docket No. FDA-2012-P-0818

Dear Dr. Kolodny:

This letter responds to the citizen petition submitted by Physicians for Responsible Opioid Prescribing (PROP), which was received by FDA on July 26, 2012 (Petition). The Petition describes PROP's concerns about the safety and efficacy of opioid analgesic drugs for long-term use in chronic non-cancer pain, and requests that the Food and Drug Administration (FDA or Agency): (1) "[s]trike the term 'moderate' from the indication [of opioid analgesics] for non-cancer pain"; (2) "[a]dd a maximum daily dose, equivalent to 100 milligrams of morphine for non-cancer pain"; and (3) "[a]dd a maximum duration of 90-days for continuous [daily] use" for non-cancer pain (Petition at 2).[1]

FDA has carefully reviewed PROP's Petition and the numerous comments submitted to the public dockets[2] by government entities, medical societies, healthcare providers, patients, and other members of the public. For the reasons described in detail in this response, the Petition is granted in part and denied in part.

Today, on the basis of the information discussed below, FDA has notified application holders for extended-release/long-acting (ER/LA) opioid analgesics that, pursuant to section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C 355(o)(4)), important safety labeling changes are needed to the labeling of ER/LA opioid analgesics.[3] It is the agency's intent that these changes, which are described more fully below, will help more effectively communicate the serious risks of misuse, abuse, neonatal opioid withdrawal syndrome (NOWS), addiction, overdose, and death associated with the use of ER/LA opioids overall, and during pregnancy. FDA has also determined that more data are needed about the safety of long-term use of opioids. Pursuant to section 505(o)(3) of the FD&C Act, FDA is therefore requiring all new drug application (NDA) sponsors of ER/LA opioids to conduct postapproval studies and clinical trials

[1] The Petition requests pertain to analgesia products; therefore, this response is limited to opioids with indications for analgesia.

[2] FDA received comments on the PROP citizen petition in the above-captioned docket and comments relevant to the PROP citizen petition in the docket for a part 15 hearing the agency held in February 2013, titled Impact of Approved Drug Labeling on Chronic Opioid Therapy (Part 15 Hearing) (*see* Docket No. FDA-2012-N-1172).

[3] Pursuant to section 505(o)(4) of the FD&C Act, FDA is notifying holders of approved NDAs and holders of approved ANDAs that reference a NDA that is not currently marketed.

(post-marketing requirements, or PMRs) to assess certain known serious risks of ER/LA opioid use: misuse, abuse, hyperalgesia, addiction, overdose, and death.

I. BACKGROUND

A. Opioids

Opioids are a class of powerful pain-relieving agents that includes oxycodone, hydrocodone, and morphine, among others. When prescribed and used properly, opioids can effectively manage pain and alleviate suffering—clearly a public health priority.[4] Chronic pain is a serious and growing public health problem: it "affects millions of Americans; contributes greatly to national rates of morbidity, mortality, and disability; and is rising in prevalence."[5] There is also evidence that pain is inadequately treated in many patients.[6] However, pain is a self-reported symptom that is difficult to quantify, and its treatment is complex.

Opioids also have grave risks, the most well-known of which include addiction, overdose, and even death. The labeling for these products contains prominent warnings about these risks. Moreover, the boxed warning states that all patients should be "routinely monitor[ed]...for signs of misuse, abuse, and addiction." Even proper use of opioids under medical supervision can result in life-threatening respiratory depression, coma, and death (see Boxed Warning and Section 5.3 of Warnings in current labeling). Indeed, a Centers for Disease Control and Prevention (CDC) analysis published in February 2013 documents an 11th straight year of increases in drug overdose deaths, with opioids being involved in 75% of pharmaceutical overdose deaths, either alone or in combination with other drugs.[7]

Most opioid-only drugs are controlled under Schedule II of the Controlled Substances Act.[8] By law, prescriptions for Schedule II drugs cannot be refilled; patients need a new prescription to obtain the drug beyond the initial number of doses prescribed.[9] There are also strict recordkeeping, reporting, and physical security requirements. This level of

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[4] *See* "Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research." Committee on Advancing Pain Research, Care, and Education; Institute of Medicine. 2011:1-364 (available at http://www.nap.edu/catalog.php?record_id=13172).

[5] *Id.* at p. 5.

[6] *Id.* at p. 1.

[7] Jones CM, Mack, KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. JAMA 2013; 309(7): 657-9.

[8] *See* 21 U.S.C. 801 *et seq*; 21 CFR 1308.12. There are some opioids in Schedule III (*e.g.*, buprenorphine, *see* 21 CFR 1308.13(e)(2)(i)) and Schedule IV (*e.g.*, butorphanol and pentazocine, *see* 21 CFR 1308.14(f)). Tramadol, a synthetic opioid, is not currently scheduled under the Controlled Substances Act, *see* www.deadiversion.usdoj.gov/drug_chem_info/tramadol.pdf.

[9] Although opioid drug labeling does not recommend a limit on the number of doses a patient should receive, the Schedule II status of most opioid drugs imposes certain restrictions on their availability. 21 CFR 1306.12(a). However, prescribers "may issue multiple prescriptions authorizing the patient to receive a total of up to a 90-day supply of a Schedule II controlled substance" as long as certain conditions are met. 21 CFR 1306.12(b)(1).

control reflects a finding that most opioid drugs have "high potential for abuse" and that "[a]buse of the drug . . . may lead to severe psychological or physical dependence."[10]

Opioid drugs have been approved for different conditions of use based on the data and information submitted by the sponsor of each drug product. Accordingly, product labeling may vary among approved opioid drugs, and such drugs may be prescribed to different patient populations.[11] The approved indications for ER/LA opioid analgesics are uniform, however. These drugs are currently indicated "for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time."[12] The current labeling for these drugs also contains a prominent statement that they are **not** for use:

- As an as-needed (prn) analgesic,
- For pain that is mild or not expected to persist for an extended period of time,
- For acute pain,
- In the immediate postoperative period, or
- For postoperative pain, unless the patient is already receiving chronic opioid therapy prior to surgery, or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time.[13]

The labeling for some ER/LA opioid analgesics also states that they are for use (or for use at higher doses) only in opioid-tolerant patients.[14]

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[10] 21 U.S.C. 812(b)(2).

[11] For example, indications for which particular IR opioid products have been approved include "the management of acute and chronic moderate to severe pain where the use of an opioid analgesic is appropriate" (Oxecta (oxycodone hydrochloride) labeling, available at www.accessdata.fda.gov/drugsatfda_docs/label/2013/202080s001lbl.pdf); "the relief of mild to moderately severe pain where the use of an opioid analgesic is appropriate" (Codeine sulfate (NDA 022402) labeling, available at www.accessdata.fda.gov/drugsatfda_docs/label/2013/022402s006lbl.pdf); and "the management of pain in patients where an opioid analgesic is appropriate" (Dilaudid (hydromorphone hydrochloride) labeling, available at www.accessdata.fda.gov/drugsatfda_docs/label/2007/019892s015lbl.pdf).

[12] OxyContin (oxycodone hydrochloride) extended-release tablets (NDA 022272) labeling, available at www.accessdata.fda.gov/drugsatfda_docs/label/2013/022272Orig1s014lbl.pdf.

[13] Labeling for OxyContin (oxycodone hydrochloride) extended-release tablets (NDA 022272), available at www.accessdata.fda.gov/drugsatfda_docs/label/2013/022272Orig1s014lbl.pdf (internal references omitted).

[14] *See, e.g.,* labeling for Exalgo (hydromorphone hydrochloride) (NDA 021217) and Duragesic (fentanyl) (NDA 019813). Further, certain opioid drugs also have limitations of use on the higher doses, with labeling stating that higher doses are for opioid-tolerant patients only. *See, e.g.,* labeling for Avinza (morphine sulfate) extended-release capsules (NDA 021260), available at www.accessdata.fda.gov/drugsatfda_docs/label/2013/021260s017lbl.pdf and OxyContin (oxycodone hydrochloride) extended-release tablets (NDA 022272), available at www.accessdata.fda.gov/drugsatfda_docs/label/2013/022272Orig1s014lbl.pdf.

B. ER/LA Opioid Analgesic Risk Evaluation and Mitigation Strategy

FDA approved a shared-system Risk Evaluation and Mitigation Strategy (REMS) for ER/LA opioid analgesics on July 9, 2012 (ER/LA Opioid Analgesic REMS).[15] The goal of the ER/LA Opioid Analgesic REMS is to "reduce serious adverse outcomes resulting from inappropriate prescribing, misuse, and abuse of [ER/LA opioids] while maintaining patient access to pain medications."[16] Under the REMS, "[a]dverse outcomes of concern include addiction, unintentional overdose, and death."[17] The REMS is currently limited to ER/LA opioid products because FDA has concluded that there are disproportionate safety concerns associated with these products compared to immediate-release (IR) opioids.[18]

Currently, more than 30 products are subject to the ER/LA Opioid Analgesic REMS.[19] The ER/LA Opioid Analgesic REMS contains requirements for distribution of a Medication Guide with each prescription filled, as well as a requirement that training be made available to all those who prescribe ER/LA opioids. Prescriber education training is considered ER/LA Opioid Analgesic REMS-compliant if, among other things, it includes the elements described in the "FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics" (FDA Blueprint).[20] The FDA Blueprint provides guidance to prescribers to enable appropriate ER/LA opioid prescribing practices, as well as information prescribers can use in counseling patients about the risks and benefits of ER/LA opioid use.

C. Public Input

FDA has received a considerable amount of input from stakeholders and other commenters on issues pertaining to the benefits and risks of opioid use. For example, FDA participated in a two-day workshop in May 2012 hosted at the National Institutes of Health (NIH), called, "Assessment of Analgesic Treatment of Chronic Pain: A Scientific Workshop."[21] Several stakeholders and other members of the public gave presentations

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[15] *See* www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf (most recently modified in April, 2013).

[16] *Id.* at p. 2.

[17] *Id.*

[18] *See* http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm309742.htm#Q5; *see also, e.g.*, Dormitzer, C. Opioid Abuse and Misuse: Data from the National Survey on Drug Use and Health and the Drug Abuse Warning Network. Joint Meeting of the Anesthetic and Life Support Drugs Advisory Committee (ALSDAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM). UMUC Inn and Conference Center by Marriott, Adelphi, MD, July 22-23, 2010 (available at http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndAnalgesicDrugProductsAdvisoryCommittee/UCM220950.pdf) (providing data showing growing harm associated with ER/LA opioids).

[19] The list of drugs required to have a REMS, grouped by application holder, may be found at www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM348818.pdf.

[20] Available at http://www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/ucm277916.pdf.

[21] *See* Docket No. FDA-2012-N-0067; *see also* http://www.fda.gov/Drugs/NewsEvents/ucm283979.htm.

about issues relating to opioid treatment of chronic pain, and additional comments and subsequent input were posted to the public docket for that meeting.[22]

On February 7 and 8, 2013, FDA held a public hearing on chronic use of opioid drug products, titled, "Impact of Approved Drug Labeling on Chronic Opioid Therapy" (Part 15 Hearing).[23] FDA requested information, particularly scientific evidence, on issues pertaining to the use of opioid drugs in the treatment of chronic pain, including diagnosis and understanding of pain, understanding and adhering to the labeling of pain-treating products, and limiting opioid prescriptions and use.[24] The Agency received input from dozens of presenters, including patients, individuals who had lost loved ones due to opioids, clinicians, public health experts, professional associations, academicians, and others, including PROP. FDA also received over 600 comments to the Part 15 Hearing docket. The majority were from patients voicing concerns that labeling changes could make legitimate patient access to opioid analgesics more difficult.[25] The remainder reflected the same diversity of viewpoints and concerns presented during the hearing itself.

FDA also received more than 1900 comments on the PROP Petition. Many public health agencies and organizations supported the requests in the Petition, citing concerns about increased opioid use and abuse.[26] However, the majority of comments opposed PROP's requests. Many professional societies (*e.g.*, the American Academy of Pain Medicine, the American Medical Association, the American Society of Anesthesiologists, the American Pain Society) did not support the Petition and stated that the data cited by PROP did not support PROP's requests (particularly those requests for limits on dose and duration of use of opioids). Professional societies also expressed concern that the labeling changes requested by PROP were not supported by scientific evidence, and that a "one-size-fits-all" approach to a maximum dose or duration of treatment would be problematic and inconsistent with the need for individualized treatment and the variability among patient responses to opioids.[27]

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[22] *See* Docket No. FDA-2012-N-0067.

[23] *See* Docket No. FDA-2012-N-1172.

[24] *See* www.gpo.gov/fdsys/pkg/FR-2012-12-19/pdf/2012-30516.pdf.

[25] However, for privacy reasons, many comments from individual patients are not publicly available on www.regulations.gov. They nevertheless are considered to be included in the public docket.

[26] *See, e.g.*, comments from the New York City Department of Health and Mental Hygiene (Docket No. FDA-2012-P-0818-0785); County of Los Angeles Public Health (Docket No. FDA-2012-P-0818-0336); Denver Public Health (Docket No. FDA-2012-P-0818-0677); and the National Center on Addiction and Substance Abuse at Columbia University (Docket No. FDA-2012-P-0818-0691).

[27] *See, e.g.*, comments from the American Academy of Pain Medicine (Docket No. FDA-2012-P-0818-0165); the American Medical Association (Docket No. FDA-2012-P-0818-0783); the American Society of Anesthesiologists (Docket No. FDA-2012-P-0818-0246); the American Pain Society (Docket No. FDA-2012-P-0818-0187); the American Academy of Physical Medicine and Rehabilitation (Docket No. FDA-2012-P-0818-0658); the American Society of Regional Analgesia and Pain Medicine (Docket No. FDA-2012-P-0818-0276); the Texas Pain Society (Docket No. FDA-2012-P-0818-0331); and the Florida Academy of Pain Medicine (Docket No. FDA-2012-P-0818-0333). Some commenters submitted critiques of PROP's cited studies that identified the studies' limitations. *See, e.g.*, comments from the American Academy of Pain Medicine (Docket No. FDA-2012-P-0818-0165). For example, the Florida Academy of Pain Medicine states, "it appears that the petitioners are asking for changes to the indications for long-term

II. SAFETY LABELING CHANGES

After evaluating stakeholder and commenter input regarding opioid labeling, and based on FDA's review of relevant literature, FDA has determined that safety labeling changes to the labeling of ER/LA opioid analgesics are needed to more effectively communicate to prescribers the serious risks associated with these drugs, and to more clearly describe the population in whom these drugs should be used in light of these serious risks—thus encouraging better prescribing, monitoring, and patient counseling practices involving these drugs. FDA is therefore exercising its authority under section 505(o)(4) of the FD&C Act to notify application holders that modifications to ER/LA opioid analgesic labeling are needed.[28] It is the agency's intent that these changes will help reduce inappropriate prescribing[29] and help curb the increase in misuse, abuse, NOWS, addiction, overdose, and death associated with ER/LA opioid analgesic use.

These safety labeling changes apply only to ER/LA opioid analgesics, and, at present, FDA is not requesting or requiring that any labeling changes be made to IR opioids or opioid/non-opioid combination products (which include both an IR opioid and a non-opioid analgesic).[30] Much of the literature FDA reviewed assessed opioid use from all opioid sources, or did not necessarily separate data according to opioid formulation (*i.e.*, ER/LA versus IR or opioid/non-opioid combinations). However, FDA recognizes that ER/LA opioids, as a class of drugs, have disproportionate safety concerns compared to IR opioids or opioid/non-opioid combination products; indeed, the recognition of

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high-dose opioid therapy (LTHDOT) for non-cancer pain, based on a small number of studies with significant methodological shortcomings and findings that are not conclusive. In short, they are basing their request for label changes on the same kind of evidence they themselves, criticize as being insufficient to support the safety and efficacy of LTHDOT for non-cancer pain" (Docket No. FDA-2012-P-0818-0333).

[28] Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amended the FD&C Act, as codified in section 505(o)(4) of the FD&C Act, to authorize FDA to require holders of approved drug applications to make safety labeling changes (SLCs) if the agency becomes aware of "new safety information" that FDA determines should be included in the labeling of the drug. *New safety information* is information derived from a clinical trial, an adverse event report, a post-approval study (including a study under section 505(o)(3) of the FD&C Act), or peer-reviewed biomedical literature; data derived from the post-market risk identification and analysis system under section 505(k) of the FD&C Act; or other scientific data deemed appropriate by the Agency about, among other things, a serious or an unexpected serious risk associated with use of the drug of which the Agency has become aware (that may be based on a new analysis of existing information) since the drug was approved, the REMS was approved, or since the last assessment of the approved REMS; or the effectiveness of the approved REMS for the drug obtained since the last assessment of such strategy. *See* section 505-1(b)(3) of the FD&C Act.

[29] Pain patients in the United States receive care from prescribers with different backgrounds and levels of experience and expertise in treating pain. IMS Health, Vector One®: National (VONA). Data Extracted September 2012. Weblink: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM337148.pdf. For example, some prescribers may not understand how to identify patients at risk for addiction, how to identify behaviors associated with misuse and abuse, and how to manage patients who are receiving opioids for chronic pain so as to reduce the risks of misuse, abuse, NOWS, addiction, overdose and death.

[30] Therefore, the agency denies PROP's Petition insofar as it requests labeling changes for IR opioids, or opioid/non-opioid combination products.

disproportionate safety concerns for ER/LA opioids informed FDA's decision to require the ER/LA Opioid Analgesic REMS. For example, data show that the risk for misuse and abuse is greater for ER/LA opioids.[31] Because they are intended to release the drug over a longer period of time, many ER/LA opioids contain higher doses of opioids compared to IR opioids or opioid/non-opioid combinations. This increases the risk of a fatal outcome in the event of an overdose, and may make ER/LA opioids more desirable in the eyes of opioid abusers and addicts. Furthermore, ER/LA opioids are often used in a chronic pain setting. Thus, in light of the risks posed by ER/LA opioids, and the totality of available data on both ER/LA opioids specifically and opioid drugs in general, the Agency has decided to make ER/LA opioid analgesics its current focus.

First, FDA is requiring changes to the boxed warning for ER/LA opioid analgesics to give greater emphasis and prominence to the risks of misuse, abuse, NOWS, addiction, overdose, and death. For example, the first sentence of the new boxed warning provides that ER/LA opioids "expose patients and other users to the risks of opioid addiction, abuse, and misuse which can lead to overdose and death." The new boxed warning also urges prescribers to "assess each patient's risk" before prescribing, and to "monitor all patients regularly for the development of these behaviors or conditions."

Second, FDA is requiring changes to the Indications and Usage section of the labeling. As noted above, ER/LA opioid analgesics currently are "indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time."[32] The Agency has concluded that use of terminology predicated only on a categorical "severity scale" (e.g., mild, moderate, severe) to characterize the intensity of pain for which ER/LA opioids are indicated does not sufficiently focus prescribers' attention on their responsibility to make an individualized assessment of patient needs in light of the serious risks of ER/LA opioids. Given these serious risks, especially those of overdose and death, the Agency believes that clarity as to the appropriate use of such drugs is of the utmost importance. The new language clearly communicates to prescribers that ER/LA opioid analgesics should be used only when alternative treatments are inadequate because of the serious risks of these drugs. The new language also identifies specific examples of alternative treatment options, namely, "non-opioid analgesics or immediate-release opioids," and provides additional guidance on when such treatments may be deemed inadequate to provide sufficient management of pain.

Furthermore, the new labeling language underscores that patients in pain should be assessed not only by their rating on a categorical pain intensity scale, but also based on a

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[31] Dormitzer, C. Opioid Abuse and Misuse: Data from the National Survey on Drug Use and Health and the Drug Abuse Warning Network. Joint Meeting of the Anesthetic and Life Support Drugs Advisory Committee (ALSDAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM). UMUC Inn and Conference Center by Marriott, Adelphi, MD, July 22-23, 2010 (available at http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndAnalgesicDrugProductsAdvisoryCommittee/UCM220950.pdf).

[32] *See, e.g.*, OxyContin (oxycodone hydrochloride) extended-release tablets (NDA 022272) labeling, available at www.accessdata.fda.gov/drugsatfda_docs/label/2013/022272Orig1s014lbl.pdf.

more thoughtful determination that their pain — however it may be defined — is *severe enough* to require daily, around-the-clock, long-term opioid treatment, *and* for which alternative treatment options are inadequate. This framework better enables prescribers to make decisions based on a patient's individual needs, given the serious risks associated with ER/LA opioids, against a backdrop of alternatives such as IR opioids and non-opioid analgesics. It allows prescribers to make an assessment of pain relative to a patient's ability to perform daily activities or enjoy a reasonable quality of life, not only on where a patient's pain falls on an intensity scale, and assess if ER/LA opioids are needed after determining whether (a) the pain is severe enough to require daily, around-the-clock, long-term opioid treatment, and (b) if alternatives to ER/LA opioids are inadequate to manage such pain, in light of the serious risks associated with ER/LA opioid analgesics.

The revised indication language reads as follows:

> **"[Tradename] is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.**
>
> **<u>Limitations of Use</u>**
> **• Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve [Tradename] for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.**
> **• [Tradename] is not indicated as an as-needed (prn) analgesic."**

This new language is intended to prompt prescribers to more closely assess each individual patient's condition, and carefully evaluate whether alternative treatment options such as non-opioid analgesics or IR opioids are appropriate. The new language is intended to reflect that ER/LA opioid analgesics should be prescribed only when the prescriber determines that such alternatives are ineffective, not tolerated, or would otherwise be inadequate.

Third, FDA is notifying application holders of the need for changes to the Dosage and Administration, Warnings and Precautions, Drug Interactions, and Use in Specific Populations sections of ER/LA opioid analgesic labeling. These changes are specifically intended to urge prescribers to weigh carefully whether the benefits of an ER/LA opioid outweigh its serious risks on a patient-by-patient basis. If an ER/LA opioid analgesic is prescribed, the labeling changes emphasize that prescribers should monitor patients carefully for signs of abuse and addiction. FDA is also notifying application holders of the need for changes to the Patient Counseling Information and the product-specific Medication Guides to improve the communication of risks to patients.[33] The Agency

[33] Following the approval of the safety labeling changes, a REMS modification will be required to incorporate the approved safety labeling changes into the REMS materials, as applicable.

believes that the changes will improve communication of serious risks associated with the use of these products and help improve the safe use of ER/LA opioid analgesics overall.

FDA intends these changes to enable not only a more careful and thorough approach to determining whether ER/LA opioid analgesics should be prescribed for a particular patient, but also allows prescribers to better assess whether the serious risks associated with ER/LA opioids, including the risks of misuse, abuse, addiction, overdose and death associated with ER/LA formulations, are offset by the benefits ER/LA opioids may provide in managing pain for an individual patient.

Accordingly, PROP's request that FDA remove the term "moderate" from the indication for ER/LA opioid analgesic drugs is granted for the reasons explained above. As explained above, the changes to the labeling also reflect a departure from an indication based solely on a severity scale, and transitions to an indication that facilitates careful prescribing decisions based on an individualized assessment of a patient's situation (*i.e.*, whether an individual's pain is severe enough to require daily, around-the-clock, long-term opioid treatment) and a heightened recognition that, because of the serious risks associated with the use of these drugs, ER/LA opioids should be used only when alternative treatment options are inadequate.[34]

All of PROP's labeling change requests are limited to "non-cancer" pain, a distinction that is not made in current ER/LA opioid analgesic labeling. It is FDA's view that a patient without cancer, like a patient with cancer, may suffer from chronic pain, and PROP has not provided scientific support for why labeling should recommend different treatment for such patients. In addition, FDA knows of no physiological or pharmacological basis upon which to differentiate the treatment of chronic pain in a cancer setting or patient from the treatment of chronic pain in the absence of cancer, and comments to the Petition docket reflect similar concerns.[35] FDA therefore declines to make a distinction between cancer and non-cancer chronic pain in opioid labeling.[36]

In accordance with section 505(o)(4) of the FD&C Act, the ER/LA opioid analgesic application holders are required to submit by October 10, 2013, a supplement proposing changes to the approved labeling to reflect the new safety information, or else notify the Agency that they do not believe labeling changes are warranted and submit a statement detailing the reasons why changes are not warranted.[37]

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[34] When other analgesics are contraindicated or ineffective, restricting the indication of opioid drugs to treatment of severe pain only could leave some patients with chronic pain with an impaired ability to carry out daily activities, resulting in a diminished quality of life. *See* National Pharmaceutical Council (2001): Pain: Current Understanding of Assessment, Management, and Treatments, http://www.npcnow.org/App_Themes/Public/pdf/Issues/pub_related_research/pub_quality_care/Pain-Current-Understanding-of-Assessment-Management-and-Treatments.pdf.

[35] *See, e.g.*, comments from National Hospice and Palliative Care Organization (Docket No. FDA-2012-P-0678); Purdue Pharma (Docket No. FDA-2012-P-0818-0707).

[36] FDA notes that some epidemiology studies make distinctions between cancer and non cancer pain. However, while such classifications may be standard in epidemiological research, FDA believes that they are not relevant to ER/LA opioid labeling.

[37] *See* section 505(o)(4)(B) of the FD&C Act.

If the ER/LA opioid application holders do not submit the requested safety labeling changes, or if FDA disagrees with alternative language that the companies propose, the FD&C Act provides timelines under section 505(o)(4) for discussions regarding the labeling changes.[38] At the conclusion of these discussions, section 505(o)(4)(E) authorizes FDA to issue an order directing labeling changes as appropriate.

III. POSTAPPROVAL SAFETY STUDIES AND CLINICAL TRIALS

ER/LA opioid drugs generally have been approved in part based on randomized, controlled clinical trials that lasted for a 12-week period. This is due, in part, to the fact that for chronic pain, it can be difficult to ensure subject participation in controlled trials beyond 12 weeks. Many commenters, including PROP, have voiced increasing concern about the lack of controlled clinical trial data evaluating opioid use longer than 12-weeks. FDA is not aware of adequate and well-controlled[39] studies of opioid use longer than 12 weeks.[40]

FDA has evaluated concerns pertaining to the serious risks of misuse, abuse, hyperalgesia,[41] addiction, overdose, and death associated with opioid use. The Agency acknowledges that the available data demonstrate an association—though not necessarily a causal relationship—between opioid dose and certain serious risks of opioid use. However, FDA also agrees that more data are needed regarding the relationship between opioid dose and adverse effects, and the relationship between opioid duration of use and adverse effects, before the Agency can determine whether additional action needs to be taken. More data are also needed on the point at which the risks of opioid use at escalating doses and longer durations of treatment may outweigh the benefits of opioid analgesic therapy.

Thus, FDA is exercising its authority under section 505(o)(3)(A) through (B) of the FD&C Act to require ER/LA opioid drug sponsors to conduct PMRs to assess the known serious risks of misuse, abuse, hyperalgesia, addiction, overdose, and death associated with the long-term use of opioid analgesics. FDA has established milestone dates for

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[38] *See* section 505(o)(4)(D) of the FD&C Act.

[39] In this setting, "well-controlled studies" exclude active-controlled trials because they lack assay sensitivity, and failure to detect a statistically significant difference is difficult to interpret—either both drugs had the desired effect or both drugs did not have the desired effect.

[40] There are numerous uncontrolled studies that have evaluated patients on opioids for as long as a year; although some patients drop out of the studies over this period of time, many remain on opioid therapy, which may suggest that they continue to experience benefits that would warrant the risks of opioid use.

[41] Hyperalgesia is a known serious risk associated with chronic opioid analgesic therapy in which the patient becomes more sensitive to certain painful stimuli over time. *See, e.g.*, Varney SM, Bebarta VS. Opioid-induced hyperalgesia--worsening pain in opioid-dependent patients . Am J Emerg Med. 2013 Feb;31(2):458.e5-6; Angst MS, Clark JD Opioid-induced Hyperalgesia A Qualitative Systematic Review. Anesthesiology 2006; 104:570–87. It also may lead to increased use of opioid analgesics. *See, e.g.*, Chapman CR, Davis J, Donaldson GW, Naylor J, Winchester D. Postoperative pain trajectories in chronic pain patients undergoing surgery: the effects of chronic opioid pharmacotherapy on acute pain. J Pain 2011;12:1240-6.

completion of these studies and clinical trials, and is encouraging ER/LA opioid application holders to work together on these studies and clinical trials to provide the best information possible. First, the sponsors will have the opportunity to discuss with the Agency the particulars of the design and conduct of these PMRs.[42] We expect that this process will be completed in time for sponsors to submit final protocols to FDA within one year (*i.e.*, no later than August 2014). Sponsors must periodically report on the status of the studies and clinical trials.[43] The milestones for completion vary by study, with some expected to be completed as early as August 2015 and others expected to be completed in 2018.

As with the safety labeling changes, FDA is requiring PMRs only of ER/LA opioid analgesic application holders. While a majority of the literature that FDA reviewed did not distinguish between opioid formulation and/or composition, such as ER/LA versus IR opioids, or single ingredient opioids versus opioid/non-opioid combination products, FDA has made the determination that PMRs should be required of ER/LA opioid analgesic application holders to assess the known serious risks of misuse, abuse, hyperalgesia, addiction, overdose and death. FDA is taking this approach for the same reasons the Agency has decided to require safety labeling changes for ER/LA opioid analgesics: as discussed in greater detail in section II, above, FDA recognizes that ER/LA opioids, as a class of drugs, have disproportionate safety concerns compared to IR opioids or opioid/non-opioid combination products[44] and because ER/LA opioids are often used in a chronic pain setting. Thus, in light of the serious risks of ER/LA opioids, and the totality of available data, the Agency has decided to make ER/LA opioid analgesics its current focus for requiring PMRs.

IV. REQUESTS FOR MAXIMUM DOSE AND DURATION OF USE

The Agency declines to specify or recommend a maximum daily dose or duration of use for any opioid at this time, for the reason described below. However, FDA has determined that PMRs are necessary to assess the known, serious risks of misuse, abuse, hyperalgesia, addiction, overdose, and death. These studies will address, among other things, the effect of dose and duration of opioid use on these serious risks.

A. Maximum Daily Dose

PROP requests that FDA "add a maximum daily dose" of the equivalent of 100 milligrams (mg) of morphine (100 mg morphine equivalent dose (MED)) to opioids

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[42] *See* Guidance for Industry, *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act* (April 2011) at 12.

[43] Section 505(o)(3)(iii) of the FD&C Act.

[44] *See, e.g.*, Dormitzer, C. Opioid Abuse and Misuse: Data from the National Survey on Drug Use and Health and the Drug Abuse Warning Network. Joint Meeting of the Anesthetic and Life Support Drugs Advisory Committee (ALSDAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM). UMUC Inn and Conference Center by Marriott, Adelphi, MD, July 22-23, 2010 (available at http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndAnalgesicDrugProductsAdvisoryCommittee/UCM220950.pdf).

(Petition at 2). In support of PROP's request, the Petition asserts that high-dose chronic opioid therapy is associated with increased risk of overdose death,[45] increased risk of emergency room visits,[46] and increased risk of fractures in the elderly,[47] (Petition at 2). PROP also maintains that "three large observational studies published in 2010 and 2011 found dose-related overdose risk" in patients on chronic opioid therapy (Petition at 2).

FDA agrees that adverse events and substance abuse of opioids occur at high doses—but adverse events can also occur at doses less than 100 mg MED. FDA also acknowledges that the available data do suggest a relationship between increasing opioid dose and risk of certain adverse events. However, the available information does not demonstrate that the relationship is necessarily a causal one. FDA has reviewed the studies cited in support of PROP's request, as well as studies cited in comments to the Petition docket and other studies described in the literature. For the reasons discussed in further detail below, the scientific literature does not support establishing a maximum recommended daily dose of 100 mg MED. Further, creating a maximum dose of 100 mg MED, or another dose ceiling, could imply a superior opioid safety profile under that set threshold, when there are no data to support such a conclusion. The Agency therefore denies PROP's request that opioid labeling specify a maximum daily dose.

1. Cited Data Do Not Define a Relationship between Opioid Dose and Risk of Fractures in the Elderly

FDA agrees that the Saunders study[48] PROP cites suggests a positive trend between opioid dose and fractures in the elderly. However, the elderly population is at risk for falls and fractures in general, and has more co-morbidities and more rapid fluctuations in health status than the overall adult population. The Saunders study did not take into account any co-morbidities in the elderly patients that arose after the initial patient visit when pain was diagnosed and an opioid was prescribed and the absence of that information may have confounded the results. Without additional data and a replication of the study's apparent finding, it would be premature to conclude that the risks of high-dose opioids outweigh their benefits in this population. Additionally, the highest dose-level in the Saunders study[40] was >50 mg MED, therefore, it did not directly address the 100 mg MED cutoff.

2. Cited Data Do Not Define a Relationship between Opioid Dose and Emergency Room Visits

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[45] *See* Gomes T, Mamdani MM, Dhalla IA, *et al.*, Opioid dose and drug-related mortality in patients with nonmalignant pain. Arch Intern Med, 2011; 171: 686-91.

[46] *See* Braden JB, Russo J, Fan MY, *et al.* Emergency department visits among recipients of chronic opioid therapy. Arch Intern Med 201 0; 170:1425-32.

[47] *See* Saunders KW, Dunn KM, Merrill JO, *et al.*, Relationship of opioid use and dosage levels to fractures in older chronic pain patients. J Gen Intern Med, 2010;25:310-5.

[48] Saunders KW, Dunn KM, Merrill JO, *et al.*, Relationship of opioid use and dosage levels to fractures in older chronic pain patients. J Gen Intern Med, 2010;25:310-5.

FDA does not agree with PROP's contention that the Braden study[49] demonstrated a clear dose-response relationship between high dose opioid therapy and emergency room visits for recipients of chronic opioid therapy for non-cancer pain. Braden *et al.* examined the association between opioid dose and emergency room visits in two populations: a national, commercially insured population and a state-based publicly insured population. The study categorized opioid dose according to 3 levels: (1) 0 MED to the median MED of the population at issue[50] (Category 1); (2) the median MED of the given population to 120 mg MED/day (Category 2); and (3) >120 mg MED/day (Category 3). When compared to Category 1 patients, Category 2 and Category 3 patients appeared to have an increased risk of emergency room visits—but only in one study population. Furthermore, Category 3 patients did not appear to have a greater risk of emergency room visits than Category 2 patients in that study population. Taken together, the findings of this study were inconclusive with respect to the relationship between opioid dose and emergency room visits. Furthermore, FDA is concerned that this study did not fully adjust for important factors that may confound the association between opioid dose and health services use, such as race and income.[51] FDA therefore concludes that the Braden study does not support PROP's request to limit the maximum daily dose of opioids.

3. *Cited Data Do Not Define a Relationship between Opioid Dose and Death*

PROP cites three observational studies (by Dunn, *et al.*,[52] Bohnert, *et al.*,[53] and Gomes, *et al*[54]) to support that higher doses of opioids are associated with higher risks of overdose-related death. Although these studies have several important limitations,[55] FDA agrees

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[49] Braden JB, Russo J, Fan MY, *et al.*, Emergency department visits among recipients of chronic opioid therapy. Arch Intern Med, 2010; 170:1425-32.

[50] Note that the mean MED was different in the two study populations.

[51] Examples of other potential confounders include past health service use, alcohol use, or numbers of total medications used concurrently with opioids. *See* Braden JB, Russo J, Fan MY, *et al.*, Emergency department visits among recipients of chronic opioid therapy. Arch Intern Med, 2010; 170:1425-32.

[52] Dunn KM, Saunders KW, Rutter CM, *et al.*, Opioid prescriptions for chronic pain and overdose: a cohort study. Annals of Internal Medicine, 2010; 152:85-92.

[53] Bohnert AS, Valenstein M, Bair MJ, et al., Association between opioid prescribing patterns and opioid overdose-related deaths. JAMA, 2011; 305:1315-21.

[54] Gomes T, Mamdani MM, Dhalla IA, et al., Opioid dose and drug-related mortality in patients with nonmalignant pain. Arch Intern Med, 2011; 171: 686-91.

[55] For example, the Dunn and Gomes studies did not discuss the reason the patients had been prescribed opioid therapy. It is possible that the patients' underlying illnesses (or the severity thereof) may have increased the risk of death or other adverse events—and without additional information, FDA cannot evaluate PROP's assumption that these adverse events can be attributed to opioid use alone. None of the three studies—Dunn, Bohnert, or Gomes—examined the role of the opioid's formulation (e.g., IR vs. ER/LA opioids) in their analyses, and it is possible that different formulations may have differing impacts on overdose-related outcomes. In addition, none of the three studies included data about what doses the patients actually took (as opposed to the doses they were prescribed), or data about whether the patients complied with the instructions they received about proper opioid use. Indeed, in the Bohnert study, almost half of the decedent population experienced an unintentional opioid-related death when the maximum prescribed dose was equal to 0 mg per day—which raises questions not only about the amount of opioids

that these studies appear to credibly suggest a positive association between high-dose opioid use and the risk of overdose and/or overdose mortality. Indeed, these studies appear to demonstrate a statistically significantly higher risk of overdose death among those taking opioid doses of >100 mg MED compared to those taking opioid doses of 1-19 mg MED.

Unfortunately, the point at which the risk of overdose-related death increases enough to change the benefit-risk assessment of the studied opioids cannot be determined from these studies. Determining such a threshold would require a better understanding of how risk of overdose and/or overdose mortality changes along the continuum of opioid dose (from 0 mg through the highest doses taken by patients). This dose-response (*i.e.* overdose and/or overdose mortality) relationship should be analyzed treating opioid use as a continuous variable or using categories defined by small increments (*e.g.*, 1 mg MED, or per 5 mg MED). Thus, even though the aforementioned studies demonstrated a statistically significantly higher risk of overdose death for patients taking the highest studied doses compared with patients taking the lowest studied doses, the threshold for an increased risk associated with these drugs could actually be considerably lower or higher than a maximum daily dose of 100 mg MED.

B. Maximum Duration of Treatment

The PROP Petition requests that FDA "[a]dd a maximum duration of 90 days for continuous (daily) use" (Petition at 2). In support of this request, the Petition alleges that "[l]ong-term safety and effectiveness of managing [pain] with opioids has not been established." After a review of the literature cited in the Petition, and an assessment of other relevant information discussed below, FDA has determined that limiting the duration of use for opioid therapy to 90 days is not supportable. Thus, the Agency denies this request.

1. Treatment Guidelines

In support of its request, PROP cites to the American Pain Society-American Academy of Pain Medicine Opioids Guidelines. However, these guidelines state that chronic opioid therapy can be an effective therapy for carefully selected and monitored patients.[56] The guidelines recommend individualized care, management plans, and monitoring—not a maximum duration of treatment.[57] For example, they note that "proper patient selection is critical," requiring "a comprehensive benefit-to-harm evaluation that weighs the

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the patients actually took, but also the possibility that other causes of death may have mistakenly been assessed as opioid-related. Furthermore, the Dunn study described only 6 deaths in its discussion of 51 overdose-related outcomes, and it did not differentiate between deaths and other overdose outcomes in its analysis. Thus, it is less informative on the question of an association between opioid dose and death.

[56] *See* Chou R, Fanciullo GJ, Fine PG, *et al.*, American Pain Society- American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic non-cancer pain. J Pain, 2009; 10:113-130.

[57] *See generally id.*

potential positive effects of opioids on pain and function against potential risks."[58] The guidelines also strongly recommend that "[o]pioid selection, initial dosing, and titration . . . be individualized according to the patient's health status, previous exposure to opioids, attainment of therapeutic goals, and predicted or observed harms."[59] The decision whether to proceed with opioid therapy, according to the guidelines, "should be intentional and based on careful consideration of outcomes" of the initial course of opioid treatment, which should be treated as a "short-term, therapeutic trial lasting from several weeks to several months."[60]

These guidelines are consistent with the new indication for ER/LA opioids: a focus on treatment decisions that include a thorough patient-specific assessment of the appropriateness of ER/LA opioids for that patient, and that reflect careful thought by prescribers and patients alike.

2. Cited Data on Persistence of Chronic Pain and Long-Term Opioid Use Are Inconclusive

PROP cites surveys by Sullivan, *et al.*[61] and Eriksen, *et al.*[62] to support its assertion that "[r]ecent surveys of [chronic non-cancer pain] patients receiving [chronic opioid therapy] have shown that many continue to experience significant chronic pain and dysfunction" (Petition at 2). The Eriksen survey supports this assertion but is insufficient to conclude that chronic opioid therapy causes or contributes to chronic pain and dysfunction, or that it is ineffective in treating chronic pain and dysfunction. Although the survey found that the pain severity reported at the time of the survey was higher among respondents who were using opioids than those who were not using opioids, there was no assessment of pain severity prior to the time of the survey. Thus, patients who were using opioids could have suffered from higher levels of pain pre-survey than those who were not using opioids. Pain *improvement* was not measured.

The Sullivan survey found that patients with chronic non-cancer pain treated with chronic opioid therapy reported being in pain 162 of the past 180 days (90% of days), and 92% of that sample reported pain on at least 90 days. These data suggest that patients on chronic opioid therapy experienced significant chronic pain, and that they continued to experience pain throughout their therapy. However, the study did not survey similar patients who did *not* receive opioid treatment. Without such a comparison group, it is unclear what the patients' pain trajectory would have been had they not been on chronic opioid therapy. Thus, this survey does not address the question of whether chronic non-cancer pain patients fare better or worse on chronic opioid therapy.

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[58] *Id.* at 115.

[59] *Id.* at 117.

[60] *Id.*

[61] Sullivan MD, Von KM, Banta-Green C, Merrill JO, Saunders K. Problems and concerns of patients receiving chronic opioid therapy for chronic non-cancer pain. Pain 2010;149(2):345-353.

[62] Eriksen J, Sjogren P, Bruera E, Ekholm O, Rasmussen NK. Critical issues on opioids in chronic non-cancer pain: an epidemiological study. Pain 2006;125(1-2):172-179.

3. *Cited Data on Long-term Opioid Use and Addiction Do Not Establish a Threshold for Maximum Duration of Use*

PROP's Petition contends that opioids should be given a maximum duration of use based in part on a study of "[a] large sample of medical and pharmacy claims records[, which] found that two-thirds of patients who took opioids on a daily basis for 90 days were still taking opioids five years later" (Petition at 2).

FDA disagrees with this statement.[63] Although the study follow-up lasted roughly 5 years, not all patients who were started on chronic opioid therapy were followed for that duration. Approximately half of the study population was followed two years or less (the median follow-up time was around 2 years). Throughout the course of the study period, some patients were censored due to death, disenrollment from health coverage, or other reasons. Patients who were censored may have had a different duration of therapy than those who continued to be followed. In FDA's view, the study showed that, among patients who were followed for 4.8 years, two-thirds were still taking opioids at the end of this period.

FDA also does not agree that these data necessarily reflect a safety concern specific to longer term use. Although some portion of these results certainly could be explained by adverse outcomes (*e.g.*, addiction in opioid therapy patients), other factors may also be associated with low discontinuation rates (*e.g.*, certain intractable or recalcitrant pain conditions that may require longer treatment periods). The referenced study did not collect data on why patients continued or discontinued opioid therapy, and without this information, it would be premature to restrict opioid use to a 90-day maximum duration treatment period.

The Petition also asserts that "[r]ecent surveys using [Diagnostic and Statistical Manual of Mental Disorders] DSM criteria found high rates of addiction in [chronic non-cancer pain] patients receiving [chronic opioid therapy]" (Petition at 2). FDA agrees with this assertion.[64] However, the cited surveys did not suggest that chronic opioid therapy causes addiction, or vice versa. Both addiction and chronic opioid therapy were measured at one point in time, so it is unknown which happened first: addiction or chronic opioid therapy.

The cited literature does not identify a duration threshold beyond which the risk of addiction outweighs the benefits of opioid treatment. PROP has selected a 90-day limit, but provides no evidence that addiction (however it is defined) increases significantly after 90 days of use such that it would support a labeling change. Nevertheless, the high

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[63] *See* Martin BC, Fan MY, Edlund MJ, DeVries A, Braden JB, Sullivan MD. Long-term chronic opioid therapy discontinuation rates from the TROUP study. J Gen Intern Med 2011;26(12):1450-1457.

[64] However, the recently published Diagnostic and Statistical Manual of Mental Disorders – V (DSM V) combines the substance abuse and substance dependence categories into a single disorder measured on a continuum, to try to avoid an inappropriate linking of "addiction" with "physical dependence," which are distinct issues. *See* American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fifth Edition. Washington, DC: American Psychiatric Association, 2013.

rates of addiction shown in the cited literature are concerning enough to require further exploration in postapproval studies.

4. Cited Data Are Insufficient to Explain Association between Opioid Use and Mental Health Co-Morbidities

The Petition asserts that "[p]atients with mental health and substance abuse co-morbidities are more likely to receive [chronic opioid therapy] than patients who lack these risk factors, a phenomenon referred to as adverse selection." In support of this assertion, PROP cites to a study by Edlund *et al.*,[65] which examined trends in opioid prescribing among individuals with non-cancer pain, with and without mental health and substances disorders.

Although the Edlund study supports the association between current mental health and substance abuse co-morbidities and current use of chronic opioid therapy, FDA is unable to determine the reasons for this association in a cross-sectional analysis. This study only depicts the frequencies and prevalence of chronic opioid therapy in different sub-populations at one point in time, and the temporal relationship between mental health and substance abuse comorbidities and opioid therapy cannot be established. Thus, it is difficult to form any conclusions based on this study regarding the relationship between mental health/substance abuse disorders and the initiation, dose and duration of chronic opioid therapy. In sum, FDA agrees with the study's authors that the cited study does not conclude that the association between opioid use and mental/substance use disorder is due to any one specific factor.[66]

FDA acknowledges that patients with these co-morbid conditions may be at higher risk of adverse outcomes—possibly because they may be more likely to be treated with other psychoactive drugs. The results of the Edlund study thus underscore the need for prescribers to evaluate carefully whether and under what circumstances to prescribe opioids (particularly in high doses) to patients with these co-morbidities.[67] However, the findings of the Edlund study do not support PROP's argument that opioid labeling should include a maximum daily dose or a maximum duration of use.

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[65] Edlund MJ, Fan MY, DeVries A, Braden JB, Martin BC, Sullivan MD. Trends in use of opioids for chronic non-cancer pain among individuals with mental health and substance use disorders: the TROUP Study. Clin J Pain 2010;26:1-8.

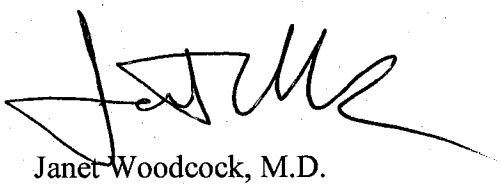
[66] The authors state that they "cannot definitively state why NCPC enrollees with MH [mental health]/SUDs [substances use disorders] were more likely to receive opioids than NCPC [non-cancer pain conditions] enrollees without MH/SUDs, and to receive them chronically[...]." *Id.* at 6.

[67] For example, section 5.1 of ER/LA opioid analgesic labeling, as provided for in the safety labeling change notification letters referred to above, contains the following language: "Risks are increased in patients with a personal or family history of substance abuse (including drug or alcohol addiction or abuse) or mental illness (e.g., major depression). The potential for these risks should not, however, prevent the prescribing of [Tradename] for the proper management of pain in any given patient. Patients at increased risk may be prescribed modified-release opioid formulations such as [Tradename], but use in such patients necessitates intensive counseling about the risks and proper use of [Tradename] along with intensive monitoring for signs of addiction, abuse, and misuse."

V. CONCLUSION

For the reasons stated above, the Petition is granted in part and denied in part.

Sincerely,



Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research

Exhibit D

The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health
250 Washington Street, Boston, MA 02108-4619

CHARLES D. BAKER
Governor

KARYN E. POLITO
Lieutenant Governor

MARYLOU SUDDERS
Secretary

MONICA BHAREL, MD, MPH
Commissioner

Tel: 617-624-6000
www.mass.gov/dph

September 15, 2016

Steven T. James
House Clerk
State House Room 145
Boston, MA 02133

William F. Welch
Senate Clerk
State House Room 335
Boston, MA 02133

Dear Mr. Clerk,

The Massachusetts Department of Public Health (DPH) is pleased to submit the attached initial report on the opioid overdose study authorized by Chapter 55 of the Acts of 2015.

The current opioid epidemic affecting our Commonwealth's communities has taken a record number of lives in each of the last four years. Opioid Use Disorder is a complex chronic disease, and this opioid epidemic is a complex and persistent problem that will not be solved through a single solution. Analytic work is ongoing, and much is yet to be learned from this effort, however, the findings of this initial report can immediately inform our collective work with new insight into overdose-related deaths and the relative risks faced by different populations.

I would like to acknowledge that this work has required a significant collaborative effort from many government agencies. To this end, we are truly grateful to the many partners which have assisted DPH in this work so far. This effort highlights government's ability to work collaboratively towards efficiently solving complex and urgent problems. With the effort of legal, technical, and analytical teams across seven state agencies (Department of Public Health, EOHHS IT, the Office of the Chief Medical Examiner, the Department of Correction, MassHealth, the Center for Health Information and Analysis, and MassIT), Massachusetts has

been able to develop a novel data model that allows for simultaneous analysis of 10 datasets with information relevant to opioid deaths. The goodwill of all parties has been a hallmark of this ongoing work.

I would also like to express my appreciation for the continued opportunity the Legislature has provided the Department of Public Health. The analytic approach authorized by Chapter 55 has enabled Massachusetts to serve as a national example for the possibilities of public health's ability to leverage data warehousing to respond to pressing policy and health concerns by allowing existing data to be leveraged in new and innovative ways to support policy development and decision making, and to allocate resources more efficiently and effectively. To this end, other states have already engaged the Department in discussions about the technical aspects of this project, and I hope that this will serve as a model for how complex problems can be tackled in the future.

Let me once again express how grateful I am for the Legislature's commitment to better understanding the root causes of this opioid epidemic by allowing us to continue this important work. I look forward to continuing to share the results of our analyses, and to our continued partnership in addressing this opioid epidemic.

Sincerely,

Monica Bharel, MD, MPH
Commissioner
Department of Public Health

Charles D. Baker
Governor

Karyn Polito
Lieutenant Governor

Marylou Sudders
Secretary

Monica Bharel, MD, MPH
Commissioner

An Assessment of Opioid-Related Deaths in Massachusetts (2013 – 2014)

September 2016

Massachusetts Department of Public Health

Table of Contents

Legislative Mandate

The following report is hereby issued pursuant to Chapter 55 of the Acts of 2015, as amended by Chapter 133 of the Acts of 2016 as follows:

Notwithstanding any general or special law to the contrary, the secretary of health and human services, in collaboration with the department of public health, shall conduct or provide for an examination of the prescribing and treatment history, including court-ordered treatment or treatment within the criminal justice system, of persons in the commonwealth who suffered fatal or nonfatal opiate overdoses in calendar years 2013 to 2015, inclusive. Any report or supplemental reports resulting from this examination shall provide any data in an aggregate and de-identified format.

Notwithstanding any general or special law to the contrary, to facilitate the examination, the department shall request, and the relevant offices and agencies shall provide, information necessary to complete the examination from the division of medical assistance, the executive office of public safety and security, the center for health information and analysis, the office of patient protection and the chief justice of the trial court, which may include, but shall not be limited to: data from the prescription drug monitoring program; the all-payer claims database; the criminal offender record information database; and the court activity record information. To the extent feasible, the department shall request data from the Massachusetts Sheriffs Association, Inc. relating to treatment within houses of correction.

Not later than 1 year from the effective date of this act, the secretary of health and human services shall publish a report on the findings of the examination including, but not limited to: (i) instances of multiple provider episodes, meaning a single patient having access to opiate prescriptions from more than 1 provider; (ii) instances of poly-substance access, meaning a patient having simultaneous prescriptions for an opiate and a benzodiazepine or for an opiate and another drug which may enhance the effects or the risks of drug abuse or overdose; (iii) the overall opiate prescription history of the individuals, including whether the individuals had access to legal prescriptions for opiate drugs at the time of their deaths; (iv) whether the individuals had previously undergone voluntary or involuntary treatment for substance addiction or behavioral health; (v) whether the individuals had attempted to enter but were denied access to treatment for substance addiction or behavioral health; (vi) whether the individuals had received past treatment for a substance overdose; (vii) whether any individuals had been previously detained or incarcerated and, if so, whether the individuals had received treatment during the detention or incarceration.

The report shall be filed with the clerks of the senate and house of representatives, the house and senate chairs of the joint committee on mental health and substance abuse, the joint committee on public health, the joint committee on health care financing and the house and senate committees on ways and means. The secretary of health and human services may publish supplemental reports on the trends identified through its examination; provided, however, that any supplemental report shall be filed not later than July 1, 2017 and shall be filed with the clerks of the senate and house of representatives, the house and senate chairs of the joint committee on mental health and substance abuse, the joint

committee on public health, the joint committee on health care financing and the house and senate committees on ways and means.

Notwithstanding any general or special law to the contrary, the executive office of health and human services may contract with a non-profit or educational entity to conduct data analytics on the data set generated in the examination, provided that the executive office shall implement appropriate privacy safeguards.

Executive Summary

Background

Since 2000, opioid-related deaths have increased in Massachusetts by 350%. The recent rate of increase is several times faster than anything seen before[1] with every community in Massachusetts impacted by the current opioid epidemic. However, beneath this statewide impact, data indicates that some areas of the Commonwealth have been disproportionately impacted by this opioid epidemic. In particular, southeastern Massachusetts and Essex County have been inordinately affected. Just as communities are differentially impacted by the current opioid epidemic, population groups are also differently burdened. Opioid-related death rates are highest among younger males – a fact that is similar in all states.[2] Opioid-related death rates are also higher among those who have recently been released from Massachusetts prisons, those who have obtained opioid prescriptions from multiple pharmacies, and those who have obtained prescription opioids in combination with other scheduled medications.

As part of a multi-faceted effort to address this unprecedented public health crisis, Chapter 55 of the Acts of 2015 (Chapter 55) was passed by the Massachusetts Legislature and signed into law by Governor Charles D. Baker in August 2015. This new law permits the linkage and analysis of existing data across state government in order to better guide policy development and programmatic decision-making to successfully tackle the current opioid epidemic. Chapter 55 articulates seven questions to be addressed in this initial report. Detailed responses to each question can be found in Appendix A. In addition, Chapter 55 permits examinations beyond these seven questions, providing the Department of Public Health (DPH) an opportunity to build an even more comprehensive picture of the current opioid crisis. To this end, DPH has connected ten datasets managed by five state agencies to build a data warehouse structure – a concept viewed by national experts as the future of successful public health.

While this initial report includes the first findings from the cross-agency analyses of these ten datasets, analytic work is ongoing, and much is yet to be learned from this nationally-leading effort. Contained within this report are descriptions of four specific analyses that directly respond to questions posed by Chapter 55, providing the state with important new insights into the profile of overdose-related deaths and the relative risks faced by the Commonwealth's diverse populations. The importance of these findings has prompted the Department to issue initial recommendations to inform policy and response efforts across the state and region.

Key Findings

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[1] Accessed at http://www.mass.gov/eohhs/docs/dph/quality/drugcontrol/county-level-pmp/data-brief-overdose-deaths-may-2016.pdf

[2] Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2014 on CDC WONDER Online Database, released 2015. Data are from the Multiple Cause of Death Files, 1999-2014, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed at http://wonder.cdc.gov/mcd-icd10.html .

Prescription Drugs Fuel This Epidemic, but Illegally-Obtained Substances More Closely Linked to Overdose Deaths: Using these data, it was determined that illegally-obtained substances are much more frequently present in post-mortem toxicology than prescription drugs (i.e., a Schedule II-III opioids, or benzodiazepines). While prescription drug use can result in addiction and may increase the long-term risk of death, illegal drugs appear more likely to be the direct cause of death. As a result, increasing the availability of harm reduction strategies and interventions that target Heroin, Fentanyl, and polysubstance use (especially opioid use concurrent with benzodiazepine and/or Cocaine use) could significantly reduce the opioid-related death rate.

Medication Assisted Treatment Reduces the Risk of Fatal Opioid Overdose: Another key finding from these data is that receiving evidence-based opioid agonist treatment following a nonfatal overdose was associated with a reduced risk of a subsequent fatal opioid overdose. This suggests that overdose survivors have a short window of opportunity after a nonfatal overdose to reduce their risk of death by undergoing an evidence-based medication-assisted treatment (MAT). A comprehensive plan for delivering evidence-based MAT, such as buprenorphine or methadone treatment, to treat opioid use disorder for those with high overdose risk could significantly lower the death rate. This report only includes data for state-funded opioid agonist treatment (i.e. Buprenorphine or Methadone). Work is ongoing to examine risk reductions associated with additional MATs including naltrexone.[3]

Women are More Likely than Men to Experience a Fatal Overdose Due to Prescription Opioid Use: While men were found to be significantly more likely to die from any opioid-related overdose, the results of this study indicate that women are more likely than men to die of a prescription opioid-related overdose. Women were more likely than men to both obtain Schedule II-III opioids and to have Schedule II-III opioids present in post-mortem toxicology following an opioid-related overdose death. While legally- and illegally-obtained opioids pose a risk for men and women alike, prescribers and pharmacists should be educated to utilize the Prescription Drug Monitoring Database (PDMP) through the Massachusetts Prescription Awareness Tool (MassPAT) in order to identify any active or past prescriptions for their patients and to provide coordinated care and overdose risk reduction.

Individuals Who Have Recently Been Released from Massachusetts Prisons are 56 Times as Likely to Die from an Opioid Related Overdose: Those who have recently been released from Massachusetts prisons have a short-term risk of death from opioid overdose that is greater than 50 times the risk for the general public. 25% of Massachusetts prison inmates received treatment during their incarceration, and there was not a notable reduction in risk of fatal overdose in those that received treatment. To further reduce the opioid-related death rate, additional focus should be paid to those being released from Massachusetts prisons, and treatment opportunities should be standardized regardless of setting.

[3] Naltrexone, also known as Vivitrol, is a Schedule VI drug. As such, it is not captured in the PDMP. In future work, All Payer Claims Database (APCD) data will be used to assess the potential risk reduction associated with Vivitrol use.

Key Findings	Recommendations
FINDING 1 – Individuals who died from opioid-related overdoses are much more likely to have an illegally-obtained substance (i.e., not Schedule II-III opioid) present in post-mortem toxicology	Harm reduction strategies and other interventions that address Heroin, Fentanyl, and polysubstance use should be increased, expanded, and enhanced.
FINDING 2 – Following nonfatal overdoses, people on opioid agonist treatment (i.e., medications that block the effect of opioids like Methadone and buprenorphine) are significantly less likely to die	Strategies for making medications for opioid use disorders more accessible to individuals who experience a nonfatal opioid overdose should be prioritized.
FINDING 3 – Women are significantly more likely than men to receive opioids from 3 or more prescribers and obtain them from 3 or more pharmacies.	MassPAT should be leveraged by prescribers and pharmacists as a decision support tool to inform clinical decision-making. Also, prescribers and pharmacists should be educated about their own personal biases.
FINDING 4 – The risk of opioid overdose death following incarceration is 56 times higher than for the general public.	MAT and overdose prevention services should be expanded in correctional facilities, and access to post-incarceration medical care and substance use prevention and treatment should be put in place prior to release.

Importantly, in addition to providing insight into the current opioid epidemic, this effort also marks the beginning of how government, academia, the health care system, and private industry can and should collaborate to ask and answer complex questions. DPH is no longer asked to simply track the incidence of disease. Instead, public health policymakers, analysts, and researchers are faced with more complex questions than ever before. Increasingly, state leadership, stakeholders, and the public are calling upon DPH to assess the effectiveness of its policies and programming and to adjust accordingly. The Department's ability to engage academic partners and private industry to support surveillance and evaluation activities will be crucial, and collaborative, data-driven efforts such as this should become standard practice in Massachusetts and beyond.

To this end, a virtual Data Warehouse – a virtual platform that links, stores, and allows for the analysis of datasets from multiple sources – should continue to be developed and expanded. Similarly to how successful businesses leverage big data to identify market opportunities, evaluate initiatives, and inform their operational and strategic decisions, a virtual Data Warehouse can serve as a business intelligence tool that would enable DPH to more efficiently and effectively target its resources, and to more precisely evaluate its programming. Furthermore, DPH will be able to support researchers and industry by being able to quickly provide these partners with information and analyses from multiple public and private data systems. Information from vital records (e.g. birth and death records), insurance

claims data, public health programs, research and educational institutions, hospitals, and other clinical partners can be aligned and examined to provide DPH, academics, and industry with answers to critical questions about health outcomes, program effectiveness, and health care costs. These and other examples – all fueled by data warehousing technology – represent public health of tomorrow.

Introduction

Addiction is a complex chronic disease characterized by compulsive alcohol/drug use and/or behaviors, cravings, and continued use despite harmful consequences. Nearly one in ten Americans over the age of 12 are classified as having a substance use disorder.[3] Among brain disorders, addiction incurs greater economic costs than Alzheimer's disease, stroke, Parkinson's disease, or head and neck injury. Addiction is also the most costly neuropsychiatric disorder.[4] According to the National Institute on Drug Abuse,[5,6] the overall cost of substance abuse in the United States exceeds half a trillion dollars, including health- and crime-related expenses, as well as losses in productivity. While the term addiction includes alcohol and drug abuse, this report focuses on opioid addiction and its impact on premature death in Massachusetts.

The consequences of addiction extend far beyond just cost. Specifically, addiction harms individuals, as well as their families, friends, and communities. Addiction to substances, like opioids, also put people at risk for the development of health problems, including life-threatening infections such as HIV and hepatitis, cirrhosis, cognitive decline, overdose, unplanned pregnancy, family disintegration, domestic violence, criminal behavior, child abuse, and death.[7]

Massachusetts is particularly affected by opioids and opioid addiction. As in other states, the 1990s and 2000s were marked with substantial increases in prescribing of opioids for acute and chronic pain. This increased access to prescription opioids has been followed by increased availability of Heroin. According to a 2013 Drug Enforcement Administration (DEA) report, the reported availability of Heroin has increased significantly from 2007 to 2013 in New England.[8] A decade ago, the most prevalent substance reported to the Bureau of Substance Abuse Services (BSAS) at the time of admission for addiction treatment in Massachusetts was alcohol. In 2015, the most prevalent reported drugs were opioids. The percentage of BSAS admissions that were opioid-related increased from 31% in 2000 to 55% in 2014.[9] The Health Policy Commission has reported similar substantial increases over the same time period for Massachusetts emergency department visits and hospitalizations. [10,11]

Center for Behavioral Health Statistics and Quality. (2015). Behavioral health trends in the United States: Results from the 2014 Nat
ional Survey on Drug Use and Health (HHS Publication No. SMA 15-4927, NSDUH Series H-50). Retrieved from http://www.samhsa.gov/ data/
rugabuse.gov/publications/drugfacts/workplace --- resources

[6] Accessed at https://www.nlm.nih.gov/medlineplus/magazine/issues/spring07/articles/spring07pg14-17.html) .

[7] American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders: **DSM**-**5**. Washington, D.C: American Psychiatric Association.

[8] Accessed at http://www.dea.gov/resource-center/DIR-017-13%20NDTA%20Summary%20final.pdf, pg. 7

[9] This includes both Heroin and other opioids.

[10] Accessed at https://www.bostonglobe.com/metro/2016/03/27/massachusetts-hospital-visits-for-opioid-abuse-soar/GGRehpwvyhY5OEea1bWO2J/story.htm

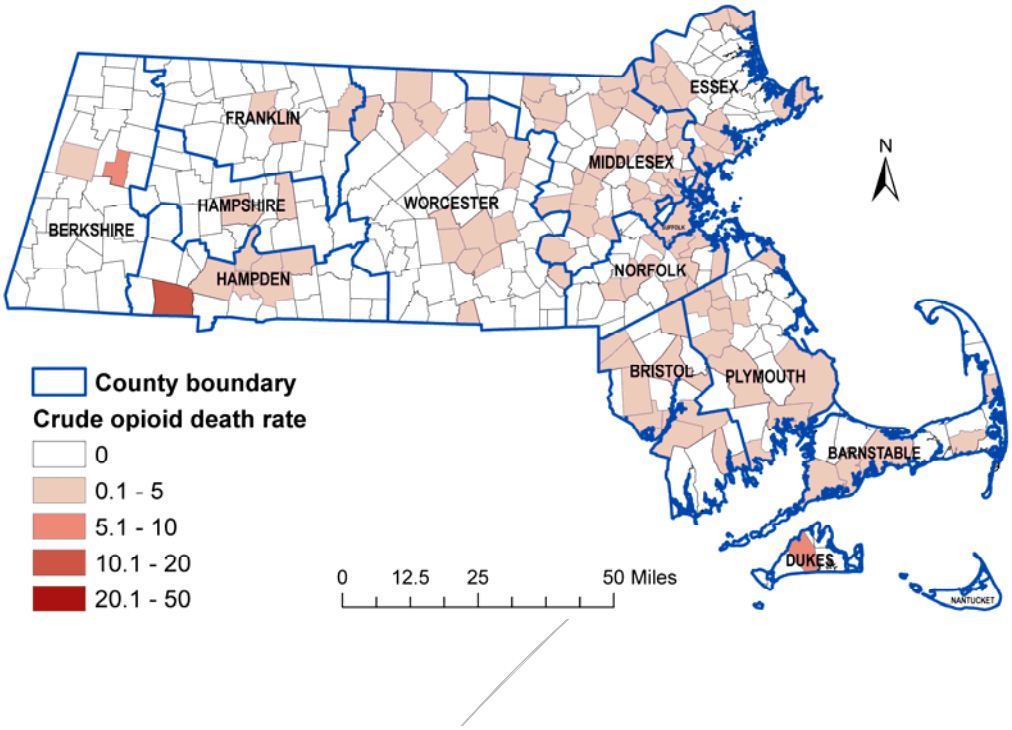
[11] Accessed at: http://www.bchumanservices.net/library/2016/04/Health-Policy-Commission-3-23-16-Opioid-Prelim.-Data-Presentation.pdf

Nationally, and in Massachusetts, there has been a dramatic increase in fatal and nonfatal opioid overdoses since 2000.[12] In May 2016, DPH reported that there were at least 1,379 confirmed opioid-related deaths in Massachusetts during 2015.[13] In comparison, there were one-quarter as many confirmed opioid-related deaths (338) in the year 2000. In 2013-2014, opioid-related deaths occurred in two-thirds of the communities in Massachusetts. While the opioid crisis has impacted every community in Massachusetts in some fashion (e.g., deaths, nonfatal overdoses, or disruptions to marriages, families, and neighborhoods), there are clearly areas that have been hit harder than others. The contrast between the community-level map from 2000 and from 2013-2014 (Figure INTR.1) clearly shows the increase in the number of communities with opioid-related deaths over a span of 15 years. Annual figures for confirmed and estimated cases can be found in Figure INTR.2. The number of confirmed unintentional opioid overdose deaths for 2015 (n=1531) represents an 18% increase over 2014 (n=1294), and the 2014 number (n=1294) represents a 41% increase over cases for 2013 (n=918). In order to obtain timelier estimates of the total number of opioid overdose deaths in Massachusetts - confirmed and probable - DPH used predictive modeling techniques for all cases not yet finalized by the Office of the Chief Medical Examiner (OCME).

[12] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/stop-addiction/current-statistics.html
[13] This report includes confirmed fatal Opioid-overdoses from 2014 – 2015 (n=2,192)

Figure INTR.1: Opioid deaths in Massachusetts 2000 and 2013 – 2014

Annual Opioid-Related Death Rate by Municipality (2000)
(per 10,000 Adults Age 18 to 64)



Annual Opioid-Related Death Rate by Municipality (2013-2014)
(per 10,000 Adults Age 18 to 64)

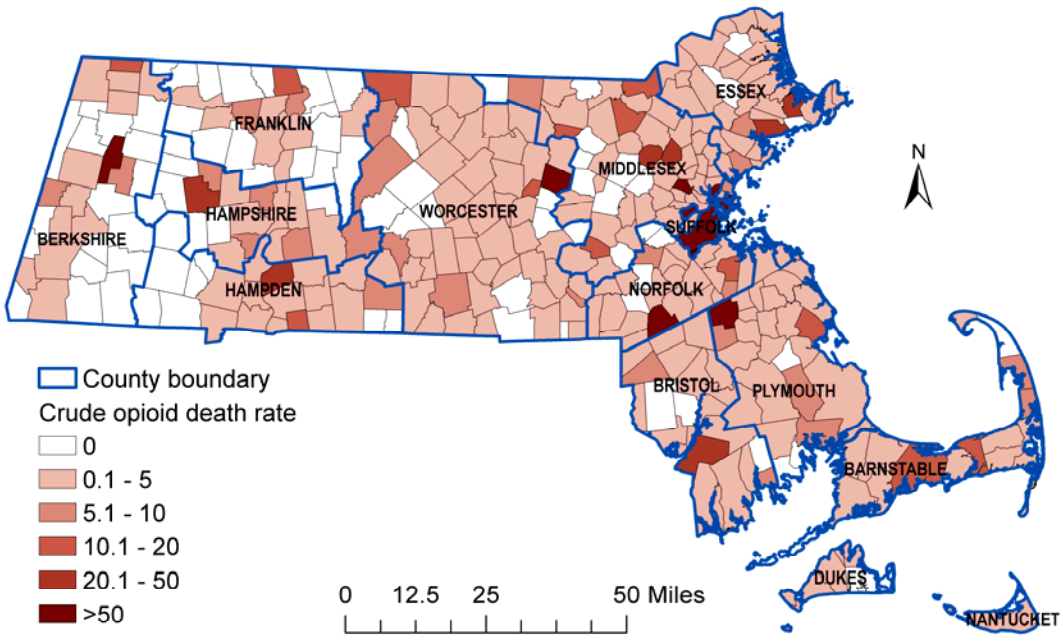
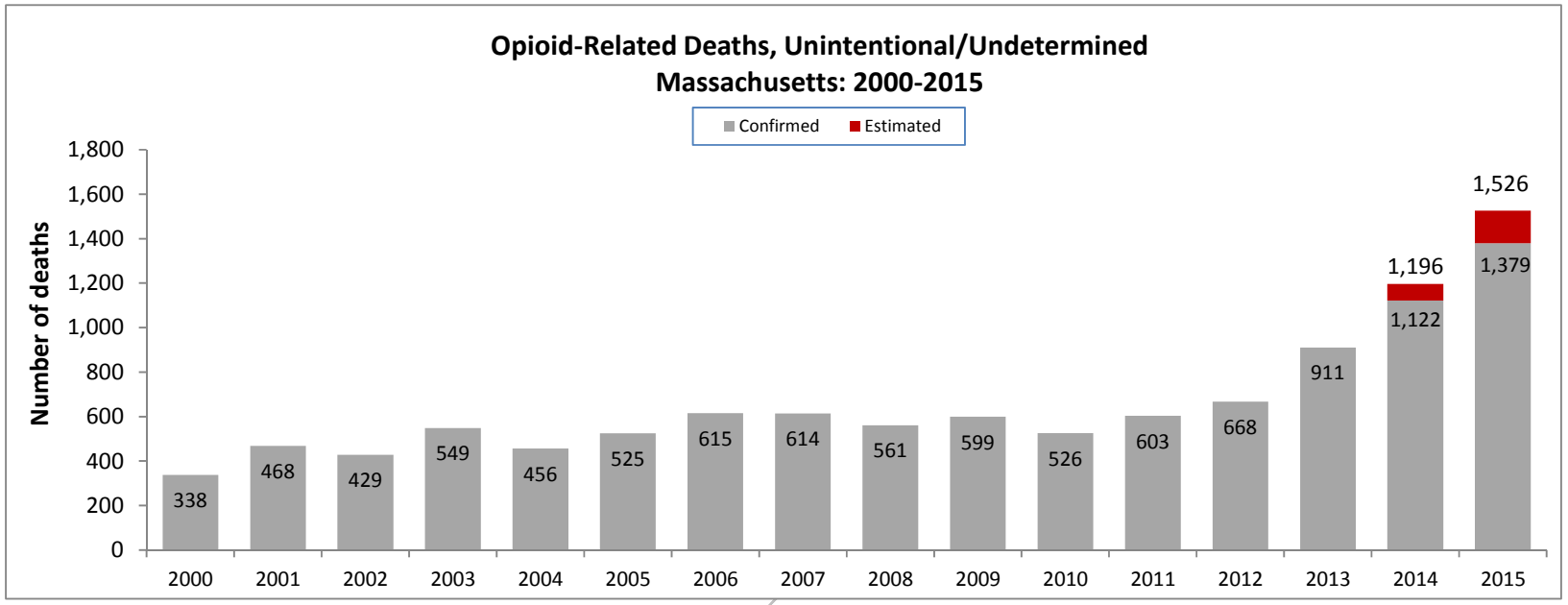


Figure INTR.2: Confirmed and estimated opioid deaths in Massachusetts between 2000 and 2015



Note: Counts for 2000 – 2013 are complete as of the date that the state's statistical file was closed. Each year, a small number of cases receive a cause of death after the file is closed.

Unintentional poisoning/overdose deaths combine unintentional and undetermined intents to account for a change in death coding that occurred in 2005. Suicides are excluded from this analysis.

Opioids include Heroin, opioid-based prescription painkillers, and other unspecified opioids.

Cases were defined using the International Classification of Disease (ICD-10) codes for mortality. The following codes were selected from the underlying cause of death field to identify poisonings/overdoses: X40-X49, Y10-Y19. All multiple cause of death fields were then used to identify an opioid-related death: T40.0, T40.1, T40.2, T40.3, T40.4, and T40.6.

This report tracks all opioid-related overdoses due to difficulties in reporting Heroin-associated overdoses separately. Many deaths related to Heroin are not specifically coded as such due to the fast metabolism of Heroin into morphine.

To maintain consistency with NCHS reporting, the ICD-10 code F11.1 is not included, which may include opioid-related overdose death.

Just as communities are differentially affected by the opioid crisis, population groups are also affected differentially. While death rates have increased for virtually every population group, the rates are highest among younger males – a fact that is similar in all states.[14] In 2013-2014, 76% of opioid overdose deaths occurred in people under the age of 50. Furthermore, men of age 18 to 34 had opioid-related death rates nearly three times higher than women of the same age. For additional detail, see Table INTR.1.

Table INTR.1: Massachusetts Opioid Annual Death Rate (2013-2014 average)

	Female			Male			
Age group	**Number of opioid death**	**Percent opioid death among all deaths**	**Death Rate (10,000)**	**Number of opioid death**	**Percent opioid death among all deaths**	**Death Rate (10,000)**	**Male to Female Rate Ratio**
18-24	49	28.5%	0.71	145	25.6%	2.12	2.98
25-34	158	32.4%	1.79	493	40.6%	5.72	3.20
35-49	253	14.5%	1.80	566	19.4%	4.22	2.34
50-64	178	3.0%	1.29	313	3.4%	2.44	1.89
65+	20	0.04%	0.18	15	0.04%	0.19	1.03
Total	658	1.2%	1.21	1532	3.1%	3.09	2.56

Potentially masked by familiar trends are other embedded trends about age and gender that this unique collection of data has allowed us to examine. Those trends are reported in subsequent sections of this report.

As stated above, opioid-related deaths began increasing very sharply in 2012.[15] While this report will not make causal statements about this increase, it will compare and contrast related trends within the same period. Two such trends are cited here. First, the number of opioids prescribed to residents of Massachusetts increased roughly 7% per year since 2000.[16] There was, however, no sharp increase in prescribed opioids beginning in 2012. In contrast, recent toxicology data suggest that the increased

[14] Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2014 on CDC WONDER Online Database, released 2015. Data are from the Multiple Cause of Death Files, 1999-2014, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed at http://wonder.cdc.gov/mcd-icd10.html .

[15] Accessed at http://www.mass.gov/eohhs/docs/dph/quality/drugcontrol/county-level-pmp/data-brief-overdose-deaths-may-2016.pdf

[16] Unpublished data from analysis of Massachusetts death records between 2000 and 2015 managed by the Registry of Vital Records and Statistics adjusted for population growth.

presence of Fentanyl in post-mortem cases roughly matches the increase in opioid-related deaths. Fentanyl is a powerful opioid that can be prescribed for pain management, but it can also be illicitly obtained either on its own, or mixed with Heroin.[17,18] Fentanyl, produced and sold illicitly as part of the Heroin supply, has become increasingly incorporated into Heroin supplies throughout the United States, but particularly in Massachusetts.[19,20] Toxicology data from post-mortem cases indicates that Fentanyl was present in blood, urine, and tissue samples in increasing numbers from 2013 through 2015. In 2015, 57% of toxicology samples tested positive for Fentanyl while the number was less than half that in 2013.[21]

These findings hint at underlying causes to the increasing opioid-related death rate, but more complex analyses are required to more firmly establish the links between numerous factors that might play important roles. The Chapter 55 effort has brought together a unique collection of datasets to gain a deeper understanding of the factors driving the crisis. To our knowledge, no state has captured as much data in one place to examine what is a national crisis. Four initial, cutting edge analyses are reported in the sections that follow. Further analysis is underway. While these findings are important, it is equally important to acknowledge that the sharp increase in opioid-related deaths has also motivated stakeholders across the Commonwealth to collaborate in an effort to better understand the risk factors that contribute to the increase in deaths, and how to collectively identify public health strategies to help reduce opioid-related death rates moving forward.

Key Takeaways

- The number of opioid-related deaths has increased 350% in 15 years
- The rate of opioid-related overdose deaths has risen sharply since 2011
- Solutions will require collaboration across stakeholders
- Analyzing linked datasets is the best way to understand the factors underlying the crisis

[17] Accessed at: https://www.dea.gov/divisions/hq/2016/hq061016.shtml
[18] Accessed at: http://www.cdc.gov/drugoverdose/opioids/fentanyl.html
[19] For more information: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm
[20] The CDC alert can be found at: http://emergency.cdc.gov/han/han00384.asp
[21] Unpublished data from analysis of Massachusetts toxicology reports managed by the Office of the Chief Medical Examiner.

Report Organization

Chapter 55 of the Acts of 2015 specifically lists seven questions pertaining to fatal opioid overdoses. Detailed examinations of these questions are included. This exercise in data linking across relevant and available datasets in Massachusetts allows us to identify systems that served individuals who died of a fatal opioid overdose prior to their death (e.g. health care settings, or criminal justice system). By identifying these points of contact, this information may shed light on future interventions to prevent opioid overdoses. The toxicology reports from the decedents may shed some light on some details of the death; however, looking back at the systems that served these individuals prior to overdose is also critical. By linking across systems, it is possible to know whether an individual had an ambulance-related event reported to the Massachusetts Ambulance Trip Record Information System (MATRIS), any prescriptions for opioid medications recorded in the Prescription Drug Monitoring Program (PDMP), contact with the healthcare system via BSAS or in the hospitalization database (Case Mix) or All Payer Claims Database (APCD), or criminal justice involvement through the Department of Correction (DoC). The body of this report describes four analyses performed with data from the ten datasets. Those analyses can be found in the section that immediately follows.

The reader is encouraged to examine the appendices as well. Please refer to Appendix A for detailed answers to the seven questions specified in Chapter 55. Among the questions were requests for information about the use of multiple prescribers, poly-prescription use, voluntary and involuntary treatment, and post-incarceration risk of overdose death. To gain a better understanding of the datasets used for analysis in this report, refer to Appendix B. Additional findings beyond the seven questions from individual datasets can be found in Appendix C. The data linkage process and a summary of how well the linkage plan worked can be found in Appendix D. In Appendix E, the reader can find the approach used to assess data quality and the strategies used to handle missing data. To understand the approach to data privacy followed by this work as well as the system architecture that allows for simultaneous examination of these 10 datasets, the reader is referred to Appendix F. Appendix G briefly summarizes the legal agreements that allowed data partners and other agencies to share data and utilize necessary resources. A full set of cross tabulations of each of the 10 Chapter 55 datasets compared to opioid deaths in 2013 and 2014 is presented in Appendix H. See Appendix I for additional information about Addiction and the Bureau of Substance Abuse Services. Finally, the partners who generously offered their time to make this report possible are listed in Appendix J.

Key Findings from the Across Chapter 55 Datasets

Linking large and complex opioid-related datasets has made it possible to take an unprecedented look at the opioid crisis in Massachusetts. In the section that follows, four analyses are presented that demonstrate the importance of looking across datasets to understand what drives the crisis and what may be done to reduce the rate of death from legal and illegal opioids. In order to support the findings and recommendations, significant technical detail has been added to each of the sections below. This may be more detail than is helpful to some readers, so a summary of the findings and the recommendations has been inserted at the beginning of each section.

Technical Notes: The linked dataset includes males and females in Massachusetts aged 11 and older. All four analyses used this starting population and filter the data according to the hypothesis of specific interest. This report uses standard conventions for naming drugs, drug classes, and chemical compounds. Specific drugs like Heroin and Fentanyl are capitalized. Drug classes and chemical compounds like benzodiazepines and 6-mono acetyl morphine are not capitalized.

Analysis #1 (Toxicology & PDMP): Key Findings and Recommendations

Analysis #1 - Toxicology & PDMP

Key Findings:

- Individuals who died from opioid-related overdoses are much more likely to have illegally-obtained substances (i.e., not Schedule II-III substances) present in post-mortem toxicology.
- Heroin was present in two-thirds of deaths. Benzodiazepines in over half. Fentanyl and cocaine were each found in roughly one-third.
- Among descendants, 22% had a positive toxicology report for a Schedule II-III opioid, but only 9.1% had a prescription for that drug in PDMP.
- Most toxicology reports had positive tests for more than one substance.

Recommendations:

- Harm reduction strategies and interventions that address Heroin, Fentanyl, and polysubstance use should be increased, expanded, and enhanced.
- Increase in real-time disease surveillance can be used as a public health tool to better understand overdose deaths.
- Data should be reported and collected in a more timely manner, allowing earlier identification of new and emerging trends.

Basic Methods: Toxicology at death was linked with PDMP records among people who died of an opioid-related overdose of unintentional or undetermined intent. Males and females age 11 and above were included. In 2013 and 2014 there were 2,192 Massachusetts residents in our analytic file who died of an opioid-related overdose. Toxicology reports including detailed information regarding specific opioids and other drugs present were available for 77% of these deaths (1,692/2,192). All data below represents these 1,692 people. A breakdown of specific substances present in the toxicology reports was also determined.

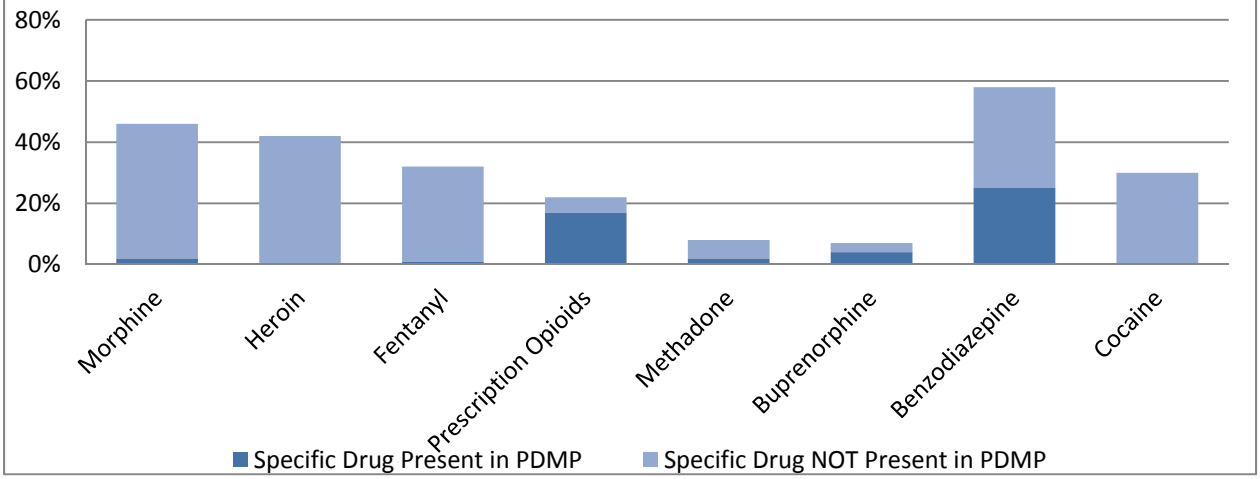
Summary of toxicology findings: Overall, 66% of the deaths had Heroin or likely Heroin present. Fentanyl was present in 32% of opioid overdose deaths. More recent data from DPH indicates that Fentanyl presence rose further to 57% in 2015[22]. Heroin or Fentanyl, which is typically sold as Heroin, was present in 85% of the opioid deaths. Schedule II and III prescription opioids were present in 22% of opioid deaths and Oxycodone, the most commonly prescribed opioid, was present in 15% of the opioid deaths. In 9.1% of overdose deaths only, Schedule II and III prescription opioids used only for pain were present, (Heroin, Fentanyl, Methadone, or buprenorphine were not present). Benzodiazepines and Cocaine were present in 58% and 30% of opioid deaths, respectively.

[22] Accessed at http://www.mass.gov/eohhs/docs/dph/quality/drugcontrol/county-level-pmp/data-brief-overdose-deaths-may-2016.pdf

Categorizing toxicology data: The toxicology tests for Fentanyl, Methadone, buprenorphine, and Cocaine are specific to those particular substances and therefore when they were present it was clear that the decedent had taken those substances prior to death. For this report, individual benzodiazepines were not distinguished on toxicology testing, but reported them as a class. Oxycodone, Hydrocodone, Hydromorphone, Oxymorphone (as a metabolite of Oxycodone or from prescription Oxymorphone), Codeine, and Tramadol are all specific toxicology results for substances where the main source is either prescribed or diverted Schedule II and III prescription opioids intended to treat pain. Therefore, these toxicology results were grouped together as "prescription opioids."

Categorizing Heroin and Morphine presence on toxicology is more complicated. One toxicology result specific for Heroin is 6-monoacetylMorphine (6-mam). However, 6-mam is rapidly metabolized to Morphine and therefore, commonly, is not present on toxicology. When Morphine and Codeine are both present, especially where the quantitative level of Morphine is greater than Codeine, this indicates Heroin use due to impurities retained during Heroin refining from Opium.[23,24] For this analysis, quantitative levels of Morphine and Codeine were not available. The presence of Morphine without Codeine in toxicology occurs due to either 1) prescription Morphine or 2) as a metabolite of Heroin. In order to determine whether to attribute deaths with Morphine present to prescription Morphine or to Heroin, the presence of Morphine prescriptions within the PDMP was reviewed.

Figure KEY1.1: Percent of Deaths (2013-2014) with Specific Drugs Present in Toxicology Results & the Relative Contribution of Prescriptions for the Drugs (2011-2014)

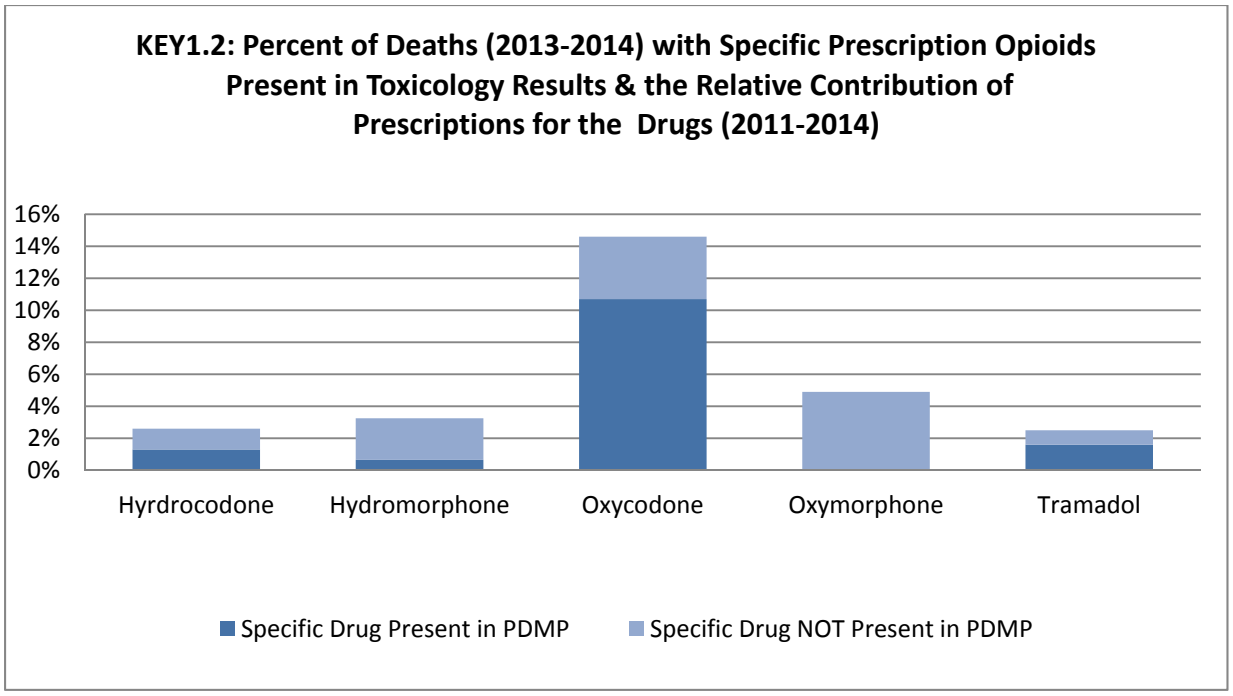


[23] Ceder G and Jones AW. Concentration ratios of Morphine to Codeine in blood of impaired drivers as evidence of Heroin use and not medication with Codeine. Clinical Chemistry. November 2001 vol. 47 no. 11 1980-1984. Accessed at: http://www.clinchem.org/content/47/11/1980.long

[24] Ellis, Ashley D., et al. "Identifying cases of Heroin toxicity where 6-acetylMorphine (6-AM) is not detected by toxicological analyses." *Forensic science, medicine, and pathology* (2016): 1-5.

Notes: Prescription opioids include Hydrocodone, Hydromorphone, Oxycodone, Oxymorphone, Codeine, and Tramadol.
Presence in PDMP includes any prescription for the particular drug between 2011 and 2014.

Figures KEY1.1 and KEY1.2 present the proportion of decedents with a specific drug (or Schedule II and III prescription opioid) in their toxicology results and the contribution of opioid prescriptions reported to the PDMP to these proportions. Breaking down the prescription opioid group into its components, substantial fractions of the decedents with Oxycodone, Hydromorphone, Hydrocodone, and Tramadol, present in toxicology had matching prescriptions for those drugs in the PDMP. Almost none had matching prescriptions for Oxymorphone, though this is a metabolite of Oxycodone.



Notes: Presence in PDMP includes any prescription for the particular drug between 2011 and 2014.
Codeine is not included in the chart because <5 prescriptions were filled by this study population.

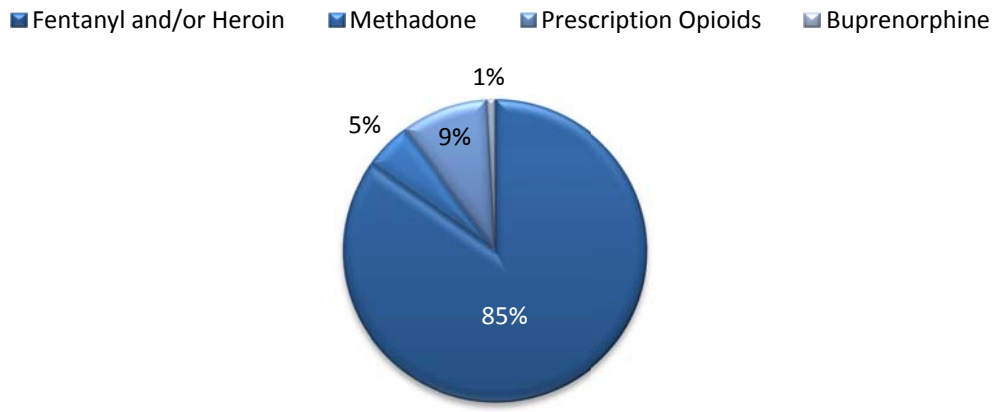
Based on these results, Morphine toxicology was further categorized as "likely Heroin." When crossed with the PDMP, people who had Morphine present at death had very low rates of Morphine prescription histories. A similar pattern for Fentanyl was observed. For Fentanyl, there is a rapidly expanding distribution of illicitly produced Fentanyl sold as Heroin,[25,26,27] which explains the low rate of Fentanyl prescriptions. In contrast, people with other prescription opioids such as Oxycodone in their

[25] Rudd, Rose A., et al. "Increases in drug and opioid overdose deaths-United States, 2000-2014." *MMWR: Morbidity and mortality weekly report* 64.50-51 (2016): 1378-1382.
[26] Accessed at: https://www.dea.gov/divisions/hq/2016/hq061016.shtml
[27] Accessed at: http://www.cdc.gov/drugoverdose/opioids/fentanyl.html

toxicology screen, were much more likely to have prescriptions for that opioid. A similar pattern with benzodiazepines and prescription opioids was observed. Morphine is uncommonly prescribed to people who die of overdose, relative to other opioids, yet it is prevalent in toxicology. Thus, most Morphine positive toxicology results are likely due to Heroin. This is supported by the presence of Codeine, but not always. In our linked data, Codeine is present in 48% of definite Heroin screens and Morphine is present >99% of the time. Further examination of the full medical examiner records of these deaths where Morphine is present would be warranted to confirm this assumption.

Opioid-related overdose deaths in mutually exclusive categories were categorized based on decreasing order of deadliness[28] of the specific drugs (*Fentanyl and/or Heroin* → *Methadone* → *other Rx* → *buprenorphine*) present in the results. A person was put into a category based on the deadliest drug present in the results, regardless of the presence of other drugs. For example, if someone had Fentanyl and Methadone present, they would be in the "Fentanyl" group. (See Figure KEY1.3)

Figure KEY1.3: Fatal Opioid-Related Overdoses (2013-2014)
Mutually Exclusive Toxicology Categories (n=1657)



Notes: Fentanyl and/or Heroin includes: Fentanyl, Heroin, and Morphine (likely Heroin).
Prescription opioids include Hydrocodone, Hydromorphone, Oxycodone, Oxymorphone, Codeine, and Tramadol.

Prescription filling by opioid decedents: The timing of Schedule II and III opioid prescriptions and their presence or absence in toxicology screens based on the above mutually exclusive categories of toxicology results demonstrates that decedents, regardless of toxicology at death, were commonly prescribed opioids during the entire study period (2011-2014). The rate of filled prescriptions for

[28] While "deadliness" is an imprecise term, drugs are considered deadlier when equivalent amounts are more likely to lead to death. In this case, equivalent amounts of Heroin or Fentanyl are more likely to result in death than buprenorphine.

opioids during this period ranged from 60% to 82% depending on the drug. (See Table KEY1.1) Looking only at prescriptions filled within 1 month of overdose death, the rate dropped in each category to a range of 8.4% to 36%. Opioid-involved decedents who died with only prescription opioids on board (representing under ten percent of opioid overdose deaths) were the most likely group to have had a prescription filled in the same month (36%) or in months proximal to their death. (See Table KEY1.1) While the majority of people filled an opioid prescription during the study period, relatively few filled a prescription for an opioid within one month of their death.

Table KEY1.1: Proportion of Decedents (2013-2014) with any Prescription[1] Opioid History (2011-2014) by Category of Opioid Present in Toxicology Screen

	Overall	Within 1 Month of Death		Within 3 Months of Death		Within 6 Months of Death		Within Study Period	
Toxicology Result	**n**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Fentanyl and Definite Heroin Present	166	16	9.6%	22	13.35	38	22.9%	104	62.7%
Fentanyl and Likely Heroin Present	83	7	8.4%	16	19.3%	21	25.3%	54	65.1%
Fentanyl Present	288	50	17.4%	64	22.2%	87	30.2%	195	67.7%
Definite Heroin Present	547	71	13.0%	104	19.0%	150	27.4%	353	64.5%
Likely Heroin Present	320	39	12.2&	68	21.3%	92	28.8%	207	64.7%
Methadone Present	84	23	27.4%	34	40.5%	39	46.4%	64	76.2%
Prescription Opioid Present	154	57	37.0%	77	50.0%	88	57.1%	127	82.5%
Buprenorphine	15	<5	N/A	<5	N/A	<5	N/A	9	60.0%
Total	1657[29]	--[2]	--[2]	--[2]	--[2]	--[2]	--[2]	1113	67.2%

1. Includes any prescription for Fentanyl, Methadone, Hydrocodone, Hydromorphone, Oxycodone, Oxymorphone, Morphine, or Codeine
2. Number not displayed because of complimentary suppression rules.

Polysubstance use: Polysubstance use can involve using 2 drugs for non-medical purposes. For example, benzodiazepines[30] are commonly taken with opioids for non-medical purposes. The combination of the medications depresses the central nervous system at a higher rate than just using one of the medications. Benzodiazepines are commonly taken with opioids for non-medical purposes. Benzodiazepines are present consistently in toxicology screens, regardless of the opioid present, in over half of overdoses. This pattern has been demonstrated in other populations.[31] The proportion of people with a prescription for a benzodiazepine within one month of death ranged from 14-25% in the toxicology subgroups while over half had a prescription during the study period. (See Table KEY1.2) Of particular note, benzodiazepines were present in 62% of overdoses when only a prescription opioid was

[29] This value (1,657) differs from the total number of cases with toxicology reports (1,692) because there were 35 cases in which no positive results for the substances listed in the table were detected.
[30] This medication is in the sedative/hypnotic drug class, and acts on the central nervous system. When used in combination with an Opioid, it poses a very high risk for overdose.
[31] Park, T. W., Saitz, R., Ganoczy, D., Ilgen, M. A., & Bohnert, A. S. (2015). Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. B*mj*, *350*, h2698.

present, and 25% of these had a prescription within a month of their death. They were present 69% of the time when Methadone was present, and 24% of these people had a prescription for a benzodiazepine within a month of death. (See Table KEY1.3)

Unlike the specific opioid products, benzodiazepines had a presence in death toxicology samples that exceeded the prevalence prescribed. While benzodiazepines were present in 982 toxicology screens, only 495 people ever had a prescription for one and less than 200 had a prescription within one month of their death. This suggests a substantial amount of diversion, and that benzodiazepines involved in opioid overdose deaths are a combination of prescribed and diverted pills. (See Table KEY1.3)

Another drug commonly seen in opioid deaths was Cocaine. Overall, 30% of opioid decedents with a toxicology screen also had Cocaine present in their system. When Fentanyl, Heroin, or buprenorphine is present, Cocaine is present about 1/3 of the time. Cocaine is less commonly present when Methadone (21%) or prescription opioids (13%) are present.

Table KEY1.2: Proportion of Decedents (2013-2014) with a Prescription Benzodiazepine History (2011-2014) by Category of Opioid Present in Toxicology Screen

	Over all	Within 1 Month of Death		Within 3 Months of Death		Within 6 Months of Death		Within Study Period	
	n	n	%	n	%	n	%	n	%
Fentanyl and Definite Heroin Present	166	14	14.7%	21	22.1%	21	22.1%	47	49.5%
Fentanyl and Likely Heroin Present	83	6	13.6%	6	13.6%	7	15.9%	14	31.8%
Fentanyl Present	288	31	18.0%	38	22.1	44	25.6%	78	45.4%
Definite Heroin Present	547	54	17.9%	75	24.9	93	30.9%	146	48.5%
Likely Heroin Present	320	40	22.0%	54	29.7	63	34.6%	94	51.7%
Methadone Present	84	14	24.1%	19	32.8%	25	43.1%	40	69.0%
RX Present	154	24	25.3%	34	35.8%	39	41.1%	60	63.2%
Buprenorphine	15	<5	N/A	<5	N/A	<5	N/A	8	57.1%
Total	1657	--[1]	--[1]	--[1]	--[1]	--[1]	--[1]	--[1]	50.4%

1. Number not displayed because of complimentary suppression rules.

Table KEY1.3: Proportion of Decedents with Benzodiazepine or Cocaine Present in Toxicology Screen by Category of Opioid Present in Toxicology Screen (2013-2014)				
	Frequency	**% of Total**	**% with Benzodiazepine**	**% with Cocaine**
Fentanyl and Definite Heroin Present	166	10.0%	57.2%	31.3%
Fentanyl and Likely Heroin Present	83	5.0%	53.0%	33.7%
Fentanyl Present	288	17.4%	59.7%	32.6%
Definite Heroin Present	547	33.0%	55.0%	30.7%
Likely Heroin Present	320	19.3%	56.9%	32.2%
Methadone Present	84	5.1%	69.1%	21.4%
RX Present	154	9.3%	61.7%	13.0%
BPN Present	15	0.9%	93.3%	33.3%

Limitations: The Chapter 55 project has facilitated the linkage of death, toxicology, and PDMP data at the individual level, which has allowed us to obtain a clearer picture of what opioids and other substances are present and how often opioids and benzodiazepines are prescribed. However, there are several limitations to our analyses at this point. First, the overdose death data are limited to 2013 and 2014 and therefore little can be said about time trends with two years of data. Expanding this analysis to more years would allow for analysis and surveillance of changes over time. The rapidly rising rates of Fentanyl present at overdose deaths from 2013 to 2015 is one example of why real-time surveillance of overdose death toxicology is an important public health tool. For the toxicology dataset, as discussed above, it is not clear how to attribute deaths where Morphine is present on toxicology. Based on a review of the PDMP data, it was decided to define these as "likely Heroin" present. A more in-depth review of the subset of deaths with this toxicology result is warranted to confirm or further inform our assumptions. The toxicology also does not include routine testing for substances like Gabapentin, Promethazine or Clonidine, which may be diverted and used in combination with opioids.[32,33,34,35,36] Further, the toxicology testing is not sensitive for alcohol, which is an established contributor to polysubstance overdose death. Therefore the role that these substances may be playing in opioid-related overdose deaths cannot be determined. The PDMP dataset includes methadone prescribed for pain management, but does not include Methadone dispensed through opioid treatment programs. In this analysis, the data was not available to link toxicology to Methadone treatment data from the Bureau of Substance Abuse Services, which would help address this limitation.

[32] Smith, RV, et al. "Gabapentin misuse, abuse and diversion: a systematic review." Addiction. 2016 Jul;111(7):1160-1174. doi: 10.1111/add.13324. Epub 2016 Mar 18.

[33] Shapiro, B. J., Lynch, K. L., Toochinda, T., Lutnick, A., Cheng, H. Y., & Kral, A. H. (2013). Promethazine misuse among methadone maintenance patients and community-based injection drug users. Journal of addiction medicine,7(2), 96.

[34] Lynch, K. L., Shapiro, B. J., Coffa, D., Novak, S. P., & Kral, A. H. (2015). Promethazine use among chronic pain patients. Drug and alcohol dependence, 150, 92-97.

[35] Dennison, S. J. (2001). Clonidine abuse among opiate addicts. Psychiatric quarterly, 72(2), 191-195.

[36] Beuger, M., Tommasello, A., Schwartz, R., & Clinton, M. (1998). Clonidine use and abuse among methadone program applicants and patients. Journal of substance abuse treatment, 15(6), 589-593.

Implications and recommendations based on Key Finding #1:

- Heroin and/or Fentanyl, and benzodiazepines are present at the majority of opioid overdose deaths and thus are likely to be driving the increases in overdose.
- Increased real-time surveillance capacity that integrates linkable data from multiple sources is crucial to understanding the rapidly increasing overdose death rates.
- Harm reduction strategies and interventions that address Heroin, Fentanyl, and polysubstance use (especially benzodiazepines and Cocaine) should be increased, expanded, and enhanced.
- More outreach and education regarding use of the online PDMP to detect patients receiving multiple drugs is essential to improve coordination of care and thus reduce overdose risk.
- People who die from opioid-related overdose are commonly prescribed opioids, though less commonly at the time close to their death. Therefore, the role of prescription opioids in overdose death is more likely part of the development of upstream risk, than a downstream proximal cause. Interventions focused on reducing access to prescription opioids should be paired with interventions that address Heroin, Fentanyl, and polysubstance use as the proximal causes of overdose.

Analysis #2 (Nonfatal Overdoses and Opioid Agonist Treatment): Key Findings and Recommendations

Analysis #2 - Non Fatal Overdoses and Opioid Agonist Treatment (OAT)

Findings

- Following nonfatal overdoses, individuals receiving opioid agonist treatment (i.e., medications such as methadone & buprenorphine that block the effect of opioids) were significantly less likely to die from a subsequent opioid overdose. (Note: Data on naltrexone/Vivitrol use comes from the APCD. Analyses are ongoing.)
- Despite previous history of nonfatal overdoses, engagement in opioid agonist treatment (OAT) remained constant (~5%) over a 12-month follow-up period, indicating lost opportunities to save lives.

Recommendations

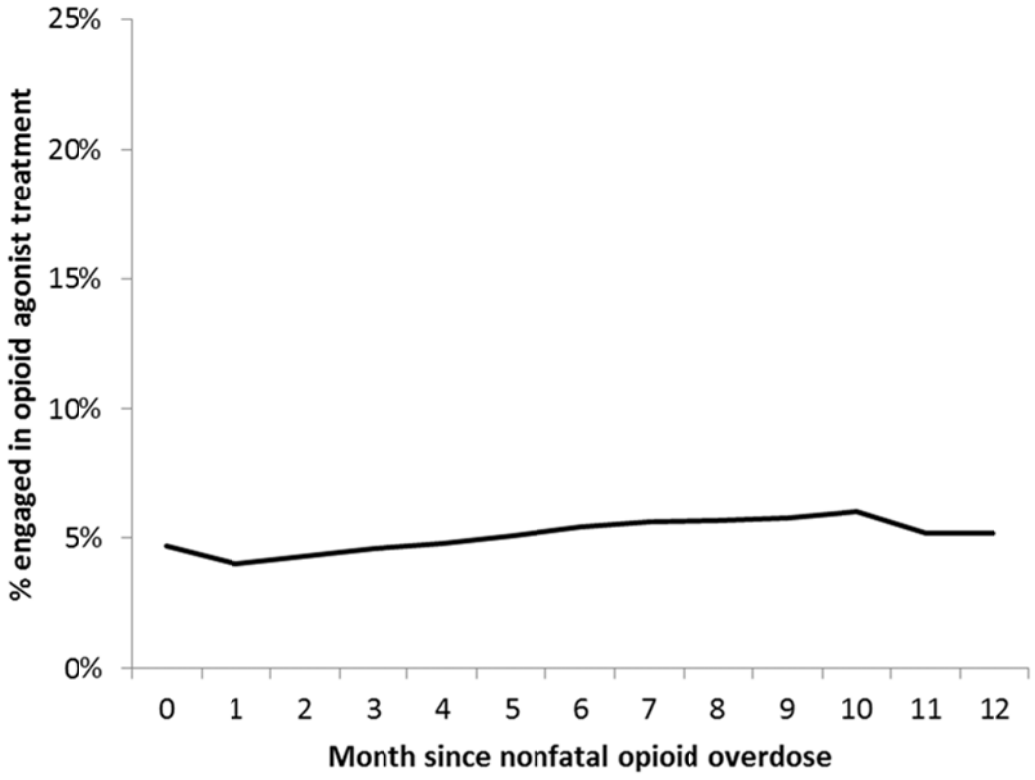
- Strategies for making MATs for opioid use disorders more accessible to individuals who experience a nonfatal opioid overdose should be prioritized.
- Follow-up period of analysis should be extended to determine whether protective factor of OAT persists beyond 12 months.

Basic Methods: Treatment patterns and outcomes following nonfatal opioid-related overdose were examined. Males and females age 11 and above were included in the analysis. By linking data from MATRIS and the death index at the individual level, 7,634 individuals were identified who survived an ambulance encounter for an opioid-related overdose in Massachusetts between 2013 and 2014.

Summary of Findings: Over a median follow-up period of 10 months, 149 individuals (2.0%) with non-fatal overdose experienced a subsequent fatal opioid-related overdose. Analyzed another way, at least 6.8% (149 of 2,192) of total opioid-related overdose deaths in Massachusetts over the relevant period were preceded by a nonfatal opioid-related overdose as detected in MATRIS. Since not all opioid-related overdoses are captured by MATRIS, these values are almost certainly underestimates.

For those individuals who experienced a nonfatal opioid overdose, engagement in opioid agonist treatment (OAT) in the period surrounding the nonfatal opioid overdose was examined. Specifically, monthly exposure to OAT was studied using BSAS records for treatment with Methadone or buprenorphine or PDMP dispensing for buprenorphine. During the month of the nonfatal opioid-related overdose, 4.7% of individuals were engaged in OAT. Engagement in OAT remained relatively constant over 12 months of follow-up, with 5.2% of individuals receiving OAT in month 12 (Figure KEY2.1).

Figure KEY2.1: Engagement in Opioid Agonist Treatment by Month Following a Nonfatal Opioid-Related Overdose (2013-2014).



Finally, time to fatal opioid-related overdose was examined. All deaths due to other causes through the end of the study period (December 2014) were removed from the analysis. Here, the cumulative incidence of fatal opioid-related overdose stratified by exposure to OAT using an extended Kaplan-Meier estimator, treating OAT exposure as a time varying covariate defined as exposed in the month of or month prior to the month at risk for opioid-related death was calculated. The cumulative incidence of fatal opioid-related overdose was 1.1% for those engaged in OAT versus 2.3% for those not engaged in OAT. Thus, among people who have a nonfatal opioid-related overdose, those who are engaged in OAT had a risk of subsequent fatal opioid-related overdose that is less half of those who are not engaged in OAT.

Limitations: There are several potential limitations of this preliminary analysis. First, these estimates likely represent a substantial underestimate of the number of nonfatal opioid-related overdoses in Massachusetts. Not all nonfatal opioid-related overdose events result in an ambulance encounter, and not all ambulance encounters are captured in MATRIS. To build on this analysis, nonfatal opioid-related overdoses identified in the emergency room and inpatient settings from the Case Mix will be included datasets once these data are available. Second, the findings related to the impact of OAT are observational and likely subject to substantial confounding. Additional analyses will be conducted to adjust for factors that may influence treatment decisions as well as fatal opioid-related

overdose. As part of this, geospatial variability will be explored to compare the intersection of where individuals experience nonfatal opioid overdose and where they access treatment that may inform hotspots that should be targeted with additional resources. Finally, a range of treatment options beyond OAT will be examined including opioid antagonist treatment (e.g. injectable extended-release Naltrexone) and detoxification admissions.

Implications and recommendations based on Key Finding #2

- A substantial portion of opioid-related overdose deaths in Massachusetts are preceded by a nonfatal opioid overdose.
- Engagement in OAT following nonfatal opioid-related overdose was found to be associated with a substantial decrease in the risk of a subsequent fatal opioid-related overdose. Despite this risk reduction (50% less risk of an overdose by those engaged in OAT versus those who did not engage in OAT), the proportion of people who engage in OAT following a nonfatal opioid overdose remains low.
- Presentation to the health care system with nonfatal opioid-related overdose represents an opportunity to engage high-risk individuals in treatment.
- There is substantial opportunity to develop novel public health approaches to identify individuals who experience nonfatal opioid-related overdose and engage them in treatment.

Analysis #3 (Gender Differences and the PDMP): Key Findings and Recommendations

Analysis #3 - Gender Differences and the PDMP

Key Findings

- Between 2011 and 2014, women filled nearly one million more Schedule II and III opioid prescriptions than men.
- Women are significantly more likely than men to receive Schedule II and III opioids from 3 or more prescribers and obtain them from 3 or more pharmacies.
- Obtaining Schedule II and III opioid prescriptions from multiple prescribers and filling them at multiple pharmacies are significant risk factors for subsequent opioid-related death.

Recommendations

- Alerts in MassPAT should be configured to assure that prescribers and pharmacists are aware of potential patient misuse and diversion of Schedule II-III opioids.
- Prescribers and pharmacists should be educated about personal biases associated with "expected" risks for certain populations.
- Providers should consider gender differences when screening, assessing, diagnosing and treating patients.

Basic Methods: Demographic differences in general and gender differences in specific were examined in outcomes related to opioid-related overdose deaths and risk factors for these deaths. Males and females age 11 and above were included in the analysis. Toxicology and PDMP data were linked to deaths. Demographics were used from all available sources. Bivariate analyses using the Chi Squares were performed in order to determine if there were any significant differences in frequencies between gender and age groups.

Summary of Findings: There are differences between the substances found in the toxicology screening of males and females who die as a result of an opioid-related overdose. While males were statistically significantly more likely to have Heroin present in their toxicology screen as compared to females who died during the study period ($\rho \leq 0.001$), females were statistically significantly more likely than males to have a prescription opioid in their toxicology screening ($\rho \leq 0.001$). Overall, in the PDMP database, females were more likely than males to have 3 or more prescribers ($p < .0001$). Females who died of an opioid overdose were more likely than males to have 3 or more prescribers ($p < .0001$) and to fill prescriptions at multiple pharmacies ($p < .0001$). For frequencies see Tables KEY3.1 and KEY3.2.

Toxicology Results and Gender: In 2013-2014, there were 1,692 opioid-related decedents where data was available for the toxicology screen. These decedents are represented in the tables below; 485 decedents were female and 1,207 were male. Table KEY3.1 displays the presence of a prescription opioid in the toxicology screen by gender. The key finding is that 27.8% of females had a prescription opioid present in their toxicology screen while only 18.5% of males did. Further analyses

indicated that this result was statistically significant. While fatal opioid overdoses occur most frequently in males, this data suggests that women are disproportionately impacted by prescription opioids. As described in other sections of this report, the presence of Morphine in a toxicology screen is due to prescription Morphine or Heroin metabolites. Decedents were categorized as deaths that were likely attributable to Heroin when there was no matching Morphine prescription documented in the PDMP database.

Table KEY3.1: Presence of a Prescription Opioid in Toxicology Screen by Gender (2013-2014)						
	Males			Females		
Toxicology Results	N	% of total	% of Males	N	% of total	% of Females
Prescription Opioid Present	223	13.2%	18.5%	135	8.0%	27.8%
No prescription opioid present	984	58.2%	81.5%	350	20.7%	72.2%

Table KEY3.2 displays the presence of Heroin in the toxicology screen by gender. The key finding is that 68.9% of males had Heroin present in their toxicology screen while only 58.6% of females did. Additional analysis demonstrated that males were statistically significantly more likely than females to have Heroin present.

Table KEY3.2: Presence of Heroin in Toxicology Screen by Gender (2013-2014)						
	Males			Females		
Toxicology Results	N	% of total	% of Males	N	% of total	% of Females
Heroin Present	832	49.2%	68.9%	284	16.8%	58.6%
No Heroin present	375	22.2%	31.1%	201	11.9%	41.4%

When differences in toxicology screening findings based upon gender are further divided into age categories – younger than 18 years, 18-44 years, 45-64 years and 65 years and older, the differences observed largely remain. Table KEY3.3 and Table KEY3.4 display the presence of Heroin and prescription opioids, respectively by gender and age group. In the first three age categories – younger than 18 years, 18-44 years and 45-64 years – males are statistically significantly more likely to have Heroin in their toxicology screens as compared to females. In the age category 45-64 years, females are statistically significantly more likely to have prescription opioids in their toxicology screens as compared to males. Only the oldest group, 65 years and older, did not observe a difference between males and females.

The size of this last group was small relative to the other three groups; there were only 25 decedents in this oldest group.

Table KEY3.3: Presence of Heroin in Toxicology Screen by Sex and Age Group (2013-2014)					
		Younger than 18 Years	**18-44 Years**	**45-64 Years**	**65 Years+**
Heroin Present	Male	76	497	256	<5
	Female	35	156	91	<5
Heroin Not Present	Male	70	350	273	12
	Female	14	166	176	18

Table KEY3.4: Presence of Prescription Opioid in Toxicology Screen by Sex and Age Group (2013-2014)					
		Younger than 18 Years	**18-44 Years**	**45-64 Years**	**65 Years+**
Prescription Opioid Present	Male	14	95	108	6
	Female	7	45	73	10
Prescription Opioid Not Present	Male	97	587	295	5
	Female	36	194	116	<5

Prescribing Patterns and Gender: Figures KEY3.1 and KEY3.2 show the breakdown of number of prescribers by the gender of the decedent. 35% of males who died of an opioid overdose had three or more prescribers of a scheduled drug, as compared with 61% of females.

Figure KEY3.1: Fatal Opioid-Related Overdoses (2013-2014) by Number of Opioid Prescribers (2011-2014): Male

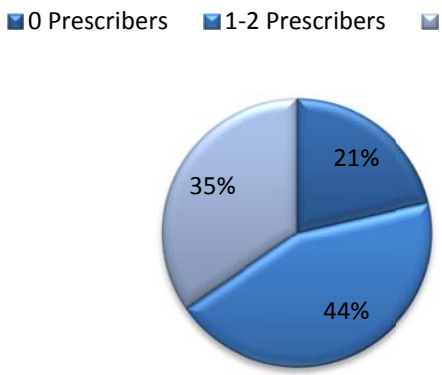
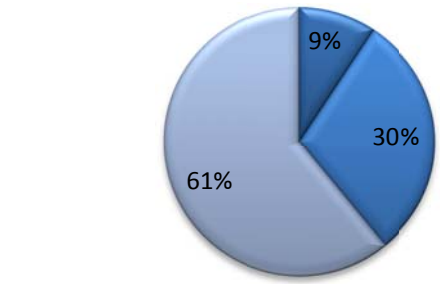


Figure KEY3.2: Fatal Opioid-Related Overdoses (2013-2014) by Number of Opioid Prescribers (2011-2014): Female



In the linked data, there were 1,206 males and 597 females who died of an opioid-related overdose and had at least one opioid prescription in the PDMP. In this group, females were more than three times as likely to have 3 or more prescribers of a scheduled drug as compared with 1-2 prescribers as males. They were also almost three times as likely to fill scheduled drug prescriptions at three or more pharmacies as males.

Limitations: There are several limitations of these analyses that should be cited. First, only about three quarters of the opioid related deaths had drug specific toxicology screens available and so it is not possible to comment on the possible drugs present in the remaining population. Second, as stated previously, the presence of Heroin is derived from the absence of a Morphine prescription in the PDMP database and the presence of a Heroin metabolite in the toxicology screen. Although very few providers prescribe Morphine to their patients, it is possible that there are Morphine prescriptions that were not entered into the PDMP database and so these decedents may represent a false negative. Third, this analysis does not include claims data from the Case Mix Database or APCD. Integrating this information in future analyses can help to identify variables associated with the differences observed between sexes.

Implications and recommendations based on Analysis #3:

- Individual providers should take the observed gender differences into consideration when screening, assessing, diagnosing, and treating patients. Providers should utilize the PDMP database to identify any active or past prescriptions for their patients, particularly females, and to provide coordinated care.

- Addiction Services and Treatment providers must incorporate the observed differences in toxicology screens by gender into the planning, development, and implementation of recovery services.
- Finally, policymakers should consider Addiction Services public service campaigns that integrate the gender-based differences observed into the messaging and advocate for additional in-depth analyses towards better understanding the gender-based differences.

Analysis #4 (Post Incarceration Risk): Key Findings and Recommendations

Analysis #4 – Post Incarceration Risk

Key Findings

- The risk of opioid-related overdose death following incarceration in Massachusetts is over 50 times higher than for the general public.
- The risk of death is highest in the month following release.
- Among those released from prison, young people aged 18 to 24 have roughly 10 times the risk of death upon release compared to individuals 45 years and older.

Recommendations

- Ensuring the availability of treatment within correctional facilities, and improved aftercare planning for inmates prior to release has the potential for life-saving impact and should be prioritized.
- Treatment and overdose prevention services should be expanded in correctional facilities and should be standardized, evidence-based, and monitored.
- Further research is warranted to identify other specific risk factors associated with the increased risk for those released from incarceration.

Basic Methods: Previous studies in the United States as well as in other countries have identified a markedly increased risk of death in former inmates, compared with the general population, particularly in the first month following release[37,38]. This excess mortality is predominantly due to an increased risk of injury death, often due to drug-related causes[39]. In order to calculate Crude Mortality Rates (CMR), person-years were calculated to account for the amount of time at risk for death for former inmates. Person-years were defined as the total number of days in the study period during which former inmates were not incarcerated during 2013-2014, including days between each release and the subsequent incarceration, the end of the study period, or death. For the rest of the Massachusetts population, the Massachusetts population counts from the 2013-2014 Modified Age, Race/Ethnicity, and Sex files (MARS) were used, which are a bridged population file produced by the National Center for Health Statistics (NCHS) and the Census Bureau Population Estimates Program and subtracted the total person-years of formerly incarcerated people. In addition, mortality rates were calculated by dividing the number of deaths by the number of person-years. To calculate the number of deaths among non-incarcerated Massachusetts residents, the total number of deaths among formerly

[37] Kariminia A, Butler TG, Corben SP, Levy MH, Grant L, Kaldor JM, Law MG: Extreme cause specific mortality in a cohort of adult prisoners – 1998 to 2002: a data-linkage study. Int J Epidemiol. 2007, 36 (2): 310-8.10.1093/ije/dyl225.

[38] Glaze L. E., Keuble D. Correctional Populations in the United States, 2013. Washington, DC: Bureau of Justice Statistics; 2014.

[39] Merrall EL, Kariminia A, Binswanger IA, Hobbs MS, Farrell M, Marsden J, Hutchinson SJ, Bird SM: Meta-analysis of drug-related deaths soon after release from prison. Addiction. 2010, 105 (9): 1545-1554. 10.1111/j.1360-0443.2010.02990.x

incarcerated people was subtracted from the total number of deaths among Massachusetts residents within each age category **for persons aged 18 to 64 years**. Finally, a multivariate analysis to examine risk factors associated with overall mortality and opioid-related mortality was conducted.

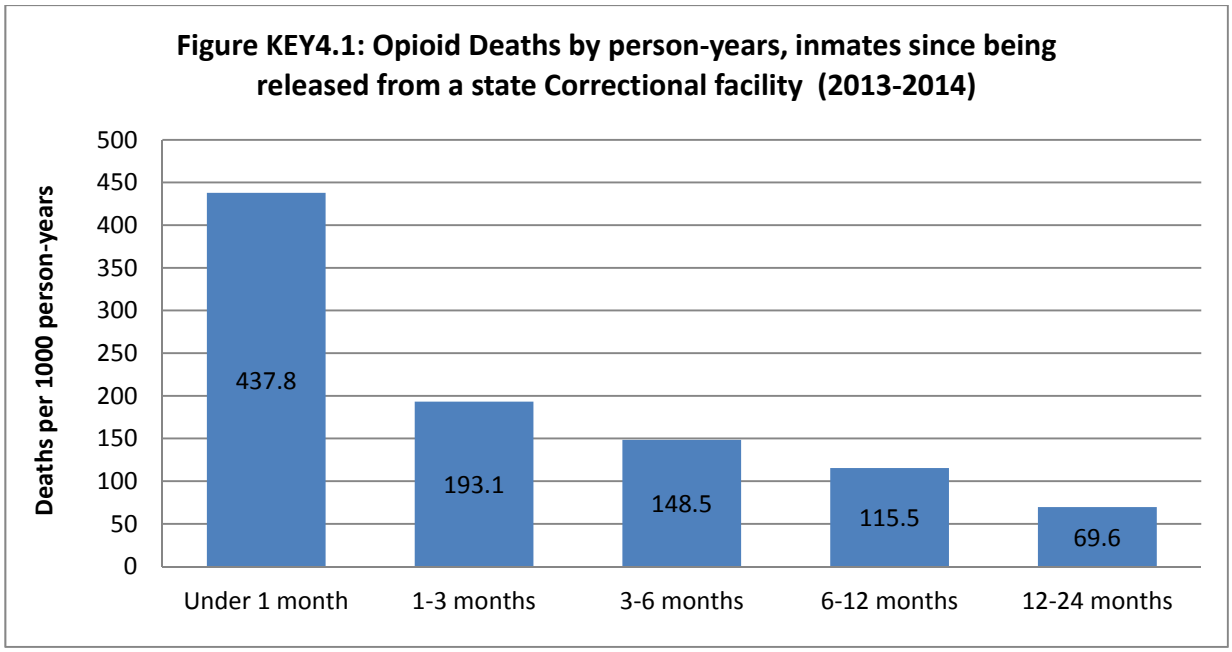
Summary of Findings: 13,918 former inmates released between 2013 and 2014 were identified. These individuals spent 5,707 person-years in the community after release, 287 died from all causes, and 121 consequently died from an opioid-related overdose during the study period. Rate of opioid-related overdose was approximately 50 times higher in formerly incarcerated people than in non-incarcerated Massachusetts residents. Former inmates also had a significantly lower overall survival than non-inmates ($p<0.0001$).

Table KEY4.1: Deaths and years at risk by time, since being released from a state Correctional facility (2013-2014)

	Opioid Deaths	Population	Rate per 100000
Former Inmates	121	13,918	869.4
Everyone else (non-former inmates)	2,071	13,423,695[40]	15.4
Rate Ratio			**56.4**

Our findings also suggest that there is a significantly elevated mortality risk in the earliest time-periods after being released from a state correctional facility, when compared with other non-critical time periods. The largest proportions of former inmates died within the first month (Figure KEY4.1).

[40] This figure represents sum of the population of the state in 2013 and 2014.



The first month after release proved to be a critical time period for former inmates, having rates that were between 2 to 6 times higher than for later times for all-cause mortality (Table KEY4.2). Likewise, when examining opioid-related overdoses, former inmates had death rates in the 1st month after release that were up to 6times higher than rates at later times.

Table KEY4.2: Overall and Opioid Deaths by person-years, inmates since being released from a state Correctional facility (2013-2014)

Time Periods	Overall Deaths		Opioid-related deaths	
	Number of deaths	CMR per 100 person-years	Number of deaths	CMR per 100 person-years
Under 1 month	86	573.4	31	437.8
1-3 months	42	218.4	18	193.1
3-6 months	59	160.3	33	148.5
6-12 months	63	116.9	26	115.5
12-24 months	37	75.6	13	69.6

A logistic regression was also conducted on all deaths and opioid-related deaths and the following variables were included in the model: age at death or at December 2014, gender, race, and 2 variables to describe the periods of incarceration: the cumulative number of days spent in jail (≤1 month vs. >1 month) and the frequency of incarceration. Although, not a high R^2 (20%), it is worth highlighting that age was a significant predictor. The youngest at the time of release were most at risk: former inmates 18-24 years of age were almost 10 times more likely to die from an opioid-related overdose than any those that were 45 years and older. Likewise, former inmates that were 25-35 and 35-44 years

of age were 4 times more likely to die from an opioid-related overdose than any those that were 45 years and older.

Table KEY4.3: Odds Ratios for Opioid Overdoses (2013-2014)			
Effect	**Point Estimate**	**95% Confidence Limits**	
Male vs. Female	0.8	0.5	1.4
18-24 vs. 45+	9.4	3.0	29.5
25-35 vs. 45+ years	3.9	2.0	7.6
35-44 vs. 45+ years	3.5	1.6	7.6
White non-Hispanics vs. All others	1.7	0.3	8.8
2 vs. 1 incarceration	0.8	0.4	1.5
3+ vs. 1 incarceration	1.0	0.3	3.0
More than 1 month vs. Under 1 month in prison	1.4	0.8	1.4

Limitations: There are some limitations associated with using DoC data to better understand the intersection of Opioid overdoses and criminal justice involvement in the Commonwealth. Even though there is a large overlap between those that are criminally involved and those that have a SUD, there is a large assumption in this analysis - not everyone who is incarcerated is in need of substance abuse treatment.

The treatment indicator within the DoC data does not specify the type of treatment an individual received, and it may in fact include self-help groups. The indicator also does not specify the date when the treatment was received; therefore, it is hard to determine for those that had a lengthy sentence, whether the treatment was received closer to the beginning or end of a sentence, which may impact the overdose outcome.

DoC data includes incarcerations for those in prison and does not include data for people in jails or houses of correction (HoC). The data from DoC used in this analyses (e.g. those incarcerated during the study period and released) is only a subset of the individuals incarcerated within Massachusetts during this study period. This analysis does not included individuals that were not released during the study period, and it does not include individuals incarcerated within Hoc. HoC servers a higher volume of inmates per year in comparison to DoC, primarily due to shorter sentences and those waiting trial within Hoc. Due to this limitation, using DOC data to understand the intersection between fatal opioid

overdoses and the criminal justice system in Massachusetts does not provide a full picture to determine associated risks. An additional limitation arises if residents of Massachusetts are incarcerated outside of Massachusetts as that data is not captured by the DoC.

Implications and recommendations based on Analysis #4:

- Of the 25,209 inmates released 13,918 were released during 2013 and 2014. Of these, 287 died during the same time period. In this group, 42.2% (n=121) died from an opioid-related overdose. In comparison, for the total population in the state, opioid-related deaths accounted for only 2.1% (n=2,192) of deaths.
- Opioid-related overdose deaths in former inmates accounted for 5.5% of all opioid-related deaths in the time period. Former inmates who died from opioid-related overdoses were on average younger, more likely to have a High School education or less, and less likely to be married at or around the time of death, compared with those who died from all other reportable causes.
- These findings corroborate previous studies indicating that recently released prisoners are at increased risk for death following their release, particularly in the early period and particularly younger released prisoners.
- Ensuring treatment behind the walls and aftercare planning for released prisoners could potentially have a large public health impact.
- Increase education for overdose prevention (e.g. abstinence while incarcerated and relapsing upon release poses a risk for overdose.
- Further research is also warranted to identify other specific risk factors associated with this increased risk.

Conclusions

The rate of opioid-related deaths in Massachusetts has increased sharply in recent years. Some communities have been very hard hit by this public health crisis, but all communities have felt the burden of deaths, nonfatal overdoses, job loss, poor health, disintegrated family structures, or disrupted neighborhoods. Important findings described in this report include the fact that illicit drugs, not prescription drugs, are much more commonly present in post-mortem toxicology. As a result, increasing the availability of interventions that address Heroin, Fentanyl, and polysubstance use (especially benzodiazepines and Cocaine) could significantly reduce the opioid-related death rate. Also, opioid agonist treatment (OAT) like methadone or buprenorphine was found to be associated with a significantly lower risk of fatal opioid overdose following a previous nonfatal opioid overdose. A comprehensive plan for delivering OAT could significantly lower the death rate. This study also determined that women are more likely than men to obtain prescription opioids and to have prescription opioids present in post-mortem toxicology. While legal and illegal opioids pose a risk for men and women alike, prescribers should be educated to utilize the PDMP database to identify any active or past prescriptions for their patients, particularly females, and to provide coordinated care. To further reduce the opioid-related death rate, particular focus could be paid to the population of individuals being released from Massachusetts prisons. Their short-term risk of death from opioid-related overdose is 56 times higher than for the general public. Given the high risk of death in this population, better care coordination should also reduce the number of deaths.

The Chapter 55 legislation permitted the development and examination of a first ever cross-sector, linked dataset related to opioid deaths. The insights highlighted in this report would not have been possible without the capacity to create a confidential and secure dataset which was developed under the authority of Chapter 55. This approach also holds promise for other critical public health concerns. The unique partnership forged between government, academia, and industry to address a critical public health problem could form the roadmap for conducting complex analytic work in the future.

Appendix A: The Seven Chapter 55 Statutory Questions

This section presents the original statutory language of each question, restates it as a specific question, discusses its significance, presents results, and discusses findings. The analytic restatement is seen as an opportunity for the researchers to confirm they understand the underlying intent motivating the questions as presented in the legislation.

Note: *For privacy purposes, the data sets used for Chapter 55 analyses record information in the month of occurrence. No exact dates are used. In most cases, the presence or absence of <u>any</u> event was recorded in the month <u>not the count</u> of those events. Therefore, statements made about these data cannot directly be interpreted as averages but instead as the average number of months that any type of event occurred.*

<u>Statutory Question 1:</u> *"Instances of multiple provider episodes, meaning a single patient having access to opiate prescriptions from more than 1 provider"*

Analytic Question 1: *"Does having multiple prescribers increase a patient's risk of fatal opioid-related overdose?"*

Individuals who obtain prescriptions for opioids from more than one prescriber may be at greater risk of death. Receiving prescription opioids from multiple prescribers with the intent of deceiving the prescriber about the volume of opioids received is often referred to as "doctor shopping." While there is general acceptance that this is a risk factor for death, it is actually unknown how many persons in Massachusetts have died of an opioid-related overdose who also obtained prescriptions from more than one health care provider. This analysis provides an opportunity to examine the assumption that persons going to multiple providers for opioid prescriptions are at increased risk of death from opioid-related overdose. To answer this question, the Prescription Drug Monitoring Program (PDMP) dataset was linked to death certificates where the causes of death were noted. The linked dataset was analyzed for opioid prescriptions by patient, their demographics (age, gender, race, marital status, employment, and geography), the number of prescribers, and the outcome (opioid-related death, any death, or still living- no death). The analysis was conducted to determine the relationship between the number of prescribers and likelihood of dying of an opioid-related overdose.

Table A1: Relative Risk of Opioid-Related Overdose (2013-2014) by Number of Prescribers in a Three Month Period (2011-2014)

Number of Prescribers vs. Risk of Fatal Opioid-Related Overdose	1 – 2 Prescribers	3+ Prescribers	Relative Risk Ratio
Total Fatal Overdoses	648	808	
Total Individuals with at least 1 opioid prescription	~2.1M	~400,000	
Incidence	~1.5 per 10,000 per year	~10.1 per 10,000 per year	~7
Summary	Based on observed data, the use of 3 or more prescribers associated		

	with a 7-fold increase in risk of fatal opioid-related overdose

Discussion: Having three or more prescribers does not necessarily or automatically imply the patient is exhibiting the behavior colloquially known as "doctor shopping." There are notable exceptions, such as multi-provider practices in which prescriptions could be written for a single patient by multiple providers as part of normal operations. Having said that, there is still a clear pattern supported by the data that once three or more prescribers write prescriptions for opioids in a three-month window there is a marked increase in the likelihood of an opioid-related overdose. It should be noted that the three-month period that defined a multi-prescriber event did not have to occur within any specific amount of time prior to death. The relationship examined was whether any multi-prescriber event (i.e., 3 or more prescribers) was associated with an increased risk of death of an opioid-related overdose.

Limitations: The identifiers in the PDMP data set are imperfect. As such, it is highly likely that the multi-prescribers events are underestimated. That said, there is no reason seen in these data to suggest that these undetected cases would substantially alter the conclusions drawn here. If anything, individuals using multiple forms of identification might logically be assumed to be at higher risk than those not attempting to avoid detection.

Statutory Question 2: *"Instances of poly-substance access, meaning a patient having simultaneous prescriptions for an opiate and a benzodiazepine or for an opiate and another drug which may enhance the effects or the risks of drug abuse or overdose"*

Analytic Question 2: *"Does the addition of a prescription benzodiazepine to opioids increase the risk of fatal opioid-related overdose relative to taking opioids alone?"*

It is generally thought that there are more deaths from overdose in people who use more than one type of central nervous system depressant. To confirm this hypothesis, the PDMP dataset was linked to death certificates to analyze the death rates for those concurrently using opioid and benzodiazepines versus opioids only. The analysis was further refined with demographic break outs to allow for the relationships between drug combinations and demographic data. The linked dataset was analyzed for concurrent opioid and benzodiazepine prescriptions by individual and their demographics (age, gender, race, marital status, employment, and geography) to identify any relationship between the number and type of depressants taken and the likelihood of dying.

Table A2: Relative Risk of Opioid-Related Overdose (2013-2014) by Presence of Benzodiazepine in PDMP Records (2011-2014)

Presence of Benzodiazepine vs. Risk of Fatal Opioid-Related Overdose	Opioids Only	Opioids + Benzodiazepines	Relative Risk Ratio
Fatal Overdoses	812	692	
Total Individuals	~2.1M	~0.4M	
Incidence	~2.0 per 10,000 per year	~8.4 per 10,000	~4.2
Summary	Based on observed data, the history of benzodiazepine concurrent with opioid prescriptions is associated with a 4-fold increase in risk of fatal opioid-related overdose		

Discussion: Preliminary findings support the hypothesis of increased risk of fatal opioid-related overdose associated with concurrent prescriptions for opioids and benzodiazepines. This risk factor should be clearly communicated to all prescribers and dispensers. Further analysis should be undertaken to see if mediating factors like demographics, previous treatment history, and co-morbid conditions like mental health histories increase or decrease this risk.

Limitations: The identifiers in the PDMP data set are imperfect. As such, it is highly likely that the instances of concurrent prescriptions for opioids and benzodiazepines are underestimated. There is no reason seen in the data that these undetected cases would substantially alter the conclusions drawn here. If anything, individuals using multiple forms of identification might logically be assumed to be at higher risk than those not attempting to avoid detection.

Statutory Question 3: *"The overall opiate prescription history of the individuals, including whether the individuals had access to legal prescriptions for opiate drugs at the time of their deaths"*

Analytic Question 3: *"Did opioid-related overdose decedents have access to legal opioids, defined as a prescription filled around time of death?"*

It is not known if there are more overdose deaths from misuse of prescribed medications or illegal drug use - drugs consumed by people for whom they were not prescribed. To ascertain the difference, the PDMP dataset was linked to death certificates to analyze the death rates for individuals with no scheduled medications[41]. The analysis was further refined with demographic break outs so relationships with demographic data could be examined. As in Question 2, the linked dataset was analyzed for opioid prescriptions by individual and their demographics (age, gender, race, marital status, employment, and geography) to identify any relationship between the number, type of opioid, and use of non-prescribed medication and the likelihood of dying of an opioid-related overdose.

Table A3a: Proportion of Opioid-Related Overdose Decedents (2013-2014) with Prescription for Opioids (2011-2014)			
Prescription in Same Month of Death vs. No Known Prescription	Rx in Month of Death	No Known Rx in Month of Death	Proportion
Fatal Overdoses	183	2009	8.3%
Summary	Based on observed data, 8.3% of opioid-related overdose decedents had an opioid prescription in the same month as their death		

Table A3b: Proportion of Opioid-Related Overdose Deaths by Toxicology Report Findings (2013-2014) (Mutually Exclusive Groups)		
Proportion of Opioid-Related Overdoses by Toxicology Report Findings	Fatal Overdoses	Percent of Fatal Overdoses
Fentanyl + Definite Heroin	166	9.8%
Fentanyl + Likely Heroin	83	4.9%
Fentanyl	288	17.0%
Definite Heroin	547	32.3%
Likely Heroin	320	18.9%
Methadone	84	5.0%
Other RX[1]	154	9.1%
Buprenorphine	15	0.9%

[41] The Comprehensive Drug Abuse Prevention and Control Act of 1970 established an initial list of five classifications or schedules of drugs. The legislation also authorized two Federal agencies (the Drug Enforcement Administration and the Food and Drug Administration) to manage the five schedules and add or subtract drugs as needed.

Remainder[2]	35	2.1%
Summary	Based on observed data of opioid-related decedents with toxicology report findings approximately 83% had illicit or likely illicit substances in their system at time of death	

1. Other RX includes: Codeine (without Morphine), Hydrocodone, Hydromorphone, Oxycodone, Oxymorphone, and Tramadol
2. Remainder includes: toxicology screen only included a non-specific "opiate" test and no specific drugs were mentioned and toxicology screen did not include an opiate

Table A3c: Contribution of Specific Drugs in Toxicology Reports (2013-2014)

Contribution of Specific Drugs in Toxicology Reports	Fatal Overdoses	Percent of Fatal Overdoses[2]
Fentanyl	537	31.7%
Definite Heroin	713	42.1%
Likely Heroin	772	45.6%
Methadone	138	8.2%
Other RX[1]	358	21.2%
Buprenorphine	122	7.2%
Summary	Based on observed data, opioid-related decedents with toxicology reports, this table agrees with Table 3b in that greater proportions of opioid-related deaths contain illicit or likely illicit substances even after relaxing the mutual exclusivity constraint.	

1. Other RX includes: codeine (without morphine), Hydrocodone, Hydromorphone, Oxycodone, Oxymorphone, and Tramadol
2. These are not mutually exclusive categories so this column adds to more than 100%

Discussion: These three tables are used to estimate the proportion of opioid-related fatal overdoses that are attributable to prescriptions. Table A3a examines prescription history in the same month of death as a way to infer if the decedent had "legal access to opioids" at time of death. Table A3b notes chemicals found in toxicology screen and is presented in decreasing order of deadliness of the specific drugs[42] (Fentanyl and/or Heroin > methadone > other Rx > buprenorphine) present in the results. A person was put into a category based on the most deadly drug present in the results, regardless of the presence of other drugs. For example, if someone had Fentanyl and methadone present, they would be in the "Fentanyl" group. These groups are mutually exclusive. For clarification, "likely Heroin" is determined based on evaluation of the toxicology data in combination with information on prescribing of Morphine from the PDMP. Toxicology screens were considered where Morphine was present in the

[42] While "deadliness" is an imprecise term, drugs are considered deadlier when equivalent amounts are more likely to lead to death. In this case, equivalent amounts of Heroin or Fentanyl are more likely to result in death than buprenorphine.

absence of Codeine to indicate that the Morphine present was likely a metabolite of Heroin (and not prescription Morphine). A final important note regarding Table A3b is that in 14 of the 15 deaths where Buprenorphine was the only opioid present, the toxicology result was also positive for a benzodiazepine. Table A3c uses a similar identification methodology but relaxes the mutual exclusivity constraint. Both 3b and 3c, in tandem with 3a, lend support to an emerging hypothesis that illicit substances are the driving force behind opioid-related deaths.

Limitations: The identifiers in the PDMP data set are imperfect. As such, it is highly likely that the opioid prescription histories for some individuals are incomplete. Toxicology data also does not precisely identify all drugs. In some cases, metabolites of opioids may suggest that either a legal or illegal drug was ingested. However, there is no reason seen in the data that these limitations would substantially alter the conclusions drawn here.

Statutory Question 4: *"Whether the individuals had previously undergone voluntary or involuntary treatment for substance addiction or behavioral health."*

Analytic Question 4: *"Substance abuse treatment history (voluntary and involuntary) of Massachusetts residents who died of opioid-related overdose"*

Addiction treatment is intended to help individuals stop compulsive drug seeking and use by providing them with medication and behavioral coping skills as tools. Treatment can occur in a variety of settings, take many different forms, and last for different lengths of time. Because addiction is typically a chronic disorder characterized by occasional relapses, a short-term, one-time treatment is usually not sufficient. For many, treatment is a long-term process that involves multiple interventions and regular monitoring. There are a variety of evidence-based approaches to treating addiction. Treatment can include behavioral therapy (e.g. cognitive-behavioral therapy or contingency management), medications, or their combination. The setting for service delivery may be inpatient or outpatient. A clinical recommendation for treatment depends on the individualistic needs of a client.[43]

While most clients enter treatment voluntarily, some are committed to treatment through the court system. Section 35 of Chapter 123 of the Massachusetts General Laws provides a mechanism for a family member, police officer, physician, or court official to petition for a person whose alcohol or drug use puts themselves or others at risk to be involuntarily committed for substance abuse treatment. If the court approves the petition, the person is sent to the Women's Addiction Treatment Center (WATC) in New Bedford or the Men's Addiction Treatment Center (MATC) in Brockton to receive up to 90 days of inpatient substance abuse treatment similar to a combination of Acute Treatment Services (detoxification) and Clinical Stabilization Services. There has been a significant increase in the number of commitments through Section 35 in recent years. In 2007 there were 1,086 individuals committed through Section 35. In 2015 that number was 3,651.Given the increasing number of commitments it is important to assess the effectiveness of the involuntary commitments in reducing adverse consequences, specifically fatal opioid-related overdoses. The current analysis measures the risk of fatal opioid-related overdose for those with a history of involuntary commitment. Death certificate data from 2013-2014 were linked to treatment data from the Bureau of Substance Abuse Services (BSAS) from 2011-2014. The analysis was further refined with demographic break outs to identify any age differences.

Results: Of the 149,351 clients served between 2011 and 2014 in the BSAS treatment system, 9,464 people were committed to involuntary treatment. Clients who had ever been admitted through Section 35 were 88% White non-Hispanic, 58% male and had a median age of 32 years old. In contrast, clients

[43] There are evidence-based guidelines from SAMHSA and associations like American Society of Addiction Medicine (ASAM) and American Psychological Association (APA) for particular treatment services and for particular populations. For instance, there are guidelines for clinically evaluating patients to determine what is medically necessary and determine individualistic needs. The guidelines outline standards of care for stabilizing patients with withdrawal symptoms during detoxification and there are recommendations for maintenance care. The guidelines also specify MAT dosing for detoxification purposes as well as maintenance. Often, people with severe addiction are poly-substance users and require treatment for all substances abused.

with only a voluntary treatment history were 75% White non-Hispanic, 68% male and had a median age of 37 years old.

Based on admissions during the study period, 67% of clients with a history of involuntary treatment had at least one opioid-related admission, 83% reported prior mental health treatment, and 44% reported a prior overdose. For clients with only a voluntary treatment history, 46% had at least one opioid-related admission, 58% reported prior mental health treatment, and 18% reported a prior overdose. Clients who received involuntary treatment were 2.2 times as likely to die of opioid-related overdoses and 1.9 times as likely to die of any cause compared to those with a history of voluntary treatment only.

Table A4: Risk of Opioid-Related Overdose Death (2013-2014) by Treatment Status (2011-2014)

Treatment Type and Risk of Fatal Opioid Overdose	Voluntary Treatment	Involuntary Treatment
Fatal Overdoses	892	134
Total Individuals	139,887	9,464
Percent Fatal Overdoses	0.63%	1.4%

Discussion: Individuals afflicted with substance use disorders often don't acknowledge having a substance use problem nor seek treatment until they have significant health and social issues as a consequence of their compulsive behavior associated with their addiction. This means that most of the individuals presenting to treatment – voluntary or involuntary – have a multitude of social, behavioral, and health issues. For example, of the BSAS treatment population included in this study 58% reported prior mental health history. That number was even higher for those committed through Section 35 (83%). Section 35 permits the courts to involuntarily commit someone whose alcohol or drug use puts themselves or others at risk. Therefore, most individuals admitted through Section 35 are not necessarily ready for treatment. Table A4 provides evidence of significant differences in outcomes between those that received voluntary treatment and those that were committed to treatment involuntarily. A higher percentage of those that had a history of involuntary treatment died of an opioid-related overdose compared to those without a history of involuntary treatment. The differences in history of prior mental health treatment and nonfatal overdoses may indicate that these clients have complex co-morbid conditions and are at a higher risk of fatal overdose. There are significant limitations in both the mental health and substance abuse treatment systems in addressing the dually diagnosed. Mental health clinicians' knowledge of substance use disorders and overdose prevention is necessary given the significant overlap between these two populations. The same is true about substance abuse providers.

Further analysis must be conducted to assess other underlying risk factors, i.e.; prescription history, drugs of choice, co-morbid disorders (e.g., mental health conditions), and demographics that may put this subpopulation at a higher risk for overdose. However, the preliminary findings are not surprising given the involuntary nature of Section 35 and thus potential lack of client treatment readiness. Future analysis should also investigate the impact on risk of overdose death of the length of

engagement as well as the transition to step down services following voluntary and involuntary acute services.

Limitations: This analysis does not include all Section 35 commitments in the Commonwealth, only those admitted through WATC and MATC, which are facilities licensed and operated under contracts from MDPH. A significant portion of people committed were sent to the Massachusetts Committing Institution (MCI) in Framingham and the Massachusetts Alcohol and Substance Abuse Center (MASAC) in Bridgewater during this time period. As a result, the findings may not fully reflect the risk of overdose for this population. Furthermore, BSAS data does not represent all substance abuse treatment provided in the Commonwealth. BSAS only collects data from its contracted providers. Of the data that is submitted to BSAS, outpatient treatment data is incomplete and does not include all non-BSAS-paid services. BSAS does not collect data from providers that prescribe Vivitrol or from non-contracted buprenorphine providers. Including substance abuse treatment data captured in other systems such as APCD may help refine these findings.

Statutory Question 5: *"whether the individuals had attempted to enter but were denied access to treatment for substance addiction or behavioral health."*

Analytic Question 5: *"Does denial of service lead to an increased risk of fatal opioid-related overdose?"*

This analysis could not be conducted with the data currently available. Addiction is a complex problem partially because there is no single path to recovery. People with addiction can recover on their own without any treatment; some use self-help strategies to recover while others enter formal treatment.[44] Evidence suggests that few people with addiction actually seek treatment, and for those that do, they often wait for many years before entering treatment.[45] Only about 10% of individuals with a substance use disorder have had any treatment.[46] This lack of treatment for those in need is unlike any other area of health care. By comparison, approximately 50% of those with a mental health disorder receive treatment.[47,48] In 2014, the Substance Abuse and Mental Health Service Administration (SAMHSA) estimated that nationally 19.9 million persons aged 12 or older needed substance use treatment but did not receive specialty treatment in the past year. Of these 19.9 million persons, only 798,000 reported that they perceived a need for treatment for their use of illicit drugs or alcohol; this corresponds to about 4.0 percent of those that needed treatment. Thus, the large majority of the roughly 20 million people aged 12 or older who needed substance use treatment but did not receive specialty treatment did not perceive a need for treatment. Of the 798,000 persons who perceived a need for treatment, only a small percentage made an effort to get treatment (Figure A5).[49]

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[44] Klingemann and Sobell, 2007; Shaffer, 2007; Shaffer and Jones, 1989; Slutske, 2006; Sobell et al., 1996

[45] Kessler, R. C., Aguilar-Gaxiola, S., Berglund, P. A., Caraveo-Anduaga, J. J., DeWit, D. J., Greenfield, S. F., ... & Vega, W. A. (2001). Patterns and predictors of treatment seeking after onset of a substance use disorder.*Archives of general psychiatry*, *58*(11), 1065-1071.

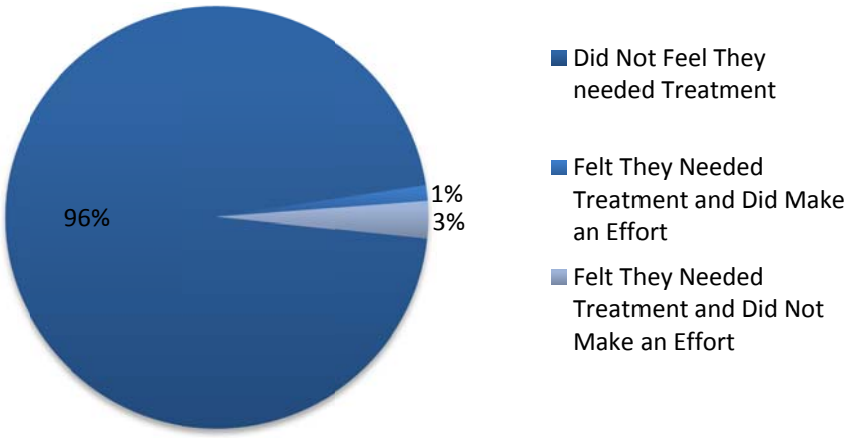
[46] Substance Abuse and Mental Health Services Administration. R*esults from the 2014 National Survey on Drug Use and Health: Summary of National Findings. R*ockville, MD: Substance Abuse and Mental Health Services Administration; 2015.

[47] Honberg R, Diehl S, Kimball A, Gruttadaro D, Fitzpatrick M. S*tate mental health cuts: A national Crisis. N*ational Alliance on Mental Illness2011.

[48] Mental Health America. Position Statement 14: The Federal Government's Responsibilities for Mental Health Services. 2011; http://www.mentalhealthamerica.net/positions/federal-role.

[49] Accessed at http://www.samhsa.gov/data/sites/default/files/NSDUH-DR-FRR3-2014/NSDUH-DR-FRR3-2014/NSDUH-DR-FRR3-2014.htm (figure 15 and 21)

Figure A5: Perceived Need for Substance Use Treatment among People Aged 12 or Older Who Needed Substance Use Treatment But Did Not Receive Substance Use Treatment in the Past Year (2014)



19.9 million needing but not receiving treatment

For individuals who would like to access treatment, a number of factors can complicate their access to care, including: homelessness, unemployment, childcare, criminal involvement, cost, wait time, distance to treatment, and other barriers that inhibit placement in treatment.

Historically, limited residential bed capacity created a bottleneck in the transition of clients from more acute levels of care into less intensive levels of treatment. As a result, providers created their own waitlists and maintained contact with clients awaiting residential beds. While this helped individual providers in serving their own clients, the redundancy of these lists made it impossible to measure the extent of unmet need throughout the state. BSAS constantly strives to better understand issues associated with access to treatment in Massachusetts. Under a current initiative, the Massachusetts Substance Abuse Helpline will maintain a centralized waitlist management process for residential treatment. The Substance Abuse Helpline tracks individual admissions into programs and will allow BSAS to report the unduplicated number of people across the state waiting for residential treatment as well as wait time.[50]

This BSAS initiative is the beginning of addressing issues associated with access to treatment. Similar initiatives must be supported to collect access-related information throughout the system. While waitlists will help to assure that most programs run at their full capacity, uniform and standardized assessment is necessary to make sure that clients admitted meet the clinical criteria for each level of care. Those not meeting the clinical criteria for residential levels of care should be redirected to appropriate treatment and wrap-around services such as housing and case management.

[50] Accessed at http://helpline-online.com/

Statutory Question 6: *"whether the individuals had received past treatment for a substance overdose."*

Analytic Question 6: *"Are those who have had a nonfatal opioid-related overdose more likely to die from a fatal opioid-related overdose?"*

It is assumed that people with substance use disorders who have a history of treatment for nonfatal opioid-related overdoses are at higher risk for eventually dying of an opioid-related overdose. As such, a history of past treatment would be a marker for individuals at higher risk for death from an overdose. There are two datasets that must be used to identify nonfatal opioid-related overdoses: the Massachusetts Ambulance Trip Record Information System (MATRIS) and Acute Case Mix. An algorithm that utilizes several pieces of information in MATRIS creates a flag to indicate opioid-related incidents. Both Case Mix and MATRIS data have been linked with death data where possible. A gap in this data is that MATRIS does not include information on opioid-related overdoses where an ambulance was not called. Case Mix data, which includes information on Emergency Department visits, Hospitalizations, and Observation stays, can be used to both corroborate the incidence of an opioid-related overdose in MATRIS and also to identify opioid-related overdoses that occurred when a person did not take an ambulance to the hospital. This data can also be linked with deaths in order to determine if the opioid-related overdose was fatal or not. None of our data systems can account for an opioid-related overdose where a person did not take an ambulance and did not end up in a Massachusetts hospital (i.e. a person who was revived with Naloxone by a friend or family member and did not seek additional treatment.)

Results: Using ICD9 codes[51], 6,335 individuals were recorded as having opioid overdoses in the Case Mix data file. Overdoses were recorded for these 6,355 people in 9,621 different months thus indicating that there were at least 1.5 overdoses per person using Case Mix data alone. *Since the Chapter 55 Case Mix data records only that one or more events occurred within a month and not the total number of events, it is not possible to compute a more accurate estimate of the average.* In Case Mix data, 71% had only one overdose. Of these, 3.7% died of an opioid-related overdose at some point in 2013 or 2014. Similarly, 29% had more than one overdose in Case Mix. Of these, 6.3% died of an opioid-related overdose at some point in 2013 or 2014. See Table A6a.

Table A6a: Overdoses by Person in Case Mix Data, Massachusetts (2011-2014)

Total ODs	Number	Percent	Cumulative Frequency	Cumulative Percent
1	4,490	70.9	4,490	70.9
2	1,127	17.8	5,617	88.7
3	389	6.1	6,006	94.8
4	171	2.7	6,177	97.5
5 or more	158	2.5	6,335	100.0

[51] The following ICD9 codes were used: 96500, 96501, 96502, E8500, E8501, E8502.

Using an algorithm developed in collaboration with the Centers for Disease Control and Prevention (CDC), 8,859 individuals were identified as having had a likely overdose from the MATRIS data. There were 10,995 overdoses recorded for these 8,859 individuals, thus indicating that there were 1.2 overdoses per person using the MATRIS data alone. *In MATRIS,* 83% had only one likely overdose. Of these, 4.5% died of an opioid-related overdose at some point in 2013 or 2014. Similarly, 17% had more than one likely overdose in MATRIS. Of these, 5.4% died of an opioid-related overdose at some point in 2013 or 2014. See Table 6b.

Table A6b: Overdoses by Person in MATRIS, Massachusetts (2013-2014)

Total ODs	Number	Percent	Cumulative Frequency	Cumulative Percent
1	7,344	82.9	7,344	82.9
2	1,134	12.8	8,478	95.7
3	242	2.7	8,720	98.4
4	82	0.9	8,802	99.4
5 or more	57	0.6	8,859	100.0

Finally, when Case Mix and MATRIS data were examined together, there were 13,154 people recorded as having or likely having an overdose event in 2013 or 2014. Although it is likely an underestimate for the reasons stated above, these overdose events occurred 20,619 event-months thus indicating that on average each individual had 1.5 overdose events per person. In Case Mix and MATRIS, 15% of the individuals had one or more overdose events recorded. Of these, 5.4% died of an opioid-related overdose at some point in 2013 or 2014. One-third (33%) of individuals with recorded overdose events could be found only in the Case Mix data. Of these, 4.0% died of an opioid-related overdose during 2013 or 2014. Slightly over half (52%) of individuals with recorded overdose events could be found only in the MATRIS data. Of these, 4.4% died of an opioid-related overdose during the study period.

Altogether, 9.3% of people with a fatal opioid-related overdose had at least 1 prior nonfatal overdose event recorded in either Case Mix or MATRIS. No differences were found by gender. In other words, the likelihood of subsequent opioid related death when preceded by a nonfatal overdose was the same for men and women. There were, however, differences by age. Compared to people aged 45+, those aged 27 and under and those 28 to 34 were nearly twice as likely to have a previous overdose event before death.

Discussion: There are at least 5 times as many nonfatal overdose events compared to fatal opioid-related overdose deaths. Each should be considered an opportunity to reduce the risk of subsequent opioid-related death. While the available data shows that a relatively small number of nonfatal overdoses precede a fatal overdose (9.3%), it is believed that this number is a significant underestimate. See the Limitations discussion below. Regardless, all opportunities should be explored to reduce the

opioid overdose death rate. For example, Emergency Medical Services (EMS) could receive alerts about high-risk communities or high-risk patient profiles. Heightened awareness could positively impact the death rate. Hospitals and EMS alike could be advised about the importance of reporting accurate data about fatal and nonfatal overdose deaths, so trends can be identified and addressed as soon as possible. Finally, since the majority of overdose events are only found in Case Mix data or MATRIS data but not in both, this suggests that a substantial number of people seek no treatment whatsoever following a nonfatal overdose. Educating users, friends, family members, and bystanders about the importance of seeking medical treatment following a nonfatal overdose is critical if the number of deaths is to be reduced.

Limitations: While only 9.3% of the individuals who had a fatal opioid-related overdose also had at least 1 prior nonfatal overdose event, it is very likely that this value is a significant underestimate of the actual number of opioid overdoses prior to opioid death that occurred in Massachusetts during 2013 and 2014. First of all, the Chapter 55 data was organized by months to protect the privacy of the individuals whose data was analyzed. Any nonfatal overdose occurring in the same calendar month as a fatal overdose would be masked and thus undercounted. Second, MATRIS data has known gaps. Some emergency medical services do not report data and others do not routinely record data that is sufficient for the algorithm to flag an ambulance trip as a likely overdose case. As least 30% of MATRIS data is missing in whole or in part. On this measure alone, it is almost certain that the actual number of individuals with overdose events preceding death far exceeds what is reported here. Third, Case Mix data is also likely to underestimate the total number of overdose cases. There could be coding errors, different coding approaches used by different hospitals, or possible physician concerns for patient privacy that could result in incomplete counts of overdose reporting in hospital settings. Finally, there are numerous testimonials of persons who survived an overdose after a being revived with Naloxone by a friend or family member. Anecdotal evidence suggests that many of these individuals did not seek additional treatment and thus were not included in the two data sets examined here. These individuals may have refused care by an EMT, refused to enter a hospital Emergency Department, or never sought any treatment whatsoever. Mathematical modeling of the full array of data available through Chapter 55 could shed some additional light on the percentage of cases. That work is ongoing.

Statutory Question 7: *"Whether any individuals had been previously detained or incarcerated and, if so, whether the individuals had received treatment during the detention or incarceration."*

Analytic Question 7: *"Does treatment during incarceration reduce likelihood of a fatal opioid-related overdose?"*

It is considered best practice to provide individuals that have a substance use disorder (SUD) with treatment as swiftly as possible. Furthermore, for individuals who are incarcerated and have a SUD, providing treatment behind the walls would be the optimal time to do so rather than waiting until release. It is hypothesized that those that receive SUD treatment behind the walls are less likely to die of an opioid-related overdose post-release in comparison to those that do not receive treatment prior to release. To confirm this hypothesis, an analysis was conducted by linking Massachusetts Department of Correction (DoC) data (jails are not included), which includes drug treatment received during incarceration in prison to death certificate data and the individual's demographic information.

There is a large overlap between people involved in the criminal justice system and people who use substances. In a survey of State and Federal prisoners, the Department of Justice's (DOJ) Bureau of Justice Statistics (BJS) estimates that about half of the prisoners in the US meet Diagnostic and Statistical Manual for Mental Disorders (DSM) criteria for substance use disorders, and yet fewer than 20 percent who need treatment receive it.[52,53] Of those surveyed, 14.8 percent of State and 17.4 percent of Federal prisoners reported having received drug treatment since admission.[54]

Inmates released from correctional facilities are at an increased risk of overdose;[55] this increased risk is due to a multitude of factors. First, evidence–based, individualized treatment may not be available within the correctional facilities. Second, due to prolonged abstinence and the resulting reduction in tolerance, a similar dose as the one used prior to incarceration may pose a significantly high risk of overdose. A large study conducted in Washington State found that within the first two weeks after release, the rate of death from overdose was 1,840 per 100,000 person-years (95% confidence interval, 1213 to 2677). In the Washington State study, inmates were 129 times as likely to die of an overdose compared to other state residents in the first two weeks after release. [56] The cases in this study were in the state system and did not include jails or houses of correction; which is very similar to Massachusetts.

During incarceration there is an opportunity to engage inmates with a substance use disorder in treatment. Of those surveyed by BJS, 14.8% of State and 17.4% of Federal prisoners reported having

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[52] Chandler RK, et. Al.. "Treating drug abuse and addiction in the criminal justice system: improving public health and safety." *Jama* 301.2 (2009): 183-190.
[53] Mumola CJ, et. Al.. "Bureau of Justice Statistics special report." *Washington, DC: Department of Justice* (2006).
[54] Ibid.
[55] Glaze L. E., Keuble D. Correctional Populations in the United States, 2013. Washington, DC: Bureau of Justice Statistics; 2014.
[56] Ingrid A. Binswanger, M.D., Marc F. Stern, M.D., Richard A. Deyo, M.D., Patrick J. Heagerty, Ph.D., Allen Cheadle, Ph.D., Joann G. Elmore, M.D., and Thomas D. Koepsell, M.D. Release from Prison – A High Risk of Death for Former Inmates.N Engl J Med 2007; 356:157-165January 11, 2007. http://www.nejm.org/doi/full/10.1056/nejmsa064115#t=articleTop

received drug treatment since admission.[57] It is also critical to refer them to community-based substance abuse treatment programs upon release to reduce the risk of overdose. Further analysis of linking DoC data with BSAS data will indicate whether inmates with a substance use disorder are: a) receiving treatment while incarcerated; and b) referred and subsequently admitted to the appropriate community-based treatment.

According to the National Institute on Drug Abuse (NIDA)[58], "only a small percentage of offenders have access to adequate services, especially in jails and community correctional facilities. Not only is there a gap in the availability of these services for offenders, but often there are few choices in the types of services provided. Treatment that is of insufficient quality and intensity or that is not well suited to the needs of offenders may not yield meaningful reductions in drug use and recidivism. Untreated substance abusing offenders are more likely than treated offenders to relapse to drug abuse and return to criminal behavior. This can lead to re-arrest and re-incarceration, jeopardizing public health and public safety and taxing criminal justice system resources. Treatment is the most effective course for interrupting the drug abuse/criminal justice cycle for offenders with drug abuse problems."[59]

Results: The DoC data includes people that were incarcerated and released during the study period (n = 25,209). 25% of the sample received treatment for substance abuse behind the walls. 12% of the fatal opioid overdose records linked with DoC data.

Table A7: Risk of Fatal Opioid Related Overdose by Treatment during Incarceration Status (2013-2014)

Treatment Status vs. Risk of Fatal Opioid Overdose	Treated while Incarcerated	Not Known to Have Been Treated while Incarcerated
Fatal Overdoses	37	84
Total Population	3758	10160
Incidence	~49.2 per 10,000 per year	~41.3 per 10,000 per year
Summary	There does not appear to be a large difference between treated versus not known to have been treated amongst those incarcerated during study period.	

[57] Mumola CJ and Karberg JC. Drug Use and Dependence State and Federal Prisoners. Accessed at: http://proxychi.baremetal.com/csdp.org/research/dudsfp04.pdf
[58] Accessed at https://www.drugabuse.gov/publications/principles-drug-abuse-treatment-criminal-justice-populations/introduction
[59] Ibid.

Discussion: There does not appear to be a difference in incidence of opioid-related overdose between those treated for SUD and those not known to have been treated for an SUD while incarcerated. Further analysis is needed to determine the risks associated with being incarcerated and risk of overdose.

A significant opportunity is missed in engaging these clients in substance abuse treatment while they are incarcerated. Recommendations for improving services and increasing understanding of these associations include:

- Increase the quantity and quality of substance abuse treatment within DoC facilities.
- Increase education for overdose prevention (e.g. abstinence while incarcerated and relapsing upon release poses a risk for overdose).
- Improve integrated mental health and substance use disorder treatment plan prior to release date, and ensure individuals are linked with these community supports at time of release.
- DoC data only includes a subpopulation of the individuals incarcerated in Massachusetts. This may impact the rates presented in Table A7. Future analyses using more comprehensive criminal justice data would shed better light on the associations between incarceration and risk for overdose.

Limitations: There are some limitations associated with using DoC data to better understand the intersection of opioid overdoses and criminal justice involvement in the Commonwealth. Even though there is a large overlap between those that are criminally involved and have a SUD, there is a large assumption in this analysis - not everyone who is incarcerated is in need of substance abuse treatment.

The treatment indicator within the DoC data does not specify the type of treatment an individual received, and it may in fact include self-help groups. The indicator also does not specify the date when the treatment was received; therefore, it is hard to determine for those that had a lengthy sentence whether the treatment was received closer to the beginning or end of a sentence, which may impact the overdose outcome.

DoC data includes incarcerations for those in prison and does not include data for people in jails or houses of correction (HoC). The data from DoC used in this analyses (e.g. those incarcerated during the study period and released) is only a subset of the individuals incarcerated within Massachusetts during this study period. This analysis does not included individuals that were not released during the study period, and it does not include individuals incarcerated within HoC. HoC servers a higher volume of inmates per year in comparison to DoC, primarily due to shorter sentences and those waiting trial within HoC. Due to this limitation, using DoC data to understand the intersection between fatal opioid overdoses and the criminal justice system in Massachusetts does not provide a full picture to determine associated risks. An additional limitation arises if residents of Massachusetts are incarcerated outside of Massachusetts, as that data is not captured by the DoC.

Appendix B: Dataset Descriptions

The following is a description of each of the ten datasets used for this report. Each description outlines the information collected, the frequency, the limitations, the lag time between data collection and data availability, the relevance to opioids, and the authorization for collecting the data. It is of note that *all* of the datasets are authorized through Massachusetts legislation, however, this is the first time these datasets have been used together to depict a more accurate and holistic picture of a public health problem.

Registry of Vital Records and Statistics (RVRS)[60] – Death Records[61]

What data are collected: Opioid-related deaths are the primary focus of this work and the most basic source of this information comes from death certificates filed with the Registry of Vital Records and Statistics (RVRS). The official cause of death and the manner of death (i.e., intentional, unintentional, or undetermined) are assigned by physicians and medical examiners. Each death certificate also includes demographic information such as age, race, Hispanic ethnicity, gender, educational attainment, marital status, and occupation. These basic demographics are recorded by the funeral director and are typically provided by a family member.

Availability of data: Mortality information is reported electronically using the Vitals Information Partnership[62] (VIP). The VIP system is web-based and receives information 24 hours a day seven days a week. For analytic purposes, data can be exported from VIP with all the data elements listed above. Opioid-related deaths and other complex cases are almost always referred to the Office for the Chief Medical Examiner (OCME) for determination of cause and manner of death. This results in a reporting lag for these deaths. That said, basic data on demographics is available on a near-real time basis.

Limitations of the data: As legal records, the information recorded on death certificates is considered highly accurate. However, some information like race, Hispanic ethnicity, educational attainment, marital status, and occupation are not always fully populated. Causes of death from the OCME often lag the date of death making some elements of death data less timely than others.

[60] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/
[61] The collection of death certificate data is authorized by MGL Chapter 46.
[62] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/vitals-information-partnership-vip.html

Bureau of Substance Abuse Services (BSAS)[63] – Substance Abuse Treatment Data[64]

What data are collected: Massachusetts Bureau of Substance Abuse Services (BSAS), of the Department of Public Health, is the single state authority responsible for regulating and licensing substance abuse treatment providers. The services provided range from acute detoxification to residential and outpatient based services. All treatment providers who receive funding from BSAS are required to submit data to BSAS to carry out the responsibilities listed under the law. The required data fields include but are not limited to: client characteristics, enrollment information, disenrollment information, services and outcomes. Currently, only treatment providers that receive funding from the Department submit this data to BSAS.

Availability of data: Processing of linked clients also allows us to construct treatment episodes and entire client histories. There is a 1-2 month lag between the time the data are reported and the time it is available for analysis/reporting from BSAS.

Limitations of the data: The BSAS data set poses several limitations. First, BSAS data does not represent all substance abuse treatment provided in the commonwealth. BSAS only collects data from its contracted providers. Of the data that is submitted to BSAS, outpatient treatment data is incomplete and does not include all non-BSAS paid services BSAS does not collect data from providers that prescribe Vivitrol or from non-contracted Buprenorphine providers. At the time of this analysis, Methadone data was incomplete. Due to challenges associated with recent system changes related to data submission, some Methadone providers have been unable to submit data. Data collected in regards to section 35 commitments are incomplete in the BSAS data set. For example, in 2015 there were 2,068 of Section 35 commitments were served in settings that are outside the scope of data submitted to BSAS (e.g. MASAC and MCI Framingham). As a result of these data limitations, it is possible that some of the analyses using BSAS treatment data may provide an incomplete picture.

Prescription Drug Monitoring Program (PDMP)[65] – Schedule II through V medications[66]

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[63] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/substance-abuse/

[64] The collection of detailed substance abuse treatment by BSAS is authorized under MGL Ch.111 B and E. All treatment providers are required to submit data to BSAS to carry out the responsibilities listed under the law. The regulations promulgated to carry out these responsibilities require the providers to submit data in a timely manner. The required data fields include but are not limited to: client characteristics, enrollment, disenrollment information, services and outcomes. Currently, only treatment providers that receive funding from the Department submit the required data to BSAS. BSAS uses this data for billing/payment and service planning purposes. Almost all BSAS licensed/contracted providers enter the required data through the Virtual Gateway. Assessment data collected at admission and disenrollment are entered into Enterprise Invoice Management/Enterprise Service Management (EIM/ESM) system daily or in batches. Data entry occurs at provider sites and is transmitted to BSAS on a monthly basis. The current database includes data from Fiscal Year 2000-2016. BSAS can readily report data at the provider level, the enrollment level, and the client level.

[65] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/hcq/drug-control/PDMP/

[66] The Department of Public Health's Office of Prescription Monitoring and Drug Control (OPMDC) established the Massachusetts Prescription Monitoring Program (MA PDMP) in 1992 pursuant to joint regulations (105 CMR 700.012) with the Board of Registration in Pharmacy (247 CMR 5.04).

What data are collected: Information about filled prescriptions for schedule II through V medications is reported electronically each business day to the Prescription Drug Monitoring Program (PDMP) in the Department of Public Health's Office of Prescription Monitoring and Drug Control (OPMDC) by all Massachusetts community, hospital outpatient and clinic pharmacies as well as from out-of-state mail order pharmacies that deliver to patients in Massachusetts. Schedules II through V medications consist of those prescription drug products with recognized potential for abuse or dependence (e.g., narcotics, stimulants, sedatives). Consequently, they are among those most sought for illicit and non-medical use. The specific medication as well as the dosage and the number of pills or amount are also captured. In order to facilitate the monitoring of individuals who receive scheduled medications, basic identifying information like full name, gender, date of birth, and full address are also recorded as well as information about the prescriber and dispensing pharmacy.

Availability of data: PDMP reporting is comprehensive for pharmacies within the Commonwealth with very few instances of non-compliance among pharmacies. PDMP data arrives daily and is considered complete and accurate for export and analysis within approximately two weeks.

Limitations of the data: The PDMP dataset has a few noteworthy limitations. First, methadone clinics do not report to the Massachusetts PDMP as they are exempt by statutory language. Specifically, the PDMP only collects data on prescriptions dispensed, and methadone in clinics is administered pursuant to medical order, not prescription. Methadone is only include when prescribed for pain. Second, controlled substance prescriptions dispensed by Veterans Administration (VA) facilities are not included. This represents a high risk population and a significant data gap. Third, prescription drugs that are obtained illegally (e.g., stolen, purchased on the street, etc.) are a potentially significant contributor to the opioid overdose epidemic and are not captured within an individual's PDMP history, but may be captured by the OCME toxicology screens. Finally, a filled prescription should not be interpreted to mean that an individual took all or even any of that medication. Linking these records with toxicology data can provide some insight into the proportion of scheduled medications that are illegally diverted for other purposes than originally intended.

Massachusetts Ambulance Trip Record Information System (MATRIS)[67] – Office of Emergency Medical Services (OEMS)[68]

What data are collected: The Department of Public Health's Office of Emergency Medicine (OEMS) established the Massachusetts Ambulance Trip Record Information System (MATRIS) in December 2010 as a statewide system collecting emergency medical service (EMS) incident data from licensed ambulance services. Under EMS System regulations, ambulance services are required to document each EMS call and include the data elements pertaining to the call that are specifically referenced in an administrative requirement issued by OEMS governing the statewide EMS minimum data set. MATRIS data elements are based on the National Emergency Medical Service Information System

[67] For more information see: www.mass.gov/dph/oems/matris

[68] The collection of detailed ambulance trip data by OEMS is authorized under 105 CMR 170.345(B).

(NEMSIS) Version 2.2.1 dataset standard developed in 2005. This includes demographic, clinical, operational, and billing data. Demographics required are patient age, birth date, gender, and patient home address. Also required are incident type, incident address, dates, times, destination facility type, destination facility name, and destination facility address. Patient name is not currently required but is submitted approximately 70% of the time. MATRIS can identify nonfatal-opioid-related events, even when the patient refuses transport to the hospital. MATRIS tracks when naloxone was administered either by the EMT or as "prior aid" by other first responders, (fire, police) or bystanders (friends, family). Evaluation on interventions provided by EMTs can be performed to correlate survival and other outcome rates when linked with outcomes from ED and death data.

Availability of data: Ambulance incident information is to be submitted into the MATRIS secure website electronically from all licensed ambulance services in Massachusetts within 14 days of the call; however frequency of submission varies by service. Many of the larger ambulance services have automated daily submission, while others can take longer to submit. There are currently over 6.4 million ambulance trip records in MATRIS. There were 1.3 million records in MATRIS for incidents occurring in both 2013 and 2014. There are 1.4 million for 2015 available for future analysis.

Limitations of the data: MATRIS has several limitations. The first is that the NEMSIS standard does not specifically identify incidents as being opioid-related, but rather "poisoning/ingestion". The second, the data are not uniformly reported by EMS providers. The third limitation is that the overall usability of the data submitted by ambulance services varies by provider, with roughly 30% of the provided data being partially or completely unusable. These issues are partially mitigated through the integration with other datasets listed above. Finally, whether a specific ambulance trip involves an opioid overdose is not a simple judgment. The classification of opioid trips was based on an algorithm developed in conjunction with the Centers for Disease Control and Prevention. Their assistance was invaluable.

Registry of Vital Records and Statistics (RVRS)[69] – Birth Records[70]

What data are collected: The collection and dissemination of this data are to facilitate the surveillance of births and birth trends in the state of Massachusetts, including those based on demographic information and data on birth outcomes. Data are reported to the Registry of Vital Records and Statistics (RVRS) by all licensed birthing hospitals and birthing centers and by city and town clerks if they are establishing a home birth that occurred in their city/town in Massachusetts. The birth data contains identifying information about the parents of record and the child. These data are critical to understand the health risk to a mother who delivers a Substance Exposed Newborn (SEN) or an infant with Neonatal Abstinence Syndrome (NAS).

[69] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/
[70] The collection of Confidential Birth Information is authorized under 105 CMR 350.000.

Availability of data: Natality information is reported electronically using the Vitals Information Partnership (VIP).[71] The VIP system is web-based and receives information 24 hours a day, seven days a week. Substantial quality control efforts are required to assess the accuracy and completeness of birth records. As a result, the final dataset of birth records is usually available by May of the following year.

Limitations of the data: As legal records, the information recorded on birth certificates is considered highly accurate. However, some information like race and Hispanic ethnicity are not always fully populated.

Massachusetts Cancer Registry (MCR)[72] – Cancer Staging[73]

What data are collected: The Massachusetts Cancer Registry (MCR), a database managed by the Department of Public Health, is a population-based registry that tracks the incidence of cancer within the Commonwealth. Since 1982, the MCR has captured key data elements such as date of diagnosis and cancer stage at diagnosis, in addition to various demographic data elements. For this purposes of this work, MCR data was included because palliative treatment for late stage cancers often includes the use of opioid medications to control pain. Being able to distinguish those cases of high opioid use for cancer treatment from cases where an individual may be abusing prescription medications was critical to this study.

Availability of data: Reporting facilities are required to report case level data to the MCR within 180 days of diagnosis or first date of patient interaction. Analysis of supporting documentation related to determining the *stage* of a cancer also takes considerable time. Typically, MCR data availability lags the calendar by approximately two years.

Limitations of the data: Defining the stage of a cancer is not an exact science. It is based on a number of written reports and laboratory tests. Furthermore, not all cancers cause significant pain even in late stages. These data can provide an indication that medications may have been prescribed for pain but they cannot definitively rule out the possibility that there was underlying abuse.

Office of the Chief Medical Examiner (OCME)[74] – Circumstances of Death and Toxicology Reports[75]

What data are collected: The OCME, a part of the Executive Office of Public Safety and Security, gathers a great deal of information about unattended and other deaths where the underlying causes may not be apparent. Not of all of the information collected is relevant to opioid overdose deaths,

[71] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/vitals-information-partnership-vip.html
[72] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/cancer-registry/
[73] The collection of detailed cancer incidence and staging by the MCR is authorized under Chapter 111, Section 111B.
[74] Accessed at http://www.mass.gov/eopss/agencies/ocme/
[75] The collection of death certificate data is authorized by MGL Chapter 38.

so the work reported here has focused on the *circumstances of death* recorded on the OCME intake forms and the toxicology reports used to determine the cause of death. The data field labeled "*circumstances of death" i*s a brief narrative that describes the setting and environment of an unattended death. It is often written by the State Police in the case of acute opioid overdoses. These narratives are analyzed by searching for the presence of key words. The toxicology reports describe the presence of hundreds of specific chemical compounds that might be found in the body of the decedent. This study has focused primarily on the presence of natural and synthetic opioids.

Availability of data: The intake forms that contain the *circumstances of death* narratives are usually available within about 72 hours of a case being accepted by the OCME. Toxicology screening and confirmatory tests are conducted by the Crime Laboratory run by the Massachusetts State Police as well as the NMS Labs (Willow Grove, PA). Toxicology tests lag the date of death by about 60 days.

Limitations of the data: Written narratives will provide initial impressions of the circumstances of death. As first impression, these can be misleading in some cases. Final causes of death must be provided by physicians and medical examiners. Toxicology results can be extremely complex to interpret. Levels of drugs found a decedent's tissue are affected by the timing of the test, the type of tissue, and other factors. Many drugs also metabolize into a variety of different chemical compounds. For all these reasons, toxicology results are generally examined in broad categories to simplify interpretation. OCME data are connected directly to the death records using the unique OCME ID number. OCME and RVRS death records link nearly 100% of the time. Finally, the vast majority of the toxicology records for early 2013 were only available on paper and thus not practical to include in this report.

Case Mix Database[76] – Inpatient hospitalization, emergency department visits, and outpatient observations managed by the Center for Health Information and Analysis (CHIA)[77]

What data are collected: The Case Mix data contains all inpatient hospitalizations, emergency department visits, and outpatient observation in the state. Massachusetts acute care hospitals are required to submit Case Mix data to the Center for Health Information and Analysis (CHIA) in order to track disease burden and associated costs statewide. Detailed information is available for each encounter, including geography (e.g., zip code, town, county, state, country), demographics (e.g., age, race, ethnicity), and costs by service (e.g., medical/ surgical, behavioral health), admission and discharge dates, diagnosis, and the facility providing patient care. Case Mix data can identify individuals who received past treatment for a substance overdose including healthcare encounters

[76] Accessed at http://www.chiamass.gov/case-mix-data/
[77] Massachusetts acute care hospitals are required to submit Case Mix data in accordance with Regulation 114.1 CMR 17.00.

associated with detoxification, psychiatric care, and overdose based on procedures rendered or diagnoses made when these services are offered by acute-care hospitals.

Availability of data: The Center for Health Information and Analysis (CHIA) receives data quarterly. Significant work is required to clean and harmonize the data across hospitals. As a result, there is approximately a one year lag between final data submission to CHIA by acute care hospitals and receipt of the data by DPH and other approved organizations.

Limitations of the data: The Case Mix data does not include hospital services rendered to Massachusetts residents by non-Massachusetts hospitals or hospitals operated by the Veterans Administration (VA), thus reducing the observable analytic universe. Similarly, CHIA does not currently collect information from behavioral health hospitals. Demographic data included in Case Mix is not considered as accurate as those recoded on birth of death records. Consequently, the linkage of these records to other datasets may be incomplete. Furthermore, the coding of encounters for overdose or for behavioral health services is not considered fully complete. Finally and possibly most important for the Chapter 55 project is that Case Mix data are available on a Federal fiscal year. The most recent data available is through 9/30/2014 which means that any data on nonfatal overdoses, substance abuse treatment, or mental health diagnosis codes won't be captured in the final three months of the study period.

Non-Scheduled Pharmacy Claims[78] – Massachusetts All Payer Claims Database (APCD)[79]

What data are collected: The Massachusetts All Payer Claims Database (APCD) is managed by the Center for Health Information and Analysis (CHIA). The APCD contains health and pharmacy insurance claims data from the approximately 80 private health care payers, public health care payers (including Medicare and MassHealth) and publicly-supported managed care organizations and senior care organizations across the entire state of Massachusetts. The APCD insurance eligibility files include basic identifying information like full name, address, gender, date of birth, race, ethnicity, and Social Security number. Most APCD data requested from CHIA focused on pharmacy claims for non-scheduled medications.

Availability of data: The APCD is overseen by CHIA, the independent state agency responsible for collecting, cleaning, maintaining, and managing access to the data. Data are reported out once a year and each report contains all data from the previous calendar year. The newest version is available approximately 6 months after the close of the preceding calendar year.

Limitations of the data: The APCD forms the backbone or spine of the linked datasets. Its completeness and accuracy are critical to the entire effort. In recent years, CHIA has expended

[78] Accessed at http://www.chiamass.gov/ma-apcd/

[79] CHIA has statutory authority to collect data from both public and private health care payers under Massachusetts General Laws Chapter 12C, section 10. By July 2010, Regulations 114.5 CMR 21.00 and 114.5 CMR 22.00 formally established the APCD in Massachusetts.

significant resources to link records across payers. The current APCD contains roughly 15 million unique records which is substantially above the 6.3 million residents in Massachusetts. Most of these records are single records unconnected to a full set of identifiable records. Other analyses undertaken for this project suggest that the unique records prepared for the APCD serve the purpose intended. Other known limitations of the APCD include exclusions such as Workers' Compensation, TRICARE/Veteran's Health Administration, and the Federal Employees Health Benefit Plan claims. Additionally, uninsured individuals (approximately 3% of the state's population) are not captured. Finally, healthcare services provided but paid for out of the patient's own finances, e.g., cash payment for a convenience care clinic service like a strep throat culture, are excluded because these services do not generate claims.

Department of Correction (DoC)[80] – Incarceration and Treatment[81]

What data are collected: The Department of Correction (DoC), a part of the Executive Office of Public Safety and Security, is required by statute to maintain adequate records of persons committed to the custody of the department. In addition, DoC must establish and maintain programs of research, statistics, and planning, and conduct studies relating to correctional programs and responsibilities of the Department. To achieve those goals, DoC maintains a database of individuals incarcerated in Massachusetts prisons. This database includes the substance abuse treatment received by prisoners. Identifiers like full name, gender, date of birth and Social Security numbers are also included.

Availability of data: As releases from prison are routine, these data are kept current.

Limitations of the data: DoC data includes incarcerations for those in prison and does not include data for people in jails or houses of correction (HoC). The data from DoC used in this analyses (e.g. those incarcerated during the study period and released) is only a subset of the individuals incarcerated within Massachusetts during this study period. This analysis does not included individuals that were not released during the study period, and it does not include individuals incarcerated within HoC. HoC servers a higher volume of inmates per year in comparison to DoC, primarily due to shorter sentences and those waiting trial within Hoc. Due to this limitation, using DOC data to understand the intersection between fatal opioid overdoses and the criminal justice system in Massachusetts does not provide a full picture to determine associated risks. An additional limitation arises if residents of Massachusetts are incarcerated outside of Massachusetts as that data is not captured by the DoC.

[80] Accessed at http://www.mass.gov/eopss/agencies/doc/

[81] The collection of detailed incarceration data by DoC authorized under MGL c. 124, s. 1(j) and MGL c. 124, s. 1(k).

Appendix C: Additional Single Table Discussion

Additional Single Table Discussion: Prescription Monitoring Program (PDMP)

Key Findings: The Chapter 55 work has allowed for a robust analysis of key PDMP measures with the other linked datasets. Looking at PDMP data alone, it is notable that although there has been a seven-percent annual increase in Schedule II filled prescriptions since CY 2000; a slowing in that trend in the most recent years has been observed. This is primarily attributed to a reduction in opioid prescribing in the recent time period. It is too early to determine whether this reduction in opioid prescribing will result in fewer opioid-related overdose deaths over time. The Chapter 55 work has highlighted the alarming increase in opioid-related overdose deaths attributed to Heroin and most notably Fentanyl. How prescription opioid use/abuse impacts transitioning to these illicit drugs will be a key area of focus moving forward and the Chapter 55 linked databases will play a critical role in addressing these questions.

Other key findings identified from analyzing the PDMP dataset are that while 2 in 5 Massachusetts adults had a prescription for an opioid during the study period, only 8 percent of people who died from an opioid-related overdose had legal access to prescription opioids within a month of their death. This is critical information because without linking the datasets and reviewing medical examiner data, there is no way to estimate the extent to which diversion of prescription opioids plays a role in the opioid overdose epidemic. Additionally, the linkage with PDMP and death files highlights the significance of polysubstance use in risk of overdose death. The data show that having a concurrent prescription for opioids and benzodiazepines results in a four-fold increased risk of opioid-related death.

One additional key finding from analyzing the PDMP dataset concerns the issue of individuals obtaining controlled substance prescriptions from multiple providers (i.e., visiting different prescribers for similar or same controlled substances and having these prescriptions dispensed at different pharmacies). The occurrence of multiple provider episodes (MPEs) can be identified from analyses of the PDMP data. Linkage with the death records provides a more complete understanding of the risk that this type of activity poses in opioid-related overdose deaths. Table C.1 presents the opioid-related overdose death incident rate analysis of having different numbers of prescribers and pharmacies (0 = individuals who died were not linked to any prescription records in the PDMP). The findings clearly show the increased incidence (more than 3-fold) of having 3 or more different prescribers compared to only 1 prescriber who writes prescriptions for controlled substances. Even more striking is the apparent increase in overdose incidence when obtaining these controlled substance medications filled from three or more pharmacies compared to using only one pharmacy (18.34 versus 1.09, respectively). This apparent risk that having dispensed controlled substance prescriptions from multiple pharmacies can help inform policy moving forward.

Table C.1: Incidence of opioid overdose deaths associated with multiple provider episodes (2011-2014)				
	Prescribers			
Incidence (per 10,000 per year)	0	1	2	3+
Opioid Deaths	0.97	0.99	2.72	9.73
	Pharmacies			
Incidence (per 10,000 per year)	0	1	2	3+
Opioid Deaths	0.97	1.09	4.28	18.34

Additional Single Table Discussion: Massachusetts Ambulance Trip Record Information System (MATRIS)

Key Findings: By utilizing the linkage authorized by Chapter 55 with MATRIS and death data, EMS response was shown to be highly successful in preventing fatal overdoses. The finding that 95.8% of the patients with an opioid-related ambulance trip did not die during the study period and only 18.6% of opioid-related decedents had one or more opioid-related ambulance trips confirms that 911 response leads to a high reversal rate. Overdose campaign strategies encouraging EMS activation should continue. Of people who had an ambulance trip for a nonfatal overdose prior to their fatal overdose, 29.3% did not have an ambulance trip for their fatal overdose. This indicates that there are possible missed opportunities for interventions after the non-fatal overdose. Some examples of these interventions are: recovery coaching, treatment, and education on withdrawal and tolerance. This finding also supports the need for further promotion of the Good Samaritan Laws to encourage calling 911 for an overdose without fear of legal repercussions.

Additional Single Table Discussion: Massachusetts Cancer Registry (MCR)

Key Findings: The MCR data are included in this project so that cancer diagnosis can be controlled for in multivariate analyses. It is not intended to be analyzed separately. There is a well-known association between late stage cancer diagnosis and opioid prescribing. It was important to be able to take this into account when looking at risk of opioid death as it relates to opioid prescribing patterns.

Additional Single Table Discussion: Department of Correction (DoC)

Key Findings: Data from the Department of Correction (DoC) included information on all inmates who have been released from DoC incarceration between January 1, 2011 and December 31, 2014. The cohort included 25,209 inmates who had a total of 38,961 releases from prison. Prior studies have demonstrated that inmates face an increased risk of death, compared with the general population,

following release from prison in the United States and abroad[82,83]. Since only 2013-2014 deaths were available, inmates released only during this same time period were used to calculate the risk of death faced by those inmates after release from prison and investigate whether they had a higher risk of death after release.

Of the 14,533 inmates released in 2013-2014, 287 died from all causes and 121 consequently died from an opioid-related overdose during the study period. In this group, 42.2% (n=121) died from an opioid-related overdose. In comparison, for the total population in the state, opioid-related deaths accounted for only 2.1% (n=2,192). The leading cause of death was injuries of all intents: 124 unintentional injuries, 16 suicides, 9 homicides and 5 injuries of undetermined intent. The second leading cause of death were ill-defined conditions-signs and symptoms (30 deaths), cancer (20 deaths), heart disease (20 deaths), and chronic liver disease (9 deaths). Looking at the leading cause of death, we see that these were mostly unintentional poisonings involving opioids. Deaths from opioid-related overdoses were more common among persons younger than 45 years, whereas deaths from cardiovascular disease and cancer were more common among those 45 years of age or older. Inmates who died from opioid-related overdoses were significantly younger than those inmates that died from other causes (35.0 vs. 47.0 years). See Table C.3.

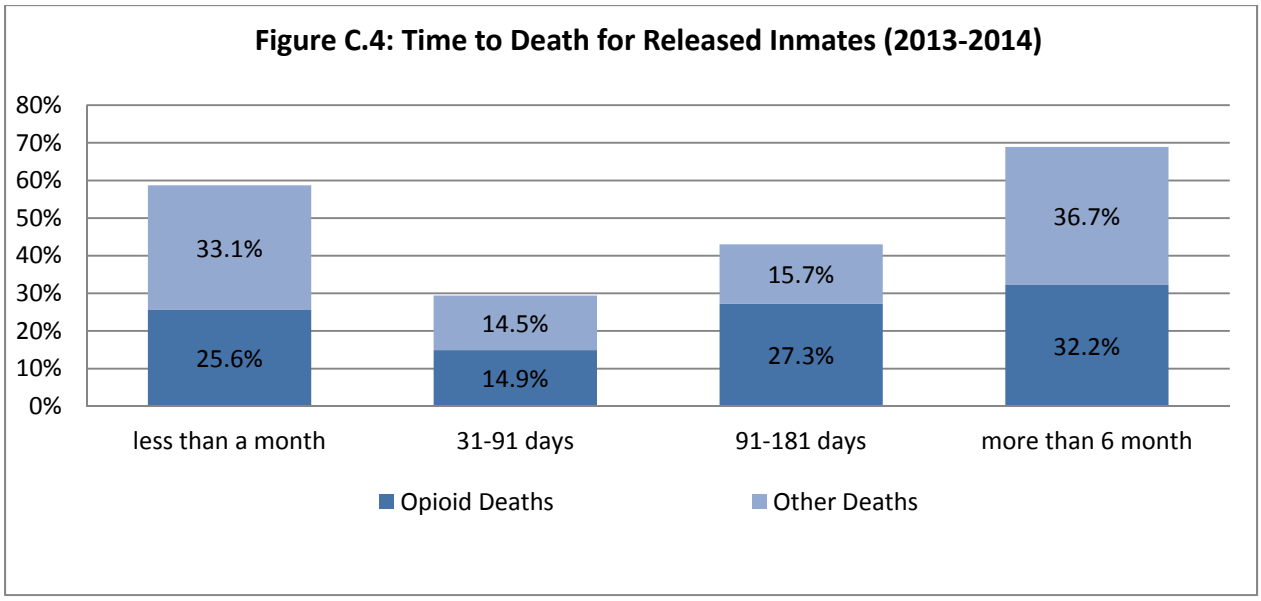
Table C.3: Mean Age at Death with 95% Confidence Intervals (2013-2014)

Age At Death (years)	Mean	Lower 95%	Upper 95%
All deaths	41.9	40.3	43.6
Opioid Deaths	35.0	33.2	36.7
Non-Opioid Deaths	47.0	44.7	49.2

Nearly one-quarter of released inmates in 2013-2014 who died of an opioid-related overdose died within 30 days of release. The mean time from release to death was 13 months, ranging from dying within the same month as release (or in prison) to 42 months later. See Figure C.4.

[82] Merrall EL, Kariminia A, Binswanger IA, *et al*: Meta-analysis of drug-related deaths soon after release from prison. Addiction 105: 1545–54, 2010

[83] Binswanger IA, Stern MF, Deyo RA, *et al*: Release from prison: a high risk of death for former inmates. NEngl J Med 356:157–65, 2007



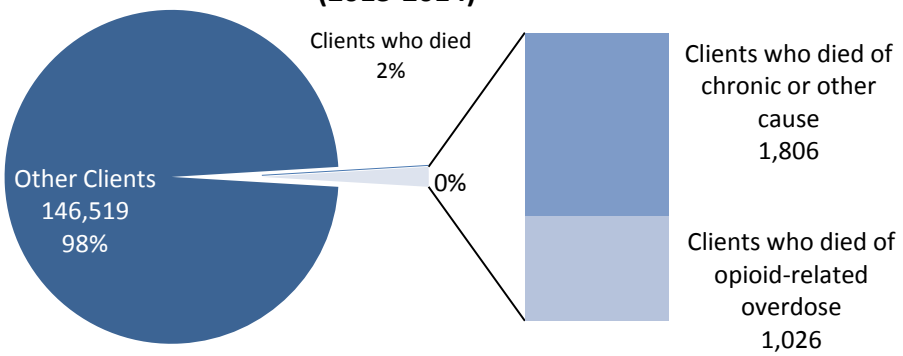
Additional Single Table Discussion: Bureau of Substance Abuse Services (BSAS)

Key Findings: Between 2011 and 2014, 149,351 people received addiction treatment or other recovery related services from providers that report to the BSAS. These clients were 76% white non-Hispanic, 68% male, had a median age of 37 years. Of the 149,351 people utilizing services, 87% (130,452) had at least one admission in 2011-2014; the remaining 13% utilized services in programs in which they were admitted to prior to 2011. Based on clients with admissions in the study period, 60% reported prior mental health treatment and 20% reported a prior overdose.

Additionally, 47% had at least one opioid-related admission. Similarly, people admitted to treatment reporting opioid use has increased since FY 2012. Of the clients reporting an opioid problem, the percentage that report a Heroin problem has increased over the last several years, as those that report a problem with other Opioids has simultaneously decreased. In fact, treatment admissions for non-Heroin opioids increased from 3.7% of all opioid admissions in 2000 to 21.8% in 2011 and then dropped to 9.9% in 2014. This suggests that Heroin is a major contributor in regards to the increase in treatment admissions for Opioid addiction. Although it is important to note that prescription opioids still play a role in opioid addiction and overdose. Over half of the individuals who received treatment through BSAS had a prescription for an Opioid in the PDMP during the study period.

2,832 of the 149,351 clients (1.9%) died in 2013 and 2014. Of these deaths, 1,026 were due to opioid-related overdoses (36.2%). The remaining 1,806 deaths were due to chronic disease or other causes (Figure C.6).

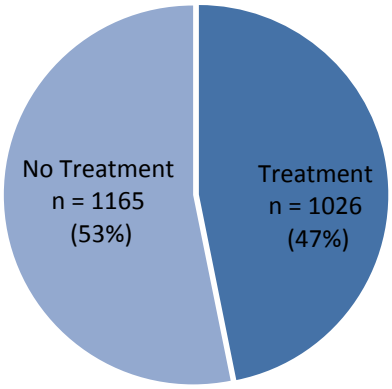
Figure C.6: BSAS Addiction Treatment (2011-2014) Clients and Deaths (2013-2014)



Total BSAS clients N = 149,351

Of all confirmed opioid-related overdose deaths in 2013-2014 (n = 2,192), 47% (n=1,026) utilized addiction treatment and recovery services in BSAS system (Figure C.7).

Figure C.7: Confirmed Opioid-Related Overdose Deaths (2013-2014) & Addiction Treatment in BSAS System (2011-2014)



Demographics of Fatal Opioid Overdoses among BSAS clients

Among the 1,026 people who died of an opioid-related overdose and utilized addiction treatment and recovery services in the BSAS system, 85% were White non-Hispanic, 71% were male, and they had a median age of 36 at the time of death.

BSAS Treatment Population: Comparing No Death vs. Fatal Opioid overdose

BSAS clients that died of an opioid-related overdose in 2013 and 2014 utilized more acute services within the BSAS treatment system relative to other clients. Of the 1,026 people utilizing services, 91% (933) had at least one recent admission in 2011-2014; the remaining 9% utilized services in programs in which they were admitted to prior to 2011. Based on these 933 clients with recent admissions, 87% had at least one opioid-related admission, 79% reported prior mental health treatment, and 51% reported a prior overdose.

Key Take Aways

- Treatment admissions for opioid problems now account for more than half of all BSAS treatment admissions.
- Treatment admissions for non-Heroin opioids increased from 3.7% of all opioid admissions in 2000 to 21.8% in 2011 and dropped to 9.9% in 2014.
- Over half of persons who received treatment through BSAS had a prescription for an opioid during the study period.
- Nearly half of individuals who died of opioid-related overdoses had a confirmed addiction treatment history in the BSAS system.
- Of the BSAS clients who died of an opioid-related overdose, 60% utilized acute treatment services and 91% had a recent admission to any BSAS treatment or service.

Appendix D: Data Linkage

Data linkage for the Chapter 55 work was conducted by the Center for Health Information and Analysis (CHIA) in consultation with the Department of Public Health (DPH). Six levels of matches were tested between individual Chapter 55 datasets and identifiers found in the All Payer Claims Database (APCD). All matches were deterministic. A conservative approach to matching was used, so no "near" or "close" matches were considered. In other words, all successful matches had to be exact at one of six levels. The complete matching scheme is described below. The most reliable match is a "1", and so on down the chart to the least reliable, a "6".

Match Level	Identifiers To Be Matched
1	Exact match on first name, last name, Social Security number, gender, birth date, street address #1, street address #2, town of residence, and zip code.
2	Exact match on last name, Social Security number, gender, birth date, town of residence, and zip code.
3	Exact match on Social Security number, gender, and birth date.
4	Exact match on first name, last name, gender, birth date, street address #1, street address #2, town of residence, and zip code.
5	Exact match on first name, last name, gender, birth date, town of residence, and zip code.
6	Exact match on first name, last name, gender, and birth date.

CHIA processed each Chapter 55 file independent of all other files. To speed the process of the linkage work, there was no requirement for CHIA to perform data standardization or to deduplicate the data within or across files. Since data fields, collection methods, oversight, and quality vary from source to source – and even record to record – it is possible that "John Smith" got a Level 1 match in ***File1*** but then the same "John Smith" appeared twice in ***File2***, getting a Level 2 and a Level 3 match due to algorithm rules and/or missing data. Alternatively, the various John Smiths may not be related. Without a focused deduplication effort, or a secondary weighted probabilistic match, it is impossible to know how often this might have occurred. Other tests of reliability of the matching scheme indicated that this was not a frequent occurrence. If duplicates were found within a file, each of these records was assigned the same project-specific ID (see Appendix F, de-identification). A summary of the matches across all datasets can be found in Table D.1 below.

Table D.1: Linkage rates across Chapter 55 datasets.									
	DEATHS 103,505	**PDMP 3,475,545**	**BSAS 149,351**	**MATRIS 515,229**	**MCR 147,066**	**OCME 4,832**	**Case Mix 1,333,862**	**APCD 14,484,061**	**DoC 25,209**
DEATHS		80508	2832	47103	20202	4781	55616	103499	565
Column %	X	2.3	1.9	9.1	13.7	98.9	4.2	0.7	2.2
Row %		77.8	2.7	45.6	19.5	4.6	53.7	>99.9	0.6
PDMP			107658	37617	122109	3504	892716	3470474	16814
Column %		X	72.1	1.1	83.0	72.3	66.9	24.0	66.7
Row %			3.1	7.3	3.5	0.7	25.7	99.9	0.48
BSAS				37811	1679	1340	55956	149252	13131
Column %			X	7.3	1.1	27.7	4.2	1.0	52.2
Row %				25.3	1.1	0.9	37.5	>99.9	8.8
MATRIS					25138	2864	221811	514866	8664
Column %				X	17.1	59.3	16.6	3.6	34.4
Row %					4.9	0.6	43.1	99.9	1.7
MCR						99	67898	146673	234
Column %					X	2.1	5.1	1.0	0.9
Row %						0.1	46.2	99.7	0.2
TOX							2332	4815	302
Column %						X	0.2	0.03	1.2
Row %							48.3	99.6	6.3
Case Mix								1333862	10298
Column %							X	9.2	40.8
Row %								100	0.7
APCD									25205
Column %								X	100
Row %									0.2
DoC									
Column %									X
Row %									

Appendix E: Data Quality and Strategies for Handling Missing Data

Data Quality Analysis:

Each data owner cleaned their data according to their usual standards. To provide some uniformity to the process of data cleaning, DPH conducted a four-step cleaning process for all analytic datasets that it held prior to delivery to the server on which all Chapter 55 datasets were stored. The first step was to screen for duplicate records; the second step was to measure the distributions of categorical and numeric variables; the third step was to assess overall data environment quality by examining various aspects of the linkages across tables; and the fourth step was to compare the linked and unlinked records for differences in demographic categories.

Step 1. Evaluation of duplicate identification values

A count of identification values was performed and compared to a count of distinct identification values for each analytic dataset. The ratio of those values indicated the level of duplication if any. The level of record duplication detected was minimal.

Step 2. Distribution of Categorical and Numeric Variables

The larger the dataset the more likely it is to contain some invalid or unknown values. For example, no age should be a negative number and it is unlikely that any age is above 110. In order to assess the quality of each variable across the datasets, it was important to quantify the frequency, percent, and cumulative percent of all valid and invalid information. High percentages of invalid data were corrected wherever possible. Assessing the quality of each numeric variable was extended to include binary variables represented by 0/1. The summary of numeric variables included quantifying the mean, maximum, and minimum values and a flag to indicate if the variable was binary. These values were calculated across all analytic datasets and applicable variables. As above, the rate of invalid data detected was minimal.

Step 3. Overall Environmental Quality

The data were evaluated for overall quality, which included determining how much overlap exists across datasets. Each unique ID was assessed for presence in each dataset and ultimately in how many and in which specific datasets the unique ID appears. The total number of ID's with a single hit as well as the total number of ID's with more than one hit were reported. Inconsistencies were evaluated based on prior knowledge of what constitutes irregular patterns among tables in which ID's appear.

Step 4. Linked Versus Unlinked Data

A six-level deterministic matching algorithm was used for matching each dataset with the APCD-Spine. For more information about this process and the percentage of matches for each dataset, please see Appendix D. Before proceeding with any analysis, it was important to understand whether there were any pronounced biases between those records that were linked to the APCD-Spine and those that were not. Individual records from original sources, such as MATRIS ambulance trip data, were excluded from the analytic environment when a match could not be

made to the CHIA spine. By comparing the demographic patterns between the linked and unlinked records, it is possible to gain a basic sense of whether the linking produced a biased dataset and thus required greater care when interpreting the results. Upon review of the datasets provided by the participating organizations, in general, there were no systemic or nonrandom patterns with two exceptions:

- 30% of all records, 25% of opioid-related records, provided by MATRIS for ambulance trips were unlinked due to missing identifiers, such as first name. This was observed to be ambulance-service-specific and therefore geographically biased, causing artificially low representation of Boston. To address this issue missing geographic information was imputed for individual rides, not patients. By imputing the geographic information, ambulance trip data could be analyzed on an aggregate basis and the 25% of opioid-related events that would have been excluded were able to be used. See the section below titled "Data Strategies" for further information about this work.
- The Department of Corrections dataset also exhibited statistically significant deviations when comparing the linked and unlinked comparison. This dataset is being examined to understand the root cause of the deviations and to determine what, if any, adjustments need to be made. The current hypothesis is that longer duration prison terms lead to shorter windows of opportunity to acquire health insurance or file a health claim and therefore appear in the Mass APCD.
- Given the large data files in use, many demographic categories showed statistically significant difference but these were not considered to be of practical importance.

Missing Data Strategy:

In any complex analytics project, data quality is a key consideration. High quality data leads to high quality results and trustworthy interpretations. Knowing the importance of the opioid threat and the criticality of providing trustworthy interpretations, the project team developed a data quality strategy to overcome known limitations in the data. These limitations are caused by imperfections in the data capturing mechanisms. For example, some fields or data elements may be optional from an operational perspective, but turned out to be critical from an analytics perspective. For this Chapter 55 Report, the team adhered to two guiding principles, identified three types of archetypal data limitations, and devised five approaches to deal with them.

Guiding Principles:

The guiding principles informed the strategy by helping to frame the problem and align the solution to the aims of the Ch. 55 Report. The first guiding principle was to be analytically rigorous and valid. This principle should allow readers to focus on results, conclusions, and interpretations rather than flaws in methodology. The second guiding principle was that a false positive was less harmful than a false negative. What this means is that the approach slightly biases toward over-reporting of critical incidents rather than under-reporting since the data capture is inherently biased towards under-capturing. To illustrate this, consider a nonfatal opioid-related overdose. The data may show 1,000 for a given time period in a given geographic area. In reality, however, if perfect data was available the real

number may be as high as 1,100. It is well known that some nonfatal overdoses are not recorded if the person is not transported by EMS or is seen in a hospital emergency department. The strategy taken here seeks to modify the data to get closer to the true value of 1,100 by using the observed values as a minimum instead of a mid-point for confidence intervals.

Common Data Limitations:

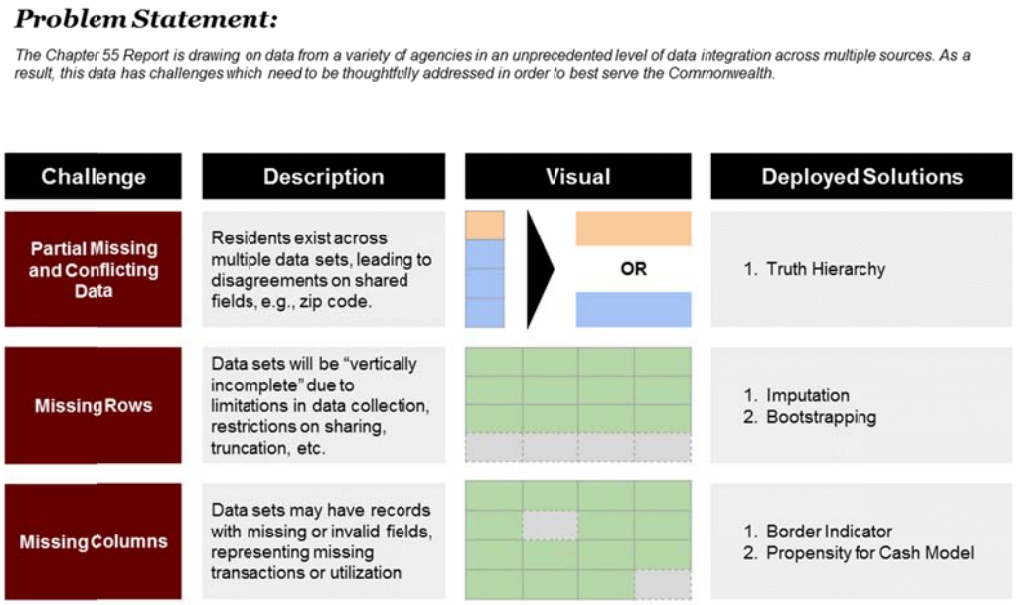
As the word implies, common data limitations are not unusual. They are seen in many datasets including the Chapter 55 datasets. They are partially-missing or conflicting data, missing columns, and missing rows. Partially-missing or conflicting data occurs when the linkage across datasets results in either one dataset having a field that another lacks (e.g., a death record for a particular individual may contain their gender while their PDMP record may not), or when two datasets have different values for the same field (e.g., a death record for a particular individual may indicate they are male while their PDMP record indicates they are female). A missing column arises when a one or more types of information are not included in a dataset. For example, education level is only recorded within the death records but not the other nine Chapter 55 datasets. A missing row arises when either a record for an individual is never recorded but service was provided or when an event occurs that is normally recorded but no record is ever made.

Data Strategies:

To address these limitations, five strategies were deployed. The first strategy addressed the partial and conflicting data challenge by establishing a "trust hierarchy" that created a single source of truth for each resident's demographic data based on reliability of the respective sources of that data. The second strategy addresses missing columns caused by "border leakage", a problem that arises when services are rendered outside of the State of Massachusetts and therefore not captured by any governmental agencies. To address this challenge, a border flag was created and appended to each record with a residence zip code that was near any Massachusetts state border. This variable could then be used as a covariate to help manage the risk of services missing due to geographic constraints. The third strategy dealt with missing columns due to cash payments. Since healthcare is so heavily claims and payer-oriented, when a resident chooses to pay cash instead of use their insurance for select services, those records would not be found in the data, with one notable exception which is the PDMP. By using the PDMP's cash payment indicator, researchers developed a Propensity to Use Cash Model, which helps account for utilization that may be hidden due to cash payments. To address missing rows, a SAS Macro was developed to create confidence intervals around summary statistics using a technique known as bootstrapping. This methodology incorporates uncertainty about the data to resample known data over and over again. This resampling leads to multiple simulated alternatives from which a distribution of outcomes can be derived and used to infer what the actual true value would be with perfect data. For example, data may show 50 opioid-related deaths in a given month, by using this methodology, one could observe that 90% of simulated alternative samples are below 57 opioid-related deaths and therefore establish a confidence interval that the true number of opioid-related deaths is between 50 and 57 for that specific month. The difference between observed and calculated is based on the trustworthiness of the underlying datasets. Finally, the fifth solution to missing data was to

impute missing geographic fields in MATRIS ambulance rides that were excluded from the integrated data warehouse due to a lack of matching. This approach allowed the researchers to use data for aggregate analytics despite not being able to use it to analyze individuals, thus retaining more of the information content of the MATRIS data extract. Without this imputation approach, roughly 25% of opioid-related ambulance rides would have had to have been excluded from the Chapter55 Report. See Figure E.1 for a visual depiction of these strategies.

Figure E.1: Visualization of Data Strategy



Appendix F: Data Privacy and System Architecture

A determination was made at the outset of the Chapter 55 project to be able to examine all datasets in relation to each other. This required the development of a linkage or crosswalk so that individuals in one set could be located in the others, yet without revealing the identity of the matched person. The privacy concerns about holding, managing, and processing direct identifiers for so many sensitive datasets are considerable, and the processes developed to address these concerns were both thoughtful and innovative. In order to protect the privacy of the individual datasets, four approaches were used:

Encryption: All data was encrypted in transport and at rest.

De-identification: Direct identifiers were removed from each dataset prior to analyst access. The unique identifiers randomly generated for individuals were *project-specific*, meaning that no record IDs could be used to trace information back to any dataset held by any data owner now or in the future.

Securing the Server: The server on which the Chapter 55 datasets were stored was secured so the likelihood of unauthorized access was minimized to the extent possible.

Preventing Misuse by Analysts: Additional restrictions were placed on authorized access to the server on which the Chapter 55 datasets were stored in order to minimize the likelihood of intentional or unintentional misuse of the data.

Each of these approaches is described briefly below.

Encryption

Given the sensitivity of the data involved in the Chapter 55 analysis, multiple levels of encryption were used with the intent to limit data access to only authorized parties.

Whenever data was stored at rest, whether on the server or other hard media, it was protected by at least 256-bit encryption and industry-standard strong passwords. Further, whenever data needed to be transported – for example between DPH and CHIA – it was placed in an encrypted file container on physical media that used hardware-based encryption. This doubly-encrypted drive was then manually transported by a trusted and authorized team member to its destination and hand-delivered to the proper recipient, or similarly retrieved for a return trip.

De-identification

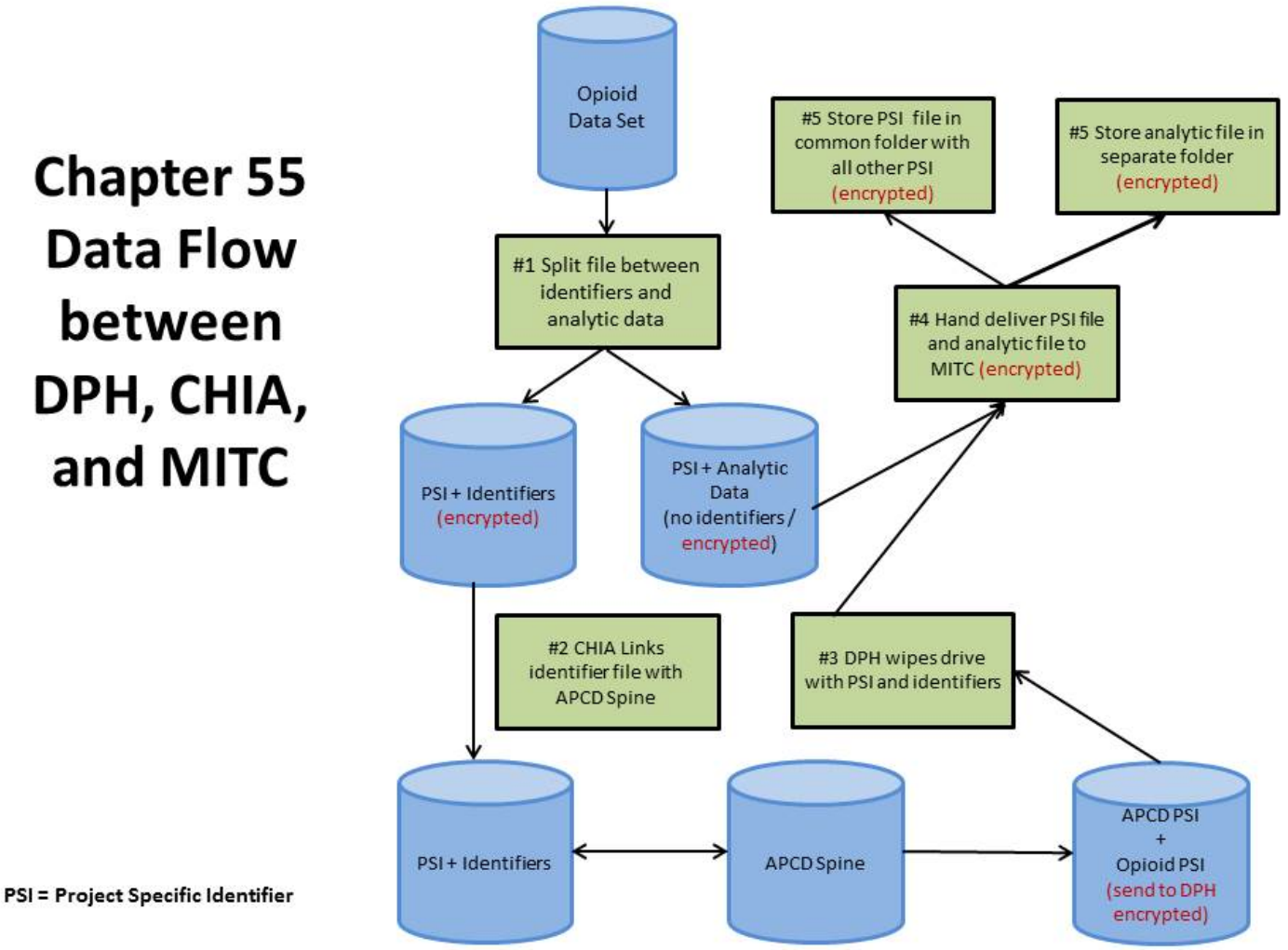
Chapter 55 datasets are not truly linked in the most commonly used sense of that word. In most cases, linkage implies a merger of datasets. For Chapter 55, a crosswalk is developed between datasets but the datasets themselves were never actually merged. This is an important distinction. By not merging data, it is argued that risk of re-identification of individuals who have information in two or more datasets is minimized. Furthermore, the unique identifiers contained in each dataset are not

found in any other project. Thus, if any breach of data or transmission protocol occurred, then the data could not be linked back to any source data file.

The specific steps taken to minimize of the risk to data privacy through de-identification are below. See Figure F.1 for a visual depiction of this process.

1) A pool of roughly 54 million random, non-sequential, 20-digit IDs (Random IDs or RIDs) was created at DPH. This number of values was sufficient to assign to every record of each of the constituent Chapter 55 raw datasets an ID that was unique across the entire project.
2) With RIDs affixed, each dataset was divided into two parts: direct identifiers (Identifier set) and analytic data (Analytic set). The only common information across both was the RID. The Identifier sets were hand delivered to CHIA. As noted under the Encryption section, all data was encrypted using 256-bit AES encryption with strong protection consistent with EOHHS and MassIT policy regarding password contents and length.
3) Distinct from DPH's RID-creation effort, CHIA created an extract of the All Payer Claims Database (APCD) that included only the fields to be used for the linkage scheme matching (Appendix D), plus an additional project-specific ID (PID). This PID was a random unique 20-digit number. It was in no way related to, nor derivative of, CHIA's Master Person Index (MPID) or any other persistent identifying code. This master extract-plus-PID is known as the APCD-Spine.
4) For each Identifier set, CHIA compared each record to the APCD-Spine. (For additional details on the data linkage, please see Appendix D.) Where a match was found, the PID and match level were associated with the RID from the Identifier set.
5) Upon confirmation from CHIA that an Identifier set was successfully matched to the APCD-Spine, DPH then deleted that Identifier set from its server.
6) The result set of matched PID/RID and match level were returned to DPH through the same secure mechanism as the delivery of the Identifier sets.
7) The RIDs within the returned result set were used to appropriately assign PIDs (and match confidence) to matching records in the Analytic sets. This allows the Analytic sets to be de-identified, but also connectable across datasets.
8) Because DPH had deleted the Identifier set, it was never in possession of the PID, RID and direct identifiers at the same time.
9) After assigning the PIDs to the Analytic sets, DPH securely delivered each Analytic file to the Massachusetts Information Technology Center (MITC) to be securely loaded onto the designated server.
10) In order to prevent merging of data, the project-specific identifiers and the analytic files for each Chapter 55 dataset were permanently stored in separate folders.
11) After all Chapter 55 Identifier sets have been matched and the Chapter 55 project no longer needs the APCD-Spine, CHIA will then delete it, destroying any connection between direct identifiers and PIDs at CHIA.

Figure F.1: Step by step process for transferring data securely from DPH tp CHIA to MITC



Securing the Server

There were three main goals in securing the SAS server:

1) Develop a clear audit process
2) Ensure proper encryption for the different needs of the users
3) Make it so that it was possible to handle more than a small number of group types in the system

These three goals were achieved in the following manner:

- The disk partition on which the Chapter 55 data was stored was encrypted using LUKS (Linux Unified Key Setup). Linux is the open-source version of the UNIX operating system and LUKS is the standard hard disk encryption method for Linux servers.
- To provide further flexibility in the design of the secure data ecosystem to the needs of the Chapter 55 project, Red Hat Enterprise Linux version 6.0 was used.
- Accounts were authenticated by LDAP, which is the MITC standard, and account creation was handled through specific (not automated) requests to the MITC Linux team.
- A unique mount point for the Chapter 55 project was created so that only group participants could gain access.
- The interface for Chapter 55 work was through the web server interface with data encrypted at rest including all individual work files.
- An audit process was implemented to record when and who was doing maintenance on/for SAS.
- All inbound requests to the server were blocked unless the requestor was on a pre-approved whitelist. The firewall restricted access to specific ports on the server. Ports were continuously monitored.

Preventing Misuse by Analysts:

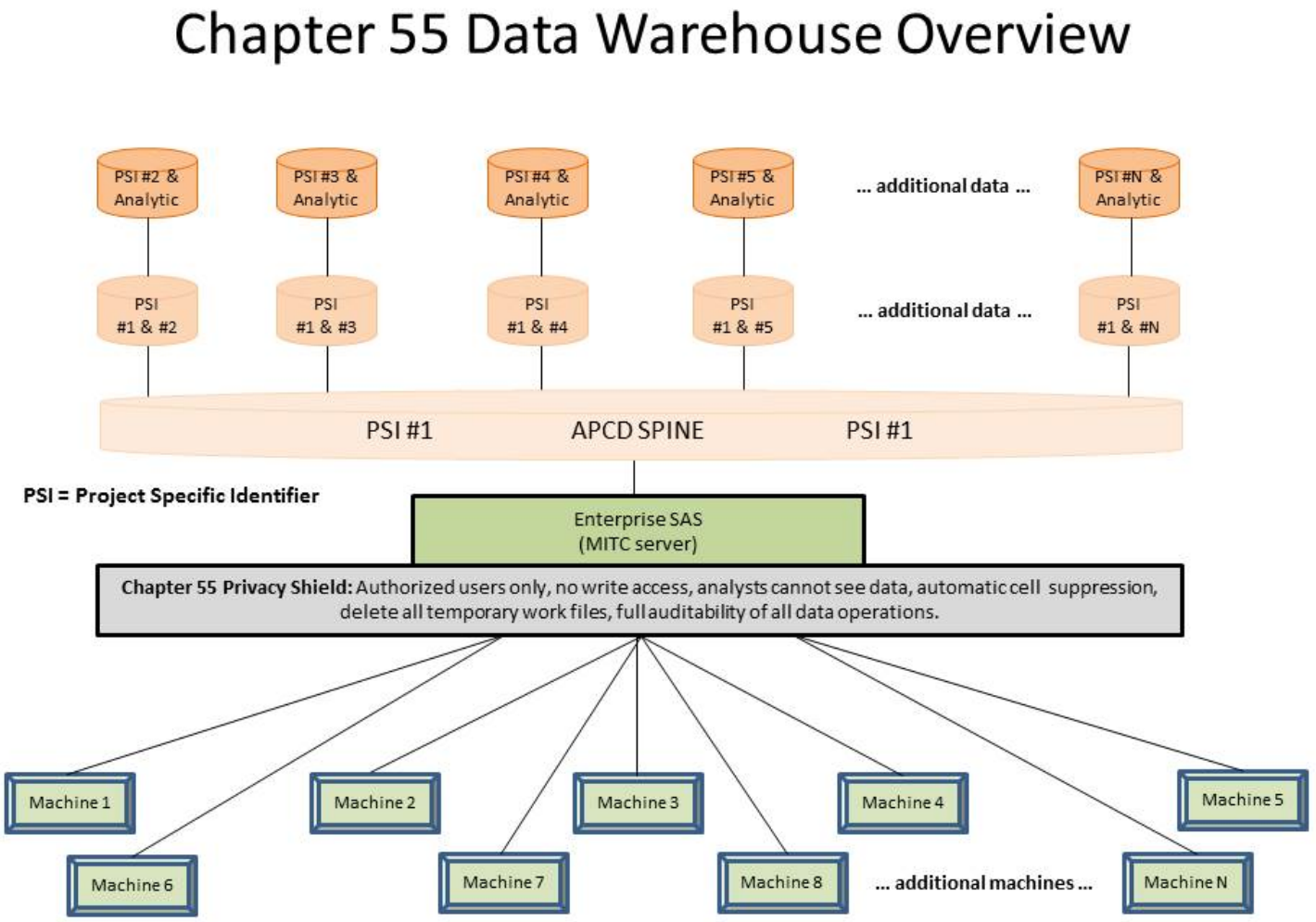
To minimize the risk of misuse of Chapter 55 data by authorized users, the following processes were implemented as what has been collectively termed a **Privacy Shield**.

- Access to Chapter 55 data was only permitted using Enterprise SAS Studio software
- Only authorized users were given User IDs and passwords to access the Chapter 55 data.
- Authorized users were required to demonstrate that DPH-required privacy and confidentiality trainings were up to date.
- Only de-identified Analytic sets were accessible by analysts.
- Analysts had “read only” access to Chapter 55 datasets. Writes were not permitted.
- Analysts were not permitted to see the raw Chapter 55 Analytic data. This was accomplished by turning off the ability of authorized users to open and view raw Analytic data files.

- Analysts were not permitted to see small cell sizes. The common SAS procedure for producing counts and cross-tabulations (PROC FREQ) was altered so that it masked (by displaying asterisks) any cell count that was between 1 and 10.
- All temporary SAS work files were deleted in one of three ways. If shutdown of a process was typical, files were deleted upon shutdown. If shutdown was atypical (e.g., power outage), the system searched for orphaned work files every 15 minutes and these files were deleted. If any data query was open for more than 72 hours, then the system administrator could manually shut down a process which would delete any associated SAS work files.
- An audit process of all commands issued to SAS was implemented. Logs were checked to ensure that no analyst made any attempt to export, print, or otherwise view any Chapter 55 data.

See Figure F.2 for a visual depiction of the Chapter 55 Data Warehouse.

Figure F.2: Data analyst access to Chapter 55 datasets through a secure hardware and software Privacy Shield.



Appendix G: Legal Agreements

In order to meet the legal requirements of working with all of these protected datasets, a number of legal documents were produced. Four different types of agreements were signed.

1) Linking – This agreement between DPH and CHIA allowed for the exchange of data for the purposes of securely connecting data at the individual level across secure datasets without exposing the identity of the individual so connected.
2) Sharing – This agreement outlined the methodology and restrictions allowing for the sharing of data between different departments or agencies that were not previously sharing – or even allowed to share, outside of the Chapter 55 project. Each of the data-supplying entities was a signatory to this ISA. Specifically, signatories include: the Department of Public Health (DPH), the Department of Correction (DoC), the Office of the Chief Medical Examiner (OCME), and the Center for Health Information and Analysis (CHIA). While CHIA has previously signed the Linking agreement, they are also intended to be a provider of Analytic data from the All Payer Claims Database (APCD) and Case Mix.
3) Hosting – An agreement between DPH and MassIT specifying the hosting responsibilities and restrictions for the data infrastructure.
4) Access – An additional agreement created for *ad hoc* access to data outside of the purview of the prior three agreements. For example: If the Data Office within MassIT were to assist in a way that required analytical data access that is not covered by the 3rd agreement (which is hosting specific). This 4th agreement essentially outlines the responsibilities of being a good data steward and requires a signature for access. There would conceivably be *n* number of these agreements signed over time.

Appendix H: Cross-tabulations of Chapter 55 Datasets with Death File Demographics

Table H.1: All Deaths in Massachusetts compared to DoC population			
Characteristic	**All Deaths in MA**	**DoC**	
Age— no. (%)		**Died**	**Living**
11-24	902 (0.87)	34 (6.0)	2473 (10.0)
25-34	1701 (1.64)	153 (27.1)	8984 (36.5)
35-44	2324 (2.25)	110 (19.5)	5998 (24.3)
45-54	6098 (5.89)	164 (29.0)	4894 (19.9)
55-64	11375 (10.99)	79 (14.0)	1896 (7.7)
65+	81072 (78.33)	25 (4.4)	399 (1.6)
Sex— no. (%)			
Male	49438 (47.8)	382 (67.6)	16140 (65.5)
Female	54067 (52.2)	183 (32.4)	8504 (34.5)
Race or ethnic group — no. (%)			
White non-Hispanic	94012 (90.8)	454 (80.4)	15443 (62.7)
Black non-Hispanic	4361 (4.2)	43 (7.6)	4757 (19.3)
Asian/PI non-Hispanic	1599 (1.5)	NA	176 (0.7)
Hispanic	2822 (2.7)	56 (9.9)	3489 (14.2)
Other	703 (0.7)	10 (1.8)	778 (3.2)
Marital status — no. (%)			
Single, never married	15042 (14.5)	337 (59.7)	NA
Married or separated	36133 (34.9)	85 (15.0)	NA
Widowed	38800 (37.5)	17 (3.0)	NA
Divorced	13307 (12.9)	123 (21.8)	NA
Education — no. (%)			
High School or Less	67362 (65.1)	445 (78.8)	NA
13+ years	34569 (33.4)	110 (19.5)	NA

Table H.2: All Deaths in Massachusetts compared to PDMP Population			
Characteristic	**All Deaths in MA**	**PDMP**	
Age— no. (%)		**Died**	**Living**
11-24	902 (0.87)	511 (0.6)	429065 (12.6)
25-34	1701 (1.64)	1256 (1.6)	531483 (15.7)
35-44	2324 (2.25)	1807 (2.2)	497742 (14.7)
45-54	6098 (5.89)	4852 (6.0)	601398 (17.7)
55-64	11375 (10.99)	9077 (11.3)	584597 (17.2)
65+	81072 (78.33)	63005 (78.3)	750752 (22.1)
Sex— no. (%)			
Male	49438 (47.8)	36829 (45.8)	1502500 (44.3)
Female	54067 (52.2)	43679 (54.3)	1892537 (55.7)
Race or ethnic group — no. (%)			
White non-Hispanic	94012 (90.8)	73881 (91.8)	NA
Black non-Hispanic	4361 (4.2)	3000 (3.7)	NA
Asian/PI non-Hispanic	1599 (1.5)	1023 (1.3)	NA
Hispanic	2822 (2.7)	2054 (2.6)	NA
Other	703 (0.7)	546 (0.7)	NA
Marital status — no. (%)			
Single, never married	15042 (14.5)	10838 (13.5)	NA
Married or separated	36133 (34.9)	28716 (35.8)	NA
Widowed	38800 (37.5)	30293 (37.6)	NA
Divorced	13307 (12.9)	10527 (13.1)	NA
Education — no. (%)			
High School or Less	67362 (65.1)	52509 (65.2)	NA
13+ years	34569 (33.4)	26918 (33.4)	NA

Table H.3: All Deaths in Massachusetts compared to BSAS Population			
Characteristic	**All Deaths in MA**	**BSAS**	
Age— no. (%)		**Died**	**Living**
11-24	902 (0.87)	154 (5.4)	17017 (11.6)
25-34	1701 (1.64)	608 (21.5)	48879 (33.4)
35-44	2324 (2.25)	522 (18.4)	31863 (21.7)
45-54	6098 (5.89)	835 (29.5)	29456 (20.1)
55-64	11375 (10.99)	577 (20.4)	15550 (10.6)
65+	81072 (78.33)	136 (4.8)	3754 (2.6)
Sex— no. (%)			
Male	49438 (47.8)	2049 (72.4)	99761 (68.1)
Female	54067 (52.2)	783 (27.6)	46753 (31.9)
Race or ethnic group — no. (%)			
White non-Hispanic	94012 (90.8)	2335 (82.5)	110482 (75.4)
Black non-Hispanic	4361 (4.2)	171 (6.0)	10789 (7.4)
Asian/PI non-Hispanic	1599 (1.5)	12 (0.4)	1266 (0.9)
Hispanic	2822 (2.7)	245 (8.6)	18433 (12.6)
Other	703 (0.7)	69 (2.4)	4468 (3.1)
Marital status — no. (%)			
Single, never married	15042 (14.5)	1541 (54.4)	NA
Married or separated	36133 (34.9)	503 (17.8)	NA
Widowed	38800 (37.5)	91 (3.2)	NA
Divorced	13307 (12.9)	673 (23.8)	NA
Education — no. (%)			
High School or Less	67362 (65.1)	2055 (72.6)	NA
13+ years	34569 (33.4)	738 (26.1)	NA

Table H.4: All Deaths in Massachusetts compared to MATRIS Population			
Characteristic	**All Deaths in MA**	**MATRIS**	
Age— no. (%)		**Died**	**Living**
11-24	902 (0.87)	312 (0.7)	66162 (14.1)
25-34	1701 (1.64)	925 (2.0)	63331 (13.5)
35-44	2324 (2.25)	1104 (2.3)	49788 (10.6)
45-54	6098 (5.89)	2808 (6.0)	64956 (13.9)
55-64	11375 (10.99)	5351 (11.4)	66644 (14.2)
65+	81072 (78.33)	36603 (77.7)	157168 (33.6)
Sex— no. (%)			
Male	49438 (47.8)	24462 (51.9)	214954 (45.9)
Female	54067 (52.2)	22641 (48.1)	253172 (54.1)
Race or ethnic group — no. (%)			
White non-Hispanic	94012 (90.8)	42253 (89.7)	160116 (34.2)
Black non-Hispanic	4361 (4.2)	2358 (5.0)	13965 (3.0)
Asian/PI non-Hispanic	1599 (1.5)	632 (1.3)	3482 (0.7)
Hispanic	2822 (2.7)	1506 (3.2)	17671 (3.8)
Other	703 (0.7)	352 (0.8)	12592 (2.7)
Marital status — no. (%)			
Single, never married	15042 (14.5)	7553 (16.0)	NA
Married or separated	36133 (34.9)	17543 (37.4)	NA
Widowed	38800 (37.5)	15135 (32.1)	NA
Divorced	13307 (12.9)	6771 (14.4)	NA
Education — no. (%)			
High School or Less	67362 (65.1)	30947 (65.7)	NA
13+ years	34569 (33.4)	15470 (32.8)	NA

Table H.5: All Deaths in Massachusetts compared to OCME Data			
Characteristic	**All Deaths in MA**	**OCME**	
Age— no. (%)		**Died**	**Living**
11-24	902 (0.87)	387 (8.1)	NA
25-34	1701 (1.64)	914 (19.1)	NA
35-44	2324 (2.25)	813 (17.0)	NA
45-54	6098 (5.89)	1230 (25.7)	NA
55-64	11375 (10.99)	865 (18.1)	NA
65+	81072 (78.33)	572 (12.0)	NA
Sex— no. (%)			
Male	49438 (47.8)	3334 (69.7)	NA
Female	54067 (52.2)	1447 (30.3)	NA
Race or ethnic group — no. (%)			
White non-Hispanic	94012 (90.8)	4017 (84.0)	NA
Black non-Hispanic	4361 (4.2)	336 (7.0)	NA
Asian/PI non-Hispanic	1599 (1.5)	47 (1.0)	NA
Hispanic	2822 (2.7)	325 (6.8)	NA
Other	703 (0.7)	56 (1.2)	NA
Marital status — no. (%)			
Single, never married	15042 (14.5)	2466 (51.6)	NA
Married or separated	36133 (34.9)	982 (20.5)	NA
Widowed	38800 (37.5)	274 (5.7)	NA
Divorced	13307 (12.9)	1005 (21.0)	NA
Education — no. (%)			
High School or Less	67362 (65.1)	3276 (68.5)	NA
13+ years	34569 (33.4)	1446 (30.2)	NA

Table H.6: All Deaths in Massachusetts compared to Cancer Population			
Characteristic	**All Deaths in MA**	**Cancer**	
Age— no. (%)		**Died**	**Living**
11-24	902 (0.87)	34 (0.2)	960 (0.8)
25-34	1701 (1.64)	73 (0.4)	2309 (1.8)
35-44	2324 (2.25)	315 (1.6)	5026 (4.0)
45-54	6098 (5.89)	1322 (6.5)	15143 (11.9)
55-64	11375 (10.99)	3688 (18.3)	28009 (22.1)
65+	81072 (78.33)	14762 (73.1)	75417 (59.5)
Sex— no. (%)			
Male	49438 (47.8)	10554 (52.2)	57280 (45.2)
Female	54067 (52.2)	9648 (47.8)	69573 (54.8)
Race or ethnic group — no. (%)			
White non-Hispanic	94012 (90.8)	18248 (90.3)	NA
Black non-Hispanic	4361 (4.2)	864 (4.3)	NA
Asian/PI non-Hispanic	1599 (1.5)	417 (2.1)	NA
Hispanic	2822 (2.7)	540 (2.7)	NA
Other	703 (0.7)	132 (0.7)	NA
Marital status — no. (%)			
Single, never married	15042 (14.5)	2372 (11.7)	NA
Married or separated	36133 (34.9)	9502 (47.0)	NA
Widowed	38800 (37.5)	5228 (25.9)	NA
Divorced	13307 (12.9)	3072 (15.2)	NA
Education — no. (%)			
High School or Less	67362 (65.1)	12533 (62.0)	NA
13+ years	34569 (33.4)	7414 (36.7)	NA

Table H.7: All Deaths in Massachusetts compared to Case Mix Population			
Characteristic	**All Deaths in MA**	**Case Mix**	
Age— no. (%)		**Died**	**Living**
11-24	902 (0.87)	318 (0.57)	122505 (9.58)
25-34	1701 (1.64)	812 (1.46)	208860 (16.34)
35-44	2324 (2.25)	1270 (2.28)	185271 (14.49)
45-54	6098 (5.89)	3618 (6.51)	190954 (14.94)
55-64	11375 (10.99)	6590 (11.85)	206109 (16.12)
65+	81072 (78.33)	43008 (77.33)	364387 (28.51)
Sex— no. (%)			
Male	49438 (47.8)	26389 (47.45)	543108 (42.49)
Female	54067 (52.2)	29227 (52.55)	735135 (57.51)
Race or ethnic group — no. (%)			
White non-Hispanic	94012 (90.8)	49491 (88.99)	989471 (77.41)
Black non-Hispanic	4361 (4.2)	2765 (4.97)	104421 (8.17)
Asian/PI non-Hispanic	1599 (1.5)	1005 (1.81)	36667 (2.87)
Hispanic	2822 (2.7)	1986 (3.57)	113818 (8.9)
Other	703 (0.7)	369 (0.66)	33869 (2.65)
Marital status — no. (%)			
Single, never married	15042 (14.5)	8883 (15.97)	NA
Married or separated	36133 (34.9)	18038 (32.43)	NA
Widowed	38800 (37.5)	20495 (36.85)	NA
Divorced	13307 (12.9)	8072 (14.51)	NA
Education — no. (%)			
High School or Less	67362 (65.1)	37245 (66.97)	NA
13+ years	34569 (33.4)	17552 (31.56)	NA

Appendix I: Background on Addiction & the Bureau of Substance Abuse Services

Addiction Background: The etiology of addiction is dependent upon biological, psychological, and social factors. Antecedents of addiction include individual vulnerability levels, drug or object exposure, and drug or object interaction. More specifically, throughout the course of development, people encounter and accumulate specific combinations of neurobiological and psychosocial elements that can influence their behavior. Some elements increase the likelihood of addiction, whereas other factors are protective and reduce the chance of addiction (e.g., social support networks). Individuals with psychopathology (e.g., major depression, generalized anxiety disorder, or posttraumatic stress disorder) often exhibit increased prevalence of drug use disorders. Furthermore, the prevalence of psychopathology is increased among individuals who are dependent on multiple psychoactive substances (e.g., Heroin, alcohol, or cocaine)[8485]. Various sociodemographic risk factors (e.g., relating to poverty, geography, family, and peer groups) can influence the onset and course of drug use that can similarly affect the likelihood of developing addiction.[868788]

Starting in fiscal year 2012, clients receiving BSAS treatment reporting an opioid problem at the time of admission exceeded the number of clients reporting a problem with any other substance (31% in 2000 compared to 55% in 2014).[89] A significant portion of the increase was due to prescribed and illicit prescription drugs up to 2011, after which there was a drop in this category and a sharp increase in Heroin admissions.

Each expression of addiction, poses similar as well as unique consequences. Opioid Addiction, for example, poses very particular risks and adverse consequences, i.e. hypoxia (decreased oxygen to the brain), sepsis, and non-fatal/ fatal overdose. There is an elevated risk of exposure to Opioids in Massachusetts given the trends in the last decade. Opioids are a class of drugs that are naturally occurring but are also produced in a synthetic and semi-synthetic fashion. When Opioids bind to receptors in the body they can reduce the perception of pain. Opioids can produce many different side effects including: respiratory depression, drowsiness, mental confusion, and nausea. However, Opioids can produce a feeling of euphoria since they affect the brain's reward circuitry. Opioids can be prescribed for pain management, but they can also be illicitly obtained. Some examples of Opioids include: Heroin, Hydrocodone, Oxycodone, Morphine, Codeine, Tramadol and Fentanyl. Fentanyl can be prescribed for pain management, but it can also illicitly be obtained either on its own, or combined with Heroin. The potency of an Opioid as well as the combination of more than one Opioid, or the combination of an Opioid with a sedative can pose elevated risks for adverse consequences. The reason

[84] Kessler RC, Crum RM, Warner LA, Nelson CB, Schulenberg J, Anthony JC. Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the National Comorbidity Survey. Arch Gen Psychiatry 1997;54:313–21.
[85] Tomasson K, Vaglum P. Psychopathology and alcohol consumption among treatment-seeking alcoholics: a prospective study. Addiction 1996;91:1019–30.
[86] Evans GW, Kantrowitz E. Socioeconomic status and health: the potential role of environmental risk exposure. Annual Review Public Health 2002;23:303–31.
[87] Robins LN. Vietnam veterans' rapid recovery from Heroin addiction: a fluke or normal expectation? Addiction 1993;88:1041–54
[88] Zinberg NE. Drug, set, and setting. New Haven, CT: Yale University Press, 1984.
[89] This includes both Heroin and other opioids.

for these adverse consequences has to do with fundamental components of the disease. People with addiction often experience episodes of abstinence, and relapse. When there is a period of abstinence which is followed by a relapse, a person is at enormous risk for overdose. This risk is due to tolerance and withdrawal. Tolerance and withdrawal can be explained as (1) an increased dose of a drug or object is needed to experience the same subjective effects as with a lower dose before,(2) the experience of withdrawal upon stopping use with the presence of three or more symptoms: dysphoric mood, nausea or vomiting, muscle aches, pupillary dilation, sweating, fever, diarrhea, convulsions, or tremors, and (3) the symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.[90] Tolerance among Heroin users, for example, refers to the observation that regular users require more Heroin to get the same level of intoxication experienced previously at a lower dose; withdrawal means that these users get sick when they stop using the drug and that using the drug again can make this stereotypical pattern of illness stop. The potency of a drug can also play a critical role in the relationship between abstinence, relapse, tolerance and withdrawal; if a similar dose is used, but the potency is stronger than the previous dose there is a risk for overdose and death.

Addiction treatment is intended to help individuals stop compulsive behaviors and drug and/or alcohol seeking and use by providing them with medication and behavioral coping skills as tools. Treatment can occur in a variety of settings, take many different forms, and last for different lengths of time. Because addiction is typically a chronic disorder characterized by occasional relapses, a short-term, one-time treatment is usually not sufficient. For many, treatment is a long-term process that involves multiple interventions and regular monitoring. There are a variety of evidence-based approaches to treating addiction. Treatment can include behavioral therapy (e.g. cognitive-behavioral therapy or contingency management), medications, or their combination. The setting for service delivery may be inpatient, or outpatient. A clinical recommendation for treatment depends on the individualistic needs of a client.[91]

People with Addiction often suffer from other health (e.g., depression, HIV, Hepatitis), occupational, legal, familial, financial, and social problems that should be addressed concurrently. The best programs provide a combination of therapies and other services to meet an individual's needs. Psychoactive medications, (e.g. antidepressants, anti-anxiety agents, mood stabilizers, and antipsychotic medications) may be critical for addiction treatment success for patients that have co-occurring mental disorders. Currently, the BSAS data set does not account for all these critical elements of people served in our treatment system; however there is potential to collect and analyze this information in the future.

---

[90] American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders: **DSM**-**5**. Washington, D.C: American Psychiatric Association.

[91] There are evidence-based guidelines from SAMHSA and associations like American Society of Addiction Medicine (ASAM) and American Psychological Association (APA) for particular treatment services and for particular populations. For instance, there are guidelines for clinically evaluating patients to determine what is medically necessary and determine individualistic needs. The guidelines outline standards of care for stabilizing patients with withdrawal symptoms during detoxification and there are recommendations for maintenance care. The guidelines also specify MAT dosing for detoxification purposes as well as maintenance. Often, people with severe addiction are poly-substance users and require treatment for all substances abused.

BSAS Data Collection: Massachusetts Department of Public Health's Bureau of Substance Abuse Services (BSAS) is the single state authority responsible for regulating and licensing substance abuse treatment providers throughout the Commonwealth. The Department's authority is defined under MGL Ch.111 B and E. Under this authority, the Department must ensure that treatment services are available along the continuum of care from detoxification to recovery. The Department can also engage into contracts with private providers and fund services. The Department currently licenses American Society of Addiction Medicine (ASAM) levels I – IV but only funds levels I – III. The services that fall under the funded categories range from acute detoxification to residential and outpatient-based services. In addition to licensing, regulating, and funding treatment services, BSAS funds prevention and recovery support services throughout the Commonwealth.

Appendix J: Partnerships

The Chapter 55 project brought together analysts and researchers from across government, six academic institutions, and two private consulting firms. First and foremost, the Department of Public Health would like to thank all those who participated in this effort. Without everyone's assistance, this report could not have been completed in time. The work done here has been groundbreaking and the collaboration has been extraordinary both inside and outside government institutions.

The concept of a shared, integrated, data environment, accessible by government, academic institutions and private enterprise predates both this opioid epidemic and the Chapter 55 legislation. The March 2015 report to the Legislature titled "Feasibility Proposal and Implementation Plan for a Public Health Data Warehouse" describes much of the infrastructure, data security plans, and the partnership goals that were central to the Chapter 55 work. One specific goal stated in the March 2015 report captures the approach taken by all parties. It was, "To design a technical architecture for a data warehouse that utilizes state resources efficiently while enabling secure access to public health data for internal and external users."

This goal was an acknowledgement that each type of organization (i.e., government, academic and private industry) had essential but incomplete resources and expertise relevant to completing the work undertaken in the Chapter 55 project. The Chapter 55 report, therefore, became the catalyst that motivated a collective and concerted effort towards bringing the vision of a shared, integrated, data environment to fruition. The collaborative, multi-sector, work done to date is a single instance of the vision. The Chapter 55 project represents a process that should be continued, adapted, and refined as new public health challenges and new collaborators emerge.

The Department would specifically like to thank the following institutions.

Academic Institutions
• Boston University School of Medicine • Brown University • Harvard Medical School • Harvard School of Public Health • Northeastern University • Tufts University School of Medicine • University of Massachusetts, Boston • University of Massachusetts Medical School • Worcester Polytechnic Institute
Private Institutions
• Boston Children's Hospital • MITRE Corporation • Price Waterhouse Coopers (PwC) • SAS Analytics

Government Agencies

• Executive Office of Health and Human Services
  o Executive Office of Health and Human Services, Information Technology Division
  o Center for Health Information and Analysis
  o MassHealth
• Executive Office of Public Safety and Security
  o Department of Correction
  o Office of the Chief Medical Examiner
• Massachusetts Office of Information Technology
  o Enterprise Data Management (“the Data Office”)
  o Infrastructure Planning Group
  o Office of the Chief Medical Examiner

Department of Public Health

• Commissioner’s Office
• Bureau of Community Health and Prevention
• Bureau of Health Care Safety and Quality
  o Office of Prescription Monitoring and Drug Control
  o Emergency Medical Services
• Bureau of Family and Community Health
• Bureau of Substance Abuse Services
• Office of the Chief Legal Counsel
• Office of Office of Data Management and Outcomes Assessment

Exhibit E

The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health
250 Washington Street, Boston, MA 02108-4619

CHARLES D. BAKER
Governor

KARYN E. POLITO
Lieutenant Governor

MARYLOU SUDDERS
Secretary

MONICA BHAREL, MD, MPH
Commissioner

Tel: 617-624-6000
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August 16, 2017

Steven T. James
House Clerk
State House Room 145
Boston, MA 02133

William F. Welch
Senate Clerk
State House Room 335
Boston, MA 02133

Dear Mr. Clerk,

Pursuant to Chapter 55 of the Acts of 2015, as amended by Chapter 133 of the Acts of 2016, enclosed, please find a report entitled "*An Assessment of Fatal and Nonfatal Opioid Overdoses in Massachusetts (2011 – 2015).*" The report was prepared under the direction of Monica Bharel, MD, MPH, Commissioner of Public Health and reaffirms the administration's commitment to provide data for public understanding and policy direction.

If you have any questions, please do not hesitate to contact us.

Sincerely,

Marylou Sudders
Secretary
Executive Office of Health and Human Services

Cc: Monica Bharel, MD, MPH
Commissioner
Department of Public Health

An Assessment of Fatal and Nonfatal Opioid Overdoses in Massachusetts (2011 – 2015)

August 2017

Massachusetts Department of Public Health

Legislative Mandate

The following report is hereby issued pursuant to Chapter 55 of the Acts of 2015, as amended by Chapter 133 of the Acts of 2016 as follows:

Notwithstanding any general or special law to the contrary, the secretary of health and human services, in collaboration with the department of public health, shall conduct or provide for an examination of the prescribing and treatment history, including court-ordered treatment or treatment within the criminal justice system, of persons in the commonwealth who suffered fatal or nonfatal opiate overdoses in calendar years 2013 to 2015, inclusive. Any report or supplemental reports resulting from this examination shall provide any data in an aggregate and de-identified format

Notwithstanding any general or special law to the contrary, to facilitate the examination, the department shall request, and the relevant offices and agencies shall provide, information necessary to complete the examination from the division of medical assistance, the executive office of public safety and security, the center for health information and analysis, the office of patient protection and the chief justice of the trial court, which may include, but shall not be limited to: data from the prescription drug monitoring program; the all-payer claims database; the criminal offender record information database; and the court activity record information. To the extent feasible, the department shall request data from the Massachusetts Sheriffs Association, Inc. relating to treatment within houses of correction.

Not later than 1 year from the effective date of this act, the secretary of health and human services shall publish a report on the findings of the examination including, but not limited to: (i) instances of multiple provider episodes, meaning a single patient having access to opiate prescriptions from more than 1 provider; (ii) instances of poly-substance access, meaning a patient having simultaneous prescriptions for an opiate and a benzodiazepine or for an opiate and another drug which may enhance the effects or the risks of drug abuse or overdose; (iii) the overall opiate prescription history of the individuals, including whether the individuals had access to legal prescriptions for opiate drugs at the time of their deaths; (iv) whether the individuals had previously undergone voluntary or involuntary treatment for substance addiction or behavioral health; (v) whether the individuals had attempted to enter but were denied access to treatment for substance addiction or behavioral health; (vi) whether the individuals had received past treatment for a substance overdose; (vii) whether any individuals had been previously detained or incarcerated and, if so, whether the individuals had received treatment during the detention or incarceration.

The report shall be filed with the clerks of the senate and house of representatives, the house and senate chairs of the joint committee on mental health and substance abuse, the joint committee on public health, the joint committee on health care financing and the house and senate committees on ways and means. The secretary of health and human services may publish supplemental reports on the trends identified through its examination; provided, however, that any supplemental report shall be filed not later than July 1, 2017 and shall be filed with the clerks of the senate and house of

representatives, the house and senate chairs of the joint committee on mental health and substance abuse, the joint committee on public health, the joint committee on health care financing and the house and senate committees on ways and means.

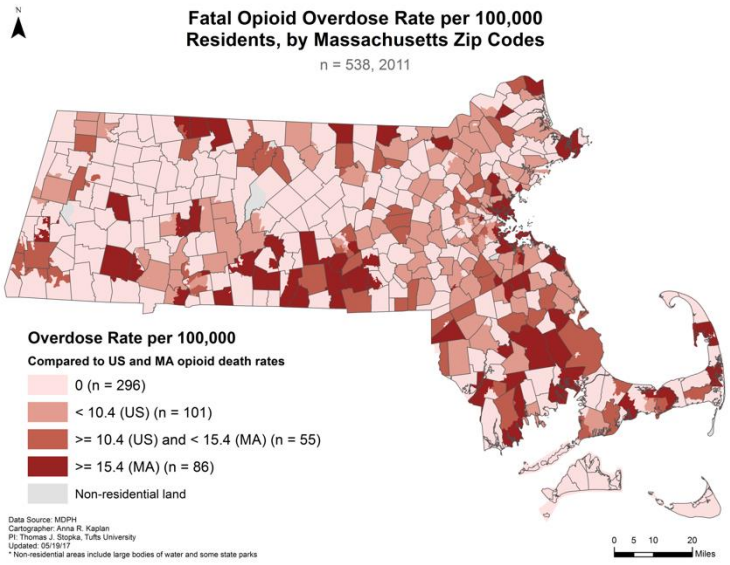
Notwithstanding any general or special law to the contrary, the executive office of health and human services may contract with a non-profit or educational entity to conduct data analytics on the data set generated in the examination, provided that the executive office shall implement appropriate privacy safeguards.

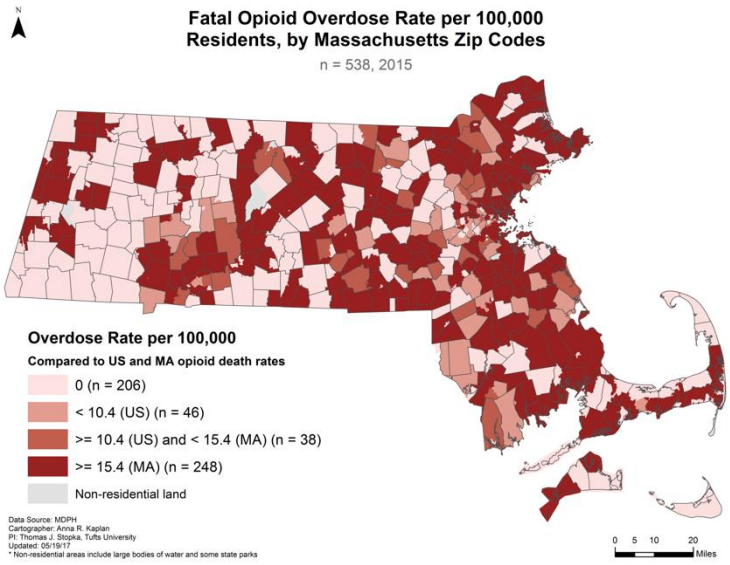
Table of Contents

Executive Summary

In the twelve months since the first Chapter 55 report was released in July 2016, nearly 2,000 Massachusetts residents have died of opioid-related overdoses. The total number of deaths has increased five-fold in the last 20 years, but the rate of increase of opioid-related overdose deaths was particularly sharp between 2013 and 2014.[1] The maps below show a graphic depiction of the increasing and spreading opioid crisis in Massachusetts between 2011 and 2015 (the darkening area on the maps below). Not since the AIDS epidemic of the 1980s and 1990s has Massachusetts seen such a sharp increase in a single category of deaths.

Increasing and Spreading Opioid-Related Overdose Death Rates in Massachusetts from 2011 to 2015[2]





2011 2015

The characteristics of the epidemic in Massachusetts are similar to other states. What is especially notable is that this epidemic does not conform to the stereotypical boundaries of race, class, gender, and geography. Almost every community is affected. Opioid-related overdose deaths and nonfatal opioid-related overdoses are highest among younger males, but all population subgroups have seen increases in recent years. Individuals released from incarceration are also at high risk of death upon re-entering the community, but so too are individuals experiencing homelessness, veterans, mothers with opioid use disorder, and individuals with serious mental illnesses.

[1] Accessed at http://www.mass.gov/eohhs/docs/dph/stop-addiction/current-statistics/data-brief-overdose-deaths-february-2017.pdf on 5/19/2017.

[2] Maps prepared by Department of Public Health and Community Medicine, Tufts University School of Medicine. In 2011, 16% of zip codes were in the highest risk category. By 2015, that number had increased to 46%. The full-sized maps can be examined in Appendix D.

Fighting the current opioid epidemic has been a priority of the Baker-Polito Administration since day one. In February 2015, Governor Baker appointed a working group to develop a plan to reduce the rate of opioid-related deaths in the Commonwealth. In June 2015, the Governor's Opioid Working Group released 65 recommendations and a comprehensive Action Plan aimed at curbing the current opioid epidemic. These short- and long-term recommendations focus on prevention, intervention, treatment, and recovery support. Today, nearly all of these recommendations are underway, making Massachusetts a national leader in terms of both investments and policy.[3]

Understanding the complexity of this epidemic with precision is imperative to respond effectively. One part of this response includes the passage of Chapter 55 of the Acts of 2015 (Chapter 55) by the Massachusetts Legislature and Governor Charles D. Baker, and its reauthorization in Chapter 133 of the Acts of 2016. These laws enabled an unprecedented linkage and analysis of existing data across state government in order to better guide policy development and programmatic decision-making. The findings included in this report are a result of the linkages and analyses of more than 20 administrative datasets.[4]

Contained within this report are descriptions of analyses providing the state with important new insights into the profile of overdose-related deaths and nonfatal opioid-related overdoses and the relative risks faced by the Commonwealth's diverse populations. The report is divided into three main sections:

- Re-Estimating Baseline Statistics: This section provides more accurate estimates for Opioid Use Disorder (OUD), Nonfatal Overdose (NFO), and Opioid-Related Overdose Deaths (OROD).
- Timeline and Influences: This section offers an initial glimpse into the length of time between the stages of opioid use from an individual's perspective from initial use of prescription medications to fatal overdose.
- Identifying At-Risk Populations: This section includes estimates of the risk of fatal and nonfatal overdose for each of seven at-risk populations including the homeless, veterans, and individuals diagnosed with severe mental illness.

In each section, the left column contains succinct take-home messages including current status, data sources, and key findings and is organized for quick reference. The larger right hand area of each page contains more information including the background, basic methods used for conducting the analysis, teams involved in the analysis, and key findings for further analysis and for policy consideration. Finally, the appendices provide in-depth explanations and background information.

[3] Accessed at http://www.mass.gov/eohhs/docs/dph/stop-addiction/recommendations-of-the-governors-opioid-working-group.pdf on 5/19/2017.
[4] Administrative data refers to information collected primarily for administrative (not research) purposes.

Key Findings: Massachusetts 2011-2015
In 2015, it is estimated that over 4% of persons age 11 and older in Massachusetts had opioid use disorder.
Nonfatal overdoses recorded by emergency medical services (EMS), hospitals, and bystander interventions increased ~200% between 2011 and 2015. The total number of nonfatal overdoses between 2011 and 2015 exceeded 65,000.
Almost half of the individuals who died of an opioid-related overdose during the study period were at one time classified as opioid naïve[5] during the study period. Risk for fatal and nonfatal opioid overdose grows as use continues.
Compared to the general population, those who received three months of prescribed opioids in 2011 were 4 times as likely to die from an opioid-related overdose within one year, and 30 times as likely to die of an opioid-related overdose within five years.
It is estimated that roughly one in every 25 adults has been homeless at some point between 2011 and 2015. The risk of opioid-related overdose death for persons who have experienced homelessness is up to 30 times higher than it is for the rest of the population.
The risk of fatal opioid-related overdose is six times higher for persons diagnosed with a serious mental illness (SMI) and three times higher for those diagnosed with depression.
Compared to the rest of the adult population, the opioid-related overdose death rate is 120 times higher for persons released from prisons and jails.
The five-year opioid-related overdose death rate of mothers with evidence of opioid use disorder was 321 times higher than the rate among mothers without evidence of opioid use disorder.

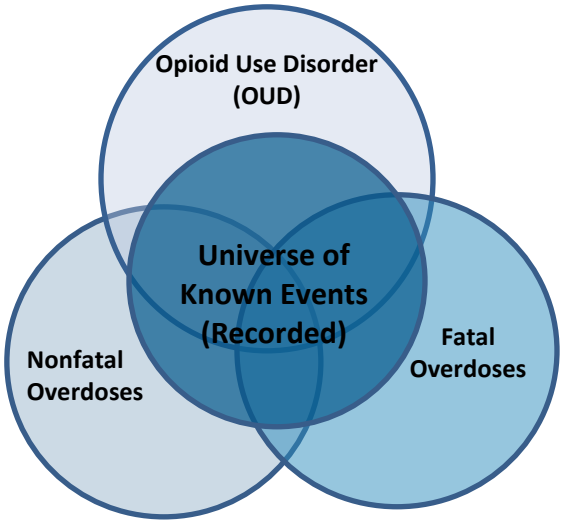
This effort also marks a continuation of the significant collaboration between state and federal government, academia, the health care system, and private industry. The Chapter 55 initiative has clearly demonstrated that partnerships can cross governmental and non-governmental boundaries to quickly address a public health problem of acknowledged urgency. However, for these types of partnerships to become institutional and routine, it is critical to formalize relationships. Access to a unique dataset in a time of crisis may temporarily attract multidisciplinary partners, but sustainability is best assured through formalizing data governance, mutually beneficial partnerships, and a plan for ongoing resourcing and data maintenance. These issues must be addressed to ensure continued success.

The Department's ability to engage academic partners and private industry to support monitoring and evaluation activities will be crucial, and collaborative, data-driven efforts such as this should become standard practice in Massachusetts and beyond.

[5] To be categorized as opioid naïve, the individual's records had to show a period of six months or more without an opioid prescription before their first opioid prescription. Patients excluded from the group were persons who had any advanced cancer (other than non-melanoma skin cancer), had a substance use disorder diagnosis in the six months preceding their first opioid prescription, or whose first prescription was for any buprenorphine formulation indicated for treatment of substance use disorder.

Section I. Re-Estimating Baseline Statistics

There were indications in the information gathered during the first year of Chapter 55 work that data collected by government agencies about the opioid crisis portrayed an incomplete picture of the scope of the problem. The figure below depicts this hypothesis. In the center of the diagram is the Universe of Known Events, consisting of data recorded in administrative data sets like medical claims, ambulance trip records, and death certificates about Opioid Use Disorder (OUD), Nonfatal Overdose (NFO), and Opioid-related overdose deaths. The fact that we are in a crisis is made clear when we look at these data. The scope of the crisis, however, is not.



Specifically, what is unknown are the actual number of *unrecorded* nonfatal overdoses and the total number of people with OUD. If we are to improve allocation of resources for individuals with OUD, we need to know how many people fit this definition and where they live. If we are to improve emergency services for people who have nonfatal opioid overdoses, we need to know how many people have overdosed, how many have overdosed repeatedly, and what proportion of reversals are overseen by bystanders. While opioid-related deaths are recorded on death certificates, there are strong indications that additional deaths may also be opioid-related. Internal data patterns suggest that publically reported counts of opioid-related deaths may still underestimate the size of the problem and also mask the impact of fentanyl on the death rates.

This section of the report examines the interrelationships among all the data sets to establish estimates for Opioid Use Disorder (OUD), Nonfatal Overdose (NFO), and Opioid-related Overdose Deaths (OROD) that are more internally consistent and consistent with all the relevant data.

Section I.a Estimating the Size of the Population with OUD

Current Status: The best available estimate is that the rate of Opioid Use Disorder (OUD) in MA is nearly one-third higher than the national rate.

Background: The rise in opioid-related overdose death rates nationally between 1999 and 2010 parallels the increase in consumption of opioid analgesics.[6] While this general trend applies to Massachusetts, reliable state-level numbers for Opioid Use Disorder (OUD) are difficult to obtain. Without citing a specific rate, one recent study using 2012 data suggested that the rate of opioid use disorder in Massachusetts was nearly one-third higher than the national rate.[7] However, opioid-related overdose deaths in Massachusetts have more than doubled since 2012. Given this increase, it is more important than ever to obtain a reliable estimate of the size of the population with OUD.

Basic Methods: In the normal course of business, government agencies collect vast amounts of administrative data to track events and transactions. While the data is often comprehensive, there are limitations to its use. One commonly cited limitation of administrative data is the likelihood that some information recorded is incomplete.[8] Events may not be captured or diagnosis codes may not be listed.

Data sources:

- Medical claims
- Hospital, ED, and outpatient data
- Death records
- Ambulance trips
- Post-mortem Toxicology
- Prescription Drug Monitoring Program
- Substance Abuse Treatment
- Birth records
- Dept of Mental Health
- Dept of Correction
- Houses of Correction
- Cancer Registry
- Dept of Housing and Community Development
- Dept of Veterans' Services

Analysts used records that were linked at the individual level across more than 10 administrative data sets. OUD is specifically coded in the All Payer Claims Database, Case Mix (hospital, ED and outpatient), death records, and the post mortem toxicology reports recorded by the Office of the Chief Medical Examiner. These values were used to form what was referred to as the "Gold Standard" measure for OUD.

A "capture-recapture" analysis[9] was used to estimate the true prevalence of opioid use. Individuals were identified using markers consistent with OUD in each Chapter 55 data source (i.e., the Gold Standard). It was assumed that this data was an incomplete accounting of OUD in Massachusetts.

Data was organized in tables by age group, sex, and county. Log linear models were used to fit the data to markers. The final model produced aggregate

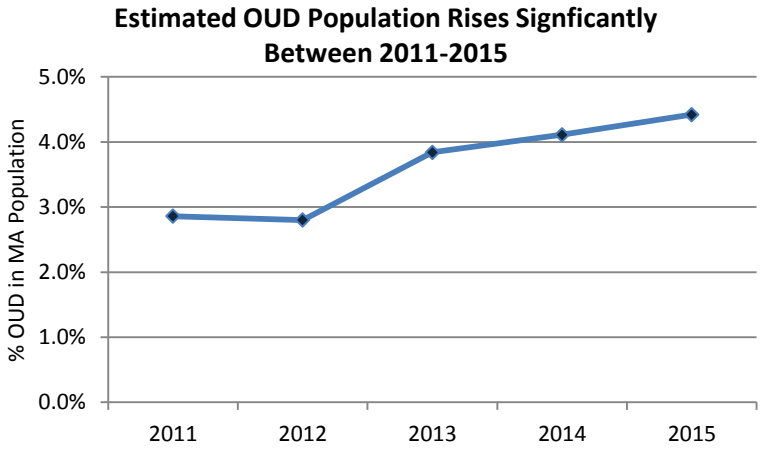
[6] Jones CM. Frequency of prescription pain reliever nonmedical use: 2002-2003 and 2009-2010. Arch Intern Med. 2012;172(16):1265-1267.
[7] Jones CM, Campopiano M, Baldwin G, McCance-Katz E. Am J Public Health. 2015 Aug;105(8):e55-63. doi: 10.2105/AJPH.2015.302664.
[8] Accessed at https://archive.ahrq.gov/data/safetynet/billings.htm on 5/19/2017.
[9] A capture-recapture analysis is often used in ecological studies to estimate the size of a population when data is incomplete.

estimates by year, county, gender, and age group. A combination of Poisson and zero inflated Poisson models were used to estimate the population prevalence. Estimates were validated by comparing projected OUD rates with rates of fatal opioid-related overdose deaths.

Key Findings:

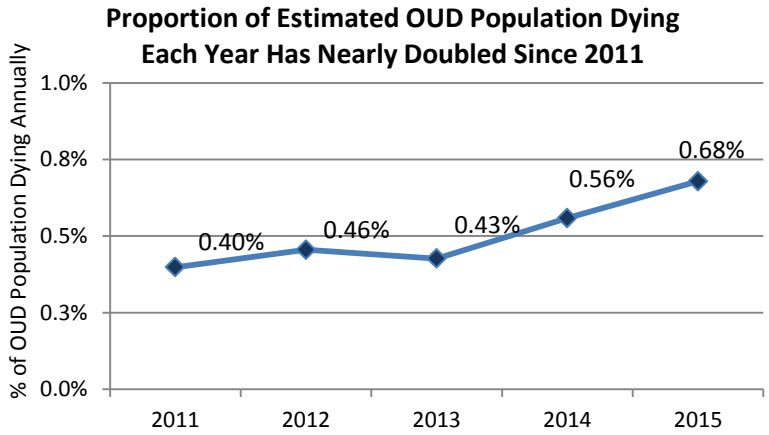
- Using only data specifically coded for OUD, it is estimated that approximately 4.4% of Massachusetts residents age 11 and older have opioid use disorder. ***No single Chapter 55 data set included all individuals identified by the Gold Standard of OUD.*** **Linkage was critical to increase accuracy.**
- The capture-recapture methodology produced annual estimates of OUD. There is an indication that the size of the OUD population may be increasing. Further study will refine these estimates.

Key Finding: In 2015, over 4% of Massachusetts residents age 11 and older had opioid use disorder.



- ***The proportion of the OUD population dying each year from opioid-related overdoses has nearly doubled between 2011 (0.40%) and 2015 (0.68%).***

Key Finding: The proportion of the OUD population dying each year from opioid-related overdoses has nearly doubled between 2011 (0.40%) and 2015 (0.68%).



- Epidemics occur in stages from growth to equilibrium to decay. The fact that the OUD population may still be increasing despite the fact that the proportion of population dying is also increasing may suggest that we have not yet reached the equilibrium phase.

Recommendations for Further Analysis:

- Develop analytic models for making estimates of OUD for individuals.
- Compare current OUD services for demographic and geographic populations to determine if services should be adjusted.
- Examine changing demographic trends to determine whether the need for specific services is likely to change over time. The population in Massachusetts is getting older and more ethnically diverse.
- Evaluate the impact of transitions of care for the OUD population on fatal and nonfatal overdose.

Section I.b Estimating the Number of Nonfatal Overdoses (NFO)

Current Status: Some research has estimated that there are 20 nonfatal opioid-related overdoses (NFO) for every fatal overdose. This estimate predates the influx of fentanyl into the drug supply system.

Background: Some research has estimated that there are 20 nonfatal opioid-related overdoses (NFO) for every fatal overdose. [10] For Massachusetts, that would suggest that there could be 30,000-40,000 nonfatal overdoses in 2015 alone. However, hospital, ED, and ambulance data record fewer than 20,000 events combined. Furthermore, the 20 to 1 ratio comes from a study that is 15 years old and predates the influx of fentanyl into drug supply system. The actual estimates could be either higher or lower. More recent data from Vancouver found that nearly half of people who die of fatal opioid-related overdose had a previous nonfatal overdose in the preceding five years. [11] Since death rates in Massachusetts have increased so markedly since 2012, [12] it is important to know whether nonfatal overdoses have increased at the same rate.

Records of nonfatal overdoses capture events when illegal activity may have been involved. As a result, those records are most likely incomplete accountings of the total number of events. To complete the picture, it is important to review data sources to ensure that estimates for different aspects of the opioid crisis are logically consistent with each other. That is why the linked Chapter 55 data set is such a valuable resource. All known sources were brought together to provide this composite estimate.

Data sources:

- Hospital, ED, and outpatient data
- Death records
- Ambulance trips
- Post-mortem Toxicology
- Census data (zip level)
- Community bystander reversals

Basic Methods: Linkage is required to identify any nonfatal overdose event in the administrative data sets available for Chapter 55. Overdoses are captured in hospital and ambulance data, but those events must be linked with death records to determine whether the overdose was fatal or nonfatal.

Overdose events for individuals are recorded in the Case Mix (hospital, ED and outpatient data), and MATRIS (ambulance trips). While the Case Mix data is thought to be a fairly complete accounting of NFO seen in Massachusetts hospitals, it is less clear that the APCD captures all NFO events for which medical claims are paid. MATRIS data has known gaps. Some emergency medical services have failed to report required data. Also, NFOs from MATRIS are based on a composite of information recorded by the EMTs to produce a likely NFO

[10] Darke S., Mattick R. P., Degenhardt L. The ratio of non-fatal to fatal heroin overdose. Addiction 2003; 98: 1169–71

[11] Caudarella A, Dong H, Milloy MJ, Kerr T, Wood E, Hayashi K. Nonfatal overdose as a risk factor for subsequent fatal overdose among people who inject drugs. Drug Alcohol Depend. 2016;162:51-55

[12] http://www.mass.gov/eohhs/docs/dph/stop-addiction/dph-legislative-report-chapter-55-opioid-overdose-study-9-15-2016.pdf

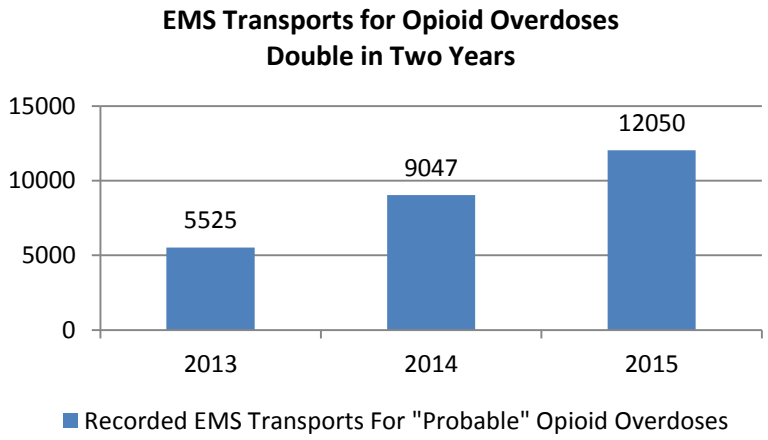
event.[13] Lastly, DPH's Bureau of Substance Abuse Services tracks some overdose reversals by community. However, this is also an incomplete picture of bystander reversals across the state. Given the variety of data sources used in this analysis, data linked at the individual as well as community level data was used to estimate the total number of NFO. Extensive de-duplication of NFO events was required across the different data sets.

All sources of data were used to develop a model of NFO that yielded a statistically reliable annual estimate of events in the state. Final estimates of missing NFO data from MATRIS were computed by comparing the ratio of projected NFO population rates at a community level to the rate of fatal overdoses by community. Values for community level "undercounts" were recorded. Finally, bystander reversals reported by communities were added to the community level "undercounts" from MATRIS.

Key Findings:

Key Finding: Ambulance trips due to a probable opioid-related overdose increased as much as by 110% in two years. Naloxone was administered by EMS in roughly 2 of every 5 of these overdoses.

- Reliable MATRIS data is only available starting in 2013. Ambulance trips due to opioid-related overdose increased by 110% in the two following years.[14] Overdoses are counted by an algorithm that incorporates many different pieces of information from the trip record for each ambulance run.



- Naloxone was administered by an EMT in roughly two of every five overdose events between 2013 and 2015. While the actual number of naloxone administrations has increased over time, the percentage of

[13] Data entered into MATRIS by EMTs was never intended to be diagnostic.
[14] This number could be an overestimate since data recorded in 2013 may have more missing information than subsequent years.

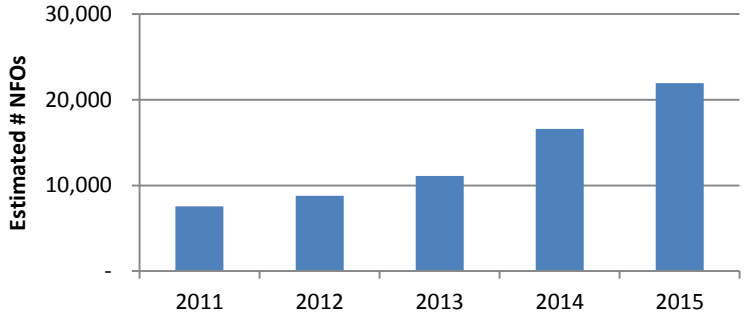
opioid-related events where naloxone was administered has remained relatively unchanged.

- Multiple naloxone administrations by EMTs were up 27% from 2013 to 2015, which aligns with the time period during which the presence of illicit fentanyl sharply increased in the drug supply system.
- No single Chapter 55 data set included all individuals identified with NFO. Linkage between data sets was critical for this analysis.
- Nonfatal opioid overdoses increased by ~200% between 2011 and 2015. The total number of nonfatal overdoses between 2011 and 2015 exceeded 65,000.[15]

Key Finding: Multiple naloxone administrations by EMTs up 27% from 2013 to 2015 which aligns with the period of sharply increased presence of illicit fentanyl in the drug supply system.

Key Finding: Nonfatal overdoses recorded by EMS, hospitals, and bystander interventions increased ~200% between 2011 and 2015. The total number of nonfatal overdoses between 2011 and 2015 exceeded 65,000.

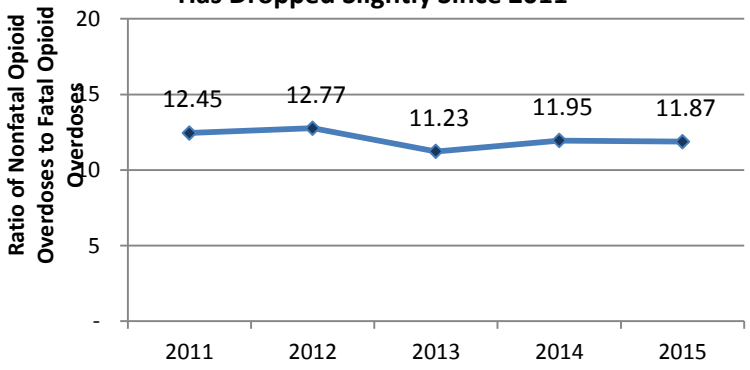
Total Nonfatal Opioid Overdoses Rise Sharply Between 2011 and 2015*



* MATRIS data only available from 2013 - 2015. EMS transports estimated.

- Annual estimates for nonfatal overdoses were compared to the number of fatal overdoses between 2011 and 2015. The figure below shows the year to year changes.

The Ratio of Nonfatal to Fatal Overdoses Has Dropped Slightly Since 2011



[15] Linking data across multiple data systems along with the use of logical estimates of missing data has allowed DPH to determine likely counts for nonfatal opioid overdoses between 2011 and 2015. Nonfatal opioid overdoses in Massachusetts have increased by ~300% in four years.

Recommendations for Further Analysis:

- Since many nonfatal overdoses go unrecorded, the total number, and geographic and demographic distributions may still be underestimated. To better understand these aspects of the opioid crisis, more complex analytic tools (e.g., machine learning) should be used to estimate the number and distribution of nonfatal opioid overdoses in Massachusetts.
- A careful examination of Naloxone distribution to communities should be studied using the Chapter 55 data sets to determine the effectiveness of this program. It will also tell us whether this program is increasing the proportion of "lives saved" to total overdoses, and where to target program resources in the future.

Section I.c Estimating the Total Number of Opioid-related Overdose Deaths (OROD)

Current Status: The rate of recorded opioid-related deaths and number of deaths are higher than ever in Massachusetts. In 2016, there were five times as many confirmed opioid-related deaths compared to 2000. This number may still be an underestimate.

Background: Nationally and in Massachusetts, fatal opioid-related overdoses have dramatically increased since 2000.[16] In May 2017, DPH reported that there were at least 1,933 confirmed opioid-related deaths in Massachusetts during 2016.[17] In comparison, there were just one-fifth as many confirmed opioid-related deaths (338) in 2000.[18]

While the number of opioid-related overdose deaths (OROD) is at the highest level ever, initial analyses of Chapter 55 data indicated that the reported total may be an undercount.[19] For example, opioid overdose was the listed cause of death for only 49.8% of those who died the same day as the naloxone administration by EMS. Similarly, there was a dip in the number of opioid-related overdose deaths for persons in their late 30's and early 40's. To better understand these unexpected results, the data was examined to determine if the reported numbers of OROD should be revised upward.

Unlike the examination of undercounts of opioid use disorder (OUD) and nonfatal overdoses (NFO), undercounts of OROD are not caused by incomplete data. The Office of the Chief Medical Examiner (OCME) certifies virtually all opioid-related deaths in the state. However, the linked Chapter 55 data provides analysts with an opportunity to examine data patterns across many data sets that the OCME could not have seen at the time the cause of death was being certified. For example, when making a determination of the cause of death, the OCME cannot systematically examine treatment and prescription histories or other administrative records indicating long-term opioid use. These additional pieces of information can be used to shed light on whether there may be an undercount of opioid-related deaths.

Data sources:

- Medical claims
- Hospital, ED, and outpatient data
- Death records
- Ambulance trips
- Post-mortem Toxicology
- Prescription Drug Monitoring Program
- Substance Abuse Treatment

Basic Methods: Analysts used 253,378 linked records of deceased individuals. These records were linked at the individual level across eight additional administrative data sets. All causes of death were included. OROD for

[16] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/stop-addiction/current-statistics.html on 5/19/2017.
[17] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/stop-addiction/current-statistics.html on 5/19/2017.
[18] While some of the increase in opioid-related deaths could be due to more careful reporting, it is unlikely that increases of this magnitude are due to reporting differences over time.
[19] Unreported data from the first Chapter 55 study showed an unusual number of deaths in different age groups with long histories of opioid use and treatment. This study examines the likelihood that some additional deaths may be opioid-related.

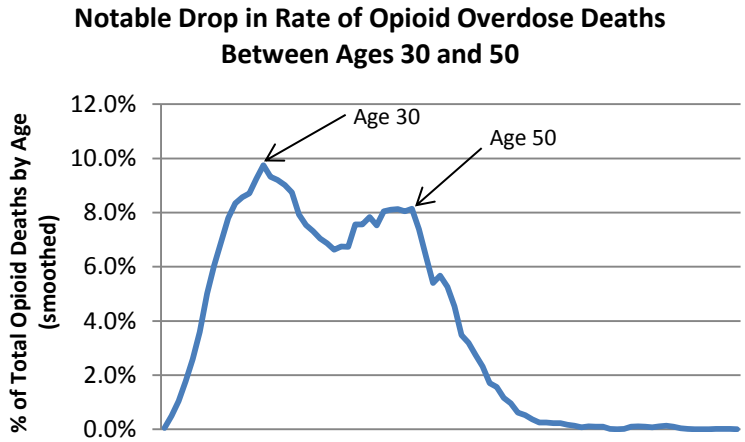
individuals was coded using the Medical Examiner's determination of cause of death. A predictive model was developed using 15 dependent variables. Causes of deaths assigned to cases that had been referred to the Medical Examiner were assumed to be correct.

The model produced results that could be interpreted conservatively or more broadly. The conservative approach focused only on a narrow range of cases with the specific ICD 10 codes for the cause of death that were drug related, related to respiratory or cardiovascular conditions, or were undefined or unknown.[20] The sum of the probabilities from the logistic model was counted as the additional opioid-related overdose deaths. The broader model utilized all cases not referred to the Medical Examiner and summed the probabilities to obtain an estimate of the additional opioid-related overdose deaths.

Key Findings:

Key Finding: Plots of opioid-related deaths suggest that fewer cases were recorded among persons age 30 to 50.

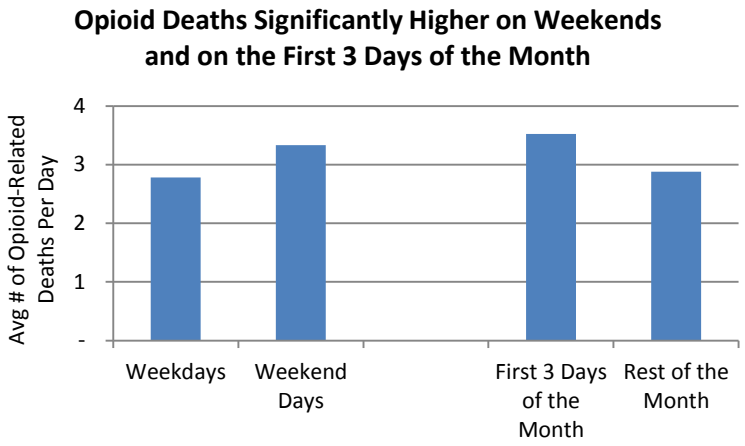
- The percent of total opioid-related deaths by age group shows a drop between age 30 and 50 suggesting the possibility that deaths may have been undercounted.



- Before estimating total deaths, opioid-related deaths were examined for several temporal patterns: seasonality, weekend/weekday differentials, and concentrations of deaths near the beginnings of months when benefit checks are often distributed. Approximately 20% more deaths occurred per day on weekends and also 20% more during the first 3 days of a month. There was no seasonality effect.

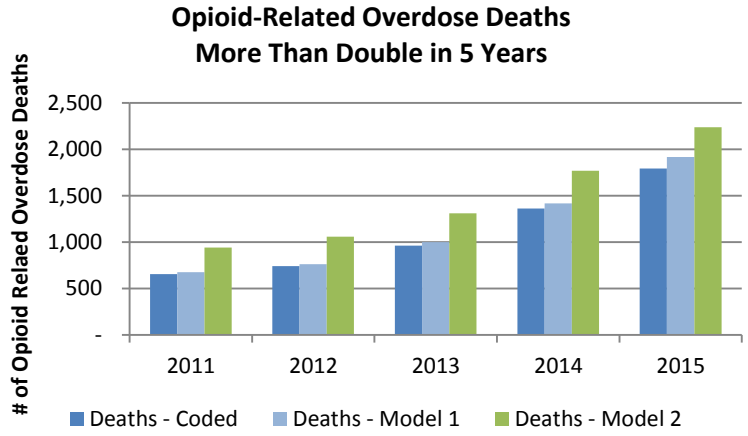
[20] The following codes were used: F11, F19, J18, J45, I11, I21, I33, I38, I49, and R99.

Key Finding: Approximately 20% more opioid-related deaths occurred per day on weekends and also 20% more during the first 3 days of a month.



- The number of opioid-related overdose deaths coded by the Office of the Chief Medical Examiner more than doubled between 2011 and 2015. Two predictive models were developed to determine if the "official" count was lower than what might be expected when looking across the breadth of Chapter 55 data.

Key Finding: Predictive models suggest that there might be an additional 6% to 33% opioid-related overdose deaths between 2011 and 2015. The more conservative estimate (6%) is thought to be closer to the "true" value.



- These models suggest that there might be an additional 6% to 33% opioid-related overdose deaths between 2011 and 2015. Model 2 estimates were highest for 2011 (43% increase) and 2012 (42% increase) compared to 2015 (25% increase).
- Since the broader model included many categories of death that were less related to long-term substance misuse or causes of death that were undefined or vague, it was felt that the re-estimate from the conservative model is most likely closer to the true value for OROD.

Recommendations for Further Analysis:

- A much deeper examination of undercounted opioid-related deaths should be undertaken. Knowledge of which demographic groups are misclassified more frequently than others, and whether patterns exist that indicate more frequent misclassification of official causes of death, can guide further work in this area.

Section II. Timeline and Influences

Introduction

In addition to being able to look across many different data sets as was the case in the previous section, the Chapter 55 data set also allows analysts to look at individuals for up to a five year time period. There has been much discussion about the role of prescription medications in fueling the opioid crisis in Massachusetts and elsewhere. There is also growing evidence of the impact of fentanyl on the sharp increase in fatal and nonfatal overdoses in the state.[21] While the Chapter 55 data can be used to establish the risk of fatal and nonfatal opioid overdose at each stage of the timeline, it can also be used to estimate the average length of time between the different stages.

What is the growing risk following first use of medications? How rapidly does that risk increase? When does more continuous use become risky and how long does that take? After a nonfatal overdose (NFO), what are the risks for a second NFO and how long does that take? Finally, how has the availability of illicit fentanyl in the drug supply system changed these timelines?

To fully understand how the transitions operate from one stage of opioid use to the next and how individual risk can be reduced, individual demographics, social determinants, medication use and other factors should be examined in concert to develop an individualized risk model. That work is beyond the scope of this report. The following section will provide an initial glimpse of timeline from opioid naive to fatal opioid overdose.

[21] Somerville NJ, O'Donnell J, Gladden RM, et al. Characteristics of Fentanyl Overdose — Massachusetts, 2014–2016. MMWR Morb Mortal Wkly Rep 2017;66:382–386. DOI: http://dx.doi.org/10.15585/mmwr.mm6614a2

Section II.a Risks for Fatal Opioid Overdose among the Opioid Naïve

Current Status: While there is consensus that long-term and high dose prescribing of opioids puts patients at increasing risk of fatal and non-fatal opioid-related overdose, additional evidence is needed about the short-, mid-, and long-term risks of opioid prescribing to the opioid naïve.

Background: In the 1990s, support was building for greater use of opioids to manage pain.[22] Throughout the early 2000s, there was a steady increase in opioid prescribing for acute and chronic pain.[23] [24] For many years, this increase closely paralleled an increasing opioid-related death rate in Massachusetts and elsewhere, but rates for opioid prescribing and opioid related overdose deaths have gone in different directions in recent years.[25] That fact could be used to argue against the importance of examining opioid naïve individuals. However, given the long-term statistical relationship between prescribing and overdose deaths from the early 2000s, it is important to better understand the rate at which this risk increases.

Studies also show that the transition from opioid naïve to opioid tolerant can be very brief – as little as one week.[26] Despite the short time it takes for the body to develop tolerance to opioids, relatively little is known about the short, mid, and long-term risks of opioid prescribing to the opioid naïve. The Chapter 55 data set provides an opportunity to examine the risk for persons with little or no exposure to prescription opioids and to track those risks over time.

Data sources:

- Medical claims
- Hospital, ED, and outpatient data
- Death records
- Ambulance trips
- Prescription Drug Monitoring Program
- Substance Abuse Treatment

Basic Methods: A binary operational definition for persons who were opioid naïve was developed using Chapter 55 data. All individuals were classified as either opioid naïve or not opioid naïve. **To be categorized as opioid naïve**, the individual's records had to show a period of six months or more without an opioid prescription before their first opioid prescription. Patients excluded from the group include those who:

- had any advanced cancer (other than non-melanoma skin cancer)
- had a substance use disorder diagnosis in the six months preceding their first opioid prescription, or
- whose first prescription was for any buprenorphine formulation indicated for treatment of substance use disorder

[22] McQuay H. Opioids in pain management. Lancet 1999, 353: 2229-2232.
[23] Kenan et al. Trends in prescriptions for oxycodone and other commonly used opioids in the United States, 2000-2010. Open Med. 2012 Apr 10;6(2):e41-7. Print 2012.
[24] Okie S. A Flood of Opioids, a Rising Tide of Deaths. N Engl J Med 2010; 363:1981-1985
[25] Pezalla et al. Secular trends in opioid prescribing in the USA. J Pain Res. 2017; 10: 383–387.
[26] Accessed at http://professionals.ufhealth.org/files/2011/11/0312-drugs-therapy-bulletin.pdf on 5/19/2017.

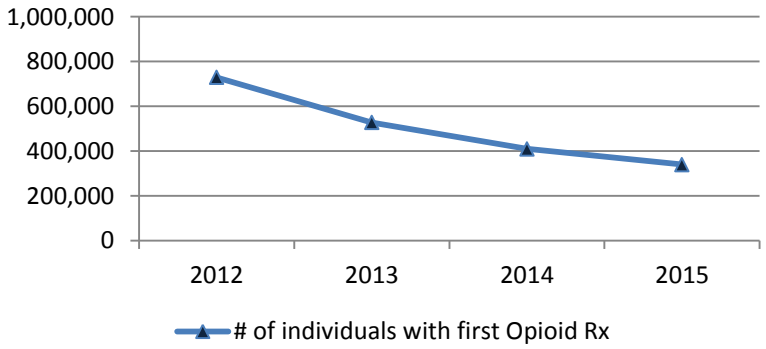
Opioid naïve populations were examined annually between 2011 and 2015. They were compared to the general population for rate of fatal opioid overdose.

Key Findings:

- The number of new opioid prescriptions dropped by roughly 50% between 2012 and 2015. Over three million individuals received new opioid prescriptions during the study period with a death rate of 6.2%. It is possible that the high death rate may reflect use of opioids for palliative care.
- The number of first prescriptions for patients classified as opioid naïve using the definition above dropped by nearly half between 2012 and 2015.

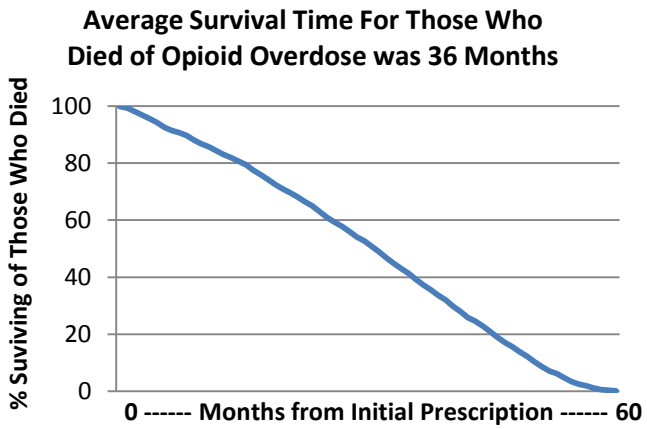
Key Finding: The number of initial prescriptions for patients classified as opioid naïve using the definition above dropped by nearly half between 2012 and 2015.

The Number of Opioid Naive Individuals with First Prescriptions Has Dropped 47% Since 2012



- Opioid naïve patients were tracked for up to 66 months following the initial prescription. For those who died of an opioid-related cause, the mean length of time from initial prescription to the opioid-related overdose death was 36 months.

Key Finding: For those who died, the mean length of time from initial prescription to opioid-related overdose death was 36 months



Key Finding: Almost half of all individuals who died of an opioid-related overdose during the study period were at one time classified as opioid naïve during the study period.

- Almost half of all individuals who died of an opioid-related overdose during the study period were at one time classified as opioid naïve during the study period.

Recommendations for Further Analysis:

- Examine the risk of this population to determine other factors which increase, decrease, or mitigate the risk of fatal opioid overdose.
- Compare the data for this population to the post-mortem toxicology reports to determine if people are dying from prescribed opioid medications or if they have made the transition to illegal drugs such as heroin.
- Measure the average length of time between opioid naivety and coding of opioid use disorder in administrative data sets.

Section II.b Continued Use of Prescription Opioids and Risk of Fatal Overdose

Current Status: Since many Massachusetts adults have filled an opioid prescription between 2011 and 2015, any increasing risk associated with continued use of prescription opioids puts hundreds of thousands of individuals at some increased level of risk for fatal and nonfatal opioid-related overdose.

Data Sources:

- Death records
- Prescription Drug Monitoring Program

Background: Concern about changes in opioid prescribing practices has been evident for over a decade.[27] Most people who receive an initial prescription for opioids after surgery or for pain do not continue to receive opioids after completing the initial prescription. [28] However, since most Massachusetts adults have filled an opioid prescription between 2011 and 2015,[29] any increasing risk associated with the continued use of prescription opioids puts hundreds of thousands of individuals at some ongoing risk for fatal and nonfatal opioid overdose. The analyses presented in this section will be a continuation of the work presented in the previous section on the opioid naïve population. The same cohorts will be tracked and estimates of fatal overdose risk will be calculated for different lengths of time of continued use.

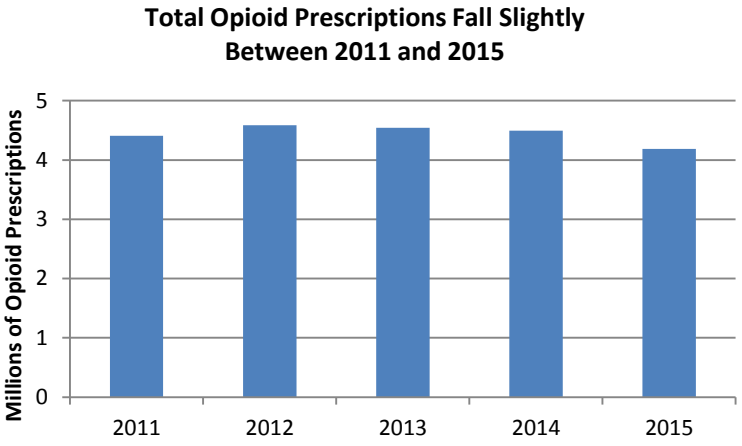
Basic Methods: A cohort who filled an opioid prescription for three months in 2011 or six months in 2011 or all 12 months in 2011 was tracked from 2011 through 2015 to see how many of them died from opioid-related overdoses each year. Data from the Prescription Drug Monitoring Program was linked to death records for this analysis. The goal was to see how risk of death increased through time and as a function of the number of months an individual had a prescription for opioids in 2011.

Key Findings:

- There has been a 47% decrease in the number of opioid naïve individuals between 2011 and 2015, and the total number of opioid prescriptions dropped 10% from its peak in 2012 to 2015.

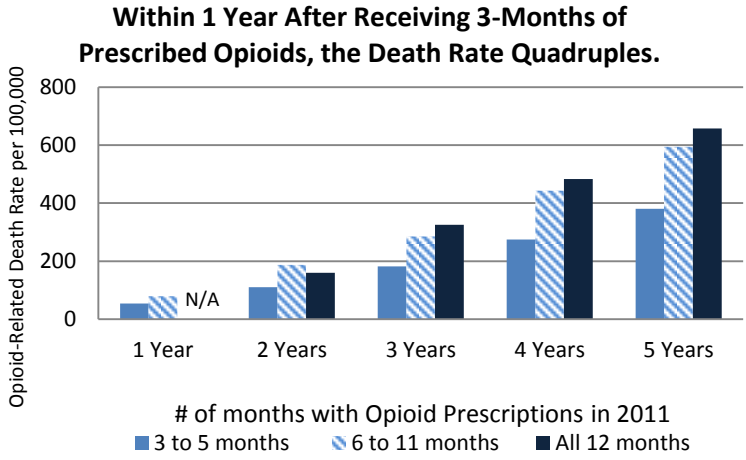
[27] Compton WM, Volkow ND. Major increases in opioid analgesic abuse in the United States: Concerns and strategies Drug and Alcohol Dependence 81 (2006) 103–107.
[28] Clarke H, et. al. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. BMJ 2014; 348 doi: https://doi.org/10.1136/bmj.g1251 (Published 11 February 2014) Cite this as: BMJ 2014;348:g1251
[29] In the previous section, it was stated that "Over three million individuals received new opioid prescriptions during the study period."

Key Finding: While there has been a 47% decrease in the number of opioid naïve individuals since between 2011 and 2015, the total number of opioid prescriptions only dropped 10% from its peak in 2012 to 2015.



- 1.1 million people who filled opioid prescriptions in 2011 were tracked over time. Of these, over 40,000 persons were prescribed opioids for the entire year, over 120,000 had more than six months of prescribed opioids, and over 220,000 persons had over three months of prescribed opioids.
- Compared to the general population, those who received three months of prescribed opioids in 2011 were four times as likely to die from an opioid-related overdose within one year, and 30 times as likely to die of an opioid-related overdose within five years.

Key Finding: Compared to the general population, those who received three months of prescribed opioids in 2011 were four times as likely to die from an opioid-related overdose within one year, and 30 times as likely to die of an opioid-related overdose within five years.



Recommendations for Further Analysis:

- A deeper analysis is required to understand the impact of fentanyl on the risk timeline for this 2011 cohort. It is possible that the trends seen for the persons prescribed opioids in 2011 may be different than in years where fentanyl was prevalent and opioid prescribing had dropped to some extent.

- The analysis should be combined with post-mortem toxicology to determine if it is possible to pinpoint with some accuracy the point at which individuals transition from legal to illegal opioids.

Section II.c Risk of Overdose and Death after a Nonfatal Opioid Overdose

Current Status: Previous research has shown that mortality among individuals with substance use disorders is high, even among those receiving treatment.

Background: Identifying individuals with a non-fatal overdose (NFO) related to opioids and determining treatment patterns and use of substance use treatment services may provide an opportunity to intervene and improve future outcomes. Previous research has shown that mortality among individuals with substance use disorders is high, even among those receiving treatment.[30] Additionally, individuals having an NFO from opioids, heroin, or related drugs may suffer from substantial morbidity from injuries and illnesses caused by the NFO.[31] Increased access to opioid agonist treatment has been shown to be associated with a decrease in heroin associated deaths.[32]

Understanding the post-NFO risk can guide government agencies and the health care system to deliver more integrated care that reduces the likelihood of subsequent fatal opioid overdose. Additionally, treating conditions related to opioid use and NFOs may be very expensive for private and government insurers,[33] so better understanding treatment access and provision may improve the evidence available for policy on appropriate treatment access and utilization.

Data Sources:

- Medical claims
- Hospital, ED, and outpatient data
- Death records
- Ambulance trips
- Post-mortem Toxicology

Basic Methods: A cohort was constructed of Massachusetts residents ages 11 years or older who had either an opioid-related fatal overdose or NFO within the 2011-2015 period.[34] Individuals were identified for this cohort using hospital discharge data, data on ambulance responses, and death records. The cohort was tracked to determine whether individuals had 1) an overdose (fatal or non-fatal) at any point, and 2) a repeat overdose after the original NFO. Insurance status was determined using the All Payer Claims Database.

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[30] Gossop M, Stewart D, Treacy S, Marsden J. A prospective study of mortality among drug misusers during a 4-year period after seeking treatment. *Addiction.* Jan 2002;97(1):39-47.
[31] Warner-Smith M, Darke S, Day C. Morbidity associated with non-fatal heroin overdose. *Addiction.* Aug 2002;97(8):963-967.
[32] Schwartz RP, Gryczynski J, O'Grady KE, et al. Opioid agonist treatments and heroin overdose deaths in Baltimore, Maryland, 1995-2009. *American journal of public health.* May 2013;103(5):917-922.
[33] Clark RE, Samnaliev M, McGovern MP. Impact of substance disorders on medical expenditures for medicaid beneficiaries with behavioral health disorders. *Psychiatric services.* Jan 2009;60(1):35-42.
[34] Note that individuals in the cohort could enter with either an original fatal overdose or a non-fatal overdose. For those whose initial overdose was fatal, we observe them as censored in our follow-up data. However, the construction of the original overdose cohort in this manner allows us to determine overall trends in the insurance status and type of individuals experiencing an opioid overdose at any point in the time period.

For the overdose cohort, we constructed two datasets – one with follow-up information for 12 months including the month of the first fatal overdose or NFO, and one with follow-up information for 24 months including the month of the first overdose. Estimates of the rate of fatal and repeat nonfatal overdoses were calculated.

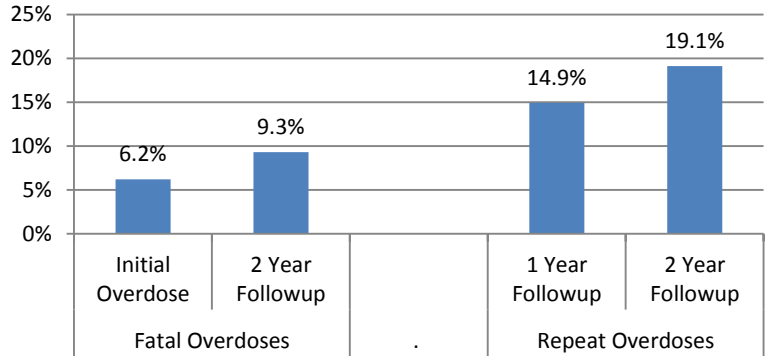
Key Findings:

- Of the Massachusetts residents who had a nonfatal overdose (NFO) between 2011 and 2015, 94.8% of them were insured for the majority of the two-year follow-up period. Of those who were insured, 76.8% were enrolled in Medicaid.
- Of the Massachusetts residents who had a nonfatal overdose (NFO) between 2011 and 2015, 6.2% had a fatal opioid-related overdose within one year following the initial overdose; 9.3% of the sample had a fatal opioid-related overdose within two years following the initial nonfatal overdose.[35]
- ***Repeat overdoses were common in the cohort, with 14.9% having one or more repeat overdoses during the one-year follow-up period and 19.1% during the two year follow-up period***.

Key Finding: 6.2% of the sample had a fatal opioid-related overdose within one year following the initial overdose. 9.3% of the sample had a fatal opioid-related overdose during the following two years.

Key Finding: Repeat overdoses were common in the cohort, with 14.9% having one or more repeat overdoses during the one-year follow-up period and 19.1% during the two year follow-up period.

Nearly 1 in 10 Die with in 2 Years After an Initial Nonfatal Overdose



- For the two year period, being insured (versus uninsured) is associated with a 5% increase in the probability of a repeat overdose, controlling for demographics and health services utilization. However, being insured (versus uninsured) is associated with a 7% reduction in the

[35] This includes individuals who had a fatal overdose as their initial entry into the overdose cohort.

probability of having a fatal opioid-related overdose at any point during the period (including the initial overdose).

Recommendations for Further Analysis:

- More advanced statistical modeling should be conducted to control for length of follow-up, comorbidities that impact medical care utilization, and differences in socioeconomic status.
- Examining associations between insurance status and type with opioid prescriptions and prescription use following an NFO is an important area for further study.
- There should be further examination of treatment provided to high-risk individuals by insurers in order to ensure that they have appropriate access to evidence-based treatment.

Section II.d Estimating the Impact of Fentanyl on Fatal Opioid-Related Overdoses

Current Status: Nationally, two in five heroin-related deaths have involved fentanyl and the rate appears to be higher in Massachusetts.

Background: Fentanyl is a synthetic opioid. It is a schedule II prescription drug,[36] and it is typically used to treat patients with severe pain or to manage pain after surgery.[37] While similar to morphine, fentanyl is estimated to be 50 to 100 times more potent.[38] [39] However, fentanyl is also increasingly manufactured illicitly and distributed for non-medical purposes often mixed with heroin or substituted for heroin without the users' knowledge.

Nationally, two in five heroin-related deaths have involved fentanyl and the rate appears to be higher in Massachusetts.[40] [41] Adding to the public health concern is the fact that new synthetic opioids are now being found in New England. A recent warning about carfentanil is evidence of the evolving risk.[42] In some cases, these new Illicit synthetics are many times as potent as fentanyl which is almost always illicit as well.

When illicit fentanyl became common in the drug supply in Massachusetts, the death rates went up sharply. While evidence is emerging that fentanyl is a strong contributor to the sharp increase in opioid-related deaths in Massachusetts.[43] this analysis will attempt to shed some additional light on that question.

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[36] Controlled Substances Act. Vol 21 CFR 1308.12. http://www.deadiversion.usdoj.gov/21cfr/cfr/1308/1308_12.htm.

[37] Nelson L, Schwaner R. Transdermal fentanyl: Pharmacology and toxicology. J Med Toxicol. 2009;5(4):230-241. doi:10.1007/BF03178274.

[38] Volpe DA, Tobin GAM, Mellon RD, et al. Uniform assessment and ranking of opioid Mu receptor binding constants for selected opioid drugs. Regul Toxicol Pharmacol. 2011;59(3):385-390. doi:10.1016/j.yrtph.2010.12.007.

[39] Higashikawa Y, Suzuki S. Studies on 1-(2-phenethyl)-4-(N-propionylanilino) piperidine (fentanyl) and its related compounds. VI. Structure-analgesic activity relationship for fentanyl, methyl-substituted fentanyls and other analogues. Forensic Toxicol. 2008;26(1):1-5. doi:10.1007/s11419-007-0039-1.

[40] Gladden RM, Martinez P, Seth P. Fentanyl law enforcement submissions and increases in synthetic opioid-involved overdose deaths — 27 states, 2013–2014. MMWR Morb Mortal Wkly Rep 2016; 65: 837-43

[41] Accessed at http://www.mass.gov/eohhs/docs/dph/stop-addiction/current-statistics/data-brief-overdose-deaths-may-2017.pdf on 5/19/2017.

[42] Ohannessian, Dana "Re: Situational Awareness Alert for the Drug Carfentanil - Message from DPH." Received 5/15/2017 via email.

[43] Somerville NJ, O'Donnell J, Gladden RM, et al. Characteristics of Fentanyl Overdose — Massachusetts, 2014–2016. MMWR Morb Mortal Wkly Rep 2017;66:382–386. DOI: http://dx.doi.org/10.15585/mmwr.mm6614a2.

Data Sources:

- Medical claims
- Hospital, ED, and outpatient data
- Death records
- Ambulance trips
- Post-mortem Toxicology
- Substance Abuse Treatment

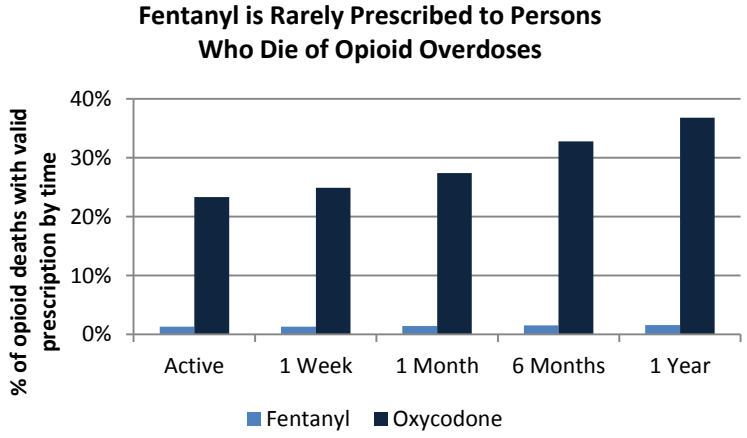
Basic Methods: Two models were developed to estimate the impact of fentanyl on opioid related deaths in Massachusetts. Model 1 used the annual counts of opioid-related deaths between 2000 and 2011 to project annual opioid-related deaths for the period from 2011 through 2015. Fentanyl was first noticed in Massachusetts deaths beginning around 2011. Actual deaths were compared to the expected deaths from the projection model to yield additional deaths that may be attributable to fentanyl.

Model 2 also used the individual death records but supplemented this information with data from post-mortem toxicology reports as well as basic demographics and the individual's history of opioid use disorder (OUD) including medication assisted and other OUD treatments. The model was designed to determine the unique contribution that fentanyl has played in the increased death rate in Massachusetts.

Key Finding: While seizures of heroin and other opioids doubled in this time, fentanyl seizures barely registered in 2011 and increased 70-fold between 2014 and 2015.

Key Findings:

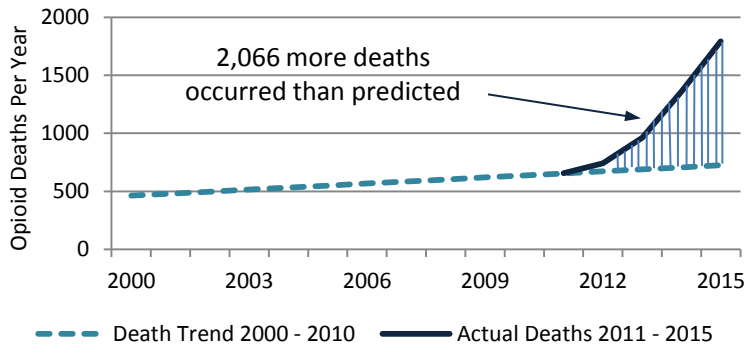
- According to the New England High Intensity Drug Trafficking Area (NE-HIDTA) group, seizures of pure fentanyl increased sharply between 2011 and 2015. While seizures of heroin and other opioids doubled in this time, fentanyl seizures barely registered in 2011 and increased 70-fold between 2014 and 2015.



Key Finding: A simple model was used to estimate that 2,066 deaths were attributable to increased levels of illicit fentanyl in the drug supply.

- Oxycodone is the most commonly prescribed opioid. One in five persons dying of an opioid overdose had an active oxycodone prescription at the time of death. Less than 2% had an active prescription for fentanyl, a number that barely changed over the course of a year. This indicates that almost all fentanyl involved in deaths is illicitly obtained.
- The fentanyl predictive model used trended death data from 2000 through 2010 to estimate likely deaths in 2011 through 2015. This is the dashed line in the figure below. Based on this model, the number of additional deaths since 2010 due to fentanyl exceeds 2,000.

More Than 2,000 Additional Deaths Attributable to Fentanyl Between 2011-2015



Recommendations for Further Analysis:

- While the increasing levels of fentanyl in the illicit drug supply roughly parallel the temporal increase in deaths, a deeper analysis looking at each individual's history of opioid use disorder, previous nonfatal overdoses, and mental and physical health co-morbidities is required to better understand the impact of fentanyl
- A geographic time series analysis should be conducted to show the spread of fentanyl and its relation to fatal and nonfatal overdose locally. If possible, algorithms should be developed to project where hot spots may occur in the future.

Section III. Identifying At-Risk Populations

The Chapter 55 data enables the state to simultaneously examine many different groups who may be at risk for fatal and non-fatal opioid overdose. This work marks the first population-specific examination of opioid related overdose risk for several of the populations characterized in this report.

The strength of the Chapter 55 data comes from the breadth of information gathered together in a single place. For example, data on homelessness is limited or not well validated in virtually all data sets. However, evidence of homelessness can be found in 12 different Chapter 55 data tables. Pulling together these data enables analysts to fill in the gaps in individual histories or even to model missing data. This approach has been used to provide a more complete picture of the homeless population in the state. The same is true for veterans, those with mental health co-morbidities, young adults, those leaving Massachusetts jails and prisons after serving a sentence, mothers with opioid use disorder, and individuals served by a number of other government agencies.

The core information presented in each subsection will provide estimates of the risk of fatal and nonfatal overdose for each of the populations studied. In addition, the overlap in these populations will be presented. This is of particular interest for persons receiving service or aid from a specific government agency. Knowing the likelihood that an individual is also connected to another agency may offer opportunities to collaborate across government to address the opioid problem.

The subpopulations examined were:

- Massachusetts Veterans served by VA Pharmacies and the Department of Veterans' Services
- Individuals experiencing an episode of homelessness or housing instability
- Individuals with Serious Mental Illness (SMI)
- Young Adults (ages 18-25)
- Individuals Recently Released from Incarceration in Prisons and Jails
- Mothers with Opioid Use Disorder
- Residents of Massachusetts Communities and Regions

Section III.a Massachusetts Veterans Using the VA Pharmacies and DVS Services

Current Status:
Massachusetts veterans report problems with binge drinking, symptoms of depression and posttraumatic stress disorder along with financial, housing, and educational needs. Little is known about the specific risk of fatal and nonfatal opioid overdose among Veterans.

Background: Veterans comprise 5% of the Massachusetts population – more than 355,000 persons. A recent survey of Massachusetts veterans indicates that they reported problems with binge drinking, symptoms of depression and post-traumatic stress disorder along with financial, housing, and educational needs,[44] making this group an at-risk population for opioid use disorder.

While a Chapter 55 analysis of the broader relationship between Veterans' status and fatal and nonfatal opioid overdose will be examined at a later date, the population of interest here are Veterans who receive services and entitlements from the Department of Veterans' Services (DVS) along with those who dually utilize the Federal VA pharmacy for prescriptions, including opiate prescriptions.

Data Sources:

- Medical claims
- Hospital, ED, and outpatient data
- Death records
- Ambulance trips
- Post-mortem Toxicology
- Dept of Veterans' Services

Basic Methods: DVS provided a complete list of persons receiving financial support with DVS funds. Fewer than 10% of the total Veteran population in the state received benefits from DVS between 2011 and 2015. In order to expand the population to other Veterans, an operational definition of "Veteran" status was developed. To be counted as a "Veteran" in the Chapter 55 data set, an individual had to meet ANY of the following criteria:

- At least one record for housing, medical or other benefits in the DVS data between 1/1/2011 and 12/31/2015 AND was at 18 years old or more.
- At least one prescription filled at a VA pharmacy between 1/1/2013 – 12/31/2015 (the period for which data were available).
- At least one prescription in the PMP data between 1/1/2011 and 12/31/2015 where the type of payment was identified as 'Military Installations and VA.'
- A record of death in which the occupation was classified as 'military.'

This definition identified 98,433 individuals. The Veterans identified using the definition above were cross-tabulated with the other at-risk groups reported on

[44] Supporting Those Who Served in Massachusetts Needs, Well-Being, and Available Resources for Veterans by Carrie M. Farmer, Terri Tanielian, Shira H. Fischer, Erin L. Duffy, Stephanie Dellva, Emily Butcher, Kristine Brown, Emily Hoch Copyright: RAND Corporation Availability: Web-Only, DOI: 10.7249/RB9945 Document Number: RB-9945-KLAFF

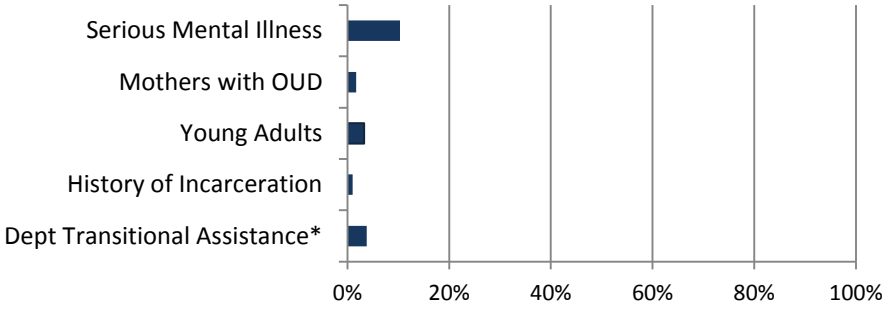
in this section. Finally, estimates of the rates for fatal overdoses were calculated for this group of Veterans.

Key Findings:

- The average veteran identified was 54 years old, but the age distribution indicated that there were two distinct groups of veterans – one with an average age of 32 and the other with an average age of 67. More than half of the Massachusetts veterans identified were men.
- Unlike most at-risk populations, the Massachusetts veterans examined here had relatively little overlap with other at-risk groups. One quarter were insured through MassHealth.

Key Finding: Unlike other at-risk populations, the Massachusetts veterans examined here had relatively little overlap with other at-risk groups.

MA Veterans Had Little Connection to Other Service Agencies and At Risk Populations

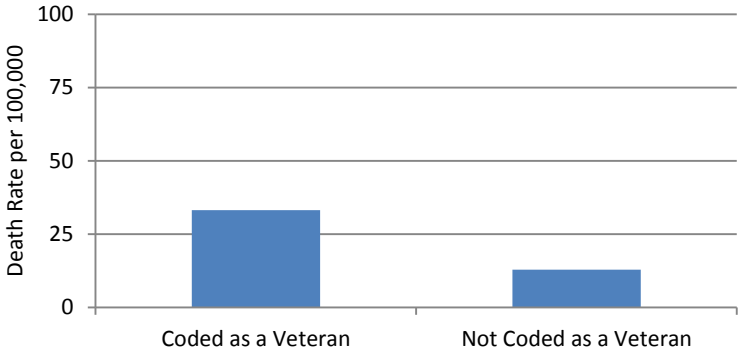


* Individuals receiving benefits through DTA.

- The percentage of identified veterans who had a fatal opioid overdose was three times the state average. This was an unadjusted estimate, which did not control for Veteran specific characteristics such as age, physical and mental health co-morbidities, etc. Generation of an adjusted estimate is planned as part of further analyses.

Key Finding: The percentage of identified veterans who had a fatal opioid-related overdose was three times the state average.

Opioid Death Rate ~3 Times Higher among MA Veterans



Recommendations for Further Analysis:

- Examine “dual use” in this Veteran sample for opioid prescriptions (i.e., how many Veterans are getting their opioid prescriptions from both VA and non-VA pharmacies as compared to only VA pharmacies). Further, examine whether these dual users are at an increased risk of opioid use disorder, non-fatal opioid overdose and fatal opioid overdose.
- Estimate prevalence of opioid use disorder, non-fatal opioid overdose, and fatal opioid overdoes in sub-groups of at-risk Veterans (i.e., homeless, depressed, and those with PTSD).
- Examine effect of the VA’s Opioid Safety Initiative launched in 2013 on the rates of opioid use disorder and opioid related deaths in Veterans in Massachusetts.

Section III.b Individuals Experiencing Homelessness

Current Status:
Homelessness has been a persistent societal problem in Massachusetts and nationwide for decades. Despite the length of time policymakers have recognized the problem, accurate and complete data on individual homelessness is difficult to obtain primarily because data systems are not well organized to track a population that is periodically transient.

Data Sources:

- Medical claims
- Hospital, ED, and outpatient data
- Death records
- Ambulance trips
- Post-mortem Toxicology
- Prescription Drug Monitoring Program
- Substance Abuse Treatment
- Birth records
- Dept of Mental Health
- Dept of Correction
- Houses of Correction
- Cancer Registry
- Dept of Housing and Comm Development
- Dept Veterans' Services

Background: Homelessness has been a persistent societal problem in Massachusetts and nationwide for decades.[45] Despite the length of time policymakers have recognized the problem, accurate and complete data is difficult to obtain primarily because data systems are not well organized to track individuals experiencing homelessness. Some estimates, however, do exist. A 2016 point-in-time count in Massachusetts found that roughly 19,600 persons were experiencing homelessness on a given night—of whom about two thirds were persons in families and the remaining one third were single homeless adults.[46] Point-in-time counts, however, do not adequately capture the issue of housing instability or episodic homelessness since an individual's or family's risk of homelessness may be transient.

With respect to risk of fatal and nonfatal opioid-related overdose, a 2003-2008 study of homeless adults in Boston found that drug overdose was the leading cause of death for this population, occurring at rates 16-24 times higher than in the general population. Opioids were a factor in over 80% of these deaths.[47] In light of dramatic recent increases in opioid-related fatalities nationally, a more comprehensive and updated assessment of opioid overdose deaths among individuals experiencing homelessness in Massachusetts is warranted.

Basic Methods: Government agencies routinely collect vast amounts of administrative data to track events and transactions. These data include information about homelessness and housing instability in various forms, and while extensive, these data are limited in important ways. One commonly cited limitation of administrative data is the likelihood that some information recorded is incomplete.[48] For example, data on emergency shelter utilization represent one of the most commonly used sources of administrative data to identify homelessness but do not identify homeless persons who do not use the emergency shelter system. Other administrative data sources such as medical records, data collected about ambulance trips, and death records include indicators of homelessness and housing instability, but not all episodes of homelessness are likely to be captured and diagnosis codes indicating

[45] Lee, B. A., Tyler, K. A., & Wright, J. D. (2010). The new homelessness revisited. *Annual review of sociology*, *36*, 501-521.
[46] https://www.hudexchange.info/resource/5178/2016-ahar-part-1-pit-estimates-of-homelessness/
[47] January 14, 2013. doi:10.1001/jamainternmed.2013.1604
[48] Accessed at https://archive.ahrq.gov/data/safetynet/billings.htm on 5/19/2017.

homelessness may not be listed during a medical encounter even for those who are experiencing an episode of homeless. For this study, mathematical modeling was therefore used to project the incomplete parts of data sets in order to yield a reliable prevalence estimate for individuals experiencing homelessness in Massachusetts.[49]

Analysts used 5,050,639 records that were linked at the individual level across 14 administrative data sets. To be included, individuals had to have data in at least one data set in addition to the All Payer Claims Database. [50]

The records were randomly split into two portions – a training data set with 75% of the records and a test data set with the remaining 25%. Homelessness was specifically coded in the All Payer Claims Database, CaseMix (hospital, ED and outpatient data), ambulance trip, Prescription Drug Monitoring Program, and Department of Mental Health data, and an indicator in any of these datasets was categorized as a coded instance of homelessness.[51] Predictive models using logistic regression were developed on the training data set to estimate the likelihood of coded homelessness using more than 100 predictors.

The resulting model was validated on the test data set on the coded homelessness measure described above and also other related variables. Since the validation demonstrated that the estimated homelessness values were predictive of expected outcomes, a final homelessness measure was created using actual coded values where available and predicted probabilities where no code existed. These values were examined with respect to fatal and nonfatal opioid overdose to determine the risk for this vulnerable population.

Key Findings:

- By linking data sets together and modeling patterns that could be related to homelessness, it is estimated that 1 in 25 adults (3.7%) was likely to have been homeless at some point between 2011 and 2015.

Key Finding: When relying exclusively on homeless-specific administrative codes, only 1% of the population was homeless between 2011 and 2015. However, by linking data sets together and modeling patterns that could be related to homelessness, it was estimated that 1 in 25 adults (3.7%) was likely to have been homeless at some point between 2011 and 2015.

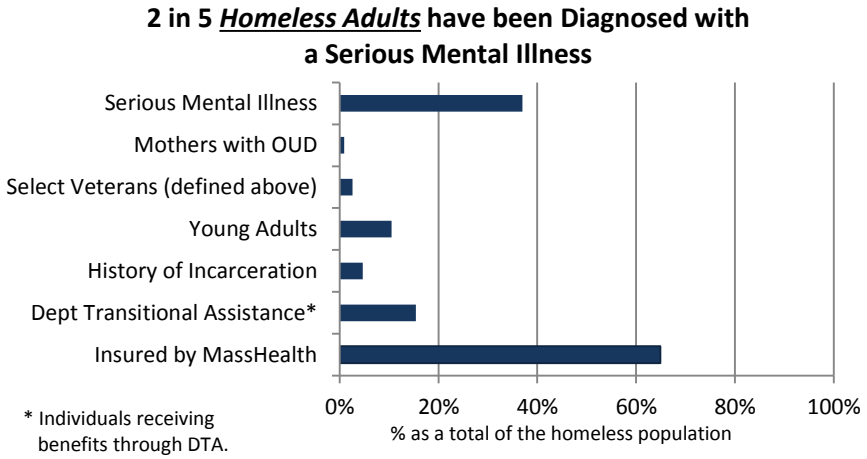
[49] Our focus in this work is primarily on the single adult homeless population with a future analysis to focus more specifically on the discrete population of persons in families experiencing homelessness. This distinction is warranted in light of evidence of differences in the characteristics of the single adult and family homeless along several dimensions.

[50] Since the APCD forms the spine of the Chapter 55 data system, all individuals have at least some data in the APCD.

[51] Records on the use of the Emergency Assistance (EA) family shelter system were available from the Department of Housing and Community Development (DHCD), but were not included as an indicator of homelessness in the current analysis, as the intent was to identify the single adult homeless population as far as was possible with the available data.

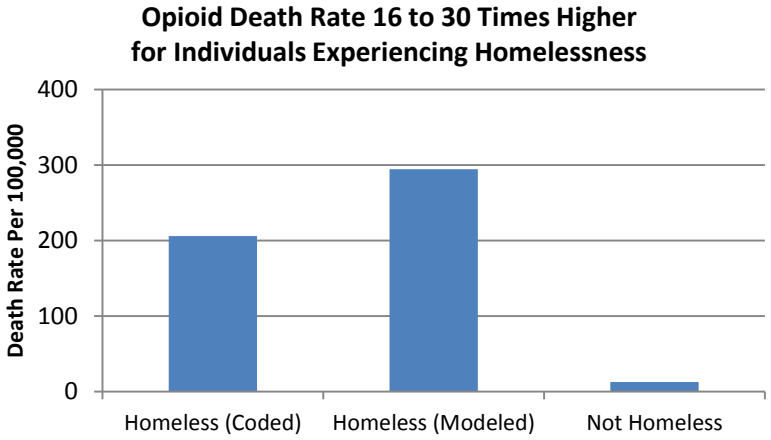
- At least three in eight adults who experienced homelessness between 2011 and 2015 have a coded diagnosis of a serious mental illness.[52]

Key Finding: 39% of Homeless adults have had contact with the Dept of Transitional Assistance while 20% have been recently incarcerated in Massachusetts jails or prisons.



- The opioid overdose death rate is between 16 and 30 times higher for the homeless individuals compared to the rest of the adult population.[53]

Key Finding: The opioid-related overdose death rate is 16 to 30 times higher for homeless individuals compared to the rest of the adult population.



Recommendations for Further Analysis:

- Build on this initial analysis of the relationship between homelessness and opioid overdose to assess other questions of interest related to homelessness housing status. Potential areas for inquiry include: examining whether homeless status modifies (either positively or negatively) the effectiveness of naloxone; assessing whether persons experiencing homelessness are more likely to experience fatal

[52] Coded in one or more of the administrative data sets.
[53] The rate is 16 times higher for coded administrative data and 30 times higher for the modeled results.

overdoses in which fentanyl is present; examine health care utilization patterns among persons experiencing homelessness to identify potential intervention points.

- Since the risk of opioid related death is significant for individuals experiencing homelessness, we should also examine fatal and non-fatal opioid overdose specifically among families who use the DHCD Emergency Assistance family shelter system.

Section III.c Individuals with Serious Mental Illness (SMI)

Current Status: SAMHSA estimated that 1.5 million adults with serious mental illnesses (SMI) had misused opioids in the previous year. While the rate of opioid misuse is higher in the SMI population, the impact on fatal and nonfatal overdoses is not known.

Background: Persons with substance use disorder (SUD) have been found to be twice as likely to have mood or anxiety disorders.[54] However, among the criminal justice involved population, almost half have both a diagnosis of a serious mental health condition and substance use disorder.[55] In January 2017, the Substance Abuse and Mental health Services Administration (SAMHSA) estimated that 1.5 million adults with serious mental illnesses (SMI) had misused opioids in the previous year.[56] SAMHSA defined SMI as "a diagnosable mental, behavioral or emotional disorder (excluding developmental and substance use disorders) of sufficient duration to cause serious functional impairment in an individual's major life activities (going to work, school, interacting with family, etc.)." The specific diagnostic categories included were mood disorders, schizophrenia, and other psychotic disorders. While the rate of opioid misuse is higher in the SMI population, the impact on fatal and nonfatal overdoses is not known. The Chapter 55 data system can shed much light on these relationships.

Data Sources:

- Medical claims
- MassHealth
- Hospital, ED, and outpatient data
- Death records
- Dept of Mental Health

Basic Methods: MassHealth prepared data that flagged persons with SMI using ICD 9 and ICD 10 diagnosis codes found in any medical claims administered by MassHealth. This flag was only available for MassHealth Clients and was based on the MassHealth definition of SMI. Other diagnosis groups were examined using the Case Mix hospital, ED, and outpatient data sets. These included Stress/Anxiety, Depression, Early Onset/ADHD, and Neuro-Cognitive diagnoses. Comparisons between the SMI group using MassHealth data and the hospital-based diagnoses using Case Mix should be done with caution.

The risk of fatal and nonfatal overdose may be overestimated if based on the opioid-related risk for the populations identified from hospital events, since hospital-related events may capture persons with more serious conditions than those identified through medical claims. All five groups examined with respect to fatal opioid overdose and comparisons were made to the rest of the adult population in Massachusetts. Additional comparisons were made between SMI and other at-risk populations.

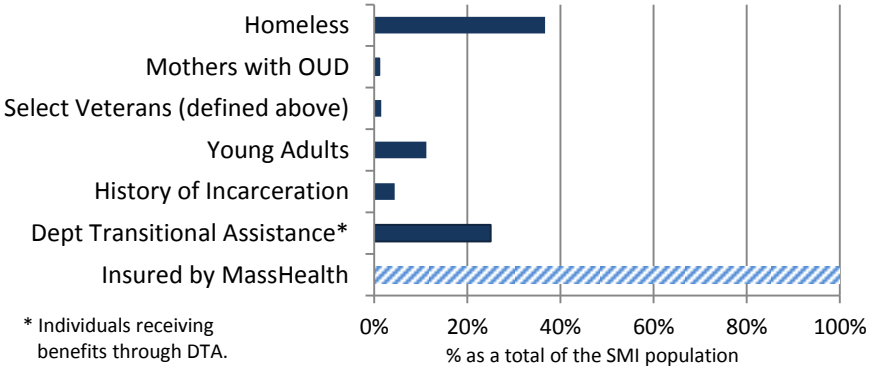
[54] Accessed at https://www.drugabuse/gov/publications/drgfacts/comorbidity-addiction-other-mental-disorder on 5/19/2017.
[55] Accessed at https://www.drugabuse.gov/sites/default/files/rrcomorbidity.pdf on 5/19/2017.
[56] Accessed at https://www.samhsa.gov/newsroom/press-announcements/201701241230 on 5/19/2017.

Key Finding: Nearly two in five MassHealth members with a serious mental illness have been homeless for some period of time between 2011 and 2015.

Key Findings:

- Roughly one in four persons ages 11 and older in the MassHealth population was identified as having a serious mental illness. Of these individuals, nearly two in five have been homeless for some period of time between 2011 and 2015 while one in four has been served by the Department of Transitional Assistance.

Persons with SMI **are More Likely to be Homeless and Receive Benefits Through Dept of Transitional Assistance**



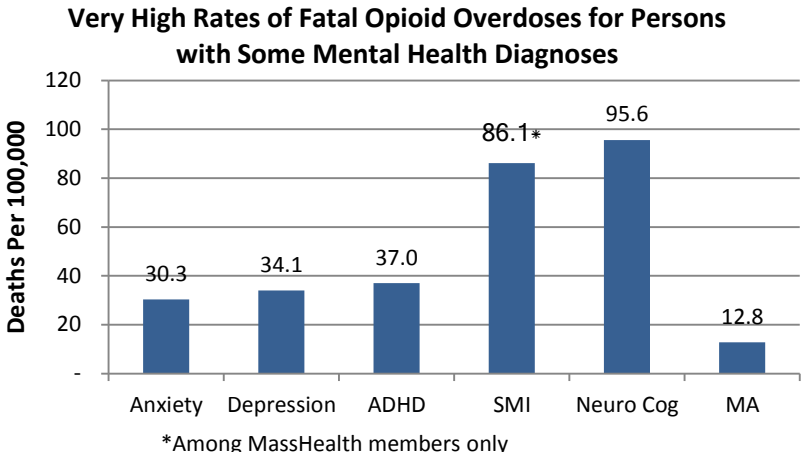
* Individuals receiving benefits through DTA.

[57]

[57] Since only MassHealth data was used to identify SMI, all persons with SMI in this study were insured by MassHealth.

- Of individuals diagnosed with SMI in the MassHealth population, the opioid-related overdose death rate is more than six times the state average.
- In the Chapter 55 data set, through hospital records, one in six persons was identified having a stress or anxiety diagnosis, one in 10 persons in was identified as having a depression diagnosis, and one in 40 persons was identified as having a neuro-cognitive diagnosis.
- The opioid-related overdose death rate was roughly two times higher than the state average for those identified as having a stress or anxiety diagnosis.
- The opioid-related overdose death rate was roughly three times the state average for those identified as having a depression diagnosis.
- The opioid-related overdose death rate was roughly seven times higher than the state average for those identified as having a neuro-cognitive diagnosis.

Key Finding: The risk of fatal opioid-related overdose is six times higher for persons diagnosed with a serious mental illness (SMI) and three times higher for those diagnosed with depression.



Recommendations for Further Analysis:

- Examine all deaths that might be considered premature in order to better understand whether a larger number of cases involving persons with a serious mental illness might actually be intentional deaths (i.e., suicides).
- Examine nonfatal overdoses to see if the proportion is related to greater degrees of isolation.

Section III.d Young Adults (18 – 25 years old)

Current Status: 18 to 25 year olds are three times more likely to report past year illicit drug dependence and misuse than the general population

Data sources:

- Medical claims
- Hospital, ED, and outpatient data
- Death records
- Ambulance trips
- Post-mortem Toxicology

Background: Eight percent of the state's population (538,000 persons) are 18-25 years old (i.e., "young adults").[58] Nationally, young adults have a higher prevalence of prescription drug misuse than any other group with 5.9 percent reporting nonmedical use in the past month.[59] Between 2002-2004 and 2011-2013, heroin use in young adults increased 108% and fatal overdoses increased 86%.[60] In 2014, young adults had the highest prevalence of past-year heroin use (0.8%) and prescription drug misuse (12.0%) compared to other age groups. When examining recent illicit drug use, young adults are almost three times as likely to report past year illicit drug dependence and misuse as the general population.[61] Young adults who use substances are also three times more likely to be HIV positive and twice as likely to have past year history of civil commitment (Section 35) to treatment.

Since young adults may respond to engagement and treatment differently than older adults, further examination into developmental differences in this age group and the need to take a tailored approach to understanding their specific risk factors and treatment needs are critical.

Basic Methods: Age is a core demographic variable in the All Payer Claims Database (APCD) and thus young adults are represented in the Chapter 55 data as fully as they are represented in the APCD. The Center for Health Information and Analysis (CHIA) estimates that annual representation of Massachusetts residents in the APCD exceeds 97%. Since the vast majority population was represented, no mathematical modeling or weighting was required.

Key Findings:

- In general, young adults did not overlap with other at-risk groups. Approximately one-third were insured by MassHealth. One in 20 had been homeless and one in 20 had a diagnosis for a serious mental illness.

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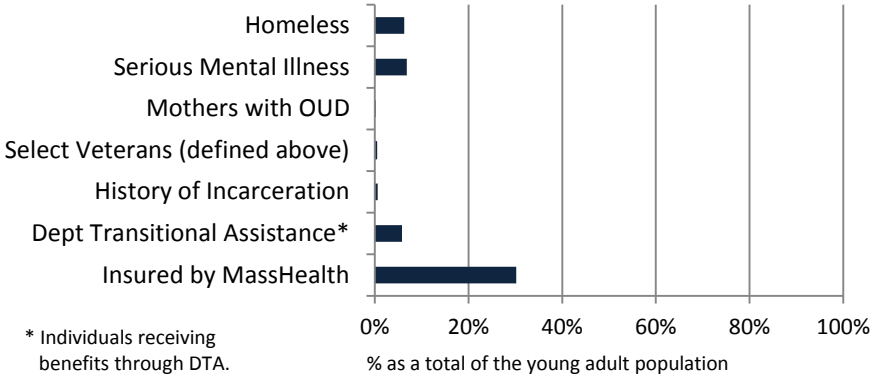
[58] Accessed at http://censusviewer.com/state/MA/2010 on 5/19/2017.

[59] Accessed at https://www.drugabuse.gov/publications/research-reports/prescription-drugs/trends-in-prescription-drug-abuse/adolescents-young-adults on 5/19/2017.

[60] Rudd R, Aleshire N, Zibbell J, Gladden M. Rudd RA, Aleshire N, Zibbell JE, Matthew Gladden R. Increases in drug and opioid overdose deaths—United States, 2000–2014. *MMWR Morb Mortal Wkly Rep*. 2016;64(50-51):1378-1382.

[61] Jones CM, Logan J, Gladden RM, Bohm MK. Vital Signs: Demographic and Substance Use Trends Among Heroin Users - United States, 2002-2013. *MMWR Morb Mortal Wkly Rep*. 2015;64(26):719-725

Young Adults Had Less Overlap with Other Subpopulations Examined

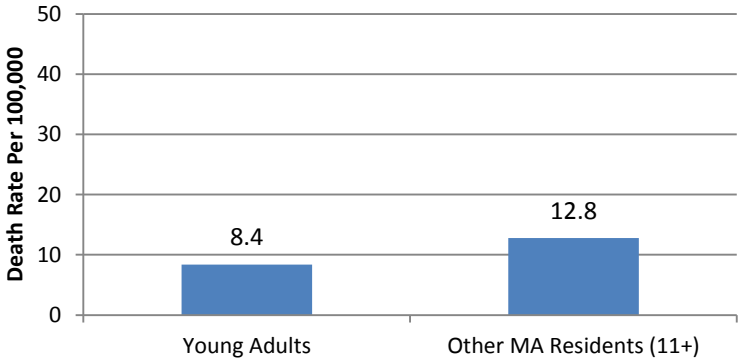


* Individuals receiving benefits through DTA.

Key Finding: Of all individuals experiencing a nonfatal opioid-related overdose between 2012 and 2014, 19% were young adults. Young adults were 189% more likely to be HIV positive and 79% more like to have a history of civil commitment to treatment within the past year.

- Of all individuals experiencing a nonfatal opioid-related overdose between 2012 and 2014, 19% were young adults (they made up 8% of the overall population).
- Young adults were 189% more likely to be HIV positive and 79% more like to have a history of civil commitment to treatment within the past year than older adults.

Opioid Death Rate is One-Third Lower Among Young Adults (18-25)



Key Finding: The opioid-related death rate is one-third lower for young adults compared to the rest of the population.

Key Finding: While the opioid-related overdose death rate is lower for young adults, it is a critical time to intervene since death rates for older adults increases dramatically.

- While the opioid-related overdose death rate is lower for young adults, it is a critical time to intervene since death rates for older adults increases dramatically. Among individuals who had a nonfatal overdose, there were no differences between young adults and older adults in gender, recurrent overdose, or subsequent fatal overdose.

Recommendations for Further Analysis:

- Catalog the specific services that are already in place for young adults in order to determine whether more (and how many more) should be allocated.

- Describe the geographic distribution of nonfatal overdoses among young adults.
- Determine whether there are gender-specific risk factors for young adults who experience a nonfatal overdose that have implications for public health interventions or policy.
- Examine the factors associated with engaging in medication treatment for young adults (buprenorphine, methadone, or naltrexone) after an overdose.
- Evaluate the rates of nonfatal opioid-related overdose in this population.

Section III.e Persons Released from Incarceration in Prisons and Jails

Current Status: the 2016 Chapter 55 opioid report found an approximately 50 times higher opioid overdose death rate in formerly incarcerated people than among non-incarcerated Massachusetts residents. Individuals incarcerated in Massachusetts jails were not examined previously.

Background: At the end of 2011, 7 million Americans were under correctional supervision, including 2.2 million held in jail or prison[62]. Of those incarcerated, nearly two-thirds (1.5 million) have substance use disorders, including up to one-quarter with opioid use disorder[63,64,65]. It has been estimated that one-third of heroin users pass through correctional facilities annually[66]. Few inmates with opioid use disorder receive addiction treatment during incarceration, and rates of relapse and opioid overdose-related deaths (109 deaths per 100,000 person years, or 15 percent of all deaths among former inmates) are tragically high following release[67] [68] [69] [70].

Data from Massachusetts prisons and jails were used in this report. The Massachusetts Department of Corrections (DOC) manages all seventeen[71] state correctional facilities or prisons. The 15 county jails[72] or Houses of Correction (HOC) are managed by the county sheriffs. According to the DOC, the MA prison population continued to decline for the fourth year, dropping 15% after a peak of 11,723 inmates on January 1, 2012 to 10,014 inmates on January 1, 2016. The number of criminal releases increased averaging 277 per month (3,329 total) during 2015.[73] The DOC has acknowledged the drug problem within the prison

Data sources:

- Medical claims
- Hospital, ED, and outpatient data
- Death records
- Ambulance trips
- Post-mortem Toxicology
- Dept of Correction
- Houses of Correction

[62] Glaze LE, Parks E. Correctional populations in the United States, 2011. Washington DC: U.S. Department of Justice; 2012.
[63] Mumola CJ, Karberg JC. Drug use and dependence, state and federal prisoners, 2004 (revised 1/19/07) Washington, DC: U.S. Department of Justice; 2006.
[64] Fazel S, Baillargeon J. The health of prisoners. Lancet. 2011;377:956–65. doi: 10.1016/S0140-6736(10)61053-7. [PubMed] [Cross Ref]
[65] Karberg JC, James DJ. Substance dependence, abuse, and treatment of jail inmates, 2002. Washington DC: U.S. Department of Justice; 2005.
[66] Boutwell AE, Nijhawan A, Zaller N, Rich JD. Arrested on heroin: a national opportunity. J Opioid Manag. 2007;3:328–32. [PubMed]
[67] Chandler RK, Fletcher BW, Volkow ND. Treating drug abuse and addiction in the criminal justice system: improving public health and safety. JAMA. 2009;301:183–90. doi: 10.1001/jama.2008.976.[PMC free article] [PubMed] [Cross Ref]
[68] Gordon MS, Kinlock TW, Schwartz RP, O'Grady KE. A randomized clinical trial of methadone maintenance for prisoners: findings at 6 months post-release. Addiction. 2008;103:1333–42. doi: 10.1111/j.1360-0443.2008.002238.x. [PMC free article] [PubMed] [Cross Ref]
[69] Binswanger IA, Blatchford PJ, Mueller SR, Stern MF. Mortality after prison release: opioid overdose and other causes of death, risk factors, and time trends from 1999 to 2009. Ann Intern Med. 2013;159:592–600. doi: 10.7326/0003-4819-159-9-201311050-00005. [PubMed] [Cross Ref]
[70] Binswanger IA, Stern MF, Deyo RA, Heagerty PJ, Cheadle A, Elmore JG, et al. Release from prison–a high risk of death for former inmates. N Engl J Med. 2007;356:157–65. doi: 10.1056/NEJMsa064115.[PMC free article] [PubMed] [Cross Ref]
[71] List of Prisons, Mass.gov
[72] Accessed at http://prisonhandbook.com/1688/massachusetts-county-jails/ on 5/19/2017.
[73] Massachusetts Department of Correction, 2015 Annual Report

population.[74] Indeed, the 2016 Chapter 55 opioid report found an approximately 50 times higher opioid overdose death rate in formerly incarcerated people compared with non-incarcerated Massachusetts residents.[75]

Basic Methods: The DOC and the county-based HOC data provided a complete listing of persons "released to the street" for the Chapter 55 study. DOC records covered the period 1/1/2011 through 12/31/2015. HOC records covered a slightly shorter period – 7/1/2011 through 12/31/2015. Since nearly the entire population was represented, it was decided that no mathematical modeling would be required to estimate the likelihood that a person had been released from a prison or jail. The linkage rate of DOC and HOC records to the APCD spine were 89.7% and 81.8% respectively.[76]

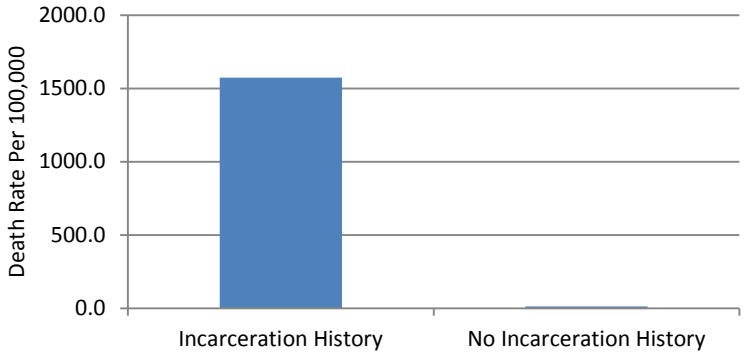
Key Finding: The majority of individuals with history of incarceration have insurance through MassHealth; 42% of former inmates were considered homeless and 54% were considered as having an opioid use disorder.

Key Findings:

- During the time period, there were 30,056 recently released inmates from the Department of Correction (DOC) and 29,068 from the House of Correction (HOC) for a total of 53,956 former inmates. Twenty-five percent of Massachusetts prison inmates from DOC received treatment during their incarceration.
- The opioid overdose death rate is 120 times higher for those recently released from incarceration compared to the rest of the adult population.

Key Finding: Compared to the rest of the adult population, the opioid-related overdose death rate is 120 times higher for persons released from prisons and jails.

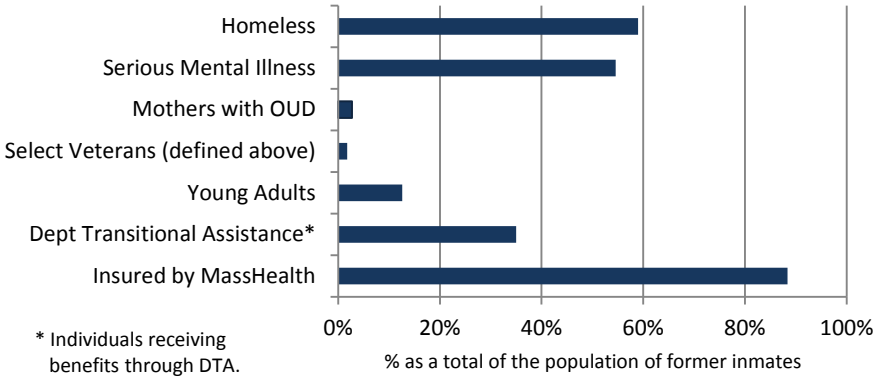
Opioid Death Rate 120 Times Higher for Individuals with Histories of Incarceration



[74] Accessed at http://www.mass.gov/eopss/agencies/doc/ on 5/19/2017.
[75] Accessed at http://www.mass.gov/eohhs/docs/dph/stop-addiction/dph-legislative-report-chapter-55-opioid-overdose-study-9-15-2016.pdf on 5/19/2017.
[76] For HOC data, incarceration dates are not reported for all county releases, so the full period of incarceration is not available for the data set. Hampshire and Berkshire counties did not submit data for FY2012 quarter 2, and Worcester County did not provide offender date of birth for CY2012 through CY2013 Q4, so their information is excluded for this analysis.

- About three in five former inmates were considered homeless (coded plus estimated), over half were considered as having an opioid use disorder. Less than 2% were also among the veterans examined in this study.

More Than Half of Individuals with *Histories of Incarceration* Have Been Homeless

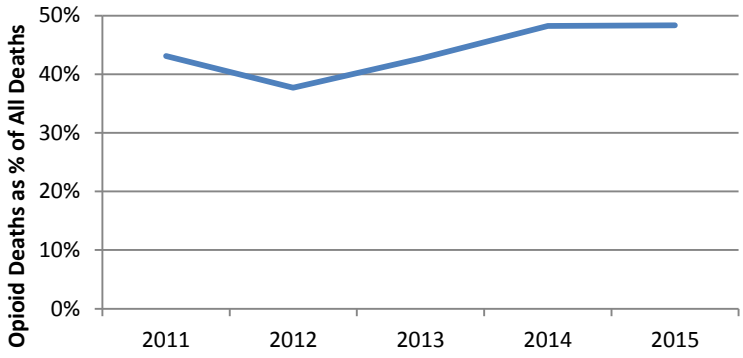


* Individuals receiving benefits through DTA.

Key Finding: Opioid-related deaths have increased over 12-fold between 2011 and 2015. Nearly one of every 11 opioid-related overdose deaths were to persons with histories of incarceration in Massachusetts jails and prisons.

- Opioid-related deaths among persons recently released from incarceration have increased over 12-fold between 2011 and 2015. Two in five deaths were opioid-related corresponding to one of every six opioid-related overdoses deaths in the state.
- In 2015, nearly 50% of all deaths among those released from incarceration were opioid-related.

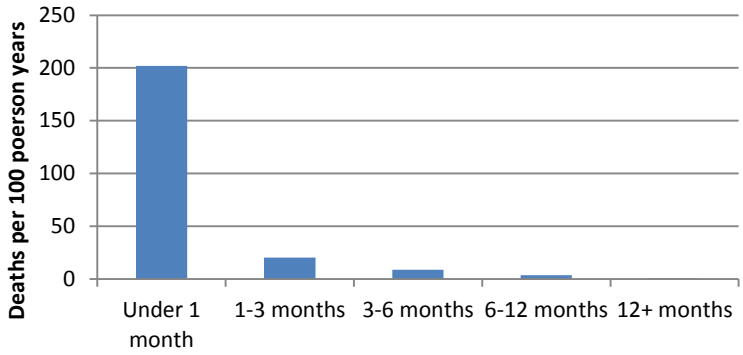
Nearly Half of All Deaths for Persons Released from Incarceration (2011-2015) are Opioid-Related



- Inmates who died from opioid-related overdoses were significantly younger than those inmates that died from other causes (36.2 vs. 46.5 years).

- For individuals who died, the mean time from release to death was 19 months, ranging from dying within the same month as release (or in prison) to 58 months later. The first month after release proved to be a critical time period for former inmates. Opioid-related overdose death rates were significantly higher than for subsequent months.[77]

Opioid-Related Death Rates for Former Inmates are Higher in the Month of Release than Later



Key Finding: Our findings also confirm that there is a significantly elevated mortality risk in the earliest time-periods after being released from a state correctional facility, when compared with other non-critical time periods.

- Former inmates who died from opioid-related overdoses were on average younger, more likely to be male, more likely to be White non-Hispanic, more likely to have a high school education or less, less likely to be married at or around the time of death, less likely to be in a management or professional occupation, more likely to be in a service and in farming/fishing/construction profession, and more likely to be recorded as a veteran on death certificates compared with those who died from all other reportable causes.

Recommendations for Further Analysis:

- Examining the impact of treatment on fatal and nonfatal overdose to determine if specific models are more effective with individuals who have been released from incarceration.
- More advanced statistical modeling should be conducted to control for length of prison time, comorbidities that impact medical care utilization, and other differences in socioeconomic status.

[77] Since the data from Houses Correction only included release data and not dates of incarceration, the analysis focused on data from the Department of Correction.

Section III.f Mothers with Opioid Use Disorder

Current Status: Pregnancy-associated deaths with an indication of substance use increased from 14% in 2011 to 41% in 2014. Little is known about the risk of nonfatal opioid-related overdose during pregnancy and following delivery.

Background: Mothers with opioid use disorder (OUD) are a population of particular concern, since perinatal opioid use is not only associated with adverse health outcomes for the mother, but also with adverse health outcomes for her offspring across the life course. While 2013 estimates of current illicit drug use among persons aged 12 and older are higher for men than for women (11.5% vs.7.3%), research indicates women progress more rapidly to problem use.[78] [79] [80]

The proportion of pregnancy-associated deaths (deaths during or within one year of the end of pregnancy) in Massachusetts related to substance use increased from 14% in 2011 to 41% in 2014.[81] Opioids were the most common substance indicated in these deaths. However, little is known about nonfatal opioid-related overdoses during pregnancy and following delivery. Because screenings of women in primary or prenatal care is not universal, opportunities are likely missed to identify women in need of OUD evaluation and treatment referral. The breadth of the Chapter 55 data set provides an opportunity to better understand whether pregnant women and new mothers with OUD are at greater or lesser risk of fatal and nonfatal overdose compared with new mothers who do not have an OUD and understand the timing of overdose events during the prenatal and postpartum periods. By linking the data of the mother and child, the Chapter 55 data set allows close tracking of the impacts on the substance-exposed dyad and estimation of future risks.

Data sources:

- Medical claims
- Hospital, ED, and outpatient data
- Death records
- Birth records
- Ambulance trips
- Post-mortem Toxicology
- Substance use treatment records
- Prescription records

Basic Methods: A cohort of women who delivered a live birth in Massachusetts between 2011—2015 was identified by linking birth certificate records to maternal records in the All Payer Claims Database (APCD). Infant diagnosis codes for neonatal abstinence syndrome (NAS) documented in APCD and CaseMix were also linked to mothers via birth certificate records. Fatal and nonfatal opioid overdose events were identified using CaseMix hospital records, MATRIS ambulance records, and death certificates. Women were classified as having evidence of OUD if any of the following were documented during the 5 year time period:

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[78] Derrington TM, Bernstein J, Belanoff C, Cabral HJ, Babakhanlou-Chase H, Diop H, Evans SR, Kotelchuck M. Refining Measurement of Substance Use Disorders Among Women of Child-Bearing Age Using Hospital Records: The Development of the Explicit-Mention Substance Abuse Need for Treatment in Women (EMSANT-W) Algorithm. Matern Child Health J. 2015; 19:2168-78.
[79] ACOG Committee Opinion No. 422: At-risk drinking and illicit drug use: ethical issues in obstetric and gynecologic practice. Obstetrics and Gynecology. 2008; 112(6):1449–60.
[80] Harrison PA, Sidebottom AC. Systematic prenatal screening for psychosocial risks. Journal of Health Care for the Poor and Underserved. 2008; 19(1):258–76. doi:10.1353/hpu.2008.0003.
[81] Massachusetts Department of Public Health, unpublished data.

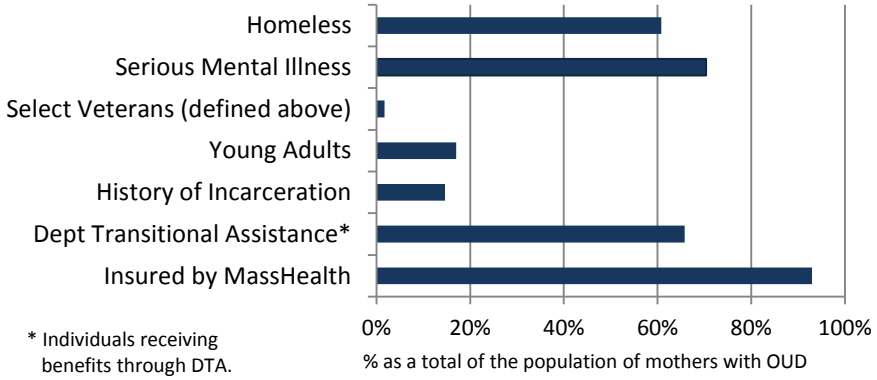
- A fatal or nonfatal opioid overdose
- A diagnosis code related to OUD
- A claim for methadone or prescription for buprenorphine
- Record of opioid-related enrollment/treatment in the Bureau of Substance Abuse Services (BSAS) database
- Record of opioid-related treatment while incarcerated

Finally, data from APCD, Case Mix, birth certificate records, and BSAS were used to describe maternal socio-demographic and substance use characteristics

Key Findings:

- A majority of mothers with OUD had interaction with the Department of Transitional Assistance, were insured by MassHealth, and had evidence of serious mental illness. One in six had a history of incarceration in Massachusetts prisons and jails.

Mothers with OUD **Had High Rates of Homelessness and Serious Mental Illness**



* Individuals receiving benefits through DTA.

Key Finding: Mothers with OUD had a significantly higher co-occurrence of mental health diagnoses. 82% of mothers with an overdose during pregnancy or the first year postpartum had a diagnosis of depression compared with 63% of mothers with OUD and 18.0% of mothers without evidence of OUD.

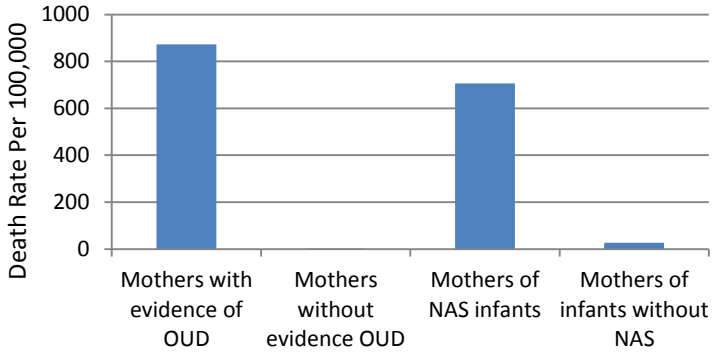
- Compared to mothers without evidence of OUD or overdose, mothers with a fatal or nonfatal overdose and mothers with OUD were significantly more likely to be less than 30 years old, White non-Hispanic race, born in the United States, unmarried, without paid employment, less educated, receive their prenatal care at a hospital clinic, and have public insurance.
- Mothers with OUD had a significantly higher co-occurrence of mental health diagnoses.
    - 82% of mothers with an overdose during pregnancy or the first year postpartum had a diagnosis of depression during the study period compared with 63% of mothers with OUD and 18% of mothers without evidence of OUD.

- 79% of mothers with an overdose during pregnancy or the first year postpartum had a diagnosis of anxiety during the study period compared with 62% of mothers with OUD and 18% of mothers without evidence of OUD.

- More than a third (38.3%) of deaths among women delivering a live birth between 2011 and 2015 were fatal opioid-related overdoses, compared to a fifth (19.9%) among women who did not deliver a live birth.
- The five-year opioid-related overdose death rate of mothers with evidence of OUD was 321 times higher than the rate among mothers without evidence of OUD and the opioid-related overdose death rate among mothers delivering an infant with NAS was 27 times higher than the rate for all other mothers.

Key Finding: The five-year opioid-related overdose death rate of mothers with evidence of opioid use disorder was 321 times higher than the rate among mothers without evidence of opioid use disorder.

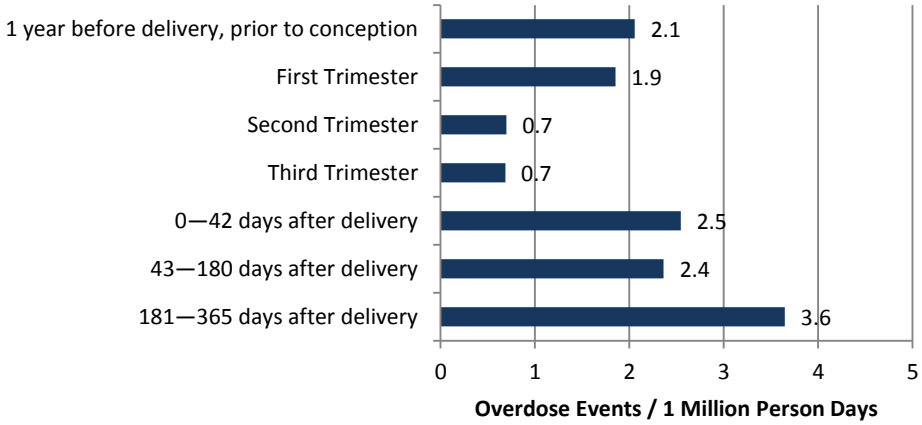
Opioid Death Rate More than 300 Times Higher for Mothers with OUD



- Among women with OUD, women who delivered a live birth between 2011-2015 were 2.1 times less likely to have a fatal overdose compared to women who did not deliver a live birth

Key Finding: The opioid-related overdose rate increases almost four-fold between the third trimester of pregnancy and the first six weeks postpartum. They are highest six to 12 months post-partum.

Rate of Opioid Overdose Events Increase Sharply After Delivery for OUD Mothers



- Rates of opioid-related overdose decrease during pregnancy and are lowest during the second and third trimesters, but significantly increase in the postpartum period, with the highest rates six months—one year after delivery.

Recommendations for Further Analysis:

- Assess the impact of treatment engagement and retention on maternal overdose during the postpartum period.
- Determine factors that may predict or protect against overdose among mothers in the first year postpartum.
- Evaluate infant outcomes for women who have nonfatal overdose events during pregnancy.

Section III.g Estimating Opioid Burden for All Massachusetts Communities

Current Status: Other than counts of opioid-related deaths (which are unstable for smaller communities), little is known about the burden of the opioid crisis in all 351 Massachusetts communities.

Background: The scope of the data assembled for the Chapter 55 project has enabled the Department of Public Health to examine trends in the data for small communities, which is a process that has not previously been possible. Standard statistics, based on very limited data, do not lend themselves to making clear statements about the burden of specific health conditions when community populations are small. However, by linking the Chapter 55 data at the community level, it is possible to gain insight into the opioid burden for all Massachusetts communities.

Basic Methods: A four-step process was used to estimate overall opioid burden for all towns in Massachusetts. An assumption was made that the overall burden of the opioid crisis at a community level could best be measured using multiple data points that captured different aspects of the crisis. While some measures might be higher in one town and lower in another, considering multiple measures across time would make the results more reliable. The graphic below depicts the basic approach of combining years, using reliable data, adjusting the population for very small towns, and using multiple data sources to make all estimates more accurate.

Step 1 (Combine Years): Averaging across years or computing rates for multiple years tends to produce more reliable estimates.[82] Because some data elements were available for all years, only data from 2013 and 2014 were used for this analysis.

Step 2 (Use Only What's Reliable): Estimating rates for very small communities is difficult, because isolated events can alter rates dramatically. It was necessary to determine the point at which data were reliable enough to use.[83] This was called the *threshold of stability*. The threshold was established to be 3,000 residents.

[82] Since the opioid crisis in Massachusetts accelerated in 2012, no data prior to 2012 was used in the analysis.

[83] To establish our "threshold of stability," we looked at the standard deviations of community level rates for each of the 4 measures using different population cut points for the communities. Community population size was determined using the 2010 US Census. Multiple population cut points were tested to determine the appropriate threshold: all communities, 1,000 2,000, 3,000 and 20,000 residents. For all four measures, the standard deviation of the rates stabilized once when communities with 3,000 residents or more were considered.

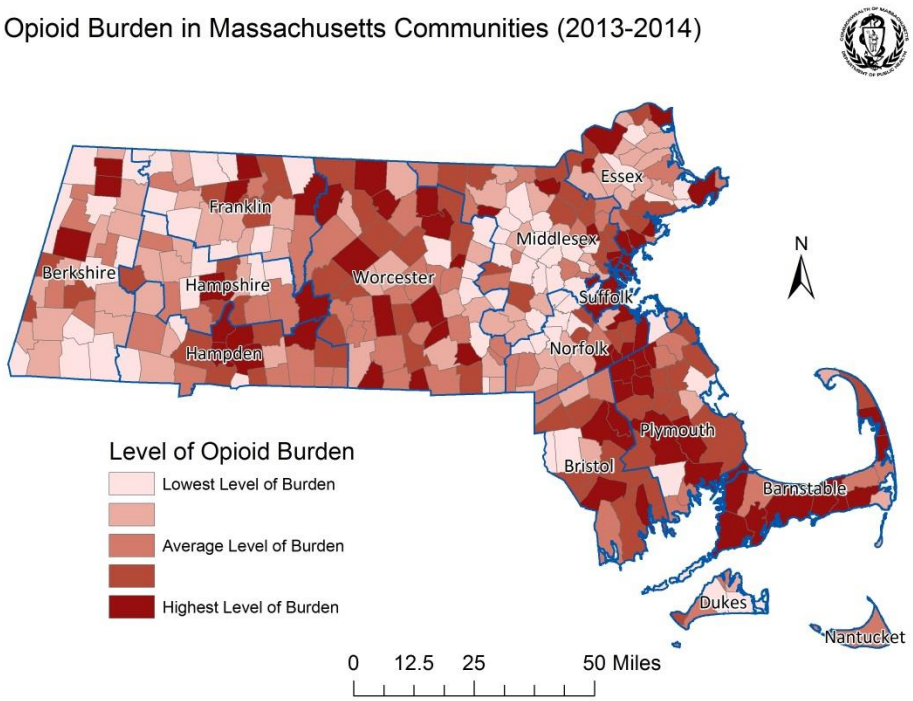
Step 3 (Make Small Towns Seem Bigger): After determining the *threshold of stability*, data for the 75 smallest towns in Massachusetts were adjusted so that changes in rates would be similar to a town of 3,000 people.[84]

Step 4 (Find Data with Similar Patterns): The level of community burden was estimated using information about fatal opioid overdoses for residents of a community, nonfatal opioid overdoses for residents of a community, Naloxone kits distributed to communities, and the number of infants born with neonatal abstinence syndrome (NAS) to mothers who lived in these communities. These four data points were chosen because they were expected to show similar changes over time and across communities. If a community was high or low on one measure, it would be similarly high or low on others.[85]

Key Findings: A measure of the overall burden of the opioid crisis on the community level was developed using four data points (described above) that captured different aspects of the crisis. The map below shows the burden for all 351 Massachusetts communities divided by quintiles (i.e., five equally-sized groups ordered from lowest to highest burden) – the darker the shade, the higher the burden of opioid use in that community.

[84] A Poisson probability of the number of actual events occurring in each community was computed for each of the 4 measures. That probability was compared to the probabilities computed for rates for a hypothetical town of 3,000 people. The rate for the hypothetical town replaced the rate for the smaller community to make it more reliable over years.

[85] The actual rates for larger towns and estimated rates for smaller towns were analyzed using a principal components analysis. A one component solution was clearly indicated as it accounted for nearly three-quarters of all differences. Therefore, adding together standardized values for the four measures was a reliable way to estimate the opioid burden on a community level.



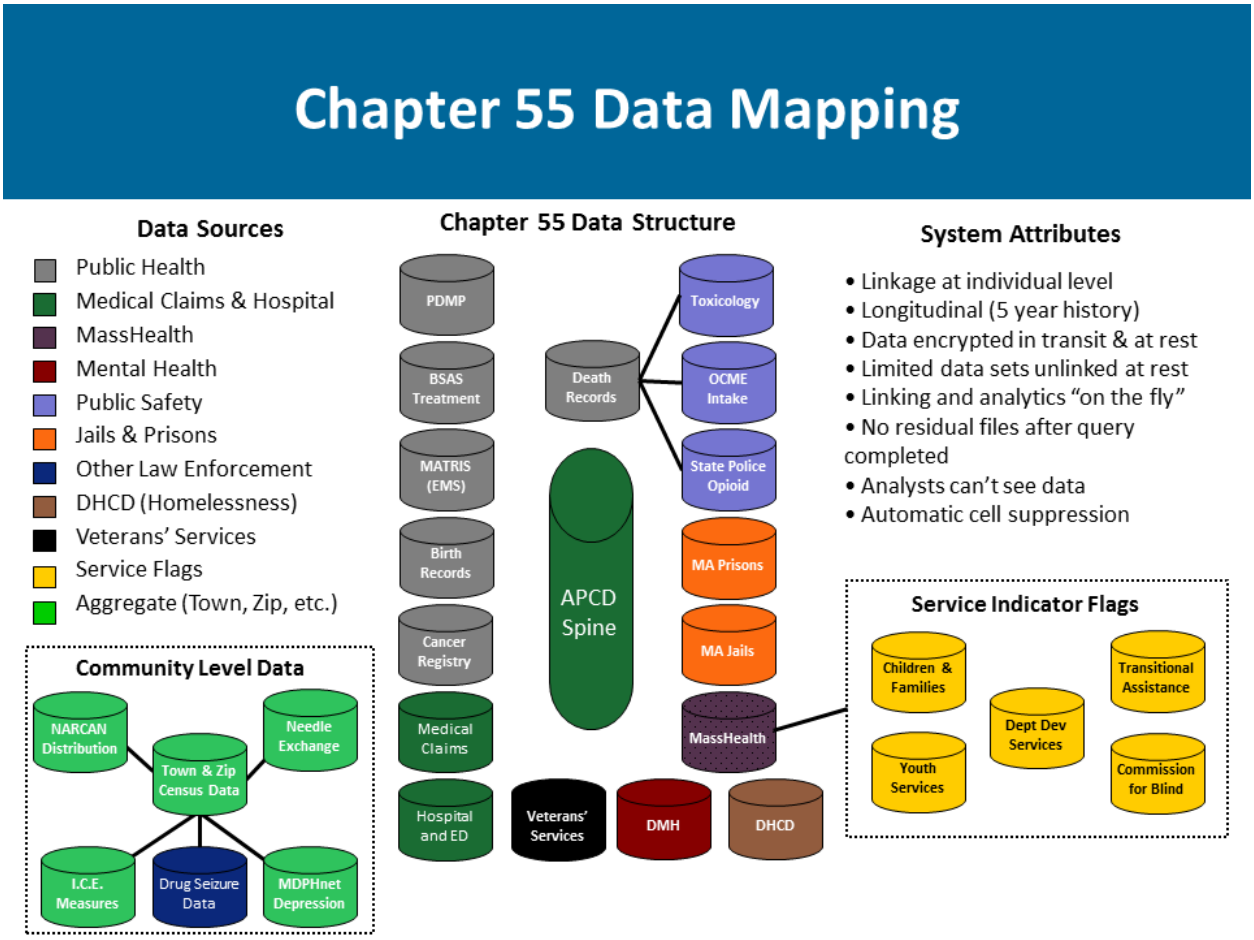
Recommendations for Further Analysis:

- A comprehensive geospatial analysis of opioid burden should be conducted at the micro-geographic-level (e.g., census tract, block group, block) to identify neighborhood level burden.
- Hotspot cluster analysis should be conducted at the census tract or block group level to identify statistically significant clusters of opioid burden on the neighborhood level across Massachusetts.
- A thorough geospatial analysis should look at the relationship between local opioid burden and available services such as pharmacies, SEPs, OEND, MAT, detox programs, hospitals, etc.
- A composite variable for available services should be developed and mapped geospatially. Several variables should be considered for this composite variable:
    - Numerator: naloxone distribution, number of people receiving medication assisted therapy (MAT: methadone maintenance, buprenorphine, suboxone), number of people in drug detoxification programs;
    - Denominator: number of people with opioid use disorder (OUD)
- Development of novel variables and analyses to assess access to services should be considered:
    - MAT services received per 1,000 fatal overdoses; MAT services per 1,000 people with OUD;

    - Naloxone kits distributed per 1,000 people with OUD
    - Ratio: number of providers to number of people with OUD
- Statistical models should be considered to identify community-level factors associated with opioid burden and access to services.
- Trends in opioid burden should be examined in order to make estimates of future risk on a community by community basis.

Appendix A: Dataset Descriptions

The diagram below shows the 22 datasets linked to produce this report. Sixteen of the data sets were linked at the individual level while six data sets provided additional community level data either at the town or zip code level. The MassHealth data also included service flags for individuals receiving services from the Department of Children & Families, the Department of Youth Services, the Department of Developmental Services, the Department of Transitional Assistance, and the Massachusetts Commission for the Blind.[86]



The remainder of Appendix A provides a description of each of the 22 datasets used for this report. Each description outlines the information collected, the frequency, the limitations, the lag time between data collection and data availability, the relevance to opioids, and the authorization for collecting the data.

[86] With the exception of data from the Department of Transitional Assistance, the data in the service flag fields was poorly populated and therefore was not used in this report.

Registry of Vital Records and Statistics (RVRS)[87] – Death Records[88]

What data are collected: Opioid-related deaths are the primary focus of this work and the most basic source of this information comes from death certificates filed with the Registry of Vital Records and Statistics (RVRS). The official cause of death and the manner of death (i.e., intentional, unintentional, or undetermined) are assigned by physicians and medical examiners. Each death certificate also includes demographic information such as age, race, Hispanic ethnicity, gender, educational attainment, marital status, and occupation. These basic demographics are recorded by the funeral director and are typically provided by a family member.

Availability of data: Mortality information is reported electronically using the Vitals Information Partnership[89] (VIP). The VIP system is web-based and receives information 24 hours a day seven days a week. For analytic purposes, data can be exported from VIP with all the data elements listed above. Opioid-related deaths and other complex cases are almost always referred to the Office for the Chief Medical Examiner (OCME) for determination of cause and manner of death. This results in a reporting lag for these deaths. That said, basic data on demographics is available on a near-real time basis.

Limitations of the data: As legal records, the information recorded on death certificates is considered highly accurate. However, some information like race, Hispanic ethnicity, educational attainment, marital status, and occupation are not always fully populated. Causes of death from the OCME often lag the date of death making some elements of death data less timely than others.

Bureau of Substance Abuse Services (BSAS)[90] – Substance Abuse Treatment Data[91]

What data are collected: Massachusetts Bureau of Substance Abuse Services (BSAS), of the Department of Public Health, is the single state authority responsible for regulating and licensing substance abuse treatment providers. The services provided range from acute detoxification to residential and outpatient based services. All treatment providers who receive funding from BSAS are required to submit data to BSAS to carry out the responsibilities listed under the law. The required data fields include but are not limited to client characteristics, enrollment information, disenrollment information, services and outcomes. Currently, only treatment providers that receive funding from the Department submit this data to BSAS.

Availability of data: Processing of linked clients also allows us to construct treatment episodes and entire client histories. There is a one to two month lag between the time the data are reported and the time it is available for analysis/reporting from BSAS.

[87] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/ on 5/19/2017.
[88] The collection of death certificate data is authorized by MGL Chapter 46.
[89] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/vitals-information-partnership-vip.html on 5/19/2017.
[90] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/substance-abuse/ on 5/19/2017.
[91] The collection of detailed substance abuse treatment by BSAS is authorized under MGL Ch.111 B and E. All treatment providers are required to submit data to BSAS to carry out the responsibilities listed under the law. The regulations promulgated to carry out these responsibilities require the providers to submit data in a timely manner. The required data fields include but are not limited to: client characteristics, enrollment, disenrollment information, services and outcomes. Currently, only treatment providers that receive funding from the Department submit the required data to BSAS.

Limitations of the data: The BSAS data set poses several limitations. First, BSAS data does not represent all substance abuse treatment provided in the commonwealth. BSAS only collects data from its contracted providers. Of the data that is submitted to BSAS, outpatient treatment data is incomplete and does not include all non-BSAS paid services. BSAS does not collect data from providers that prescribe Vivitrol or from non-contracted Buprenorphine providers. At the time of this analysis, Methadone data was incomplete. Due to challenges associated with recent system changes related to data submission, some Methadone providers have been unable to submit data. Data collected in regards to section 35 commitments are incomplete in the BSAS data set. For example, in 2015 there were 2,068 Section 35 commitments served in settings outside the scope of data submitted to BSAS (e.g. MASAC and MCI Framingham). As a result of these data limitations, it is possible that some of the analyses using BSAS treatment data may provide an incomplete picture.

Prescription Drug Monitoring Program (PDMP)[92] – Schedule II through V medications[93]

What data are collected: Information about filled prescriptions for schedule II through V medications is reported electronically each business day to the Prescription Drug Monitoring Program (PDMP) in the Department of Public Health's Office of Prescription Monitoring and Drug Control (OPMDC) by all Massachusetts community, hospital outpatient and clinic pharmacies as well as from out-of-state mail order pharmacies that deliver to patients in Massachusetts. Schedules II through V medications consist of those prescription drug products with recognized potential for abuse or dependence (e.g., narcotics, stimulants, sedatives). Consequently, they are among those most sought for illicit and non-medical use. The specific medication as well as the dosage and the number of pills or amount are also captured. In order to facilitate the monitoring of individuals who receive scheduled medications, basic identifying information like full name, gender, date of birth, and full address are also recorded as well as information about the prescriber and dispensing pharmacy.

Availability of data: PDMP reporting is comprehensive for pharmacies within the Commonwealth with very few instances of non-compliance among pharmacies. PDMP data arrives daily and is considered complete and accurate for export and analysis within approximately two weeks.

Limitations of the data: The PDMP dataset has a few noteworthy limitations. First, methadone clinics do not report to the Massachusetts PDMP as they are exempt by statutory language. Specifically, the PDMP only collects data on prescriptions dispensed, and methadone in clinics is administered pursuant to medical order, not prescription. Methadone is only included when prescribed for pain. Second, controlled substance prescriptions dispensed by Veterans Administration (VA) facilities are not included. This represents a high risk population and a significant data gap. Third, prescription drugs that are obtained illegally (e.g., stolen, purchased on the street, etc.) are a potentially significant contributor to the opioid overdose epidemic and are not captured within an individual's PDMP history, but may be captured by the OCME toxicology screens. Finally, a filled prescription should not be interpreted to mean that an individual took all or even any of that medication. Linking

[92] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/hcq/drug-control/PDMP/ on 5/19/2017.

[93] The Department of Public Health's Office of Prescription Monitoring and Drug Control (OPMDC) established the Massachusetts Prescription Monitoring Program (MA PDMP) in 1992 pursuant to joint regulations (105 CMR 700.012) with the Board of Registration in Pharmacy (247 CMR 5.04).

these records with toxicology data can provide some insight into the proportion of scheduled medications that are illegally diverted for other purposes than originally intended.

Massachusetts Ambulance Trip Record Information System (MATRIS)[94] – Office of Emergency Medical Services (OEMS)[95]

What data are collected: The Department of Public Health's Office of Emergency Medicine (OEMS) established the Massachusetts Ambulance Trip Record Information System (MATRIS) in December 2010 as a statewide system collecting emergency medical service (EMS) incident data from licensed ambulance services. Under EMS System regulations, ambulance services are required to document each EMS call and include the data elements pertaining to the call specifically referenced in an administrative requirement issued by OEMS governing the statewide EMS minimum data set. MATRIS data elements are based on the National Emergency Medical Service Information System (NEMSIS) Version 2.2.1 dataset standard developed in 2005. This includes demographic, clinical, operational, and billing data. Demographics required are patient age, birth date, gender, and patient home address. Also required are incident type, incident address, dates, times, destination facility type, destination facility name, and destination facility address. Patient name is not currently required but is submitted approximately 70% of the time. MATRIS can identify nonfatal-opioid-related events, even when the patient refuses transport to the hospital. MATRIS tracks when naloxone was administered either by the EMT or as "prior aid" by other first responders, (fire, police) or bystanders (friends, family). Evaluation on interventions provided by EMTs can be performed to correlate survival and other outcome rates when linked with outcomes from ED and death data.
Availability of data: Ambulance incident information is submitted into the MATRIS secure website electronically from all licensed ambulance services in Massachusetts within 14 days of the call; however frequency of submission varies by service. Many of the larger ambulance services have automated daily submission, while others can take longer to submit. There are currently over 6.4 million ambulance trip records in MATRIS. There were 1.3 million records in MATRIS for incidents occurring in both 2013 and 2014. There are 1.4 million for 2015 available for future analysis.
Limitations of the data: MATRIS has several limitations. The first is that the NEMSIS standard does not specifically identify incidents as being opioid-related, but rather "poisoning/ingestion." The second, the data are not uniformly reported by EMS providers. The third limitation is that the overall usability of the data submitted by ambulance services varies by provider, with roughly 30% of the provided data being partially or completely unusable. These issues are partially mitigated through the integration with other datasets listed above. Finally, whether a specific ambulance trip involves an opioid overdose is not a simple judgment. The classification of opioid trips was based on an algorithm developed in conjunction with the Centers for Disease Control and Prevention. Their assistance was invaluable.

[94] For more information see: www.mass.gov/dph/oems/matris
[95] The collection of detailed ambulance trip data by OEMS is authorized under 105 CMR 170.345(B).

Registry of Vital Records and Statistics (RVRS)[96] – Birth Records[97]

What data are collected: The collection and dissemination of this data are to facilitate the surveillance of births and birth trends in the state of Massachusetts, including those based on demographic information and data on birth outcomes. Data are reported to the Registry of Vital Records and Statistics (RVRS) by all licensed birthing hospitals and birthing centers and by city and town clerks if they are establishing a home birth that occurred in their city/town in Massachusetts. The birth data contains identifying information about the parents of record and the child. These data are critical to understand the health risk to a mother who delivers a Substance Exposed Newborn (SEN) or an infant with Neonatal Abstinence Syndrome (NAS).

Availability of data: Natality information is reported electronically using the Vitals Information Partnership (VIP).[98] The VIP system is web-based and receives information 24 hours a day, seven days a week. Substantial quality control efforts are required to assess the accuracy and completeness of birth records. As a result, the final dataset of birth records is usually available by May of the following year.

Limitations of the data: As legal records, the information recorded on birth certificates is considered highly accurate. However, some information like race and Hispanic ethnicity are not always fully populated.

Massachusetts Cancer Registry (MCR)[99] – Cancer Staging[100]

What data are collected: The Massachusetts Cancer Registry (MCR), a database managed by the Department of Public Health, is a population-based registry that tracks the incidence of cancer within the Commonwealth. Since 1982, the MCR has captured key data elements such as date of diagnosis and cancer stage at diagnosis, in addition to various demographic data elements. For this purposes of this work, MCR data was included because palliative treatment for late stage cancers often includes the use of opioid medications to control pain. Being able to distinguish those cases of high opioid use for cancer treatment from cases where an individual may be abusing prescription medications was critical to this study.

Availability of data: Reporting facilities are required to report case level data to the MCR within 180 days of diagnosis or first date of patient interaction. Analysis of supporting documentation related to determining the *stage* of a cancer also takes considerable time. Typically, MCR data availability lags the calendar by approximately two years.

Limitations of the data: Defining the stage of a cancer is not an exact science. It is based on a number of written reports and laboratory tests. Furthermore, not all cancers cause significant pain even in late stages. These data can provide an indication that medications may have been prescribed for pain but they cannot definitively rule out the possibility that there was underlying abuse.

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[96] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/ on 5/19/2017.

[97] The collection of Confidential Birth Information is authorized under 105 CMR 350.000.

[98] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/vitals-information-partnership-vip.html on 5/19/2017.

[99] Accessed at http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/cancer-registry/ on 5/19/2017.

[100] The collection of detailed cancer incidence and staging by the MCR is authorized under Chapter 111, Section 111B.

Office of the Chief Medical Examiner (OCME)[101] – Circumstances of Death and Toxicology Reports[102]

What data are collected: The OCME, a part of the Executive Office of Public Safety and Security, gathers a great deal of information about unattended and other deaths where the underlying causes may not be apparent. Not of all of the information collected is relevant to opioid-related overdose deaths, so the work reported here has focused on the *circumstances of death* recorded on the OCME intake forms and the toxicology reports used to determine the cause of death. The data field labeled "*circumstances of death" i*s a brief narrative that describes the setting and environment of an unattended death. It is often written by the State Police in the case of acute opioid-related overdoses. These narratives are analyzed by searching for the presence of key words. The toxicology reports describe the presence of hundreds of specific chemical compounds that might be found in the body of the decedent. This study has focused primarily on the presence of natural and synthetic opioids.

Availability of data: The intake forms that contain the *circumstances of death* narratives are usually available within about 72 hours of a case being accepted by the OCME. Toxicology screening and confirmatory tests are conducted by the Crime Laboratory run by the Massachusetts State Police as well as the NMS Labs (Willow Grove, PA). Toxicology tests lag the date of death by about 60 days.

Limitations of the data: Written narratives will provide initial impressions of the circumstances of death. As first impression, these can be misleading in some cases. Final causes of death must be provided by physicians and medical examiners. Toxicology results can be extremely complex to interpret. Levels of drugs found a decedent's tissue are affected by the timing of the test, the type of tissue, and other factors. Many drugs also metabolize into a variety of different chemical compounds. For all these reasons, toxicology results are generally examined in broad categories to simplify interpretation. OCME data are connected directly to the death records using name, date of birth and date of death. A unique OCME ID number is used to link to toxicology reports. Finally, the vast majority of the toxicology records for early 2013 were only available on paper and thus not practical to include in this report.

Case Mix Database[103] – Inpatient hospitalization, emergency department visits, and outpatient observations managed by the Center for Health Information and Analysis (CHIA)[104]

What data are collected: The Case Mix data contains all inpatient hospitalizations, emergency department visits, and outpatient observation in the state. Massachusetts acute care hospitals are required to submit Case Mix data to the Center for Health Information and Analysis (CHIA) in order to track disease burden and associated costs statewide. Detailed information is available for each encounter, including geography (e.g., zip code, town, county, state, country), demographics (e.g., age, race, ethnicity), and costs by service (e.g., medical/ surgical, behavioral health), admission and discharge dates, diagnosis, and the facility providing patient care. Case Mix data can identify individuals who received past treatment for a substance overdose including healthcare encounters

[101] Accessed at http://www.mass.gov/eopss/agencies/ocme/ on 5/19/2017.
[102] The collection of death certificate data is authorized by MGL Chapter 38.
[103] Accessed at http://www.chiamass.gov/case-mix-data/ on 5/19/2017.
[104] Massachusetts acute care hospitals are required to submit Case Mix data in accordance with Regulation 114.1 CMR 17.00.

associated with detoxification, psychiatric care, and overdose based on procedures rendered or diagnoses made when these services are offered by acute-care hospitals.

Availability of data: The Center for Health Information and Analysis (CHIA) receives data quarterly. Significant work is required to clean and harmonize the data across hospitals. As a result, there is approximately a one year lag between final data submission to CHIA by acute care hospitals and receipt of the data by DPH and other approved organizations.

Limitations of the data: The Case Mix data does not include hospital services rendered to Massachusetts residents by non-Massachusetts hospitals or hospitals operated by the Veterans Administration (VA), thus reducing the observable analytic universe. Similarly, CHIA does not currently collect information from behavioral health hospitals. Demographic data included in Case Mix is not considered as accurate as those recoded on birth of death records. Consequently, the linkage of these records to other datasets may be incomplete. Furthermore, the coding of encounters for overdose or for behavioral health services is not considered fully complete. Finally and possibly most important for the Chapter 55 project is that Case Mix data are available on a Federal fiscal year. The most recent data available is through 9/30/2014 which means that any data on nonfatal overdoses, substance abuse treatment, or mental health diagnosis codes will not be captured in the final three months of the study period. The low linkage rate for infant records produced a smaller number of NAS-related records for mothers.

Non-Scheduled Pharmacy Claims[105] – Massachusetts All Payer Claims Database (APCD)[106]

What data are collected: The Massachusetts All Payer Claims Database (APCD) is managed by the Center for Health Information and Analysis (CHIA). The APCD contains health and pharmacy insurance claims data from the approximately 80 private health care payers, public health care payers (including Medicare and MassHealth) and publicly-supported managed care organizations and senior care organizations across the entire state of Massachusetts. The APCD insurance eligibility files include basic identifying information like full name, address, gender, date of birth, race, ethnicity, and Social Security number. Most APCD data requested from CHIA focused on pharmacy claims for non-scheduled medications.

Availability of data: The APCD is overseen by CHIA, the independent state agency responsible for collecting, cleaning, maintaining, and managing access to the data. Data are reported out once a year and each report contains all data from the previous calendar year. The newest version is available approximately six months after the close of the preceding calendar year.

Limitations of the data: The APCD forms the backbone or spine of the linked datasets. Its completeness and accuracy are critical to the entire effort. In recent years, CHIA has expended significant resources to link records across payers. The current APCD contains roughly 15 million unique records which is substantially above the 6.3 million residents in Massachusetts. Most of these records are single records unconnected to a full set of identifiable records. Other analyses

[105] Accessed at http://www.chiamass.gov/ma-apcd/ on 5/19/2017.

[106] CHIA has statutory authority to collect data from both public and private health care payers under Massachusetts General Laws Chapter 12C, section 10. By July 2010, Regulations 114.5 CMR 21.00 and 114.5 CMR 22.00 formally established the APCD in Massachusetts.

undertaken for this project suggest that the unique records prepared for the APCD serve the purpose intended. Other known limitations of the APCD include exclusions such as Workers' Compensation, TRICARE/Veteran's Health Administration, and the Federal Employees Health Benefit Plan claims. Additionally, uninsured individuals (approximately 3% of the state's population) are not captured. Finally, healthcare services provided but paid for out of the patient's own finances, e.g., cash payment for a convenience care clinic service like a strep throat culture, are excluded because these services do not generate claims.

Department of Correction (DOC)[107] – Incarceration and Treatment[108]

What data are collected: The Department of Correction (DOC), a part of the Executive Office of Public Safety and Security, is required by statute to maintain adequate records of persons committed to the custody of the Department. In addition, DOC must establish and maintain programs of research, statistics, and planning, and conduct studies relating to correctional programs and responsibilities of the Department. To achieve those goals, DOC maintains a database of individuals incarcerated in Massachusetts prisons. This database includes the substance abuse treatment received by prisoners. Identifiers like full name, gender, date of birth and Social Security numbers are also included.

Availability of data: As releases from prison are routine, these data are kept current. Releases from January 1, 2011 to December 31, 2015 were included.

Limitations of the data: DOC data includes incarcerations for those in prison and does not include data for people in jails or houses of correction (HOC). That data is separate and does not include all the same information as the DOC data. Analyzing only the DOC data could yield misleading results since HOC serves a higher volume of inmates per year in comparison to DOC, primarily due to shorter sentences and those waiting trial within HOC. An additional limitation arises if residents of Massachusetts are incarcerated outside of Massachusetts as that data is not captured by DOC.

Department of Mental Health (DMH)[109]

What data are collected: The Department of Mental Health, as the State Mental Health Authority, assures and provides access to services and supports to meet the mental health needs of individuals of all ages, enabling them to live, work and participate in their communities. The Department of Mental Health (DMH), under the umbrella of the Executive Office of Health and Human Services (EOHHS), is required by statute to maintain adequate records of persons receiving services of the department. This database includes psychiatric hospitalizations, substance abuse treatment and the desire for change and stage of change, loss of housing, incarceration, use of crisis stabilization beds and employment status between January 1, 2011 and December 31, 2015. Identifiers included gender, race, and age.

Availability of data: Different programs and services provided by DMH are kept current and are available for the period from 1/1/2011 through 12/31/2015.

[107] Accessed at http://www.mass.gov/eopss/agencies/doc/ on 5/19/2017.
[108] The collection of detailed incarceration data by DoC authorized under MGL c. 124, s. 1(j) and MGL c. 124, s. 1(k).
[109] Accessed at http://www.mass.gov/eohhs/gov/departments/dmh/ on 5/19/2017.

Limitations of the data: The Chapter 55 DMH data only includes data for services provided by DMH such as Community Based Flexible Supports (CBFS) and Clubhouse Coalition programs. It does not include routine or crisis mental health services provided in hospitals, emergency departments, and the private offices of licensed mental health providers. Some of these data can be found in the APCD and Case Mix data sets.

Department Housing and Community Development (DHCD)[110] – Family Homelessness

What data are collected: DHCD's mission is to strengthen cities, towns and neighborhoods to enhance the quality of life of Massachusetts residents. This agency provides leadership, professional assistance and financial resources to promote safe, decent affordable housing opportunities, economic vitality of communities and sound municipal management. DHCD collects and maintains data on all persons receiving services from the Department. For this report, DHCD created a subset of the records of families (heads of household) who received services from the Emergency Assistance Program between January 1, 2011 and December 31, 2015. Identifiers included gender, race, age, veteran status and disability.

Availability of data: Different programs and services provided by DMH are kept current and are available for the period from 1/1/2011 through 12/31/2015.

Limitations of the data: While DHCD offers supportive services for individuals who are homeless, the Chapter 55 data only includes services provided to families. The linkage to the APCD is made through the listed Head of Household in the DHCD data set. This may represent an underestimate of housing instability even for individuals within families because only the head of household is linked to the APCD.

Department of Veterans' Services (DVS)[111] – Benefits Programs

What data are collected: The mission of the Department of Veterans' Services (DVS) is to be the chief advocate for the nearly half-million veterans of the Commonwealth and their families. DVS establishes policy, proposes legislation, ensures that adequate funding for veterans' programs is included in the Governor's budget, and represents the interests of veterans in matters coming before the General Court. In addition, DVS represents all state agencies and individual veterans before the federal Department of Veterans Affairs in securing federal compensation and other benefits that might be available. DVS collects information of all Massachusetts veterans receiving benefits through DVS. Among other data, DVS collects data on persons who received DVS medical, housing or other benefits from DVS through communities. Identifiers included name, date of birth, social security number, race, gender and address.

Availability of data: For Chapter 55, DVS provided DPH with payment information for medical, housing or other benefits made between January 1, 2011 and December 31, 2015.

[110] Accessed at http://www.mass.gov/hed/economic/eohed/dhcd/ on 5/19/2017.
[111] Accessed at http://www.mass.gov/veterans/about-veterans-services/ on 5/19/2017.

Limitations of the data: These data include only benefits directed to Massachusetts veterans by DVS. Any federal, private, other donations are not captured in the DVS data set. Therefore, these data will be an underestimate of all services provided to Massachusetts veterans.

MassHealth[112] – Opioid Related Services for the Massachusetts Medicaid population

What data are collected: In Massachusetts, Medicaid and the Children's Health Insurance Program (CHIP) are combined into one program called MassHealth. MassHealth maintains and updates reports quarterly on member enrollment, application activity and services provided. Identifiers included name, date of birth, social security number, gender, race and city of residence. Variables included disability status, type of MassHealth Plan and coverage type, dually eligible status (Medicare and Medicaid), and number of enrollment days per month. Variables also included if client received services from Department of Developmental Services, Department of Mental Health, Department of Children & Families, Department of Transitional Assistance, Department of Youth Services, and Massachusetts Commission for the Blind. Using CCS, ICD-9 and 10 codes other variables included inpatient psychiatric hospital, semi-acute hospital, specialty hospital for substance use disorder, Serious Mental Illness diagnosis, Mental Illness diagnosis, Substance Use Disorder diagnosis. Payment variables included MassHealth payments, patient payment amounts, third party payment amounts, pass through claim payments and claims passing through MassHealth for federal match. Unstable housing was an additional variable (defined as three or more street addresses in a calendar year).

Availability of data: MassHealth medical claims are included in the APCD dataset. The additional data provided by MassHealth for Chapter 55 includes information on type of coverage, disability status, payment amounts, specific types of opioid related services and whether an individual was served by any of the following agencies: Department of Developmental Services, Department of Mental Health, Department of Children & Families, Department of Transitional Assistance, Department of Youth Services, and the Massachusetts Commission for the Blind.

Limitations of the data: As with any medical claim, the information contained in the MassHealth records cannot be tied directly to a specific clinical judgment about an individual or about that person's behavior. For example, diagnosis codes may be included for the purposes of billing and may not provide a full picture of a patient's health. Similarly, the fact that a payment was made for a medication cannot guarantee that an individual used the medications as prescribed. Opioid -services tracked and paid for by MassHealth will not include any services privately paid for or provided free of charge; therefore, these services could be underrepresented if only MassHealth records are included. Finally, the information provided by MassHealth only includes person covered by MassHealth for the period they were covered. If a person had interruptions in their MassHealth, equivalent services may have been provided by other insurers or entities for which we do not have comparable data.

Massachusetts Sheriff's Association[113] – Incarceration in Houses of Correction

What data are collected: It is the mission of the Massachusetts Sheriffs' Association to promote,

[112] Accessed at http://www.mass.gov/eohhs/gov/departments/masshealth/ on 5/19/2017.
[113] Accessed at http://www.mass.gov/msa/ on 5/19/2017.

advocate and support the office of sheriff in all fourteen counties of the Commonwealth, to secure their cooperative working relationship with one another, to enhance their work as the chief law enforcement officers of the counties, and to advance efforts to unify their efforts in policy development, operations and training while preserving the autonomy of each office. The Houses of Correction operate on a county level. They are required to track releases to the public through the Executive Office of Public Safety and Security. Individual releases are the basis for the data included in Chapter 55. The information includes basic identifiers as well as specific release dates.

Availability of data: The Chapter 55 data set include releases of sentenced offenders between July 1, 2011 through December 31, 2015 as reported by the county sheriffs' departments. These data are reported to the Massachusetts Executive Office of Public Safety (EOPSS) quarterly.

Limitations of the data: Incarceration dates are not reported for all county releases, so the full period of incarceration is not available for the data set. Hampshire and Berkshire counties did not submit data for FY2012 quarter 2, and Worcester county did not provide offender date of birth for CY2012 through CY2013 Q4, so their information is excluded for this analysis. These data should be combined with data from the Department of Correction to provide a fuller perspective of incarcerations for Massachusetts residents. However, residents of Massachusetts incarcerated outside of Massachusetts are not captured.

Community Level Data

Census:

What data are collected: name of city/town, EOHHS Region, EMS Region, total population, age group (18 age groupings), median age, gender, race, spoken language, unemployed individuals, food assistance received, income below poverty level, median household income, own or rent, and education level.

Availability of data: Data from the American Community Survey, five year-Estimates: 2006-2010

Limitations of the data: Since the data from a community or a zip code are applied to all residents of that community or zip code, the data can help in understanding the context in which an individual lives but not whether that data applies to any specific individual in the data set.

Naloxone:

What data are collected: Data from the MDPH Naloxone program from 2011-2015 including enrollments by month and town, refills by month and town and rescues by month and town.

Availability of data: 2011-2015 by city/town

Limitations of the data: Since the data from a community or a zip code are applied to all residents of that community or zip code, the data can help in understanding the context in which an individual lives but not whether that data applies to any specific individual in the data set.

Needle Exchange:

What data are collected: The Bureau of Substance Abuse Services has gathered data on needle exchange programs by town.

Availability of data: 2011-2015 by city/town

Limitations of the data: Since the data from a community or a zip code are applied to all residents of that community or zip code, the data can help in understanding the context in which an individual lives but not whether that data applies to any specific individual in the data set.

MDPHnet Depression Scores by Town:

What data are collected: MDPHnet is a distributed network of EHR-based data depositories. MDPHnet utilizes custom algorithms to detect cases that integrate diagnosis codes, laboratory tests, prescriptions, and other clinical indicators to accurately identify key conditions. In this case, MDPHnet was used to produce town level estimates of depression.

Availability of data: 2011-2015 by city/town

Limitations of the data: Since the data from a community or a zip code are applied to all residents of that community or zip code, the data can help in understanding the context in which an individual lives but not whether that data applies to any specific individual in the data set.

Drug Seizure Data:

What data are collected: Massachusetts Executive Office of Public Safety & Security records the number of incidents where drugs were seized between 2011-2015 by month. Each seizure is recorded by town. Variables included the type and amount of each drug seized.

Availability of data: 2011 to 2015.

Limitations of the data: These data report the number of incidents where drugs were seized, many may have resulted in arrests but not all of them.

ICE (Index of Concentration at the Extremes):

What data are collected: There are three ICE measures by census tract – one for income, another for race/ethnicity and the third which combines race/ethnicity. **ICEinc** sets as the extremes the American Community Survey household income categories that most closely approximate cutpoints for the US 20th and 80th household income percentile, currently <$25k and >=$100k. **ICErace** sets as the extreme groups persons who self-identify as non-Hispanic White vs. non-Hispanic Black, over the total population for whom race/ethnicity data are available. **ICEwbinc** combines race/ethnicity and income and sets as the extreme groups non-Hispanic White persons whose household income is great than or equal to the 80th income percentile vs. non-Hispanic Black persons in households below the 20th income percentile, over the total population for whom data on race x income are available.

Availability of data: American Community Survey five year estimates (2011- 2015).

Limitations of the data: Since the data from a community or a zip code are applied to all residents of that community or zip code, the data can help in understanding the context in which an individual lives but not whether that data applies to any specific individual in the data set.

Appendix B: Data Linkage

Data linkage for the Chapter 55 work was conducted by the Center for Health Information and Analysis (CHIA) in consultation with the Department of Public Health (DPH). Ten levels of matches were tested between individual Chapter 55 datasets and identifiers found in the All Payer Claims Database (APCD). All matches were deterministic. A conservative approach to matching was used, so no "near" or "close" matches were considered. In other words, all successful matches had to be exact at one of ten levels. The complete matching scheme is described below. The most reliable match is a "1," and so on down the chart to the least reliable, a "10."

Match Level	Identifiers To Be Matched
1	Exact match on first name, last name, Social Security number, gender, birth date, street address #1, street address #2, town of residence, and zip code.
2	Exact match on last name, Social Security number, gender, birth date, town of residence, and zip code.
3	Exact match on Social Security number, gender, and birth date.
4	Exact match on first name, last name, gender, birth date, street address #1, street address #2, town of residence, and zip code.
5	Exact match on first name, last name, gender, birth date, town of residence, and zip code.
6	Exact match on first name, last name, gender, and birth date.
7	Exact match on first name, last name, gender, and birth date
8	First and third letters of first name, first and third letters of last name, gender, birth date
9	Street address #1, street address #2, town of residence and zip code
10	Exact match on first name, last name, and birth date

CHIA processed each Chapter 55 file independent of all other files. To speed the process of the linkage work, there was no requirement for CHIA to perform data standardization or to deduplicate the data within or across files. Since data fields, collection methods, oversight, and quality vary from source to source – and even record to record – it is possible that "John Smith" got a Level 1 match in ***File1*** but then the same "John Smith" appeared twice in ***File2***, getting a Level 2 and a Level 3 match due to algorithm rules and/or missing data. Alternatively, the various John Smiths may not be related.

Without a focused deduplication effort, or a secondary weighted probabilistic match, it is impossible to know how often this might have occurred. Other tests of reliability of the matching scheme indicated that this was not a frequent occurrence. If duplicates were found within a file, each of these records was assigned the same project-specific ID. A summary of the matches across all datasets can be found in table below.

1. All Payer Claims Database	100.0%
2. Births Records linking Mothers (Vitals)	91.7%
3. Bureau of Substance Abuse Services (Treatment)	88.6%
4. Cancer Registry	88.3%
5. Case Mix (Hospital, ED, and Outpatient Records)	~70.0%[114]
6. Deaths Records (Vitals)	96.7%
7. Department of Housing & Community Development	82.6%
8. Department of Mental Health	97.8%
9. Department of Correction	89.7%
10. Department of Veterans Services	78.4%
11. Houses of Correction (MA Sheriffs' Association)	81.8%
12. MassHealth	99.8%
13. Massachusetts Ambulance Trip Information System (MATRIS)	71.1%
14. Office of the Chief Medical Examiner	96.7%
15. Prescription Drug Monitoring Program	92.3%

After reviewing the detailed matching data for each table, it was determined that match level 9 was too vague to be useful. It was dropped from consideration for record level matches. That issue aside, the matching procedure described above produced matches across all the tables in that data set that ranged from 71.1% on the low end for MATRIS to above 95% on the high end for the APCD (100%), Death records from the Registry of Vital Records and Statistics (96.7%), Department of Mental Health (97.8%), and MassHealth (99.8%).[115]

[114] Case Mix records are stored without the usual complement of identifiers making estimates of linkage rates difficult to compute. Comparisons of non-fatal events in raw Case Mix were made with those same events in the linked data set. Approximately 30% more nonfatal opioid events were found in the raw records, thus the estimate of a 70% linkage rate.

[115] Data from Partners Healthcare for a project proposed by Harvard School of Public Health and Partners was also linked to the APCD data. Since this data was not available to other researchers, it is not included in the table above.

Appendix C: Data Privacy and System Architecture

A determination was made at the outset of the Chapter 55 project to be able to examine all datasets in relation to each other. This required the development of a linkage or crosswalk so that individuals in one set could be located in the others, yet without revealing the identity of the matched person. The privacy concerns about holding, managing, and processing direct identifiers for so many sensitive datasets are considerable, and the processes developed to address these concerns were both thoughtful and innovative. In order to protect the privacy of the individual datasets, four approaches were used:

- **Encryption:** All data were encrypted in transport and at rest.
- **De-identification:** Direct identifiers were removed from each dataset prior to analyst access. The unique identifiers randomly generated for individuals were *project-specific*, meaning that no record IDs could be used to trace information back to any dataset held by any data owner now or in the future.
- **Securing the Server:** The server on which the Chapter 55 datasets were stored was secured so the likelihood of unauthorized access was minimized to the extent possible.
- **Preventing Misuse by Analysts:** Additional restrictions were placed on authorized access to the server on which the Chapter 55 datasets were stored in order to minimize the likelihood of intentional or unintentional misuse of the data.

Each of these approaches is described briefly below.

Encryption

Given the sensitivity of the data involved in the Chapter 55 analysis, multiple levels of encryption were used with the intent to limit data access to only authorized parties. Whenever data was stored at rest, whether on the server or other hard media, it was protected by at least 256-bit encryption and industry-standard strong passwords. Further, whenever data needed to be transported – for example between DPH and CHIA – it was placed in an encrypted file container on physical media that used hardware-based encryption. This doubly-encrypted drive was then manually transported by a trusted and authorized team member to its destination and hand-delivered to the proper recipient, or similarly retrieved for a return trip.

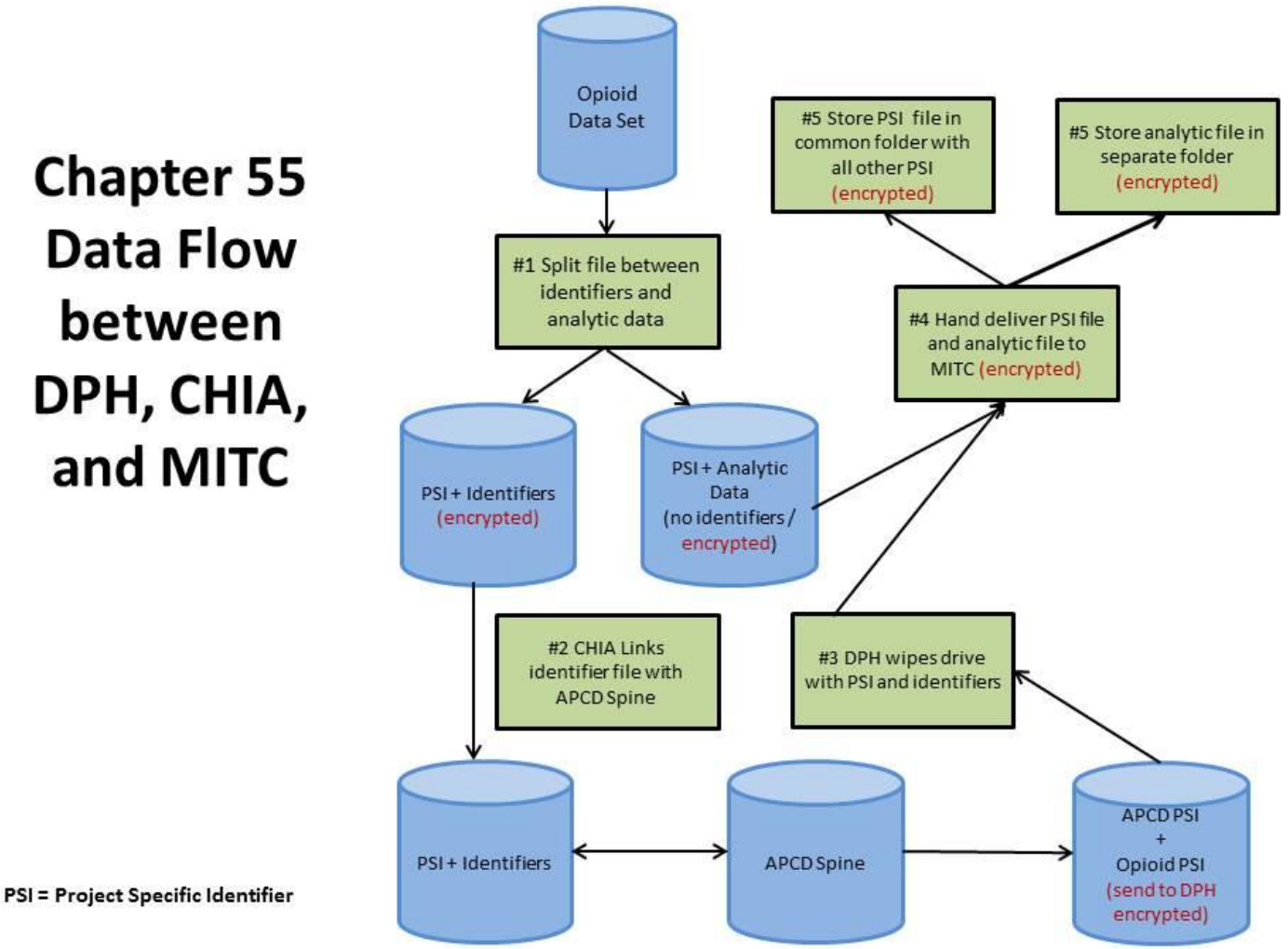
De-identification

Chapter 55 datasets are not truly linked in the most commonly used sense of that word. In most cases, linkage implies a merger of datasets. For Chapter 55, a crosswalk is developed between datasets but the datasets themselves were never actually merged. This is an important distinction. By not merging data, it is argued that risk of re-identification of individuals who have information in two or more datasets is minimized. Furthermore, the unique identifiers contained in each dataset are not found in any other project. Thus, if any breach of data or transmission protocol occurred, then the data could not be linked back to any source data file.

The specific steps taken to minimize of the risk to data privacy through de-identification are below. See Figure F.1 for a visual depiction of this process.

1) A pool of roughly 54 million random, non-sequential, 20-digit IDs (Random IDs or RIDs) was created at DPH. This number of values was sufficient to assign to every record of each of the constituent Chapter 55 raw datasets an ID that was unique across the entire project.
2) With RIDs affixed, each dataset was divided into two parts: direct identifiers (Identifier set) and analytic data (Analytic set). The only common information across both was the RID. The Identifier sets were hand delivered to CHIA. As noted under the Encryption section, all data was encrypted using 256-bit AES encryption with strong protection consistent with EOHHS and MassIT policy regarding password contents and length.
3) Distinct from DPH's RID-creation effort, CHIA created an extract of the All Payer Claims Database (APCD) that included only the fields to be used for the linkage scheme matching (Appendix D), plus an additional project-specific ID (PID). This PID was a random unique 20-digit number. It was in no way related to, nor derivative of, CHIA's Master Person Index (MPID) or any other persistent identifying code. This master extract-plus-PID is known as the APCD-Spine.
4) For each Identifier set, CHIA compared each record to the APCD-Spine. (For additional details on the data linkage, please see Appendix D.) Where a match was found, the PID and match level were associated with the RID from the Identifier set.
5) Upon confirmation from CHIA that an Identifier set was successfully matched to the APCD-Spine, DPH then deleted that Identifier set from its server.
6) The result set of matched PID/RID and match level were returned to DPH through the same secure mechanism as the delivery of the Identifier sets.
7) The RIDs within the returned result set were used to appropriately assign PIDs (and match confidence) to matching records in the Analytic sets. This allows the Analytic sets to be de-identified, but also connectable across datasets.
8) Because DPH had deleted the Identifier set, it was never in possession of the PID, RID and direct identifiers at the same time.
9) After assigning the PIDs to the Analytic sets, DPH securely delivered each Analytic file to the Massachusetts Information Technology Center (MITC) to be securely loaded onto the designated server.
10) In order to prevent merging of data, the project-specific identifiers and the analytic files for each Chapter 55 dataset were permanently stored in separate folders.
11) After all Chapter 55 Identifier sets have been matched and the Chapter 55 project no longer needs the APCD-Spine, CHIA will then delete it, destroying any connection between direct identifiers and PIDs at CHIA.

Figure C.1: Step by step process for transferring data securely from DPH tp CHIA to MITC



Securing the Server

There were three main goals in securing the SAS server:

1) Develop a clear audit process.
2) Ensure proper encryption for the different needs of the users.
3) Make it so that it was possible to handle more than a small number of group types in the system.

These three goals were achieved in the following manner:

- The disk partition on which the Chapter 55 data was stored was encrypted using LUKS (Linux Unified Key Setup). Linux is the open-source version of the UNIX operating system and LUKS is the standard hard disk encryption method for Linux servers.
- To provide further flexibility in the design of the secure data ecosystem to the needs of the Chapter 55 project, Red Hat Enterprise Linux version 6.0 was used.
- Accounts were authenticated by LDAP, which is the MITC standard, and account creation was handled through specific (not automated) requests to the MITC Linux team.
- A unique mount point for the Chapter 55 project was created so that only group participants could gain access.
- The interface for Chapter 55 work was through the web server interface with data encrypted at rest including all individual work files.
- An audit process was implemented to record when and who was doing maintenance on/for SAS.
- All inbound requests to the server were blocked unless the requestor was on a pre-approved whitelist. The firewall restricted access to specific ports on the server. Ports were continuously monitored.

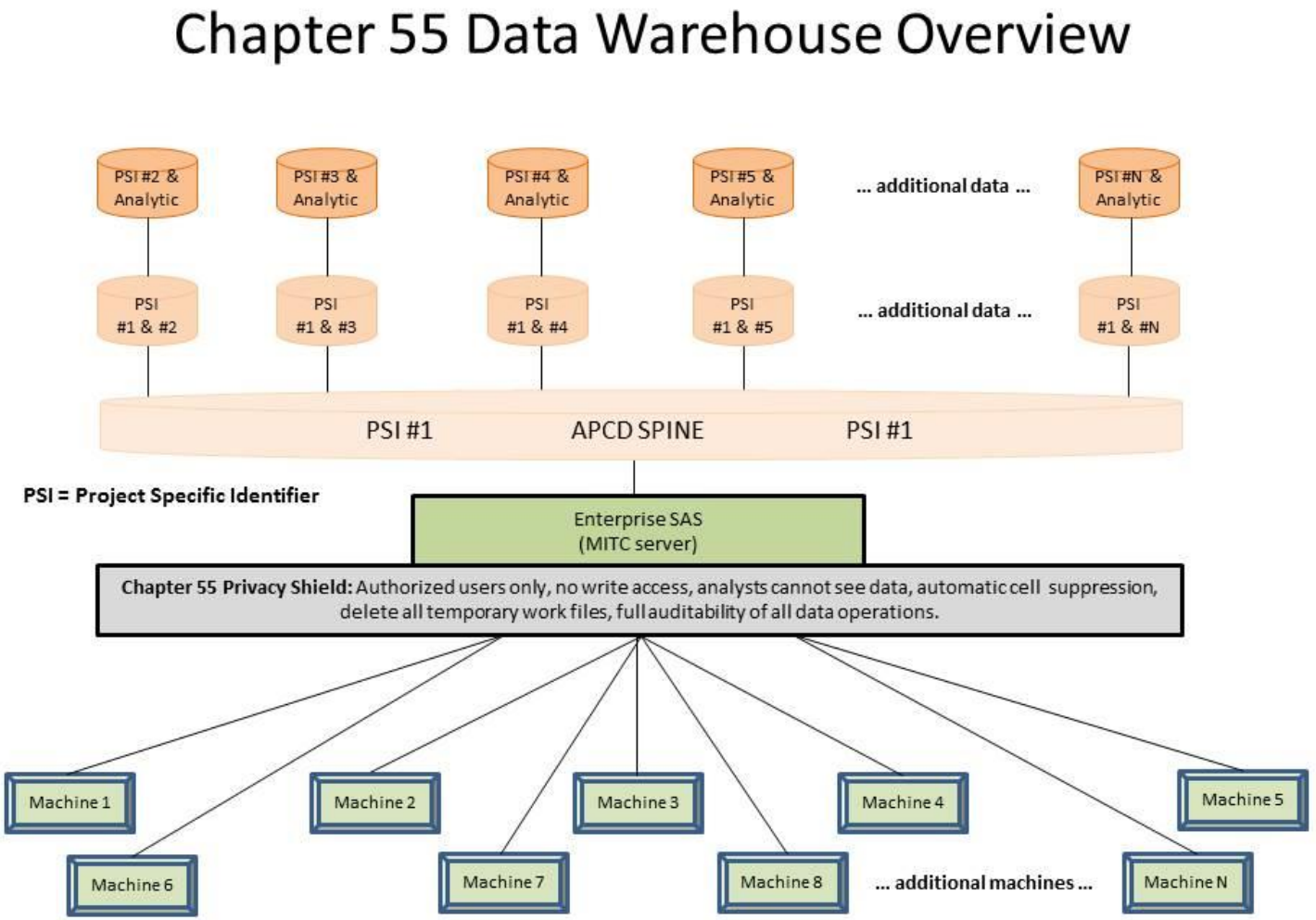
Preventing Misuse by Analysts:

To minimize the risk of misuse of Chapter 55 data by authorized users, the following processes were implemented as what has been collectively termed a **Privacy Shield**.

- Access to Chapter 55 data was only permitted using Enterprise SAS Studio software
- Only authorized users were given User IDs and passwords to access the Chapter 55 data.
- Authorized users were required to demonstrate that DPH-required privacy and confidentiality trainings were up to date.
- Only de-identified Analytic sets were accessible by analysts.
- Analysts had “read only” access to Chapter 55 datasets. Writes were not permitted.
- Analysts were not permitted to see the raw Chapter 55 Analytic data. This was accomplished by turning off the ability of authorized users to open and view raw Analytic data files.
- Analysts were not permitted to see small cell sizes. The common SAS procedure for producing counts and cross-tabulations (PROC FREQ) was altered so that it masked (by displaying asterisks) any cell count that was between one and 10.
- All temporary SAS work files were deleted in one of three ways. If shutdown of a process was typical, files were deleted upon shutdown. If shutdown was atypical (e.g., power outage), the system searched for orphaned work files every 15 minutes and these files were deleted. If any data query was open for more than 72 hours, then the system administrator could manually shut down a process which would delete any associated SAS work files.
- An audit process of all commands issued to SAS was implemented. Logs were checked to ensure that no analyst made any attempt to export, print, or otherwise view any Chapter 55 data.

See Figure C.2 for a visual depiction of the Chapter 55 Data Warehouse.

Figure C.2: Data analyst access to Chapter 55 datasets through a secure hardware and software Privacy Shield.



Appendix D: Supplemental Data

Section 1: Chapter 55 Approved Projects

Project Title: Linking Toxicology at Death with Prescription Monitoring Program Records: Implications for Defining Fentanyl and Heroin-related Deaths
Project Lead: Alex Walley (BMC)
Project Team: Marc LaRochelle (BMC), Traci Green (Brown), DPH Resources
Approved: 1/30/2017
Project Summary: Specific opioid toxicology in cause of deaths records has been imprecisely and inconsistently defined and reported across medical examiner jurisdictions. Specifically, likely heroin-related overdoses are inconsistently distinguished from morphine-related deaths because they have similar toxicology. Furthermore, fentanyl-related deaths have been classified as "prescription opioid-related" although young evidence has demonstrated that the fentanyl that is causing increased overdoses is illicitly made outside of the pharmaceutical fentanyl distribution system. Study will thoroughly examine historical and active prescribing along with post-mortem toxicology and how timing of prescriptions relates to fatal and non-fatal overdose. What fraction of overdoses with opioid A are attributable to opioid A prescriptions versus other sources for opioid A?

Project Title: Factors Associated with Overdose Death Among Inpatient Detoxification Patients
Project Lead: Alex Walley (BMC)
Project Team: Marc LaRochelle (BMC), DPH Resources
Approved: 1/30/2017
Project Summary: The population of patients who undergo inpatient detoxification represents a narrow, but specific group of those who have baseline risk for opioid overdose. People who seek inpatient detoxification are trying to reduce their risk of overdose; however, detox lowers opioid tolerance, thus increases overdose risk in the immediate post-detox time period. Patients who seek inpatient detoxification are both easy to define and recognize in the dataset, as well as, relatively easy to reach in the real world if an intervention comes out of this project. The protective and risk factors will be data elements that are both available in the datasets and have clinical and public health implications. This study will examine the protective and risk factors associated with different modalities of substance use disorder treatment.

Project Title: Developing a Predictive Model for Homelessness in Massachusetts and Relating Risk Estimates to Fatal and Non-Fatal Opioid Overdose
Project Leads: Tom Byrne (BU)
Project Team: Marc Dones (C4SI), Travis Baggett (BHCHP), David Smelson (UMASS Med), Asaad Traina (HSPH), Abraar Karan (HSPH), DPH Resources
Approved: 1/30/2017

Project Summary: Homelessness has been related to substance abuse, low education levels, incarceration status, co-morbidity with other chronic conditions, financial catastrophe, and other factors. Identifying the homeless or those at risk of homelessness is challenging because we do not have data directly from homeless shelters, nor is there a direct flag for "homelessness" in most databases. The study will use logistic regression models to identify data patterns associated with homelessness. This predictive model of homelessness will be used to assess ongoing risk of fatal and non-fatal opioid overdose for this population.

Project Title: Multivariate Analysis of Risk Factors for Death Using Data from the PDMP and Fatal Overdoses
Project Lead: Carly Levy (MCPHS)
Project Team: Abhidnya Kurve (MCPHS), Roger Studd (MCPHS), Rania Mekary (MCPHS), Francis Melaragni (MCPHS), DPH Resources
Approved: 1/30/2017
Project Summary: This application proposes to develop a PDMP-specific risk model. All potential factors for risk will be examined and included in a multivariate model if they are supported by the data. The goal is to develop a tool or alert system that could be incorporated into the PDMP to guide prescribers and pharmacists about risks linked specific patients. All algorithms will be self-contained in that they would only utilize PDMP data to compute risk assessments on which alerts would be based.

Project Title: Examination of opioid prescriptions across the VA and non-VA systems to reduce fatal and non-fatal opioid overdoses in Massachusetts
Project Lead: Guneet K. Jasuja (BU/ Bedford VA Medical Center)
Project Team: Omid Ameli (Bedford VA), David Smelson (UMASS Med), Dan Berlowitz (Bedford VA), Donald R. Miller (BU), Keith McInnes (BU), Adam Rose (RAND), Jim Burgess (BU), Avron Spiro (BU), DPH Resources
Approved: 1/30/2017
Project Summary: Veterans may be at particular risk for opioid overdose given that they have high rates of pain that is often treated with prescription opioids. Further, many Veterans are "dual users" who get both VA and non-VA medical care, and this dual use has been shown to increase risk for adverse outcomes in other areas of care. Thus, the objective of these analyses is to examine whether Veterans who receive prescriptions for opioids in both systems (VA and non-VA) are at an increased risk of fatal and non-fatal opioid overdose as compared to Veterans who receive all their opioids in one system. Further, we will examine whether the pattern and times of transition of opioid prescriptions between VA and non-VA systems would increase this risk of opioid overdose.

Project Title: Developing a Dynamic Model for Predicting Opioid Overdoses with the Opportunity to Identify Effective Points of Intervention
Project Lead: Harry Sleeper (MITRE)

Project Team: Project Team Six – The MITRE Corporation, DPH Resources
Approved: 1/30/2017
Project Summary: The team hypothesizes that patterns exist in the timing and type of interactions preceding fatal and non-fatal overdose occurrences. Their objective is to identify patterns in the timing and type of interactions that precede fatal and non-fatal overdose occurrences. Interactions include those that occur with the healthcare and behavioral health systems, the criminal justice system, social services and other interactions that can be analyzed with the available data. The study plans to use most or all Chapter 55 data sets to examine complex interactions related to timing of events and subsequent fatal and non-fatal overdose. A dynamic model will be developed. Survival analyses and logistic regression will be used to define the states of change and the amount of change in the model.

Project Title: Non-Fatal Overdoses, Differential Health Services Utilization, and Subsequent Risk
Project Lead: Kimberley Geissler (UMASS Med)
Project Team: Jennifer Whitehill (UMASS Med), Chelsea Young (UMASS Med), DPH Resources
Approved: 1/30/2017
Project Summary: Based on previous research examining substance use disorders, treatment after an initial non-fatal overdose is likely to vary based on insurance type (e.g., Medicaid, private insurance). Differences in treatment patterns may change the likelihood of repeat overdoses. We hypothesize that individuals with Medicaid insurance receive less treatment after an initial non-fatal overdose and are more likely to have a repeat overdose. Therefore, we will examine differences in repeat non-fatal and fatal overdoses among individuals with different insurance types after an initial non-fatal overdose.

Project Title: A Machine Learning Approach to Identify Patients at Risk of Fatal and Non-Fatal Opiate Overdose
Project Leads: Joscha Legewie (Yale) and Mathijs de Vaan (UC Berkeley)
Project Team: Joscha Legewie (Yale) and Mathijs de Vaan (UC Berkeley), and DPH Resources
Approved: 1/30/2017
Project Summary: The objective of the analysis is to develop a predictive model based on PDMP that produces patient-level risk scores for opioid-related deaths and overdose. The key hypothesis is that consumption of prescription opioids captured in PDMP together with socio-demographic data is predictive of opioid-related deaths. This hypothesis is a pre-requirement for developing a risk score based on PDMP. We will use logistic regression and random forests as our initial models and experiment with other machine learning methods such as support vector machines, adaptive boosting and decision trees. Machine learning methods automate analytical model building and iteratively "learn" from data, which allows computers to find hidden patterns such as complex non-linearities or interactions. These non-linearities and interactions are particularly relevant for the case at hand considering the different pathways and likelihoods of transitioning into illicit drug use. This work may embed other machine learning models within the larger model (e.g., homelessness). The methods proposed in this study promise to significantly improve the prediction of fatal and non-fatal opioid overdose. Cross-validation

will be used to limit problems like overfitting and assess how the results of our model generalize to an independent data set.

Project Title: Risk of Opioid Poisoning Associated with Medical Opioid Prescribing
Project Leads: Laura Burke (BIDMC)
Project Team: Austin Frakt, Ashish Jha, and DPH Resources
Approved: 1/30/2017
Project Summary: Medical opioid prescribing is thought to play a key role in this trend and there has been concern that providers have had inadequate information about the risks of medical opioid. There are a number of studies in different settings looking at patient-level risk factors for an opioid poisoning (overdose). However, the absolute risk of an overdose for an individual receiving a new opioid prescription is not well characterized. Empirical evidence about the risk of poisoning is crucial for providers to better evaluate the risk-benefit profile of opioid treatment in patients with potential medical indications for opioid treatment. The objective of this analysis is to characterize the risk of opioid overdose for individuals receiving a new opioid prescription.

Project Title: Risk of Overdose and Death after a Nonfatal Opioid Overdose
Project Leads: Laura Burke (BIDMC)
Project Team: Austin Frakt, Ashish Jha, and DPH Resources
Approved: 1/30/2017
Project Summary: There are a number of studies in different settings looking at patient-level risk factors for an opioid poisoning (overdose). However, more information is needed about the risk of death after a healthcare encounter for opioid overdose and the factors that mediate this risk. The objective of this analysis is to characterize the risk of subsequent death after a healthcare encounter (EMS, ED visit or hospitalization) for opioid poisoning and to understand individual demographic characteristics and co-morbidities as well as indications for opioids that mediate the risk of death after a nonfatal overdose.

Project Title: Receipt of Pharmacotherapy among Adolescents and Young Adults with Opioid Use Disorder and its Impact on Fatal and Non-Fatal Overdose
Project Lead: Scott Hadland (BMC)
Project Team: Sarah Bagley (BMC), Marc Larochelle (BMC), Alex Walley (BMC), and DPH Resources
Approved: 1/30/2017
Project Summary: Despite preexisting clinical practice guidelines and a new policy statement from the American Academy of Pediatrics recommending pharmacotherapy for youth with OUD, no prior studies have examined the extent to which youth in Massachusetts receive medications (buprenorphine, naltrexone, or methadone) and how these medications reduce the likelihood of fatal and non-fatal overdose. The BMC team will address this knowledge gap by obtaining valid, precise, and up-to-date estimates of the percentage of youth receiving pharmacotherapy and relate this information to fatal and non-fatal events. They will also examine retention in care and rate of drug use relapse among youth

receiving pharmacotherapy. They will identify time trends and potential disparities in receipt of pharmacotherapy among youth with OUD in Massachusetts using the All Payers Claim Data (APCD), and measure retention in care and rates of drug use relapse among youth receiving pharmacotherapy.

Project Title: Mortality of Patients who Received Pre-hospital Administration of Naloxone
Project Lead: Scott Weiner (Harvard/BWH)
Project Team: Sabrina Poon (Harvard/BWH), Olesya Baker (Partners), and DPH Resources
Approved: 1/30/2017
Project Summary: There has been significant emphasis on availability of naloxone for the lay public and prehospital administration as a means to prevent overdose death. Naloxone is now available as a standing order prescription from most commercial pharmacies, and by a special waiver, it can be administered by Basic Life Support medics. It is theorized that naloxone is saving a significant number of lives in the Commonwealth, but paradoxically, the opioid-related death rate continues to climb despite increased availability of naloxone. The purpose of this study is to determine the medium- and long-term mortality of patients who receive naloxone prehospital. The applicant hypothesizes that naloxone administration is a temporary life-saving measure for many patients, that >50% of patients who eventually died from an overdose had a previous episode of reversal with naloxone.

Project Title: GIS, Spatial Epidemiological, and Geostatistical Analysis of Opioid Overdose in MA
Project Lead: Tom Stopka (Tufts)
Project Team: Kenneth Chui (Tufts), Anna Kaplan (Tufts), Rachel Hoh (Tufts), and DPH Resources
Approved: 1/30/2017
Project Summary: The study will characterize the geospatial distribution and clustering of non-fatal and fatal opioid overdose and its associated outcomes in MA. We will employ descriptive GIS mapping and hotspot cluster analyses that look to control for time, geography, and demographics as we work to portray the unfolding of the opioid epidemic in terms of deaths, non-fatal overdoses, and repeat overdoses in Massachusetts between 2011 and 2015. We will determine whether changes in the epidemic are related to relevant community-level factors to better understand the current state of the opioid epidemic and to project future patterns.

Project Title: Examining Intervention Points to Reduce Fatal and Non-Fatal Opioid Overdoses in Massachusetts
Project Lead: Tom Stopka (Tufts)
Project Team: Marc LaRochelle (BMC), Adam Rose (RAND), Alex Walley (BMC), Kenneth Chui (Tufts), Anna Kaplan (Tufts), David Landy (Tufts), Rachel Hoh (Tufts) , and DPH Resources
Approved: 1/30/2017
Project Summary: This study will examine touchpoints to identify potential opioid use disorder (OUD) interventions in the health care delivery, criminal justice, and public health systems. We will identify distinct subpopulations, times, and venues for which potentially inappropriate prescribing (PIP) is

associated with fatal and non-fatal overdose. We will conduct spatial epidemiological analyses to characterize the geographic distribution and clustering of PIP, touchpoints before overdose events, non-fatal and fatal overdoses, and access to OUD services across Massachusetts (MA).

Project Title: Opioid Prescription and Utilization after Orthopedic Surgery
Project Lead: Brandon Earp (BIDMC)
Project Team: Ariana Mora (BIDMC), Praveen Murthy (BIDMC), Jamie Collins (BIDMC), Philip Blazar (BIDMC), and DPH Resources
Approved: March 6, 2017
Project Summary: The purpose of this study is to identify the incidence and risk factors for prolonged use or misuse of opioids, opioid overdose, and opioid-related mortality in patients who have undergone orthopedic procedures in different orthopedic subspecialties. Understanding the characteristics of these patients and their prescribers will facilitate development of future protocols that minimize early opioid dependence after orthopedic surgery, and thereby minimize the risk of long-term opioid-related morbidity and mortality. We hypothesize that there is a substantial and underestimated incidence of prolonged post-operative opioid use beyond the initial perioperative period, and that there are identifiable risk factors that predispose to ongoing prescription opioid use in this population, including both patient factors and prescriber factors listed below.

Project Title: Effect of treatment for opioid use disorder on opioid-related death among patients with intravenous drug associated endocarditis
Project Lead: Simeon Kimmel (BMC)
Project Team: Alex Walley (BMC), Ben Linas (BMC), Marc LaRochelle (BMC), and DPH Resources
Approved: March 6, 2017
Project Summary: In this analysis, we will define the effect of medications for opioid use disorder on opioid related mortality in intravenous drug associated endocarditis (IE-IDU). Reporting the number of patients in Massachusetts with IE-IDU who receive recommended treatment for opioid use disorder after an episode of endocarditis will add to our understanding of the current opioid epidemic. Moreover, describing the impact of treatment for underlying opioid use on overdose and overall mortality can guide public health and clinical strategies to improve mortality in this high-risk population. Treatment with medication for opioid use disorder (MOUD) in patients with injection drug associated endocarditis is associated with reduced opioid-related and all-cause mortality utilization and opioid overdose among families involved in the Emergency Assistance (EA) shelter system

Project Title: Assessing the relationship between patterns of shelter and behavioral health services utilization and opioid overdose among families involved in the Emergency Assistance (EA) shelter system
Project Lead: Thomas Byrne (BU)
Project Team: Margaret Thomas (BU), Daniel Miller (BU), Yoonsook Ha (BU), Travis Baggett (BHCFH) , and DPH Resources

Project Summary: The proposed project seeks to assess the extent to which, among families using the Emergency Assistance (EA) shelter system, different patterns of shelter and behavioral health services utilization are associated with the risk of fatal and non-fatal opioid overdose. . The project is motivated by prior research demonstrating that heads of households in families that make episodic (i.e. multiple discrete episodes over time) use of EA shelter have higher rates of substance abuse and mental health treatment histories than do their counterparts in families that make either transitional (i.e. a single, brief episode) or long term (i.e. a single extended episode) use of EA shelter. By assessing whether such variation in shelter utilization and behavioral health services use is associated with opioid overdose, the project stands to provide actionable information that could be used to help prevent future overdoses among EA-involved families. Specifically, findings could be used to inform the development of a tool that would identify EA-involved families who may be appropriate candidates for targeted screening and intervention efforts.

Project Title: Understanding the Impact that Mental Health has on the Likelihood of Opiate Addiction, Overdose, and Death
Project Lead: Christer Johnson (Ernst & Young)
Project Team: Ankur Jindal (Ernst & Young), Debra Cammer Hines (Ernst & Young), and DPH Resources
Project Summary: Much of the analytical focus in creating insights to reduce the number of opiate related overdoses and deaths has been focused on medical claim and prescription data, but very little focus has been given to behavioral health claims associated with mental health diagnosis and treatment. We propose to use exploratory data mining techniques to examine the relationship between a patient's mental health diagnosis and treatment history and opiate abuse and overdose. This analysis will allow us to create a patient risk profile for opiate abuse which can be used to inform treatment plans and help health care providers identify patients who are good candidates for interventions before they become addicted and thus prevent opiate related overdose and death

Project Title: Benzodiazepines, ADHD stimulants and overdose in buprenorphine maintenance treatment
Project Lead: Tae Woo Park (BMC)
Project Team: Marc LaRochelle (BMC), Alex Walley (BMC) , and DPH Resources
Project Summary: Benzodiazepines (BZD) and ADHD stimulants are commonly prescribed for psychiatric co-morbidities in patients receiving buprenorphine maintenance treatment (BMT). BZD and stimulant-related poisoning deaths have increased in the US. No large epidemiological study has tested the association between BZD or stimulants and fatal or non-fatal overdose in people receiving BMT. Additionally, the benefits of BZD or stimulants in the BMT patient population are largely unknown. Prescribing BZD or stimulants may increase patient adherence to BMT (see BZD maintenance treatment studies in methadone maintenance) and thus decrease risk of overdose. The study will focus on two primary questions. Is receipt of BZD or stimulant associated with BMT treatment retention? Is the relationship between BZD or stimulant and OD mediated by BMT treatment retention?

Project Title: Assessing Racial Differences In Accessing Treatment Subsequent To A Non-fatal Opioid Overdose Related Hospital Patient Encounter
Project Lead: Dan Dooley (BPHC)
Project Team: Snehal Shah (BPHC), and DPH Resources
Project Summary: Our purpose is to gain a better understanding of the relationship between opioid-related hospital care and subsequent substance abuse treatment admissions. Specifically, we seek to assess whether race and other factors in the hospital record predict follow-up substance abuse treatment among individuals who experienced a non-fatal opioid overdose. To determine if and to the what extent there are racial/ethnic differences in the rates of individual residents receiving subsequent substance abuse treatment services among those who have received acute hospital care for non-fatal opioid overdose and for any substance abuse-related diagnosis within the prior month and to assess factors within the Case Mix record that may play a role in predicting direct follow-up to treatment services.

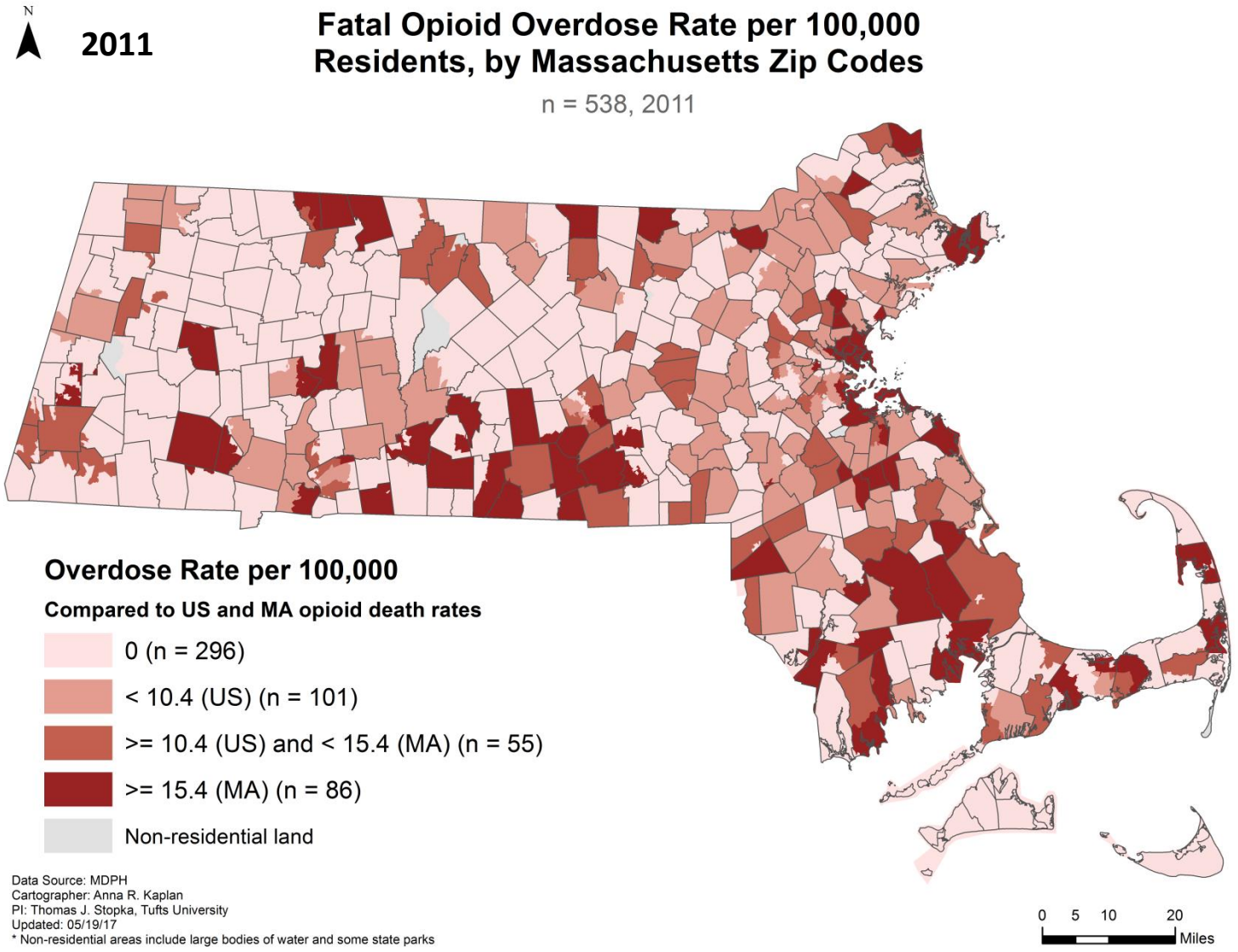
Project Title: Defining the cascade of care for substance use disorder detoxification in Massachusetts
Project Lead: Jake Morgan (BU)
Project Team: Josh Barocas (BU), Ben Linas (BU), Jenny Wang (BU), Alex Walley (BMC), Jenifer Jaeger (BPHC) , and DPH Resources
Project Summary: The goal of this project is to describe the cascade of care and churn (i.e., frequent relapse and readmission) in substance use disorder (SUD) treatment in Massachusetts for those entering acute treatment services (ATS, detoxification) to inform policies to reduce the risk of fatal and non-fatal opioid overdoses in the Commonwealth. We will describe the movement from ATS post-detox treatment (lower levels of care including CSS and TSS) to longer term residential services, and to outpatient treatment such as outpatient based opioid treatment (OBOT), describing relapse associated with each treatment level and transition (time between treatment services) as well as the rate of successful transitions to lower levels of care. The flexibility of our model will incorporate the variety of paths from ATS through the cascade, and we will describe the impact of each point in the cascade on fatal and non-fatal opioid-related overdose outcomes.

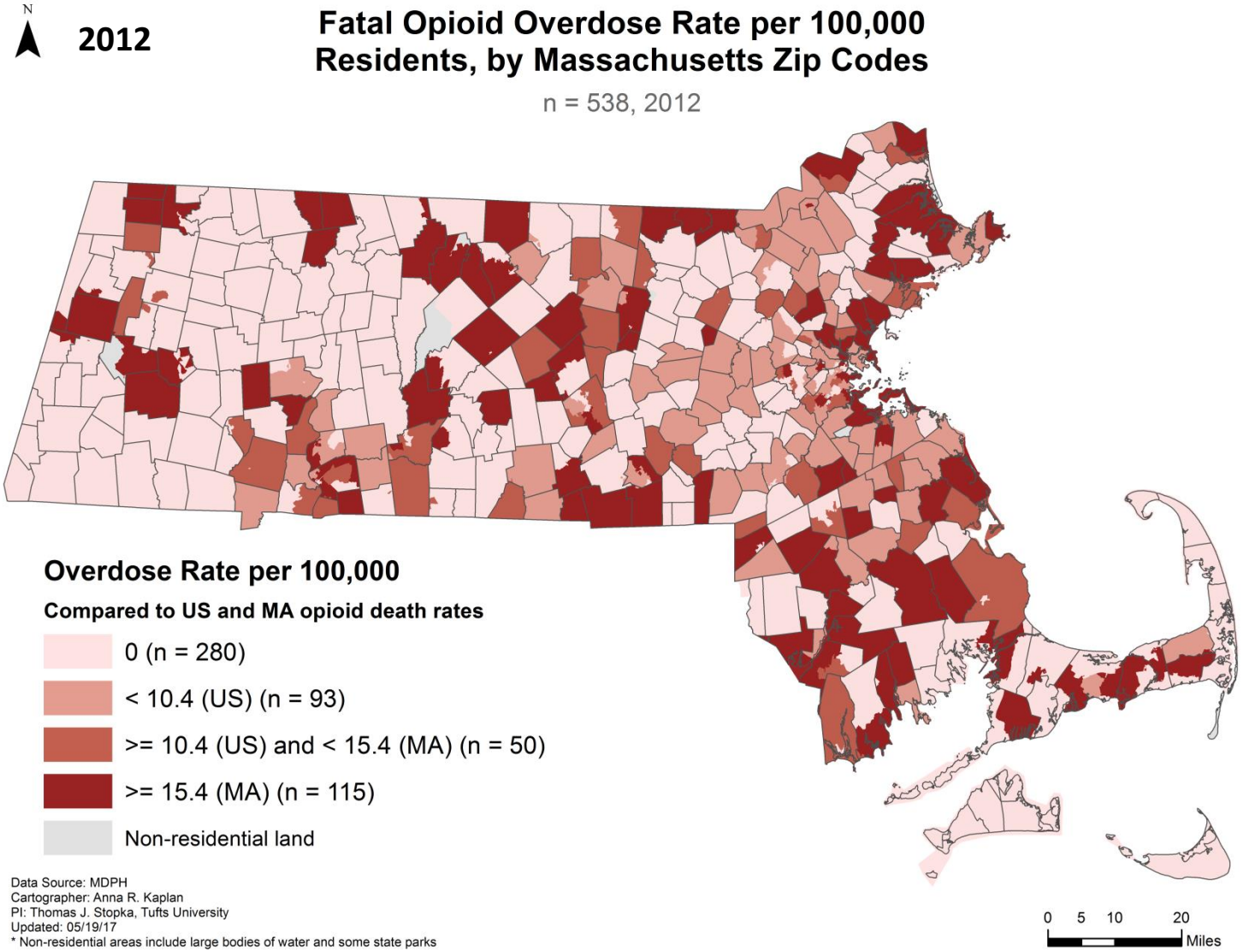
Project Title: Community Distribution of Naloxone Kits and Naloxone Rescues
Project Lead: Alex Walley (BMC)
Project Team: Traci Green (Brown), Tom Stopka (Tufts), Marc Larochelle (BMC), Na Wang (BMC), and DPH Resources
Project Summary: Community overdose response with naloxone is one of the core strategies identified by the US Department of Health and Human Services to address the opioid epidemic. The Massachusetts' Governor's Opioid Working Group identified access to naloxone as a key strategy to addressing the opioid crisis. Massachusetts is an early adopter of community overdose education and naloxone distribution. The objectives of this analysis are to use the Chapter 55 databases to generate the amount of naloxone distributed to the community per community (municipality, zip code) over time and the amount of naloxone administered by community members during rescue attempts per

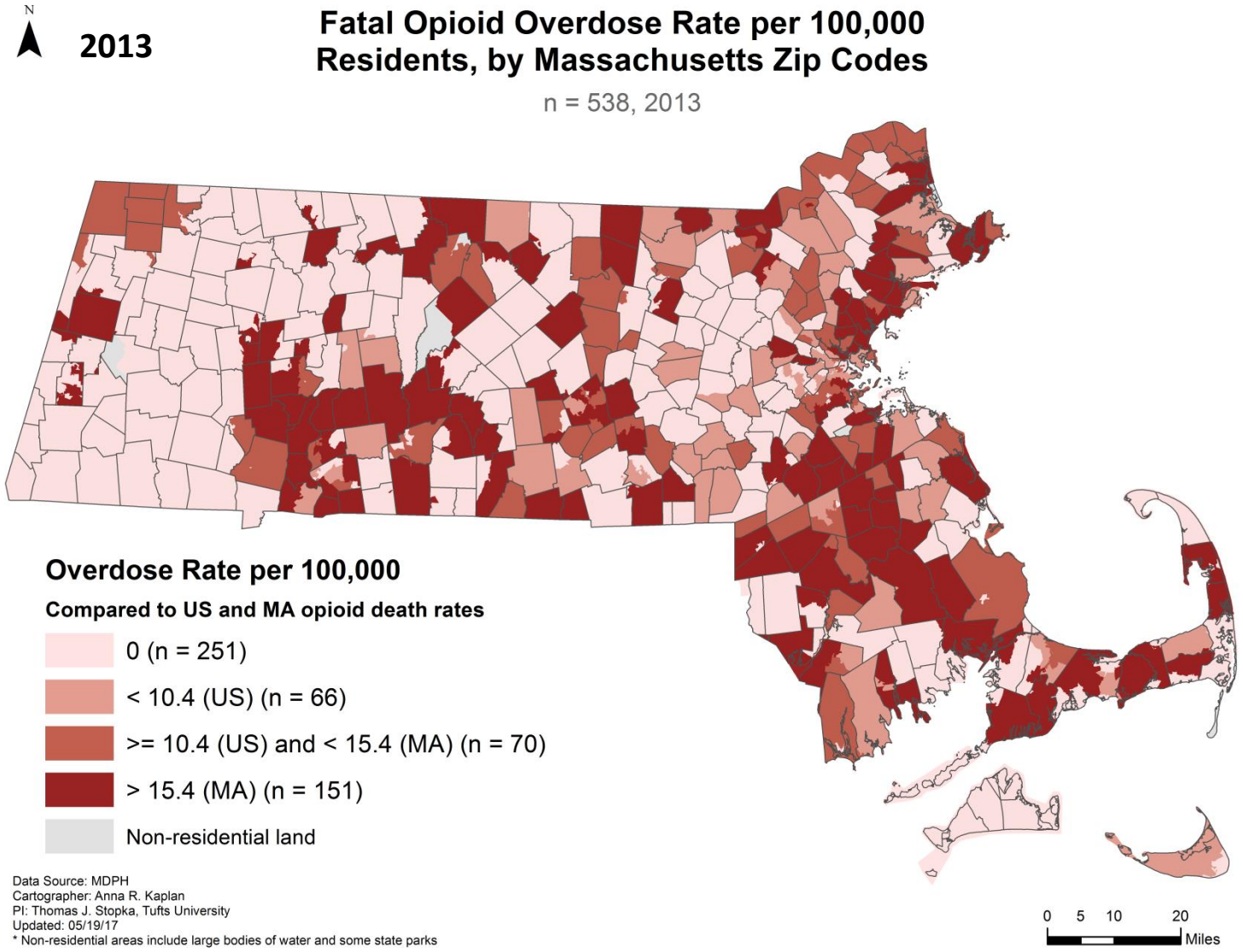
community per month. A secondary objective of the project is to assess the geospatial distribution of naloxone, as well as rescue attempts, by zip code. This project will generate community level rates of naloxone distribution and naloxone rescue attempts from multiple sources linked through the chapter 55 databases.

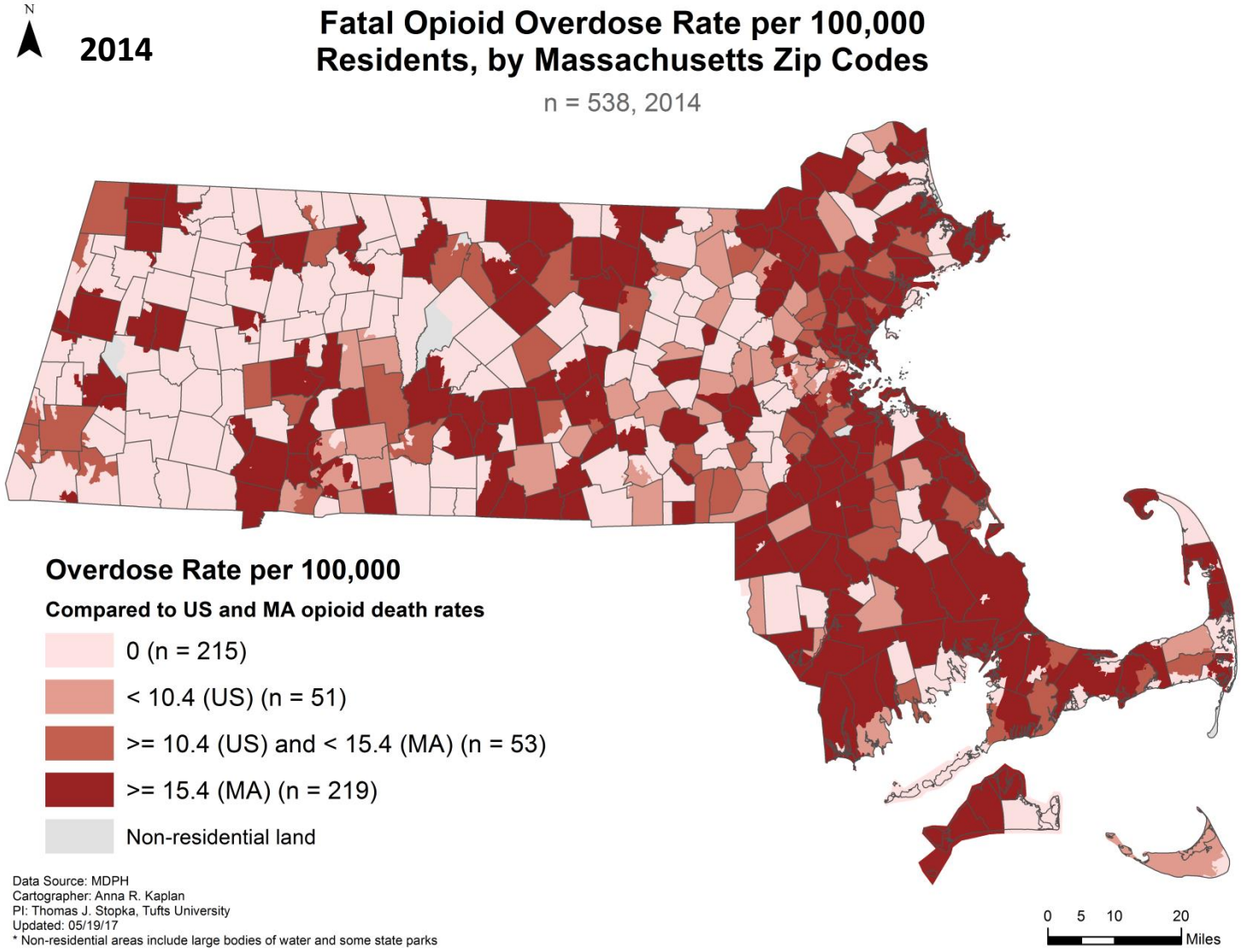
Project Title: Iatrogenic Opioid Addiction and Overdose in Orthopaedic Trauma: Examining a Natural Experiment
Project Lead: Matthew Basilico (Harvard)
Project Team: Abhiram Bhashyam (Harvard), Marilyn Heng (Harvard), Alan Xie (Harvard), Chethan Bachireddy (Harvard), and DPH Resources
Project Summary: This natural experiment utilizes the insight that clinicians differ in their individual propensities to prescribe a particular treatment course among many available options. To identify the relationship between opioid prescribing and addiction, they will use the econometric technique of "instrumental variables," and use first-year resident assignment as the discharging clinician in orthopedic trauma surgery as an "instrument"—a feature that is essentially random in its assignment—for the opioid prescription the patient receives. For comparison, they will also utilize two additional instruments, differing levels of trauma severity in a motor vehicle accidents, and facility-level propensities to refer to medication assisted treatment after discharge, as well as predictive techniques from machine learning to give context to our causal estimates.

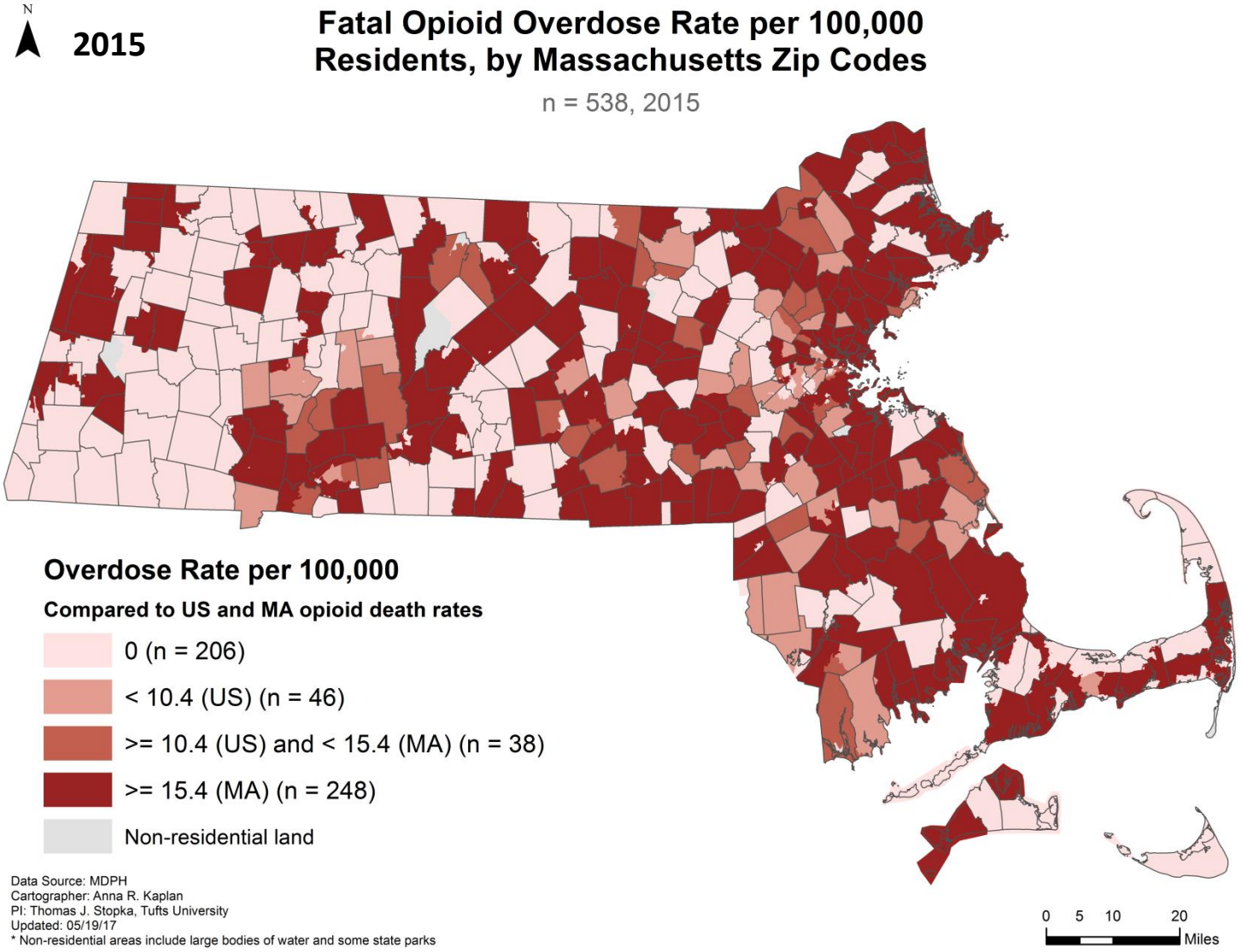
Appendix D Section 2: Full-sized maps of opioid overdose death rates by year.




N
2012
Fatal Opioid Overdose Rate per 100,000 Residents, by Massachusetts Zip Codes
n = 538, 2012
Overdose Rate per 100,000
Compared to US and MA opioid death rates
0 (n = 280)
< 10.4 (US) (n = 93)
>= 10.4 (US) and < 15.4 (MA) (n = 50)
>= 15.4 (MA) (n = 115)
Non-residential land
Data Source: MDPH
Cartographer: Anna R. Kaplan
PI: Thomas J. Stopka, Tufts University
Updated: 05/19/17
* Non-residential areas include large bodies of water and some state parks
0 5 10 20
Miles


N
2013
Fatal Opioid Overdose Rate per 100,000 Residents, by Massachusetts Zip Codes
n = 538, 2013
Overdose Rate per 100,000
Compared to US and MA opioid death rates
0 (n = 251)
< 10.4 (US) (n = 66)
>= 10.4 (US) and < 15.4 (MA) (n = 70)
> 15.4 (MA) (n = 151)
Non-residential land
Data Source: MDPH
Cartographer: Anna R. Kaplan
PI: Thomas J. Stopka, Tufts University
Updated: 05/19/17
* Non-residential areas include large bodies of water and some state parks
0 5 10 20
Miles


N
2014
Fatal Opioid Overdose Rate per 100,000 Residents, by Massachusetts Zip Codes
n = 538, 2014
Overdose Rate per 100,000
Compared to US and MA opioid death rates
0 (n = 215)
< 10.4 (US) (n = 51)
>= 10.4 (US) and < 15.4 (MA) (n = 53)
>= 15.4 (MA) (n = 219)
Non-residential land
Data Source: MDPH
Cartographer: Anna R. Kaplan
PI: Thomas J. Stopka, Tufts University
Updated: 05/19/17
* Non-residential areas include large bodies of water and some state parks
0 5 10 20
Miles


N
2015
Fatal Opioid Overdose Rate per 100,000 Residents, by Massachusetts Zip Codes
n = 538, 2015
Overdose Rate per 100,000
Compared to US and MA opioid death rates
0 (n = 206)
< 10.4 (US) (n = 46)
>= 10.4 (US) and < 15.4 (MA) (n = 38)
>= 15.4 (MA) (n = 248)
Non-residential land
Data Source: MDPH
Cartographer: Anna R. Kaplan
PI: Thomas J. Stopka, Tufts University
Updated: 05/19/17
* Non-residential areas include large bodies of water and some state parks
0 5 10 20
Miles

Appendix D Section 3: Community Quintile Scores (Alphabetical Order)

Community	Quintile[116]	Community	Quintile	Community	Quintile
Abington	1	Braintree	2	Dudley	3
Acton	4	Brewster	3	Dunstable	4
Acushnet	2	Bridgewater	2	Duxbury	5
Adams	1	Brimfield	2	East Bridgewater	1
Agawam	2	Brockton	1	East Brookfield	3
Alford	2	Brookfield	3	East Longmeadow	2
Amesbury	2	Brookline	5	Eastham	1
Amherst	5	Buckland	4	Easthampton	2
Andover	4	Burlington	3	Easton	3
Aquinnah	2	Cambridge	4	Edgartown	5
Arlington	4	Canton	3	Egremont	4
Ashburnham	4	Carlisle	5	Erving	2
Ashby	3	Carver	1	Essex	5
Ashfield	5	Charlemont	3	Everett	1
Ashland	4	Charlton	3	Fairhaven	2
Athol	1	Chatham	4	Fall River	1
Attleboro	2	Chelmsford	4	Falmouth	1
Auburn	3	Chelsea	1	Fitchburg	1
Avon	1	Cheshire	5	Florida	5
Ayer	1	Chester	4	Foxborough	3
Barnstable	1	Chesterfield	4	Framingham	2
Barre	1	Chicopee	1	Franklin	3
Becket	4	Chilmark	3	Freetown	2
Bedford	4	Clarksburg	4	Gardner	1
Belchertown	3	Clinton	1	Georgetown	4
Bellingham	3	Cohasset	3	Gill	3
Belmont	5	Colrain	5	Gloucester	1
Berkley	2	Concord	5	Goshen	4
Berlin	5	Conway	4	Gosnold	5
Bernardston	1	Cummington	3	Grafton	3
Beverly	2	Dalton	4	Granby	3
Billerica	2	Danvers	2	Granville	4
Blackstone	4	Dartmouth	2	Great Barrington	4
Blandford	3	Dedham	2	Greenfield	1
Bolton	4	Deerfield	4	Groton	4
Boston	1	Dennis	1	Groveland	4
Bourne	1	Dighton	4	Hadley	4
Boxborough	5	Douglas	3	Halifax	2
Boxford	5	Dover	5	Hamilton	4
Boylston	3	Dracut	2	Hampden	3

[116] Lower quintiles indicate highest relative burden. Higher quintiles indicate lowest relative burden.

Community Quintile Scores (Alphabetical Order)

Community	Quintile[117]	Community	Quintile	Community	Quintile
Hancock	5	Ludlow	2	New Bedford	1
Hanover	3	Lunenburg	2	New Braintree	2
Hanson	2	Lynn	1	New Marlborough	5
Hardwick	2	Lynnfield	3	New Salem	3
Harvard	5	Malden	1	Newbury	4
Harwich	1	Manchester	5	Newburyport	4
Hatfield	2	Mansfield	4	Newton	5
Haverhill	1	Marblehead	5	Norfolk	4
Hawley	5	Marion	3	North Adams	1
Heath	4	Marlborough	3	North Andover	4
Hingham	5	Marshfield	2	North Attleboro	3
Hinsdale	3	Mashpee	1	North Brookfield	3
Holbrook	1	Mattapoisett	3	North Reading	3
Holden	3	Maynard	3	Northampton	1
Holland	3	Medfield	5	Northborough	5
Holliston	4	Medford	2	Northbridge	1
Holyoke	1	Medway	5	Northfield	2
Hopedale	3	Melrose	2	Norton	2
Hopkinton	4	Mendon	4	Norwell	3
Hubbardston	2	Merrimac	4	Norwood	2
Hudson	2	Methuen	2	Oak Bluffs	4
Hull	1	Middleborough	1	Oakham	4
Huntington	3	Middlefield	2	Orange	1
Ipswich	3	Middleton	4	Orleans	3
Kingston	4	Milford	3	Otis	4
Lakeville	2	Millbury	1	Oxford	2
Lancaster	2	Millis	5	Palmer	1
Lanesborough	3	Millville	5	Paxton	3
Lawrence	1	Milton	4	Peabody	2
Lee	2	Monroe	5	Pelham	5
Leicester	2	Monson	3	Pembroke	2
Lenox	4	Montague	2	Pepperell	2
Leominster	1	Monterey	5	Peru	5
Leverett	5	Montgomery	5	Petersham	3
Lexington	5	Mount Washington	5	Phillipston	4
Leyden	5	Nahant	3	Pittsfield	1
Lincoln	5	Nantucket	3	Plainfield	5
Littleton	5	Natick	4	Plainville	3
Longmeadow	5	Needham	5	Plymouth	2
Lowell	1	New Ashford	3	Plympton	2

[117] Lower quintiles indicate highest relative burden. Higher quintiles indicate lowest relative burden.

Community Quintile Scores (Alphabetical Order)

Community	Quintile[118]	Community	Quintile	Community	Quintile
Princeton	2	Springfield	1	West Boylston	3
Provincetown	4	Sterling	5	West Bridgewater	1
Quincy	1	Stockbridge	3	West Brookfield	3
Randolph	2	Stoneham	2	West Newbury	5
Raynham	1	Stoughton	1	West Springfield	1
Reading	3	Stow	5	West Stockbridge	4
Rehoboth	5	Sturbridge	4	West Tisbury	5
Revere	1	Sudbury	5	Westborough	4
Richmond	2	Sunderland	4	Westfield	2
Rochester	5	Sutton	4	Westford	5
Rockland	1	Swampscott	3	Westhampton	5
Rockport	3	Swansea	2	Westminster	3
Rowe	5	Taunton	1	Weston	5
Rowley	4	Templeton	2	Westport	3
Royalston	2	Tewksbury	2	Westwood	5
Russell	4	Tisbury	3	Weymouth	1
Rutland	4	Tolland	5	Whately	5
Salem	1	Topsfield	4	Whitman	1
Salisbury	1	Townsend	2	Wilbraham	4
Sandisfield	5	Truro	2	Williamsburg	5
Sandwich	3	Tyngsborough	3	Williamstown	5
Saugus	1	Tyringham	3	Wilmington	2
Savoy	4	Upton	5	Winchendon	1
Scituate	2	Uxbridge	2	Winchester	5
Seekonk	5	Wakefield	2	Windsor	4
Sharon	4	Wales	3	Winthrop	1
Sheffield	4	Walpole	4	Woburn	1
Shelburne	2	Waltham	3	Worcester	1
Sherborn	5	Ware	1	Worthington	4
Shirley	3	Wareham	1	Wrentham	4
Shrewsbury	4	Warren	2	Yarmouth	1
Shutesbury	4	Warwick	5		
Somerset	2	Washington	5		
Somerville	2	Watertown	3		
South Hadley	2	Wayland	5		
Southampton	3	Webster	1		
Southborough	5	Wellesley	5		
Southbridge	1	Wellfleet	1		
Southwick	3	Wendell	4		
Spencer	1	Wenham	5		

[118] Lower quintiles indicate highest relative burden. Higher quintiles indicate lowest relative burden.

Community Quintile Scores (Quintile 1: Highest Relative Burden)

Community	Quintile[119]	Community	Quintile	Community	Quintile
Abington	1	Greenfield	1	Rockland	1
Adams	1	Harwich	1	Salem	1
Athol	1	Haverhill	1	Salisbury	1
Avon	1	Holbrook	1	Saugus	1
Ayer	1	Holyoke	1	Southbridge	1
Barnstable	1	Hull	1	Spencer	1
Barre	1	Lawrence	1	Springfield	1
Bernardston	1	Leominster	1	Stoughton	1
Boston	1	Lowell	1	Taunton	1
Bourne	1	Lynn	1	Ware	1
Brockton	1	Malden	1	Wareham	1
Carver	1	Mashpee	1	Webster	1
Chelsea	1	Middleborough	1	Wellfleet	1
Chicopee	1	Millbury	1	West Bridgewater	1
Clinton	1	New Bedford	1	West Springfield	1
Dennis	1	North Adams	1	Weymouth	1
East Bridgewater	1	Northampton	1	Whitman	1
Eastham	1	Northbridge	1	Winchendon	1
Everett	1	Orange	1	Winthrop	1
Fall River	1	Palmer	1	Woburn	1
Falmouth	1	Pittsfield	1	Worcester	1
Fitchburg	1	Quincy	1	Yarmouth	1
Gardner	1	Raynham	1		
Gloucester	1	Revere	1		

[119] Lower quintiles indicate highest relative burden. Higher quintiles indicate lowest relative burden.

Community Quintile Scores (Quintile 2: Higher Than Average Relative Burden)

Community	Quintile[120]	Community	Quintile	Community	Quintile
Acushnet	2	Hardwick	2	Plymouth	2
Agawam	2	Hatfield	2	Plympton	2
Alford	2	Hubbardston	2	Princeton	2
Amesbury	2	Hudson	2	Randolph	2
Aquinnah	2	Lakeville	2	Richmond	2
Attleboro	2	Lancaster	2	Royalston	2
Berkley	2	Lee	2	Scituate	2
Beverly	2	Leicester	2	Shelburne	2
Billerica	2	Ludlow	2	Somerset	2
Braintree	2	Lunenburg	2	Somerville	2
Bridgewater	2	Marshfield	2	South Hadley	2
Brimfield	2	Medford	2	Stoneham	2
Danvers	2	Melrose	2	Swansea	2
Dartmouth	2	Methuen	2	Templeton	2
Dedham	2	Middlefield	2	Tewksbury	2
Dracut	2	Montague	2	Townsend	2
East Longmeadow	2	New Braintree	2	Truro	2
Easthampton	2	Northfield	2	Uxbridge	2
Erving	2	Norton	2	Wakefield	2
Fairhaven	2	Norwood	2	Warren	2
Framingham	2	Oxford	2	Westfield	2
Freetown	2	Peabody	2	Wilmington	2
Halifax	2	Pembroke	2		
Hanson	2	Pepperell	2		

[120] Lower quintiles indicate highest relative burden. Higher quintiles indicate lowest relative burden.

Community Quintile Scores (Quintile 3: Average Relative Burden)

Community	Quintile[121]	Community	Quintile	Community	Quintile
Ashby	3	Hampden	3	Orleans	3
Auburn	3	Hanover	3	Paxton	3
Belchertown	3	Hinsdale	3	Petersham	3
Bellingham	3	Holden	3	Plainville	3
Blandford	3	Holland	3	Reading	3
Boylston	3	Hopedale	3	Rockport	3
Brewster	3	Huntington	3	Sandwich	3
Brookfield	3	Ipswich	3	Shirley	3
Burlington	3	Lanesborough	3	Southampton	3
Canton	3	Lynnfield	3	Southwick	3
Charlemont	3	Marion	3	Stockbridge	3
Charlton	3	Marlborough	3	Swampscott	3
Chilmark	3	Mattapoisett	3	Tisbury	3
Cohasset	3	Maynard	3	Tyngsborough	3
Cummington	3	Milford	3	Tyringham	3
Douglas	3	Monson	3	Wales	3
Dudley	3	Nahant	3	Waltham	3
East Brookfield	3	Nantucket	3	Watertown	3
Easton	3	New Ashford	3	West Boylston	3
Foxborough	3	New Salem	3	West Brookfield	3
Franklin	3	North Attleboro	3	Westminster	3
Gill	3	North Brookfield	3	Westport	3
Grafton	3	North Reading	3		
Granby	3	Norwell	3		

[121] Lower quintiles indicate highest relative burden. Higher quintiles indicate lowest relative burden.

Community Quintile Scores (Quintile 4: Lower Than Average Relative Burden)

Community	Quintile[122]	Community	Quintile	Community	Quintile
Acton	4	Granville	4	Phillipston	4
Andover	4	Great Barrington	4	Provincetown	4
Arlington	4	Groton	4	Rowley	4
Ashburnham	4	Groveland	4	Russell	4
Ashland	4	Hadley	4	Rutland	4
Becket	4	Hamilton	4	Savoy	4
Bedford	4	Heath	4	Sharon	4
Blackstone	4	Holliston	4	Sheffield	4
Bolton	4	Hopkinton	4	Shrewsbury	4
Buckland	4	Kingston	4	Shutesbury	4
Cambridge	4	Lenox	4	Sturbridge	4
Chatham	4	Mansfield	4	Sunderland	4
Chelmsford	4	Mendon	4	Sutton	4
Chester	4	Merrimac	4	Topsfield	4
Chesterfield	4	Middleton	4	Walpole	4
Clarksburg	4	Milton	4	Wendell	4
Conway	4	Natick	4	West Stockbridge	4
Dalton	4	Newbury	4	Westborough	4
Deerfield	4	Newburyport	4	Wilbraham	4
Dighton	4	Norfolk	4	Windsor	4
Dunstable	4	North Andover	4	Worthington	4
Egremont	4	Oak Bluffs	4	Wrentham	4
Georgetown	4	Oakham	4		
Goshen	4	Otis	4		

[122] Lower quintiles indicate highest relative burden. Higher quintiles indicate lowest relative burden.

Community Quintile Scores (Quintile 5: Lowest Relative Burden)

Community	Quintile[123]	Community	Quintile	Community	Quintile
Amherst	5	Lincoln	5	Seekonk	5
Ashfield	5	Littleton	5	Sherborn	5
Belmont	5	Longmeadow	5	Southborough	5
Berlin	5	Manchester	5	Sterling	5
Boxborough	5	Marblehead	5	Stow	5
Boxford	5	Medfield	5	Sudbury	5
Brookline	5	Medway	5	Tolland	5
Carlisle	5	Millis	5	Upton	5
Cheshire	5	Millville	5	Warwick	5
Colrain	5	Monroe	5	Washington	5
Concord	5	Monterey	5	Wayland	5
Dover	5	Montgomery	5	Wellesley	5
Duxbury	5	Mount Washington	5	Wenham	5
Edgartown	5	Needham	5	West Newbury	5
Essex	5	New Marlborough	5	West Tisbury	5
Florida	5	Newton	5	Westford	5
Gosnold	5	Northborough	5	Westhampton	5
Hancock	5	Pelham	5	Weston	5
Harvard	5	Peru	5	Westwood	5
Hawley	5	Plainfield	5	Whately	5
Hingham	5	Rehoboth	5	Williamsburg	5
Leverett	5	Rochester	5	Williamstown	5
Lexington	5	Rowe	5	Winchester	5
Leyden	5	Sandisfield	5		

[123] Lower quintiles indicate highest relative burden. Higher quintiles indicate lowest relative burden.

Appendix E: Legal Agreements

In order to meet the legal requirements of working with all of these protected datasets, a number of legal documents were produced. Four different types of agreements were signed.

1) Linking – This agreement between DPH and Center for Health Information and Analysis (CHIA) allowed for the exchange of data for the purposes of securely connecting data at the individual level across secure datasets without exposing the identity of the individual so connected.
2) Sharing – This agreement outlined the *methodology* and *restrictions* allowing for the sharing of data between different departments or agencies that were not previously sharing – or even allowed to share, outside of the Chapter 55 project. Each of the data-supplying entities was a signatory to this ISA. Specifically, signatories include: the Department of Public Health (DPH), the Department of Correction (DOC), the Executive Office of Public Safety and Security (EOPSS) for Houses of Correction data (HOC), the Office of the Chief Medical Examiner (OCME), the Department of Veterans' Services (DVS), the Department of Mental Health (DMH), the Department of Housing and Community Development (DHCD), MassHealth, and the Center for Health Information and Analysis (CHIA). While CHIA has previously signed the Linking agreement, they are also the provider of analytic data from the All Payer Claims Database (APCD) and Case Mix.
3) Hosting – An agreement between DPH and MassIT specifying the hosting responsibilities and restrictions for the data infrastructure.
4) Access – An additional agreement created for *ad hoc* access to data outside of the purview of the prior three agreements. For example: If the Data Office within MassIT were to assist in a way that required analytical data access that is not covered by the 3rd agreement (which is hosting specific). This 4th agreement essentially outlines the responsibilities of being a good data steward and requires a signature for access. There would conceivably be *n* number of these agreements signed over time.

Appendix F: Partnerships

The Chapter 55 project brought together analysts and researchers from across government, more than a dozen academic institutions, and two private consulting firms. First and foremost, the Department of Public Health would like to thank all those who participated in this effort. Without everyone's assistance, this report could not have been completed in time. The work done here has been groundbreaking and the collaboration has been extraordinary both inside and outside government institutions.

State Agencies	
• Center for Health Information and Analysis • EOHHS IT • EOPSS • Department of Correction • Department of Housing and Community Development • Department of Mental Health	• Department of Public Health • Department of Veterans' Services • Massachusetts Sheriffs' Association • Massachusetts State Police • MassHealth • Mass IT – Data Office • Office of the Chief Medical Examiner
Academic Institutions and Private Industry	
• Beth Israel Deaconess Hospital • Boston Children's Hospital Boston Health Care for the Homeless • Boston Medical Center • Boston Public Health Commission • Boston University School of Medicine • Brigham & Women's Hospital • Brown University • Center for Social Innovation • Centers for Disease Control and Prevention • Commonwealth Medicine • Ernst & Young • General Electric Foundation • Harvard Medical School • Harvard School of Public Health • Harvard University	• Mass College of Pharmacy and Health Sciences • Massachusetts Institute of Technology • MITRE Corporation • Northeastern University • Partners Healthcare • Price Waterhouse Cooper • RAND Corporation • SAS Analytics • Tufts University School of Medicine • University of Massachusetts, Amherst • University of Massachusetts, Boston • University of Massachusetts Medical School • University of California, Berkeley • Veterans Administration • Yale University

Exhibit F

THE MASSACHUSETTS OPIOID EPIDEMIC

A data visualization of findings from the Chapter 55 report

View latest report ➜ (http://www.mass.gov/eohhs/gov/departments/dph/stop-addiction/chapter-55-overdose-assessment.html)

A Deadly Problem

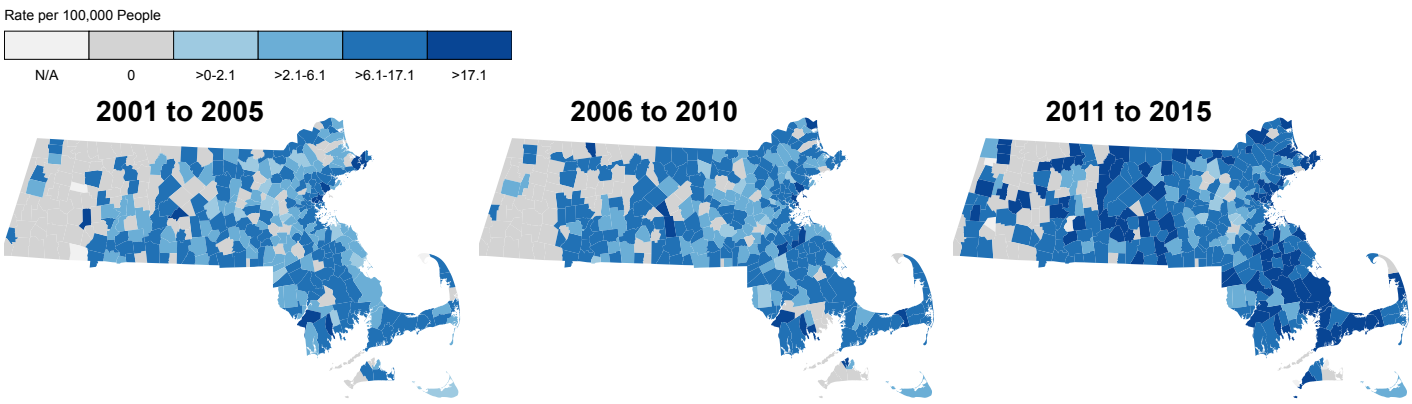
Massachusetts is currently experiencing an epidemic of opioid-related overdose and death.

These overdoses are driven by the underlying chronic disease of opioid addiction or opioid use disorders. People with opioid addiction are at high risk of overdose and death.

Opioid-related deaths in the state were more than four times higher in 2015 than in 2000. This recent rate of increase is several times faster than anything seen here before. In 2013–2014 alone, opioid-related deaths occurred in two-thirds of the cities and towns in Massachusetts.

Average Annual Opioid-related Death Rate per 100,000 People[1,2,3,4,5]

The maps below, representing average annual rates of opioid-related deaths across five-year spans, demonstrate the increase in both the spread and intensity of the problem across Massachusetts.



View the dataset powering this visualization (js/data/csv/Introduction_MassMuni_5yrOpioidDeathRate.csv)

Sources: Massachusetts Registry of Vital Records and Statistics (http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/), Massachusetts Department of Public Health (http://www.mass.gov/eohhs/gov/departments/dph/).

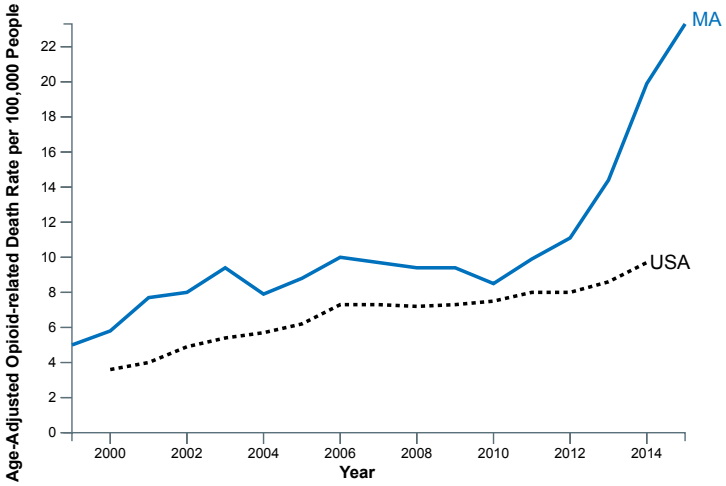
The opioid-related death rate in Massachusetts has surpassed the national average, with an especially sharp rise in the last two years.

In fact, 2014 marked the first year since 1999[6] that the fatal overdose rate in the Bay State was more than double the national average. While opioid-related deaths have been on the rise across the country during that period, the situation in the Commonwealth has become especially worrying.

In one way or another — through deaths, nonfatal overdoses, or disruptions to jobs, marriages, families, and neighborhoods — every community in Massachusetts has been impacted by this growing crisis.

Age-Adjusted Opioid-related Death Rate by Year[4,7,8]

Comparing the opioid-related death rate of Massachusetts to the nation overall.



View the dataset powering this visualization (js/data/csv/Introduction_USA_vs_MA_OpioidDeathRate.csv)

Sources: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2014 on CDC WONDER Online Database (http://wonder.cdc.gov/mcd-icd10.html), released 2015. Massachusetts Registry of Vital Records and Statistics (http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/), Massachusetts Department of Public Health (http://www.mass.gov/eohhs/gov/departments/dph/).

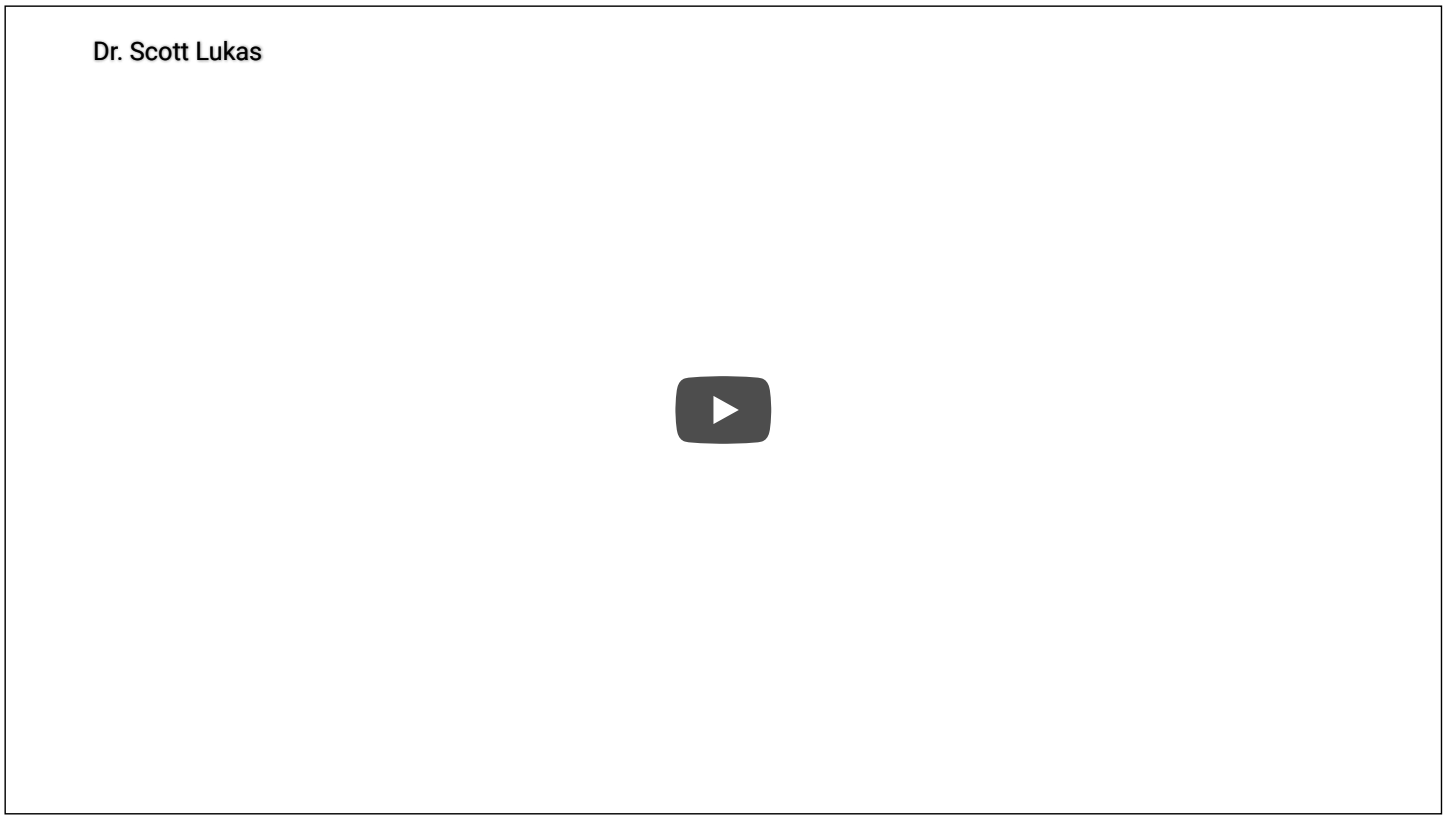
Understanding the causes and deadly effects of this issue can be a challenge. It's a complex problem that has many layers and no single solution. It often raises more questions than answers. Why do people start — and why do they continue – taking opioids? How many people does this affect? What can be done about it and what steps are being taken? What is an opioid, anyway?

Learn More About Opioids

Definition | Uses | Side Effects

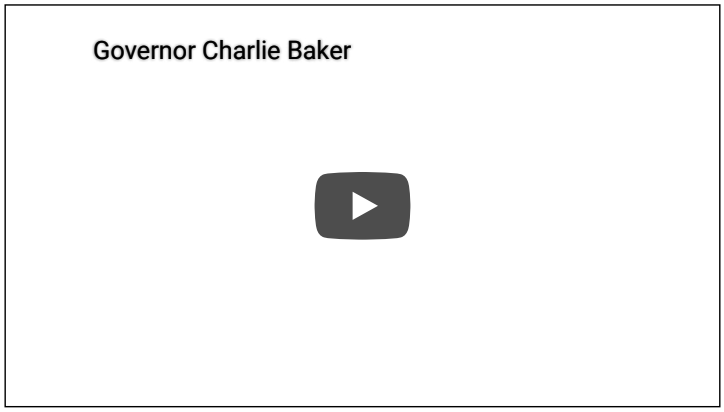
What are opioids?

The term opioid means "opiate-like." It generally refers to a family of substances that include natural opiates (like Morphine and Codeine), as well as synthetic and semi-synthetic opioids like Heroin, Oxycodone, and Fentanyl.



CHAPTER 55

In the face of this emergent public-health issue, the Commonwealth of Massachusetts took an unprecedented deep dive into available data on opioid-related deaths to investigate the crisis. As part of a multi-faceted effort to combat the epidemic, Chapter 55 of the Acts of 2015 (https://malegislature.gov/Laws/SessionLaws/Acts/2015/Chapter55) was passed by the Legislature and signed into law by Governor Baker in August 2015.



This new law permits the analysis of different government datasets to guide policy decisions and to better understand the opioid epidemic. Recently, a groundbreaking report highlighting the current state of the crisis was released as part of this effort.
Led by the Department of Public Health (DPH), the Chapter 55 analysis involved 10 datasets (http://www.mass.gov/eohhs/docs/dph/stop-addiction/dph-legislative-report-chapter-55-opioid-overdose-study-9-15-2016.pdf#page=58) from five different government agencies. In total, 29 groups (http://www.mass.gov/eohhs/docs/dph/stop-addiction/dph-legislative-report-chapter-55-opioid-overdose-study-9-15-2016.pdf#page=95) from government, higher education, and the private sector provided information and expertise. This level of partnership is what makes the Chapter 55 report (http://www.mass.gov/eohhs/docs/dph/stop-addiction/dph-legislative-report-chapter-55-opioid-overdose-study-9-15-2016.pdf) a milestone achievement in Massachusetts. Before this legislation was passed, such a comprehensive look at the opioid epidemic in the Commonwealth would not have been possible.

In addition to providing significant insights into the opioid crisis by answering seven key questions (http://www.mass.gov/eohhs/docs/dph/stop-addiction/dph-legislative-report-chapter-55-opioid-overdose-study-9-15-2016.pdf#page=41), this project demonstrates how private and public organizations can collaborate to answer complex public-health questions. This model of cooperative data analysis has the potential to become the standard in Massachusetts and across the United States. The Chapter 55 project represents a process that should be continued, adapted, and refined as new public health challenges and new collaborators step forward.

Below are examples of opioid use trends that were uncovered by Chapter 55 analysis. Real, actionable steps to curb the epidemic can be taken as a direct result of this innovative data effort.

ADDICTION AND SUBSTANCE USE DISORDER

Similar to diabetes or cancer, addiction is a complex disease impacted by certain risk factors like behavior and family history. Compulsive substance abuse, cravings, and continued use despite known harmful consequences are hallmarks of the condition. This disease is also more widespread than some may realize — according to a study from the Substance Abuse and Mental Health Services Administration (SAMHSA) (http://www.samhsa.gov/data/sites/default/files/NSDUH-FRR1-2014/NSDUH-FRR1-2014.pdf#page=6), nearly 1 in 12 Americans over the age of 12 have a substance abuse disorder.

Cost of Addiction

Economically, addiction is more costly than other brain conditions like Alzheimer's disease, Parkinson's disease, and stroke. In fact, data from the National Institutes of Health (NIH) (https://www.drugabuse.gov/related-topics/trends-statistics) shows that costs related to substance abuse top more than $700 billion annually in the United States.

However, economic impact is hardly the most negative aspect of addiction and, more specifically, the opioid epidemic. Addiction to opioids can put people at greater risk for infectious diseases like HIV or hepatitis, deteriorating conditions like cirrhosis or cognitive decline, family disruption like domestic violence or child abuse, job loss, exposure to criminal behavior, overdose, and death.

Growth of Addiction in Massachusetts

Data from the DPH Bureau of Substance Abuse Services (BSAS) shows an increasing need for opioid-related treatment in Massachusetts. In 2000, about one third of admissions to substance abuse treatment centers and programs were opioid-related[9]. By 2015, that figure had increased to more than half, overtaking alcohol as the most prevalent substance recorded by BSAS at treatment intake. The Health Policy

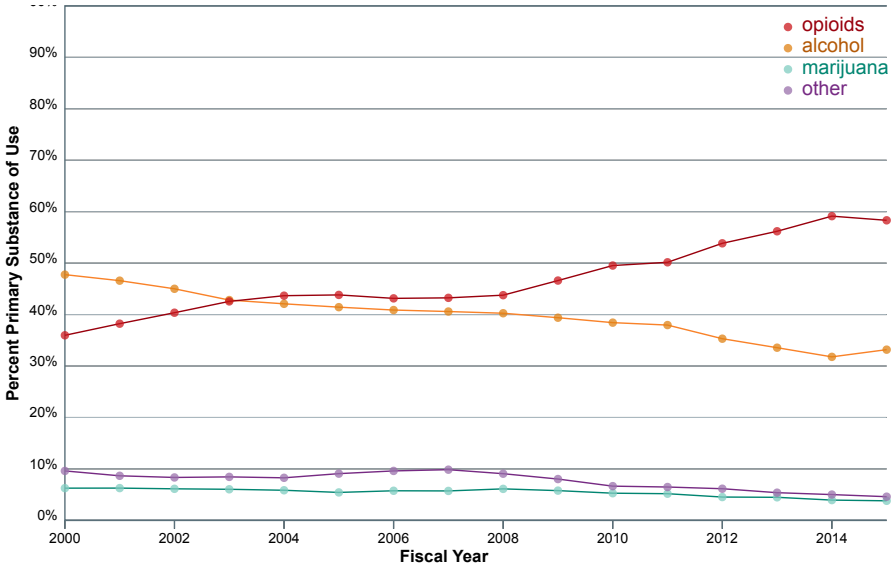
Commission (HPC) (http://www.mass.gov/anf/budget-taxes-and-procurement/oversight-agencies/health-policy-commission/public-meetings/board-meetings/20160907-commission-opioid-presentation.pdf#page=11) recorded similar numbers for emergency room visits and hospitalizations during that time.

Along with the rise in demand for opioid use treatment, nationally and in Massachusetts, there has been an increase in opioid-related overdoses, both fatal and nonfatal.

Primary Substance of Use When Entering Treatment by Town[9,10,11,12,13]

At admission, clients identify a primary substance of use for which they are seeking treatment. Below, view the changes in the percentage of primary substances identified at admission from 2000 to 2015.

Filter by town name e.g. Arlington or view all of Massachusetts



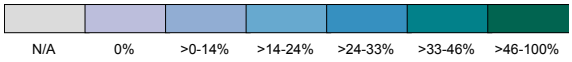
View the dataset powering this visualization (js/data/csv/Addiction_BSAS-LineChart.csv)

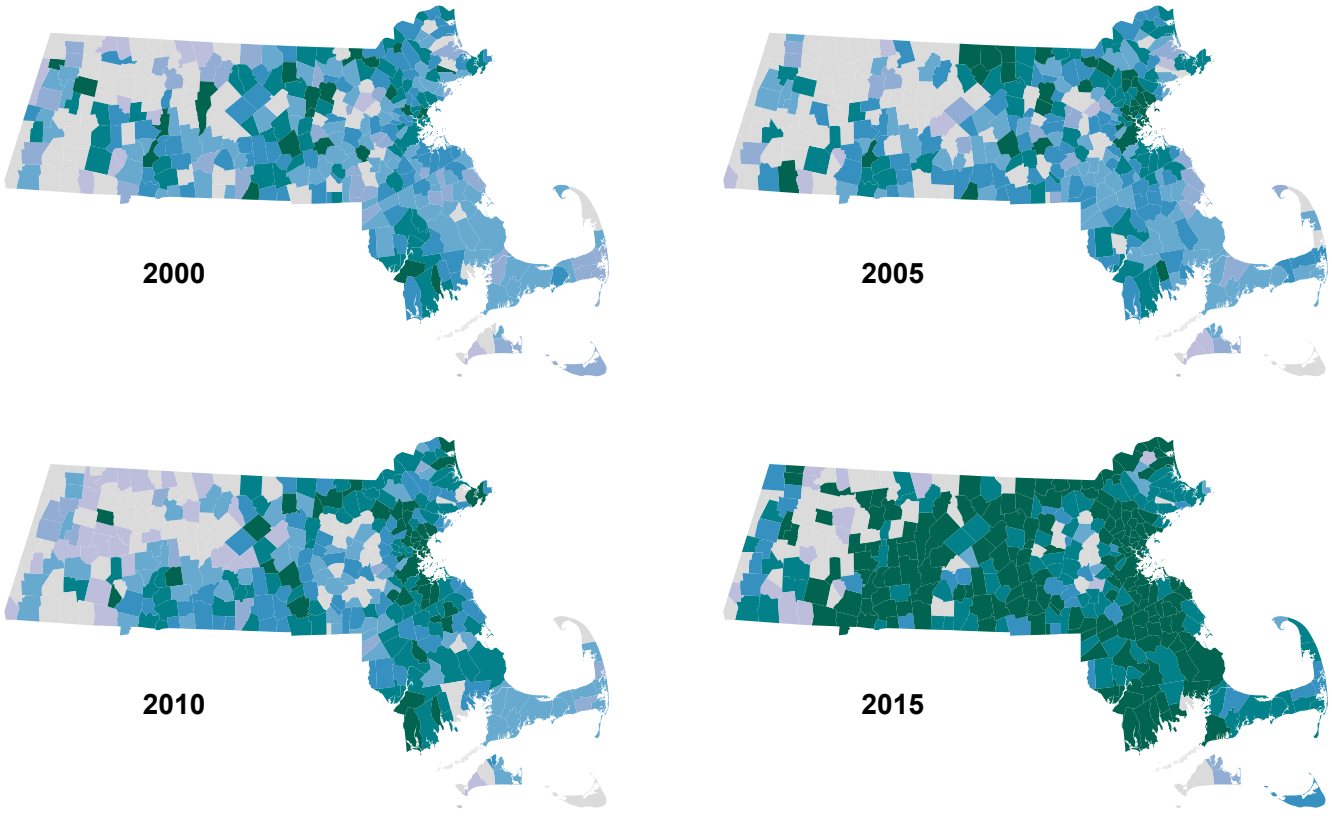
Sources: Massachusetts Bureau of Substance Abuse Services (http://www.mass.gov/eohhs/gov/departments/dph/programs/substance-abuse/), Massachusetts Department of Public Health (http://www.mass.gov/eohhs/gov/departments/dph/)

Percentage of Patients in Treatment Listing Heroin as their Primary Substance of Use[11,12,13]

At admission, clients identify a primary substance of use for which they are seeking treatment. Below, view maps at five-year intervals which show the increase in the percentage of admissions identifying heroin as their primary substance of use.

Heroin Primary Substance of Abuse upon Seeking Treatment (%)





View the dataset powering this visualization (js/data/csv/Addiction_HeroinAbuseMap.csv)

Sources: Massachusetts Bureau of Substance Abuse Services (http://www.mass.gov/eohhs/gov/departments/dph/programs/substance-abuse/), Massachusetts Department of Public Health (http://www.mass.gov/eohhs/gov/departments/dph/)

SUBSTANCE USE

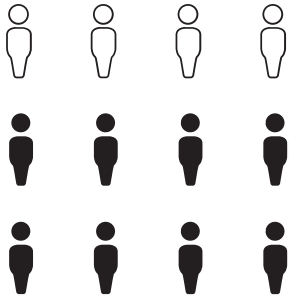
Opioids are incredibly powerful drugs that have transformed the way the health care world treats and manages pain. However, because they are so potent, they can be dangerous if misused. To understand the opioid epidemic, it's important to realize how both legal prescription medications and illegal substances impact the crisis in Massachusetts. To investigate the scope of the problem, the entire population of adults[14] was analyzed.

Prescriptions

The number of opioids prescribed to residents of Massachusetts has increased roughly 7% annually since 2000. In 2015, nearly one in six Massachusetts residents obtained an opioid prescription from a health care provider. Those receiving prescriptions obtained more than three filled prescriptions on average.

Prescription History for Fatal Overdoses

2011 – 2014 | 1 Month Before Death



About **8 in 12** people who died from opioids in 2013 and 2014 had an opioid prescription at some point from 2011–2014

Sources: Massachusetts Registry of Vital Records and Statistics (http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/), Massachusetts Prescription Drug Program (http://www.mass.gov/eohhs/gov/departments/dph/programs/hcq/drug-control/pmp/), Massachusetts Department of Public Health (http://www.mass.gov/eohhs/gov/departments/dph/)

Whether using them for legitimate medical reasons or not, anyone can become dependent on or addicted to opioids. When this happens, the body's craving for an opioid continues even if a prescription runs out. In these cases, many people keep using opioids, but illegally. More than two-thirds of people who died from an opioid-related overdose had a legal opioid prescription at some point from 2011–2014. However, only about 1 in 12 of those who died had an opioid prescription in the month before their death.

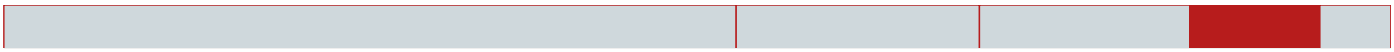
It should be noted that opioid-related deaths began increasing sharply in 2012, no similar increase in opioid prescriptions was recorded. This suggests that no single substance or health care practice is solely responsible for the current opioid crisis. Rather, it's a complex issue with a number of contributing factors.

Deadly Trend: Switching from Legal to Illegal Opioids

Some people make the transition from legal to illegal opioid use, driven by the disease of addiction. This becomes clear by looking at the amount of people who had a prescription six months, three months, and one month before death. This is found regardless of the substance that caused a fatal overdose.

154 people had a positive toxicology screen for **prescription opioids**[15] from 2013-2014

Heroin | Fentanyl | Both Fentanyl & Heroin | Precription Opioids | Methadone

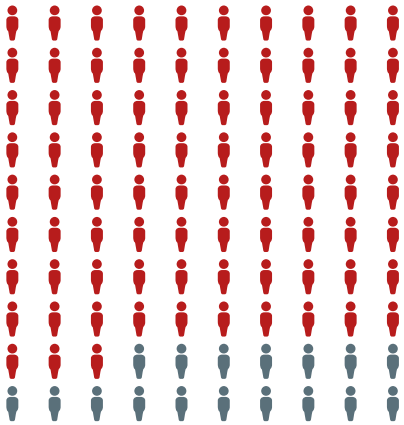


Of those with a positive toxicology screen for **prescription opioids**[15], **83%** had a legal opioid prescription[17] at some point from 2011-2014

2011–2014 | 6 Month Before Death | 3 Month Before Death | 1 Month Before Death

Had legal prescription	Did not have legal prescription
83%	17%

= 1% of people with a positive toxicology screen for prescription opioids



View the dataset powering this visualization (js/data/csv/SubstanceAbuse_RxHistory.csv)

Sources: Massachusetts Office of the Chief Medical Examiner (http://www.mass.gov/eopss/agencies/ocme/), Massachusetts Registry of Vital Records and Statistics (http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/), Massachusetts Prescription Drug Program (http://www.mass.gov/eohhs/gov/departments/dph/programs/hcq/drug-control/pmp/), Massachusetts Department of Public Health (http://www.mass.gov/eohhs/gov/departments/dph/)

Multiple Prescribers

One risk factor for fatal overdose that was identified was the number of opioid prescribers for an individual. There are legitimate reasons why someone might have multiple prescribers — primary care plus specialists[18] or multi-provider practices[19] — but there is an elevated risk for this group. The fatal opioid-related overdose rate for individuals with three or more opioid prescribers is seven times higher than the rate for other people.

Multiple Substances

Using multiple substances at the same time is also a risk factor. For example, Cocaine showed up in 30% of toxicology screens for opioid-related deaths from 2013–2014. Nearly 60% of post-mortem toxicology screens were positive for benzodiazepines. Benzodiazepines are a type of tranquilizer, including drugs like Valium, Xanax, and Ativan, and are typically used to treat anxiety.

While Cocaine is always illegal, benzodiazepines are legally available but might be used outside a prescription. Although benzodiazepines were present in nearly 1,000 toxicology screens from 2011–2014, only about half that many people ever had a prescription for one during that period. Fewer than 200 had a benzodiazepine prescription within a month of death. This suggests that the supply of benzodiazepines involved in overdoses includes both prescribed and diverted pills.

Illegal Drugs

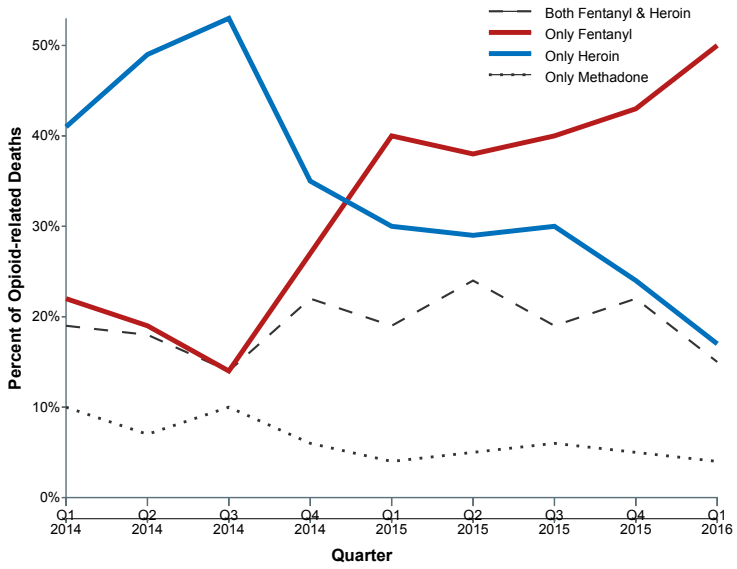
When it comes to illegal opioids, Massachusetts is facing a dangerous combination of trends. Some individuals are transitioning from legal to illegal opioid use, perhaps due to dependence and addiction developing beyond prescribed thresholds. At the same time, the availability of illegal drugs is strengthening across the region. The Drug Enforcement Administration (DEA) surveyed law enforcement officials about the availability of Heroin in eight regions across the country from 2007 to 2014[20]. Each year, New England led all regions in the percentage of respondents who reported high Heroin availability

Heroin, perhaps expectedly, is commonly found in toxicology reports for opioid-related deaths. Data from 2013–2014 shows Heroin was likely or definitely in the individual's system at the time of death in more than 60% of opioid-related overdose deaths. What might be surprising is the increasingly deadly role Fentanyl is playing in the crisis.

While Fentanyl can be available as a legally-prescribed medication, it is most often used illegally. Only about 3% of people who died from an opioid-related overdose and had Fentanyl present in their toxicology screen during the study period had a prescription for Fentanyl at the time of death. However, toxicology data shows Heroin, Fentanyl, or both substances were present in 85% of cases.

Fentanyl: Legal and Illegal[16]

Fentanyl is an opioid that can be prescribed for pain management. However, it's also used illegally either on its own or combined with Heroin, often without the user's knowledge. According to the DEA, illegally produced Fentanyl can be up to 50 times more potent than Heroin. Fentanyl is increasingly recognized as a problem across the United States, and particularly in Massachusetts. Toxicology data from recent post-mortem cases indicates Fentanyl is adding to the state's deadly epidemic more than Heroin. In 2015, more than 60% of toxicology samples tested positive for Fentanyl. In the previous year, that mark was about 40%.



View the dataset powering this visualization (js/data/csv/SubstanceAbuse_FentanylTox.csv)

Sources: Massachusetts Office of the Chief Medical Examiner (http://www.mass.gov/eopss/agencies/ocme/)

DEMOGRAPHICS

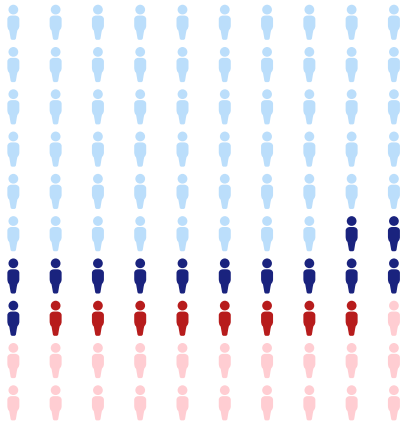
Opioid addiction doesn't discriminate. The crisis in Massachusetts affects people from all backgrounds. The widespread nature of the epidemic makes addressing it an especially challenging task, because the path to opioid addiction has different starting points from person to person. While definite solutions might still be a mystery, knowing how the epidemic plays out among different sections of society can help Massachusetts find ways to strongly and effectively address this problem.

Male and Female

Despite the fact more men die from opioid overdoses than women, both genders are at risk, yet in different ways. Toxicology reports show men are more likely than women to have Heroin in their systems, while prescription opioids are more likely to be found in women than in men at the time of death. Part of this discrepancy may be down to a simple fact — women are more likely to use the health care system. This could present a particular risk for women because they are also more likely than men to have multiple prescribers for opioids, which is a risk factor as mentioned above.

Prescriber and Opioid Use Trends by Gender[21]

= 1% of **1,692** Opioid-related Deaths from 2013-2014



Prescription Opioids | Heroin | Multiple Prescribers

Prescription Opioids in Toxicology Screen

	Present	Not Present
Male	13%	58%
Female	8%	21%

View the dataset powering this visualization (js/data/csv/Demographics_TrendsGender.csv)

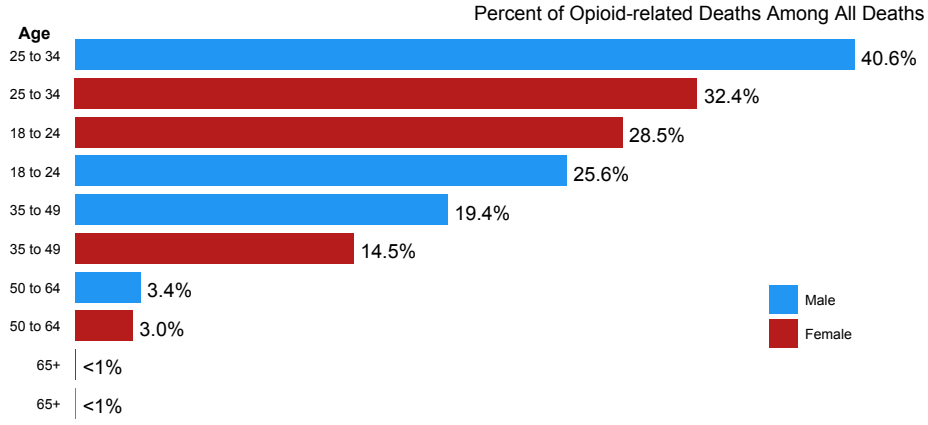
Sources: Massachusetts Office of the Chief Medical Examiner (http://www.mass.gov/eopss/agencies/ocme/), Massachusetts Registry of Vital Records and Statistics (http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/), Massachusetts Prescription Monitoring Program (http://www.mass.gov/eohhs/gov/departments/dph/programs/hcq/drug-control/pmp/), Massachusetts Department of Public Health (http://www.mass.gov/eohhs/gov/departments/dph/)

Young People

The fight to curb the opioid epidemic in Massachusetts is also a battle to protect future generations. The percentage of opioid-related deaths for different age groups shows the young people of Massachusetts are especially at risk. From 2013–2014, opioids accounted for more than a quarter of all fatalities in the 18–24 age group. For individuals from 25–34, opioids were responsible for more than a third of all deaths, rising to more than 40% for men in this group. In 2015, roughly two out of every three people who died from opioids were younger than 45.

Fatal Opioid Overdoses by Age and Gender[21]

Percent of Opioid Deaths | Opioid Death Rate per Year | Number of Opioid Deaths



View the dataset powering this visualization (js/data/csv/Demographics_AgeGender.csv)

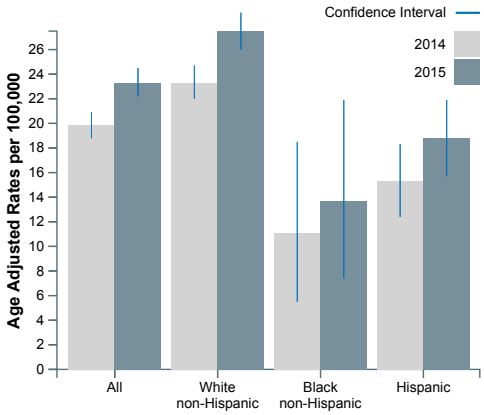
Sources: Massachusetts Registry of Vital Records and Statistics (http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/), Massachusetts Department of Public Health (http://www.mass.gov/eohhs/gov/departments/dph/)

Race and Ethnicity

In 2000, the rate of opioid-related fatal overdose was 5.8 per 100,000 people in Massachusetts, according to DPH data. That rate has increased steadily since then, with the figure hitting 11.1 per 100,000 in 2012. However, the increase in the last three years has been especially sharp. By 2015, there were 23.3 fatal overdoses for every 100,000 residents.

While the death rate within Massachusetts differs for various racial and ethnic groups, people from all backgrounds in the Bay State are caught up in the deadly epidemic. In the adjoining graph, we can see the overdose rates of three of the state's largest groups for the last two years. By comparison, the national average was 9.7 per 100,000 in 2014. As seen in the graph, the age-adjusted, normalized data reveals that the epidemic is hitting the White non-Hispanic population at a rate around twice that of Black non-Hispanic population for the last two years, and roughly 50% more than the rate for the Hispanic population over that time.

Opioid-related Deaths by Race and Ethnicity



View the dataset powering this visualization (js/data/csv/Demographics_RaceEthnicity.csv)

Sources: Massachusetts Registry of Vital Records and Statistics (http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/), Massachusetts Department of Public Health (http://www.mass.gov/eohhs/gov/departments/dph/).

Interpreting Data

Age-Adjusted Rates | Confidence Intervals | Normalizing Rates

Using age-adjusted data is important because different groups have different age distributions, whether those groups are broken out by racial/ethnic, gender, or geographic lines. For example, the Hispanic population in Massachusetts is relatively younger than other racial/ethnic groups in the state. Without taking age distribution into account, the fact that younger people are more likely to die from opioid-related overdoses could result in an over-estimated death rate for the Hispanic community as a whole. We might experience similar mischaracterization when looking at cities and towns that skew older or younger than the rest of the state. In these ways and others, age-adjusting population data helps public health officials get a more accurate picture of the crisis and better target the most problematic areas and populations.

Incarcerated Population

When an inmate is released from prison in Massachusetts, their ability to re-enter society is being threatened by the opioid crisis. The risk of opioid-related death following release from incarceration is more than 50 times greater than for the general public. What's more concerning is that the threat is immediate. Fatal overdoses during the first month after release are six times higher than for all other post-incarceration periods.

Among inmates who both were released and died between 2013 and 2014, opioid-related overdose was the cause of death for 40% of these people. Following the age trend noted above, the risk of death for people aged 18–24 in this group is roughly 10 times higher than for individuals 45 or older. While some inmates receive substance use treatment while incarcerated, the data from this study does not include how, when, or for how long that treatment takes place.

THE FUTURE

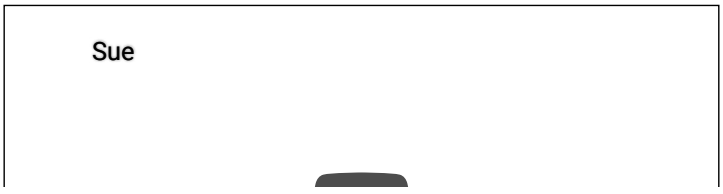
The opioid epidemic won't be solved overnight, and there's no easy solution to make this problem disappear. However, there are signs of hope and a turning tide.

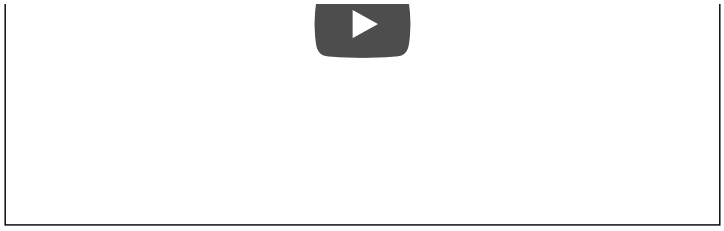
The state has recently taken a number of important steps to address the crisis. From campaigns aimed at shifting the culture around how the public views addiction, to giving our health care professionals the tools they need to responsibly prescribe opioids and monitor prescriptions, Massachusetts is working to end the epidemic.

While there is still a lot to do, findings from the Chapter 55 report have helped elected officials and public health leaders determine what should be done next.

Recent Steps Taken | What to Do Next

- **Stopping Stigma** — Shifting the way that people view addiction and individuals with substance use issues is a top priority. DPH launched the State Without StigMA (http://www.mass.gov/eohhs/gov/departments/dph/stop-addiction/state-without-stigma/) campaign to encourage the public to rethink how they perceive and treat people with addiction. Stories from people in recovery — like Sue and Stephanie, and Cotto — have helped reframe addiction as the disease it is.
- **Promoting the Good Samaritan Law** — Another state campaign, Make the Right Call (http://www.mass.gov/eohhs/gov/departments/dph/programs/substance-abuse/make-the-right-call-public-information-campaign.html), has helped spread awareness about the state's Good Samaritan Law. It ensures a person won't be charged with possession of a controlled substance if they call 9-1-1 to report an overdose.
- **Prescription Monitoring Reforms** — To help pharmacists and doctors better monitor active opioid prescriptions, DPH launched the Massachusetts Prescription Awareness Tool (MassPAT) (http://www.mass.gov/eohhs/gov/newsroom/press-releases/dph/admin-launches-new-prescription-monitoring-program.html). This new online system is more efficient and user-friendly than older technologies.
- **Expanding Prescription Drug Training** — More resources and programs have been offered to dental schools (http://www.mass.gov/eohhs/gov/newsroom/press-releases/eohhs/dental-core-competencies-to-combat-addiction-announced.html) and nursing and physician assistant programs (http://www.mass.gov/eohhs/gov/newsroom/press-releases/eohhs/core-competencies-to-combat-opioid-epidemic-expanded-.html) to train students and professionals on how to prevent prescription drug misuse.





Opioid Addiction and Use Resources

- Massachusetts Substance Abuse Helpline
  (800) 327-5050 (tel:8003275050)
- Substance Use Treatment Services Locator ➜ (https://findtreatment.samhsa.gov/locator/home)
- Prescription Dropbox Locations ➜ (https://www.mass.gov/eohhs/gov/departments/dph/programs/substance-abuse/prevention/prescription-dropbox-locations.html)
- Parents: Talk to Your Kids about Opioids ➜ (https://www.mass.gov/eohhs/gov/departments/dph/programs/substance-abuse/prevention/prescription-drug-misuse-abuse-and-your-kids.html)

Massachusetts Department of Public Health
250 Washington St, Boston, MA 02108
(617) 624-6000 (tel:6176246000)

1. The confirmed opioid-related death rate was suppressed in towns that were detected as strong outliers using Tukey's outlier filter. All values that fell outside of the upperbound, calculated using three times the interquartile range, were considered strong outliers. Rates for Provincetown, Cummington, and Granville were suppressed from 2001 to 2005. Rates for Aquinnah, New Ashford, and Tyringham were suppressed from 2011 to 2015.
2. In both 2014 and 2015, there was one death of a Massachusetts resident whose city/town of residence was not known.
3. Please note that data for 2000-2013 have been updated following a review of cases that did not receive an official cause of death at the time the file was closed. Death data for 2014-2015 are preliminary and subject to updates. Case reviews of deaths are evaluated and updated on an ongoing basis. A large number of death certificates have yet to be assigned final cause-of-death codes. These counts are based on the estimates rather than confirmed cases.
4. Cases were defined using the International Classification of Disease, Tenth Revision (ICD-10) codes for mortality. The following codes were selected from the underlying cause of death field to identify poisonings/overdoses: X40-X49, Y10-Y19. All multiple cause of death fields were then used to identify an opioid-related death: T40.0, T40.1, T40.2, T40.3, T40.4, and T40.6.
5. The average annual opioid-related death rate was calculated in five-year intervals. The death rate displayed is the crude, non age-adjusted rate.
6. In 1999, the International Classification of Diseases, Tenth Revision (ICD-10) replaced the International Classification of Diseases, Ninth Revision (ICD-9) for coding all mortality data. Because there were changes made in the codes that are assigned to causes of death, changes to the rules used to determine the underlying cause of death, and changes in the codes that comprise the leading cause of death categories, direct comparisons of causes of death between 1999 and previous years cannot be made.
7. The Massachusetts age-adjusted opioid-related death rate was provided by the Massachusetts Department of Public Health.
8. The national level data was extracted from the Centers for Disease Control and Prevention, National Center for Health Statistics Wonder Databases.
9. "Opioids" includes "Heroin" and "Other Opioids". "Other Opioids" includes non-prescription Methadone, Oxycodone, non-prescription Suboxone, prescription opiates, non-prescription opiates, and other opiates.
10. "Other" includes Crack/Cocaine, PCP, other hallucinogens, Methamphetamine, other amphetamines, other stimulants, benzodiazepines, other tranquilizers , barbiturates, other sedatives, inhalants, OTC, club drugs, and other.
11. All out-of-state enrollments and Massachusetts County Correction Facility enrollments are excluded.
12. Data were prepared on Sep 12, 2016 with data as of July 15, 2016.
13. To protect client confidentiality, categories with 5 or fewer admissions are supressed.
14. For the purposes of the study, "adults" is defined as the nearly 3.5 million residents aged 11 and older.
15. "Prescription opioids" includes Hydrocodone, Hydromorphone, Oxycodone, Oxymorphone, Codeine, and Tramadol.
16. "Both Fentanyl and Heroin" includes Fentanyl, Heroin, and Morphine (likely Heroin).
17. "Legal opioid prescription" includes any prescription for Fentanyl, Methadone, Hydrocodone, Hydromorphone, Oxycodone, Oxymorphone, Morphine, or Codeine.
18. Some individuals may see a primary care physician who then directs them to a specialist, depending on the medical issue. In some cases, both the primary physician and specialist may provide opioids to the patient for various reasons, including for immediate pain relief. Emergency room visits might also fall under this category.
19. Some health centers or clinics could have a pool of multiple physicians who collectively treat all patients. This could result in one patient receiving multiple opioid prescriptions from different physicians on separate visits for various reasons, including for immediate pain relief.
20. Data from the National Drug Threat Assessment Summary. Sources: 2013 (https://www.dea.gov/resource-center/DIR-017-13%20NDTA%20Summary%20final.pdf#page=15), 2014 (https://www.dea.gov/resource-center/dir-ndta-unclass.pdf#page=53). Data is not available for 2012.
21. Data from 2013-2014.

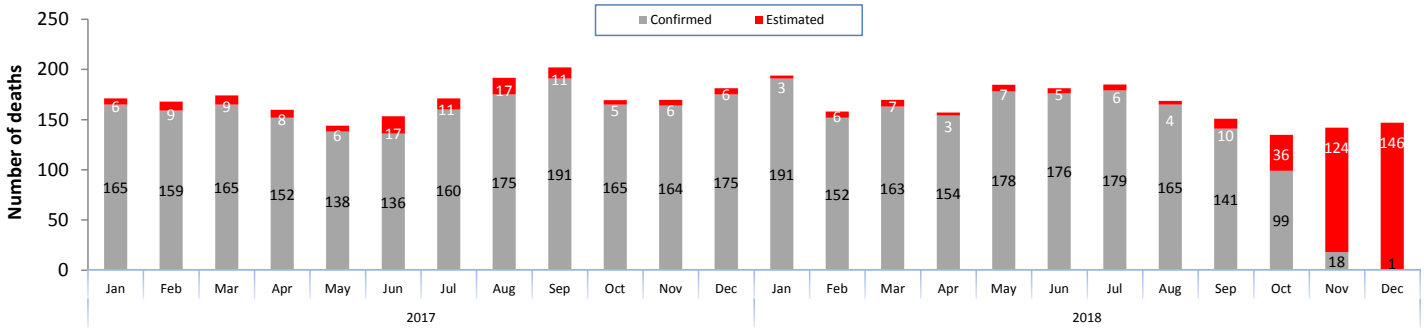
Exhibit G

Data Brief: Opioid-Related Overdose Deaths among Massachusetts Residents

Massachusetts Department of Public Health | POSTED: FEBRUARY 2019

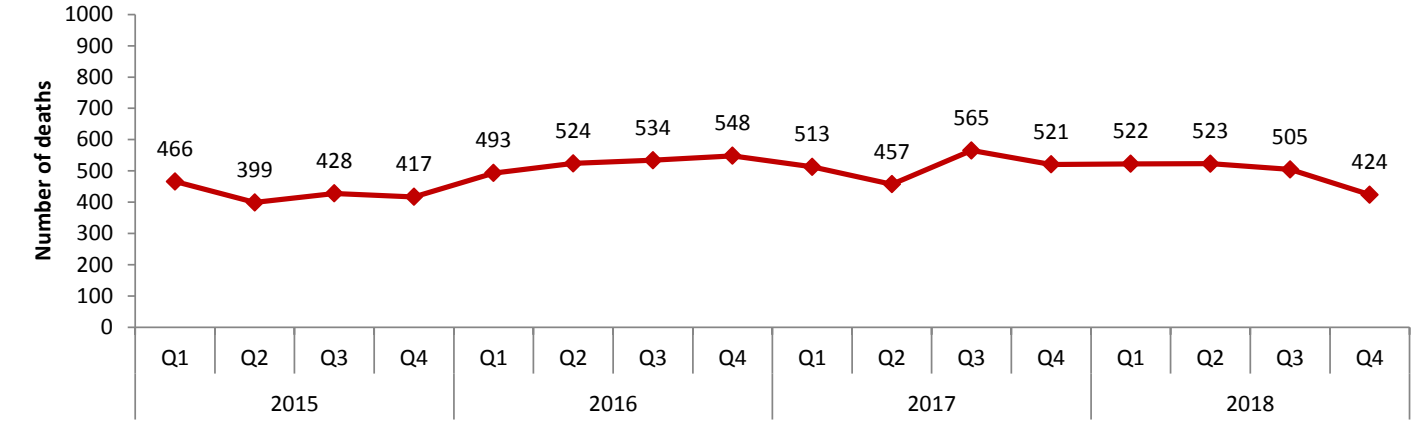
This report contains both confirmed and estimated data through December 2018.

Figure 1. Opioid-Related Overdose Deaths, All Intents by Month
Massachusetts Residents: January 2017 - December 2018



The chart above shows the month-by-month estimates for fatal opioid-related overdoses for all intents from January 2017 through December 2018. In 2018, there are 1,617 confirmed opioid-related overdose deaths and DPH estimates that there will be an additional 320 to 394 deaths.

Figure 2. Confirmed and Estimated Opioid-Related Overdose Deaths, All Intents by Quarter
Massachusetts Residents: 2015 - 2018



Despite the spike in the third quarter of 2017, overall, there was an estimated 2% decrease in the number of opioid-related overdose deaths in 2017 compared with 2016, followed by another 4% estimated decrease in 2018 compared with 2017. The count for 2018 represents an estimated 6% decrease from 2016.

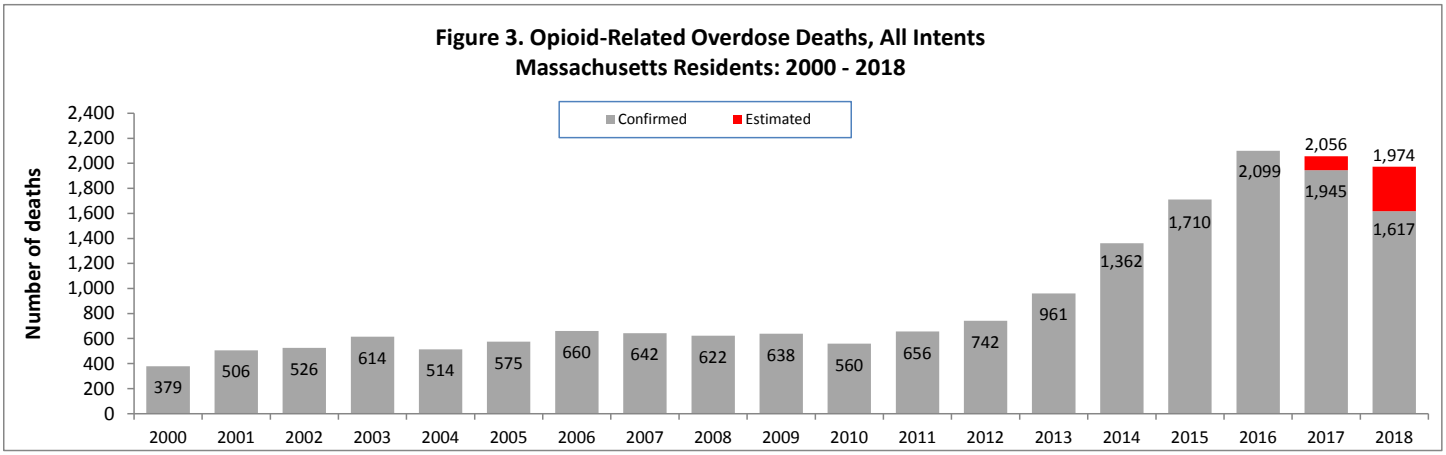
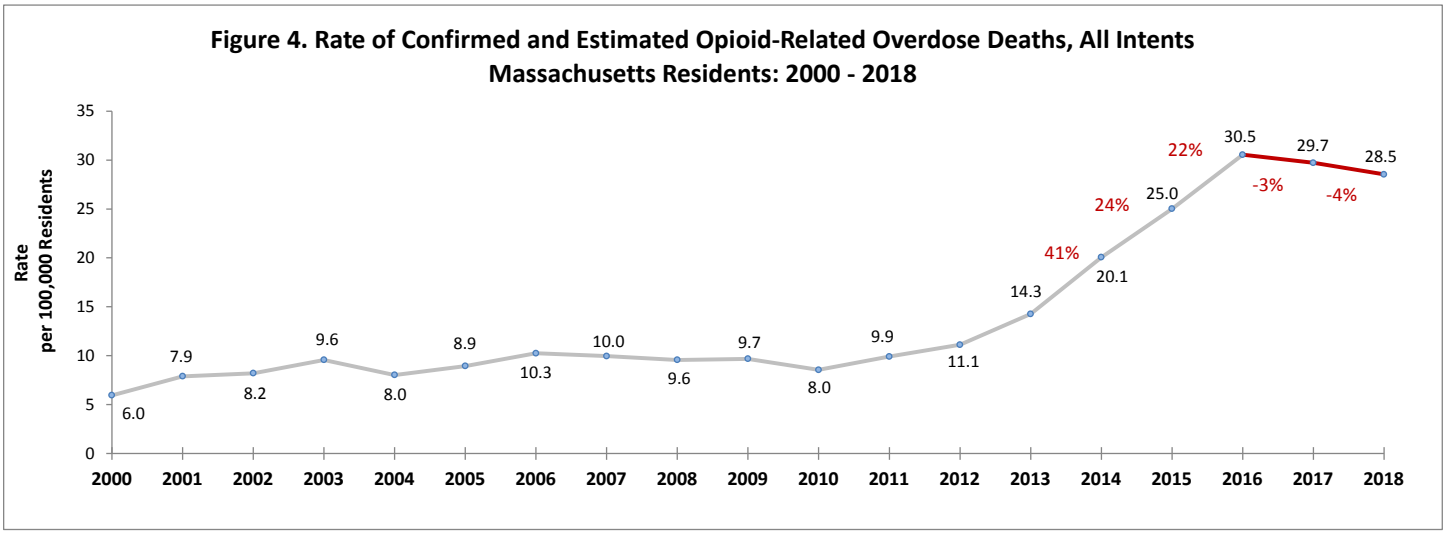


Figure 3 shows the trend in annual number of confirmed and estimated cases of opioid-related overdose deaths for all intents from 2000 to 2018. In order to obtain timelier estimates of the total number of opioid-related overdose deaths in Massachusetts - confirmed and probable - DPH used predictive modeling techniques for all cases not yet finalized by the Office of the Chief Medical Examiner (OCME). Based on the data available as of January 15, 2019, DPH estimates that there will be an additional 104 to 117 deaths in 2017 and an additional 320 to 394 deaths in 2018, once these cases are finalized.

Opioid-Related Overdose Death Rates, All Intents

In 2018, DPH estimates a 4% decrease in the rate of opioid-related overdose deaths compared with 2017. This follows an estimated 3% decline in the rate of opioid-related over deaths from 2016 to 2017.



Toxicology Analysis: Fentanyl and Other Drugs

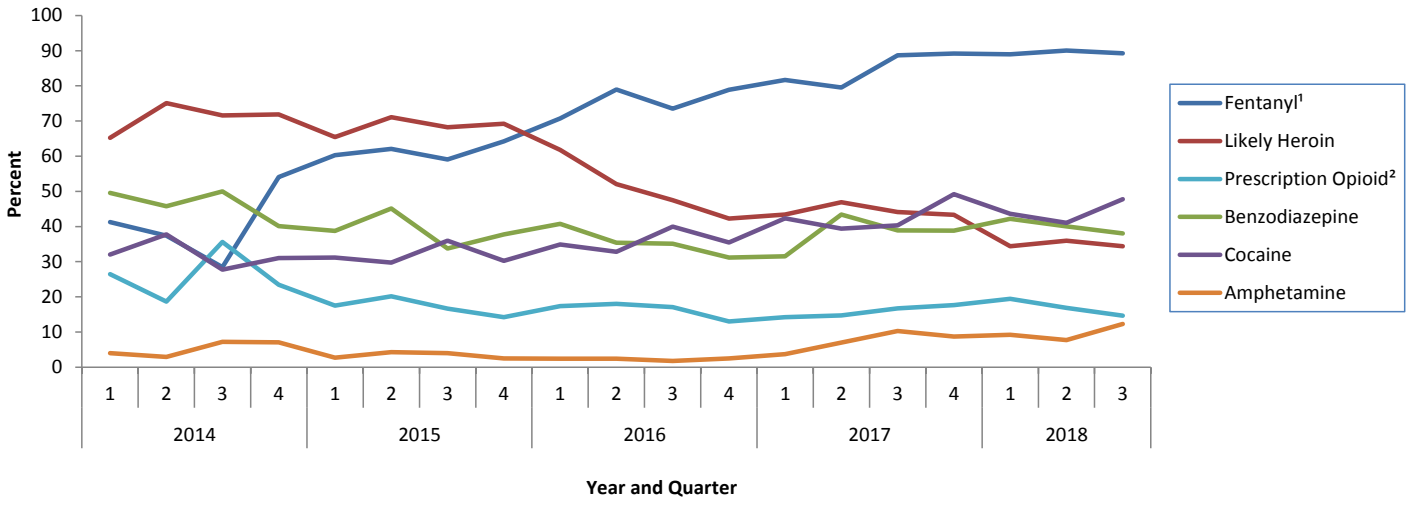
Fentanyl is a synthetic opioid that has effects similar to heroin. It can be prescribed for severe pain. According to the U.S. Department of Justice, Drug Enforcement Administration's 2015 Investigative Reporting, while pharmaceutical fentanyl (from transdermal patches or lozenges) is diverted for abuse in the United States at small levels, much of the fentanyl in Massachusetts is due to illicitly-produced fentanyl, not diverted pharmaceutical fentanyl.

The standard toxicology screen ordered by the Office of the Chief Medical Examiner includes a test for the presence of fentanyl. Among the 1,445 opioid-related overdose deaths in 2018 where a toxicology screen was also available, 1,292 of them (89%) had a positive screen result for fentanyl. In the third quarter of 2018, heroin or likely heroin was present

in approximately 34% of opioid-related overdose deaths that had a toxicology screen. Cocaine was present in approximately 48% of these deaths and benzodiazepines were present in approximately 38%. In the first quarter of 2014, amphetamines were present in 4% of opioid-related overdose deaths that had a toxicology screen. The presence of amphetamines has been increasing since 2017 to approximately 12% of opioid-related overdose deaths in the third quarter of 2018. Since 2014, the rate of heroin or likely heroin present in opioid-related overdose deaths has been decreasing while the presence of fentanyl and cocaine is still trending upward.

While screening tests can be used to note the rate at which certain drugs are detected in toxicology reports, they are insufficient to determine the final cause of death without additional information. The cause of death is a clinical judgment made within the Office of the Chief Medical Examiner.

Figure 5. Percent of Opioid-Related Overdose Deaths with Specific Drugs Present Massachusetts Residents: 2014 - 2018



1. This is most likely illicitly produced and sold, **not** prescription fentanyl
2. Prescription opioids include: hydrocodone, hydromorphone, oxycodone, oxymorphone, and tramadol

Please note that previous estimates may change slightly as DPH routinely receives updated toxicology data from the Office of the Chief Medical Examiner and the Massachusetts State Police.

Technical Notes

- Opioids include heroin, illicitly manufactured fentanyl, opioid-based prescription painkillers, and other unspecified opioids.
- Data for 2017-2018 deaths are preliminary and subject to updates.
- Beginning with the May 2017 report, DPH started reporting opioid-related deaths for all intents, which includes unintentional/undetermined and suicide.
- This report tracks opioid-related overdoses due to difficulties in identifying heroin and prescription opioids separately. The Department regularly reviews projections as more information becomes available. Information from the Office of the Chief Medical Examiner and the Massachusetts State Police are now incorporated into the predictive model. This additional information has improved the accuracy of the models that predict the likelihood that the cause of death for any person was an opioid-related overdose. DPH applied this model to death records for which no official cause of death was listed by the OCME. The model includes information from the death certificate, Medical Examiner's notes, and the determination by the State Police of a suspected heroin death. DPH added this estimate to the number of confirmed cases in order to compute the total number of opioid-related overdoses. Should new information become available that changes the estimates to any significant degree, updates will be posted.

Sources

- Massachusetts Registry of Vital Records and Statistics, MDPH
- Massachusetts Office of the Chief Medical Examiner
- Massachusetts State Police
- Population Estimates 2000-2010: National Center for Health Statistics. Postcensal estimates of the resident population of the United States, by year, county, age, bridged race, Hispanic origin, and sex (Vintage 2000-2010).
- Population Estimates 2011-2018: Small Area Population Estimates 2011-2020, version 2017, Massachusetts Department of Public Health, Bureau of Environmental Health. Population estimates used for years following the decennial census were developed by the University of Massachusetts Donahue Institute (UMDI) in partnership with the Massachusetts Department of Public Health, Bureau of Environmental Health.

Exhibit H

The Massachusetts OxyContin and Other Drug Abuse Commission

Final Report

Dear Reader,

I am pleased to present the **OxyContin Commission Report.**

The "Massachusetts OxyContin and Other Drug Abuse Commission" was established through Chapter 189 of the Acts of 2004 which commissioned the legislature to investigate the effects of the abuse of prescription medications and illicit drugs on the citizens of the Commonwealth. The Commission held hearings across the state from March through October of 2005.

The Commission heard from concerned citizens from Lynn, Framingham, Bridgewater, Somerville and Boston. Police chiefs, law enforcement officials, physicians, pharmacists, substance abuse treatment professionals, and community members testified before the commission. Parents, spouses, and children from across the state testified about the extraordinary challenges of recognizing the signs of abuse, finding treatment and maintaining recovery and support for themselves and family members.

I would like to take this opportunity to thank my esteemed colleagues that were members of the OxyContin Commission:

Michael Botticelli, DPH
Representative Garrett J. Bradley
Ernest Gates, Jr., R.Ph., F.A.S.C.P
Gary Gilmore, MassHealth
David Hoffman, MD, MFA - DMH
Robert Jamison, Ph.D.
Janice Kauffman, R.N. MPH,
Senator Richard T. Moore, (Co-Chair)
Representative Steven M. Walsh
Eric Weil, M.D. - MGH

Critical guidance and input was received from the following legislators:

Representative Ruth Balser, House Chair on the Joint Committee on Mental Health and Substance Abuse and
Senator Steven Tolman, Senate Chair on the Joint Committee on Mental Health and Substance Abuse.

I would also like to offer special acknowledgement to my research staff and Richard H. Dougherty, Ph. D. DMA Health Strategies.

Please join me in this ongoing effort to improve the health of our communities by addressing this serious and complex problem. Thank you.

Sincerely,

Representative Peter J. Koutoujian
OxyContin Commission Chair
Chairman, Joint Committee on Public Health

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INTRODUCTION

The Massachusetts OxyContin and Other Drug Abuse Commission (the "OxyContin Commission" or the "Commission") was established in 2004 by the Massachusetts' Legislature to investigate the effects of the abuse of prescription medications and illicit drugs on people of all ages in the Commonwealth. The Commission consists of 11 members including four members of the Legislature, pharmacists, physicians, nurses and experts in the field of drug abuse. The Commission held hearings across the state from March through October of 2005. In addition, the Commission met numerous times to review public hearing information, hear from key informants and develop its recommendations.

The Commission heard compelling and troubling stories about the personal toll that prescription and other drug abuse have wrought on individuals and families in the Commonwealth. Parents, spouses, and children in all parts of the Commonwealth and in every socio-economic group have experienced the extraordinary challenges of recognizing the signs of abuse, finding treatment and maintaining recovery and support for themselves and family members. As a result, the Commission expanded the scope of its review to consider public policy options for all age groups for the prevention, control and treatment of drug abuse in general, not just prescription drugs.

The problems associated with the abuse of prescription drugs are significant. OxyContin[1] abuse is perhaps the most troubling because it is highly addictive and is a gateway drug for the use of cheaper, illicit opiates such as heroin. Recent stories confirm that other medications, such as Klonopin, are also frequently abused, particularly by our youth. During the Commission testimony and meetings, numerous other drugs were reviewed and discussed, including transdermal fentanyl, methadone, morphine, hydrocodone (e.g. Vicodin), oxycodone (e.g. Percocet) and other prescription drugs of abuse.

Prescription drug abuse differs in several important ways from alcohol abuse and other illicit drug use. Control of prescription medications needs to involve manufacturers, prescribers, pharmacists, hospitals, state regulators, and consumers in a comprehensive approach for the control of these drugs. Educational efforts must address the fact that consumers often feel that use and any resulting abuse of these drugs is less risky than other drugs because a physician is involved and because the drugs are legally sold at a pharmacy. Finally, insurers, Medicaid, and other state systems rather than the prescribers and manufacturers, often bear the financial costs of abuse. A comprehensive solution to prescription drug abuse must be a systemic approach.

This report begins with policy and legislative recommendations because that is and should be the principal focus of the work from this point forward. The background and summary of the work of the Commission is included at the end of the report.

[1] Note that OxyContin is a registered trademark of Purdue Pharma for a controlled release tablet they produce consisting of oxycodone hydrochloride. For simplicity in this report we have not included the registration symbol in reference to OxyContin or other brand name drugs.

POLICY RECOMMENDATIONS

Recommendations for policy actions and legislation are outlined below. These include the following areas: 1) prevention and education; 2) distribution, dispensing and handling; 3) prescribing and monitoring; and 4) expansion of access to treatment services. Following the detailed recommendations, a set of recommended action steps are outlined. This is a comprehensive plan and the Commission recognizes that prioritization will need to occur and that we cannot accomplish all these steps at once.

Prevention and Education

The Commonwealth's existing prevention and education programs for consumers, community agencies and professional groups need to be expanded and enhanced to more comprehensively and specifically address the problem of prescription drug abuse. Primarily funded with federal funds, the Commonwealth's current prevention programs include the Massachusetts Department of Public Health (MDPH), Bureau of Substance Abuse Services (BSAS), law enforcement agencies, local partnerships with schools, health organizations and others. However, the role of physicians, pharmacies, drug manufacturers and others in prescription drug diversion and abuse requires a different and expanded focus for prevention. To this end, the Commonwealth began a public service announcement campaign in January 2006 and the MDPH has recently announced enhanced capabilities for its prescription drug monitoring program from a federal grant. These are important steps forward, but more needs to be done.

In addition to these efforts, the prevention of prescription drug abuse should include the following:

1. Additional support provided to Parent Advisory Councils. This support shall include training to educate parents on: prescription drug abuse; the link between prescription drugs and the so-called lesser drugs of abuse (alcohol and marijuana); mental illness in adolescents; the need for proper storage of drugs, and; additional prevention approaches for communities and parents across the Commonwealth.
2. Additional materials on prescription drug abuse shall be provided to community and statewide organizations in order to expand peer support networks such as the Massachusetts Organization of Addiction Recovery (MOAR).
3. Continued development of parenting curricula and resource guides to teach parents that most abusers of prescription drugs start by using alcohol and marijuana. Education should also include information about controlling access to drugs of abuse, safe storage and proper disposal of unused prescription medications.
4. Continued support of the use and development of evidence-based educational materials for teachers, law enforcement and other health professionals. These materials should address substance abuse prevention, the warning signs of drug abuse and methods of intervention and identification of treatment resources available to consumers across the Commonwealth.

5. Improved training on the identification of and intervention in prescription and illicit drug abuse. Prescribing clinicians seeking to obtain or renew a Massachusetts Controlled Substances license shall be required to demonstrate completion of defined training in effective pain management, identification of patients at high risk for substance abuse and other aspects of drug abuse. DPH shall convene a task force to develop a plan for the prompt implementation of these recommendations.
6. Improved pharmacist training on the identification of prescription drug abuse and the security measures necessary to deter such abuse. The Board of Registration for Pharmacists shall develop a required course as an integral part of the continuing education requirements for pharmacists who store, distribute and dispose of drugs subject to abuse.
7. Continued efforts to educate the citizens of the Commonwealth through public service announcements and advertising campaigns. The Commonwealth shall continue funding to further develop the public service announcements on OxyContin and other prescription drugs of abuse that began in January 2006.

Distribution, Dispensing, Handling and Disposal

In collaboration with manufacturers, pharmacies and state agencies, the Commonwealth shall develop a comprehensive plan to encourage pharmaceutical manufacturers, pharmacists and consumers to securely and safely store, dispense and dispose of Schedule II and other prescription drugs that are prone to abuse. The plan should include the following:

1. Continued efforts by pharmaceutical drug manufacturers to expand upon the use of tamper proof drugs and packaging for Schedule II opioids and other abused drugs.
2. Expanded use of warning labels on drugs to warn of the potential for dependence and addiction.
3. Collaboration between pharmacies and the Board of Registration in Pharmacy to educate pharmacists on and set standards for the safe storage of Schedule II drugs.
4. Develop a plan to educate consumers on the need for proper and effective disposal of unused drugs.
5. Development of a statewide program for controlled drug disposal.

Prescribing and Monitoring

Working with the members of the Prescription Monitoring Program Advisory Board of the Department of Public Health, the Commonwealth shall expand the scope, timeliness and availability of reports and data on prescribing of Schedule II and other high-risk drugs, including irregular patterns of use. The Commonwealth shall explore legislation, similar to mandatory reporting laws, that provides a process for reporting prescription drug abuse to proper authorities within the Commonwealth.

Twenty-one states currently have some form of Prescription Drug Monitoring Program; 19 of them are comprehensive programs, similar to Massachusetts'. Increasingly states are enhancing their capabilities to monitor prescribing in order to more readily detect fraud and abuse. In 2004, five states provided reports to physicians upon request on patients who had multiple prescribers for Schedule II drugs. A federal grant recently announced by DPH provides funds for the enhancement of the Prescription Monitoring software.

The expanded prescription monitoring capabilities shall include the following:

1. Increased analytic capability of the current Prescription Drug Monitoring Program so that prescriptions can be analyzed by patient and by the prescriber and, therefore, irregular patterns detected.
2. Development of a confidential and fair reporting system for prescribing physicians in order to identify atypical patterns of prescription refills among patients.
3. Expanded list of drugs monitored by the Prescription Drug Monitoring Program. The list shall include other abused drugs beyond the Schedule II drugs currently being reported.
4. Modify current regulations as permitted under existing privacy laws to allow the transfer of necessary prescription data for more timely and comprehensive access to data for pharmacies, prescribing physicians, the Board of Registration, law enforcement and others as necessary. Provide education and training to clarify the limits and scope of privacy regulations.
5. Improved Prescription Drug Monitoring Program software and applications to take advantage of current technologies that include a secure, internet-based application. This application should increase the timeliness of data and improve the speed with which prescribers, pharmacies and others can identify individuals with multiple prescriptions and patterns of abuse.
6. The Commonwealth shall prepare a report to the legislature on the costs and benefits of developing a tamper-proof prescription pad system, similar to the one employed in New York State.
7. Consistent with existing privacy and other legislation, the Commonwealth shall also improve the overdose and Emergency Room monitoring system so that patterns of abuse can be detected and actions taken to mitigate additional health risks. Specifically, the Commonwealth shall revise any necessary regulations to increase hospitals' and other health care providers' compliance and reporting of any drug overdoses, including alcohol and all Schedule II drugs.

Expanded Access to Treatment

Consistent with the strategies and activities outlined in the Commonwealth's Substance Abuse Strategic Plan, Massachusetts shall support and coordinate access to treatment services and shall provide expanded access to evidence-based and promising treatments for drug abuse in a broad array of settings. Specifically, as funds are available, the Commonwealth shall:

1. Provide additional funding for effective treatments that are currently provided including Detox, Methadone, Residential, Transitional Support Services, Day/Evening Treatments and Youth Services.
2. Expand access to newer medication treatments such as Suboxone which can be administered in office- based settings by primary care physicians and psychiatrists, dramatically altering the nature of and access to medications that can reduce withdrawal symptoms in dependent opiate and other drug users. Plans for expanded access to these medications shall also include protocols to ensure that these medications are prescribed appropriately.
3. Support the efforts of the Department of Public Health to expand the use of more evidence-based treatments through new purchasing standards, purchasing incentives and pay for performance initiatives, training and other educational activities.
4. Ensure access to and coverage of substance abuse treatment services for individuals through the prompt passage of substance abuse and mental health parity legislation. Far too often, insurers maintain standards for the utilization of substance abuse services that are not based upon the same medical necessity standards as with other physical conditions.
5. Continually monitor the adequacy of the supply of and funding for treatment services, particularly Section 35 beds.
6. Convene a panel of substance abuse experts, members of the judiciary, law enforcement, the Department of Probation, the Parole Board and District Attorneys to develop recommendations for diversion, treatment and monitoring of offenders.
7. Review the efficacy of Drug Courts and the costs and benefits of expanding the number of Drug Courts in the Commonwealth for prescription, alcohol-related and illegal drug abuse.

Action Steps

To follow up on the various detailed recommendations outlined above, and pursuant to the authority outlined in Joint Rule 1, paragraph I, the Committee on Public Health requests the Department of Public Health and other relevant state agencies to report back to the Committee no later than March 31, 2007 and annually thereafter on their activities and progress in implementing the recommendations, any barriers encountered and proposed approaches to overcome these barriers. Specifically the reports should address:

1) **Prevention and Education**: The Department of Public Health and other applicable state agencies shall provide a report and testimony to the Committee on Public Health on their progress in implementing the prevention, education and training efforts outlined above.

2) **Distribution, Dispensing, Handling and Disposal:** The Department of Public Health and the Board of Registration in Pharmacy shall present plans to the Committee on Public Health on their implementation of the recommendations outlined above for the proper distribution, dispensing, handling and disposal of schedule II drugs and other prescription drugs that are prone to abuse.

3) **Prescribing and Monitoring:** The Department of Public Health shall prepare a report and provide testimony to the Committee on Public Health on the progress DPH has made in redesigning and expanding the scope of its Prescription Monitoring Program and reporting procedures to accomplish the recommendations outlined above.

4) **Expanded Access to Treatment:** The Department of Public Health shall provide an annual report and testimony to the Committee on Public Health on the access and availability of treatment services for prescription and other drug dependence and abuse.

SCOPE OF THE PROBLEM

OxyContin and Prescription Drug Abuse

The high cost of OxyContin on the street stands as witness to the demand and need created by its large-scale abuse. However, OxyContin is the tip of the much larger social problem of prescription drug abuse and the abuse of other substances including alcohol. While the Massachusetts OxyContin Commission has focused much of its attention on OxyContin abuse, the recommendations of the Commission are designed to target both prescription and other drug abuse in general and for all ages.

The abuse of prescription drugs now stands only second (as a group) behind marijuana on the list of commonly abused drugs.[2] For those in the treatment community and others affected by prescription drug abuse the need is clear. Many of the solutions lie with the legislature through special legislation and increased funding.

While prescription drug abuse is a significant problem, we recognize that its control cannot occur at the cost of patients who suffer from chronic pain and who can benefit from these medications. For some people, OxyContin and other Schedule II drugs are the only way they can live comfortably. Physicians often face a dilemma in offering the optimal opioid medication for legitimate pain while weighing concerns about abuse and diversion. Public policies must not impede the legitimate access to these effective medications.

What is OxyContin?

In 1996 Purdue Pharma launched OxyContin as a highly effective painkiller: oxycodone hydrochloride, used to treat moderate to severe chronic pain. To many dealing with chronic pain it is the only adequate solution for pain management[3]. OxyContin is classified as a Schedule II opioid because of its high potential for abuse.[4]

When taken correctly, OxyContin has a controlled-release feature, slowly releasing into the blood stream over a twelve-hour period. Due to the quantity and purity of the drug being released, patients suffering from chronic pain are able to function normally and nearly pain-free.

[2] Rannazzisi, Joseph T. "Status of the Efforts of the FDA and DEA in regulating Schedule II Prescription Painkillers, Specifically OxyContin® and Other Opioid Analgesics." DEA Congressional Testimony. Government Reform Subcommittee on Regulatory Affairs. Boston, MA: September 13, 2006.

[4] "DEA Fact Sheet." United States Drug Enforcement Agency 2005. Web site: http:www.dea.gov/concern/oxycodone_factsheet.html

How is OxyContin Abused?

Abusers of OxyContin destroy its controlled-release feature by crushing and snorting the tablet, chewing the tablet, or dissolving it in water and injecting the solution. Without the time-release properties, OxyContin produces an immediate heroin-like high.[5] Poly-drug users often use OxyContin interchangeably with heroin because of the similar high—heroin is actually cheaper and more readily available in some areas, making heroin addiction the ultimate destination for many OxyContin abusers.[6]

How is OxyContin Trafficked?

Like other prescription drugs, OxyContin is supplied to pharmacies legally and enters the black market through diversion, health care fraud, pharmacy robberies, false prescriptions, and/or prescription exploitation. Abusers also may doctor-shop or order from illegal online pharmacies. Less frequently, patients sell legitimate prescriptions on the black market for profit.[7]

The cost of OxyContin on the black market ranges from $0.50 to $1.50 per milligram. Pills come in 10, 20, 40, 80, and 160-milligram tablets.[8] The 40 and 80 strength pills are most commonly abused selling from $40 to $100 per tablet.[9] The large profit in the sale of OxyContin—initially being either stolen or covered by insurance—is a significant motivator for dealers, doctors, and patients involved in diversion of the drug.

National Summary: Data and Policies

OxyContin abuse has become an issue of national concern. The problem first became apparent in rural areas of the mid-Atlantic region, Maine, and Appalachia during the late nineties. Since then, cities and states around the country have reported OxyContin as either an emerging problem or a current problem in their communities.[10]

According to the Office of National Drug Control Strategy's fact sheet on OxyContin, approximately 9% of Americans have misused prescription opioids in their lifetime. The number of Americans who abuse prescription opioids is still growing, and the danger to society must be addressed.

"Jeff Allison, a standout pitcher from Peabody was a first-round draft pick of the Florida Marlins. But his blossoming career derailed when he became addicted to OxyContin. Instead of fighting for a spot in the starting rotation, he was fighting for his life."

(Health on the Hill 3/05) Koutoujian, Peter J. "Understanding OxyContin: new commission begins work on drugs and abuse." Health on the Hill. March 10, 2005.

[5] "OxyContin® Fast Facts" National Drug Intelligence Center August 2003. Web site: http://www.usdoj.gov/ndic/pubs6/6025/
[6] Coakley, Martha. Middlesex District Attorney. Testimony to the OxyContin Commission. May 24, 2005.
[7] "Intelligence Bulletin: OxyContin Diversion, Availability, and Abuse." National Drug Intelligence Center. August 2004.
[8] "Pulse Check: Trends in Drug Abuse." White House Drug Policy. April 2002. Web site: http://www.whitehousedrugpolicy.gov/publications/drugfact/pulsechk/apr02/synthetic_opiods.html
[9] "OxyContin FAQs." United States Drug Enforcement Agency. 2005. Web site: http://www.deadiversion.usdoj.gov/drugs_concern/oxycodone.oxycontin_faq.htm
[10] "Pulse Check: Trends in Drug Abuse." op. cit.

National Data

Oxycodone Related Emergencies, Treatments, and Deaths

- The National Household Survey on Drug Abuse demonstrated that 1.6 million individuals reported abusing prescription painkillers for the first time in 1998; in 1999 there were 2.6 million abusers of prescription opioids.[11]
- DAWN (Drug Awareness Warning Network) reports that Emergency Department mentions of oxycodone tripled between 1999 and 2002.[12]
- Reports from the Treatment Episode Data Set (TEDS) describe a significant increase in the number of oxycodone-related admissions to public treatment centers: from 138 in 1999 to 1,039 in 2001.[13]
- In 2000 and 2001, the DEA with the National Association of Medical Examiners verified 146 deaths directly caused by OxyContin. There were an additional 318 deaths in which the most likely cause of death was OxyContin.[14]

The Number of Users is Growing - Many are Young and First-Time Drug Users

- In 2004, the average age for first-time prescription opioid abuse was 23.3 years old.
- The National Survey on Drug Use and Health shows that OxyContin and other prescription opioids had a total of 2.4 million new users in 2004—the highest of all drug categories.
- In 2004, the number of new OxyContin-specific users was 615,000 persons.[15]

National Policies and Programs

The FDA and the DEA regulate prescription drugs with high potential for abuse under the Controlled Substances Act (CSA.) The CSA outlines five schedules for classifying drugs: Schedule I drugs have no legitimate medical uses and are highly addictive and likely to be abused; Schedule II drugs are highly addictive and likely to be abused, but have legitimate medical uses; Schedule III, IV, and V have approved medical uses and decreasing likelihoods of being abused.

Schedule II opioids, like OxyContin, are regulated by the DEA and put on watch for diversion and abuse. OxyContin, though introduced in 1996, did not emerge as a national problem until 1998. When it became clear that OxyContin was being heavily abused and diverted onto the black market across the country, the FDA in coordination with Purdue Pharma developed a risk management plan. Such a plan was recently recommended as a

[11] Hutchinson, Asa. "Statement before the House Committee on Appropriations Subcommittee on Commerce, Justice, State, and Judiciary." DEA Congressional Testimony. December 11, 2001.
[12] DEA Statistics. 2005. Web site: http://www.dea.gov/statisticsp.html
[13] "Intelligence Bulletin: OxyContin Diversion, Availability, and Abuse."
[14] "Summary of Medical Examiner Reports on Oxycodone-Related Deaths." Drugs and Chemicals of Concern. United States Drug Enforcement Agency. 2005. Web site: http://www.deadiversion.usdoj.gov/drugs_concern/oxycodone/oxycontin7.htm
[15] Cote, Paul. Public Hearing written statement.

requirement for pharmaceutical companies applying for approval of new Schedule II opioids.[16]

OxyContin's classification as a Schedule II opioid under the CSA means that the DEA has the power to set annual quotas on the production of the raw materials necessary to manufacture the drug. Such quotas allow the DEA to regulate the amount of drug produced and therefore the amount of drug diverted.[17] Though the DEA sets annual quotas, the production of OxyContin has continued to increase since its introduction ten years ago.[18]

A National Action Plan

In 2001, the Administrator of the Drug Enforcement Administration, Asa Hutchinson, declared that the rising concern surrounding the diversion of OxyContin and other prescription painkillers called for a national action plan. The DEA developed a Prescription Drug Strategy combining education, law enforcement, and the disruption of the drug trade in hopes of eradicating prescription drug abuse.[19] The strategy includes collaboration with other governmental and non-governmental agencies, specifically the Food and Drug Administration, the Justice Department, and the National Association of Medical Examiners.[20]

Results of the National Action Plan

Education and Community Outreach

The FDA immediately worked with Purdue Pharma to change the labeling of OxyContin in an effort to better educate practitioners, pharmacists, and patients. The new label clearly states, "Oxycodone can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing OxyContin." It also is very clear that tablets are not to be broken, chewed, or crushed, but that they must be swallowed whole.[21]

The DEA has been working in conjunction with popular Internet search engines like Google and AOL to launch public service announcements about prescription drug abuse. The announcements will automatically appear when Internet users search for prescription drugs online. The DEA has also taken steps to better educate physicians of the dangers of prescribing controlled substances.[22]

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[16] Rannazzisi, op. cit.
[17] Lynch, Stephen. "OxyContin and Beyond: Examining the Role of FDA and DEA in Regulating Prescription Painkillers." Government Reform Subcommittee on Regulatory Affairs. Boston, MA: September 13, 2006.
[18] Cruz, Timothy J. "OxyContin Abuse & Addiction" Plymouth County District Attorney. Testimony to the OxyContin Commission. June 27, 2005.
[19] Rannazzisi, op. cit.
[20] Hutchinson
[21] OxyContin Label. Food and Drug Administration: 2001. Web site; http://www.fda.gov/cder/foi/label/2001/20553s022lbl.htm
[22] Rannazzisi, op. cit.

Targeting Diversion

The DEA began an effort to target key points of diversion and encourage states to establish Prescription Drug Monitoring Programs (PDMP's). In August of 2005 the President signed the "National All Schedules Prescription Drug Reporting Act" and transferred oversight of PDMP's to the Department of Health and Human Services.[23] When PDMP's work correctly, the state should be able to monitor prescription activity and identify doctor-shoppers and unscrupulous physicians and pharmacists.

In addition to encouraging states to adopt PDMP's, the DEA is targeting the diversion of prescription drugs through law enforcement. By interrupting the economic stability of the prescription drug trade, the DEA hopes to cut off the availability of the drugs. Through seizure of assets, arrests, and imprisonments, the DEA believes that the diversion of prescription drugs can be slowed, if not stopped completely.[24]

> "Christine has been in and out of hospitals and rehabs 24 times… 3-5 days of detox is NOT, by any stretch of the imagination, enough time for a heroin addict to have any chance of staying clean, and that's all the insurance companies will pay for. They need long-term treatment."
>
> *Mary of Abington, mother of an OxyContin turned heroin addict*

Improving the Availability of Office Based Treatment

DEA registration identification numbers are issued to qualified physicians treating opioid addiction. The unique identification numbers allow such physicians to treat a limited number of individuals with opioid addiction from their offices. Since September 2005, the DEA has registered close to 6,000 physicians qualified to treat opioid addiction. The program is intended to improve the quality and availability of new and effective treatment regimens.[25]

Collaborating with Pharmaceutical Companies

In addition, the DEA has communicated to Purdue Pharma its concern with the direct marketing of drugs that fall under the Schedule II classification of the Controlled Substances Act. The DEA believes that such drugs should not be marketed directly to consumers because of the drugs' huge potential for abuse.

Purdue Pharma has recently taken the 160-miligram OxyContin tablet off the market. Both the DEA and Purdue Pharma deny that the removal of this product is related to the DEA's Prescription Drug Strategy. However, the removal of the 160-miligram OxyContin tablet does significantly reduce the threat of overdose due to misuse of the large dose of OxyContin.[26]

[23] Rannazzisi, op. cit.
[24] "Drugs and Chemicals of Concern: Action Plan to Prevent the Diversion and Abuse of OxyContin." United States Drug Enforcement Agency. April 2001. Web site: http://www.deadiversion.usdoj.gov/drugs_concern/oxycodone/abuse_oxy.htm
[25] Rannazzisi, op. cit.
[26] "OxyContin FAQs."

Educating State Governments

The National Action Plan's Prescription Drug Strategy forces states to examine their role in curbing prescription drug abuse. OxyContin is no longer just a rural Appalachian problem. Major cities across the country have large-scale prescription drug abuse problems that need to be addressed and subsequently eradicated.

Massachusetts' Prescription Drug Problem

In Massachusetts, prescription drug abuse has become an epidemic. According to both epidemiologists and the Massachusetts police, OxyContin is widely available in the Greater Boston Area.[27]

Increase in Non-Heroin Opioid-Related Deaths and Addiction

To demonstrate how out-of-control the prescription drug problem in Massachusetts has become, the Commissioner of the MA Department of Public Health, Mr. Paul Cote, presented the following statistics during one of the public hearings held in 2005 by the OxyContin Commission.

> "This drug has ruined more lives than anything I've seen in 28 years of policing. Imagine taking a road, and that road leads to your own destruction. Trying OxyContin is that very road."
>
> *Ken Coye, Chief of Police, Malden (from A Prescription for Pain brochure)*

- Opioid-related deaths increased 600% between 1990 and 2003 in MA.
- Emergency Department visits for non-heroin related opioid use, which includes OxyContin and other prescription drugs use, increased 134% between 1999 and 2002.
- SAMHSA data show that treatment admissions in MA for the abuse of "other opiates," which includes OxyContin and other prescription drug treatment, increased 950% between 1992 and 2002 (325 persons to 3,089 persons.)
- DAWN data for metro-Boston show that in 2003 66% of opioid-related deaths were caused by the misuse of non-heroin opioids, which include OxyContin and other prescription drugs.

Increase in Criminal Activity

Consider, also, that in 2002, 148 of the 166 pharmacy thefts that were reported in New England occurred in Massachusetts.[28] According to Martha Coakley, Middlesex District Attorney, because of the high price of OxyContin, many people who are addicted resort to crime to satisfy their needs. She also notes that "there is an increasing trend of OxyContin addicts resorting to heroin or other harmful opiates, which are significantly cheaper, yet provide a similar high."[29] In Massachusetts the average price of OxyContin

[27] "Pulse Check: Trends in Drug Abuse.", op.cit.
[28] "Other Dangerous Drugs." Massachusetts Threat Assessment Update. National Drug Intelligence Center. May 2003. Web site: http://www.usdoj.gov/ndic/pubs3/3980/odd.htm
[29] Coakley, op. cit.

on the secondary market is $1.00 per milligram ($40 per 40-milligram tablet,) whereas heroin is $3.00 or $4.00 per bag.[30]

OxyContin Users in Massachusetts Graduate to Heroin

A 2002 survey of Boston-area non-methadone treatment centers determined that OxyContin was second only to heroin as the primary drug of choice.[31] Prescription drug abuse cannot be ignored—the dangerous consequences of death, prison, or life-long addiction are often the only options for individuals addicted to OxyContin.[32]

According to Plymouth County District Attorney Timothy J. Cruz, OxyContin is often called "Baby Heroin" because abusers start with OxyContin and quickly graduate to heroin. The DEA is clear that heroin and cocaine are currently still the most widely used and distributed illicit drugs in Massachusetts, but since the introduction of OxyContin, the number of individuals addicted to heroin has continued to rise whereas the number of individuals dependent upon cocaine has dramatically decreased.

In 1992, about 15% of patients in MA treatment programs reported heroin as their drug-of-choice; in 1996, about 25% reported heroin as their drug-of-choice; in 2002, just fewer than 40% reported heroin as their drug of choice. Conversely, admission rates in MA for people with addictive disorders who list their primary drug of choice as cocaine decreased 72% between 1992 and 2002, from 214 to 60 per 100,000 aged 12 or older.[33]

Who is Affected by Prescription Drug Abuse in Massachusetts?

The emergence of prescription drug abuse as a near epidemic in Massachusetts affects entire communities, from friends and family members of people suffering from addiction to police and school officials. The abuse of prescription medications is present in all socio-economic strata of society.[34] Some argue that OxyContin is what Valium was 30 years ago or what Percocet was 10 years ago and that in another ten years it will be another prescription drug that will emerge as the problem.[35] While this may be true, OxyContin has caused enough destruction in our communities—it is time to try to stop the continued abuse of this heroin-like drug.

> "And even though the situation is almost an epidemic through-out the country, many parents and their teens still don't seem to get the message, so the problem continues to grow. This is one war you need to face no matter which party you belong to."
>
> *Kerry, resident of Lynn whose close friend lost two siblings to OxyContin abuse.*

[30] Kowalski, Carol. Director Brockton Treatment Center. Testimony Presented to the Massachusetts OxyContin Commission. June 27, 2005
[31] Lynch, op. cit.
[32] Coakley, op. cit.
[33] "Trends in Cocaine Treatment Admissions by State: 1992-2002." The Drug and Alcohol Services Information System Report. June 28, 2005. Web site: http://www.drugabusestatistics.samhsa.gov/2k5/CocaineTX/CocaineTX.htm
[34] "Intelligence Bulletin: OxyContin Diversion, Availability, and Abuse."
[35] Kowalski, op. cit.

Existing Programs and Policies in Massachusetts

The Commission heard testimony from many individuals during the course of our hearings across the state. The Department of Public Health has taken efforts to develop a public service campaign on prescription drug abuse and to improve the Prescription Drug Monitoring Program. Additionally, the state's law enforcement agencies have initiated an OxyContin Task Force to target the diversion and abuse of OxyContin and prescription drugs. However, many prevention efforts are locally based. The current statewide efforts to curb prescription drug abuse primarily focus on preventing diversion through prescription drug monitoring and law enforcement—with an increasing emphasis on education.

Current Statewide Efforts

Prevention

While it is true that many OxyContin abusers begin using that drug specifically, most abusers have been using alcohol and/or marijuana for sometime. Many have been introduced to OxyContin while under the influence of another drug, and even after they begin using OxyContin and other opiates, they continue to abuse alcohol and marijuana. It is important to understand how people begin drug use in order to interrupt the cycle. Heavy use of alcohol and marijuana by young people, particularly those younger than 15, is a very clear warning sign that the abusers are at greatly increased risk for other drug use and later dependence and/or addiction.

In a Provider Discussion report written for MDPH in 2003, eight different treatment providers indicated that, based on their experience, practically everyone they saw in their treatment programs who was having a problem with OxyContin or another opioid, began their drug addiction by abusing alcohol and or marijuana.

Good prevention needs to take a comprehensive approach realizing that most drug abusers are poly–drug abusers and most abusers begin by abusing alcohol and marijuana.

Prescription Drug Monitoring Program

The Massachusetts Prescription Drug Monitoring Program is the front line of statewide efforts to control prescription fraud and abuse. In order to effectively prevent diversion and monitor the illicit use of prescription drugs, certain aspects of the program need to be improved.

The Department of Public Health has received grants from the U.S. Department of Justice to implement changes to the PDMP. The plan includes improving data collection and reporting technology. The goal of these enhancements is to allow the Department of

Public Health to effectively monitor Schedule II prescriptions and communicate the misuse of such drugs to the appropriate agencies.[36]

Increasing the capacity for treatment

The 2005 Strategic Plan for Substance Abuse in the Commonwealth included a significant increase in the number of detox beds, step-down beds, and residential beds for families and youths. There will soon be a new 15-bed facility for adolescent women opening in Boston. Though these new treatment facilities are not specifically targeted to prescription drug abusers, the new programs and facilities will allow the state to provide treatment services for many more of those who require detox and recovery support services.[37] As a result of a broad- based coalition of state agencies and the legislature who have recognized the needs for treatment, the availability of funding for treatment resources, including detox beds, transitional supports and other services, has increased in the last year and a half. However, the number of detox beds still remains below 2001 levels.

> "Law enforcement, by itself, has little deterrent effect on many people. People addicted to drugs are going to continue to do whatever they need to do to get more drugs. The same goes for people who sell drugs. Many see the prospect of being arrested as little more than an inconvenience or a 'cost' of doing business. This should be a concern to all of us."
>
> *John W. Suslak, Chief of Police, Lynn*

New treatment modality: Buprenorphine

A new treatment regimen using Buprenorphine appears to have great promise with younger users according to the Department of Public Health. DPH is collaborating with the Boston Medical Center to train physicians in the best uses of this drug.

Buprenorphine is not a substitute for methadone treatment; patients who are not suited for it should enter methadone treatment. The benefit of Buprenorphine is that, for the appropriate patient and with the appropriate supports, it can be administered in a physician's office.

Town and City-Based Efforts

The Commission heard testimony from a number of local initiatives to combat alcohol, illegal drug and prescription drug abuse in cities and towns across the Commonwealth. While there are many more efforts working in our communities throughout the state, we have summarized the work of the initiatives that testified below.

Lynn *Communities That Care* Coalition

In response to growing concerns in the community related to opiate abuse, overdoses, and overdose deaths, a network of individuals representing the provider network, public schools, law enforcement, city officials, and youth have identified a number of strategies aimed at reducing and preventing substance use among youth. This initiative has emphasized preventing the use of gateway drugs such as alcohol and marijuana and has been concentrating on raising public awareness about risks associated with substance

[36] Cote, op. cit.
[37] Cote, op cit.

abuse, alternatives to substance use, and available resources. Current and proposed activities include sponsorship of community forums geared toward parents on topics related to substance use, conducting compliance checks on alcohol vendors to reduce underage drinking, youth driven media campaigns, neighborhood improvement plans, and programming to provide families and youth at risk with greater access to needed services. This level of collaboration has been essential to the process of reducing the risk factors that contribute to substance abuse and related issues (including violence, delinquency, and school dropout) and promoting positive youth development.

Revere CARES Coalition Opiate Task Force

Revere Cares is a nationally recognized, award- winning community anti-drug coalition that has been working together in Revere with the Massachusetts General Hospital Revere Health Care Center, to reduce substance abuse among youth. The Opiate Task Force presented testimony to the Commission on their efforts and recommendations to combat opiate use among youth in Revere. Their recommendations relating to the need for treatment resources and prevention efforts for prescription drug abuse are incorporated into this report.

The City of Malden

Malden currently uses an effective substance abuse prevention and education brochure on OxyContin called *A Prescription for Pain: OxyContin*. The brochure describes both the licit and illicit uses of the drug, the warning signs of OxyContin abuse, how OxyContin has devastated families in the community, and where to get help.

Somerville Cares About Prevention

Somerville Cares About Prevention is a community coalition working to reduce substance use/abuse and addiction in all residents of Somerville. They seek to mobilize community members and retailers to protect youth, reduce underage drinking and increase the understanding of risks associated with substance use.

Framingham Public Schools

Framingham Public Schools have not seen a large-scale prescription drug problem; they attribute their success to comprehensive, prevention health education in the public schools. Framingham Public Schools currently begin health education programs in fifth grade. The programs focus on promoting a healthy lifestyle through physical and emotional wellbeing. Drug use and abuse are covered initially in Middle School and further in depth in High School.

Christopher H. Martes, the Superintendent of Schools in Framingham believes that the absence of prescription drug abuse in the Framingham Public Schools is due to

- progressive city-wide alcohol abuse prevention policies
- active family and community involvement
- aggressive health education programs

- effective communication and collaboration between school personnel, law enforcement, and community leaders.[38]

Norfolk County Heroin Task Force

The Norfolk County Heroin Task Force is composed of law enforcement representatives, probation officers, the parents of people with addictive disorders, treatment providers, and members of the office of the Norfolk County District Attorney. The group has the huge responsibility of educating parents, teachers, and community leaders about opioid addiction—preventative measures, warning signs, and treatment options.

Learn2Cope.org is a website developed by the task force. The website serves as a resource to parents who want or need to learn more about heroin and OxyContin abuse in the suburbs. The website also hosts an online support forum for the parents of people with addictive disorders.

Additionally, the Task Force has been involved in public school health education. Health educators used back-to-school meetings in 2005 as a time to educate teachers and administrators on the influx of heroin and prescription drugs in their communities. For the students, the Task Force encouraged a middle school educational program in which the sibling of a heroin addict speaks about the effect of addiction on a family. So far, the program has received very positive feedback from both students and teachers.

The group also regularly holds regional educational forums for parents and community members interested in understanding the nature of opioid addiction and it is training medical professionals to educate their patients on the dangers of OxyContin.[39]

Middlesex County District Attorney's office

The Middlesex County District Attorney's office created a 17-minute educational video called, "All Jammed Up: A Prescription for Disaster." The video is intended to educate parents, teachers, and other school personnel on how to recognize and address prescription drug abuse, specifically OxyContin abuse. In addition the office has a tip line, 1.866.OXY.TIPS, which allows people to anonymously report potential prescription drug dealers.[40]

Essex County District Attorney's Office

The Essex County District Attorney's office, led by District Attorney Jonathan Blodgett, developed an education curriculum titled "Choose To Refuse: A Heroin and OxyContin Prevention Education Program." This six-session curriculum helps young people, ages 13–18, understand the hazards of heroin and OxyContin and the damage these drugs do to their bodies and minds. They learn decision making skills and ways to refuse drugs, gain the ability to recognize risky situations, and rehearse their responses to people who may pressure them to take drugs. The program is offered to state agencies, and all of the schools and police departments in Essex County.

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[38] Martes, Christopher. Superintendent of Schools Framingham Public Schools. Testimony to the OxyContin Commission. May 23, 2006.
[39] Keating, William R. Norfolk County District Attorney. Testimony before the OxyContin Commission. June 27, 2005.
[40] Coakley, op. cit.

Addressing the Gap: A Missing Link

The Department of Public Health and other statewide and local organizations have taken numerous steps to address the issue of prescription drug abuse. Prevention funds have been provided to local organizations and governments to educate their communities on the dangers of substance abuse in general and of prescription drug abuse in particular. Law enforcement agencies and social and community service agencies have begun to work together to target prescription drug diversion and to enforce existing laws focused on alcohol and other drug use. Recently, public service ads were created and disseminated to educate the community. However, there is not yet an overarching prevention and treatment plan with coherent action steps that can be easily followed.

Massachusetts Responds by Forming the OxyContin Commission

In response to this missing link, the Massachusetts legislature convened and appointed members for the OxyContin Commission. The Commission was charged with understanding the problem of OxyContin abuse and developing a coherent set of recommendations to curtail the growing problem of prescription drug abuse in Massachusetts. This report is a direct result of the Commission's charge. We, the Commission, believe that the aforementioned legislative recommendations, when implemented, will respond to the urgent need for improved prevention and treatment of OxyContin abuse.

Legislative History

Chapter 189 of the Acts of 2004 outlined an act providing for the investigation by a special commission into the effects of OxyContin and other drug abuse beginning on July 1, 2004.

Section 1 of the Act determined that the commission would study "the prescription, dispensing, treatment, and education with respect to those drugs [OxyContin and other prescription and illicit drugs] and shall submit a report, including legislative recommendations, if any, to the clerk of the house of representatives who shall forward the same to the joint committee on health care and the house and senate committee on ways and means."[41]

Membership

The membership of the commission outlined in Section 1 of Chapter 189 of the Acts of 2004 comprised eleven members from various governmental and non-governmental posts. These eleven included four members of the Massachusetts General Court, a representative from the state's Department of Mental Health and the state's Department

[41] Massachusetts State Legislature. Section 1 of Chapter 189 of the Acts of 2004.

of Public Health Bureau of Substance Abuse Services. In addition to these governmental representatives, there were five members of the public who have expertise in the drug abuse field, two of whom were appointed by the Senate President and three by the Governor.

After appointments were made, the membership of The OxyContin Commission included the following:

- Representative Peter J. Koutoujian, Commission Co-chair
- Senator Richard T. Moore, Commission Co-chair
- Representative Steven M. Walsh
- Representative Garrett J. Bradley
- Eric Weil, M.D., MGH Revere Health Care Center
- Ernest Gates, Jr., R.Ph. F.A.S.C.P
- Gary Gilmore, MassHealth
- Robert Jamison, Ph.D. Pain Management Center, Brigham and Women's Hospital
- Janice Kauffman, R.N. MPH, LADC I, Department of Psychiatry, Brigham and Women's Hospital and North Charles, Inc.
- David Hoffman, MD, MFA, Department of Mental Health
- Michael Botticelli, Assistant Commissioner for Substance Abuse Services, DPH

Critical guidance and input was received from the following legislators:

- Representative Ruth Balser, House Chair on the Joint Committee on Mental Health and Substance Abuse
- Senator Steven Tolman, Senate Chair on the Joint Committee on Mental Health and Substance Abuse

Process Followed by the OxyContin Commission

We followed a simple two-stage process to complete the task:

1. Understanding the problem
2. Considering the policy options

Understanding the problem

The communities affected by OxyContin abuse are the best resource for information in regards to the prescribing, abuse, trafficking, prevention, and/or effects of the drug abuse. In order to develop the coherent set of policy recommendations listed above, we held five public hearings on OxyContin and other drug abuse in cities across the Commonwealth.

The hearings were held in Lynn, Framingham, Bridgewater, Somerville, and Boston. Speakers included Chiefs of Police, other law enforcement officials, physicians, pharmacists, substance abuse treatment professionals and members of the community who have been affected by drug abuse personally and in their families.

Considering Policy Options

During the preparation of this report and in meetings held at the end of 2005 and in the first months of 2006, the Commission members and elected officials reviewed policy options and considered approaches to address the growing concerns. During this period several external events occurred including: the receipt of a federal grant for revisions to and improvements in the Prescription Monitoring program operated by DPH; the initiation of a set of public service announcements as a part of the State's on-going prevention efforts; and continued tragedy including the death of a youth from Arlington as a result of prescription drug abuse.

This report is the result of all these efforts and reflects a true collaboration between the DPH Bureau of Substance Abuse Services and the members of the OxyContin Commission.

Exhibit I

FDA Perspective on Abuse-Deterrent Opioid Development

Douglas C. Throckmorton, MD
Deputy Director for Regulatory Programs
CDER, FDA

CBI Abuse Deterrent
Formulations Summit

March 7-8, 2017

The opinions and information in this presentation are my own and do not necessarily reflect the views and policies of the FDA

Outline

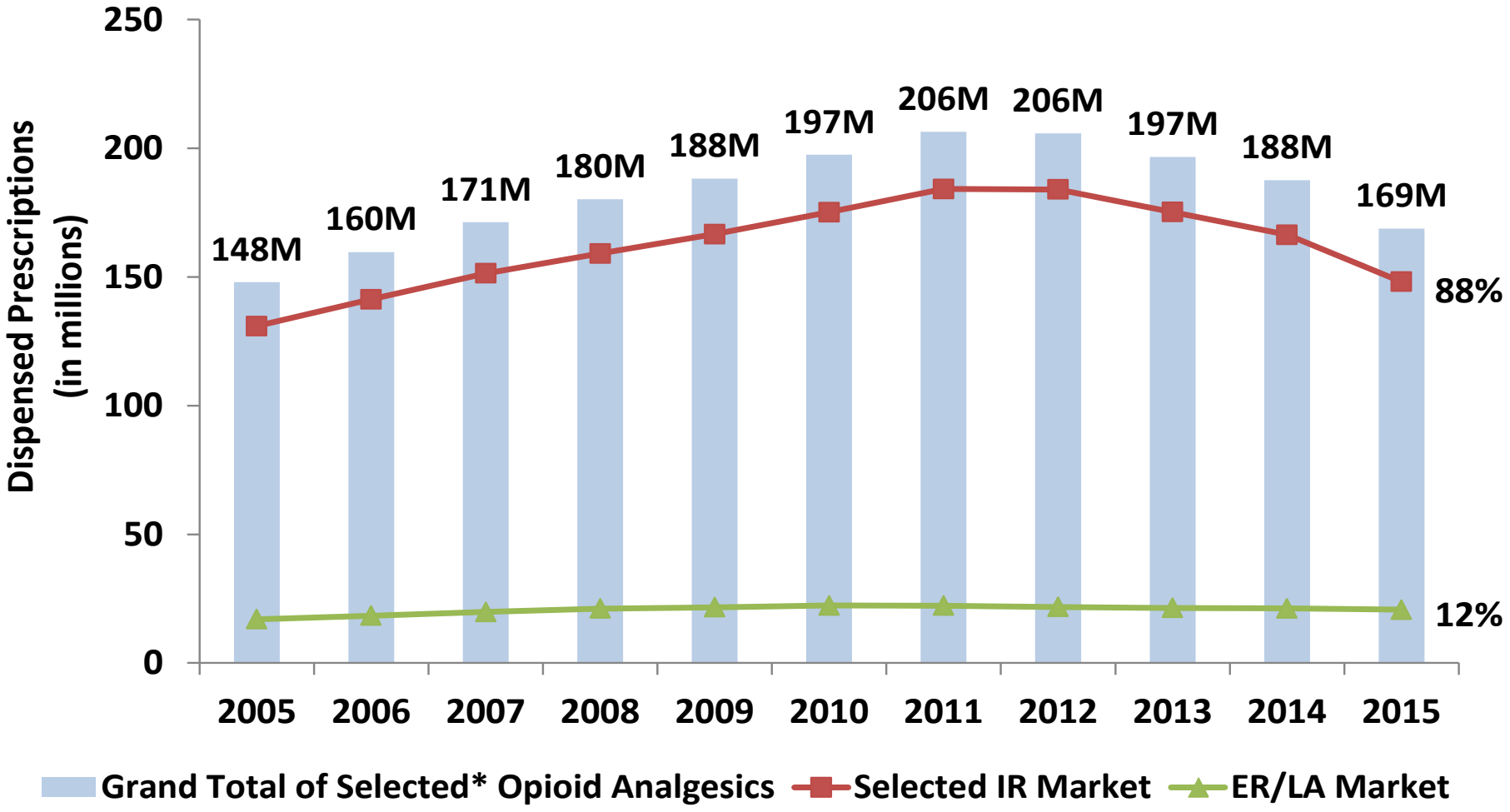
- Background on Epidemic
- Federal Context for FDA Efforts to Address Prescription Opioid Abuse
  - Other Federal Efforts
- FDA Action Plan
- FDA Focus on Abuse-Deterrent Formulations of Opioids

Overall Message

- The FDA work to improve the safe use of opioids is taking place within a larger policy framework aimed at addressing opioid abuse while assuring appropriate access to pain treatment
- Abuse Deterrent Opioids are one important part of FDA work to address opioid epidemic
- Ongoing and planned activities reflect the commitment by FDA to integrate the use of all of our available tools to achieve our goals related to the safe use of prescription opioids

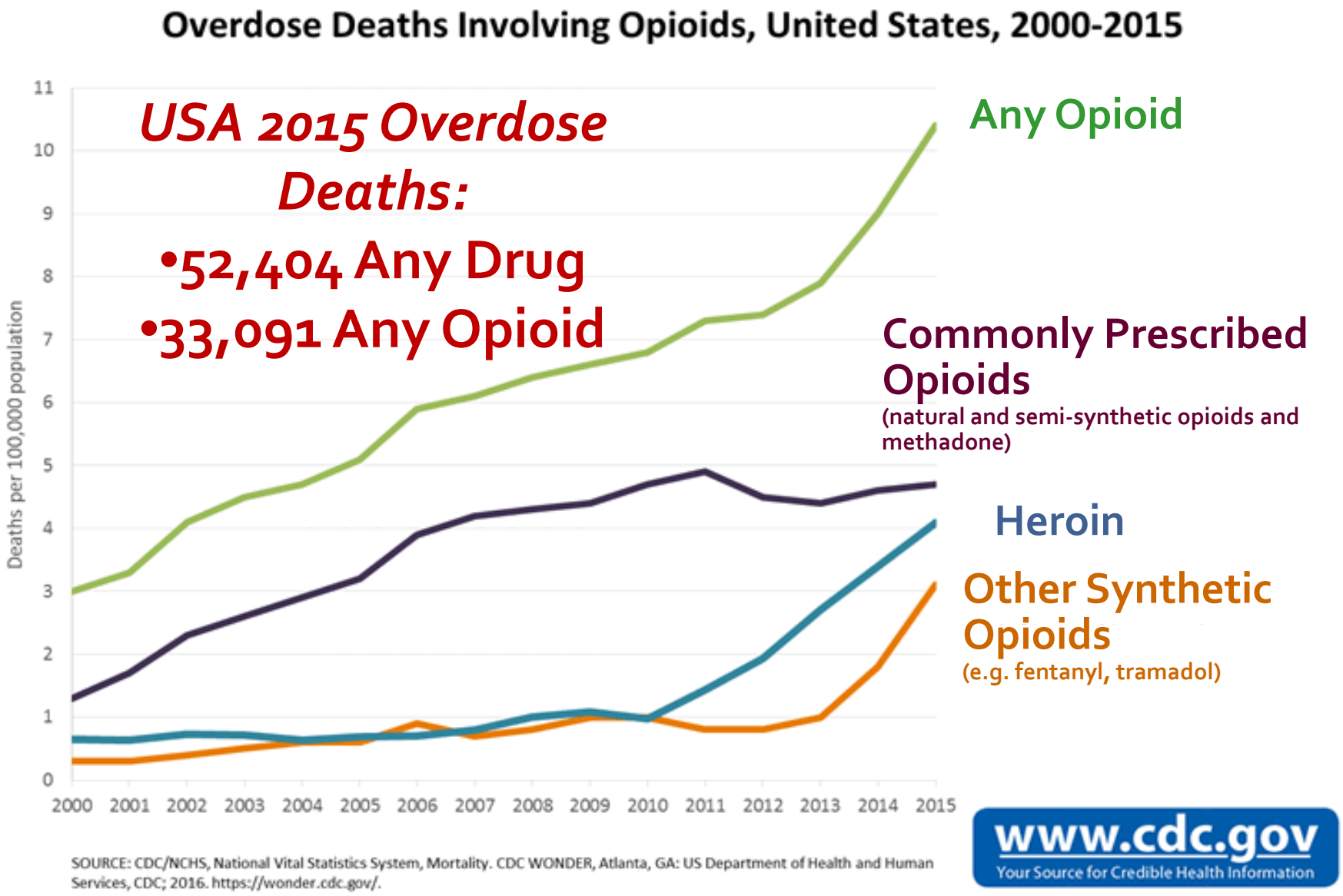
FDA U.S. FOOD & DRUG ADMINISTRATION

Nationally Estimated Number of Prescriptions Dispensed for Selected* Opioid Analgesics Oral Solids and Transdermal products from U.S. Outpatient Retail Pharmacies



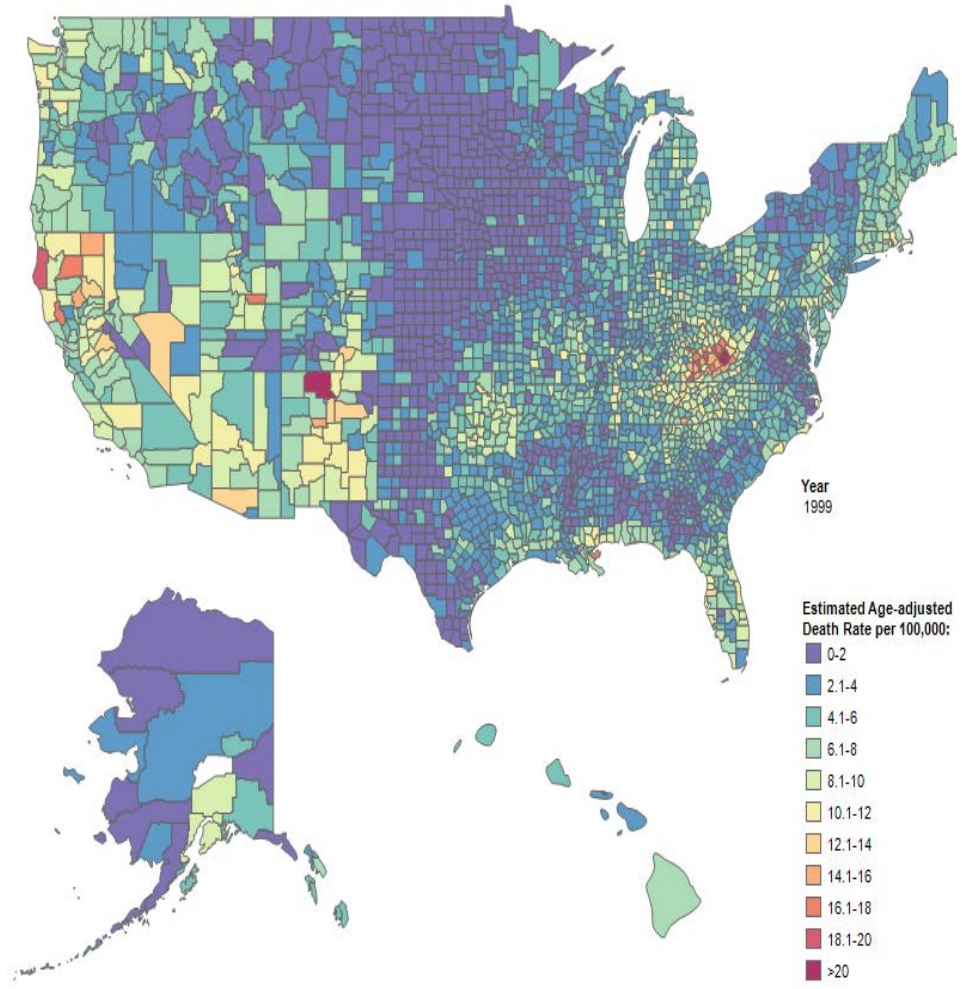
Source: National Prescription Audit (NPA). Extracted May 2015 (For 2005-2014 data) and November 2016 (For 2015 data).

Marked *Increases in Prescription Opioid and Heroin Overdose Deaths* in the USA 2000 to 2015

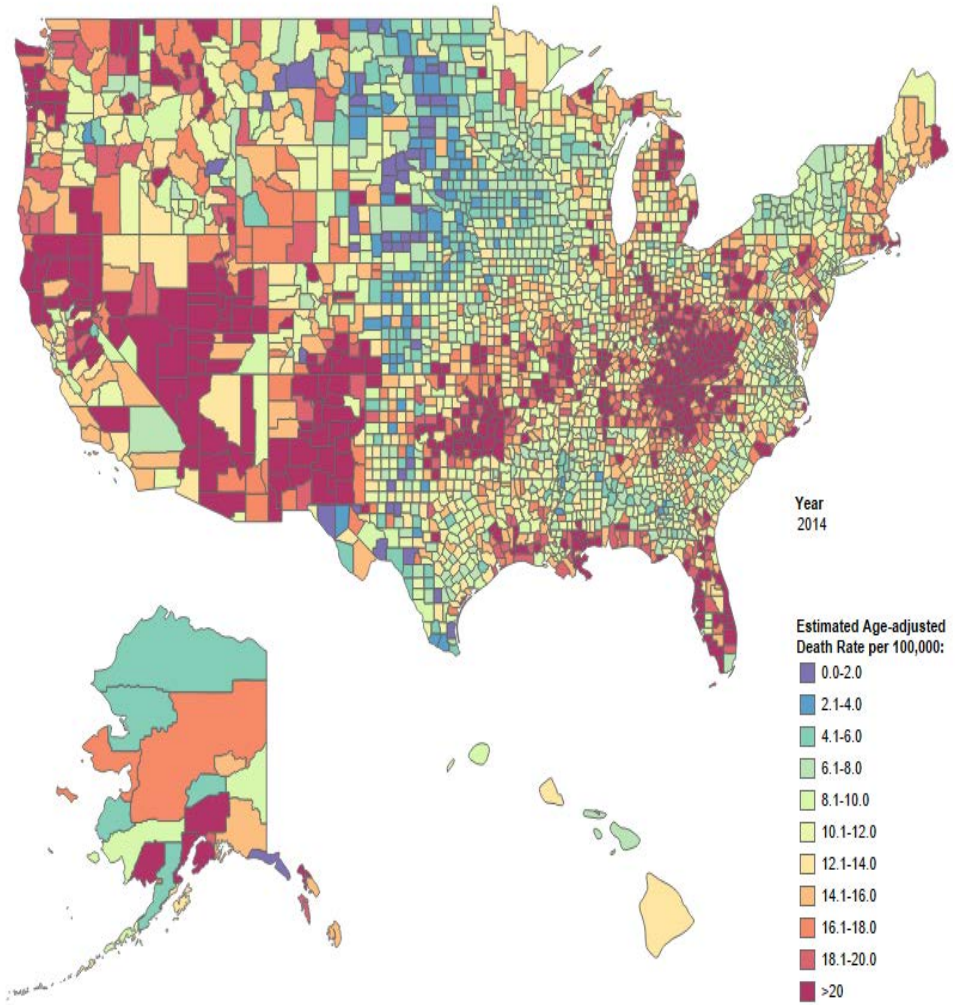


Overdose Death Rates

1999



2014

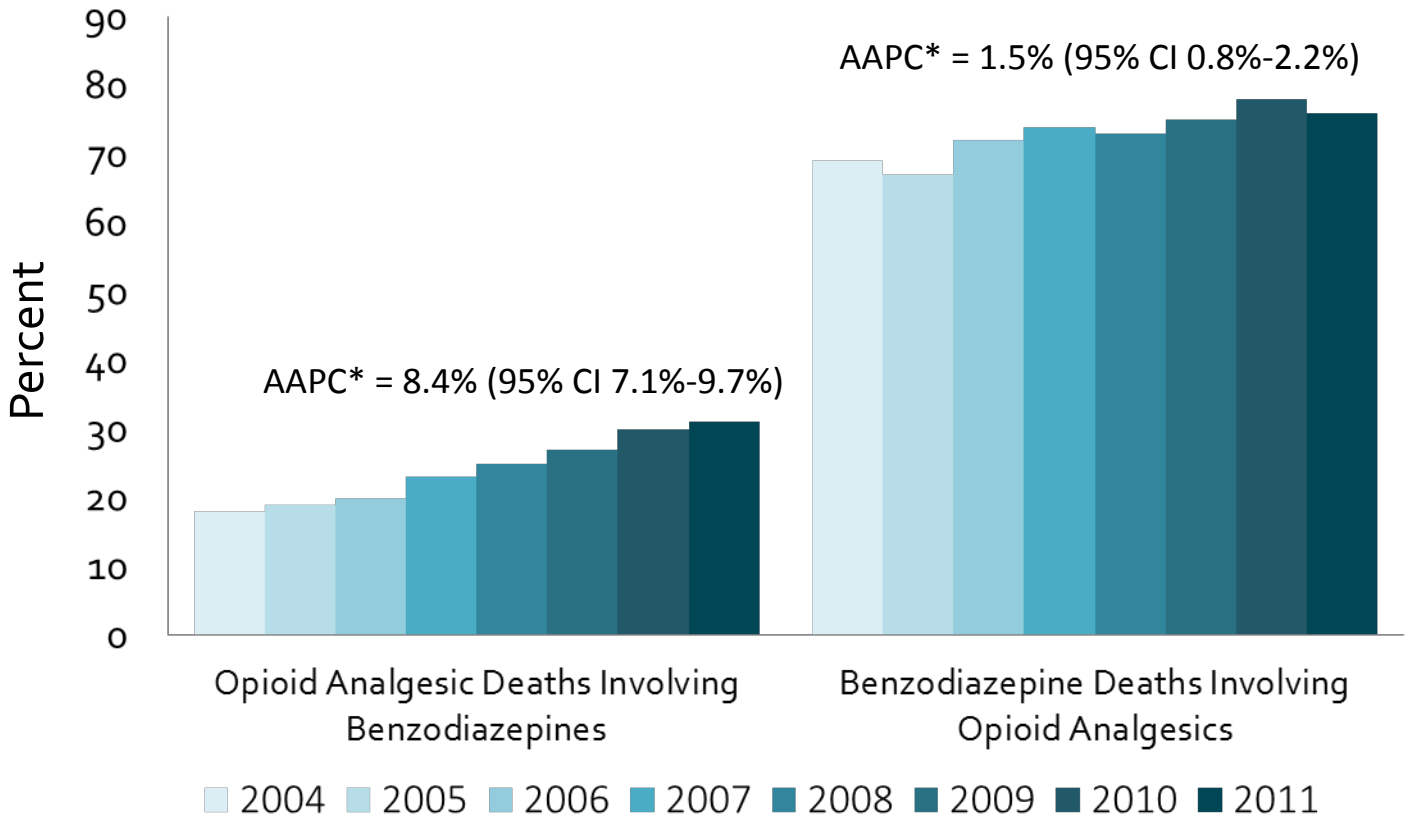


Designed by L. Rossen, B. Bastian & Y. Chong. SOURCE: CDC/NCHS, National Vital Statistics System

Science = Solutions

Overlap of *Benzodiazepines and Opioids*

Opioid OD Deaths Involving Benzodiazepines & Benzodiazepine OD Deaths Involving Opioids



*AAPC = Average annual percent change

Source: CM Jones, JK McAninch. *American Journal of Preventive Medicine* 2015;49:493-501.

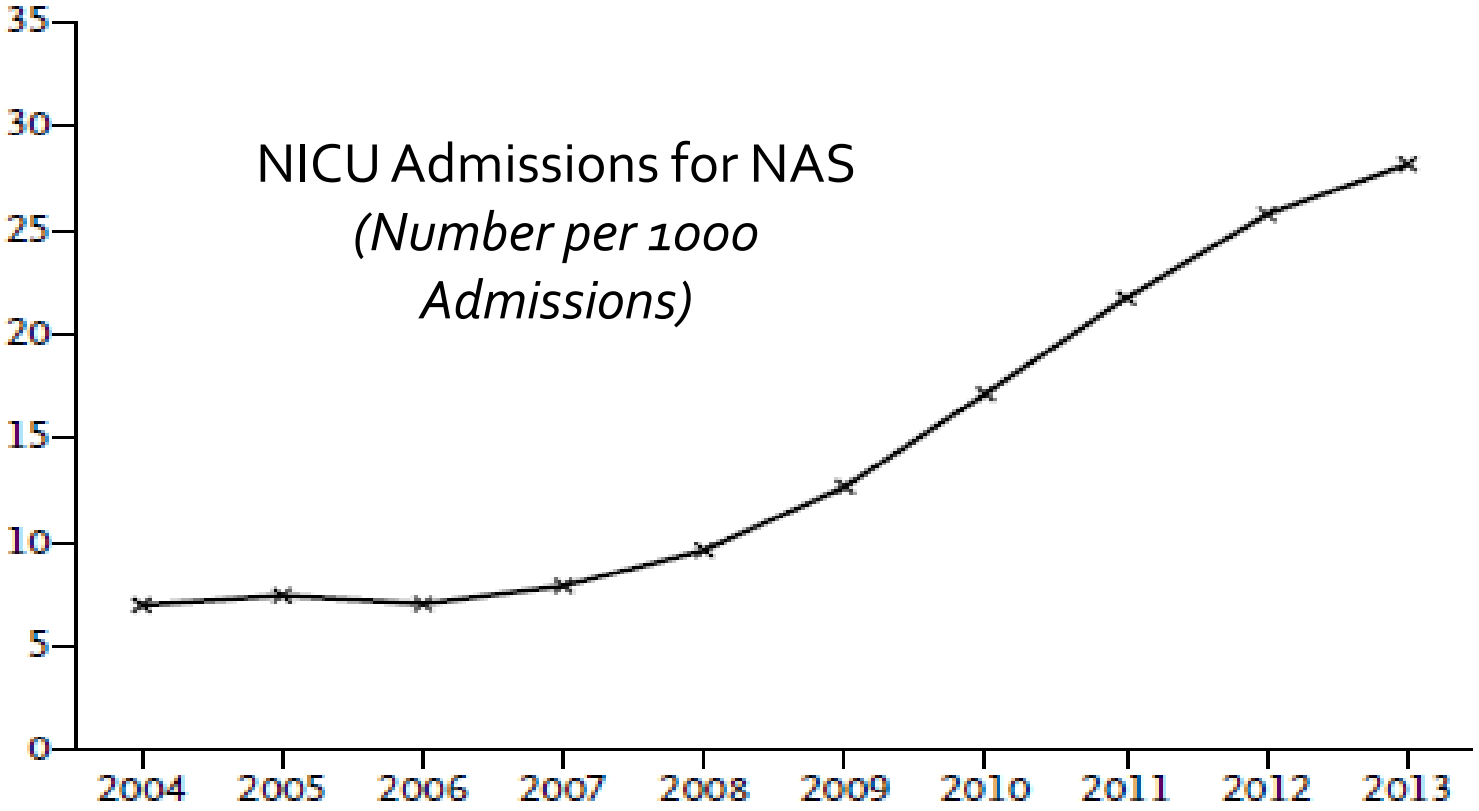
Science = Solutions

Outbreak of HIV Linked to IDU of Oxymorphone in Indiana, 2014-2015

- Through November 2015, **181 cases of HIV** identified in county of ~15,000
- 96% reported injection drug use
- Of these, **92% reported injecting prescription oxymorphone in past 12 months**
  - Frequently described preparing and injecting extended-release oxymorphone (Opana ER, Endo Pharmaceuticals)
- Public health emergency declared—syringe exchange program established

Source: Peters et al. *New England Journal of Medicine* 2016; 375:229-39.

Increasing
Neonatal Abstinence Syndrome



Source: Tolia VN, Patrick SW, et al. *NEJM* 2015;372:2118-2126

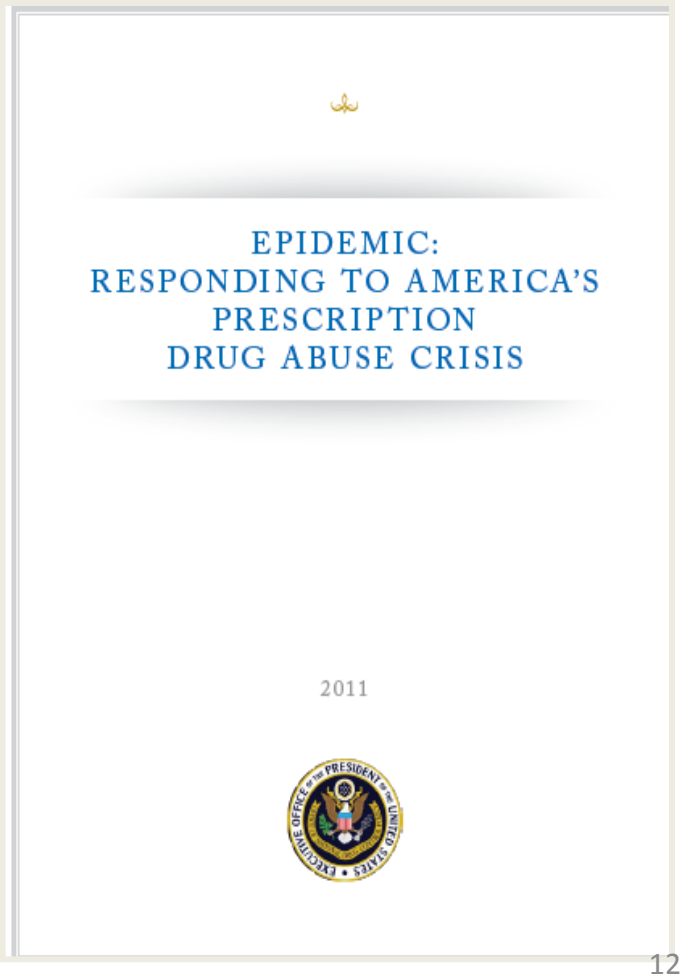
FDA is a Part of a Larger Governmental Response to Opioids Abuse

Office of the National Drug Control Policy (ONDCP) Plan

Health and Human Services (HHS) Secretary's Plan

ONDCP National Drug Abuse Prevention Plan

- Issued April 2011
- Four major areas of focus to reduce prescription drug abuse and other harm from drugs
  - Education
  - Monitoring
  - Proper medication disposal
  - Enforcement



HHS Secretary's Initiative to Combat Opioid Abuse

- Improving opioid prescribing practices to reduce opioid use disorders and overdose
- Expanding use and distribution of naloxone
- Expanding medication-assisted treatment (MAT) to reduce opioid use disorders and overdose

--http://aspe.hhs.gov/basic-report/opioid-abuse-us-and-hhs-actions-address-opioid-drug-related-overdoses-and-deaths

Other Critical U.S. Governmental Efforts FDA is Supporting

- **National Pain Strategy**
  - Focuses on key areas of pain and pain care, including professional education and training, public education and communication, service delivery and reimbursement
    - http://iprcc.nih.gov/docs/DraftHHSNationalPainStrategy.pdf
- **National Pain Research Strategy**
  - Strategic plan under development for pain research across federal agencies
- **Surgeon General's Call to End the Opioid Crisis**
  - Launched a new prescriber education campaign, Turn the Tide
  - Issued the first-ever Surgeon General's Report on Alcohol, Drugs and Health: Facing Addiction in America
- **CDC Guidelines for Prescribing Opioids for Chronic Pain**
  - Provides recommendations for the prescribing of opioid pain medication focused on the use of opioids in treating chronic pain
    - http://www.cdc.gov/drugoverdose/prescribing/guideline.html

U.S. FOOD & DRUG ADMINISTRATION

FDA Response to Opioids Abuse

FDA Action Plan (February 4, 2016)

- In response to the opioid abuse epidemic, FDA called for a far-reaching action plan to reassess the agency's approach to opioid medications. The plan focused on policies aimed at reversing the epidemic, while still providing patients in pain access to effective relief.

--http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm484765.htm

FDA Opioids Action Plan

- Expand the use of advisory committees
- Develop warnings and safety information for immediate-release (IR) opioid labeling
- Strengthen postmarket requirements to get needed data
- Update Risk Evaluation and Mitigation Strategy (REMS) Program for Prescription Opioids
- **Expand access to abuse-deterrent formulations (ADFs) to discourage abuse**
- Support better treatment for prescription opioid abuse and overdose
- Reassess the risk-benefit approval framework for opioid use

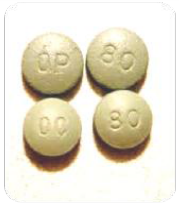
--www.fda.gov/NewsEvents/Newsroom/FactSheets/ucm484714.htm

FDA and Abuse-Deterrent Formulations of Opioids

Part of Larger FDA/HHS Efforts to Improve Tools for Pain Management

Development of New Pain Treatments

Abuse-deterrent Opioid formulations



Pro-drugs

Crush/extraction resistant formulation

Drug combinations with adverse effects if injected

Non-Opioid based analgesics
Cannabinoids;
Inflammatory mediators;
Ion channel blockers

Non-pharmacological treatments
Surgical interventions;
Neural stimulation;
Spinal cord stimulation

Transcranial Magnetic Stimulation

Spurring Development of Abuse-Deterrent (AD) Opioids: FDA Goals

- Incentivize the development of opioid medications with progressively better AD properties and support their widespread use
- Assure appropriate development and availability of generics, reflecting their importance in U.S. healthcare
  - Generic drugs play a critical role in U.S. healthcare, including important role in controlling costs and expanding access

FDA Tools to Support AD Formulation Development

- **Scientific Research**
- **Regulatory Activities**
  - Decisions on applications
  - Sponsor discussions as a part of individual product development
- **Guidances**
  - Final guidance on developing AD formulations of opioids issued April 2015
  - Draft guidance on generics development and testing issued March 2016
- **Public Discussion and Comment**
  - Public meetings, including meeting held October 2014 and 2016
  - Comments on draft guidance
  - Citizen petitions

Policy Development: Generic AD Opioids

- Generic drugs play a critical role in U.S. healthcare, including important role in controlling costs and expanding access
- March, 2016: FDA released draft guidance: "General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products"
- October, 2016: FDA held a 2-day meeting to discuss draft guidance and standardization of in vitro testing for AD opioids
- FDA plans to publish a final guidance to the March 2016 draft in 2017 in accordance with the requirements of the Comprehensive Addiction and Recovery Act of 2016.

Regulatory Activity: Supporting AD Opioid Development

- **9** new opioids approved with abuse-deterrent formulations (latest January, 2017)

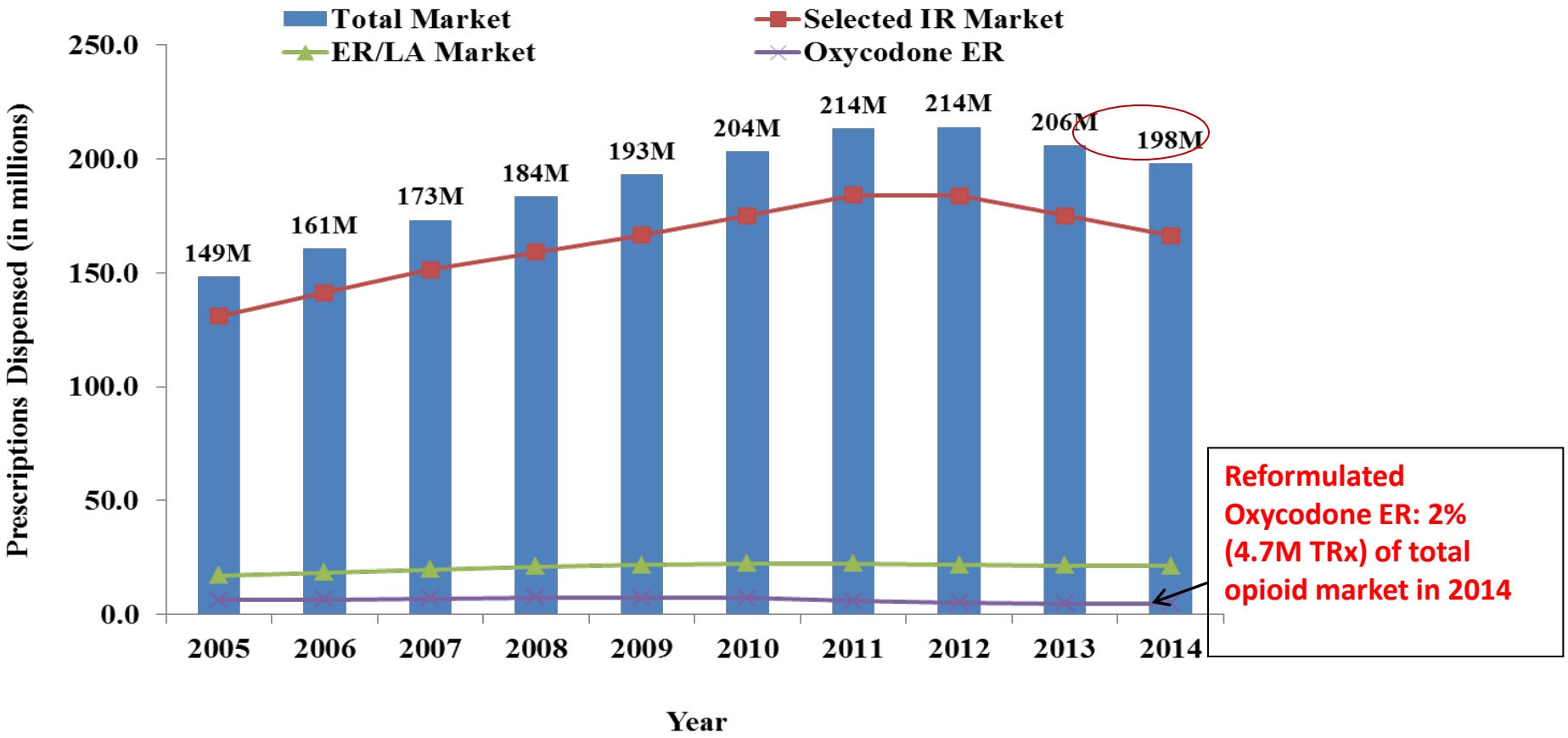
  (OxyContin, Targiniq ER, Embeda, Hysingla ER, MorphaBond, Xtampza ER, Troxyca ER, Arymo ER, Vantrela ER)

  - Work to date has often focused on use of crush/extraction-resistant and agonist/antagonist technologies, but many new approaches being explored
  - More than 30 active investigational new drug applications (INDs) being discussed for AD formulations
    - New technologies being explored by industry (e.g., pro-drugs that require activation to prevent IV abuse and snorting)

Next Steps: Need for Assessment of Impact on Real-world Abuse

- Current labels based on clinical and in vitro data to predict the formulation will reduce abuse
- Real-world assessment needed (and ongoing) as we know AD formulations are not silver bullets and can be defeated
- DECIDE WHAT WORKS AND WHAT DOESN'T

IR and ER/LA Opioid Prescriptions



Nationally estimated number of prescriptions dispensed for selected IR and ER/LA opioid analgesics from U.S. outpatient retail pharmacies

- No prescriptions captured for Hysingla ER or Embeda in 2014

Source: IMS Health, National Prescription Audit ™ Extracted May and August 2015

Challenges in Getting to the Future for AD Opioids

- Incentivizing innovation: Current FDA incentives include product labeling and Hatch-Waxman exclusivity
- Encouraging iterative development and use of effective abuse-deterrent formulations
  - Challenge to assess impact of individual formulations
  - Challenge to encourage uptake of effective products by payers
- Managing expectations: abuse-deterrent opioid--
  - Are part of larger effort on opioids
  - Will not ‘prevent’ abuse, and are not ‘silver bullets’

Summary and Conclusions

- FDA working to address opioids epidemic as a part of the larger HHS response
  - One of the FDA's highest priorities
- FDA Opioids Action Plan provides framework for FDA response to the challenge of opioids abuse epidemic
- Supporting development and use of progressively better abuse deterrent opioids one important FDA goal within the Action Plan
  - FDA looks forward to the day, not far in the future, when the majority of opioids on the market are known to be abuse deterrent

Thank you


FDA
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ADMINISTRATION

Exhibit J

FDA's Actions to Address the Opioid Epidemic

Douglas C. Throckmorton, MD
Deputy Director for Regulatory Programs
Center for Drug Evaluation and Research
FDA

CBI Abuse-Deterrent Formulation Summit

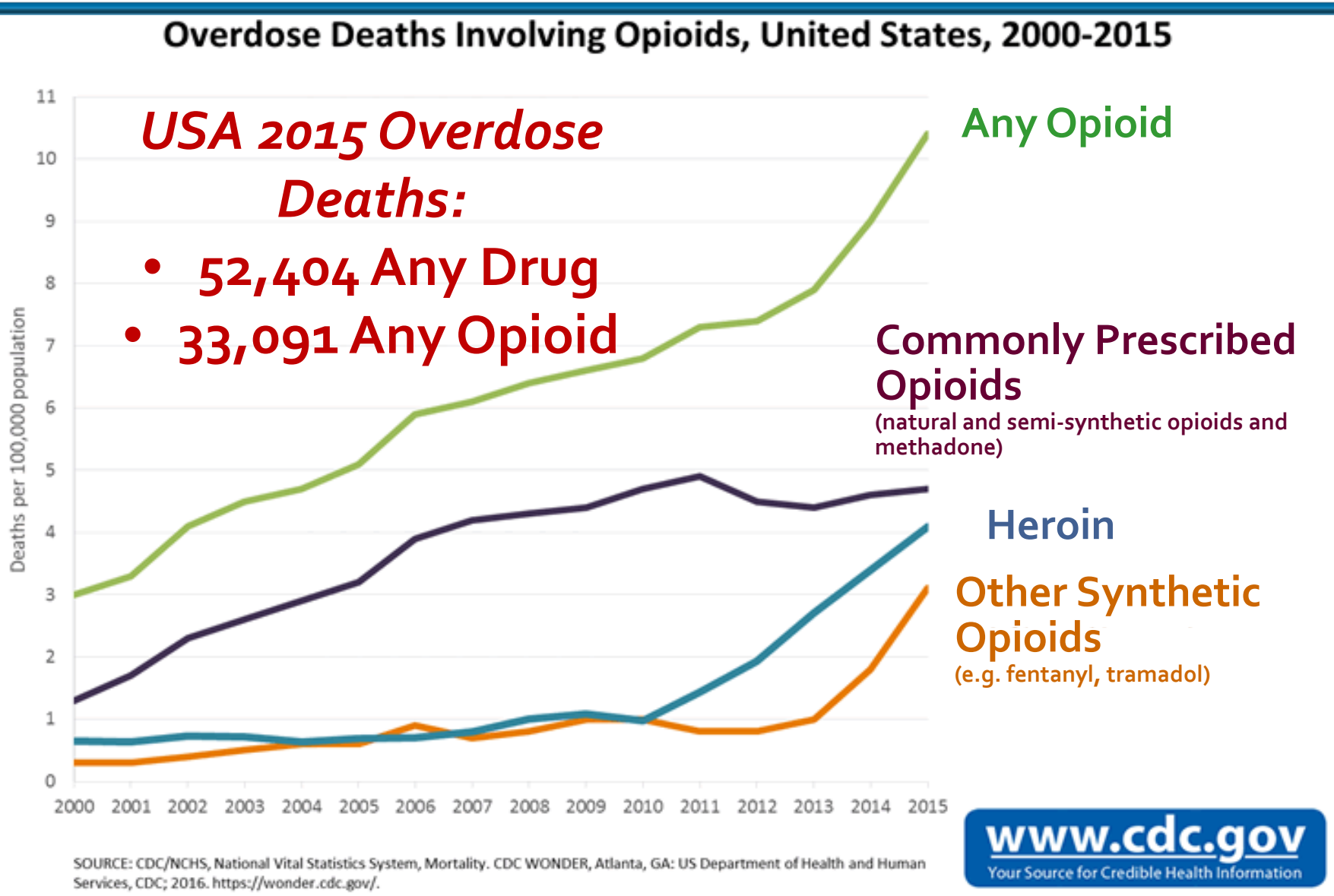
March 14, 2018

The opinions and information in this presentation are my own and do not necessarily reflect the views and policies of the FDA

Overall Messages

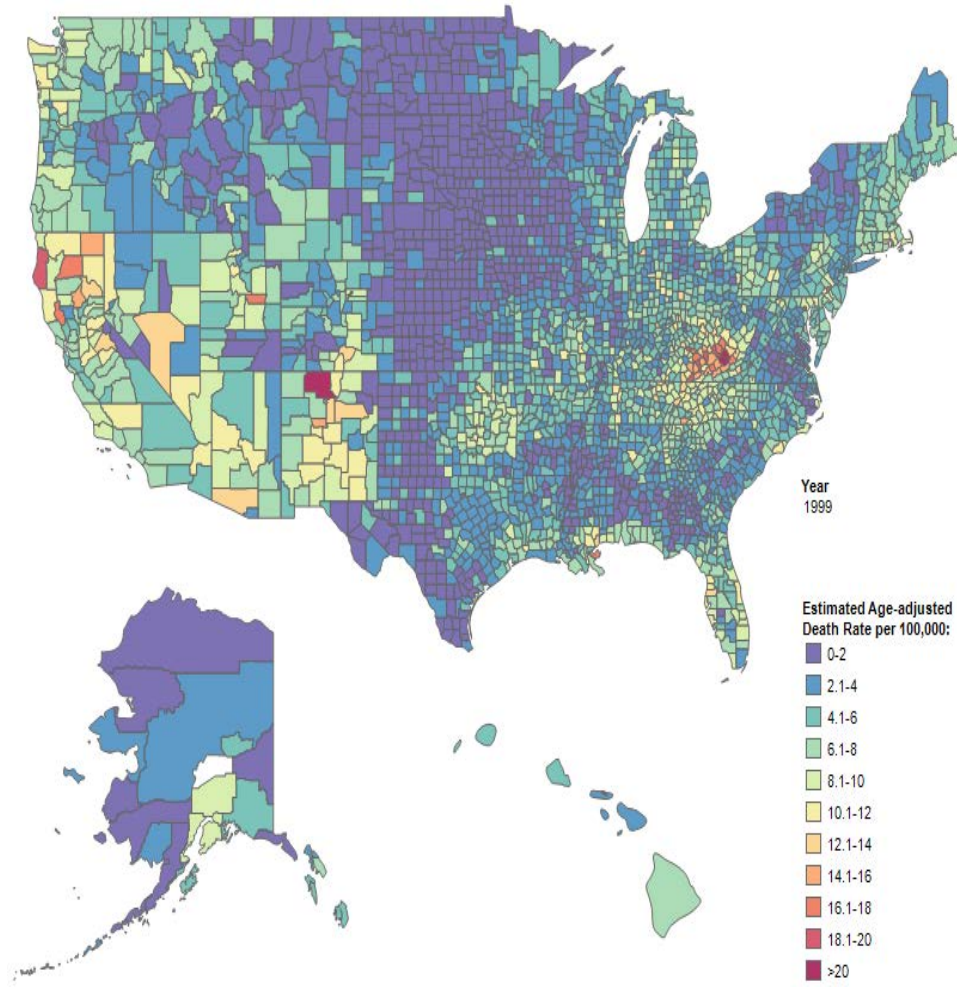
- The FDA work to improve the safe use of opioids is taking place within a larger policy framework aimed at addressing opioid abuse while assuring appropriate access to effective pain treatment
- Ongoing and planned activities reflect the commitment by FDA to use of all of our available tools to appropriately manage pain while also addressing the opioids crisis

Marked *Increases in Prescription Opioid and Heroin Overdose Deaths* in the USA 2000 to 2015

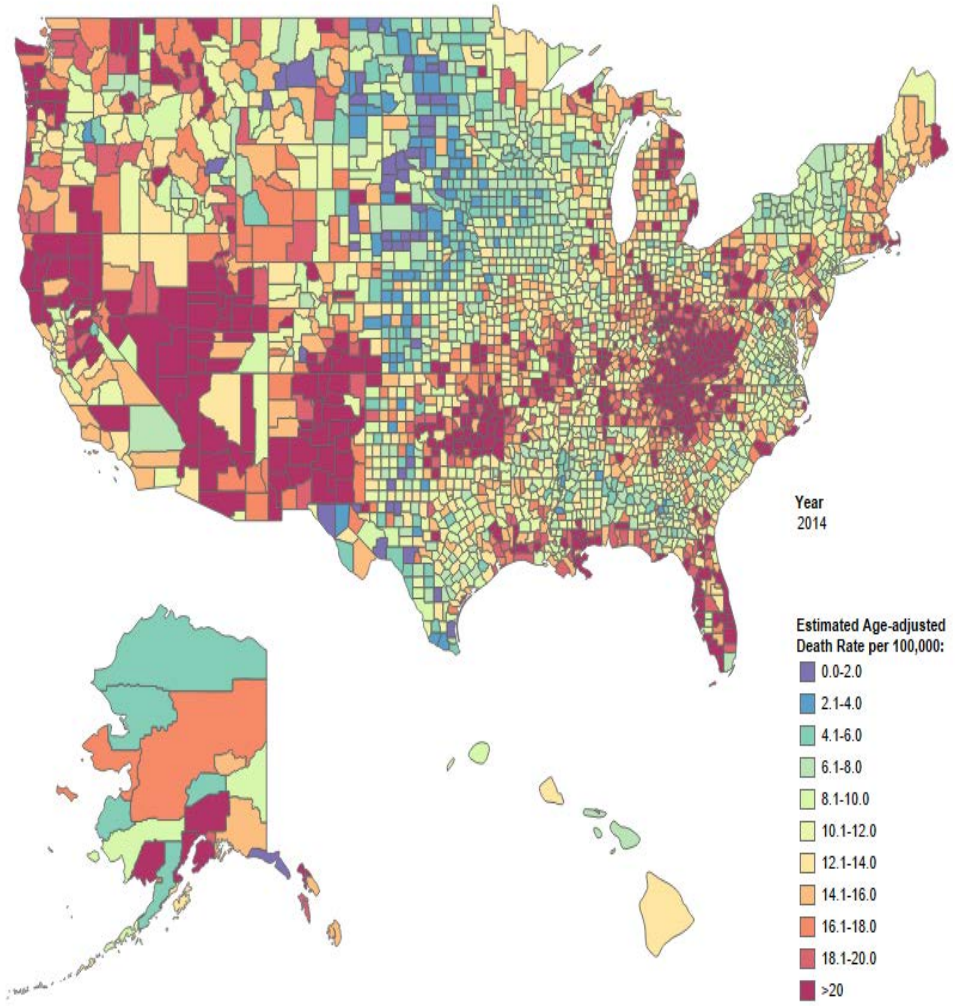


Overdose Death Rates

1999



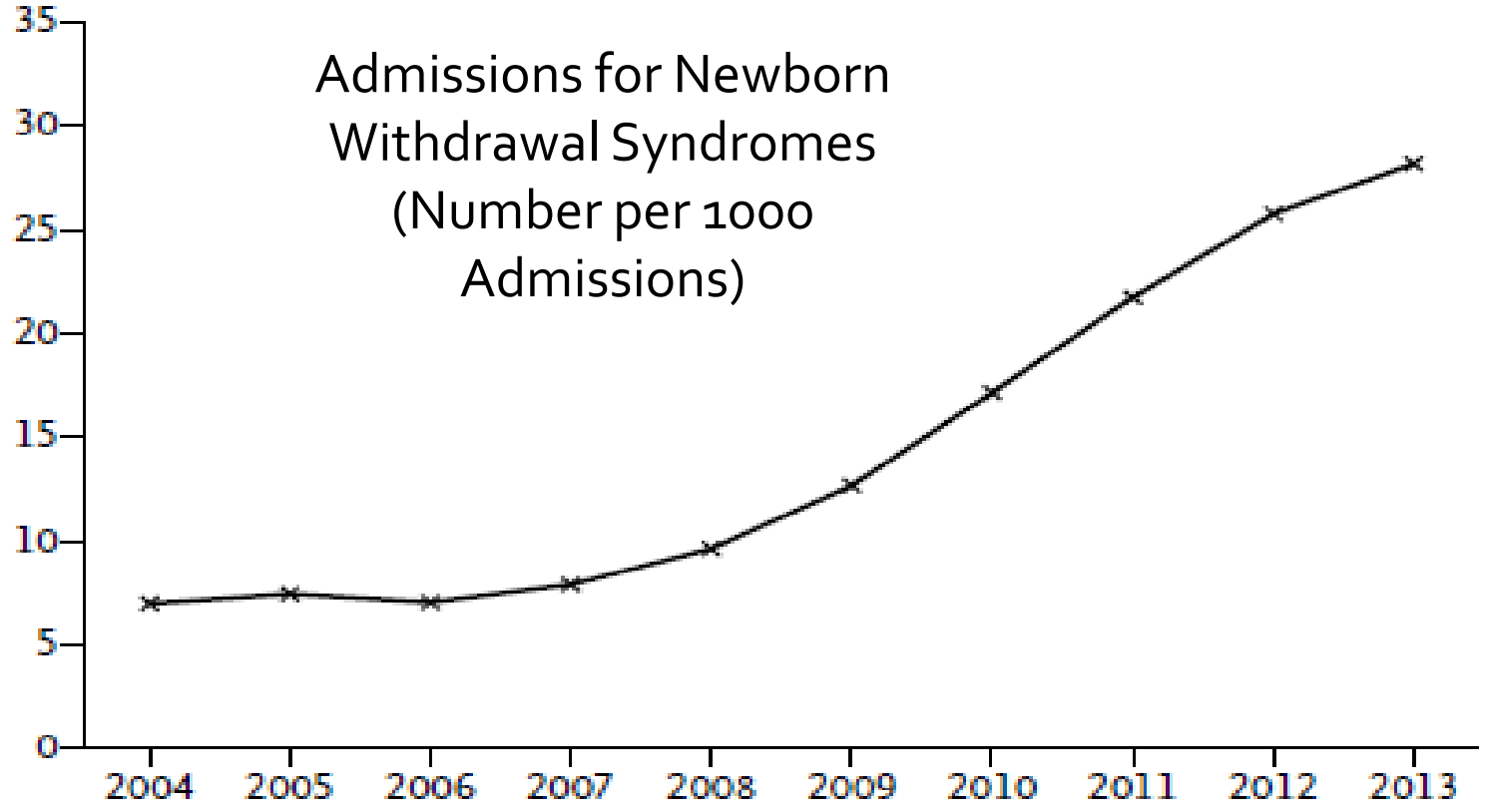
2014



Designed by L. Rossen, B. Bastian & Y. Chong. SOURCE: CDC/NCHS, National Vital Statistics System

Science = Solutions

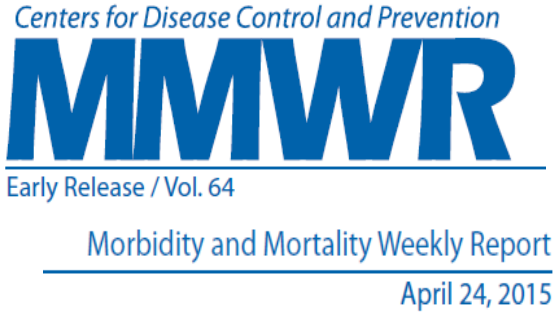
Impact of Crisis: Increasing Prenatal Exposure



Tolia VN, Patrick SW, et al. NEJM 2015;372:2118-2126

Impact of Crisis: Infectious Disease Transmission

HIV and Hepatitis C Outbreak Linked to Oxymorphone Injection Use in Indiana, 2015



Peters et al.

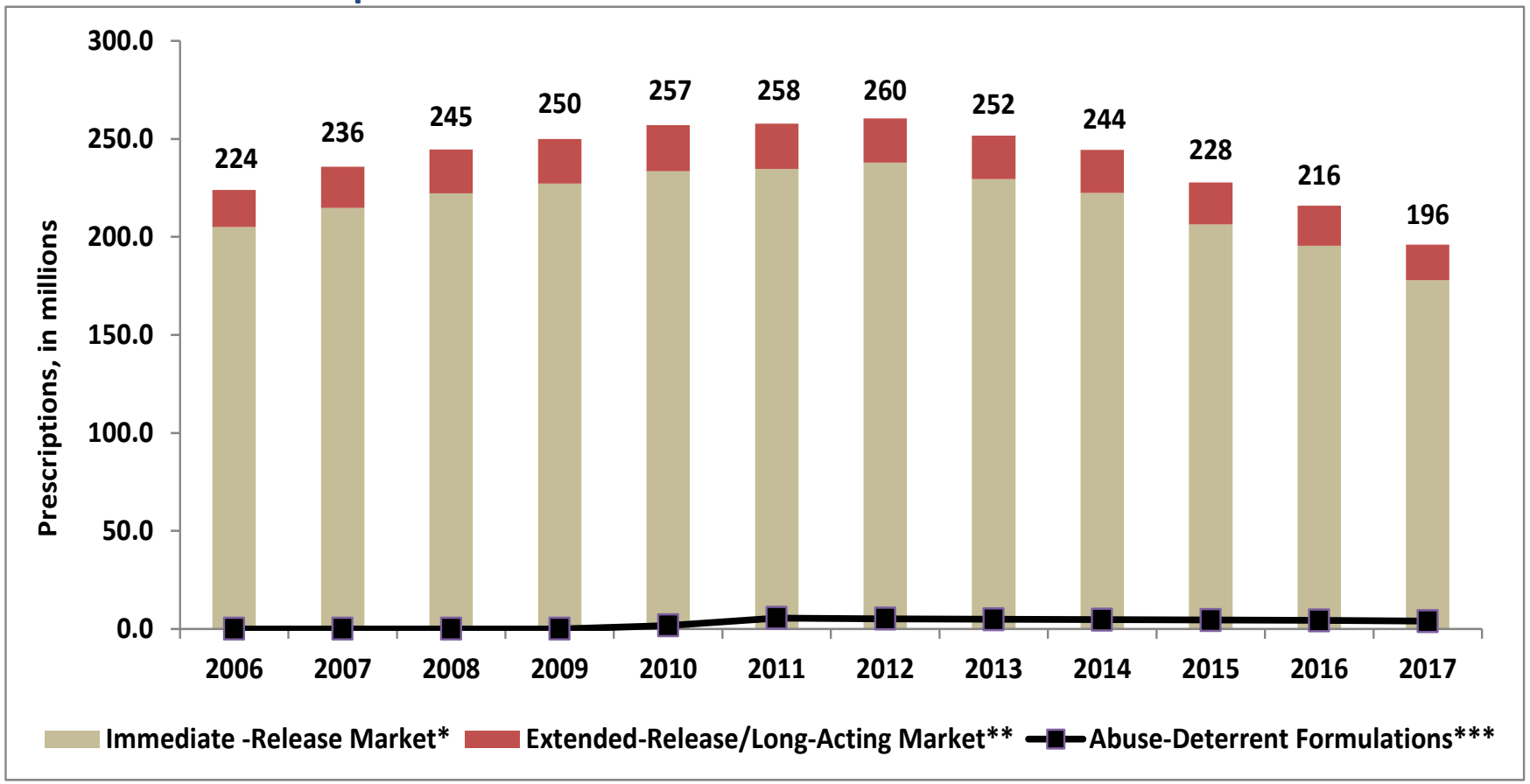
The New England Journal of Medicine

2016;375:229-239

U.S. Prescribing Rates - Trends

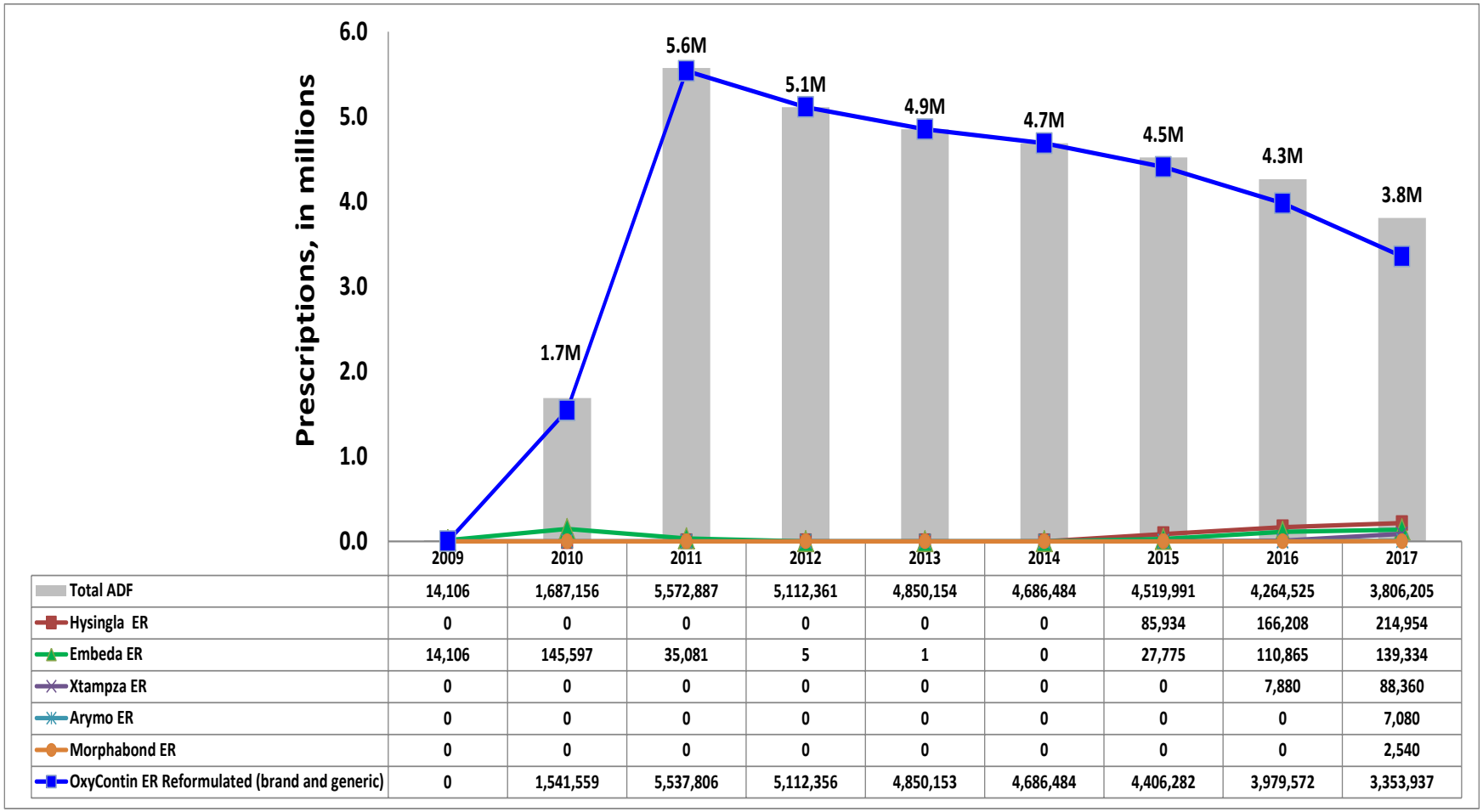
- U.S. prescribing rates peaked in 2012 at 81.3 prescriptions per 100 persons[11]
  - Total: 255 million prescriptions
- Opioid prescribing has been decreasing between 2012 and 2016.
- U.S. prescribing rate in 2016 was 66.5 prescriptions per 100 people
  - 214 million prescriptions
- Rates continue to vary widely
  - Some counties had rates 7 times the national average

Nationally Estimated Number of Prescriptions Dispensed for Opioid Analgesics Products from U.S. Outpatient Retail Pharmacies



Source: IQVIA, National Prescription Audit (NPA) and static data 2006-2011. January 2006-December 2017.
Static data extracted March 2017 and 2012-2017 data extracted February 2018.
*Immediate-Release formulations include oral solids, oral liquids, rectal, nasal, and transmucosal
**Extended-Release/Long-Acting formulations include oral solids and transdermal patches
***Abuse-deterrent formulation opioid products include Arymo ER, Embeda ER, Hysingla ER, Morphabond ER, Xtampza ER, OxyContin ER Reformulated (Approval in April 2010)
Note: Include opioid analgesics only, excluding injectable formulations as well as opioid-containing cough-cold products and opioid-containing medication-assisted treatment (MAT) products

Nationally Estimated Number of Prescriptions Dispensed for Abuse-Deterrent Formulation (ADF) Opioid Analgesic Products* from U.S. Outpatient Retail Pharmacies



	2009	2010	2011	2012	2013	2014	2015	2016	2017
Total ADF	14,106	1,687,156	5,572,887	5,112,361	4,850,154	4,686,484	4,519,991	4,264,525	3,806,205
Hysingla ER	0	0	0	0	0	0	85,934	166,208	214,954
Embeda ER	14,106	145,597	35,081	5	1	0	27,775	110,865	139,334
Xtampza ER	0	0	0	0	0	0	0	7,880	88,360
Arymo ER	0	0	0	0	0	0	0	0	7,080
Morphabond ER	0	0	0	0	0	0	0	0	2,540
OxyContin ER Reformulated (brand and generic)	0	1,541,559	5,537,806	5,112,356	4,850,153	4,686,484	4,406,282	3,979,572	3,353,937

Source: IQVIA, National Prescription Audit™, Years 2009-2017. Data Extracted February 2018.

*ADF Products not marketed during study period: RoxyBond (Oxycodone IR) - Approved 04/2017; Targiniq ER (oxycodone/naloxone ER) - Approved 07/2014; Troxyca ER (Oxycodone/naltrexone ER) - Approved 08/2016; Vantrela ER (Hydrocodone ER) - Approved 01/2017

Equally Critical Social and Medical Issue: Pain in America

- From the Functioning and Disability Supplement of the 2012 National Health Interview Survey
  - 126.1 million adults reported some pain in the previous 3 months
  - 25.3 million adults (11.2%) suffering from daily (chronic) pain
  - 23.4 million (10.3%) reporting a lot of pain.
  - Based on the persistence and bothersomeness of their pain, 14.4 million adults (6.4%) were classified as having the highest level of pain, category 4, with an additional 25.4 million adults (11.3%) experiencing category 3 pain.

Nahin RL, J.Pain, 2015 Aug;16(8):769-80

Pain in America (cont)

- Treatment options for pain: pharmacologic, physical medicine, behavioral medicine, neuromodulation, interventional, and surgical
- Optimal patient outcomes often result from a comprehensive multidisciplinary approach where pharmacologic treatment is not the sole focus
- Patients experience ongoing barriers to adequate pain management
  - "many related to non-existent or insufficient insurance coverage and reimbursement for evidence- and consensus-based therapies"

    -American Academy of Pain Medicine, 2014
- As a result, treatments have largely focused on prescription drugs, mainly opioids, and procedures, at least, in part, because of the reimbursement structure of our healthcare system

FDA Response to this Crisis

"Unquestionably, our greatest immediate challenge is the problem of opioid abuse. This is a public health crisis of staggering human and economic proportion … we have an important role to play in reducing the rate of new abuse and in giving healthcare providers the tools to reduce exposure to opioids to only clearly appropriate patients, so we can also help reduce the new cases of addiction."

- Scott Gottlieb, FDA Commissioner
  Address to FDA staff, May 15, 2017

The Opioid Crisis: An FDA Priority

Take immediate steps to reduce the scope of the epidemic of opioid addiction

- **May 2017:** Established an FDA Opioid Policy Steering Committee (OPSC)
- **2017-2018:** Soliciting public input on how **FDA authorities** can or should be **used to address the crisis**
  - **Sept 2017, January 2018: Public meetings**
  - **December 2017: Packaging solutions**
  - **February 2018: Healthcare system solutions**

The Opioid Crisis: FDA's Priorities

1. Decreasing Exposure & Prevent New Addiction

2. Supporting the Treatment of Those With Opioid Use Disorder

3. Fostering the Development of Novel Pain Treatment Therapies

4. Improving Enforcement & Assessing Benefit-Risk

FDA Priorities align to HHS Strategic Priorities and other National Activities

HHS STRATEGIC PRIORITIES	*FDA PRIORITIES*	*OTHER ACTIVITIES*
Strengthening public health surveillance	1. Decreasing Exposure & Prevent New Addiction	President's Commission on Combating Drug Addiction
Targeting availability and distribution of overdose-reversing drugs	2. Supporting the Treatment of Those With Opioid Use Disorder	Office of National Drug Control Policy Recommendations
Supporting cutting-edge research	3. Fostering the Development of Novel Pain Treatment Therapies	Comprehensive Addiction and Recovery Act (CARA)
Improving access to treatment and recovery services	4. Improving Enforcement & Assessing Benefit-Risk	National Pain Strategy Recommendations
Advancing the practice of pain management		National Public Health Emergency

1. Decreasing Exposure and Prevent New Addiction

	HOW?	*WHAT?*
Appropriate Dose/Duration Labeling	• **Facilitate appropriate prescribing** of opioid analgesics. • Evaluate **indication specific doses**.	• **Jan 30, 2018:** FDA **public meeting** to gain input on how FDA's authorities could **facilitate appropriate prescribing**. • **Feb 15, 2018:** Duke Margolis **public workshop** – "Strategies for Promoting the **Safe Use** and **Appropriate Prescribing** of Prescription Opioids".
Appropriate Packaging, Storage, and Disposal	• Explore how opioid analgesic drug products are **packaged, stored, and discarded**. • Examine use of packaging strategies, such as **unit-of-use packaging** to improve opioid analgesic safety.	• **Jun 1, 2017:** FDA/Duke Margolis **workshop and white paper** on packaging, storage, and disposal solutions. • **Dec 11-12, 2017:** FDA **public workshop** to gain input on **packaging strategies**.

1. Decreasing Exposure and Prevent New Addiction

Health Care Provider Education

HOW?	*WHAT?*
• Consider appropriateness of **mandatory education** and **how FDA would operationalize** such a requirement. • Ensure **training** is made **available to non-physician prescribers**, including nurses and pharmacists.	• **May 9-10, 2017:** FDA **public workshop** on pain management training. Issued **revised Blueprint**. • **Sept 28, 2017:** FDA issued **letters** notifying sponsors of IR opioids their drugs will be subject to more stringent set of requirements under REMS & should be approved Sept 2018. The **training** must be made available to **health care providers** who prescribe **IR opioid analgesics**.

2. Supporting the Treatment of Those With Opioid Use Disorder

	HOW?	*WHAT?*
Naloxone	• Exploring ways to **expand access** to naloxone and **facilitate the switch** to **OTC naloxone**.	• **Precedent setting research**: **FDA-led labeling study** to facilitate the **switch** from prescription to **OTC naloxone**.
Medication Assisted Treatment (MAT)	• Facilitate the development of **new MAT options**. • Take steps **promote the more widespread use** of existing, safe and effective, FDA approved therapies. • Join efforts to **break the stigma** associated with medications used for treatment of addiction.	• Issuing Guidances for product developers to **facilitate the development of new treatments**. • NIH **collaboration** to identify **new endpoints** in MAT drug development and **facilitate new formulations**.

3. Fostering the Development of Novel Pain Treatment Therapies

Partnerships & Meetings

HOW?	*WHAT?*
• Expand use of partnerships with **non-profit organizations**, **public** meetings, and **Advisory Committee** meetings. • **Collaborate** across HHS.	• **FDA grant** supporting Drug-Free Kids campaign. • **Public-private-partnership (PPP) with NIH and developers** under the Critical Path initiative. • **Jul 2017:** Commissioned NASEM **consensus report**. • **Feb 14, 2018: Advisory Committee** meeting for Hydexor (hydrocodone/APAP/promethazine) – for short term **management** of **acute pain** while **preventing** and **reducing** opioid-induced **nausea** and **vomiting**.

3. Fostering the Development of Novel Pain Treatment Therapies

	HOW?	WHAT?
Abuse Deterrent Formulations (ADFs)	• Support development of **innovative** ADFs, **data** to inform benefit-risk assessment, and **transition to an ADF-prominent market**. • Ensure ADF **label nomenclature** enables providers to adequately distinguish between the risk of abuse and the risk of addiction.	• **Jul 2017: Public workshop** for postmarketing **ADF data and evaluation methods**. • Issued final **guidance** on **generic ADFs**. • **2018:** Contracts to improve **data for ADF assessment** and understand **nomenclature**.
Pain Treatment Alternatives	• Explore use of Fast Track and Breakthrough Therapy Designations. • Encourage novel therapies, including **medical devices**.	• **Summer 2017:** FDA/NIH **meeting series** on pain treatment alternatives.

4. Improving Enforcement & Assessing Benefit-Risk

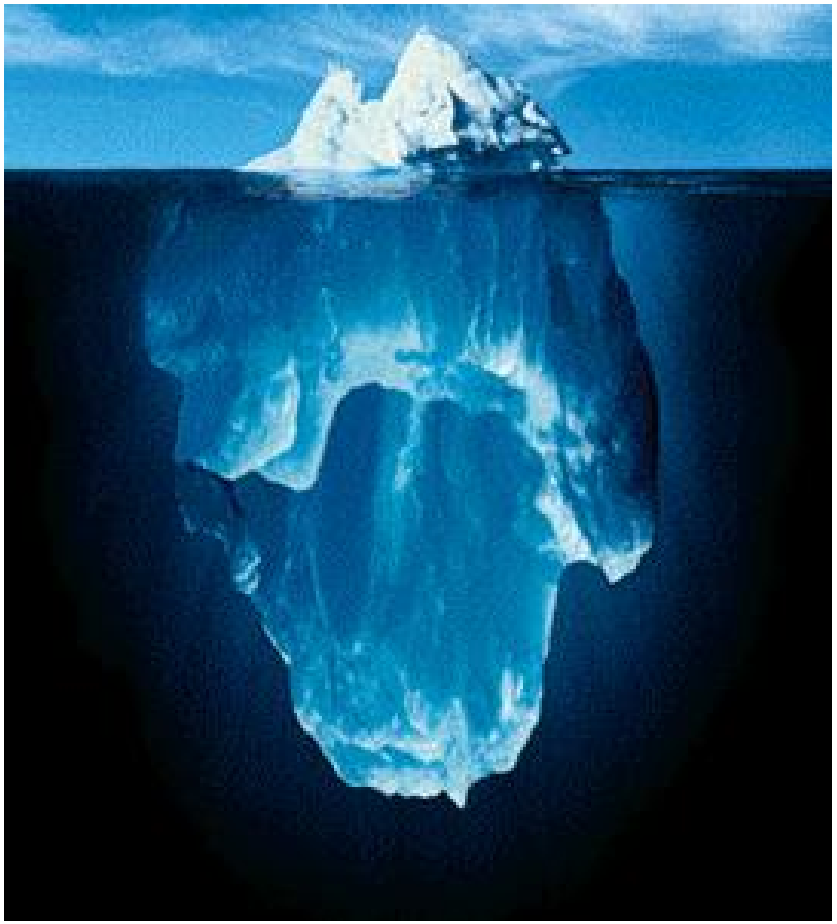
	HOW?	*WHAT?*
Improving Enforcement	• Consider how to fully **leverage** FDA's current **seizure authorities**. • Increase oversight of **Illicit** trade.	• **Collaboration** with Customs and Border Protection to **increase FDA staff** stationed at international mail facilities (IMFs) to increase **seizure of opioids** being smuggled into the United States through **international mail facilities (IMFs)**.
Assessing Benefit-Risk	• **Take action**, including product market **withdrawal recommendation**. • **Improve robustness** of **benefit-risk assessment framework** for opioid analgesic formulations.	• **Jun 2017:** Requested market **withdrawal** of Opana ER due to **abuse risks**. • **Sep 2017:** Pediatric **Advisory Committee** for hydrocodone or codeine containing cough treatment in **pediatric patients**.

FDA Will Use All of its Available Tools to Accomplish These Goals

- Improving the safe use of opioids through careful and appropriate regulatory activities
- Improving the safe use of opioids through careful and appropriate policy development
- Improving the treatment of pain through improved science
- Improving the safe use of opioids through communication, partnership and collaboration

Solutions Must Come from Many Sources

- FDA is one of many Federal agencies addressing issues involving opioids
- Many Federal Agencies working together on issue
- Each state has programs to address opioids
- Guidelines and educational programs are available from specialty societies and State Medical Boards
- Healthcare institutions
- Advocacy groups
- Individual providers (n = 800,000+)
- Patients (n = millions)



Summary and Conclusions

- FDA working to address opioid epidemic as a part of the larger HHS response
  - One of the FDA's very highest priorities
  - FDA one of many groups focused on the issue
- Going forward, FDA is committed to taking decisive actions, grounded in the available science and appropriate public input to address this critical challenge to the US health and welfare
- Our focus is addressing opioid abuse while assuring appropriate access to effective pain treatment

Thank You

Exhibit K

Abuse-Deterrent Opioid Analgesics

The FDA is encouraging the development of prescription opioids with abuse-deterrent formulations (ADFs) to help combat the opioid crisis. The agency recognizes that abuse-deterrent opioids are not abuse- or addiction-proof but are a step toward products that may help reduce abuse. The FDA fully supports efforts to better understand the impact of these products in the real-world setting and convened a **public workshop on July 10-11, 2017 (/Drugs/NewsEvents/ucm540845.htm)**, to discuss the current data and methods for evaluating ADF products postmarketing and what can be done to improve national data and methods moving forward.

The FDA also supports the development of innovative formulations that have the potential to make abuse of these products more difficult or less rewarding. This does not mean a product is impossible to abuse or that abuse-deterrent properties necessarily prevent addiction, overdose, and death. Notably, currently marketed technologies do not effectively deter one of the most common forms of opioid abuse -- swallowing the tablet or capsule. Because opioid medications must in the end be able to deliver the opioid to the patient, there may always be some potential for addiction and abuse of these products.

What does abuse-deterrent really mean?
Abuse-deterrent formulations target the known or expected routes of abuse, such as crushing in order to snort or dissolving in order to inject, for the specific opioid drug substance. The science of abuse deterrence is relatively new, and both the formulation technologies and the analytical, clinical, and statistical methods for evaluating those technologies are rapidly evolving. The FDA is working with many drug makers to support advancements in this area and helping drug makers navigate the regulatory path to market as quickly as possible. In working with industry, the FDA is taking a flexible, adaptive approach to the evaluation and labeling of potentially abuse-deterrent products.

Opioids with FDA-Approved Labeling Describing Abuse-Deterrent Properties
FDA has approved these opioids with labeling describing abuse-deterrent properties consistent with the FDA's Guidance for Industry: Abuse-Deterrent Opioids – Evaluation and Labeling:

- **OxyContin (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=022272)**
- **Targiniq ER (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=205777)**
- **Embeda (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=022321)**
- **Hysingla ER (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=206627)**
- **MorphaBond ER (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=206544)**
- **Xtampza ER (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=208090)**
- **Arymo ER (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=208603)**

- **RoxyBond (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=209777)**

There are currently NO generic opioids with FDA-approved abuse-deterrent labeling.

How does the FDA decide what drugs are considered abuse-deterrent?
To meet the FDA's standards, it is essential that every opioid with labeling describing its abuse-deterrent properties be grounded in science and supported by evidence. Any claims regarding abuse-deterrent properties must be truthful and not misleading based on a product's labeling, and supported by sound science taking into consideration the totality of the data for the particular drug. Absent sufficient science, there can be no claim of abuse deterrence. Permitting insufficiently proven claims does not serve the public health.

The FDA has issued two guidances to help industry understand how the agency currently is evaluating these innovative products.

- "**Guidance for Industry: Abuse-Deterrent Opioids – Evaluation and Labeling (/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM334743.pdf)**" (final guidance) explains the FDA's current thinking about the studies that should be conducted to demonstrate that a given formulation has abuse-deterrent properties. It also makes recommendations about how those studies should be performed and evaluated, and discusses what labeling claims may be approved based on the results of those studies.
- "**General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products (/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM492172.pdf)**" (final guidance) includes recommendations about the studies that should be conducted to demonstrate that a generic opioid is no less abuse-deterrent than the brand name product, with respect to all potential routes of abuse.

How will abuse-deterrent opioids help with the epidemic?
Because abuse-deterrent products are expected to reduce abuse compared to non-abuse-deterrent products, the agency is very interested in exploring new methods for analyzing and evaluating abuse-deterrent features; evaluating the nomenclature use to describe abuse-deterrent features; facilitating development of science for generic versions of these drugs; and taking new steps to encourage the conversion of the market to effective ADFs as part of the FDA's Opioid Policy Work Plan. The FDA looks forward to a future in which most or all opioid medications are available in formulations that are less susceptible to abuse than the formulations that are on the market today. To achieve this goal, FDA is taking steps to incentivize and support the development of opioid medications with progressively better abuse-deterrent properties. These steps include working with individual sponsors on promising abuse-deterrent technologies; developing appropriate testing methodologies for both innovator and generic products; and publishing guidance on the development and labeling of abuse-deterrent opioids.

We continue to encourage the development of innovative abuse-deterrent technologies, and we are also prioritizing the need for data that will help determine the impact of products incorporating abuse-deterrent technology on misuse and abuse. To collect this important information, all the companies that have brand name opioids with abuse-deterrent labeling claims are being required to conduct post-market studies to determine the impact those products are having in the real world. Having that information is critical and will allow us to take the next important steps in this area.

In addition, FDA supports the development of assessment tools to evaluate packaging, storage, delivery, and disposal solutions, as well as product formulations, designed to prevent and deter misuse and abuse of opioids. To further this effort, the agency held a **public workshop on December 11-12, 2017 (/Drugs/NewsEvents/ucm571797.htm)**, regarding the role of packaging, storage, and disposal options within the larger landscape of activities aimed at addressing abuse, misuse, or inappropriate access of prescription opioid

drug products. **A Broad Agency Agreement was amended (https://www.fbo.gov/index?s=opportunity&mode=form&id=62f0f64bbb3aff58da7ba3569f099485&tab=core&_cview=1)** to add this additional area of research to those previously noted to be of interest to FDA to address our current knowledge gap in this area.

More in Postmarket Drug Safety Information for Patients and Providers (/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/default.htm)

Index to Drug-Specific Information (/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111085.htm)

Exhibit L

FDA Analysis of Long-Term Trends in Prescription Opioid Analgesic Products: Quantity, Sales, and Price Trends

March 1, 2018

Introduction

To provide improved understanding and support Agency efforts to address the current opioids crisis, we have assembled a dataset of sales and quantities of retail prescription opioid analgesics sold spanning 25 years. This report summarizes data and methods that we use to evaluate the trends in sales, volume, and prices of prescription opioid analgesics over time.

Definitions of the retail prescription opioids analgesic market

The complexity of opioid risks, such as with misuse, abuse, addiction, overdose and death and the increasing rates at which they are occurring, all contribute to the significant public health burden of the opioid epidemic. Opioid products dispensed for outpatient use may be more likely to be misused and abused than opioid products used in the inpatient setting.[1] This may be due to greater availability and easier access and the difference in healthcare provider oversight in outpatient settings compared to inpatient settings. For example, for years 2012-2016, sales data, measured in dollars, of products sold from manufacturers to pharmacies and other settings of care show that sales to the retail setting accounted for the majority of annual opioid analgesic sales (>80%) and injectable formulations accounted for less than 0.2% of those sales.[2] Therefore, this analysis focuses on sales to the retail setting and includes all formulations of opioid analgesics except for injectable formulations, which are not commonly dispensed in an outpatient setting. Additionally, we focused on opioid analgesic products for the purposes of this analysis; opioid-containing products used as part of medication-assisted treatment (MAT) for opioid dependence and opioid-containing cough/cold products are not included in our analysis because of their different indications and patterns of use.

Results

Quantity

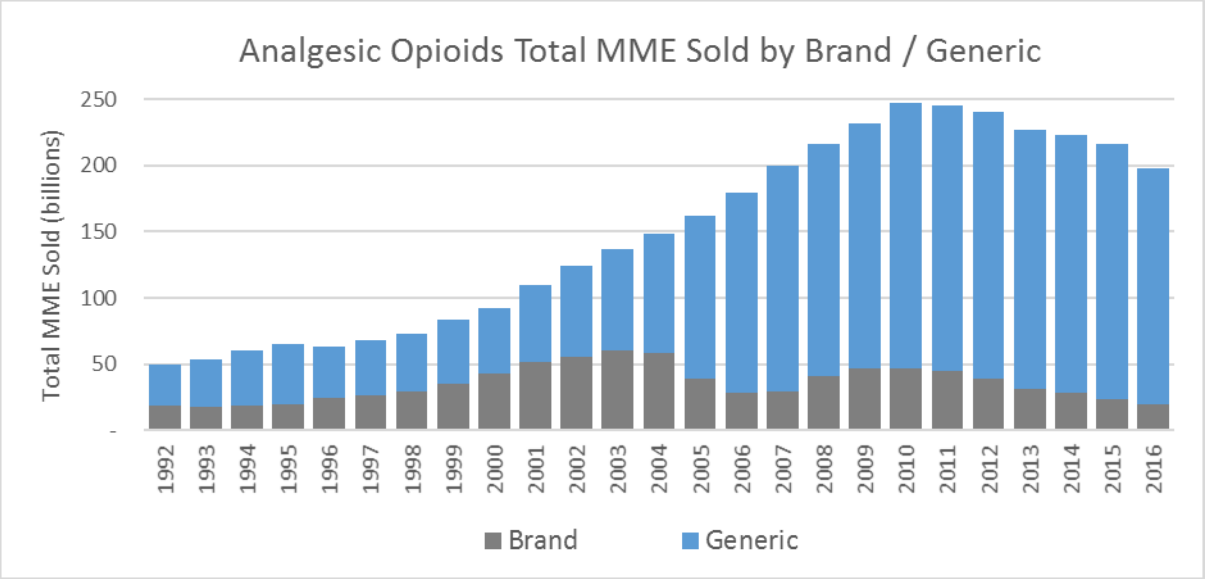
Quantities of analgesic opioids, as measured in morphine milligram equivalents (MMEs) sold from manufacturers to retail pharmacies gradually increased from nearly 50 billion MME in 1992 to about 73 billion MME in 1998, increased more steadily in 1999 – 2000 to 92 billion MME, and then rapidly increased by an average rate of more than 15 billion MMEs per year for the next decade, peaking at nearly 250 billion MME of opioids sold in 2010 (figure 1). Over the entire timeframe, generic versions of opioids were available for many of the opioid products on the market, and comprised most of the MMEs sold to pharmacies over the entire timeframe studied. The generic share of MMEs has steadily increased in the most recent timeframe with generics comprising 53% of MMEs sold in 2000, and rising

[1] Notification letters for the expansion of the Extended-release and long-acting opioid analgesic REMS https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm305245.htm.

[2] IQVIA National Sales Perspective (NSP). 2012-2016; extracted January 2018.

to account for over 90% of MMEs sold in 2016. Overall prescribing trends have similarly shown increased dispensing rates for generic drugs, including non-opioid drugs, during this interval.[3]

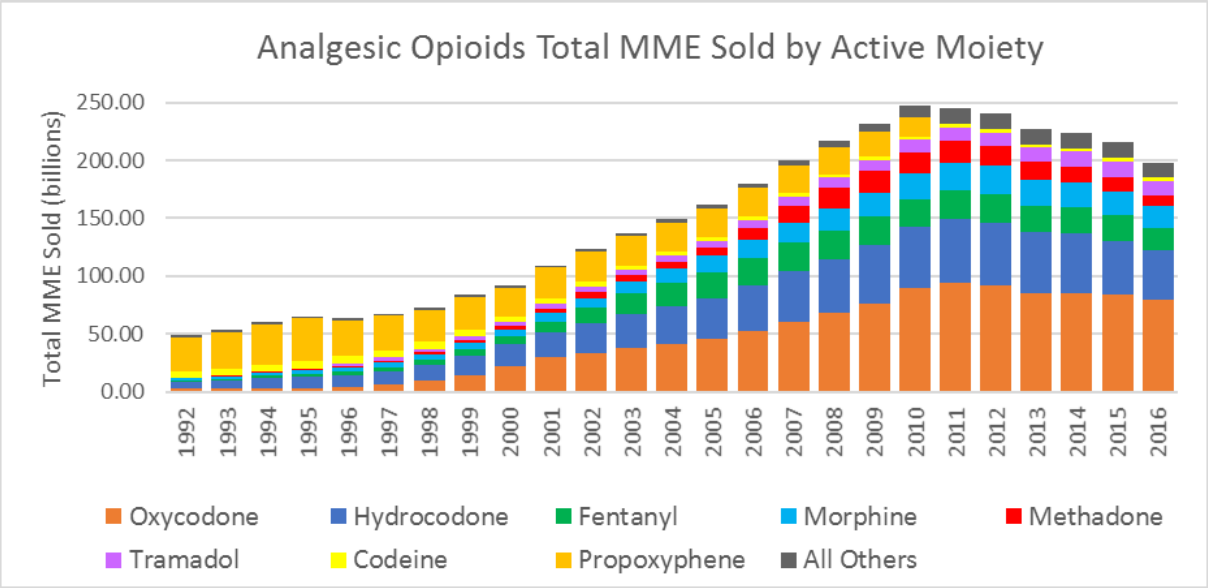
Figure 1: Total MMEs sold for aggregate opioid analgesic market – by brand / generic



The rapid uptake of opioids sold was primarily produced by a few key active moieties: oxycodone, hydrocodone, fentanyl, morphine, methadone, and tramadol (figure 2). Of these, oxycodone, hydrocodone, fentanyl, and morphine products, which comprised less than 25% of MME sold in 1992, grew to account for over 80% of MME sold by 2011. Propoxyphene, which is no longer marketed, comprised the majority of opioids MME sold between 1992 and 1995. Sales of propoxyphene products had gradually declined over time, until its removal from the US market in 2010 because of serious heart risks associated with its use.

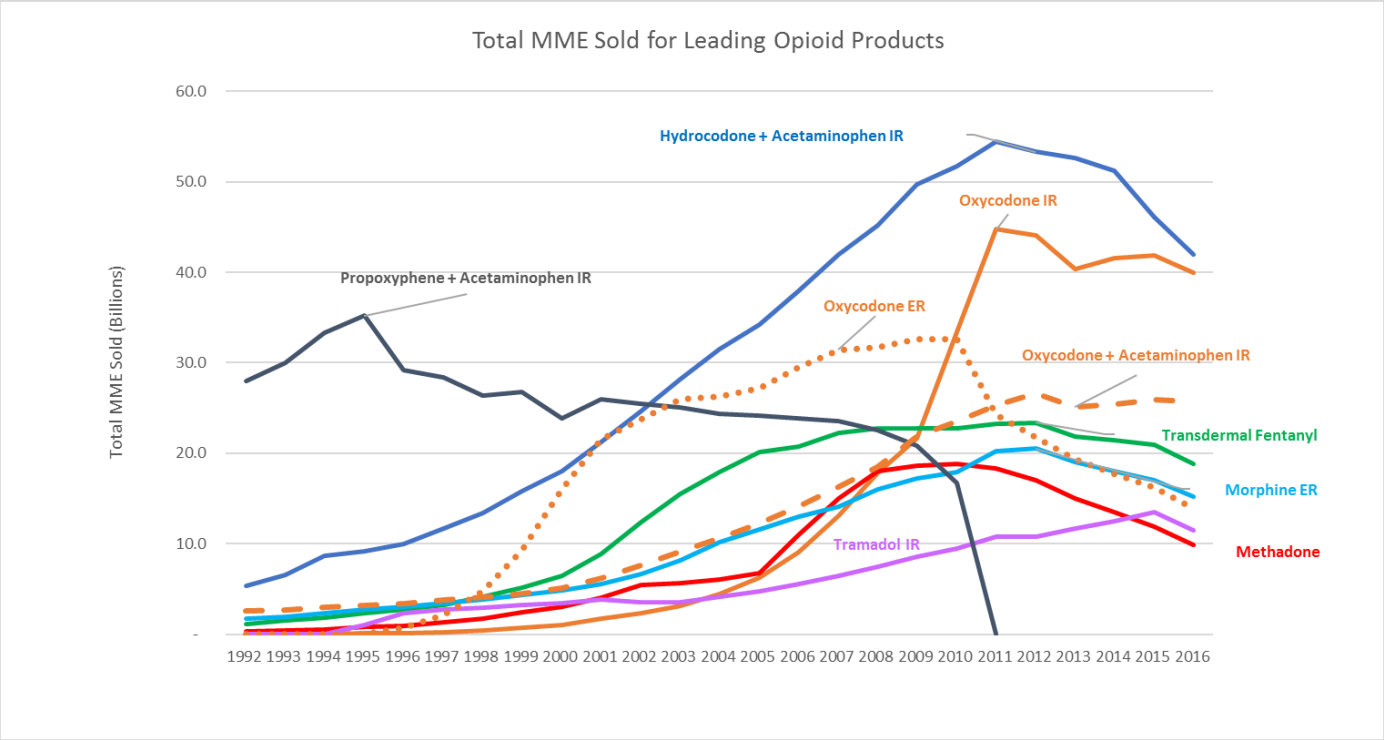
[3] Generic Pharmaceutical Association Annual Report 2014; http://www.gphaonline.org/media/wysiwyg/PDF/GPhA2014AnnualReport.pdf

Figure 2: Total MMEs sold for aggregate opioid analgesic market – by active moiety



Within these active moiety groupings, it is important to note that most of these opioids are marketed under multiple formulations, including immediate-release and extended-release versions as well as opioids in combination with other analgesics such as acetaminophen. To evaluate these aggregate trends at a more granular level, we identified specific products (i.e., the opioid active moiety and/or other analgesic, and the formulation, but not the strength), which comprised most MMEs sold for each opioid. (figure 3)

Figure 3: Total MME Sold for Leading Opioid Products



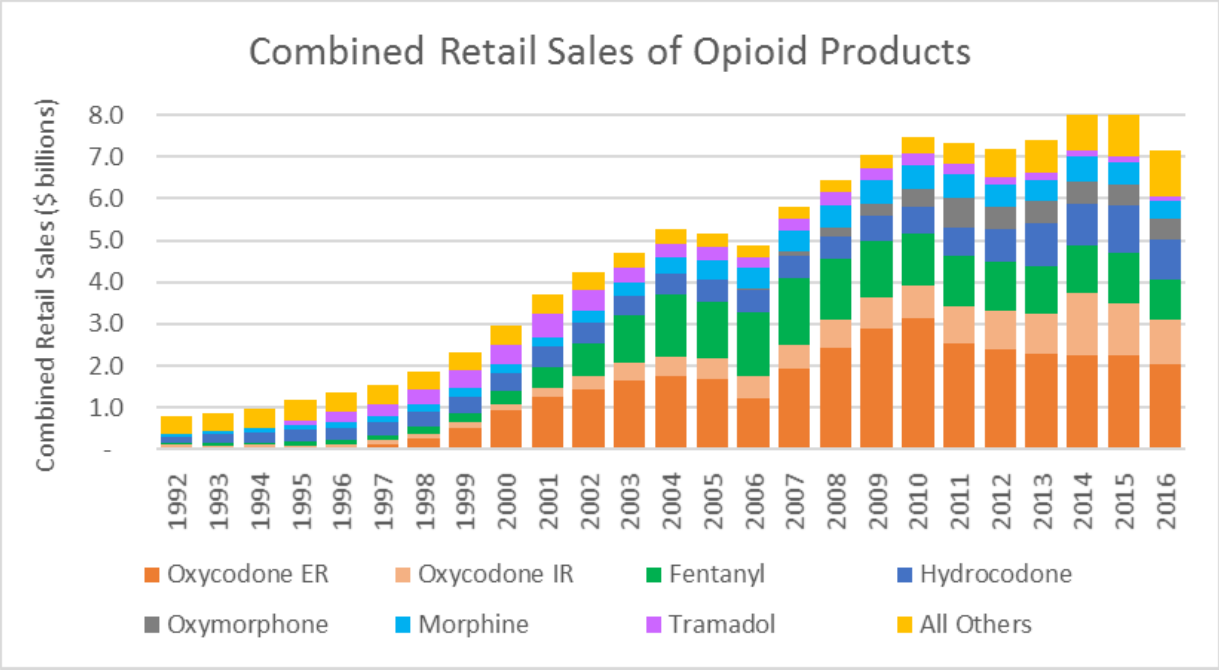
Particularly notable in figure 3 are the differences in the rates of change in quantities sold (in MME) of these different products and in the dates for the peak quantities sold, which precede 2016 for all products with the (apparent) exception of Oxycodone + Acetaminophen IR relative to the overall aggregate trends in opioid MME observed in figure 1. Changes in the annual total of morphine milligram equivalents sold may be due to a number of factors such as drug product, dosage, strength, or quantities ultimately prescribed and dispensed; further investigation is necessary to fully understand the complex factors contributing to these pattern changes over time.

Sales and Prices

We also evaluated total sales and quantities sold in MME to calculate average annual prices per MME for these products to see if any clear relationship between prices and sales volume were present. It is important to point out that the sales measures provided by IQVIA represent invoice prices that pharmacies pay to manufacturers and drug wholesalers, and not prices paid by patients or insurance providers. The price measure is interpretable as an average price per unit of analgesic relief, and is not the price of the pharmaceutical product per se. Unlike the standard price indices used by economists to measure the average price level of sundry goods, the measure $ / MME provides an interpretation based on equivalent analgesic effects across various opioid active moieties.

The retail opioid market had grown dramatically over this timeframe, from less than $1 billion in sales in 1992, peaking at $8 billion dollars in 2015 (Figure 4). Oxycodone and fentanyl products, which had combined retail sales of less than $150 million in 1992, accounted for $5 billion dollars in sales and over 70% of the retail opioid market share by 2009.

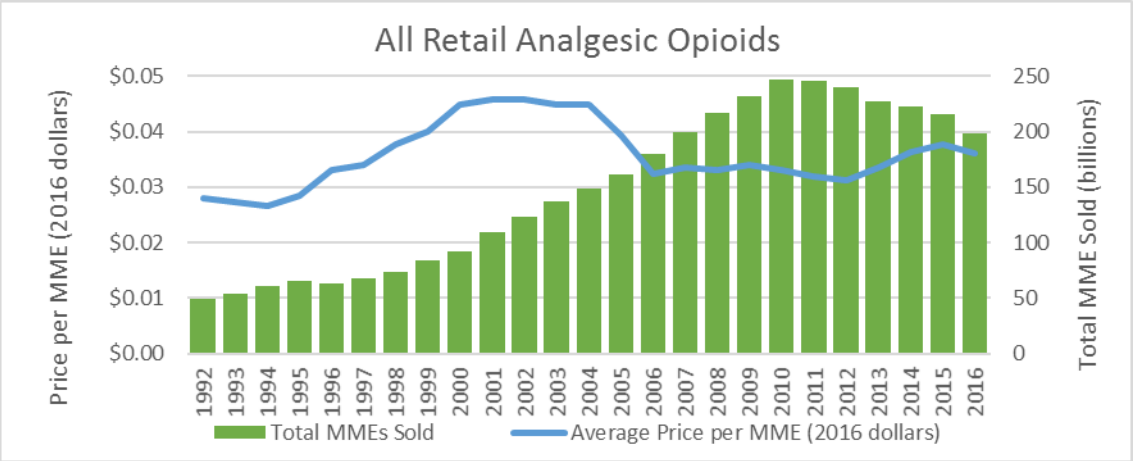
Figure 4: Combined Retail Sales of Analgesic Opioid Products



As shown in Figure 5a, the average price of retail analgesic opioids rose significantly from about 1993 to 2000. It then plateaued until 2004 before dropping to a new lower level for the years 2004 to 2005.

This trend shows no clear relationship with the total prescription retail analgesics sold as measured in MME.

Figure 5a: Total MMEs Sold and Price per MME for Aggregate Opioid Analgesic Market



We also decomposed average price by brand and generic version (figures 5b and 5c) and similarly find no clear price / quantity relationships, with prices for both brand and generic products generally increasing over time. The average price for generic opioids were found to be less than 2.5 cents per MME over the entire timeframe, while average brand prices ranged from roughly 6 cents per MME in 1992 to 12 cents per MME in 2012. Beginning in 2013, branded prices increased more sharply to 20 cents per MME in 2016.

Figure 5b: Total MMEs Sold and Price per MME for Brand Opioids

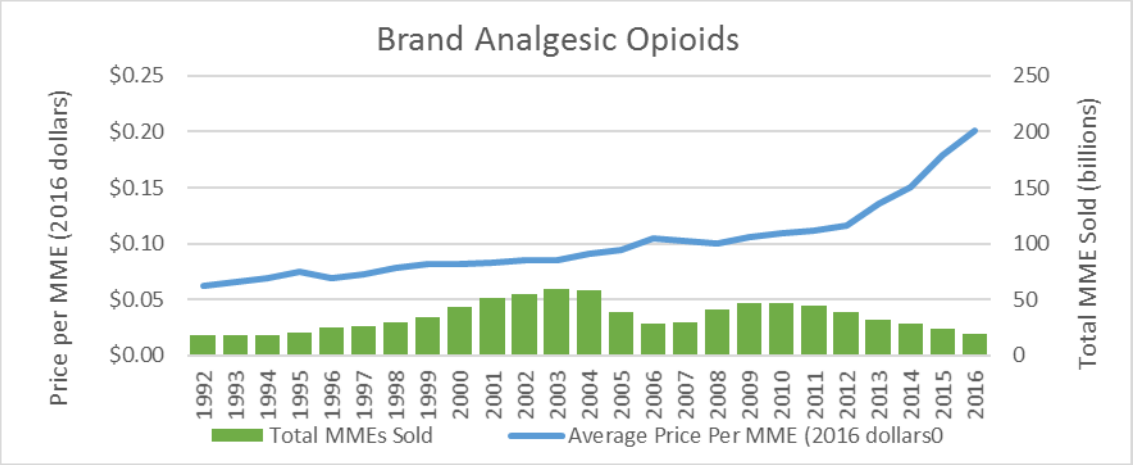
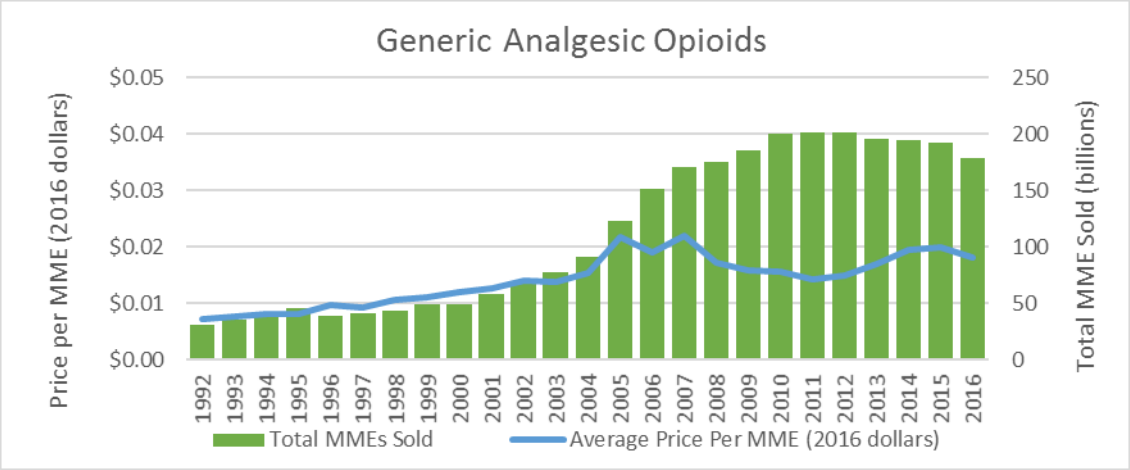
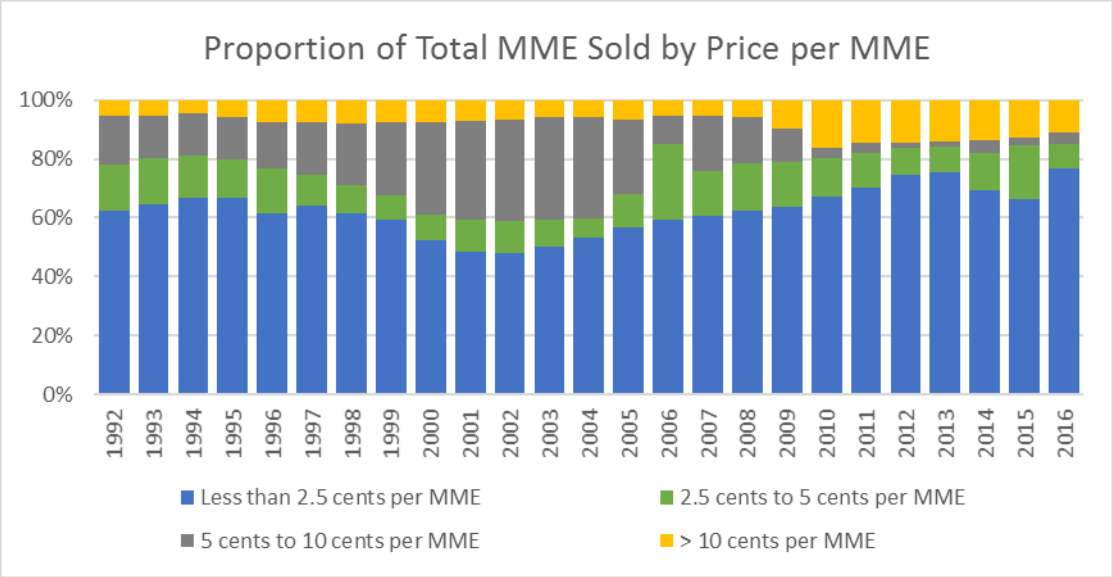


Figure 5c: Total MMEs Sold and Price per MME for Generic Opioids



Although no price / volume relationships are observable in the data, we do find that products having a lower price per MME tend to do well relative to higher-priced products. (Figure 6). In 1992, 78% of MMEs sold were for products with an average price of less than 5 cents per MME, with this ratio steadily declining to 59% by 2002. Beginning in 2003 that trend reversed and has steadily increased with 85% of MMEs sold in 2016 coming from products with an average price below 5 cents per MME.

Figure 6: Proportion of MMEs Sold by Average Price

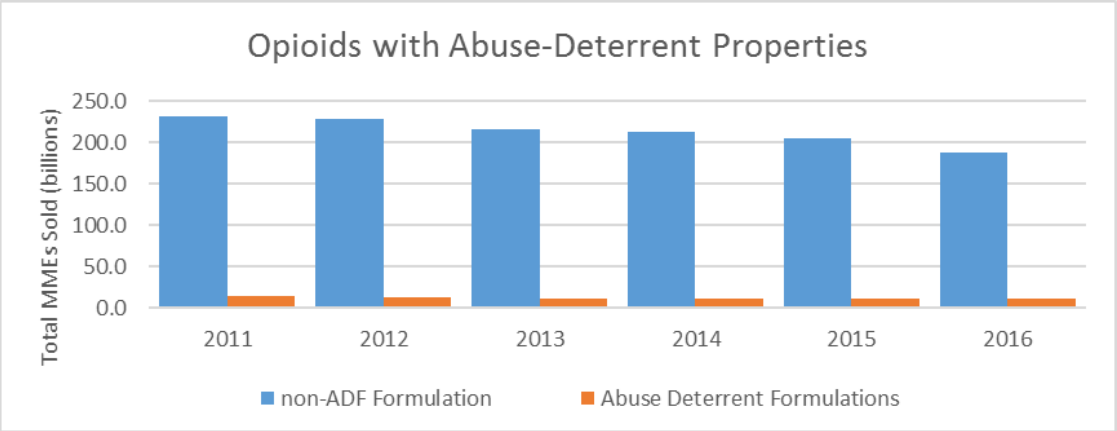


Formulation Trends

We also evaluated these data to quantify trends in use of abuse-deterrent formulations of opioid products. These formulations are intended to make certain types of abuse, such as crushing a tablet to snort or dissolving a capsule to inject, more difficult or less rewarding. For the purposes of our analysis we only included products which have received FDA-approved abuse-deterrent labeling. The science of

abuse deterrence is relatively new, and we evaluated these trends beginning in 2011 and found very low uptake of these new products, with only 5-6% of MMEs sold during that timeframe coming from ADF-formulated opioids. In 2016 the average price per MME for ADF formulated opioids was roughly 15 cents per MME, compared to only 3 cents per MME for non-ADF opioid products. There are currently no generic opioids with FDA-approved abuse-deterrent labeling.

Figure 7: Proportion of MMEs that are for Abuse Deterrent Properties



We also analyzed trends in MMEs sold for both immediate release (IR) opioids and extended release/long acting (ER/LA) opioids (Figure 8a and 8b). From 1992 – 2010 the quantity of MMEs sold for both IR and ER/LA opioids increased dramatically. However, during that timeframe, ER/LA opioids which comprised only 7% of MMEs sold in 1992, accounted for 1/3 of MMEs sold in 2000, and over 40% of MMEs sold by 2003 (figure 8c). While MMEs for ER/LA products began to decline in 2010, the decline in the quantity of IR MMEs did not begin until 2013. Over 60% of the roughly 50 billion MME decrease in MMEs sold observed from 2010 – 2016 are from decreased sales in ER/LA products.

Figure 8a: Total MMEs sold for Immediate Release (IR) Opioids

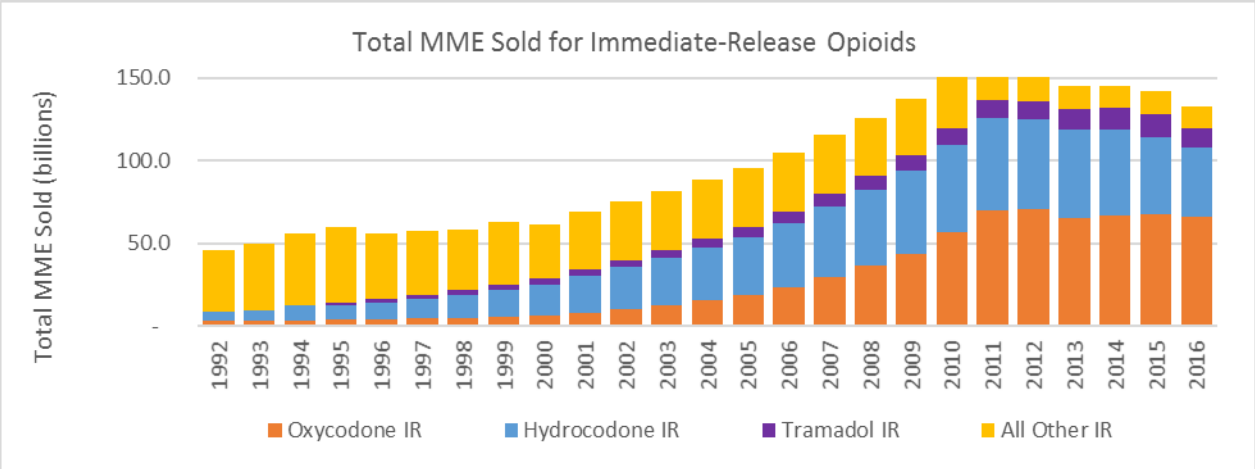


Figure 8b: Total MMEs sold for Extended Release / Long-Acting (ER/LA) Opioids

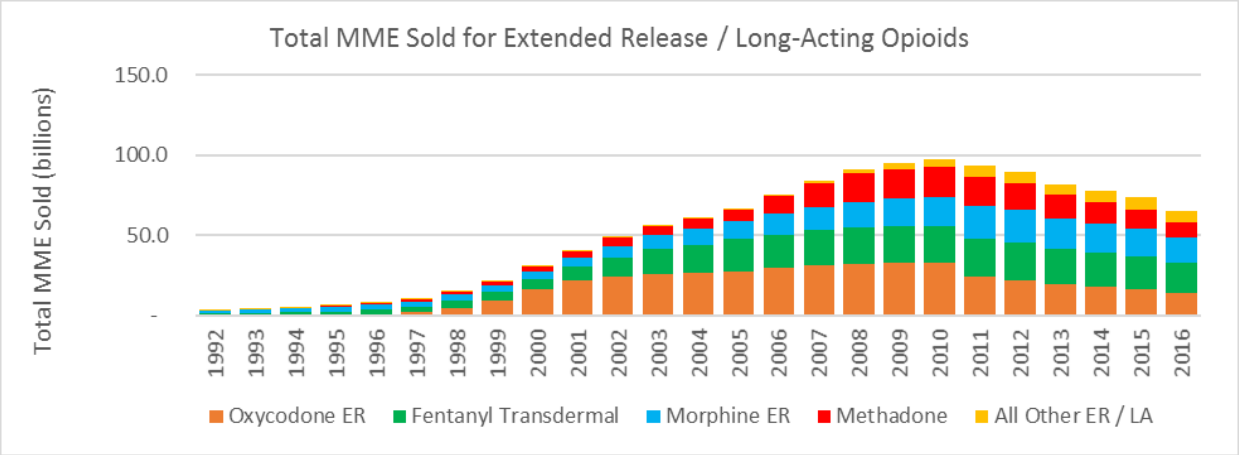
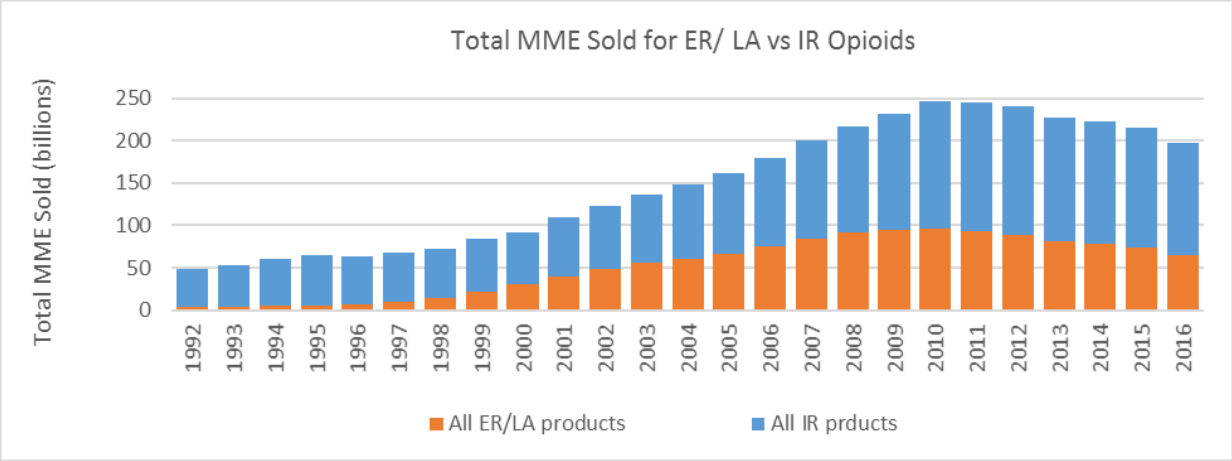


Figure 8c: Total MMEs sold by IR and ER / LA



Appendix:

Key characteristics of the IQVIA data file for the retail opioid analgesics market

Data was extracted from the IQVIA, National Sales Perspectives™: Retail and Non-Retail Database.

The IQVIA National Sales Perspectives™ measures the volume of drug products, both prescription and over-the-counter, and selected diagnostic products moving from manufacturers into various outlets within the retail and non-retail markets. Volume is expressed in terms of sales dollars, "eaches", which may be interpretable as bottles of pills, extended units, which may be interpretable as number of pills, and share of market. These data are based on national projections. Outlets within the retail market include the following pharmacy settings: chain drug stores, independent drug stores, mass merchandisers, and food stores.

Data were provided from 1992 – 2016 for all retail analgesic opioids grouped by molecule, formulation, manufacturer, and strength. Brand and generic drug identifiers were also provided. Annual measures of extended units sold and total sales dollars were provided for each product. The definitions of these variables are provided below.

Definitions of key IQVIA variables

Sales$

This variable is a measure of the amount of money non-retail and retail outlets spent on a drug product acquired from manufacturers and drug distributors/wholesalers based on the outlet's invoice for bulk order purchasing, since 1992.

Combined Molecule

This variable identifies products with a unique molecule or combination of molecules.

Strength

This variable identifies the different potencies or strengths. These are expressed in different ways depending on the presentation of the product, for example milligrams for oral tablets and capsules, milligrams per milliliter for oral and injectable liquids, micrograms per hour for transdermal products, and such.

Brand/Generic

This data element classifies products by their status as brand, generic, branded generic, or other, as classified by IQVIA. It enables identification of products by this status and reports on totals and trends for brand and generic products in a particular market.

Overall, this classification of products may differ from FDA's standard terminology based on whether a product approval derived from a New Drug Application or an Abbreviated New Drug Application (ANDA). IQVIA appears to classify all trade name products as brand or branded generic. "Generic" products appear to include only those products with no trade name. Products approved as NDAs and ANDAs are classified as "brand" prescriptions if they have a trade name, while prescriptions for products with no trade name, including some approved as NDAs are defined by FDA as "generic" prescriptions.

Extended Units

Extended units are the number of tablets, capsules, milliliters, ounces, etc. of a product shipped in each unit. Extended often are not meaningful above the package level, because a product may have different forms and strengths and, therefore, a different type of unit for each presentation.

Product Form

This data element refers to the physical dosage form of a drug, such as oral or injectable. This system consists of three levels, with each successive level containing more detail about the product form. For example:

Product Form 1 = O contains all orals

Product Form 2 = OL contains all oral liquids

Product Form 3 = OLS contains all oral liquids in syrup form

Our data captures opioid products at the more granular product form 3 level.

Limitations of these data

Numerous metrics are not available consistently for the types of historical data we were seeking. In addition, IQVIA made changes to the underlying source data and projection methodologies over time. Therefore, our analysis focused on data for the variables and metrics available consistently from 1992-2016 in a form that allowed for the calculation of a prices based on morphine milligram equivalents (MME) of the selected opioid analgesics. Of note, National Drug Code (NDC) product identifier data are not available historically back to 1992, therefore we used product formulation and strength of molecules to calculate MME based on the volume of extended units sold.

Findings from this review should be interpreted in the context of the known limitations of the databases used. These data do not provide a direct estimate of use but do provide a national estimate of units bought by retail outlets from distributors and wholesalers through the U.S. pharmaceutical supply chain. Sales of products outside of the supply chain are not captured, for example illicit sources of opioids such as fentanyl. The amount of product purchased by these channels of distribution may be a reasonable surrogate for use, if we assume the facilities purchase drugs in quantities reflective of actual patient use, i.e., that waste or diversion is constant or negligible.

Standardization of data using morphine milligram equivalents (MME)

Morphine is often used as the reference point for other opioids. The CDC developed a conversion reference table that contains MME conversion factors for opioid medications, organized by molecule and National Drug Code (NDC). The table contains all the fields necessary to compute the MMEs. A summary table of opioid MME conversions is provided in Table 1.

Table 1: Opioid Morphine Milligram Equivalent (MME) Conversion Factors[4]

Type of Opioid (strength units)	MME Conversion Factor
Buprenorphine film/tablet (mg)	30
Buprenorphine patch (mcg/hr)	12.6
Buprenorphine film (mcg)	0.03
Butorphanol (mg)	7
Codeine (mg)	0.15
Dihydrocodeine (mg)	0.25
Fentanyl buccal or SL tablets, or lozenge/troche (mcg)	0.13
Fentanyl film or oral spray (mcg)	0.18
Fentanyl nasal spray (mcg)	0.16
Fentanyl patch (mcg)	7.2
Hydrocodone (mg)	1
Hydromorphone (mg)	4
Levorphanol tartrate (mg)	11
Meperidine hydrochloride (mg)	0.1
Methadone (mg)	3
Morphine (mg)	1
Opium (mg)	1
Oxycodone (mg)	1.5
Oxymorphone (mg)	3
Pentazocine (mg)	0.37
Tapentadol (mg)	0.4
Tramadol (mg)	0.1

For all products in our dataset, the opioid component and corresponding extended unit (tablet, capsule, milliliters of liquid, transdermal patch, lozenge, spray, etc.) were identified, along with the strength, strength unit (mg for most oral dosage forms, mcg or mcg/hr for other presentation such as transdermal patch, spray, lozenge, etc.). For all products and presentations, we expressed all strength units from the IQVIA data in terms which directly corresponded with the strength units in the MME conversion reference table. We then calculated the quantity of MMEs sold per product per year by multiplying opioid strength times the MME conversion factor times the total number of extended units sold in each calendar year.

Sales and Pricing

IQVIA data provide total annual purchases by retailers from manufacturers and wholesalers and distributers for each product. For each product, the average price per MME is calculated by dividing

[4] Source: CMS.gov for additional details see: https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Opioid-Morphine-EQ-Conversion-Factors-Aug-2017.pdf for more technical details on calculating MMEs see: http://www.pdmpassist.org/pdf/BJA_performance_measure_aid_MME_conversion.pdf

total annual sales by total annual quantity of MMEs sold as described above, thus prices are expressed as an average annual price per MME.

We convert prices to constant 2016 dollars using the BLS Consumer Price Index for All Urban Consumers (CPI-U)

Summary Data on Price and Volume:

Year	Total MME Sold (billions)	Price Per MME (2016 dollars)
1992	49.3	$ 0.028
1993	53.7	$ 0.027
1994	60.5	$ 0.027
1995	65.5	$ 0.029
1996	63.6	$ 0.033
1997	67.7	$ 0.034
1998	73.1	$ 0.038
1999	84.0	$ 0.040
2000	92.1	$ 0.045
2001	109.3	$ 0.046
2002	123.7	$ 0.046
2003	137.2	$ 0.045
2004	148.9	$ 0.045
2005	161.5	$ 0.039
2006	179.5	$ 0.032
2007	200.0	$ 0.034
2008	216.7	$ 0.033
2009	232.1	$ 0.034
2010	247.3	$ 0.033
2011	245.7	$ 0.032
2012	240.5	$ 0.031
2013	226.8	$ 0.034
2014	223.2	$ 0.036
2015	215.8	$ 0.038
2016	198.0	$ 0.036

Exhibit M

Recommendations of the

OxyContin and Heroin Commission

Commonwealth of Massachusetts

November 2009

Commission Members	Organization Affiliation
Legislative Appointments	
Senator Steven Tolman, Chairman **Appointee of the Senate President**	Senator, Massachusetts Senate
Senator James Timilty **Appointee of the Senate President**	Senator, Massachusetts Senate
Senator Scott Brown **Appointee of the Senate Minority Leader**	Senator, Massachusetts Senate
Representative Brian Wallace **Appointee of the Speaker of the House**	Representative, Massachusetts House of Representatives
Representative Martin Walsh **Appointee of the Speaker of the House**	Representative, Massachusetts House of Representatives
Representative Jeffrey Perry **Appointee of the House Minority Leader**	Representative, Massachusetts House of Representatives
Gubernatorial Appointments	
Michael Botticelli	Director, Bureau of Substance Abuse Services
The Honorable David Capeless	Berkshire District Attorney President, MA District Attorneys Association
Dr. Douglas Ziedonis	Chair, Department of Psychiatry, University of Massachusetts Medical School & UMass Memorial Health Care
William Luzier	Executive Director, Interagency Council on Substance Abuse and Prevention
Patricia Horne	Deputy Director of the Office of Community Corrections
Dr. David Hoffman	Medical Director Metropolitan Boston Area of the Department of Mental Health
Terre Marshall	Assistant Deputy Commissioner of the Department of Correction
The Honorable Rosemary Minehan[1]	Massachusetts Trial Courts

[1] In accordance with § 4C(2) of the Code of Judicial conduct, Judge Minehan was prohibited from participating in discussions pertaining to law enforcement, corrections or clinical policies and issues which are the concern of the Executive and Legislative branches of government. For a copy of the Supreme Judicial Court, Committee on Judicial Ethics Opinion see Appendix A.

Table of Contents

Executive Summary

The Commonwealth is in the midst of a serious and dangerous epidemic. Prescription drug use is skyrocketing, opioid overdose deaths are steadily increasing and while support for these addiction treatment programs has increased, it is not sufficient to meet the needs of this growing problem.

The Massachusetts OxyContin and Heroin Commission was established under Chapter 302 Section 56 of the Acts of 2008 by the Massachusetts State Legislature to investigate and study the impact of the OxyContin and heroin epidemic on the state and municipal governments and recommended policy solutions to help stem the tide of this epidemic.

Between 2002 and 2007 the Commonwealth lost 78 soldiers in Afghanistan and Iraq. In the same time period, 3,265 Massachusetts residents died of opiate-related overdoses. The Commonwealth is losing men and women on its streets at a rate of 42 to 1 compared to what the state is losing in two wars overseas. Addiction is a medical disorder, and we have a public health epidemic on our hands that is larger than the flu pandemic. If the H1N1 virus killed 3,000 people in a five year period in Massachusetts, the crisis would be center stage and the entire Commonwealth would be working to find a solution to protect the public. However, because of the stigma surrounding substance abuse the opiate epidemic is left in the shadows and little light has been put upon reforming the policies involving substance abuse in the Commonwealth.

In 2005, 21.8 percent of the total state budget was spent on substance abuse and addiction related programs.[1] This funding represents a broken system as 202 people entered an ATS treatment program over 10 times in 2007.

- In 2007 there were 105,552 admissions to DPH-funded substance abuse programs in Massachusetts.[2]

- The total amount spent on substance abuse and addiction in the justice system in 2005 was $1.084 billion, which was 5.3 percent of the state budget.[3]

- Nearly 70 percent of inmates in state and local prisons throughout the country admit to regular drug abuse.[4]

The cost of opiate addiction is seen in the families who deal with the disease each day and in the increasing costs to the state. The pain and heartache that this disease inflicts on families across the Commonwealth is widespread. It appears that regardless of socioeconomic status, race, religion, or sex, the disease of addiction is devastating families at an alarming rate. Throughout the Commission hearings family members and loved ones provided some of the most powerful evidence of this terrible problem. Our understanding of the problems surrounding addiction and the new wave of prescription drug abuse is constantly evolving and as a state we have a duty to our citizens to provide comprehensive programs and treatment for those affected with this terrible disease.

Summary of Recommendations

In looking at the specific problems with OxyContin and heroin abuse, the Commission was able to tailor its recommendations to the particular concerns surrounding opioid addiction. Substance abuse affects each individual differently and there is no single solution to ending opioid addiction in the Commonwealth. The Commission believes that there are a variety of steps that can be taken to improve the prevention, treatment, safety and long-term outcomes of this devastating disease. Thus, the recommendations that are made in this report offer the widest array of policy solutions.

Based on the nearly 30 hours of oral testimony, thousands of pages of written testimony and the many heartfelt stories the Commission received, the recommendations reflect twenty broad areas of public policy pertaining to addiction and treatment of addiction. The major points of reform include; improving education and prevention measures in schools, revamping our prescription monitoring program to fall in line with more comprehensive plans from other states, regulating pain management training for doctors, dentists and nurse practitioners, ensuring that health insurance companies cover the necessary treatment for each individual, implementing a comprehensive jail diversion program for first-time, non-violent offenders, developing more effective strategies to support long-term engagement in treatment, and correcting the CORI system to better reflect the nature of substance abuse related crimes.

I. Massachusetts Prescription Monitoring Program

One of the most efficient ways at the state level to stop fraud, and reduce the availability of dangerous prescription drugs, is an active and effective Prescription Monitoring Program.

a. The Massachusetts Prescription Monitoring Program should be overhauled so that it is a useful resource for the many state agencies, and non-governmental entities that have a stake in the careful monitoring of pharmaceutical distribution.
b. The Commission believes that if the Department of Public Health is unable to assist in making these overwhelming changes in the PMP, the system may need to be moved to another regulatory agency.

II. Pain Management Training and Education

The Commission believes that educating our doctors, dentists, physician's assistants, nurses and pharmacists is a major tool in fighting the legal prescription drug abuse trade.

a. Continued support of the use and development of evidence-based educational materials for teachers, law enforcement and other health professionals.
b. Improved training on the identification and intervention of prescription and illicit drug abuse.
c. Improved pharmacy training on the identification of prescription drug abuse and the security measures necessary to deter such abuse.

III. Tamper-Resistant Prescription Pads

Implementing a fraud-resistant prescription pad program would allow additional safeguards to be built into the prescription delivery system without incurring major additional expense or creating a major disruption to the system saving the Commonwealth millions of dollars in counterfeit prescription costs.

a. The Commission recommends that all prescriptions for controlled substances be written on official state prescription pads, which contain tamper resistant features, and that no exemptions to this rule may exist.

IV. Preventing Overdose Deaths with Limited Liability Legislation

Limited liability legislation would provide limited immunity from drug possession charges and prosecution when a drug-related overdose witness or victim calls for medical attention.

a. Sensible Good Samaritan legislation should be enacted similar to New Mexico's that will be effective in decreasing the number of overdose deaths.

V. Overdose Prevention for Minors

Under current statutes and regulations, minors can check themselves out of the hospital and a parent may never be informed. This has obvious consequences for both the minor and parent and leads to a complete breakdown in communication.

a. The Commission urges that legislation be enacted to mandate that hospitals report to parents in the event of a minor overdose and enable parents to take the necessary steps to seek treatment for their child.

VI. Case Management

Case management could provide some of the necessary supports to assist individuals with substance use disorders in moving through a difficult process with many obstacles.

a. The Commonwealth should further investigate the state's capabilities to provide case management services to individuals identified with a substance use disorder.

VII. Insurance

The Commission understands the current climate in which Massachusetts finds itself in and the overwhelming support for cost containment and reform in the health care industry as a whole.

a. The Commission recommends strengthening Federal and state mental health parity laws to limit loopholes and provide comprehensive services in the form that is best suited to the individual suffering from substance use disorder.
b. Mandating a medical necessity definition which includes a determination for behavioral health issues, providing for consistency across the state.

c. Ensuring that should an individual chose the course of treatment that requires medication assisted treatment, proper coverage by insurance companies be mandated through the state.

VIII. Addiction and the Criminal Justice System

The Commission recommends that probation supervise post-release so that the substance abuse treatment afforded through the Community Corrections Centers (CCCs) can be implemented for a time duration that is consistent with evidence-based practice.

a. Adopting practices such as the Bureau of Justice Assistance's Sequential Intercept Model, where interventions can occur at any and every point along a person's involvement with the criminal justice system.
b. Enacting mandatory post-release supervision that could compel a person leaving prison into treatment.
c. Sentencing reform should include a variety of components, those which allow the Department of Correction to "step down" inmates through the various security levels prior to release.
d. Enhanced residential and outpatient substance abuse treatment programs which are essential during incarceration.
e. Permitting substance abuse intervention not only for probationers who are "sentenced" post-disposition but those who are awaiting trial and under pre-trial probation supervision.
f. Additional substance abuse treatment intervention through the reintroduction of "split" and "suspended" sentences to state prison adjudicated in the superior court.

IX. Jail Diversion

The Commission believes that we must drastically alter the manner in which we deal with those suffering with substance use disorders before they enter our criminal justice system.

a. The diversion of first time, low-level offenders from a correction setting into treatment is the best first step towards reforming a system in dire need of attention.
b. A jail diversion model requires up to 90 days of inpatient treatment, followed by a year of case management and support.

X. Interdiction and Law Enforcement

Law enforcement officials play an important role in the substance abuse equation as they are often the first responders in instances of illegal activity and play a crucial role in the implementation of policies throughout the Commonwealth.

a. The Commonwealth can be better served by improving the methods of communication with federal enforcement agencies responsible for targeting internet suppliers which are often found to be the route source for expansive criminal enterprises.
b. Improving educational awareness and providing access to the Massachusetts Prescription Monitoring Program (PMP) would be the next step in the drive to better

equip our law enforcement professionals to fight prescription drug abuse and illegal activity.

XI. Long-Term Treatment

Long-term treatment programs are needed in the Commonwealth to provide a continuum of care for individuals with substance use disorder.

a. The Commission recommends that a comprehensive approach to long-term treatment, providing individuals with comprehensive substance abuse monitoring, case management, support groups, pharmacotherapy and behavioral therapy.
b. Additionally, long-term treatment must include family and child care services, vocational rehabilitation, mental health services, housing, financial and medical services.

XII. Education and Prevention

The Commission believes that raising awareness about the harms of drugs, alcohol and substance abuse is an issue that must be addressed at an early age.

a. Given the changes in substance abuse in the Commonwealth, drug awareness programs must be updated to include illicit drug use such as prescription drugs.
b. A statewide program should be implemented to require the program throughout all levels of a child's education, including the upper grades of elementary school.
c. Licensed drug and alcohol counselors should be present in each middle school and high school throughout the state providing diagnostic services and referrals for students with substance use disorders.

XIII. Recovery High Schools

For many students suffering from substance use disorder, having an environment such as a recovery high school provides them with a safe haven, where they can both learn the state mandated curriculum and receive proper addiction treatment.

a. The Commission recommends that the state continue to support recovery high schools, by increasing the number of recovery high schools in the Commonwealth through more funding and legislative support.

XIV. Disabled Population

The Commission believes that as with all substance abuse issues, treatment must be individualized and must adapt to meet the needs of specific populations, such as those who are also physically disabled.

a. Vocational rehabilitation counselors and social service case managers need to recognize and address substance in their clientele and increase referral to treatment.
b. Provider sensitivity to treatment barriers training (political, attitudinal, or physical) is crucial while devising evaluations and individual treatment plans.
c. Treatment programs will need to address the attitudes of their staff and improve accessibility of their facilities, policies, and materials.

d. Substance abuse treatment professionals must pay close attention to the unique aspects of the lifestyle of persons with disabilities, which may affect the outcomes of substance abuse treatment.

XV. Co-occurring Mental Illness and Addiction

Co-occurring disorders place additional restraints on the treatment and recovery process and deserve special attention for the type of treatment required.

a. The Commission would recommend implementing lessons learned from the SAMHSA Co-Occurring State Initiative Grant (COSIG) that evaluated how 17 states addressed the common problem and developed more effective ways to identify and treat individuals with co-occurring mental illness and addiction (dual diagnosis).

XVI. Cultural Competencies

The Commission were struck by the lack of information about the problem which this section discusses and, similarly, about the lack of suggested solutions.

a. The Commonwealth should increase support for the worthwhile translator services provided by the Commonwealth and improve access for those who need them.

XVII. Veterans' Issues

The Commission recommends continued funding support for veterans outreach, referral services, and the Department of Veterans' Services.

a. The Commonwealth must continue to improve upon its methods for identifying returning veterans so that they may benefit from the services available to them.

XVIII. CORI/Job Training

An integral part of recovery is reintroducing those who have recovered from addiction both into society and the job market. This process is stymied by the inability of former substance abusers to find work because of CORI offenses, even after they have shown that they are rehabilitated and are making every attempt to stay sober.

a. Increasing funding of the Correctional Recovery Academy (CRA) and other programs that focus on treatment and reentry.
b. Mandating a program for Certificates of Rehabilitation and Recovery for offenders who complete correctional programs.
c. When CORI reform takes place in the upcoming legislative sessions in the Commonwealth, the issue of better displaying individual crimes be examined.

XIX. Family Issues

Addiction is a family disease and recovery is a family process. It is important for families to be both educated on the illness and supported throughout the recovery process as caring for a loved one who is struggling with an addiction is one of the most difficult situations that any individual or family will have to endure in their lifetime.

a. Increasing availability, access and funding to family services and peer support groups to ensure that families are given all options regarding treatment and services both for families and individuals with substance use disorder.
b. Increasing access to information on drug overdoses so that parents and loved ones have the lifesaving tools in the event of an emergency.

XX. Federal Issues

These issues are intertwined throughout many of the recommendations in this report; however, the Commission felt it necessary to include a separate section in the report on the specific issues that are beyond the purview.

a. Federal law enforcement and regulatory programs must be involved in the policing of illegal prescription drug activity on the internet.
b. Mental health parity must be strengthened nationally to include provisions for substance abuse coverage by insurance companies.
c. Continuing and increasing assistance from the Massachusetts Congressional delegation in obtaining funding for vital programs in the Commonwealth.
d. Continuing progress is necessary in regards to prescription medication monitoring through the Risk Evaluation and Mitigation Strategy (REMS) process at the Federal Drug Administration.

Opioid Abuse in the Commonwealth of Massachusetts

The rate of substance abuse in the Commonwealth is not a new topic, and the widespread abuse of opiates has increased to epidemic levels. Since the mid-1990s the widespread abuse of opiates became evident when substance abuse treatment systems in Massachusetts and several other states were inundated with opiate addicts. Addiction to the powerful painkiller, OxyContin, became evident almost immediately following FDA approval of the drug in 1995. In Massachusetts, OxyContin became so widely abused, that the addiction rate for the drug in Massachusetts increased by 950 percent over the last ten years.[5] The problem also became clear from the immediate rise in opioid related hospitalizations in the Commonwealth. In 2002, Boston had the highest rate of OxyContin related emergency department visits in the country and in 2005, there were more than 18,000 opioid related emergency department hospitalizations and hospital stays.[6]

Public and private treatment systems have been overwhelmed by the increase in those seeking treatment. Consider this startling statistic. Between 2002 and 2007 the Commonwealth lost 78 soldiers in Afghanistan and Iraq. In the same time period, 3,265 Massachusetts residents died of opiate-related overdoses. The Commonwealth is losing men and women on its streets at a rate of 42 to 1 to what the state is losing in two wars overseas. From these statistics one can see the increasing need for an in-depth look at the public policies surrounding substance abuse issues. A tremendous burden has been put on state and local governments, courts, corrections and hospitals. The state paid almost $200 million in emergency room costs related to overdoses in 2005, the Massachusetts Department of Corrections is at 143 percent occupancy, and the Bureau of Substance Abuse Services, MassHealth and the uncompensated care pool account for more than 75 percent of the dollars spent on substance abuse services in the Commonwealth[7]. In fact, private insurance payments for substance abuse treatment decreased 11 percent from 1991 to 2001 while public payments increased by 68 percent.[8]

Addiction is a medical disorder, and we have a public health epidemic on our hands that is larger than the flu pandemic. If the H1N1 virus killed 3,000 people in a five year period in Massachusetts, the crisis would be center stage and the entire Commonwealth would be working to find a solution to protect the public. However, because of the stigma surrounding substance abuse, this epidemic is left in the shadows and little light has been put upon reforming the policies involving substance abuse in the Commonwealth.

Purpose of the Commission

The Massachusetts OxyContin and Heroin Commission ("The Commission") was established in Chapter 302 Section 56 of the Acts of 2008 by the Massachusetts State Legislature to investigate and study the impact of the OxyContin and heroin epidemic on state and municipal government, the substance abuse treatment system and to identify potential strategies to more effectively cope with substance use disorders in the Commonwealth. The Commission is comprised of 14 members; 3 members from the State Senate; 3 members from the State House of Representatives; 1 member from the Bureau of Substance Abuse Services; 1 member from the Massachusetts District Attorneys Association; the chair of the Department of Psychiatry at the

University of Massachusetts Medical School; 1 member from the trial court; 1 member from the Department of Correction; 1 member from the Department of Mental Health; 1 member from the Department of Community Corrections; and 1 member from the Interagency Council on Substance Abuse and Prevention.

The Commission was charged, through the enacting legislation, with examining a variety of policy issues as they pertain to substance abuse. Specifically, the Commission looked at an evaluation of the total direct and indirect cost of substance abuse to the Commonwealth; the sources of heroin, OxyContin and other prescription opiates available on the street; the number of repeat detoxifications which take place on an annual basis; the number of inmates suffering from opiate dependency; and the recidivism rates of those committed in civil commitment programs for abuse of OxyContin or heroin. Secondly, the Commission looked at policy changes in the following areas: civil commitment laws; long-term residential programs that are of at least 90 days; neurobiological impacts that affect the time an addicted individual may need to be committed for OxyContin or heroin abuse; an intensive case management system; the establishment of a system of regional secure treatment centers; statutory restrictions on parents and families with adolescents addicted to OxyContin or heroin; enhancements to the Commonwealth's prescription monitoring program; and the establishment of an outpatient commitment program.

Commission Format

From March 2009 through September 2009, the Commission held seven public hearings throughout the Commonwealth on a variety of issues pertaining to substance abuse. The hearings were held in Boston (2), Salem, Fall River, Pittsfield, Worcester, and Hyannis and each focused on a specific area of substance abuse. The Commission heard from the public and private healthcare industries, medical experts, probation and police officers, unique populations, including the elderly and veterans, treatment coordinators and many addicts, parents and family members directly affected by substance use disorders. The public hearings provided the Commission the opportunity to hear from experts from all aspects of substance abuse policy and receive public feedback on where changes can be made to policies in the Commonwealth. Throughout the hearing process the Commission came to know the many intricacies of this disease and the many pieces that contribute to solving the disease of addiction. The Commission was deeply moved by the overwhelming support that was received throughout the hearing process.

In addition to the public hearings the Commission met on several occasions to discuss various aspects of the recommendations.

OxyContin and Heroin Commission Meeting Schedule			
	Meeting Date	Location	Subject
Meeting 1 Commission Member Informational Meeting	Wednesday, March 4, 2009	State House, Room 312C Boston, MA	Introduction of Commission Members and discussion of Commission layout
Meeting 2 Public Hearing	Friday, March 27, 2009	Massachusetts State House Room A2 Boston, MA	Introduction of substance abuse problem in Massachusetts
Meeting 3 Public Hearing	Friday, April 17, 2009	Salem State College, Veteran's Hall Salem, MA	Public health system and substance abuse
Meeting 4 Public Hearing	Friday, May 15, 2009	University of Massachusetts, Dartmouth Advanced Technology and Manufacturing Center Fall River, MA	The courts, jail diversion, interdiction and public safety
Meeting 5 Public Hearing	Friday, June 5, 2009	Berkshire Community College, Room K111 Pittsfield, MA	Western Massachusetts issues, prescription monitoring program, Berkshire Health Systems Pain Management Project
Meeting 6 Public Hearing	Friday, June 26, 2009	University of Massachusetts Medical School, Room S1-607 Worcester, MA	Neurobiological effects of substance abuse, adolescent populations
Meeting 7 Public Hearing	Friday, July 10, 2009	Barnstable High School, Knight Auditorium Hyannis, MA	Unique populations; including veteran's, the elderly, co-occurring disorders
Meeting 8 Public Hearing	Thursday, September 10, 2009	Massachusetts State House Gardner Auditorium Boston, MA	Insurance companies stake in substance abuse issues

It is the Commission's hope that this report be the next step in a continuing conversation in curbing the disease of addiction in the Commonwealth. This report is not meant to be the end of the discussion, but rather the beginning of the next chapter for substance abuse policy in Massachusetts.

Findings

As part of the enacting legislation, the Commission was charged with finding data on a variety of issues. This included the following information: "the number of inmates suffering from opiate dependence; recidivism in the criminal justice system for OxyContin and heroin abuse" as well as "the total direct and indirect cost to the commonwealth as a result of substance abuse; the number of repeat detoxifications on an annual basis; recidivism of those committed in civil commitment programs for abuse of OxyContin or heroin."[9] The following section details the findings of the Commission pursuant to the enacting legislation.

The total cost of substance abuse and addiction to the Commonwealth in 2005, the most recent year for which aggregate data is available, was over $4.5 billion, which represented 21.8 percent of the total state budget in 2005.[10] Out of the over $4.5 billion, less than 2 percent, or just over $66 million, was spent on prevention, treatment and research outside of the money that the state is required to spend. The other 98 percent represents the cost to public programs, which includes spending on justice, education, mental health services, and public safety.

Massachusetts ranks in the lower 50 percent of states in terms of spending on prevention, treatment and research. For every $100 the state spends on substance abuse and addiction, only $1.45 goes towards prevention, treatment and research. By comparison, for every $100 the state of Connecticut spends on substance abuse and addiction, over $10 goes towards prevention, treatment and research.[11]

[A pie chart showing that 1% of Massachusetts' overall state spending is spent on prevention, treatment, and research]

National Center on Addiction and Substance Abuse at Columbia University. S*hoveling Up II: The Impact of Substance Abuse on Federal, State and Local Budgets*. May 2009. Print.

[A pie chart showing that 10% of Connecticut's overall state spending is spent on prevention, treatment, and research]

National Center on Addiction and Substance Abuse at Columbia University. S*hoveling Up II: The Impact of Substance Abuse on Federal, State and Local Budgets*. May 2009. Print.

Hospitalizations/Overdoses in Massachusetts

An overdose occurs when excessive use of an opioid requires a [illegible]k immediate hospitalization. In 2006, there were 23,369 alcohol and substan[illegible]ospitalization discharges for non-fatal opioid-related overdoses associated with opioid abuse, dependence or poisoning. This accounted for 2.93 percent of all hospitalizations in Massachusetts that year.[12]

The number of poisoning deaths in Massachusetts increased by 23 percent in 2006 with nearly 65 percent of poisoning deaths associated with opioids.[13] In 2007, 645 Massachusetts residents died from an opioid-related overdose.[14] This is a conservative estimate, as often times other causes of death are listed on a death certificate.

Acute Treatment Services

Acute Treatment Services (ATS) programs, also known as "detox," are medically monitored detoxification services that provide 24-hour care under the consultation of a medical director to monitor an individual's withdrawal from alcohol and other drugs and alleviate symptoms.[15] In 2007, there were 18,516 individuals admitted to a state-funded ATS program for at least one ATS admission. Most of these individuals—about 64 percent—were admitted to an ATS program just once. However, 202 people entered an ATS treatment program over ten times in 2007. The burden of paying for state-funded ATS programs falls under the Bureau of Substance Abuses Services and MassHealth, with each ATS costing the state around $1,000. Therefore, the total cost to the state from ATS programs in 2007 was over $22 million.[16]

[Pie chart shows the number of Acute treatment service admissions. 64% people had one admission, 17% had 2, 8% had 3, 4% had 4, 2% had 5, 1.2% had 6, .8% had 7, .5% had 8, .4% had 9, and .9 had 10 or more.]

Massachusetts Department of Public Health. "Substance Abuse Services Description. n.d. Web. 12 Oct. 2009.

Substance Abuse Treatment Program Admissions

The Department of Public Health's Bureau of Substance Abuse Services keeps data on over 500 substance abuse treatment programs throughout the state, including Acute Treatment Services (ATS) and post-ATS inpatient and outpatient services. In 2007, there were 105,552 admissions to DPH-funded substance abuse programs in Massachusetts.[17] Of the people admitted, 39 percent reported heroin use in the year prior to admission.[18] Of the 41,850 hospitalized who admitted heroin use in the previous year, 85 percent also reported heroin as their primary drug and a majority reported heroin as their reason for seeking treatment.[19]

[Line chart shows Admissions to Treatment Facilities in Massachusetts. All Admissions to Treatment Facilities in Massachasutts begins at about 25,000 and steadily increases until 2002 where they reached 35,000 admissions. From 2004-2007 admissions plateaued around 30,000 - 32,500.]

Commonwealth of Massachusetts. Department of Public Health. *Substance Abuse Treatment Fact Sheet - FY 2007 Heroin Users*. Bureau of Substance Abuse Services, 2008. Web. 25 Sept. 2009.

Criminal Justice

The impact on the criminal justice system of the Commonwealth is demonstrated by the number of substance abusers in the corrections system, how many crimes are related to illicit opiate abuse, and the total impact on the judiciary system relating to substance abuse. These crimes burden the Department of Correction, the courts, and public safety agencies. The total amount

spent on substance abuse and addiction in the justice system in 2005 was $1.084 billion, which was 5.3 percent of the state budget.[20]

[Pie chart showing 5.3 percent of Total State Spending Spending is Criminal Justice Spending]

National Center on Addiction and Substance Abuse at Columbia University. S*hoveling Up II: The Impact of Substance Abuse on Federal, State and Local Budgets*. May 2009. Print.

Corrections

In Massachusetts today over 200,000 adults, or nearly one in twenty four, are under some kind of correctional supervision, including prison, jail, parole or probation.[21] Research has shown that 80 percent of offenders nationwide are either addicted to alcohol or drugs, or alcohol or drugs were involved in the commission of the crime.[22] Therefore, it can be established that up to 150,000 offenders in the Commonwealth have a substance abuse issue or are in correctional supervision because of their past substance abuse. The total cost to the Commonwealth on substance abuse for adult corrections in 2005 was $810 million, over four percent of the state budget that year.[23]

Judiciary

The total cost to the judiciary on substance abuse and addiction was $168 million in 2005.[24] The impact on the judicial system on substance abuse and addiction cases involves criminal, drug, family and juvenile courts. This includes personnel, contracted services and administration costs. Incorporated in the total cost to the judiciary are cases in which arrestees tested positive for drugs or reported recent drug or alcohol abuse, had previously been in a treatment program or were in need of treatment, and cases that were linked to substance abuse in other ways.[25]

Crime

Under Massachusetts law, heroin and other opiates are classified as Class A substances.[26] According to the Massachusetts Sentencing Commission's Survey of Sentencing Practices, 1,705 offenders were convicted for an offense involving a Class A substance. Out of these offenders, 771 were convicted of distributing and 934 were convicted of possessing a Class A substance.[27]

MassHealth

The impact of opiate abuse on MassHealth relates to the number of members who receive drug therapy, in the form of methadone or buprenorphine (Suboxone and Subutex). In addition to the cost of drug therapy, MassHealth's annual expenditures relating to opiate abuse include hospitalizations, transportation, and physician services. The following data represent total Medicaid costs, including expenditures from the Medicaid Managed Care partner organizations.

The number of MassHealth members who received any methadone or buprenorphine in fiscal year 2007 was 18,102.[28] The total annual expenditures for members receiving methadone and for buprenorphine was $276.2 million and $49 million, respectively, for a total expenditure for

drug therapy of over $325 million.[29] Out of the 13,951 members who received methadone in fiscal year 2007, over 40 percent (6,240) received twelve continuous months of methadone, at a cost of over $91 million.[30] The average cost per member for methadone was $19,799 and for buprenorphine was $11,820.[31]

Municipalities – City of Boston

As the largest municipality in the Commonwealth, the City of Boston serves as an excellent illustration of how the substance abuse epidemic impacts the services and budgets of large cities. The large population of Boston provides a data set that enables the Commission to gauge the impact of substance abuse on a densely populated city. Furthermore, in recent years Boston has been one of the Commonwealth's epicenters of illicit OxyContin and heroin abuse. This increase correlates to a spike in hospitalization and mortality rates. From 1999-2007 the mortality rate surrounding substance abuse increased 77.3 percent.[32]

The Drug Unit of the Boston Police Department (BPD) tracks of the number of samples of illegal controlled substances that are obtained by officers through arrests and controlled buys. These samples are submitted to a laboratory that determines the type of substance. The number of heroin seizures made by the BPD in 2008 was 1,099 and the number of OxyCodone seizures was 247.[33]

Opiate abuse also has a significant effect in the daily work of Boston's Emergency Medical Services (EMS). The cost transporting of a patient to a hospital is difficult to quantify given the level of service needed, either basic life support or advanced life support, and the possibility that two units respond to the same incident. In 2008, Boston EMS personnel spent over 140 hours responding to heroin-related incidents, with 117 basic life support responses and 86 advanced life support responses.[34] The total charge for the basic and advanced responses are $935 and $1,870 respectively, so the total cost to the city on EMS relating to heroin in 2008 was $270,215.[35]

State Workforce

While not originally required from the enacting language, this data contribute to a more comprehensive understanding of substance abuse and addiction in Massachusetts. Substance abuse and addiction have a significant negative impact on the state's workforce. Employees with drug or alcohol problems are more likely to miss work, be involved in workplace accidents, file workers' compensation claims, and are 33 percent less productive than their non-abusing coworkers. Nationally, it is estimated that productivity loss due to substance abuse was close to $15 billion in 2000.[36] In 2005, it is estimated that the Commonwealth spent $21.37 million on state workforce costs relating to substance abuse and addiction.[37]

[Bar chart showing Projections of National Costs Due to Drug Abuse is Steadily increasing.]

National Center on Addiction and Substance Abuse at Columbia University. S*hoveling Up II: The Impact of Substance Abuse on Federal, State and Local Budgets*. May 2009. Print.

Recommendations

The following section outlines the twenty issue areas for which the Commission recommends policy changes. Throughout the public hearing process these core issue areas were brought up on numerous occasions and therefore represent the most important areas for policy change. The Commission feels that by utilizing multiple aspects of these solutions the most effective outcomes can be achieved.

Regulations

A variety of changes in regulations have been proposed to improve the services the state provides and give better insight to various under-monitored areas of substance abuse regulation. It is the hope of the Commission that through the Commonwealth's regulatory process many policy changes can occur in a manner that enables state agencies the greatest flexibility and control. These regulatory changes include improving the prescription monitoring program (PMP), which entails expanding the schedule medications that are monitored and allowing physicians and law enforcement to access the valuable information that the PMP can provide; requiring those administering prescriptions which may include prescription opioids to use tamper-resistant prescription pads, ensuring that doctors can more safely administer medications and save the Commonwealth millions of dollars in prescription fraud; require pain management training for all doctors, nurses, physician's assistants and dentists; preventing overdose deaths with limited liability legislation and requiring that should a minor overdose and be taken to a hospital, that their parents be informed of the overdose and provided with information about seeking treatment.

Massachusetts Prescription Monitoring Program

A consistent theme at the Commission's hearings was the failure of the Massachusetts Prescription Monitoring Program (PMP) to be an effective resource to combat the opiate epidemic. The opiate crisis in Massachusetts is largely fueled by the misuse of prescription medication; to this end the Commission analyzed the variety of ways that legally manufactured pharmaceuticals end up being used for illegitimate purposes. In almost every case of the ways which these medications reach the street, the PMP could have acted as a preventative measure.

One of the most apparent uses of the PMP as a resource to cut off access to these dangerous prescription opiates is ending the deceptive practice of "doctor shopping" by addicts. Doctor shopping, or pharmacy shopping, is a common practice among those addicted to opiates; whereby drug seeking individuals target doctors who are known to be busy or sympathetic, or visit multiple doctors and pharmacies until the addict has the desired prescription filled. Doctor Carol Bates, Primary Care Program Director at Beth Israel Deaconess Medical Center, said in testimony regarding updates to the PMP:

> "There is a strong sense across teaching institutions that we see a flood of drug seeking patients - particularly in July when new interns arrive in training. Drug seekers are knowledgeable about the healthcare system and often target those with the least experience… Programs in other states with complete registry information have been highly effective. As I understand it, there have been no examples of breach of confidentiality or inappropriate access to systems in those states that have complete registry provider access."[38]

While it is impossible to completely end the misuse of prescription medication, drastically reducing the flow of these drugs so that they are not as prevalent in communities across the Commonwealth is an attainable goal. One of the most efficient ways at the state level to stop

fraud, and reduce the availability of dangerous prescription drugs on the street, is an active and useful PMP. For the past decade while Massachusetts has been faced with a prescription drug crisis, at the same time, our PMP system has fallen behind other states. The lack of attention to its status, and utilization of this program, has further enabled this epidemic to flourish unchecked. For these reasons, the resuscitation of the PMP is one of the most promising recommendations of this Commission and we believe its proper administration will be a tremendous asset going forward.

The state's inability to use this system to intervene in clear cases of prescription drug abuse, to reduce the frequency of "doctor shopping" or use data from this program to target resources is, perhaps, one of the greater tragedies in this decade long struggle with opiate abuse. The lack of dedicated resources to the Commonwealth's PMP continued across several administrations and, as a result, cost the state hundreds of millions of dollars. The PMP is funded in part by the Massachusetts Drug Control Program and by federal grants and is assigned one half of a full-time employee for its administration.

Through several administrations the program lacked staffing and was ignored as fraudulent prescriptions and prescription overdose death rose at alarming rates. In addition to being a preventative tool for public health officials, the PMP presents an opportunity for the state to prevent Medicaid fraud and keep close track of its spending on this class of pharmaceuticals, on which Massachusetts spends millions of dollars each year.

Background on Prescriptions Drug Monitoring Program (PDMP)

A Prescriptions Drug Monitoring Program (PDMP) is an electronic database managed by the state to collect data on substances prescribed within the state. The database management and reporting structure is housed in a specific state agency, generally a law enforcement or public health agency. The responsible agency will send notifications, reports and information to specific groups or individuals authorized by the state to receive this information. This data may be relayed to a patient, medical practice, or law enforcement agency.

According to a report by the National Alliance for Model State Drug Laws (NAMSDL) a PDMP may serve multiple purposes, including:

- To support access to legitimate medical use of controlled substances.
- To help identify and deter or prevent drug abuse and diversion.
- To facilitate and encourage the identification, intervention with and treatment of persons addicted to prescription drugs.
- To help inform public health initiatives through outlining of use and abuse trends.
- To help educate individuals about PDMPs and the use, abuse and diversion of an addiction to prescription drugs.[39]

The Massachusetts Prescription Monitoring Program (PMP) was developed in 1992 through a joint regulation of the Massachusetts Department of Public Health (DPH) Drug Control Program (DCP) and the Massachusetts Board of Registration in Pharmacy (Board) with funding from a

federal grant.[40] The program uses a computer-based, electronic data transfer (EDT) system to collect prescription data. Medical Review Groups (MRG's) comprised of practitioners and pharmacists provide peer review of the medical data and assist the Drug Control Program in reviewing data for release to law enforcement and regulatory agencies.

The Massachusetts Prescriptions Drug Monitoring Program was developed in 1992 through The Mass PMP receives data on all Schedule II controlled substances dispensed by Massachusetts community pharmacies and Massachusetts registered hospital outpatient and clinic pharmacies. Information is sent through an electronic data transmission (EDT) through a third party vendor, Atlantic Associates Inc. The information is analyzed by the Department to look for prescribing and dispensing trends, and to provide case information to regulatory and law enforcement agencies concerning drug distribution and potential diversion."[41]

In FY2008 3.3 million Schedule II prescriptions were monitored by the Massachusetts PMP.[42] Reports are provided to authorized end users (regulatory boards, state and federal law enforcement); however they are not available for prescribers or pharmacies to research their client base. Some of the types of diversion cases reviewed by Massachusetts PMP include illicit prescribing, doctor shopping, forgery and pharmacy diversion. Additionally, pharmacies and registered health care facilities are required to submit a monthly report to Atlantic Associates.[43]

[Line chart showing prescriptions of schedule II Opioids is Steadily Increasing beginning in 1996 at $750,000 to around $2 million in 2007]

Massachusetts Department of Public Health (MDPH). Drug Control Program. *Prescription Monitoring Program (PMP) Handbook for the Pharmacist and Pharmacy Software Provider.* 16 Sept. 2008. Print.

This reporting structure means that the information being used to analyze reports is 3-4 weeks old, limiting the ability for law enforcement agencies investigate potential illegal behavior. The most egregious failures of the Commonwealth's PMP may well be Dr. Michael Brown, a Cape Cod Doctor who practiced in Sandwich. According to evidence presented to the Board of Registration in Medicine, Dr. Brown was the single leading prescriber of OxyContin in the entire state, with his prescriptions accounting for 288,859 of the 922,985 OxyContin tablets filled through pharmacies in 2004. If the PMP was operating as an active bureau processing incoming data in real-time, an analyst working at the PMP would have immediately recognized this disproportionate trend and provided notices to law enforcement.

The Prescription Monitoring Program's records show that Brown, an internist working alone in Sandwich, prescribed about 1.7 percent of the OxyContin prescribed in the state in 2004. The 144,435 tablets of the narcotic he prescribed in the first six months of this year led the state's doctors by a wide margin. Although monitors collect information on more than 2 million prescriptions for potentially addictive drugs each year, they rarely release information about individual doctors unless police or regulators request it – and then only if a panel of doctors and pharmacists agrees that release of information will not unfairly raise suspicions. Dr. Brown's case highlights the gap in the prescription drug monitoring system.[44]

One of the most compelling stories the Commission heard was a mother from Pittsfield who testified about her daughter's struggle with prescription drugs after being legitimately prescribed

painkillers. Her story is a prime example of both the nature of this disease, and the failures of the prescription monitoring system. In several instances, the daughter went to multiple pharmacies and doctors that prescribed her opiates, each doctor and pharmacy not knowing she was receiving prescriptions from multiple sources. In this case the PMP should have been a preventative tool, to both stop the fraudulent prescriptions and call her addiction and multiple prescriptions to the attention of her health care providers. Unfortunately, the young woman is no longer with us.

Comparison Programs

Two examples of progressive, gold standard PMP programs exist in the Kentucky and Connecticut models. These programs provide real-time, online access to their data for several groups of stakeholders, and have demonstrated their ability to effectively monitor and intervene with illegal prescription drug use.

Kentucky, similarly impacted by a prescription drug epidemic, created Kentucky All Schedule Prescription Electronic Reporting (KASPER) in 1999. KASPER is a PMP that has set a high standard for effectiveness. While Kentucky is able to collect and update data from prescription monitoring every 8 days, the Massachusetts PMP updates data once a month. The Kentucky program has some 5,500 requests for reports every month while Massachusetts averages 10 requests per month. Of the requests in Kentucky, 92 percent are from prescribers, as compared to Massachusetts where 61 percent of requests come from law enforcement and 30 percent from licensing boards.[45]

The Kentucky program can provide doctors and police agencies with information on suspected prescription-drug abusers within 24 hours.[46] Kentucky's program, which is being used as a model for other states, has been successful because it includes privacy protections and tracks all scheduled prescriptions that can be addictive or misused. The effectiveness of this program can be seen in the ability for several stakeholders to use the data immediately in order to limit the ability for people to mis-prescribe, or to abuse the prescription medication.

Kentucky has implemented KASPER trend data reporting and analysis to produce Geographic Information System (GIS) maps identifying controlled substance usage along with increases and decreases over time by geographic area. These reports are intended to provide a tool for the licensure boards and law enforcement to identify where they need to focus investigative resources. The trend reports will also provide a tool to increase the awareness of health care providers about potential problems with controlled substances in selected geographic areas.

Similar to the Kentucky program the Connecticut PMP, which went into effect on 2008, requires pharmacies to submit their orders for all Schedule II – V prescriptions. The Connecticut PMP is a web-based application that allows prescribers and pharmacists to access a patient's prescription information online. As a safety measure these licensed healthcare professionals must register for access to the database by supplying the PMP with the appropriate credentials prior to receiving any patient information.[47] The website is accessible 24/7, and in many cases a patient report can be viewed in a matter of seconds. The report data is based on information submitted by the dispensing pharmacy. The information in a report can alert a physician or a law enforcement

group to the number/times a prescription has been filled for a patient, as well as who prescribed the prescription. This real-time information allows for physicians and law enforcement agencies to monitor, and quickly react to the individual abuse of prescription drugs. Effective management and monitoring of this information can limit the amount of narcotics in the market, as well as limit access points for illegally obtaining the drugs.

Many states would like to see the integration of a national program, which would create a standard model for reporting, and use of this data. The success that states are having with the tracking systems has led advocates to push for a national system that would link together the states' databases. A national program would deter individuals from crossing state lines to fill prescriptions in other states.

The Commission recommends that the Massachusetts Prescription Monitoring Program be overhauled so that it is a useful resource for the many state agencies, and non-governmental entities that have a stake in the careful monitoring of pharmaceutical distribution. This system must be a real-time database; prescribers should have the most information at their disposal when making decisions relevant to pain management. Law enforcement and state accounting agencies should have access to these records to detect patterns of fraud and illegal activity. Public health officials must be able to use this data to target state resources to combat startling rates of addiction.

If the technology must be updated for this to occur, it would be money that would almost be immediately recouped by the state in savings. New York, after implementing an active PMP in conjunction with serial prescription pads, realized a 500 percent savings in their health care accounts. While improvements in the ability to access this data is important, the role of the PMP must be redefined.

A culture change and redefinition of the role of the PMP is necessary to make this a worthwhile program. The structure of how the information gathered by the PMP is disseminated appears to be one of the primary obstacles for. While ideally this program should be housed at the Department of Public Health, many other states run their PMPs out of the Board of Pharmacy, or in the Attorney General or Inspector General's offices. The structure of how the data is processed should also be re-evaluated; the current system is entirely too restrictive and does not provide any entity, aside from the medical review group, with the requisite information.

The flow of information must be streamlined, and the current bottlenecks in the system must be removed. Staffing this system must also be made a priority by the Department of Public Health. Currently, the PMP acts as a repository for information with few examples of usefully investigatory or analytical activity. For the PMP to be a useful tool for the Commonwealth, the PMP must be more than that, changes need to be made so that the PMP actively provides information to the many entities that find this data critical.

The reinvention of the PMP represents an opportunity for this state to make a practical and immediate change for the better. A substantive reform of the Massachusetts Prescription Monitoring Program is one of this Commission's highest priority recommendations for immediate action that has the ability to make a worthwhile impact on the opiate epidemic.

Pain Management Training and Education

Studies show that nationally, fewer than 40 percent of physicians receive any type of pain management training in medical school.[48] This includes training indentifying prescription drug abuse, proper prescribing methods and drug diversion. According to Dr. Nathanial Katz, Director of Program on Opioids Risk Managements at Tufts University School of Medicine, "many specific prescription opioid fatal overdoses and cases of addiction are linked to prescribing errors, primarily prescribing to patients at high risk of abuse and addiction, and failure to monitor for adverse outcomes." According to national data from the National Survey of Drug Use and Health (NSDUH), 17 percent of individuals abusing prescription drugs received them from one doctor. This is more than those who bought the drug off a friend or relative, stole the drug from a friend or relative and bought the drug from a dealer combined.

[Pie Chart: Source of Pain Relievers for Non-Medical Use. 60% Free from friend or relative, 17% from one doctor, 7% from other source, 4% bought from dealer, 4% took from friend or relative without asking, 8% bought from friend or relative.]

Substance Abuse and Mental Health Services Administration. Results from the 2005 National Survey on Drug Use and Health: National Findings. Office of Applied Studies, NSDUH Series H-30, DHHS Publication No. SMA 06-4194. Rockville, MD. Web. 22 Oct. 2009.

The Commission believes that educating our doctors, dentists, physician's assistants, nurses and pharmacists is a major tool in fighting the legal prescription drug abuse trade. Given the increased need for pain management and abuse training, the Commission recognizes three areas of improvement for the Commonwealth.

1. Continued support of the use and development of evidence-based educational materials for teachers, law enforcement and other health professionals.

2. Improved training on the identification and intervention of prescription and illicit drug abuse.

3. Improved pharmacy training on the identification of prescription drug abuse and the security measures necessary to deter such abuse.

Continued support of the use and development of evidence-based educational materials for teachers, law enforcement and other health professionals.

The Bureau of Substance Abuse Services has developed a pocket-sized guide for clinicians, "Opioid Analgesics and Stimulant Medications: A Clinician Guide to Prevent Misuse." It contains screening tools for adults and adolescents, points for prescribing medications and counseling patients, and further clinical resources. It has been sent to physicians across the Commonwealth. Over 3,000 of these guides have been distributed, primarily to prescribers of these medicines. The Commission recommends that the Bureau prepare an updated guide for re-distribution. These materials should address substance abuse prevention, the warning signs of drug abuse and methods of intervention and identification of treatment resources available to consumers across the Commonwealth.

Improved training on the identification and intervention of prescription and illicit drug abuse.

The Commonwealth should take steps to ensure that Massachusetts physicians who prescribe narcotic medications receive substantive training in: 1) effective pain management, 2) identification of patients at high risk for substance abuse, and 3) other aspects of drug abuse. DPH and the Board of Registration in Medicine should work closely together to further develop effective strategies to ensure that physicians are properly and effectively trained.

Clinician training should be targeted to individuals with identified needs to ensure the most effective, focused and meaningful programs as well as the most efficient use of resources. The professional Boards of Registration (e.g., Medicine, Dentistry, Podiatry, Veterinary Medicine, Nursing and Physician Assistants) have the authority as well as the infrastructure and expertise to oversee clinical practice issues, including training requirements. The Commission recommends that the Department of Public Health (DPH) work through the Prescription Monitoring Program Advisory Council, which includes the professional Boards of Registration, to identify ways to improve information sharing and coordination that will assist the Boards in targeting programs to improve clinical skills assessment, pain management, drug diversion, and abuse. In 2004, the Board of Registration in Medicine adopted the Federation of State Medical Boards' Model Policy for the Use of Controlled Substances for the Treatment of Pain, which is a communication to physicians on the best practices for safely prescribing pain medications. Continuing education courses are presented many times each year at various locations throughout the Commonwealth. Moreover, DPH has proposed regulations to authorize providing clinicians with prescription monitoring information to help them identify their patients' potential diversion or harmful use of Schedule II pain medications through an online prescription monitoring data system. DPH is developing guidelines to help clinicians reduce opportunities for drug diversion and increase prevention of and facilitate intervention in drug addiction and abuse.

At present there is no mechanism to mandate prescriber training as a condition of obtaining a Drug Enforcement Administration (DEA) Controlled Substance Registration Certificate. Similarly, by current statute the Massachusetts Controlled Substances Practitioner Registration issued by DPH provides no basis to mandate prescriber training. While the Massachusetts professional Boards of Registration mandate continuing education as a basis for licensure, the Boards do not require specific training in this area, and are reluctant to embark on a precedent of mandating focal training for all practitioners. Any new mandate for training would likely require legislative action in the form of a statute or regulation.

The Commission also recommends that opportunities for encouraging voluntary prescriber education should also be pursued. For example, collaboration between the professional Boards of Registration, the Department of Public Health and the University of Massachusetts Medical School could result in a web-based training curriculum for physicians and dentists which could provide free risk management Continuing Medical Education. Such a resource, if well-designed and publicized, could result in a significant number of prescribers receiving targeted training in the absence of any mandate for a relatively modest appropriation.

Improved pharmacy training on the identification of prescription drug abuse and the security measures necessary to deter such abuse.

The Board of Registration in Pharmacy should consider developing a required course as an integral part of the continuing education requirements for pharmacists who store, distribute and dispose of drugs subject to abuse. Both pharmacies and pharmacists licensed by the Board of Registration in Pharmacy (the Board) are mandated to maintain strict security controls of all prescription medications ordered, received and dispensed, in accordance with deferral and state statutory and regulatory requirements. The Board provides training to pharmacists regarding security requirements as part of the continuing education course curriculum present on multiple dates and at various locations throughout the Commonwealth each year. Pharmacists complete coursework in these areas as part of the school of pharmacy curriculum. To qualify for licensure as a pharmacist in the Commonwealth, individuals must successfully complete the Multistate Pharmacy Jurisprudence Examination that includes federal and Massachusetts laws and regulations on the topics. The Commission recommends that the Board revise 247 CMR sections pertaining to the Prescription Monitoring Program (PMP) that apply to the dispensing of controlled substances by pharmacists when the revisions currently proposed to the PMP regulations are promulgated to reduce opportunities for drug diversion and facilitate intervention. In addition, the Drug Control Program (DCP), in cooperation with the Board, will develop training programs and materials for pharmacists to implement the proposed amendments. The training will include guidance on utilization of PMP information to assist patients with potential Schedule II pain medication problems and facilitate prevention of and interventions with drug addiction and abuse. The DCP will also cooperate with the Board on the development of information on dispensing, storage and disposal of controlled substances to reduce opportunities for drug diversion.

Tamper-Resistant Prescription Pads

Currently in Massachusetts, there are far too many ways for individuals who have not lawfully been prescribed OxyContin to obtain it. An individual could unlawfully obtain the drug, buy it on the street, or obtain a prescription for the drug by presenting a fraudulent prescription at a pharmacy. Fraudulent prescriptions have become a growing problem in the Commonwealth since the advent of OxyContin and other strong prescription pain medications.

Three basic categories of false prescriptions exist. The first is writing a fraudulent prescription on a legitimate prescription pad—an individual might steal a doctor's prescription pad and then, at a later time, write a prescription. The second is writing a forged prescription on a counterfeit prescription pad—an individual might copy a legitimate prescription written for them by a doctor and manipulate it in such a way to create a forged prescription pad on which they are then able to write counterfeit prescriptions. Lastly, is altering a legitimate prescription to increase the quantity, dosage or to add an additional drug.[49] [50] [51]

It should be made clear that falsified prescriptions are not solely related to abuse from OxyContin. Instead, the issue of fraudulent prescriptions is one that affects all drugs which have off-label uses (illegal and otherwise). The issue then is how the Commonwealth can eliminate the ability of people to obtain drugs and therapies without legitimate medical need.[52]

One solution to eliminating the number of fraudulent prescriptions is inexpensive and would not require a complete redesign of the current prescription drug delivery system. The creation of a tamper-resistant prescription pad program would allow Massachusetts to take action toward limiting the abuse of all three types of prescription fraud without having to eliminate written prescriptions and move toward a web-based prescription program. The Commission believes that the implementation of such a program has the ability to dramatically cut the number of fraudulent prescriptions that are filled in the Commonwealth each year.

Many states such as New York have implemented such programs and are seeing great success. Additionally, tamper-resistant prescription pads are already required by the federal government in order for Medicaid to reimburse patients and states for the cost of prescription drugs. Starting on October 1, 2008 all written, non-electronic prescriptions were required to contain at least three tamper-resistant features, one from each of the three baseline characteristics outlined by the Centers for Medicare & Medicaid Services, in order for Medicaid to reimburse.

A "regular" prescription pad may include the name of the doctor's practice; the doctor's address and telephone number; the name of the patient to whom the drug or therapy is being prescribed; the date the prescription was written; perhaps the address of the patients; whether the prescription maybe refilled (and how many times); and, space is also provided for the prescribing medical professional to write the name and dosage of the drug being prescribed and to sign the prescription. These pads are not regulated, except in the case of Medicaid prescriptions and a doctor may print them him/herself. A tamper-resistant prescription pad, on the other hand, is essentially the same as a "regular" prescription pad save the paper that has been used to produce the pad itself and the addition of several security features. First, instead of being normal copy paper the tamper resistant pad has been made of special paper which is resistant to erasures and alterations. This means that a prescription cannot be amended to increase the dosage or to increase the number of renewals available to the patients. Additionally, a tamper-resistant prescription pad is also printed in such a way that an individual is unable to photocopy the prescription for duplication. This is done much in the same way that bank checks are protected against photocopied reproductions. Finally, a tamper-resistant prescription pad has a security back print.[53] [54] [55] [56] [57]

As stated above, New York recently adopted a tamper-resistant prescription pad program. The New York program requires that all prescriptions for controlled substances be written on official New York State prescription pads, which contain tamper-resistant features, and that no exemptions to this rule may exist. Additionally, under the New York State program prescriptions for non-controlled substances must also adhere to strict requirements. In order to be accepted a prescription for a non-controlled drug must either be written on an official New York State pad, or it must be written on a facility's own prescription pad with a facility label affixed to it.[58] A facility label is a label on which a bar code has been printed that contains facility specific information readable by a computer. In addition, a facility label also contains safeguard which protect against the production of fraudulent labels in order to authenticate an illegitimate prescription.[59] For example, an authentic facility label in New York State contains a light blue pharmacist test area on the right side of the label, slight perforations along all sides of the label which prevent the label from being easily removed once it has been affixed to a

prescription, and the labels are individually serialized in the same way as official prescriptions. A New York style program would benefit Massachusetts greatly by minimizing the illegitimate prescriptions and standardizing the prescription pad system in the Commonwealth.

[Image showing a photocopied prescription pad where VOID appears throughout]
[Text Box: The word VOID appears on the prescription if it has been copied, scanned, or physically or chemically erased.

The Pharmacist Test Area on the front of the prescription is heat-sensitive ink and the color will change from blue to light blue or transparent when rubbed.

The Secure Standard Register on the back of the prescription is heat-sensitive ink and the color will change from orange to yellow when rubbed.]

New York State. Department of Health. Bureau of Narcotic Enforcement; *Pharmacy Update*, Winter 2008. Web. 19 Oct. 2009.

Implementing a tamper-resistant prescription pad program would allow additional safeguards to be built into the prescription delivery system without incurring major additional expense or creating a major disruption to the system while significantly limiting prescription fraud and saving the Commonwealth millions of dollars in counterfeit prescription costs. A sound policy such as this would provide Massachusetts with yet another tool to combat prescription drug abuse and curb this dangerous epidemic.

Preventing Overdose Deaths with Limited Liability Legislation

From 1990 to 2006, the Massachusetts age-adjusted poison death rate more than doubled from 5.6 to 14.9 per 100,000 residents. Almost 65 percent of Massachusetts' poisoning deaths in 2006 were caused by opiate overdoses.[60] Many of these deaths could have been prevented if the opioid abuser had received proper emergency medical services. Research shows that only 15 percent of fatal overdoses result in instant death, meaning that many lives could be saved if people who overdose receive prompt medical attention.[61]

The fear of arrest and prosecution often keeps opioid abusers from calling authorities when a friend or family member overdoses. Recent studies indicate that over half of the drug users interviewed did not call 911 during an overdose for fear that the police would prosecute them for illegally using drugs.[62] Many of these deaths could be avoided if Good Samaritan legislation were enacted in the Commonwealth. A Good Samaritan law would provide limited immunity from drug possession charges and prosecution when a drug-related overdose witness or victim calls for medical attention. The law would not however, protect people from prosecution from offenses other than possession of illegal drugs when calling 911, nor would it protect individuals with outstanding warrants against them or those who interfere with law enforcement procedures to secure crime scenes.

New Mexico was the first state to enact limited immunity legislation in 2007 and has seen very positive results. Several other states – Connecticut, Hawaii, Illinois, Nebraska, New York, Rhode Island – are considering similar bills. Many colleges and universities around the country have

also led the way on this issue by including limited liability policies for their student population. Currently, at least 91 schools in the country have implemented a Good Samaritan policy for alcohol or drug abuse.[63] A recent study showed that after Cornell University implemented a medical amnesty protocol, calls for emergency medical services for alcohol-related incidents increased.[64]

The Commission recommends that the Commonwealth enact a sensible limited liability law similar to New Mexico's that will be effective in decreasing the number of overdose deaths. The Commission also recognizes the need to include language that will ensure that offenders will not be able to exploit the law to evade prosecution and that it will only apply to potentially fatal situations. The implementation of this law will also require a significant effort to educate the public on the components of the law. Educating the public on these laws will enable the Commonwealth to prevent many senseless and preventable overdose deaths.

Overdose Prevention for Minors

The Commission believes that parents should be given the right to know when their child has an overdose. Many parents told the Commission that when their child experienced an overdose and was taken to the hospital they were never notified. Under current statutes and regulations, minors can check themselves out of the hospital and a parent may never be informed. This has obvious consequences for both the minor and parent and leads to a complete breakdown in communication. Currently, if a minor is caught under the influence of drugs or alcohol in a public space, such as a park, a police officer is required to return that minor to the custody of their legal guardian. However, if a minor is admitted to a hospital with the symptoms of an overdose, they can be released from the hospital on their own accord and no notice is given to the minor's legal guardian. Healthcare providers have the right to report to parents; however, most do not follow that protocol and as a result parents are never informed of their child's life threatening disease. There appears to be significant inconsistencies in the ways in which we handle overdoses of minors. While there are issues with patient/doctor confidentiality, the Commission believes that parents do have a right to know if their minor has experienced an overdose.

The Commission urges that legislation be enacted to mandate that hospitals report to parents in the event of a minor overdose and enable parents to take the necessary steps to seek treatment for their child. This is not meant to deter young adults from seeking proper medical treatment, but provide parents with a tool that they cannot currently use. Currently, 75 percent of colleges and universities in the Commonwealth have policies in place that require that school officials notify parents in the event of a student receiving medical attention or any illegal activity that occurs on a college campus. Including such a regulation in the Commonwealth would allow for intervention by parents, enabling them to take the action necessary to help their child.

Case Management

It is widely accepted in the mental health profession that case management is necessary to assist individuals in moving through the complex treatment process. The same can be said of the substance abuse field and the need for intensive case management in a constantly changing,

difficult to navigate and complex system. Case management could provide some of the necessary supports to assist individuals with substance use disorders in moving through a difficult process with many obstacles. The Commission recommends that the Commonwealth further investigate the state's capabilities to provide case management services to individuals identified with a substance use disorder and ensure that the case management provided in the Commonwealth includes the framework provided below various established programs.

The Substance Abuse and Mental Health Services Administration (SAMHSA) defines case management as "a set of social service *functions* that helps clients access the resources they need to recover from a substance abuse problem." [65] It is understood that effective case management is comprised of (1) assessment, (2) planning, (3) linkage, (4) monitoring, and (5) advocacy.[66] Clinical practice and empirical observation suggest that individuals with substance use disorders who seek treatment have significant exterior issues in addition to using psychoactive substances. In addition to substance use disorders, individuals often suffer from additional health issues including liver disease, HIV/AIDS, and strains of hepatitis. Further, they may have problems with procuring housing, employment, and difficulty in their relationships.[67] [68] When combined, these additional problems can exacerbate the underlying substance use disorder. The principal goal of case management is to keep an individual in effective treatment for the desired length of time. By focusing on the whole individual, case management allows for the external issues to be handled in combination with treatment, providing better long-term outcomes for the individual.

The Commission understands the role that case management plays in effective treatment, and believes that in order for case management to be effective, it must cross all agencies and allow the case manager to fully encompass all areas, including, housing, employment, medical, health insurance and substance use disorder treatment. Further, all agencies must be willing to work together for the common goal. SAMHSA along with the Center for Substance Abuse Treatment provides the necessary framework upon which for the Commonwealth to model a successful case management program. Given that many managed care organizations reimburse for case management services, the Commonwealth should be able to combine this funding with that of competitive federal block grants through SAMHSA.

Positive results have been seen in mental health and children's mental health services that involve intensive case management and the same results are possible with substance abuse issues in the Commonwealth. Additionally, various treatment providers in the Commonwealth have implemented a model of case management within their pain management and addiction treatment programs. Berkshire Health Systems (BHS), operating in Berkshire County, provides comprehensive health services in western Massachusetts. The BHS Pain Management Initiative includes inclusive case management and combines the "effort of healthcare providers, substance abuse specialists and members of law enforcement and the court system, designed to address the twin goals of improving chronic pain management services and combating drug diversion and misuse in the Berkshires."[69] The program has received acclaim for this innovative model which combines interagency services to patients seeking treatment for chronic pain with prescription pain medication and patients who have become addicted and are seeking treatment for their substance use disorder. Their model relies on the coordination with multiple disciplines to best facilitate treatment for their patients.

[Image is a flow chart showing Berkshire County Community Pain Management Project at the center of Pain Providers, Mental health Providers, Emergency medicine Providers, Primary Care Providers, Community Partners, Academic Partners, Regulatory Agencies: MA DPH, and Criminal Justice all communicating with each other]

Berkshire Health Systems, Inc. Pain Care Resource Manual: A Practical Guide for Health Care Professionals. n.d. Print.

[Bar chart showing Average Monthly healthcare Costs to Individuals Pre Treatment and One Year After Starting Treatment.

Pre Treatment:
Inpatient Medica/Sugrical Services - $1200, Emergency Department Visits - $400, Behavioral health Services - $2700, Women's and Children's Services - $700

In Treatment:
Inpatient Medica/Sugrical Services - $0, Emergency Department Visits - $0, Behavioral Health Services - $400, Women's and Children's Services - $1100]

Berkshire Health Systems, Inc. Pain Care Resource Manual: A Practical Guide for Health Care Professionals. n.d. Print.

While still in the early years of the initiative, the program is seeing great success, not only in lowering the number of individuals with substance use disorders, but in health care costs for individuals in need of chronic pain management. Individuals who were enrolled in the program for one year have seen dramatic decreases in healthcare costs, especially in the area of behavioral health visits.

Case management is a cost saving tool. Individuals who are enrolled in a program providing case management have fewer multiple detoxifications, relapses and unnecessary treatment. Connecticut provides a good program model through their Targeted Case Management (TCM) Services. TCM Services are determined by "persistent substance dependence as evidenced by one or more of the disorders indicated below as defined by the current edition of the DSM and by a history of multiple unsuccessful treatment episodes." [70] The Connecticut program provides diagnosis, treatment and follow up for individuals who have not responded to previous treatments, such as multiple detoxifications or outpatient care. In one year the case management program in Connecticut saw a 66 percent decrease in the total number of days that residential detoxifications were used.[71] The Commission recommends that a model, such as the one Connecticut or Berkshire Health Systems provides, be examined for possible application in the treatment model in the Commonwealth. It is the hope of the Commission that this tool would not only save money but provide more comprehensive services for those suffering from substance use disorders.

Insurance

Mandated coverage for substance abuse and mental health disorders has been an issue in state legislatures since the 1970s.[72] California was the first to pass legislation regarding mental illness in 1974, followed by 32 other states in the past 30 years.[73] There are two generally mandated types of state legislated insurance coverage. Mandated offering, which required that a plan offered in the state must treat physical and mental illnesses the same only if the insurance company offers coverage for those specific ailments in a given health care plan.[74] Mandated benefits on the other hand provides that coverage for mental and substance use disorders be complete and that minimum inpatient and outpatient coverage is specified by the state. It was not until 2001 that the Commonwealth recognized any form of substance use disorders as a form of mental health and required mandated benefits from the insurance industry.[75] Prior to the passage of the updated mental health parity laws of 2001, alcoholism and mental and nervous conditions were the only conditions covered under the mandated benefits model.[76] To Massachusetts's credit, the state is one of only nine states that have adopted parity statutes for substance use disorders.[77]

The Bureau of Labor Statistics data shows that the use of limits on substance abuse treatment has steadily increased since the 1980s, when such data began to be tracked.[78] According to the survey, in 1988, less than 60 percent of insured workers in medium and large firms were subject to limits on impatient treatment.[79] By 2002, 89 percent of workers insured through medium and large firms had limits placed on their inpatient treatment for substance abuse.[80] This dramatic decrease in services, coupled with the increase in deductibles, have negatively affected the treatment of individuals suffering from substance use disorders, even as federal and state laws have attempted to increase benefits, end discrimination for substance use disorders and reduce costs for those seeking both inpatient and outpatient treatment.

In this rapidly changing system, health insurance companies are moving to a "carve-out" system to provide mental health and substance abuse services. "Carve-outs, the management of mental health care by firms that are legally and administratively separate from the firm managing general medical care, have become common in both the public and private health care sectors."[81] Currently in Massachusetts the top insurance providers, including MassHealth, Blue Cross Blue Shield, Harvard Pilgrim Health Care, Tufts Health Plan and Fallon Community Health, contract their mental health and substance abuse services out to United Behavioral Health, Beacon Health Strategies and the Massachusetts Behavioral Health Partnership. Research on the effects of carve-outs is still not conclusive; however, given the testimony provided to the Commission, there is ample reason to be concerned that health insurance providers in the Commonwealth are able to reduce spending on mental health and substance abuse services by using the carve-out programs as gatekeepers and decreasing the services provided to individuals requesting mental health and substance abuse services.

Throughout the Commission's public hearings parents, loved ones, doctors, treatment providers and addicts continually brought up the various issues addressed above regarding insurance companies. One parent at the September 10, 2009 hearing stated that her son was denied further treatment after receiving an initial five-day detox until he had medically overdosed and was rushed to the hospital. At that point her insurance company approved a 14-day inpatient care; however her insurance later denied coverage for because the ways in which the provider coded

the treatment. She is still fighting with her insurance company to have that treatment paid for and has gone to the Massachusetts Attorney General's office to get the state involved.

The Commission understands the current climate in which Massachusetts finds itself in and the overwhelming support for cost containment and reform in the health care industry as a whole. Given these factors the Commission recognizes three areas of reform that must occur in the insurance industry to better enable those with substance use disorders to receive the treatment they, as individuals, needs:

1. Strengthen federal and state mental health parity laws to limit loopholes and provide comprehensive services in the form that is best suited to the individual suffering from substance use disorders. The state must ensure that insurance companies do not apply different utilization management standards to mental health and substance abuse treatments than they do to other medical interventions.

2. Mandate a medical necessity definition which includes a determination for behavioral health issues, providing for consistency across the state.

3. Ensure that should an individual chose the course of treatment that requires medication assisted treatment, proper coverage by insurance companies be mandated through the state.

While these reforms will not completely solve the discrepancies and inconsistencies within the insurance industry in regards to substance abuse treatment coverage, they will help to close the loopholes and work to end the heartache and frustration that many individuals in the Commonwealth experience.

> *Strengthen state mental health parity laws to limit loopholes and provide comprehensive services in the form that is best suited to the individual suffering from substance use disorder.*

As referenced above, federal and state mental health parity are often at odds with one another. The Federally mandated requirements do not specifically include substance use disorders at this time and the state mandated parity is only now beginning to require coverage for substance use disorders. Federal issues will be discussed at length in a corresponding section of the report. As of July 1, 2009, substance use disorders have been added to the list of mandated coverage disorders under the Massachusetts Mental Health Parity legislation. The law requires the coverage include up to 30 days inpatient treatment and $500 worth of outpatient treatment.

According to the Executive Office of Health and Human Services, Department of Mental Health;

> "Health plans must provide mental health benefits on a nondiscriminatory basis for the diagnosis and treatment of biologically-based mental health disorders, as described in the most recent edition of the Diagnostic and Statistical Manual of Mental Disorders published by the American Psychiatric Association ("DSM"). "Nondiscriminatory basis" means that copayments, coinsurance, deductibles, unit of service limits (e.g., hospital days, outpatient visits), and/or annual or lifetime maximums are not greater for mental

disorders than those required for physical conditions, and office visit copayments are not greater than those required for primary care visits."[82]

The state is still in the process of implementing these new regulations, and insurance companies are beginning to change their internal regulations on substance use disorder coverage to fall in line with the state law. The Commission believes it is of the upmost importance to ensure that insurance providers continue to uphold the central tenet of this legislation. Additionally, the Commission believes that the state must actively enforce the legislation, through the Office of Patient Protection and the Attorney General's office. Without strict enforcement insurance companies will find loopholes to covering treatment

Mandate a medical necessity definition which includes a determination for behavioral health issues, providing for consistency across the state.

There are two issues that arise within state insurance law as it applies to medical necessity. First, is the issue of the definition of medical necessity and how to best define the term while requiring all insurance companies in the Commonwealth to comply with a standard definition. Pennsylvania requires that medical necessity for drug and alcohol treatment be determined by a licensed physician external from the insurer.[83] Given the Commission's understanding of the difficulties that loved ones and individuals with substance use disorders face in securing adequate treatment, a recommendation is made to include a referral process by the Division of Insurance, in coordination with the Bureau and Substance Abuse Services, to the standardized definition of medical necessity.

Second, is the issue of the appeals process when individuals are denied coverage by their insurance company. While the Office of Patient Protection does allow for external reviews of denials of treatment for medical necessity, the Commission recommends strengthening the regulations to include more stringent guidelines. Further, if the above statutory change is made, a change in the appeals process will need to be made to reflect the state's comprehensive medical necessity criteria. Again, coordination with the Division of Insurance and the Bureau of Substance Abuse Services is needed. Vermont has the most rigorous criteria for appeals involving mental health services and substance abuse treatment. Their criterion establishes an independent seven member review board for mental health services and substance abuse treatment.[84] The Commission recommends using Vermont's statute as a model for legislation in the Commonwealth on medical necessity review boards.

Finally, an issue that was not widely addressed but deserves further attention is the distinction between fully-insured/fully-funded plans and self-ensured/self-funded plans. Currently there are two ways in which an employer may contract health insurance benefits for employees. Fully-insured/fully-funded plans require that all premiums be paid to a specific insurance company who pays the various providers for treatment. Self-ensured/self-funded plans require that employers pool all premiums and put said premiums into an escrow account and then contract with a health insurance company as a third-party provider. The original employer pays for all services out of the escrow account. The second type of employer supplied health insurance is not under state regulations or mandates and because this type of plan can save the employer the profit margin that they would have to pay to the insurance company, they make up nearly 50

percent of all employer supplied health insurance plans in the Commonwealth. The Commission recommends that further research be done, in conjunction with the Commonwealth's delegates in Congress, to determine the best course of action for federal laws to close loopholes involving self-ensured/self-funded plans.

> *Ensure that should an individual chose the course of treatment that requires maintenance and harm reduction medication, proper coverage by insurance companies be mandated through the state.*

Of the six insurance companies surveyed, four provide some level of methadone maintenance coverage and five of the six provide some level of buprenorphine/suboxone maintenance. Most companies stated that co-pays are required for maintenance medications and that there were no plans in place for individuals to move off maintenance medications at any time. For many individuals this is the best course of treatment and the Commission applauds the insurance industry for investing in this valuable tool towards sobriety. However, the Commission recommends that this is not the only tool for individuals to use and it can be misused and abused, just as other prescription opiates can. There should be strict guidelines to ensure that these medications are regulated and not abused. These alternative treatments must be covered by all insurance plans in the Commonwealth. As mentioned above, comprehensive follow up care from doctors and case managers is also a necessary component of effective opioid treatment and working with insurance companies to ensure that this occurs should be included in Department of Public Health regulations.

Addiction and the Criminal Justice System

The number of adults involved in the criminal justice system has soared from approximately 1.8 million in 1980 to 7.3 million in 2007.[85] During that same period, the number of people in prison for drug offenses rose roughly from 41,000 in 1980 to 500,000 today.[86] Nearly 1 in 31 adults in the United States is currently under some form of correctional supervision. In Massachusetts, that number is 1 in 24, up from 1 in 127 in 1982.[87]

[Line charting showing increasing demands on the department of corrections 1998-2007. Chart shows Individuals in MA Corrections System - women in system fluxuates between 908 females to 1089 between 1998 - 2007. Male individuals in the Correction System beginning in 1998 at 1,923 reduces until 2001 where 1,347 males were in the system. The total males in the Correction system then increases steadily until 2007 where 2,227 males are in the system.]

Commonwealth of Massachusetts. Department of Correction. *DOC Reentry Initiative*. DOC, 2008. Print.

The connection between drug abuse and crime is well known. Substance abuse is implicated in at least three types of drug related offenses: a) offenses defined by drug possession or sales, b) offenses directly related to the substance use (prostitution to get money for drugs, stealing to get money for drugs, etc.), c) offenses related to crimes committed while under the influence of substances (DUIs, etc.). Individuals who use illicit drugs are more likely to commit crimes and it is common for many offenses, including violent crimes, to be committed by individuals who had used drugs or alcohol prior to committing the crime, or who were using at the time of offense. In fact, according to the National Institute of Health, over 70 percent of inmates in state and local

prisons abuse drugs regularly.[88] Clearly, harsh punishment for drug offenders swells state and county prison populations, but does little, if anything, to reduce drug use. The Commission recognizes the need for reforms in drug policy and sentencing practices. These recommendations will be reviewed in detail below.

It is estimated that nationally 97 percent of individuals who are incarcerated will eventually return to living in the community.[89] In Massachusetts approximately 8 percent of the Department of Correction population is serving first or second degree life sentences; therefore, 92 percent of the inmates within the prison system will return to Massachusetts communities. More than 2,800 inmates were released in 2008 from the state corrections agency. A much higher number of individuals are processed through the Commonwealth's jails and Houses of Corrections on a routine basis. Most of these individuals are returning to Massachusetts neighborhoods with an untreated substance use disorder, which significantly increases the likelihood of their engaging in a variety of high risk behaviors, including criminal offending. However, there is an abundance of research which indicates that substance abuse treatment works for drug abusing offenders, even when it is entered involuntarily. Research also shows that the outcomes for drug abusing offenders transitioning to the community following incarceration can be dramatically improved through participation in aftercare programs. Left untreated, drug abusing offenders can relapse and return to criminal behavior, often within the first 72 hours after release. This jeopardizes public safety, leads to re-arrest and further stretches an already over-burdened criminal justice system. In light of these facts, the Commission recommends adopting practices such as the Bureau of Justice Assistance's Sequential Intercept Model, where interventions can occur at any and every point along a person's involvement with the criminal justice system, and enacting mandatory post-release supervision, that could compel a person leaving prison into treatment. These recommendations will be reviewed in detail below.

Spending on corrections has been the fastest growing or second fastest growing item in state budgets over the last fifteen years. In FY2009, the budget for corrections spending in Massachusetts was greater than the budget for higher education.[90] Despite this increased spending, recidivism rates have remained largely unchanged. Research shows that strong community supervision programs for lower-risk, non-violent offenders cost significantly less than incarceration. According to NIH, $1 spent in treatment results in savings of at least $4 to $7 dollars for the state.[91] The Commission supports the formulation of effective, cost-efficient recommendations that support treatment and insure public safety for this unique population. These recommendations will be reviewed in detail below.

Sentencing Reform and Post-Release Supervision

In the mid 1990s sentencing reform focused on "truth in sentencing." Reformers sought to restore integrity to the criminal justice system through statutory changes that ensured that the sentence that was indicated was the sentence that was served. This meant increasing incarceration capacity through alternative sentencing, amending arcane sentencing rules, and funding new prison construction through municipal bonds. Today, scarce resources mean that reform must do more than create additional capacity. For sentencing reform to be effective, it must promote evidence-based approaches that target recidivism and debilitated offenders.

Sentencing reform should include a variety of components, including those which allow the Department of Correction to "step down" inmates through the various security levels prior to release. In this way, individuals are better prepared to reenter the community, having progressed to minimum security and pre-release status. Such preparation prior to release is shown to reduce recidivism by gradually introducing the individual back into the community environment. Individuals currently serving mandatory minimum sentences are not allowed to participate in such programs, thus increasing their likelihood of reoffending. Many if not most of these "mandatory" sentences are related to drug use in one way or another. Given that these same individuals will be released to the community at some point, it is in the best interest of the state to better prepare them for such release by availing them of necessary reentry services through lower security programs.

Despite the overwhelming evidence that substance abuse programming is effective, if for a sufficient duration, even when required, the Department of Correction was only able to provide such services to approximately 45 percent of the inmates in need of such services in 2008 due to a shortage of resources. Since that time, the outpatient services component has been eliminated due to mandated executive funding cuts and budget reductions, further reducing the availability of critical services. Given that the majority of individuals incarcerated have either offended while under the influence of drugs or alcohol or committed crimes to procure such substances, enhanced residential and outpatient substance abuse treatment programs are essential during incarceration. Linkage with aftercare services upon release and the incentive to participate, as dictated by post-release supervision, is extremely important.

The Massachusetts Trial Court, Office of Community Corrections (OCC) is a government agency founded in 1996, to establish and implement intermediate sanction programs for the intensive supervision of probationers, parolees and inmates returning to the community after a period of incarceration. The OCC operates 27 Community Corrections Centers (CCC) statewide in collaboration with county sheriff's and community-based human service agencies. CCC's combine sanctions and services through Intermediate Sanction Levels, as promulgated by the Massachusetts Sentencing Commission. Sanctions include community-service, day-reporting, drug and alcohol screening and electronic monitoring. Services include substance abuse treatment, education, life-skills training and job development.

In FY2009 more than 4,000 criminal offenders received substance abuse treatment as a component of intensive supervision at a CCC. In order to increase access to substance abuse treatment at another point in the criminal justice process, consistent with the Sequential Intercept Model, the Commission recommends amending existing statutory law at Chapter 211F, Section 3 so that individuals on pre-trial probation can be referred to a CCC at ISL III or IV. Currently, by law, probationers must be "sentenced to" an intermediate sanction program as a condition of probation. A change in this law would permit substance abuse intervention not only for probationers who are "sentenced" post-disposition but those who are awaiting trial and under pre-trial probation supervision. This simple change would thereby create a ready-made, substance abuse treatment diversion program for those involved in the criminal justice system.

Additional substance abuse treatment intervention can be promoted through the reintroduction of "split" and "suspended" sentences to state prison adjudicated in the superior court. Under

current law, superior court judges do not have the authority to suspend a sentence of incarceration in whole or in part. Thus, superior court judges must choose exclusively between probation and incarceration. As a result, judges who might opt for a combination substance abuse intervention through intensive supervision and a period of incarceration are likely to take the "safer" approach of incarceration alone. The Commission recommends the restoration of suspended and split sentences. This move would provide judges with the authority to combine intensive supervision probation with a period of incarceration for single offense convictions in the superior court. This change will permit judges to more readily access substance abuse treatment either before or after a period of incarceration for a single offense conviction.

So-called "split" sentences provide the opportunity for additional post-release supervision. The Commission recommends that this post-release supervision be administered by probation so that the substance abuse treatment afforded through the CCC can be implemented for a time duration that is consistent with evidence-based practice. According to the National Institute of Drug Abuse, substance abuse treatment in criminal justice applications is effective when it lasts long enough to produce stable behavioral changes.[92] Consistent with this principle the OCC mandates the use of benchmarks to determine when a participant is able to make a transition to standard supervision. While all criminal justice supervision can be intensified through the CCC, only probation has the institutional focus and apparatus to coerce longer duration substance abuse treatment. The duration of parole or sheriff department supervision is often less than 90 days, which is inconsistent with evidence-based practice for substance abuse treatment in criminal justice supervision as articulated by NIDA.

Voluntary and Involuntary Commitments

There are currently two ways that an individual with substance use disorder can be placed into a locked-down setting, either through a civil ruling or as a result of a criminal offense. Massachusetts General Laws Chapter 123, Section 35 ("Section 35") permits the courts to involuntarily commit someone whose alcohol or drug use puts themselves or others at risk. Such a commitment can lead to an inpatient substance abuse treatment for a period of up to 30 days. Under the law, the person can be committed to a licensed treatment facility or, if none are available, to a separate unit at the correctional facility.

Those who commit a crime, and are found to be addicted to a controlled substance, can be placed in a locked-down treatment center through a number of innovative programs currently operating in the Commonwealth. There are 20+ drug courts in Massachusetts that can place an individual with substance use disorder in a locked-down facility for treatment as an alternative to incarceration. The Legislature, in the FY2007 Supplemental Budget, provided $1 million to start a pre-arraignment pilot program in the Essex County District Attorney's Office. The District Attorney is able to direct non-violent offenders into a locked-down substance abuse treatment facility, in lieu of arraignment and a subsequent Criminal Offender Record Information (CORI) record. Additionally, these offenders agree to enter and remain in treatment as well as pay restitution for any crimes committed in exchange for their arraignment being held in abeyance. Thus far, this program has been a great success and merits consideration for its application state-wide to serve as a siphon for the secure treatment centers.

In the summer of 2009 the Department of Corrections announced the closure of the Massachusetts Alcohol and Substance Abuse Center (MASAC). An immediate public outcry occurred, as many parents and loved ones who turn to the involuntary commitment statute as a means of protecting their loved ones when they have nowhere else to turn. Due to the overwhelming support for this program the Department of Corrections has put an indefinite hold on the closure of the facility. While this is a short-term victory for those who need this type of secure treatment, long-term solutions must be put in place.

Additionally, two treatment centers, the Men's Addiction Treatment Center (MATC) in Brockton, and the Women's Addiction Treatment Center (WATC) in New Bedford, have recently opened to provide secure treatment facilities for those individuals who are civilly committed. Approximately 92 percent of individuals who enter MATC successfully complete the program and 13.6 percent voluntarily extend their stay for further treatment.[93] While these units are providing much needed services for this population is individuals, including detoxification, case management and aftercare, they are constantly at capacity and in need of resources.

These programs are providing many individuals with a viable option to treat their opiate addiction. However, without proper funding these programs will not be able to sustain their current treatment levels. The Commission recommends that in light of current budgetary constraints secure treatment facilities, including MASAC remain in place until suitable alternatives can be established.

Jail Diversion

The Commission believes that we must drastically alter the manner in which we deal with those suffering with substance use disorders in our criminal justice system. The diversion of low-level offenders from a correctional setting into treatment is an excellent first step towards reforming a system in dire need of attention.

A jail diversion program will not only save the state tens of millions of dollars in correction costs, but also ensure that those with substance use disorders are receiving proper treatment. The findings thus far of the OxyContin and Heroin Commission have substantiated that the state is not providing a comprehensive treatment infrastructure and is, therefore, hemorrhaging money from this broken system. National estimates show that states disburse up to 15 percent of their budgets on substance abuse related costs. In Massachusetts this amounts to $4.2 billion of our state budget being used on corrections, public safety, children and family services, and health care costs associated with substance abuse.[94]

Jail diversion will create immediate savings and will take the pressure off of our overburdened corrections and court systems, allowing those branches to concentrate on their core missions. The Department of Corrections is clearly fulfilling a role that they are ill-equipped to handle. Evidence shows that 17 percent of all inmates claim to have committed their crime solely to obtain money to buy drugs. The neurobiological evidence proves that the impulse to get high becomes a survival function for individuals affected by this disease. For the most part, these individuals are not bad people, they are sick and in need of proper treatment.

A jail diversion model that requires up to 90 days of inpatient treatment, followed by a year of case management and support has the ability to change the way Massachusetts handles substance abuse issues. Many other states are adopting this model for treatment and seeing great success. We cannot afford to let Massachusetts fall behind other states in this area. We are a state that provides strong social services, excellent universal healthcare, top-rated schools, outstanding workforce development, mental health services, and resources for low-income individuals. Making a substantial change in our approach to this epidemic will make Massachusetts a national leader on this issue, and an example for other states to follow.

In 2007, Texas chose to address a projected shortfall of 17,000 available prison beds by 2012 by taking $241 million out of the prison budget and spending it on increased drug and alcohol treatment programs and other diversion efforts. It also expanded its drug courts.[95] Texas officials estimate that expanding the treatment and diversion programs will eliminate the 2012 bed shortfall and in will save the state $430 million over FY2008 and FY2009.[96]

The Commission believes that we must care for these sick individuals through a jail diversion program and that through this program, the Commonwealth will save money and lives.

Interdiction and Law Enforcement

Law enforcement officials play an important role in the substance abuse equation as they are often the first responders in instances of illegal activity and play a crucial role in the implementation of policies throughout the Commonwealth. In 2008, the United States Drug Enforcement Agency seized, 211.9 kilograms of cocaine, 7.6 kilograms of heroin, 2.9 kilograms of Methamphetamine and 988.6 kilograms of marijuana. Consequently, arrests for drug violations have risen in the last year with 540 taking place in 2007.[97]

[Bar chart shows drug violation arrests in Massachusetts from 2003 - 2007

2003: 431
2004: 409
2005: 402
2006: 402
2007: 540

Chart clearly shows a large increase from 2006-2007]

United States. Drug Enforcement Administration. *DEA Briefs and Backgrounds –Massachusetts*. Drug Enforcement Administration, 2008. Web. 19 Oct. 2009.

With the majority of state budgets concerning substance abuse going towards the aftermath of substance abuse, including crime and law enforcement, the Commission has a particular interest in ensuring that there is efficient funding and programming in place.

Internet

The availability of opioid analgesics on the internet is a concern that has garnered significant attention on both a state and federal level. The internet is riddled with online pharmacies that provide access to opioids, including those that do not require a prescription. In 2005, The Drug Enforcement Agency (DEA) concluded "Operation CYBERx" successfully shutting down over 22 pharmacies and nearly 5,000 web sites that were not requiring prescriptions.[98]

While the Commission acknowledges that the complexities involved in policing the internet remain largely a federal matter, it is imperative that emphasis is placed at the state level to monitor these transactions. The Commonwealth can be better served by improving the methods of communication with federal enforcement agencies responsible for targeting these internet suppliers which are often found to be the route source for expansive criminal enterprises.

Law Enforcement

The role of law enforcement in combating the proliferation of illegal opioid use is critical, yet often complicated and expensive. The Commission heard testimony from law enforcement officials who cited difficulty in disrupting the illegal sale of opioids without devoting significant time and resources to developing what eventually leads to a lengthy investigation. Due to the highly organized structure of the groups involved in trafficking opioids, the investigators rely heavily on long drawn out wire tap operations that become a particularly costly endeavor.

With this in mind, the Commission feels it is imperative that work be done to expand the available tools our law enforcement officers have to combat this illegal activity. Law enforcement officials need to work in conjunction with the medical professionals who prescribe these pain medications. Improving educational awareness and providing access to the Massachusetts Prescription Monitoring Program (PMP) would be the next step in the drive to better equip our law enforcement professionals. With limited funding available and the majority of the cost burden associated with assistance based programs, access to the PMP would be a very effective tool for law enforcement.

Long-Term Treatment

Research from the mid-1970s demonstrates that treatment can help patients addicted to drugs to "stop using, avoid relapse, and successfully recover their lives".[99] However, more often than not addictions go unnoticed or untreated. Substance Abuse and Mental Health Services Administration's (SAMHSA) National Survey on Drug Use and Health (NSDUH), indicates that in 2007, 23.2 million people in the US (9.4 percent of the population) age 12 and old require treatment for drug or alcohol use.[100] Of the 23+ million people needing addiction treatment

services only 2.4 million (10 percent of the population needing treatment) received the necessary treatment to successfully move into recovery, thus, 20.8 million persons (8.4 percent of the population aged 12 or older) needed treatment for an illicit drug or alcohol use problem but did not receive it.[101] Long term treatment programs are needed to provide a continuum of care to move the individuals from addiction to recovery.

Long-term treatment programs are designed to provide individuals with a treatment program that includes residential treatment, stabilization services, vocational rehabilitation and social support structures. These programs provide a continuity of care that extends through the life cycle of an individual with substance use disorder. Studies show that the best long-term programs are characterized by "a combination of therapies and other services to meet an individual patient's needs. Specific needs may relate to age, race, culture, sexual orientation, gender, pregnancy, other drug use, comorbid conditions (e.g., depression, HIV), parenting, housing, and employment, as well as physical and sexual abuse history."[102] Among the needed treatment programs, the best programs focus on substance abuse monitoring, case management, support groups, pharmacotherapy and behavioral therapy. Coupled with these treatment efforts, are the support structures needed for the individual to move into successful recovery. These support structures include family and child care services, vocational rehabilitation, mental health services, housing, financial and medical services. See all the components of comprehensive drug abuse treatment listed below.[103] The Commission recommends that a comprehensive approach to long-term treatment, include the following:

- Treatment program attributes: substance abuse monitoring, case management, support groups, pharmacotherapy and behavioral therapy.
- Recovery support attributes: family and child care services, vocational rehabilitation, mental health services, housing, financial and medical services.

Several studies have demonstrated the importance and efficacy of long-term treatment programs, especially those that institute a continuum of care program that serve the individual's specific needs and vulnerabilities. A study by the Institute for Behavioral Health found that "adolescents who received another service within 14 days of their residential discharge had approximately a 92 percent higher likelihood of being in recovery at the end of the 3-month follow-up than adolescents who did not receive another service within this time frame."[104] In a similar report the *Journal for Drug Education* found a significant relationship between social supports, economic self sufficiency and substance abuse outcomes in long-term programs.[105] Evidence about this relationship has been provided before, yet many programs have reduced their services and lengths of stay.[106] This study found that "reductions in substance abuse were associated with measures of self-sufficiency…among women who participated in our study; economic outcomes, substance abuse, and general functioning went hand-in-hand."[107] This research demonstrated that eliminating services, specifically employment related services will negatively impact the clientele.[108]

Short-term treatment should not be ignored or dismissed in regards to the overall spectrum of treatment options. However, with individuals who have a history of substance abuse, long-term treatment and continuum of care must be available. In 2001, the *Journal Psychiatric Services* looked at outcomes for short-term and long-term programs. The study determined that "patients

in the long-term program were significantly more likely to become engaged in treatment, and after discharge they were more likely to maintain abstinence and less likely to experience homelessness."[109]

A middle aged woman who is a resident of Phoenix House in Springfield testified at the commissions hearing at the State House on March 27, 2009 about her experiences with treatment programs. "The Phoenix House is the first long-term treatment facility I have tried and it is EXACTLY what I need… In my opinion is the only thing that gives addicts a chance at a so called normal life. Giving us structure and a chance to work on our issues and take care of things that we have put off for so long gives us hope that we can leave here and stay drug free."

Substance abuse treatment needs to be flexible and adjusted to the needs of the individual. Long-term treatment can provide the flexibility and adequate time to obtain the services needed to support the individual in their recovery effort. Research suggests that the length of treatment should not be pre-determined and should meet the need of the individual.[110] Similarly, "for residential or outpatient treatment, participation for less than 90 days is of limited effectiveness, and treatment lasting significantly longer is recommended for maintaining positive outcomes."[111] Recovery from drug addiction is a process that takes time and in some cases may require multiple episodes of treatment.[112]

In Massachusetts FY2007 there were 45,902 admissions to treatment programs, reporting heroin use. Of these admissions 8.8 percent (4,047) were admitted to Long-Term Residential Services for longer than 30 days.[113] These programs included Recovery Homes, Therapeutic Communities, social models, residential programs specifically for offenders, and women and family oriented shelters. It is interesting to note there are only 1,885 of long-term treatment beds available in Massachusetts. With calls from providers and consumers for more long-term treatment options, and no shortage of people needing the beds, the number of long-term treatment programs needs to be increased to meet this rising demand.

[Pie chart shows 8.8 percent of total treatment admissions are Long Term Treatment Admissions in FY2007]

Commonwealth of Massachusetts. Department of Public Health. *Substance Abuse Treatment Fact Sheet - FY 2007 Heroin Users*. Bureau of Substance Abuse Services, 2008. Web. 25 Sept. 2009.

John McGahan, President of the Gavin Foundation testified before the Commission on March 27, 2009 on his experience in working with long-term treatment programs. He stated that there are only 105 residential beds for adolescents in the Commonwealth. Cushing House, a 30-bed adolescent program run by the Gavin Foundation, is currently running at maximum capacity with a two month waiting list. The waiting list for Gavin House, a 33 bed residential program for men is just as long.[114] McGahan also commented that regulatory options need to consider the importance of cost effective treatment versus the high cost of incarcerations, social consequences, and that those affected are real people, mothers, fathers, sons and daughters. Long-term treatment programs need to be expanded to address this epidemic that is continuing to grow.

"Long-term residential treatment provides care 24 hours a day, generally in non-hospital settings. The best-known residential treatment model is the therapeutic community (TC), with planned lengths of stay between 6 and 12 months. TCs focus on the "re-socialization" of the individual and use the program's entire community— including other residents, staff, and the social context— as active components of treatment. Addiction is viewed in the context of an individual's social and psychological deficits, and treatment focuses on developing personal accountability and responsibility as well as socially productive lives. Treatment is highly structured and can be confrontational at times, with activities designed to help residents examine damaging beliefs, self-concepts, and destructive patterns of behavior and adopt new, more harmonious and constructive ways to interact with others. Many TCs offer comprehensive services, which can include employment training and other support services, on site.[115]

While many of these concepts are not foreign to treatment programs in the Commonwealth, the concept of long-term treatment is considered an expensive course of action. In-patient treatments, involving intensive 24-hour care can also be a commitment that an individual with a substance use disorder may not be willing to take. This being said, for some individuals it is the only way to recover from their disorder and maintain sobriety long term.

Youth

OxyContin, other prescription medication and heroin abuse has continued to be a prevailing problem with the Commonwealth's youth. In 2007, there were 4,544 substance abuse treatment admissions in the Commonwealth for citizens ages 15-19.[116] This age group accounts for 4.3 percent of all substance abuse treatment admissions.[117] An increasing number of young adults are being exposed to prescription painkillers. The Commission heard from parents and family members whose young adults became addicted in a variety of ways. According to statistics from the National Survey on Drug Use and Health (NSDUH), of youths misusing prescription opioids, one third reported that they obtained the drugs for free from family and friends. The second most common source for obtaining prescription opioids was through a physician.[118] Whether as the result of using painkillers after a major surgery or from experimentation with friends, the devastating and long-term effects of opioids in one's system are tremendous and the Commission feels that drastic steps must be taken to curb this epidemic in today's youth.

Education and Prevention

There are a variety of issues that affect young adults. First, is the need for prevention through schools and other community measures educating students about the dangers of substance abuse and working to deter them from trying drugs. Additionally, there is a need for licensed drug and alcohol counselors to be present in schools and provide the needed support to students who may be afflicted with addiction. The Commission found that many early points of interception for the Commonwealth's young adults are not being addressed.

Throughout the public hearing process the Commission heard many stories from community organizations and schools about the need for education and prevention programs. Due to strains in the budget since 2003, national programs such as D.A.R.E. have been cut from the state budget and as a result all but died out from the Massachusetts elementary and middle school

curriculums. Many schools were not able to keep up with the burden of paying for the program themselves. Raising awareness about the harms of drugs, alcohol and substance abuse is an issue that must be addressed at an early age. Additionally, given the changes in substance abuse in the Commonwealth, these programs must be updated to include illicit use of prescription drugs. D.A.R.E. Massachusetts has seen a recent resurgence and to date between 75 and 95 towns use the program in their schools. This is a drastic cut from the mid-1990s when most of the 351 towns in the Commonwealth accessed the program.[119] The program is attempting to modernize many of their original lesson plans, including topics on prescription medications, bullying and lesson plans for parents, however without widespread use, the program lacks the coherency to be broadly analyzed. The Commission recommends that a statewide program be put into place and required throughout all levels of a child's education, including the upper grades of elementary school. The curriculum should include lessons on the dangers of prescription medication abuse, as well as many of the other modern abused narcotics. A recent study from the National Institute of Health suggests that when school-based prevention programs began in elementary school they significantly reduced the number of students that engaged in substance abuse, violent behavior, or sexual activity.[120] It is the hope of the Commission that with a program in place in all schools, the rate of drug use would decrease among our youth.

In addition to improving education programs in schools, the Commission recommends that licensed drug and alcohol counselors are present in each middle school and high school throughout the state. While it is not necessary that a counselor be a separate staff member within the school, providing a teacher, health professional, principle or other staff member with the necessary training to recognize drug and alcohol abuse in youth, and assist parents and students with the available resources should a problem arise. Pennsylvania has a comprehensive approach to counseling and support services in schools, including a professionally trained team which includes school staff and experts from community substance abuse agencies that work together to monitor issues in the school and provide the best learning environment possible.[121]

Recovery High Schools

Recovery high schools are not a new concept to Massachusetts, however in recent months they have received increased attention and praise both within the state and nationally. In April 2009, CNN did a large print and television story on the students at the Beverly Recovery High School.[122] The three Massachusetts Recovery high schools are boasting great successes and in the 2006-2007 school year 72 percent of the youth referred to the three schools completed the school year.[123] Massachusetts Recovery high schools follow the traditional public high school format, meeting the Massachusetts Department of Elementary and Secondary Education Curriculum Framework, but incorporate the traditional addiction recovery 12-step program. These schools have seen success since their inception in the Commonwealth in 2006. In recent months, legislation in Massachusetts has been approved to require public school districts to put the portion of expenses for a given student attending a recovery high school towards that student's education at one of the three state recovery high schools. This is a vast improvement over the previous system and will aid the recovery high schools in continuing their mission and expanding the number of students they are able to serve. The Commission met with several students who attended a recovery high school in the Commonwealth and each student spoke that their success was due entirely to the drug-free zone the schools provided and are now giving

back to the schools, as teachers, mentors and staff members. The Commission recommends that the state continue to support these worthwhile schools, by increasing the number of recovery high schools in the Commonwealth through more funding and legislative support.

Throughout the hearing process the Commission heard from a variety of parents who expressed similar sentiments. We must do all that we can when children are young to expose them to the dangers of drug and alcohol abuse. Further, if a child has issues with alcohol or substance abuse, schools must be equipped to aid parents in knowing their options and assisting them in getting treatment for their child. Finally, when necessary, students should be given the option to attend an area recovery high school, as their success is clearly seen in the positive and successful graduates of these programs. The Commission believes that with these recommendations, the youth of Massachusetts who may become addicted or are currently addicted can be given a better chance of success.

Unique Populations

Throughout the Commission's public hearings, a variety of individuals spoke about so-called unique populations, which has their own special needs and considerations. The hearing in Hyannis focused solely on these unique populations dealing with substance abuse, including veterans and those with co-occurring disorders. The following section outlines the individual issues surrounding unique populations as they pertain to substance use disorders. Overall, the Commission believes that more attention must be paid to these individuals and the special needs they have.

Disabled Populations

In America there are 7 million people with disabilities (PWD) who receive federal support and health care benefits from the Supplemental Security Income (SSI) program.[124] Individuals who receive SSI have a long-term disability which will bring them in contact with state and federal health care systems as well as social service systems. These individuals receive treatment for their disabilities in many forms; however, the prevalence of substance abuse disorders among this population can increase the cost and complexity of those services.[125] One report focusing on substance abuse rates among people with multiple sclerosis (MS) found that "substance abuse may be present in up to 19 percent of this sample and contribute to high rates of depression. There may be greater risk of harm due to substance abuse in people with MS because of the potential magnification of motor and cognitive impairments."[126] With the prevalence of substance abuse among PWD, it is critical for treatment programs to be cognizant of the access barriers to treatment for this population. In addition much of the treatment for co-occurring disorders focuses on substance use disorders and mental health disorders, not on physical disabilities.[127]

Much of the difficulty in providing services for PWD is meeting the physical needs and access issues related to this population. A study by the Massachusetts Department of Public Health, in conjunction with the Center for Survey Research out of the University of Massachusetts Boston found that there were three main barriers to accessing needed health care.

[Pie chart showing reasons for not accessing proper healthcare
Cost Prohibitive - 30%
Difficulty in figuring out who to see - 37%
Hard to leave home - 33%]

Massachusetts Department of Public Health. (MDPH) Office of Health and Disability. *Study of the Unmet Needs of Adults with disabilities in Massachusetts*, 2007. Center for Survey Research. University of Massachusetts, Boston. July 2008.

Given the differences that PWDs face, substance abuse treatment programs for PWD must look to provide adequate access, treatment specific programs that take into consideration the physical impairments of the population.

Another barrier to accessing treatment for PWD who also have a substance use disorders is that "typical policy in state vocational rehabilitation (VR) agencies requires people with substance use disorder to be "clean and sober" for six months prior to receiving services."[128] For PWD to receive vocational training as a point of increasing independent living and quality of life, these services need to be available during, not after substance abuse treatment. This research demonstrated that vocational rehabilitation programs should be integrated into substance abuse treatment, not provided after the fact to improve an individual's independence and quality of life.

Recent studies have demonstrated that current best practice programs for PWD seeking treatment will merge the biopsychosocial theoretical perspective of addictive disorder. According to the study conducted by the Department of Alcohol and Drug Services in California, this model includes "supportive counseling, motivating client readiness for change and coping skills-training techniques. The goals of treatment are to establish and maintain abstinence from the illicit use of all psychoactive drugs, foster development of (nonchemical) coping and problem-solving skills to stop and ultimately eliminate impulses to "self-medicate" with psychoactive drugs, and to enhance and sustain client motivation for change."[129]

A report by the Oregon Health and Science University in Portland provided guidelines for removing access barriers to substance abuse treatment. This report cited that "interventions to address disparities in treatment access will need to coordinate across multiple communities to address the numerous barriers."[130] The study cited the following findings.

1. Vocational rehabilitation counselors and social service case managers will need to recognize and address substance in their clientele and increase referral to treatment.

2. Treatment programs will need to address the negative attitudes of their staff and improve accessibility of their facilities, policies, and materials.

3. Substance abuse treatment professionals must pay close attention to the unique aspects of the lifestyle of PWDs, which may affect the outcomes of SA treatment.

4. Provider sensitivity to treatment barriers (political, attitudinal, or physical) is crucial while devising evaluations and individual treatment plans. Leaders in the disability community have a role to play in informing their members about SA and treatment.[131]

The Executive Office of Health and Human Services (EOHHS) is striving to ensure that reasonable accommodations for access to programs and services needed by PWD are met. In accordance with the American with Disabilities Act, EOHHS is "committed to facilitating compliance with these important Civil Rights Acts among agencies that provide prevention, intervention and treatment services for alcoholism and other drug abuse."[132]

The Commission recognizes that there is a lack of specialized services for this population. Access to care is a major burden for individuals with substance use disorders who are also disabled. As with the other unique populations, many of the issues coincide with one another. The Commission believes that as with all substance abuse issues, treatment must be individualized and must adapt to meet the needs of specific populations, such as those who are also physically disabled. The Commission recommends more research to ensure that proper care is given to this unique population.

Co-Occurring Mental Illness and Addiction

According to the US Department of Health and Human Services, the term *dual diagnosis, or co-occurring disorders* is a common term that indicates the simultaneous presence of two independent medical disorders.[133] Recently, within the fields of mental health, psychiatry, and addiction medicine, the term has been popularly used to describe the coexistence of a mental health disorder and a substance abuse disorder.

Substance abuse is a common and devastating disorder among persons with severe mental illness (SMI). "Dual disorders occur in about 50 percent of individuals with SMI and is associated with a variety of negative outcomes, including higher rates of relapse, violence, hospitalization, homelessness, and incarceration."[134] [135] According to the National Alliance on Mental Illness (NAMI), "persons with a co-occurring disorder have a statistically greater propensity for violence, medication noncompliance, and failure to respond to treatment than consumers with just substance abuse or a mental illness."[136] In many cases mental health programs and services are not prepared or able to handle individuals with both a mental illness and substance abuse disorder. Often substance use disorders come out of mental illness due to the environment in which a mentally ill individual lives. Mentally ill individuals tend to live in low-income environments with little social support and easy access to drugs and alcohol.[137]

The statistics on the dual diagnosis population are startling. For example, 42.7 percent of individuals with a 12-month addictive disorder had at least one 12-month mental disorder, and 14.7 percent of individuals with a 12-month mental disorder had at least one 12-month addictive disorder.[138] Studies have also found that individuals with severe mental disorders were at significant risk for developing a substance use disorder during their lifetime. Individuals with schizophrenia are more than four times as likely as the general population to have a substance abuse disorder.[139] Further, individuals with bipolar disorder are more than five times as likely as the general population to have a substance abuse disorder.[140]

In many cases individuals classified with dual diagnosis struggle to obtain the services needed to support both disorders. According to the Massachusetts Executive Office of Health and Human

Services (EOHHS) "an individual with a substance abuse problem is eligible for continuing care services if he or she is determined to have a qualifying mental disorder, meets impairment and duration criteria, requires DMH continuing care services, and has no other means for obtaining them. The qualifying mental disorder must be confirmed before assessing whether the applicant meets duration and functional impairment criteria. The individual may need substance abuse services in addition to mental health services."[141]

It is generally understood amongst the treatment community that treatment programs designed for people whose problems are primarily substance abuse are generally not recommended for people who also have a mental illness. These programs tend to be confrontational and coercive and most people with severe mental illnesses are too fragile to benefit from them. Heavy confrontation, intense emotional jolting, and discouragement of the use of medications tend to be detrimental. These treatments may produce levels of stress that exacerbate symptoms or cause relapse."[142]

There are a variety of programs in Massachusetts that attempt to handle dual diagnosis patients in a way to better enable the success over the disease. "Desirable programs for this population should take a more gradual approach. Staff should recognize that denial is an inherent part of the problem. Patients often do not have insight as to the seriousness and scope of the problem. Abstinence may be a goal of the program but should not be a precondition for entering treatment. If dually diagnosed clients do not fit into local Alcoholics Anonymous (AA) and Narcotics Anonymous (NA) groups, special peer groups based on AA principles might be developed."[143]

Massachusetts the programs who received grants from the US Department of Health and Human Services offer services designed for individuals with co-occurring disorders is listed below.

- **Henry Lee Willis Community Center**, Worcester, Massachusetts – $400,000 each year for five years to address the needs of person 16 years of age and older who are chronically homeless and have mental illness and/or physical disability and substance abuse problems.

- **Casa Esperanza**, Roxbury, Massachusetts – $400,000 for five years to develop aftercare services for persons of the Latino population in an existing residential treatment program.

- **Boston Medical Corporation**, Boston, Massachusetts – $589,304 per year for three years, to support the BMC ACCESS Project that will work with the Massachusetts Department of Mental Health to create an enhanced safe haven shelter for homeless persons providing mental health, substance abuse and primary care services.

- **ServiceNet, Inc.**, Northampton, Massachusetts – $534,846 per year for three years, to support the Integrated Sheltering and Treatment Program to address the complex needs of homeless adults struggling with co-occurring mental health and substance abuse disorders.[144]

While these programs are good initial steps in improving services to those classified as dual diagnosis, more must be done to increase understanding of these multi-layer disorders. The Commission would recommend implementing lessons learned from the SAMHSA Co-Occurring State Initiative Grant (COSIG) that evaluated how 17 states addressed the common problem and developed more effective ways to identify and treat individuals with co-occurring mental illness

and addiction (dual diagnosis). This effort would require a joint plan between the Department of Mental Health and the Bureau of Substance Abuse Services.

Cultural Competencies

According to the 2000 U.S. Census 12.2 percent of Massachusetts residents are foreign born and 18.7 percent of all Massachusetts residents speak a language other than English at home.[145] Obviously then, Massachusetts possesses a significant population for whom English is not their first language and who, potentially, have limited English proficiency. There are many cultural, racial and ethnic differences that drastically change effective treatment for each subgroup of individuals. In 2007, the Latino population in Boston had the highest substance abuse mortality rate among all the racial/ethnic groups. In fact from 1999 to 2007, the Latino rate increased more than 500 percent.[146] It is important to note that the rate for African American and Caucasian populations decreased 20.3 percent and 8.3 percent, respectively, from 2006 to 2007, but those decreases are still well above the 1999 levels for mortality.[147] The Bureau of Substance Abuse Services provides interpreter services for those individuals in need of translators. For many people culturally appropriate treatment is an important piece of the continuum of care for substance abuse treatment.

[Substance Abuse Treatment Admissions by Race/Ethnicity, 2001-2008

Chart shows percent of total admissions by race. Chart shows Latino admissions staying relatively consistent but decrease by 4%. Black admissions decrease from 35.6% decreasing to 22.5%. White admissions steadilyl increase from 40.2% to 57.6%]

Health of Boston 2009. Boston Public Health Commission. Research and Evaluation Office. Boston, Massachusetts. n.d. Print.

Casa Esperanza in Roxbury is a model in Massachusetts seeing initial success. By creating a situation where everyone speaks and understands the same language one eliminates the possibility that an incorrect translation might occur or that some misunderstanding could take place. Perhaps more importantly though eliminating the need for a third party—a translator—allows for treatment provider and client, and for the clients themselves, to interact naturally.[148] While this is an obvious benefit to non-English speakers there are some unintended consequences to factor in. Allowing for natural interactions to take place has several benefits in and of itself, most intuitive but some not. First, placing individuals with substance abuse disorder who speak the same language exclusively into the same facility could lead to charges that members of that community are being ghettoized. While this obviously would not be the intension of such a program there is no doubt that it could possibly be an unintended consequence. Second, one has to be concerned that in increasing the availability of treatment services for a specific language population the total number of beds would remain the same and treatment for individuals with a substance abuse disorder who are not a member of a minority language population would have a more difficult time finding a treatment bed; in short creating magnet centers de facto decreases the number of bed available, and the flexibility of those beds, for the majority of those seeking substance abuse treatment. The Commission recommends that further funding be given to the current programs in place that support cultural competency.

Veterans' Concerns

The Commission believes that veterans are a demographic increasingly at risk for substance abuse. To date, Massachusetts has over 430,000 veterans throughout the state, including 30,000 veterans from Operation Enduring Freedom and Operation Iraqi Freedom.

The Commission found that substance abuse is most often related to Post Traumatic Stress Disorder (PTSD), Traumatic Brain Injury (TBI) or other mental health issues in veterans. The Massachusetts Department of Veterans Services' (DVS) Statewide Advocacy for Veterans Empowerment Program (SAVE) issued a report finding that approximately 4 percent of veterans admitted to problems of substance abuse coupled with PTSD, TBI or other issues.[149] However, the percentage only reflected veterans who had self-identified substance abuse and mental health issues. Current service members are facing an increased number of deployments as compared to older veterans. DVS notes that there has been increased concern over service members who may not report mental health issues or an increase in symptoms and will instead turn to self-medication through substance abuse.[150]

Veterans dealing with PTSD and related issues reported most often abusing narcotics (specifically heroin and morphine), alcohol and marijuana. Outreach coordinators with the SAVE program have also seen an increased number of veterans abusing both their own and other's prescription drugs to cope with lingering mental health issues.[151]

The Statewide Advocacy for Veterans Empowerment Program is Massachusetts' leading advocacy program for veterans suffering from mental health issues. SAVE was created in 2008 as collaboration between DVS and the Department of Public Health and offers outreach, advocacy and referrals for veterans and their families. Their main focus is on issues facing returning veterans such as PTSD, TBI and mental health issues, substance abuse issues and suicide prevention.

Program coordinators track and refer veterans to the proper resources for the issues they are facing. SAVE notes that substance abuse is most-often occurring in conjunction with other mental health issues and is not isolated to veterans of current conflicts. It is important to note that DVS does not offer specific treatment options for substance abuse but rather has the SAVE program direct veterans to other state and local resources who can properly help them.

The Commission recommends continued funding support for veterans outreach, referral services, and the Department of Veterans Services. In order for this recommendation to be effective the Commonwealth must continue to improve upon its methods for identifying returning veterans so that they may benefit from the services available to them. Massachusetts offers some of the most comprehensive benefits and services to veterans and should continue to set an example for the rest of the country through effective veteran advocacy and recognition of the issues facing returning service members.

CORI/Job Training

Today in Massachusetts approximately 2.8 million people have records in the Criminal Offender Record Information (CORI) system.[152] Many former offenders have trouble finding employment, securing housing or taking out loans because they have criminal records. The lack of opportunity provided to ex-offenders and the stigma of having a CORI leads many to fall back into old habits, which often include addiction and limits their ability to put their lives back together. An integral part of recovery is reintroducing those who have recovered from addiction both into society and the job market. This process is stymied by the inability of former substance abusers to find work because of CORI offenses, even after they have shown that they are rehabilitated and are making every attempt to stay sober.

A parent of an individual with a substance abuse disorder testified at the Commission's hearing in Salem that when her son was unable to continue on a path of sobriety after going through a 30-day treatment program, she concluded that the best way to help her son was to have him arrested for a drug offense. Unfortunately, her son is now in jail and while he is on his way to recovery, she expressed remorse that she is the reason why her son is in jail and now has a criminal record for the rest of his life. The Commission recognizes that many families struggle with the decision of helping their children beat addiction, even if that requires incarceration and a CORI for life.

According to national studies, jails and prisons around the country are crowded with offenders who have substance abuse issues. Research has shown that 80 percent of offenders are either addicted to alcohol or drugs, or alcohol or drugs were involved in the commission of the crime.[153] Those who are in the Commonwealth's jails and prisons are not immune from this high level of substance abuse. According to state data, 20 percent of prisoners in Massachusetts are incarcerated because of a drug-related crime, and another 20 percent of defendants turned to crime to support a drug habit.[154]

To deal with the high rate of incarcerated substance abusers, the Department of Corrections offers a six to eight month program called the Correctional Recovery Academy (CRA), which targets substance abuse, anger management, criminal thinking and relapse prevention. However, the program's capacity does not come close to meeting its demand; the program has 552 inmates participating across seven facilities with a waiting list of 400 inmates. In 2007, only 48 percent of the releasing offenders eligible for the program attended.[155] The lack of support for the majority of incarcerated addicts is detrimental to the recovery process. Once offenders are let out of jail, their problems do not end. Often many employers will not hire a potential employee simply because they have a CORI. Ex-offenders currently have no way to prove they are rehabilitated, creating an undue burden for the rest of their lives.

The Commission recognizes that CORI reform is a major issue that must be addressed. Therefore, the Commission recommends increasing funding of the CRA and other programs that focus on treatment and reentry. The Department of Correction recommends that increasing the CRA by 240 beds would cost approximately $900,000.[156] The additional funding will save money by preventing future incarcerations for minor drug offenses, which at $47,679 per offender in fiscal year 2008, are a great burden on the state.[157] In addition to increasing funding, the Commission recommends that a program for Certificates of Rehabilitation and Recovery for offenders who complete correctional programs like the CRA be created and included in CORI

reform legislation. A program such as this would enable ex-offenders to show prospective employers and landlords that they have gone through a recovery process.

Finally, the Commission recommends that when CORI reform takes place in the upcoming legislative sessions in the Commonwealth, the issue of better displaying individual crimes be examined. By allowing potential employers, landlords and other officials to see a clearer picture of an ex-offender's record, the hope is that the official would take into account a person's complete background. Further, such proposals as sealing CORI records for felonies and misdemeanors after less time would enable ex-offenders to get their lives back on track more quickly. The Commission expects that these incremental changes will provide those with CORIs who have chosen to continue on a sober path the opportunities they deserve.

Family Issues

Families traveled from across the state to each of the seven public hearings held by the OxyContin and Heroin Commission in order to testify and break the silence of this deadly epidemic. The members of the Commission received both written and oral testimony that openly and honestly spoke to the struggles and devastating effects that opiate use and abuse has had on the families living in the Commonwealth. The testimonies spoke to the uniqueness of each family's situation, yet provided a window into the similarities of the lives of the families living with the repeated heartache and devastation caused by opiate addiction. The Commission recognizes that addiction is a family disease and recovery is a family process. It is important for families to be both educated on the illness and supported throughout the recovery process as caring for a loved one who is struggling with an addiction is one of the most difficult situations that any individual or family will have to endure in their lifetime.

Throughout the public hearing process the Commission listened to heartfelt testimony from individuals who described the overwhelming experience of trying to blindly navigate through a system they knew little or nothing about to get treatment for an illness they knew just as little or nothing about. Many who testified admitted that they did not realize that a member of their family was addicted or that they didn't see any of the signs until there was a crisis that brought it to the forefront. At the July 10, 2009, hearing a mother spoke about her oldest son's addiction to heroin:

> "Until three years ago my only exposure to heroin had been in the movies and popular culture. I had never known anyone who had used it, and never thought it would ever become a part of my reality. But it did."

Many individuals stated in their testimony that they lived in an "idyllic" neighborhood, raised "good kids" and didn't know that such "hard" drugs were even being used or could be purchased within their community. National surveys of substance abuse, including the 1999 National Household Survey on Drug Abuse, "strongly suggest that most new users of heroin are young," exemplifying the fact that today's opiate addict and opiate addiction cannot longer be confined to the old stereotypes of an older street addict lurking in the shadows of an urban high rise and shooting up in an alleyway.[158]

The Commission listened to individuals as they provided testimony detailing how painful and exhausting it was when discovering a loved one was addicted to opiates and the shame and isolation that followed. They described feeling embarrassed and that they were reluctant and scared to tell anyone about the situation. Their lack of information and desperation to do anything to help their loved one caused them to frantically search for answers, often times resulting with more questions and feelings of helplessness.

The longer the addiction goes untreated, the higher the chance those members of the family who are not addicted will also develop destructive behaviors such as denial, enabling and co-dependency.[159] Research has shown that when an alcoholic or drug addict is progressing with the disease, the loved ones in their lives often become worse off than the addict themselves and suffer from emotional and psychological stress.[160] In addition, these individuals often suffer from physical problems such as headaches, allergies, insomnia, and cardiovascular disease.[161] At the July 10, 2009 hearing held in Hyannis, another mother spoke about needing treatment for not only the addict in her family but everyone in her family. She said that the support they received help them make some of the most difficult decisions they would have to make but it was, "the best thing we could have done, for it brought us to where we are today- recovery for not only for our son, but for the whole family." Education and support for the family will bring much stability into the life of chaos that they are experiencing.

The Commission identifies that the role of the family needs to be valued and recognized in the delivery of drug treatment and has the following recommends:

- Increasing availability, access and funding to family services and peer support groups to ensure that families are given all options regarding treatment and services both for families and individuals with substance use disorder.

- Increasing access to information on drug overdoses so that parents and loved ones have the lifesaving tools in the event of an emergency.

Increasing availability, access and funding to family services and peer support groups to ensure that families are given all options regarding treatment and services both for families and individuals with substance use disorder.

The support and education received in this type of program provides a valuable tool for loved ones to cope with the different stages of addiction and recovery and have proved effective. These programs support family members in addressing their own unwarranted self-blame and alleviate the feelings of pain and suffering caused by the shame and isolation of this disease. Often times the isolation and stigma attached to addiction cause families to suffer in silence. Many family members find the support they need from the members who lead and participate in these groups; as they educate and involved loved ones and family members in the treatment and recovery process.

Local and national peer groups, such as Al-Anon, Nar-Anon, Learn to Cope, and the Massachusetts Organization for Addiction Recovery (MOAR) offer the friends and family members of individuals who are addicted a safe and supportive environment to learn about the

disease, care for their loved ones, and themselves. The 2006 Al-Anon Family Groups Member Survey stated that members were "significantly affected" by another person's drinking. It was also reported that 82 percent of the responders stated that their attendance and participation within the group much improved their mental health, 58 percent reported "much improved" overall health status and 73 percemt reported "much improved" daily functioning at home, school and work.[162] These groups offer individuals who feel very much alone, a connection to those who have or are currently going through a similar situation and strength to carry on.

Increasing access to information on drug overdoses so that parents and loved ones have the lifesaving tools in the event of an emergency.

Programs such as the Opioid Overdose Prevention and Reversal Project in the Commonwealth should be utilized to prevent dangerous overdoses. Further, parents and loved ones should be trained in administering Naloxone in the event of a opioid overdose. According to research, "death from a heroin overdose most commonly occurs 1 to 3 hours after injection, most deaths occur in the company of other people and that medical help is not sought or is sought too late.[163] The estimated mortality rate in heroin overdoses managed at home is 10 percent.[164]

Beginning in Europe and Australia in the mid-1990s and moving to the United States in the 1999, naloxone is intravenous or intranasal prescription, with no abuse potential. Naloxone effectively blocks the opioids and restores normal breathing when used on an individual experiencing a drug overdose.[165] Currently, 11 communities participate in the pilot project in the Commonwealth. The Opioid Overdose Prevention and Reversal Project offers counseling and referrals to substance abuse treatment for all participants who are misusing opioids. These programs train opioid users, their families and their friends on how to prevent and recognize an opioid overdose, and what to do if one occurs.[166] In addition to training individuals on using the prescription naloxone, the programs cover the importance of calling 9-1-1, how to perform rescue breathing, how to administer nasal naloxone, and how to provide after-naloxone care.[167] The Commonwealth has seen some of the most promising results of any community using naloxone with enrollment to date in the program at over 3,000 with 350 reported reversals.

Naloxone Prescription Programs in the United States 1999-2007

City/State	Year of Establishment	Number of Trainings/ Prescriptions	Number of Reported Overdose Reversals
Chicago	1999	4600	416
New Mexico	2001	1312	222
San Francisco	2003	650	141
Baltimore	2004	951	131
New York City	2005	938	73
Massachusetts		3000	350

Sporer, Karl A. MD and Alex H. Kral, PhD. Prescription Naloxone: A Novel Approach to Heroin Overdose Prevention. Annals of Emergency Medicine. Vol. 49, No. 2: Feb 2007. 172-177.

These programs have proven effective and lifesaving in the communities they have been administered. Thus, the Commission recommends increasing funding to expand the current pilot program to a statewide program in all communities. At the Commission hearing in Fall River on May 15, 2009, Joanne Peterson, founder of Learn to Cope, set her prescription for Narcan out of the table as she began to testify and spoke about how she and other parents in the area carry Narcan in case they must use the lifesaving medication on an overdose victim. These individuals are well-trained in administering the drug and know the proper follow up steps to ensure a continuum of care. New Mexico saw a 20 percent decrease in overdose deaths after the state Department of Health began a naloxone distribution program in 2001.[168] The Commission recommends increasing access to this lifesaving program and providing continuing support to parents and families seeking use of Narcan and other similar drugs.

Federal Issues

In many ways the opiate epidemic in Massachusetts and around the country started at the federal level with the failure of the Food and Drug Administration to adequately monitor prescription medications. Federal issues are intertwined throughout many of the recommendations in this report; however, the Commission felt it necessary to include a separate section in the report on the specific issues that are beyond the purview. The following areas have been identified as key components to federal interaction with the Commonwealth in reaction to the opioid epidemic.

- Federal law enforcement and regulatory programs must be involved in the policing of illegal prescription drug activity on the internet.

- Mental health parity must be strengthened nationally to include provisions for substance abuse coverage by insurance companies.

- Continued and increased assistance from the Massachusetts Congressional delegation in obtaining funding for vital programs in the Commonwealth.

- Continued progress is necessary in regards to prescription medication monitoring through the Risk Evaluation and Mitigation Strategy (REMS) process at the Federal Drug Administration.

The Commission believes that for the state to be truly successful in combating the problem of addiction, coordination with the federal government is essential in the above areas. Swift action should be taken by the federal government to engage the state in capacity building measures and better equip the state the handle the opioid epidemic the state is facing.

Federal law enforcement must be involved in the policing of illegal prescription drug activity on the internet.

As was mentioned in the Interdiction section of this report, internet monitoring is acknowledged as a federal issue with little state interaction. The federal government is best equipped to take steps to counteract the illegal prescription market online. The Drug Enforcement

Administration, along with the American Medical Association and state boards of medicine and pharmacy have all condemned the illegal activity of filling a prescription through so-called "cyber doctors."[169] While many individuals use the internet to legally obtain prescriptions at a lower cost, the internet has become an increasingly dangerous place to purchase prescription pain relievers. Unreliable suppliers, faulty dosages, expired medication and lack of warnings and directions all contribute to this faulty industry. The Commission therefore recommends that federal law enforcement increase their involvement in internet policing for illegal narcotics prescription websites and that more federal dollars go towards this important program.

Mental health parity must be strengthened nationally to include provisions for substance abuse coverage by insurance companies.

Nationally, mental health parity lagged behind those of individual states. In 1996, President Bill Clinton signed the first federal legislation to require mental health benefits, prohibit the use of special annual and prohibit lifetime dollar limits on coverage for services associated with mental health.[170] The bill was reauthorized most recently in 2007. The law does not explicitly list substance use disorder and a mandated benefit or mandated offering, but rather instructs the Comptroller General to issue a study on the implementation of a mandated substance abuse treatment requirement for insurance companies. At this time it is unclear about any potential changes to the legislation that may occur to include substance abuse in the definition of mental health parity.

Assistance from the Massachusetts Congressional delegation in obtaining funding for vital programs in the Commonwealth.

Better coordination with the Massachusetts Congressional delegation, officials in Massachusetts must acquire the resources for innovative programs such as jail diversion and recovery high schools. The Commission believes that the Commonwealth could greatly benefit from additional funding and resources from the federal government, especially in the areas of treatment and prevention. The Obama Administration is developing a new model for drug addiction policy in the United States and there is evidence showing that the focus is on treatment and prevention measures. As this process continues, the state must concentrate on harnessing the possible new federal dollars in these areas to improve current programs and install new ones.

Continued progress is necessary towards prescription medication monitoring through the Risk Evaluation and Mitigation Strategy (REMS) process at the Federal Drug Administration.

In 2007, the Food and Drug Administration (FDA) was given the authority to assess drug and biological products for the risks they pose to those taking them. Additionally, the FDA was given the authority to use the Risk Evaluation and Mitigation Strategy (REMS) to deem a drug unsafe and issue regulations on the proper use of the medication. This year the FDA issued new guidelines regarding the re-evaluation of certain opioid drug products previously approved by the federal guidelines. A total of 24 products were called in for evaluation, including Hydromorphone, OxyCodone, Fentanyl and Methadone. The FDA is planning on holding a series of public meetings regarding prescription medication safety, some of which have already

occurred, with the hopes of issuing new guidelines for the medications later this year. This process is essential to the original intent of the FDA and will ensure that the FDA is mitigating risk of these powerful prescription medications.

The Commonwealth must engage the Congressional delegation at all levels in the reform process and ensure that as the Commission moves forward with policy recommendations the federal government is kept involved.

Conclusion

Throughout the many hours of Commission testimony and conversations with citizens in the Commonwealth who deal with substance abuse on a daily basis, it is evident to the Commission that more must be done to provide for this vulnerable and often overlooked population. The face of addiction has drastically changed in the last 30 years and no longer is an individual with substance use disorder one who should be shunned and pushed to the bottom of the list for adequate services.

Each day in the Commonwealth, two citizens die of an opioid-related overdose. This statistic is a call to action for the state to reconsider long-standing policies surrounding substance abuse and treatment.

We are faced with a public health crisis. Like any other public health emergency, whether the pandemic influenza infection of the early part of the last century, the polio epidemic of the 1950's, the HIV/AIDs health crisis, or the rapid spread of H1N1 influenza we face today, resources must be allocated to minimize the scourge that is substance abuse disorder and, specifically, opiate abuse and addiction. Unlike some of these crises, there is no vaccine or medication that offers hope of elimination. We must concentrate our efforts at every interstice where we can lessen the impact of this dreaded disease.

In addressing the opiate epidemic the one thing we do understand is that there is not a one size fits all solution. The treatment community is divided between two philosophies. Those who believe in medication assisted treatment, such as methadone and buprenorphine/suboxone, and those who believe in abstinence. While there are merits to both sides, and the Commission does not endorse one mode of treatment over another, as long as there is evidence that supports a specific mode of treatment or a method of prevention, it must be considered. The Commission has suggested an ambitious set of recommendations for the Commonwealth to adopt and while the policy process can be tedious at times, we must continue to fight for the individuals who are suffering from the deadly disease of addiction.

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Exhibit N

RECOMMENDATIONS OF THE GOVERNOR'S OPIOID WORKING GROUP

JUNE 11, 2015

WWW.MASS.GOV/STOPADDICTION

Overview

The Commonwealth has a long history of trying to combat addiction. We began to address the harm of opioids in 2004, when 456 individuals died of an opioid overdose. Since 2004, more than 6,600 members of our community have died, and behind those deaths are thousands of hospital stays, emergency department visits, and unquantifiable human suffering.

We are in the midst of an epidemic. Our response requires a strong partnership between the medical community, law enforcement, the judiciary, insurers, providers, health and human services agencies, elected officials, and the public. Our law enforcement agencies are a critical part of the opioid solution; however, we cannot arrest our way out of this epidemic. These recommendations aim to ensure access to pain medication for individuals with chronic pain while reducing opportunities for individuals to access and use opioids for nonmedical purposes.

The Commonwealth must **build upon** and **accelerate** the prevention, intervention, treatment, and recovery support strategies recommended by prior task forces and commissions and acted upon by the legislature. Equally important, we must implement **BOLD NEW STRATEGIES**. To that end, the working group developed more than 65 actionable recommendations for the administration to consider for implementation.

The challenge is great. Addiction is a complex disease. There are no easy or quick solutions, nothing short of a comprehensive approach to this opioid epidemic will turn the tide of overdose deaths and reduce the harms that opioids are inflicting upon individuals, families and our communities.

Objective

Produce actionable recommendations to address the opioid epidemic in the Commonwealth

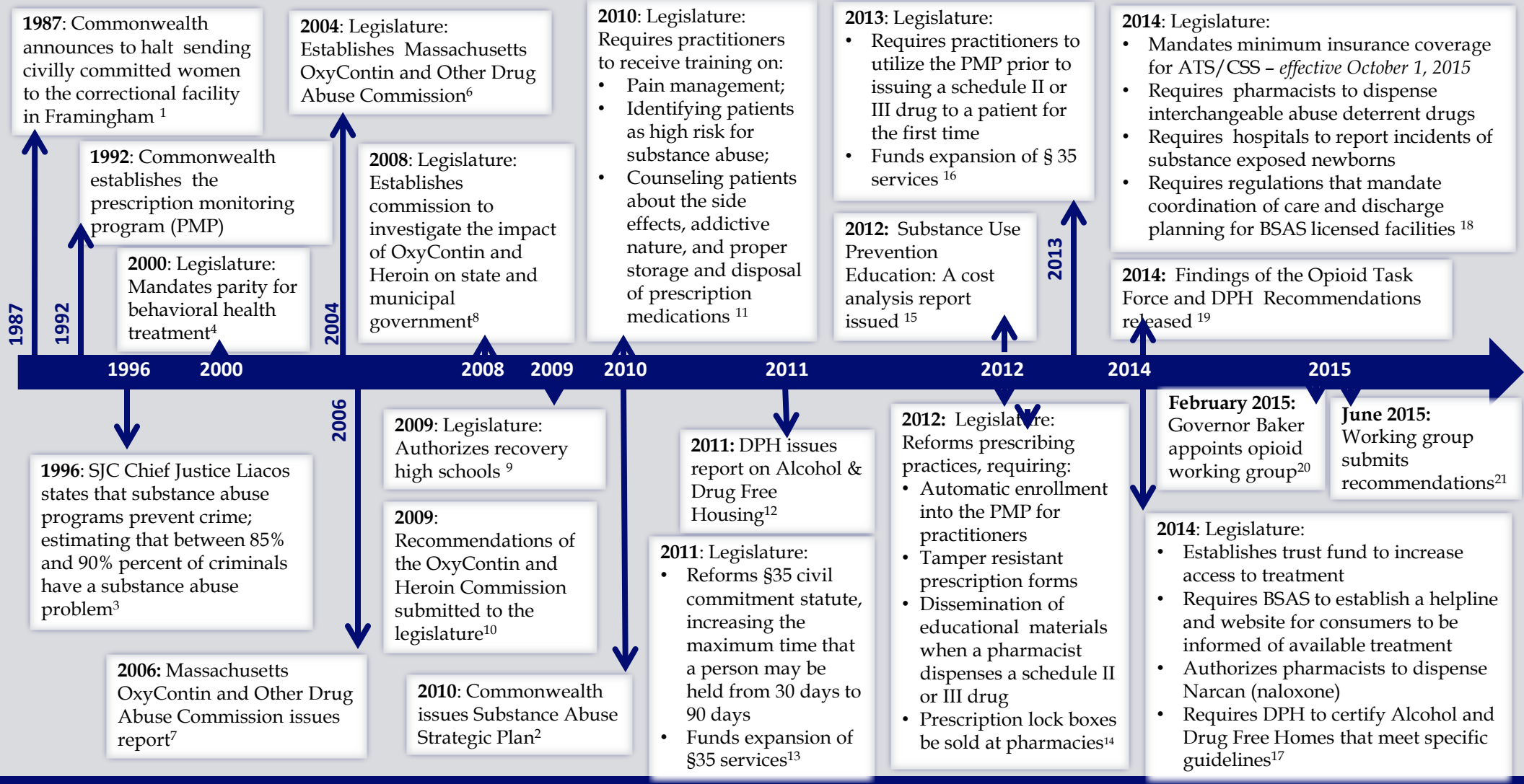
Goals

- Reduce the magnitude and severity of harm related to opioid misuse and addiction
- Decrease opioid overdose deaths in the Commonwealth

To Meet the Objective the Working Group

- Hosted 4 listening sessions in Boston, Worcester, Greenfield, and Plymouth
- Held 11 in person meetings
- Received and examined documents and recommendations from more than 150 organizations
- Heard from more than 1,100 individuals from across the Commonwealth
- Reviewed academic research, government reports, and reports of previous task forces and commissions

30 Years of Combatting Addiction in the Commonwealth



1987: Commonwealth announces to halt sending civilly committed women to the correctional facility in Framingham [1]

1992: Commonwealth establishes the prescription monitoring program (PMP)

2000: Legislature: Mandates parity for behavioral health treatment[4]

1996: SJC Chief Justice Liacos states that substance abuse programs prevent crime; estimating that between 85% and 90% percent of criminals have a substance abuse problem[3]

2004: Legislature: Establishes Massachusetts OxyContin and Other Drug Abuse Commission[6]

2006: Massachusetts OxyContin and Other Drug Abuse Commission issues report[7]

2008: Legislature: Establishes commission to investigate the impact of OxyContin and Heroin on state and municipal government[8]

2009: Legislature: Authorizes recovery high schools [9]

2009: Recommendations of the OxyContin and Heroin Commission submitted to the legislature[10]

2010: Legislature: Requires practitioners to receive training on:
- Pain management;
- Identifying patients as high risk for substance abuse;
- Counseling patients about the side effects, addictive nature, and proper storage and disposal of prescription medications [11]

2010: Commonwealth issues Substance Abuse Strategic Plan[2]

2011: DPH issues report on Alcohol & Drug Free Housing[12]

2011: Legislature:
- Reforms §35 civil commitment statute, increasing the maximum time that a person may be held from 30 days to 90 days
- Funds expansion of §35 services[13]

2012: Substance Use Prevention Education: A cost analysis report issued [15]

2012: Legislature: Reforms prescribing practices, requiring:
- Automatic enrollment into the PMP for practitioners
- Tamper resistant prescription forms
- Dissemination of educational materials when a pharmacist dispenses a schedule II or III drug
- Prescription lock boxes be sold at pharmacies[14]

2013: Legislature:
- Requires practitioners to utilize the PMP prior to issuing a schedule II or III drug to a patient for the first time
- Funds expansion of § 35 services [16]

2014: Legislature:
- Mandates minimum insurance coverage for ATS/CSS – *effective October 1, 2015*
- Requires pharmacists to dispense interchangeable abuse deterrent drugs
- Requires hospitals to report incidents of substance exposed newborns
- Requires regulations that mandate coordination of care and discharge planning for BSAS licensed facilities [18]

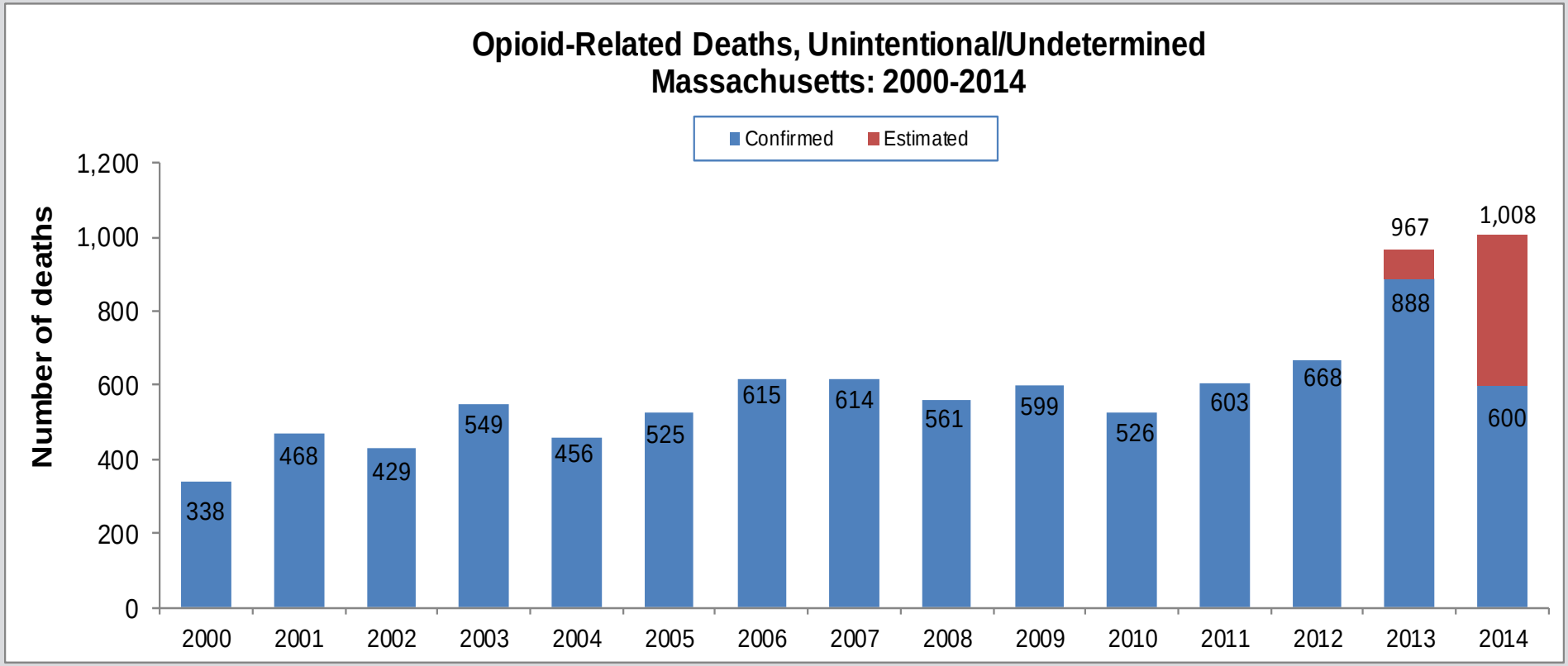
2014: Findings of the Opioid Task Force and DPH Recommendations released [19]

February 2015: Governor Baker appoints opioid working group[20]

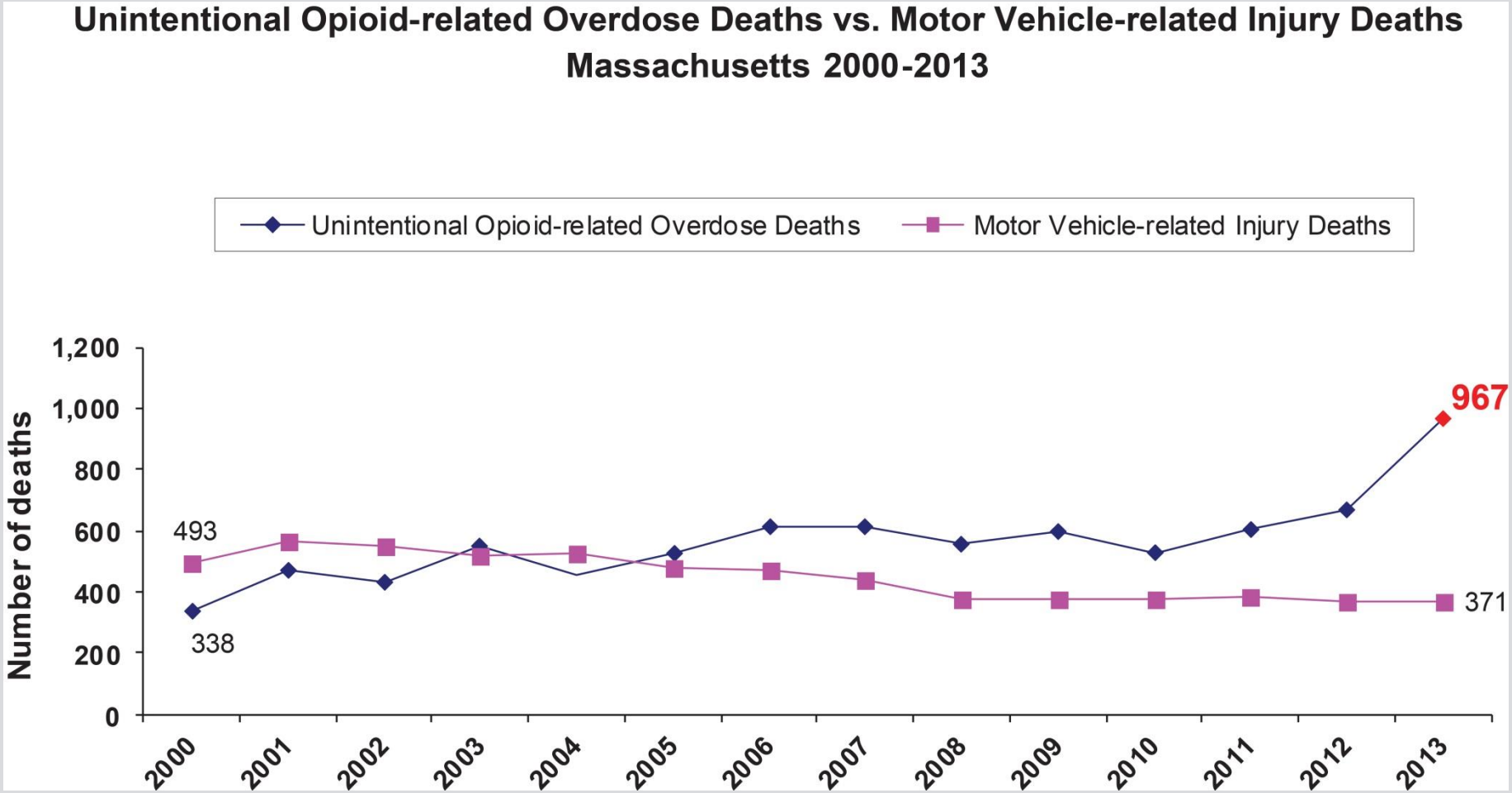
June 2015: Working group submits recommendations[21]

2014: Legislature:
- Establishes trust fund to increase access to treatment
- Requires BSAS to establish a helpline and website for consumers to be informed of available treatment
- Authorizes pharmacists to dispense Narcan (naloxone)
- Requires DPH to certify Alcohol and Drug Free Homes that meet specific guidelines[17]

Sources listed in Appendix A



MA Department of Public Health Data Brief, April 2015
http://www.mass.gov/eohhs/docs/dph/quality/drugcontrol/county-level-pmp/data-brief-apr-2015-overdose-county.pdf



MA Department of Public Health Data, February 2015

The Working Group's KEY STRATEGIES:

1. Create new pathways to treatment

Too many individuals seeking treatment utilize acute treatment services (ATS) as their entry point, even when a less acute level of treatment may be appropriate. By creating new entry points to treatment and directing individuals to the appropriate level of care, capacity will be managed more efficiently and the Commonwealth will be better able to meet the demand for treatment.

2. Increase access to medication-assisted treatment

Medication-assisted treatment for opioid use disorder (e.g. methadone, buprenorphine, naltrexone) has been shown to reduce illicit opioid use, criminal activity, and opioid overdose death. Increasing capacity for long-term outpatient treatment using medications as well as incorporating their use into the correctional health system, can be a life-saving intervention.

3. Utilize data to identify hot spots and deploy appropriate resources

By the time DPH receives overdose death data from the medical examiner, the data is stale. The Commonwealth should partner with law enforcement and emergency medical services to obtain up-to-date overdose data, which can be used to identify hot spots in a timely manner and allocate resources accordingly.

4. Acknowledge addiction as a chronic medical condition

Primary care practitioners must screen for and treat addiction in the same way they screen for and treat diabetes or high blood pressure. This will expedite the process for timely interventions and referrals to treatment.

5. Reduce the stigma of substance use disorders

The stigma associated with a substance use disorder (SUD) is a barrier to individuals seeking help and contributes to: the poor mental and physical health of individuals with a SUD; non-completion of substance use treatment; higher rates of recidivism; delayed recovery and reintegration processes; and increased involvement in risky behavior.

The Working Group's KEY STRATEGIES:

6. Support substance use prevention education in schools

Early use of drugs increases a youth's chances of developing addiction. Investing in the prevention of youth's first use is critical to reducing opioid overdose deaths and rates of addiction.

7. Require all practitioners to receive training about addiction and safe prescribing practices

Opioids are medications with significant risks; however, safer opioid prescribing practices can be accomplished through education.

8. Improve the prescription monitoring program

The Commonwealth's prescription monitoring program (PMP) is an essential tool to identify sources of prescription drug diversion. By improving the ease of use of the PMP and enhancing its capabilities, it will no longer be an underutilized resource.

9. Require manufacturers and pharmacies to dispose of unused prescription medication

Reducing access to opioids that are no longer needed for a medical purpose will reduce opportunities for misuse.

10. Acknowledge that punishment is not the appropriate response to a substance use disorder

Arrest and incarceration is not the solution to a substance use disorder. When substance use is an underlying factor for criminal behavior, the use of specialty drug courts are effective in reducing crime, saving money, and promoting retention in drug treatment. It is important that treatment occur in a clinical environment, not a correctional setting, especially for patients committed civilly under section 35 of chapter 123 of the General Laws.

11. Increase distribution of Naloxone to prevent overdose deaths

Naloxone saves lives. It should be widely distributed to individuals who use opioids as well as individuals who are likely to witness an overdose.

12. Eliminate insurance barriers to treatment

Removing fail first requirements and certain prior authorization practices will improve access to treatment. By enforcing parity laws, the Commonwealth can ensure individuals have access to behavioral health services.

In order to reduce opioid deaths, the Commonwealth must use all the tools in the toolkit

Prevention

- School based prevention education
- Parent education about signs of addiction
- Community coalition initiatives
- Local drug-free school initiatives
- Prescriber and patient education
- Drug take-back programs
- Public awareness

Intervention

- Evidence-based screening for risk behaviors and appropriate intervention methods
- Prescription monitoring program
- Civil commitment
- Utilization of data to identify hot spots
- Access to naloxone
- Recovery coaches in Emergency Departments

Treatment

- Continuum of treatment from acute inpatient services to outpatient services
- Civil commitment: court-ordered SUD treatment
- Medication assisted treatment
- Outpatient counseling
- Emergency services
- Central database of treatment resources

Recovery Support

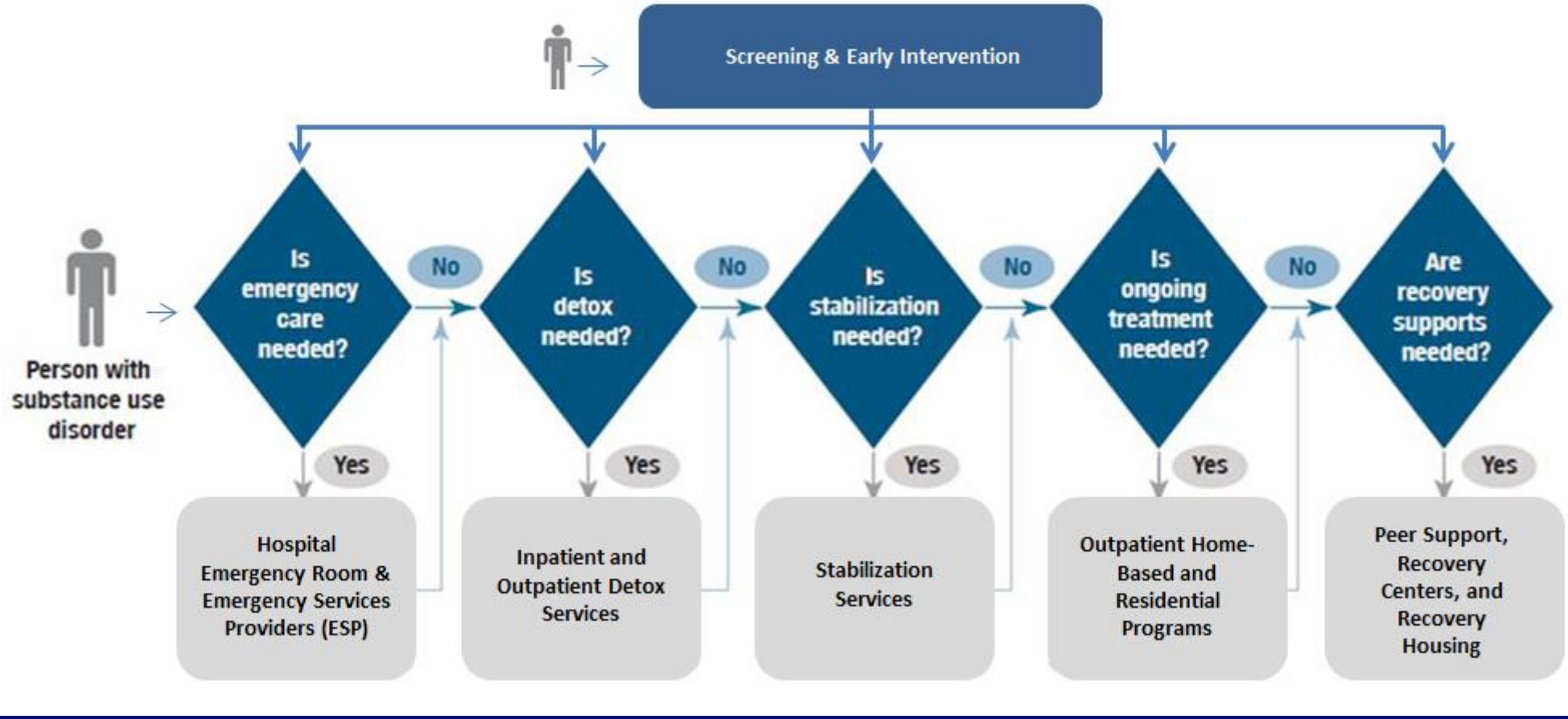
- Residential rehabilitation programs
- Alcohol and drug free housing
- Family and peer support
- Recovery high schools
- Resource navigators and case management

FINDINGS AND RECOMMENDATIONS

**Recommendations appearing in red are included in the Governor's action plan

The Working Group's Findings:

The Commonwealth must realign the treatment system to reflect the nature of opioid use disorder as a chronic disease to allow for multiple entry points to treatment



Revised figure from Center for Health Information and Analysis, Report: Access to substance use disorder treatment in Massachusetts, 2015

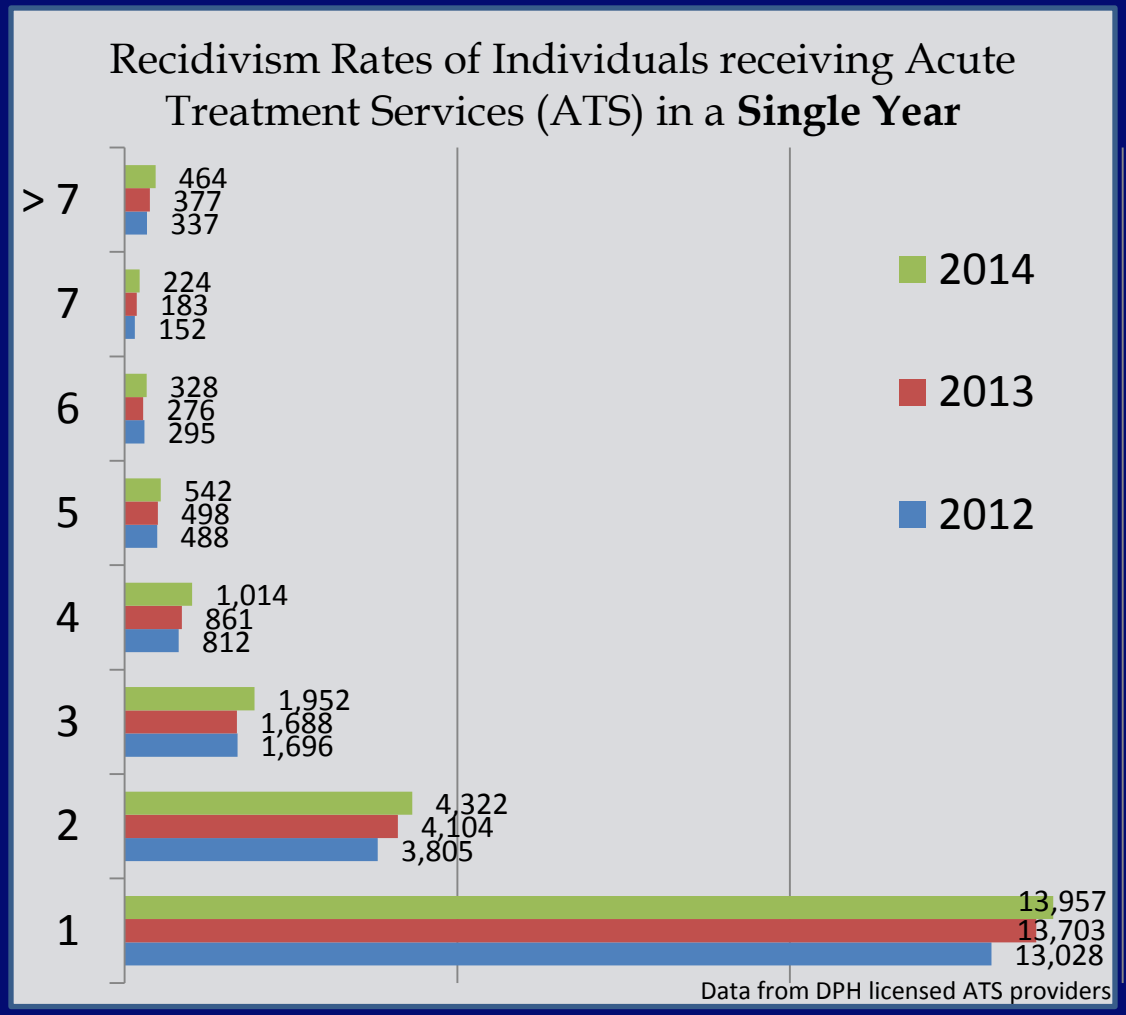
Finding 1: Individuals in crisis cannot access the right level of treatment at the right time

Focusing on patient care can increase access without having to add beds

In 2014, **4,524 individuals** utilized ATS services 3 or more times

Two individuals utilized ATS services
23 times

In 2014, if these individuals had received ongoing treatment, at least **16,000 additional** individuals could have received ATS services



Finding 1: Individuals in crisis cannot access the right level of treatment at the right time

Number of Adult Treatment Beds & Licensed Programs for a Substance Use Disorder

County	Acute Treatment Service Beds (ATS)	Section 35: Acute Treatment Service Beds (ATS)	Clinical Stabilization Service Beds (CSS)	Section 35: Clinical Stabilization Service Beds (CSS)	Transitional Support Service Beds (TSS)	Residential Beds	Outpatient Detox Programs	Opioid Treatment Programs (Methadone)	Outpatient Counseling Programs
Barnstable	35	0	55	0	0	61	1	1	2
Berkshire	21	0	13	0	0	24	0	2	2
Bristol	52	24	30	66	80	333	0	5	8
Dukes	0	0	0	0	0	0	0	0	1
Essex	86	0	23	0	25	137	0	7	15
Franklin	0	0	0	0	0	70	0	1	2
Hampden	60	0	30	0	27	224	0	4	11
Hampshire	0	0	0	0	0	0	0	1	1
Middlesex	79	40*	0	0	0	347	0	5	23
Nantucket	0	0	0	0	0	0	0	0	1
Norfolk	75	0	62	0	60	52	0	0	5
Plymouth	89	132**	64	76	0	43	0	3	6
Suffolk	188	0	22	0	80	690	0	6	30
Worcester	207	0	30	0	72	377	1	5	15
Total	**892**	**196**	**329**	**142**	**344**	**2358**	**2**	**40**	**122**

Bed & Program data, May 2015
*MCI Framingham has 40 infirmary beds, 12 designated as detoxification beds, for its entire population
**Department of Correction beds included

Finding 1: Individuals in crisis cannot access the right level of treatment at the right time

- 61 of the 122 adult outpatient counseling programs in the Commonwealth treat adolescent patients
- There are 4 recovery high schools in the Commonwealth, with 1 additional planned in Worcester

Number of Licensed Youth & Family Treatment Beds

County	Family Residential (# of Families Served)	Adolescent Residential Beds (13-17)	Transitional Aged Youth Residential Beds (16-21)	Youth Stabilization Beds (ATS/CSS)
Barnstable	**13**	0	0	0
Berkshire	0	0	0	0
Bristol	0	0	0	0
Dukes	0	0	0	0
Essex	0	**15**	0	0
Franklin	0	0	0	0
Hampden	0	**16**	0	0
Hampshire	**14**	0	0	0
Middlesex	**37**	**26**	0	0
Nantucket	0	0	0	0
Norfolk	0	0	0	0
Plymouth	0	0	0	**24**
Suffolk	**34**	**15**	**30**	0
Worcester	**12**	**33**	0	**24**
Total	**110**	**105**	**30**	**48**

Bed & Program data from May, 2015

Finding 1: Individuals in crisis cannot access the right level of treatment at the right time

Recommendations Related to Treatment

- Realign Treatment System to Reflect Nature of Opioid Use Disorder as a Chronic Disease with Periods of Acute Needs and Periods of Stability
  - Increase points of entry to treatment, eliminating the need for individuals to access other levels of care only through acute treatment services (ATS) and clinical stabilization services (CSS)
  - Establish and promote a longitudinally based treatment system and continuum of care
- Increase Treatment Access by Matching Demand and Capacity
  - Develop a real-time, statewide database of available treatment services, making information available via phone and the internet
  - Increase the number of post-ATS/CSS beds (transitional support service, residential recovery homes)
  - Fund patient navigators and case managers to ensure a continuum of care
  - Pilot a program that provides patients with access to an emergent or urgent addiction assessment by a trained clinician and provides direct referral to the appropriate level of care
  - Establish revised rates for recovery homes, effective July 1, 2015

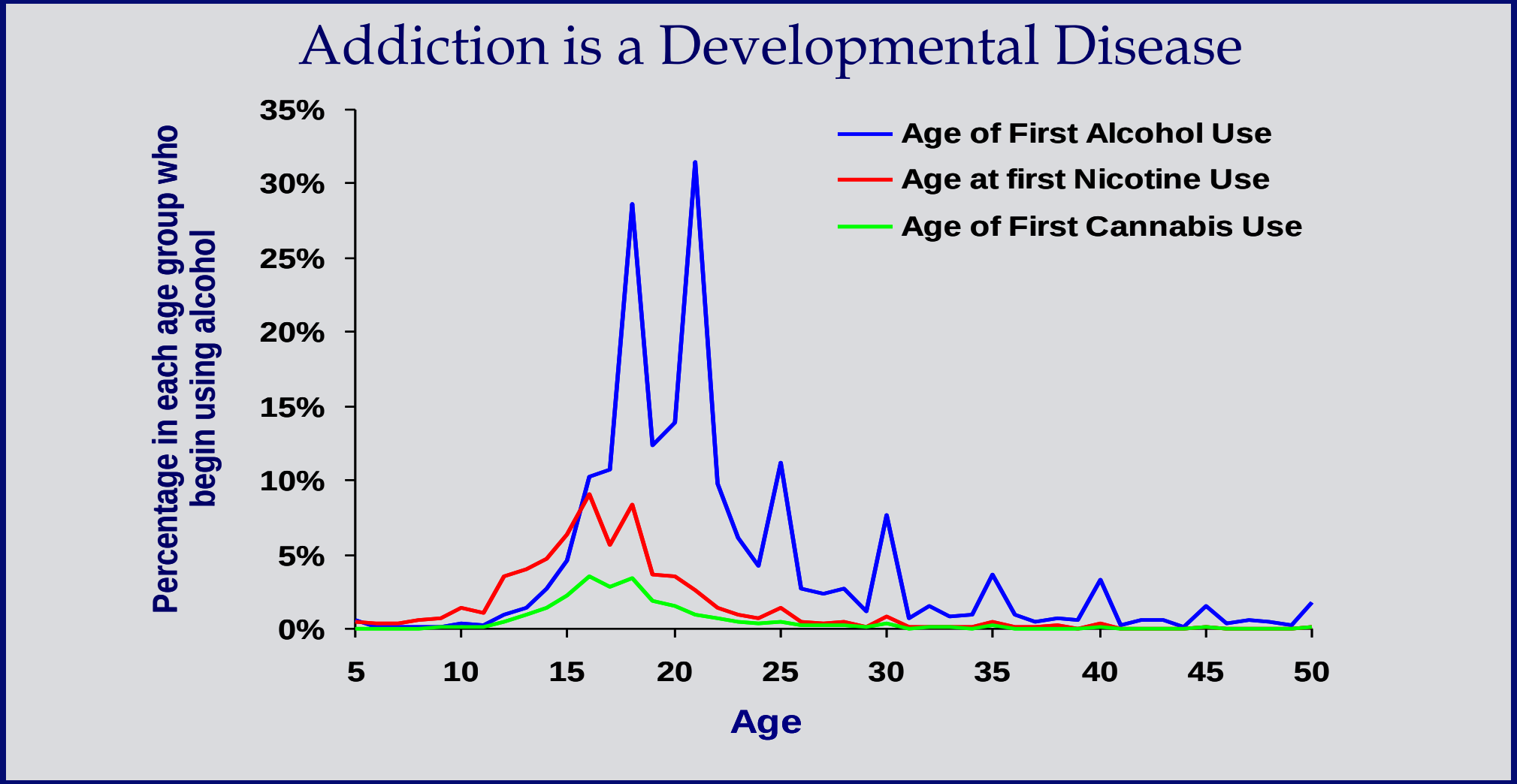
Finding 1: Individuals in crisis cannot access the right level of treatment at the right time

Recommendations Related to Treatment

- Increase Access to Evidence-Based Medication-Assisted Treatment
  - Increase the number of office-based opioid treatment programs and the number of practitioners prescribing buprenorphine and naltrexone
  - Enforce and strengthen the requirement that all licensed addiction treatment programs accept patients on an opioid agonist therapy
- Promote Integration of Mental Health, Primary Care, and Opioid Treatment
  - Create a consistent public behavioral health policy by conducting a full review of all DPH and DMH licensing regulations for outpatient primary care clinics, outpatient mental health clinics, and BSAS programs removing all access barriers
  - Explore state mechanisms to establish opioid treatment programs as Health Homes
  - Conduct a review of the license renewal process for programs accredited by The Joint Commission or Commission on Accreditation of Rehabilitation Facilities (CARF) and evaluate whether Massachusetts should implement a "deemed status" for BSAS license renewals
  - Permit clinicians to hold an individual with a substance use disorder involuntarily in order to conduct an assessment of whether release poses a likelihood of serious harm

Finding 1: Individuals in crisis cannot access the right level of treatment at the right time

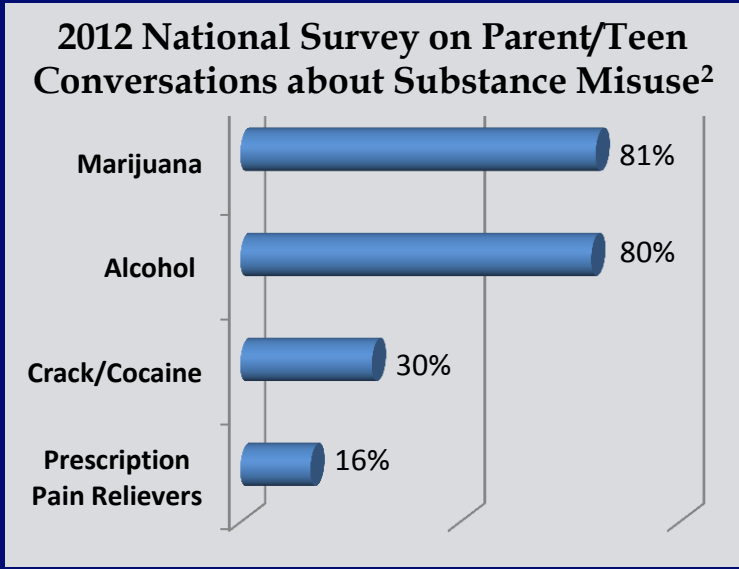
Studies demonstrate that youth begin to use alcohol and drugs as early as 10 years old



Source: Li, Ting-Kai, *Alcohol Use, Abuse, and Dependence*, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, U.S. Department of Health and Human Services, p.30, *citing* NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2003, retrieved from: Retrieved from: www.pitt.edu/~super7/25011-26001/25521.ppt

Finding 2: Youth drug use and addiction trends must be addressed through prevention education

- Universal evidence-based preventive interventions can effectively and efficiently reduce nonmedical prescription opioid use[1]
- According to a 2012 National Survey, parents generally do not discuss the dangers of prescription pain relievers with their teens[2]
- 74% of individuals with a substance use disorder began substance use at the age of 17 or younger; 10.2% initiated use at the age of 11 or younger [1]



- 40% of kids who begin drinking at age 15 will become alcoholics, while only 7% of those who begin drinking at age 21 become alcoholics[3]
- Adolescent males who participate in sports may have greater access to opioid medication, which puts them at greater risk to misuse these controlled substances [4]

1. Crowley, D. M., Jones, D. E., Coffman, D. L., & Greenberg, M. T. (2014). Can we build an efficient response to the prescription drug abuse epidemic? Assessing the cost effectiveness of universal prevention. Preventive Medicine, 62, 71-77. doi: 10.1016/j.ypmed.2014.01.029. PMCID: PMC4131945 .
2. 2012 Partnership Attitude Tracking Study (2013). MetLife Foundation. Retrieved from: http://www.drugfree.org/newsroom/full-report-and-key-findings-the-2012-partnership-attitude-tracking-study-sponsored-by-metlife-foundation/
3. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. (July 17, 2014). The TEDS Report: Age of Substance Use Initiation among Treatment Admissions Aged 18 to 30. Rockville, MD. Retrieved from: http://www.samhsa.gov/data/sites/default/files/WebFiles_TEDS_SR142_AgeatInit_07-10-14/TEDS-SR142-AgeatInit-2014.htm
4. Veliz, P, Epstein-Ngo, Q.M., Meier, E., Ross-Durow, P.L., McCabe, S.E., Boyd, C.J., (2014). Painfully obvious: a longitudinal examination of medical use and misuse of opioid medication among adolescent sports participants. J Adolescent Health, 2014 Mar;54(3), 333-40.

Finding 2: Youth drug use and addiction trends must be addressed through prevention education

Recommendations Related to Youth & Parent Education & Interventions

- Support the implementation of substance use prevention curricula in schools. School districts should have the autonomy to choose the evidence-based curricula and the grade level that it is implemented in their district. Programs must be proven to reduce nonmedical opioid use. Examples of programs include: LifeSkills and All Stars
- Integrate information about the risks of opioid use and misuse into mandatory athletic meetings and trainings for parents, students, and faculty
- Increase the use of screenings in schools to identify at-risk youth for behavioral health issues
- Develop targeted educational materials for school personnel to provide to parents about closely monitoring opioid use if their child is prescribed opioids after an injury, as well as, signs and symptoms of drug and alcohol use
- Partner with state universities that have strong education programs to develop substance use prevention curricula for school districts throughout the Commonwealth
- Require state universities that educate teachers to integrate screening and intervention techniques as well as substance use prevention education into the curriculum

Finding 2: Youth drug use and addiction trends must be addressed through prevention education

The Department of Children and Families (DCF) received 2,376 reports of a substance exposed newborn (SEN) between March, 2014 and March, 2015

A SEN designation is given when 1 or more of the following occurs:

- A positive toxic screen on the newborn;
- A positive toxic screen on the mother during her pregnancy or at delivery;
- A newborn has been diagnosed with Neonatal Abstinence Syndrome (NAS);
- Evidence of withdrawal symptoms from alcohol or drugs on the mother or the baby;
- A newborn shows signs of Fetal Alcohol Syndrome (FAS);
- A newborn tests positive for methadone, buprenorphine (Subutex), or buprenorphine with naloxone (Suboxone); or
- A self report by the mother or a verifiable report from a treatment provider that during pregnancy the mother used illicit drugs.

SEN reports to DCF	
Mar, 2014	133
Apr, 2014	142
May, 2014	157
Jun, 2014	159
Jul, 2014	168
Aug, 2014	206
Sep, 2014	244
Oct, 2014	219
Nov, 2014	160
Dec, 2014	200
Jan, 2015	177
Feb, 2015	203
Mar, 2015	208
Total	2,376

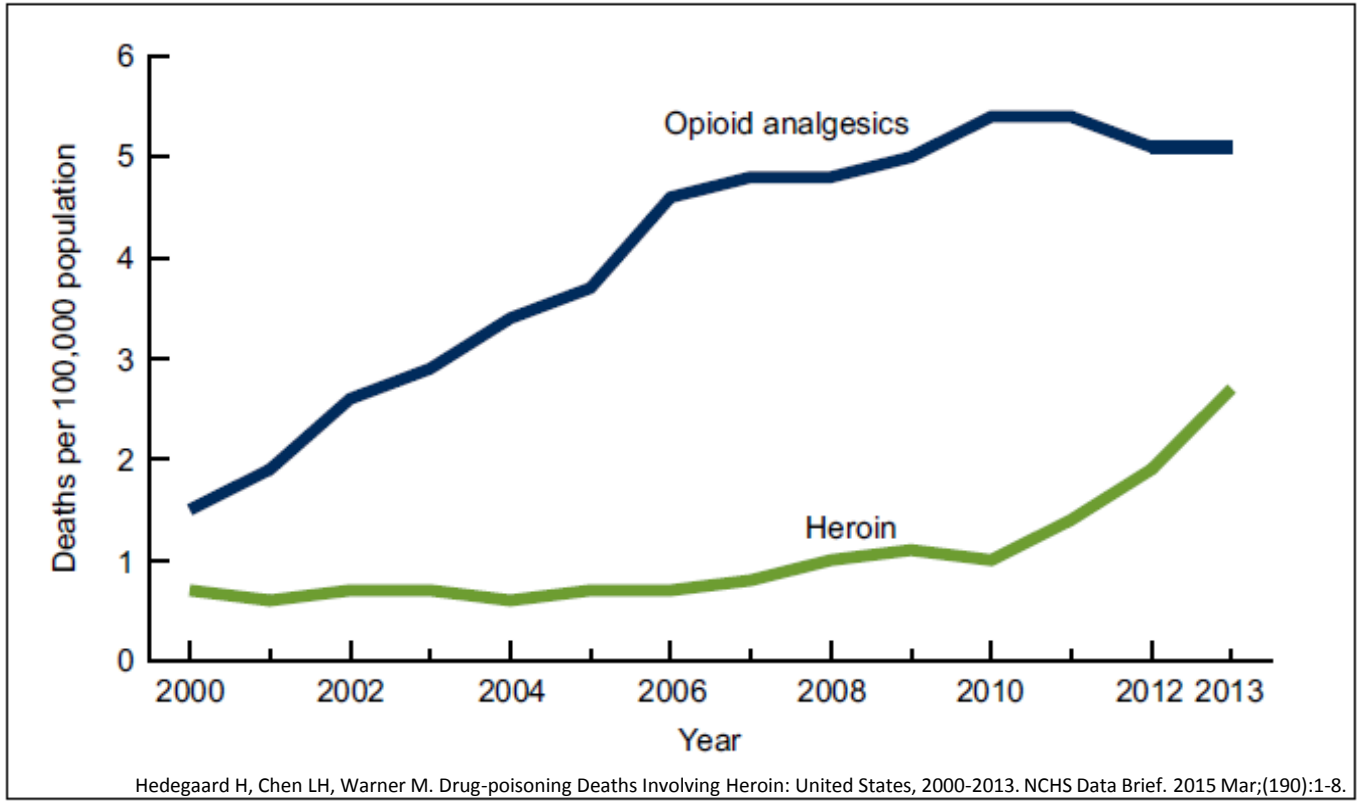
Finding 3: Pregnant women and mothers with a substance use disorder need specialized care

Recommendations Related to Neonatal Abstinence Syndrome, Prenatal Care & Neonatal Care

- Outreach to prenatal and postpartum providers to increase training about: screening, intervention, and care for women with a substance use disorder
- Promote early identification and proper treatment, raise awareness of NAS within the public health and medical communities
- Review the costs and benefits of mandating testing for in utero exposure to alcohol and drugs at every birth
- Ensure adequate capacity for pregnant women in the treatment system
- Develop and institute a training program focused on NAS and addiction for Department of Children and Families staff
- Work with health care providers to ensure all infants with NAS are referred to early intervention by the time of hospital discharge
- Partner with early intervention (EI) leadership and developmental experts to study the value of increasing automatic EI eligibility for infants with NAS from one year to two years

Finding 3: Pregnant women and mothers with a substance use disorder need specialized care

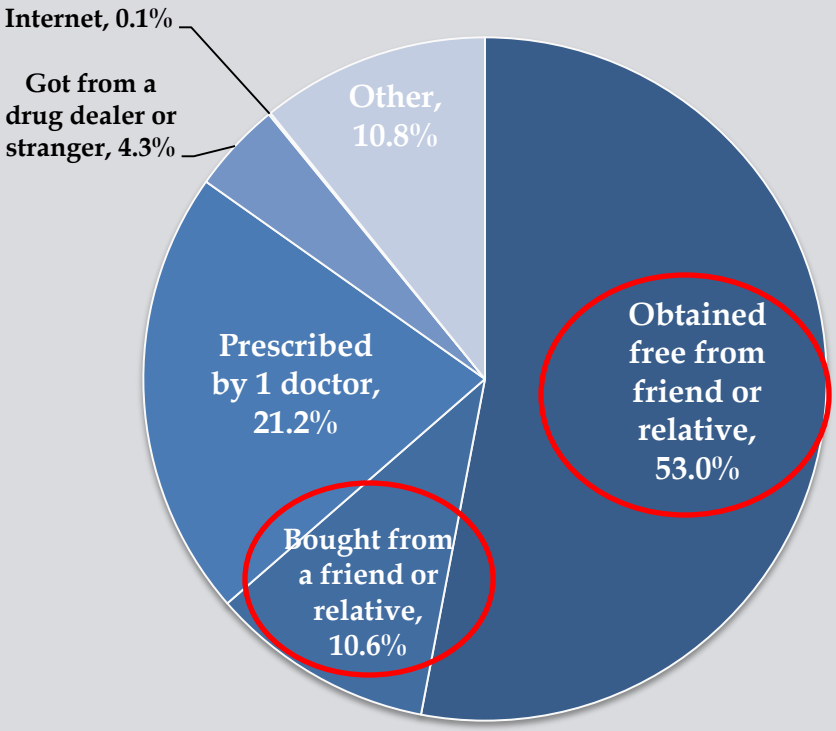
RATES OF OVERDOSE DEATH FROM PRESCRIPTION PAINKILLERS & HEROIN UNITED STATES, 2000-2013



Hedegaard H, Chen LH, Warner M. Drug-poisoning Deaths Involving Heroin: United States, 2000-2013. NCHS Data Brief. 2015 Mar;(190):1-8.

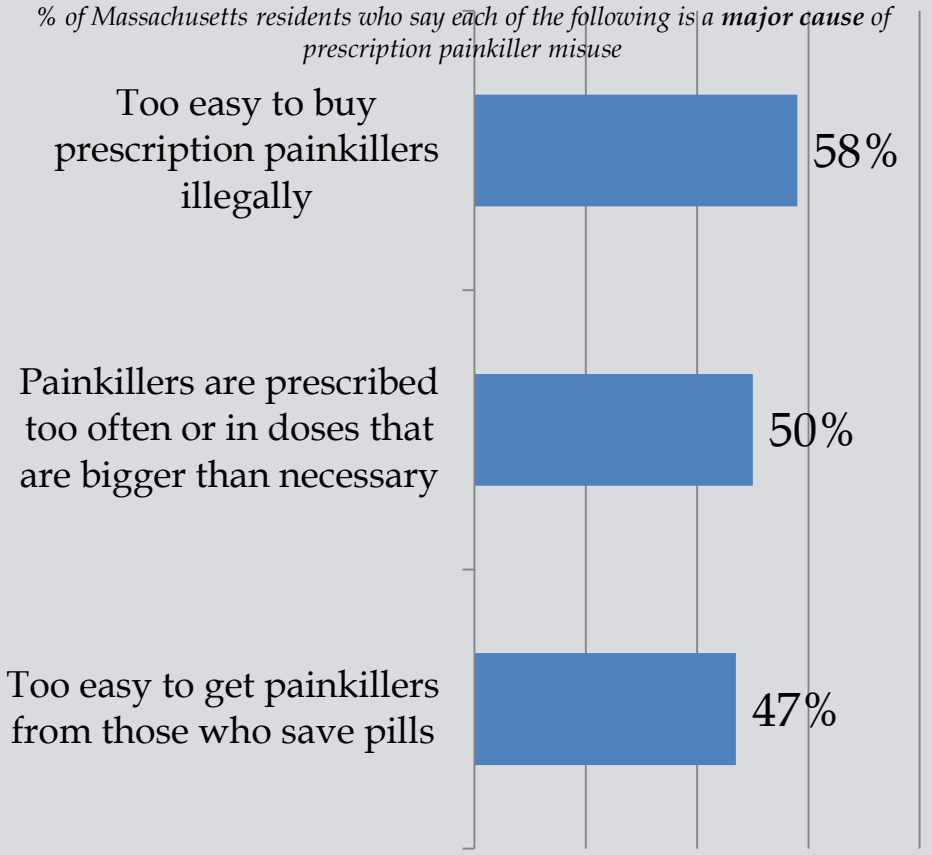
Finding 4: Opioid medications must be safely managed by prescribers, pharmacists, and patients

SOURCE, AMONG THOSE AGED 12 OR OLDER, WHO USED PAIN RELIEVERS NONMEDICALLY (2012-2013)



Source: Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings, U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality

SURVEY: REASON FOR PRESCRIPTION PAINKILLER MISUSE



Source: Boston Globe and Harvard T.H. Chan School of Public Health, Prescription Painkiller Abuse: Attitudes among Adults in Massachusetts and the United States

Finding 4: Opioid medications must be safely managed by prescribers, pharmacists, and patients

Enrollment of Providers and Delegates in the MA Online PMP (March, 2015)

- 25% of enrolled prescribers have logged into the PMP and searched for a patient at least 1 time in the past year
- Over 50% of enrolled prescribers have never logged into the system
- 58% of prescribers enrolled in the PMP issued more than 10 Schedule II-V prescriptions during 2014

	Total Enrolled	Estimated Number Practicing in MA	Total Percentage Enrolled (of Eligible Providers)
Practitioners (MD / DO / Dentist / Podiatrist)	25,977	34,173	76%
Mid-Levels (APRN / PA)	2,671	8,626	31%
Pharmacists	3,521	12,000*	29%
Total Provider Enrollment	32,169	54,799	51%
Delegates (New Entry)	139	N/A	N/A

* This number represents an estimate of all registered pharmacists that are licensed in MA. Many licensed pharmacists do not work in retail pharmacy settings and are not dispensing controlled substances; therefore, the percentage enrolled for this provider category will be biased on the low side.

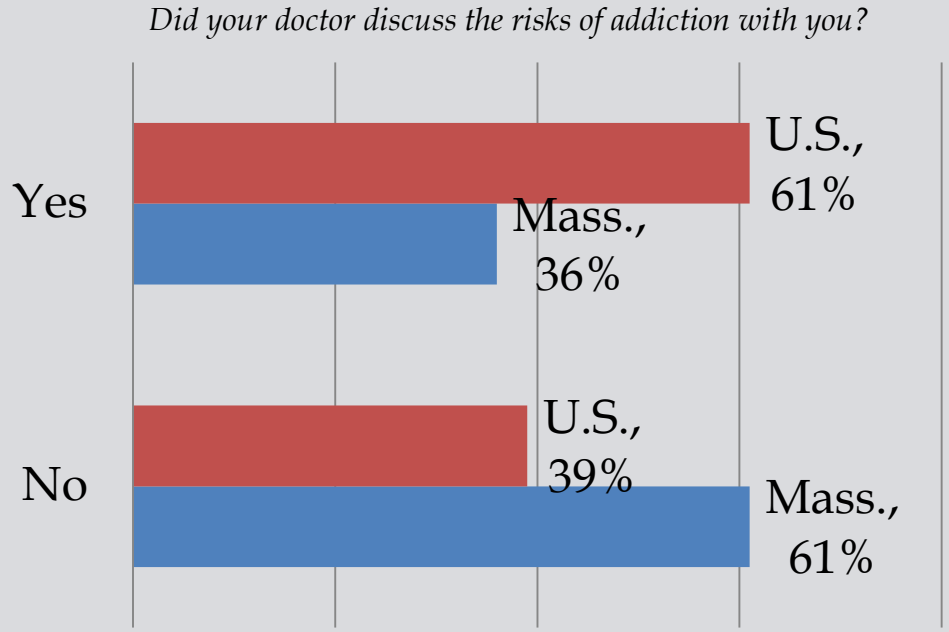
Finding 4: Opioid medications must be safely managed by prescribers, pharmacists, and patients

MASSACHUSETTS DOCTORS DISCUSS THE RISKS OF PRESCRIPTION PAINKILLERS WITH PATIENTS LESS THAN DOCTORS IN OTHER PARTS OF THE COUNTRY

In a 2015 survey, individuals who, in the past 2 years, **HAD** taken a strong prescription painkiller, such as Percocet, OxyContin, or Vicodin that was prescribed by a doctor for more than a few days, were asked the following question:

"Before or while you were taking these strong prescription painkillers, did you and your doctor talk about the risk of prescription painkiller addiction, or haven't you talked about that?"

Only 36% of Massachusetts residents said "yes", compared to 61% nationally



Source: Boston Globe and Harvard T.H. Chan School of Public Health, Prescription Painkiller Abuse: Attitudes among Adults in Massachusetts and the United States

Finding 4: Opioid medications must be safely managed by prescribers, pharmacists, and patients

Recommendations Related to Prescriber & Safe Disposal Practices

- Mandate pain management, safe prescribing training, and addiction training for all prescribers as a condition of licensure (physician assistants, nurses, physicians, dentists, oral surgeons, and veterinarians)
- Allow partial refills across all payers with a one-time co-payment
- Eliminate prescription refills by mail for schedule II medications
- Improve the Prescription Monitoring Program (PMP):
  - Increase utilization by improving ease of use and expanding abuse alerts from the PMP to prescribers
  - Ensure data compatibility of the PMP with other states & interface the PMP with electronic health records
  - Enforce mandatory use of the PMP
  - Require PMP data to be submitted within 24 hours by pharmacies
  - Improve data analytics and educate prescribers about how to utilize the information
- Implement electronic prescribing for opioids
- Partner with the medical and provider community to improve and increase educational offerings for prescribers and patients to promote safe prescribing
- Promote awareness and support for alternate pain therapies
- Appoint individuals with expertise in addiction to the medical profession licensing boards
- Develop universal distribution of easy to read materials at pharmacies on the safe use of medications
- Expand and promote drug take-back days and permanent drug take-back locations, financed by pharmacies and manufacturers
- Require practitioners, including dentists, to educate patients on the risks and side effects associated with opioids and document such discussions at the point of prescribing
- Increase screening for substance use at all points of contact in the medical system
- Appoint members to the drug formulary commission established under Chapter 258 of the Acts of 2014

Finding 4: Opioid medications must be safely managed by prescribers, pharmacists, and patients

The Harms of Stigma Associated with a Substance Use Disorder:

- Stigma is a barrier to individuals seeking help[1]
- Stigma contributes to the poor mental and physical health of individuals with a SUD[2]
- Stigma contributes to non-completion of substance use treatment[2]
- Stigma delays recovery and reintegration processes[2]
- Stigma increases involvement in risky behavior (e.g. needle sharing) [2]

Recommendations Related to Reframing Addiction as a Disease

- Create a public awareness campaign, with messaging that targets various ages, focused on:
  - Reframing addiction as a medical disease
  - Promoting medication safety practices
- Promote the Good Samaritan law
- Reduce stigma among medical and treatment professionals [1]

1. Kelly, J. F., Wakeman, S. E., & Saitz, R. (2015). Stop Talking 'Dirty': Clinicians, Language, and Quality of Care for the Leading Cause of Preventable Death in the United States. The American Journal of Medicine, Vol. 128, Issue 1, 8-9. Retrieved from: http://www.amjmed.com/article/S0002-9343(14)00770-0/pdf.
2. Livingston, J. D., Milne, T., Fang, M. L., & Amari, E. (2012). The effectiveness of interventions for reducing stigma related to substance use disorders: a systematic review. Addiction (Abingdon, England), 107(1), 39–50.

Finding 5: The stigma associated with a substance use disorder is a barrier to treatment and recovery

Recommendations Related to Enhancing the Utilization of Data to Improve Transparency

- Require and support universal and timely reporting of overdose deaths, through a partnership between the Department of Public Health, the Attorney General's Office, the Massachusetts State Police, the District Attorneys, local police departments, emergency medical services, hospitals, and others
- Make EMS overdose data available
- Utilize overdose reports to identify geographical hot spots for targeted intervention and to alert law enforcement, public health entities, community coalitions, and the public
- Create a unified EOHHS privacy policy and implement a process for sharing confidential data

Recommendations Related to Government & Provider Accountability

- Establish a single point of accountability for the Commonwealth, *Director of Addiction and Recovery Policy*
- Enhance provider accountability by requiring treatment programs at all levels (inpatient and outpatient) to report on outcomes
- Incentivize and support providers to develop and test innovative treatment approaches
- Create provider accountability for the successful transition from one level of care to the next and incentivize providers to reduce re-admissions; the current "system" inadvertently "rewards" providers for repeat detoxes and rehabs
- Require the Department of Public Health to advance standards of care by establishing industry benchmarks

Finding 6: Lack of transparency and accountability hinder our ability to respond to the opioid crisis

Recommendations Related to the Courts

- Increase drug and specialty court capacity
- Increase access to beds for patients who are civilly committed under section 35 of chapter 123 of the General Laws and provide a roster of currently available beds to judges for section 35 commitments
- Review and revise discharge policies for section 35 patients; facilities must be required to follow the law and issue a written determination that release will not result in a likelihood of serious harm when individuals are discharged from the facility
- Improve the continuum of care for patients committed under section 35
- Ensure notification to the Court when a section 35 patient escapes from treatment

Recommendations Related to Policing & Correctional Institutions

- Transfer responsibility for civil commitments from the Department of Corrections to the Executive Office of Health and Human Services
- Suspend, rather than terminate, MassHealth coverage during incarceration
- Partner correctional facilities with community health centers to ensure individuals can access treatment upon release
- Analyze treatment spending in correctional facilities
    - Inmates should be able to continue medication-assisted treatment while incarcerated
    - Inmates should be able to begin treatment while incarcerated and be connected to treatment upon release
- Encourage and support alternatives to arrest, making police a partner in obtaining treatment for individuals
- Bulk purchase opioid agonist and naltrexone therapies for county corrections

Finding 7: Courts and Jails should not be the primary mode of accessing long-term treatment

Recommendations Related to Recovery & Support

- Leverage and increase support for community coalitions to address the opioid crisis
  - Create an online repository of resources and best practices for community coalitions
  - Improve statewide coordination and information sharing among coalitions
- Expand peer and family support organizations such as *Learn to Cope*
- Pilot recovery coaches in emergency rooms and hot spots
- Implement a process to certify alcohol and drug free housing to bring accountability and credibility to this recovery support system
- Partner with businesses to remove employment barriers that recovering individuals experience, specifically review regulations related to CORI checks
- Incentivize employers to hire individuals in early recovery
- To improve outcomes for recovery, explore the benefits and costs associated with issuing certificates of recovery

Finding 8: Recovery resources are insufficient and difficult to access

Recommendations Related to Naloxone

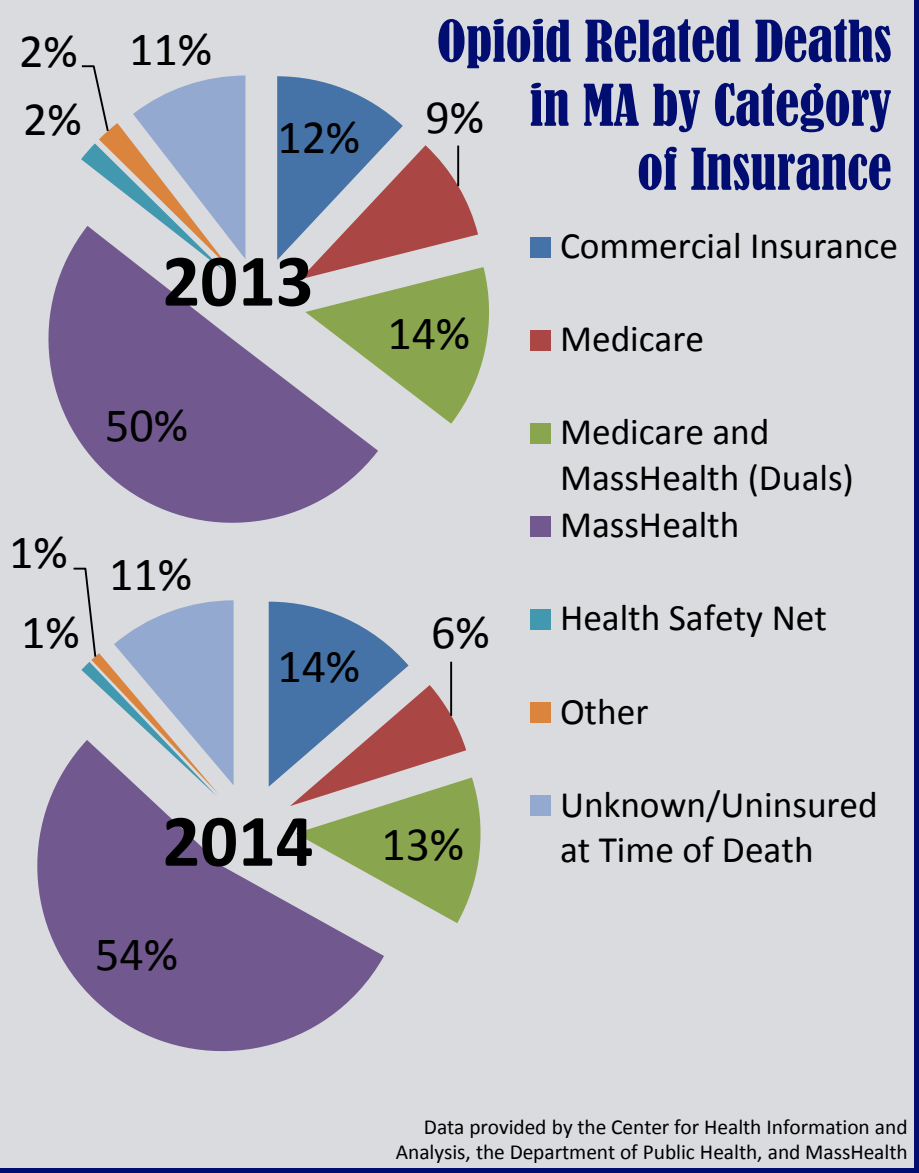
- Investigate the feasibility of having Naloxone in public spaces
- Improve affordability of Naloxone
  - Through bulk purchasing agreements
  - By eliminating all copayment requirements
- Encourage Naloxone to be co-prescribed with opioids

Date	Price Per Naloxone "Kit" 2 Naloxone Doses and 2 Atomizers
November 2007	$22.98
March 2008	$31.55
January 2009	$31.87
September 2009	$31.49
June 2011	$31.77
March 2012	$32.35
May 2012	$40.56
January 2014	$42.82
July 2014	$41.69
November 2014	$74.06
May 2015	$74.06

Finding 9: Increasing access to Naloxone will save lives

Recommendations Related to Insurance

- Require the Division of Insurance to implement guidance for commercial insurers about the implementation of chapter 258 of the acts of 2014 prior to October 1, 2015
- Eliminate insurance barriers that impede integration of addiction and mental health care into the primary care setting
- Require consistent coverage and prior authorization practices and policies throughout all MassHealth programs
- Bring meaning to federal and state behavioral health parity laws through enforcement actions to remove inappropriate barriers to treatment
- Encourage insurers to support non-opioid pain therapies
- Prepare a public report on what non-pharmacological treatments for pain are covered by all private and public insurers
- Encourage insurers to support recovery coaches for individuals with a substance use disorder
- Encourage insurers to support new pathways to treatment



Finding 10: Insurance barriers prevent individuals from receiving treatment

Recommendations Related to Federal-State Partnerships

- Partner with federal leaders to recommend that the American College of Graduate Medical Education adopt requirements for pain management and substance use disorder education for all medical and residency programs (i.e. surgical, pediatrics, internal medicine, family medicine, obstetrics, and gynecology)
- Partner with federal leaders to recommend that the Commission on Dental Accreditation adopt requirements for education on safe opioid prescribing practices for all dental programs
- Partner with federal leaders to recommend that the American Veterinary Medical Association adopt requirements for education on safe opioid prescribing practices for all veterinary programs
- Partner with federal leaders to increase support for substance use prevention, intervention, treatment, and recovery efforts uniquely tailored for our Veterans

Finding 11: The opioid crisis is a national issue that requires both state and federal solutions

Recommendations Related to Federal-State Partnerships

- Request the Drug Enforcement Agency (DEA) to permit medical residents to prescribe buprenorphine under an institutional DEA registration number, thus allowing residents to learn how to manage patients with an opioid addiction
- Implement nationwide standards for pharmaceutical take back programs
  - Require manufacturers and pharmacies nationwide to finance the disposal of unused prescription medication
- Change the laws and regulations related to prescribing buprenorphine
  - Increase the cap - the number of patients a physician can treat - or remove it entirely
  - Permit nurse practitioners and physician assistants to prescribe buprenorphine
- Facilitate the interoperability of prescription monitoring programs nationwide
- Review 42 CFR Part II to ensure that it facilitates integrated care and the use of electronic health records and does not exacerbate the stigma associated with a substance use disorder
- Request that the Pain Management Question from the HCAHPS not be linked to hospital reimbursement

Finding 11: The opioid crisis is a national issue that requires both state and federal solutions

Summary of Short-Term Action Items (6 months to 1 year)

Prevention

- **Increase educational offerings for prescribers and patients to promote safe prescriber practices**
- **Develop targeted educational materials for schools**
- **Appoint members to the drug formulary commission**
- **Integrate information about the risks of opioid use and misuse into school athletic programs**
- **Conduct a public awareness campaign**

Intervention

- **Improve the PMP**
- **Outreach to prenatal and postpartum providers to increase screening for women with a substance use disorder**
- **Improve reporting of overdose death data**
- **Enhance data transparency, including EMS data**
- **Encourage naloxone to be co-prescribed with opioids**
- **Amend civil commitment process**
- **Identify hot spots for targeted intervention, using EMS, hospital, and police data**
- **Promote the Good Samaritan law**
- Consider mandating testing for in utero exposure to alcohol and drugs at every birth
- Encourage and support alternatives to arrest
- Expand availability of Naloxone

Treatment

- **Develop a central statewide database of available treatment services**
- **Transfer section 35 civil commitment responsibility from DOC to EOHHS**
- **Increase the number of office based opioid treatment programs**
- **Require DOI to issue bulletins on chapter 258 of the Acts of 2014 prior to Oct. 2015**
- **Pilot recovery coaches in emergency rooms and hot spots**
- **Bulk purchase opioid agonist and naltrexone therapies for correctional facilities**
- **Add 100 new ATS/CSS beds**
- **Open Recovery High School in Worcester**
- Review capacity in the treatment system for women/families
- Analyze treatment spending in correctional facilities
- Increase the number of stepdown beds and services

Recovery

- **Promulgate chapter 257 rates for recovery homes effective July 2015**
- **Establish a single point of accountability for addiction and recovery policy at EOHHS**
- **Suspend rather than terminate MassHealth coverage during incarceration**
- **Certify alcohol and drug free housing**
- **Enforce the requirement that BSAS treatment programs accept patients on an opioid agonist therapy**
- Strengthen connections between law enforcement and community providers for individuals upon release
- Explore issuing certificates of recovery
- Review and revise discharge/court notification policies for section 35

Summary of Mid-Term Action Items (1 year to 3 years)

Prevention

- **Support substance use prevention curricula in schools**
- **Mandate pain management, safe prescribing and addiction training for all prescribers**
- **Partner with federal government regarding graduate medical education**
- Require manufacturers and pharmacies to dispose of unused prescription medication
- Require prescribers to discuss opioid side effects at point of prescription
- Allow partial refills across all payers
- Eliminate prescription refills by mail for schedule II medications
- Amend the curriculum for teachers as state universities to include training on screening and intervention techniques
- Have state universities develop substance use prevention curricula for schools

Intervention

- **Improve the PMP to ensure data compatibility with other states**
- **Develop training on neonatal abstinence syndrome and addiction for DCF staff**
- **Improve affordability of Naloxone**
- **Increase access to beds for section 35 patients**
- Implement electronic prescribing for opioids
- Increase screening for substance use at all points of contact in the medical system
- Increase the use of screenings in schools to identify at-risk youth for behavioral health issues

Treatment

- **Create a consistent public behavioral health policy through licensing reforms**
- **Pilot providing patients with access to an emergent/urgent addiction assessment by a trained clinician and direct referral to the appropriate level of care**
- **Increase points of entry to treatment**
- **Ensure section 35 patients receive a continuum of care**
- Enhance provider accountability by requiring treatment programs to report on outcomes
- Reform purchasing of substance use disorder treatment services
- Require DPH to advance standards of care by establishing industry benchmarks
- Add new non-ATS/CSS treatment beds

Recovery

- **Fund patient navigators and case managers**
- **Leverage community coalitions to address opioids**
- Ensure all infants with NAS are referred to early intervention by time of hospital discharge
- Increase drug and specialty court capacity
- Expand peer/family support
- Partner with businesses to remove employment barriers that recovering individuals experience

Summary of Long-Term Action Items (3+ years)

Prevention

- Support alternate pain therapies through commercial and public insurers & prepare a public report on what non-pharmacological treatments for pain are covered by all private and public insurers

Intervention

- Improve the PMP by interfacing the PMP with electronic health records

Treatment

- Establish and promote a longitudinally based system of addiction care
- Integrate primary care into substance use treatment programs

Recovery

- Reduce stigma among medical and treatment professionals

Opioid Working Group Members

Marylou Sudders, Chair, Secretary of the Executive Office of Health and Human Services
Maura Healey, Attorney General
George Bell, General Catalyst Partners
Monica Bharel, MD, MPH, Commissioner of the Department of Public Health
Hon. Paula M. Carey, Chief Justice of the Trial Court
Bill Carpenter, Mayor of Brockton
Alan Ingram, Ed.D., Deputy Commissioner of the Department of Elementary and Secondary Education
Colleen Labelle BSN, RN-BC, CARN, Boston Medical Center
Judy Lawler, Chelsea District Drug Court
Joseph D. McDonald, Sheriff, Plymouth County
John McGahan, The Gavin Foundation
Hon. Rosemary B. Minehan, Plymouth District Court
Fred Newton, Hope House, Inc.
Robert Roose, MD, MPH, Sisters of Providence Health System
Cindy Steinberg, Massachusetts Pain Initiative, U.S. Pain Foundation
Raymond V. Tamasi, Gosnold on Cape Cod
Steve Tolman, Massachusetts AFL-CIO
Sarah Wakeman, MD, Massachusetts General Hospital

Organizations that Submitted Information to the Working Group

AdCare Hospital of Worcester, Inc.
AIDS Action Committee of Massachusetts, Inc.
AIDS Project Worcester
Alkermes, Inc.
Alosa Foundation
American Academy of Addiction Psychiatry
American Academy of Pain Management
American Round Table to Abolish Homelessness
Associated Industries of Massachusetts Mutual Insurance Company
Association for Behavioral Healthcare
Barnstable County Human Services
Barnstable County Sheriff's Office
Baystate Mary Lane Hospital
Baystate Wing Hospital
Berkshire District Attorney's Office
Berkshire Opioid Abuse Prevention Collaborative
Berkshire Public Health Alliance
Berkshire Regional Planning Commission
Beth Israel Deaconess Hospital – Plymouth
Blake Works
Blue Cross Blue Shield of Massachusetts
Boston Homeless Solidarity Committee
Boston Medical Center
Boston Municipal Court
Boston Public Health Commission
Boston University School of Medicine: Continuing Medical Education Program
Boston University School of Public Health
Boston Warm
Boys and Girls Club Massachusetts Alliance
Brockton Area Multi-Services, Inc. (BAMSI)
Brook Retreat
Cambridge Health Alliance
Cambridge Needle Exchange
Cape and Islands District Attorney's Office
Carlson Recovery Center
Casa Esperanza, Inc.
Center for Early Relationship Support at Jewish Family & Children's Service
Center for Human Development, Inc.
Children's Mental Health Campaign
Christian Service and Outreach Committee
Clean Slate Centers
Collaborative for Educational Services
Commission on the Status of Grandparents Raising Grandchildren
Committee for Public Counsel Services
Communities United For A Drug Free Environment
Community Catalyst

Organizations that Submitted Information to the Working Group

Community Substance Abuse Centers
Cordant Health Solutions
Covectra
Coverys
Education Development Center, Inc.
Emerson Hospital
EvansCutler
Families Against Mandatory Minimums
Family Health Center of Worcester
Franklin County Home Care Corporation
Franklin County House of Corrections – Residents
Franklin County Sheriff's Office
Franklin Regional Council of Governments
Gate House
Gosnold on Cape Cod
Granada House
Greenfield Health Center
Greenfield Public Schools
Hampden County Sheriff's Department
Harvard Pilgrim Health Care
Health Care For All
Health Innovations, Inc.
Healthy Gloucester Collaborative
Healthy Streets Outreach Program
Heroin Education Awareness Task Force
High Point Treatment Center
Holyoke Recovery Support Center
Hope Health / Hope Hospice
Hope House, Inc. – Boston - Residents
Hyde Park Pain Management
Imprivata
Inflexxion
Institute for Health and Recovery
Journal of Opioid Management
Learn to Cope
Locke Lord, LLP
Lowell House, Inc.
Main South Alliance for Public Safety
March of Dimes Massachusetts
Massachusetts Association of Behavioral Health Systems, Inc.
Massachusetts Association of Health Plans
Massachusetts Attorney General's Office
Massachusetts Behavioral Health Partnership
Massachusetts Chiropractic Society, Inc.
Massachusetts Council of Human Service Providers, Inc.
Massachusetts Department of Children and Families
Massachusetts Dept. of Elementary and Secondary Education
Massachusetts Department of Mental Health
Mass. Dept. of Mental Health: Franklin/North Quabbin Area
Massachusetts Department of Public Health

Organizations that Submitted Information to the Working Group

Massachusetts Division of Insurance
Massachusetts Health Council
Massachusetts Hospital Association
Massachusetts Medical Society
Massachusetts Organization for Addiction Recovery
Massachusetts Pain Initiative
Mass Society for the Prevention of Cruelty to Children
Mass Technical Assistance Partnership for Prevention
Massachusetts Trial Court
MassHealth
MCI-Norfolk Project Youth Program
Medford Substance Abuse Task Force
Melrose Substance Abuse Prevention Coalition
Meridian House
Merrimack Valley Prevention and Substance Abuse Project
Middlesex County Opioid Task Force
Middlesex District Attorney's Office
Monson HEARS
Mystic Valley Public Health Coalition's Opioid Abuse Prevention Collaborative
Narcotics Anonymous
Never Another Death
New Beginnings Peer Recovery Center
Norfolk County Sheriff's Office
Norfolk District Attorney's Office
North Adams Mayor's Office
Northern Berkshire Community Coalition
Northwestern District Attorney's Office
Number 16
Opioid Task Force of Franklin County and North Quabbin
Ostiguy School
Partnership for Drug-Free Kids
Peabody Police Department
Pfizer
Phoenix Multisport
Pioneer Valley Regional School District
Plymouth County Correctional Facility
Plymouth Fire Department
Plymouth Police Department
Plymouth Public Schools
Project Cope
Project NESST (Newborns Exposed to Substances: Support and Therapy)
Project Youth
Quaboag Hills Community Coalition
Quincy Community Action Programs, Inc.
Real You Revolution
Recovery Homes Collaborative
RW Massage Therapy
SAS Solutions

Organizations that Submitted Information to the Working Group

Scituate FACTs
SEIU Local 509
Shrewsbury High School
Shilts Chiropractic Offices
Somerville Overcoming Addiction
South Bay Mental Health
South Hadley High School
Spectrum Health Systems, Inc.
Square Medical Group
State Representative Joseph McKenna, 18th Worcester District
State Representative Kay Khan, 11th Middlesex District
State Senator Eric Lesser
Suffolk County Sheriff's Office
Team Morrison
The Alex Foster Foundation
The Alliance of Massachusetts YMCA's
The Brien Center
The Carson Center for Human Services, Inc.
The Herren Project
The New Testament Church, Plymouth
The Social-Emotional Learning Alliance for Massachusetts (SAM), Inc.
Town of Greenfield
Tufts Medical Center
U.S. Pain Foundation
Victory Programs, Inc.
WellCrest
Wellesley College Health Service
Western Mass Recovery Learning Community
Wicked Sober Inc.
Worcester District Attorney's Office
Worcester Sheriff's Office

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Appendix A

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Exhibit O

Mass.Gov

The Official Website of the Executive Office of Health and Human Services (EOHHS)
Health and Human Services

Search

Input Drug Search Query Select an Area to Search

Drug Name

Search Button SEARCH

Main Menu

Breadcrumbs

Table 8: Opioids and Analgesics

Drug Category: Pain and inflammation

Medication Class/Individual Agents: Opioids and Analgesics

I. Prior-Authorization Requirements

Opioids and Analgesics – Long-Acting Opioids			Clinical Notes
Drug Generic Name	**Drug Brand Name**	**PA Status**	**Please note: In the case where the prior authorization (PA) status column indicates PA, both the brand and generic (if available) require PA. Typically, the generic is preferred when available unless the brand-name drug appears on the MassHealth Brand Name Preferred Over Generic Drug List. In general, when requesting the non-preferred version, whether the brand or generic, the prescriber must provide medical records documenting an inadequate response or adverse reaction to the preferred version, in addition to satisfying the criteria for the drug itself.** **Acetaminophen Hepatotoxicity:** • Acetaminophen has been associated with severe hepatotoxicity following acute and chronic ingestion. • Maximum recommended dose of acetaminophen for adults is 4 grams/day. • Be sure to consider and ask about all potential sources of acetaminophen (e.g., OTC, combination analgesics) when determining daily acetaminophen dose. • Risk may increase with concurrent alcohol use, underlying liver disease, and/or the fasting state. • **PA is required for any acetaminophen-containing product that exceeds 4 grams/day.** **Aspirin Dose Limit:** • The maximum recommended dose of aspirin for adults is 4 grams/day.
buprenorphine buccal film	Belbuca	PA	
buprenorphine transdermal	Butrans BP	PA - > 20 mcg/hr and PA > 4 patches/28 days	
fentanyl 12, 25, 50 mcg/hr transdermal system	Duragesic #	PA - > 50 mcg/hr and PA > 10 patches/month	
fentanyl 37.5, 62.5, 87.5 mcg/hr transdermal system		PA	
fentanyl 75, 100 mcg/hr transdermal system	Duragesic	PA	
hydrocodone extended-release capsule	Zohydro ER	PA	
hydrocodone extended-release tablet	Hysingla ER	PA	
hydromorphone extended-release	Exalgo	PA	
levorphanol powder		PA	
levorphanol tablet		PA	
methadone injection		PA	
methadone oral-Dolophine	Dolophine	PA	
methadone oral-Methadose	Methadose	PA	
methadone powder		PA	
morphine / naltrexone	Embeda	PA	

morphine controlled-release tablet	MS Contin #	PA - > 120 mg/day
morphine extended-release capsule	Kadian	PA
morphine extended-release capsule		PA
morphine extended-release tablet-Arymo ER	Arymo ER	PA
morphine extended-release tablet-Morphabond ER	Morphabond ER	PA
oxycodone extended-release capsule	Xtampza	PA
oxycodone extended-release tablet	Oxycontin BP	PA
oxymorphone extended-release, oral		PA
oxymorphone extended-release, oral-Opana ER	Opana ER	PA
tapentadol extended-release	Nucynta ER	PA
tramadol extended-release capsule	Conzip	PA
tramadol extended-release tablet	Ultram ER	PA

Opioids and Analgesics – Other Analgesics

Drug Generic Name	Drug Brand Name	PA Status
acetaminophen	*	PA - > 4 g/day
clonidine injection	Duraclon #	
pentazocine	Talwin	
pentazocine / naloxone		PA
ziconotide	Prialt	PA

- **PA is required for any aspirin-containing product that exceeds 4 grams/day.**

Ibuprofen Dose Limit:

- The maximum recommended dose of ibuprofen for adults is 3.2 grams/day.
- **PA is required for any ibuprofen-containing product that exceeds 3.2 grams/day.**

Duplicate Opioid Therapy:

- Standard practice in chronic pain management includes a long-acting opioid for chronic pain and a short-acting opioid for acute/breakthrough pain as needed.
- **PA is required for ≥ two long-acting opioids for > two months.**
- **PA is required for ≥ two short-acting opioids for > two months.**

Allergy:

- True systemic opioid allergy, such as a generalized rash, or angioedema, is unusual. A local, itchy wheal formation at the site of narcotic injection, generalized pruritus (no rash), or flushing may occur, and is due to histamine release.

Renal Dysfunction:

- Accumulation of certain opioids in patients with significant renal dysfunction can lead to excess sedation, respiratory depression, delirium, myoclonus, or seizures.
  - avoid use: meperidine, tapentadol (severe impairment), tramadol (severe impairment)
  - cautious use: acetaminophen, codeine, hydrocodone, morphine, oxycodone

Constipation:

- Common adverse effect with chronic opioid use; prescribe

Opioids and Analgesics – Short-Acting Opioids

Drug Generic Name	Drug Brand Name	PA Status
acetaminophen / codeine	Tylenol / Codeine #	PA - < 12 years and PA > 4 g/day acetaminophen and PA > 360 mg/day codeine
buprenorphine injection	Buprenex	PA
butorphanol nasal spray		PA
codeine		PA - < 12 years and PA > 360 mg/day
codeine powder		PA
dihydrocodeine / acetaminophen / caffeine		PA
dihydrocodeine / aspirin / caffeine	Synalgos-DC	PA
fentanyl buccal tablet	Fentora	PA
fentanyl injection		
fentanyl nasal spray	Lazanda	PA
fentanyl powder		PA
fentanyl sublingual spray	Subsys	PA
fentanyl sublingual tablet	Abstral	PA
fentanyl transmucosal system	Actiq	PA
hydrocodone / acetaminophen		PA - > 80 mg/day
hydrocodone /		PA

laxative +/- stool softener with opioid.

Hydrocodone and oxycodone in combination with acetaminophen:

- Generically available solution formulations continue to be available without PA within dose limits.
- Select generic tablet formulations continue to be covered without PA within dose limits. These include the following products:

Hydrocodone or Oxycodone Strength	Acetaminophen Strength
2.5 mg	325 mg
5 mg	325 mg
7.5 mg	325 mg
10 mg	325 mg

Please click on the link below to see the Opioid and Pain Initiative.
MassHealth Pharmacy Initiatives and Clinical Information

acetaminophen 300 mg		
hydrocodone 2.5 mg, 5mg, 10 mg / ibuprofen		PA
hydrocodone 7.5 mg / ibuprofen	Vicoprofen #	PA - > 80 mg/day
hydrocodone powder		PA
hydromorphone	Dilaudid #	PA - > 32 mg/day
hydromorphone powder		PA
meperidine	Demerol	PA
morphine immediate-release		PA - > 120 mg/day
morphine infusion	Infumorph	
morphine powder		PA
morphine suppositories		
morphine, injection-Astramorph-PF	Astramorph-PF	PA - > 120 mg/day
morphine, injection-Duramorph	Duramorph	PA - > 120 mg/day
oxycodone / acetaminophen		PA - > 80 mg/day
oxycodone / acetaminophen 300 mg		PA
oxycodone / acetaminophen extended-release	Xartemis XR	PA
oxycodone / acetaminophen-Percocet	Percocet #	PA - > 80 mg/day
oxycodone / aspirin		PA - > 4 g/day aspirin
oxycodone / ibuprofen		PA
oxycodone	Roxicodone #	PA - > 80 mg/day

immediate-release-Roxicodone		
oxycodone powder		PA
oxycodone-immediate-release-Oxaydo	Oxaydo	PA
oxymorphone immediate-release, oral	Opana IR	PA
oxymorphone injection	Opana	PA
sufentanil injection	Sufenta	
sufentanil powder		PA
tapentadol	Nucynta	PA
tramadol	Ultram #	PA - < 12 years
tramadol / acetaminophen	Ultracet	PA

This designates a brand-name drug with FDA "A"-rated generic equivalents. Prior authorization is required for the brand, unless a particular form of that drug (for example, tablet, capsule, or liquid) does not have an FDA "A"-rated generic equivalent.

BP Brand Preferred over generic equivalents. In general, MassHealth requires a trial of the preferred drug or clinical rationale for prescribing the non-preferred drug generic equivalent.

***** The generic OTC and, if any, generic prescription versions of the drug are payable under MassHealth without prior authorization.

II. Therapeutic Uses

FDA-approved, for example:

- acute pain
- chronic pain

Note: The above list may not include all FDA-approved indications.

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III. Evaluation Criteria for Approval

Please note: In the case where the prior authorization (PA) status column indicates PA, both the brand and generic (if available) require PA. Typically, the generic is preferred when available unless the brand-

name drug appears on the MassHealth Brand Name Preferred Over Generic Drug List. In general, when requesting the non-preferred version, whether the brand or generic, the prescriber must provide medical records documenting an inadequate response or adverse reaction to the preferred version, in addition to satisfying the criteria for the drug itself.

- All PA requests must include clinical diagnosis, drug name, dose, frequency, and formulation.
- A preferred drug may be designated for this therapeutic class. In general, MassHealth requires a trial of the preferred drug or clinical rationale for prescribing a non-preferred drug within a therapeutic class. Additional information about these agents, including PA requirements and preferred products, can be found within the MassHealth Drug List at www.mass.gov/druglist.
- Additional criteria may apply, depending upon the member's condition, requested medication, and Duplicate Therapy, High Dose, High Dose Short-Acting Monotherapy, and Quantity Limit restrictions (see below).
- If MassHealth pharmacy claims history of required trials is not available, medical records documenting such trials may be required.

Abstral (fentanyl sublingual tablet), Fentora (fentanyl buccal tablet), Lazanda (fentanyl nasal spray), Subsys (fentanyl sublingual spray)

- Documentation of the following is required:
  - indication of breakthrough cancer pain; **and**
  - adverse reaction or contraindication to all of the following:
    - hydromorphone immediate-release; **and**
    - morphine immediate-release; **and**
    - oxycodone immediate-release; **and**
    - fentanyl transmucosal system (generic Actiq) (requires PA - see criteria below); **and**
  - member is maintained on a long-acting opioid regimen; **and**
  - prescriber is an oncologist or pain specialist.

Arymo ER (morphine extended-release tablet), Embeda (morphine/naltrexone), Exalgo (hydromorphone extended-release), Hysingla ER (hydrocodone extended-release tablet), Morphabond ER (morphine extended-release tablet), Nucynta ER (tapentadol extended-release), Opana ER (oxymorphone extended-release), oxymorphone extended-release, Xtampza (oxycodone extended-release capsule), Zohydro ER (hydrocodone extended-release capsule)

- Documentation of the following is required:
  - appropriate diagnosis; **and**
  - adverse reaction or contraindication to all of the following that cannot be expected or managed as a part of opioid therapy:
    - fentanyl transdermal; **and**
    - morphine extended-release; **and**
    - oxycodone extended-release tablet (requires PA - see criteria below).

Belbuca (buprenorphine buccal film)

- Documentation of the following is required:
  - appropriate diagnosis; **and**
  - one of the following:

        - adverse reaction or contraindication to long-acting morphine sulfate that cannot be expected or managed as a part of opioid therapy; **or**
        - medical necessity for buccal formulation; **or**
        - prescriber wants to avoid using a full opioid agonist; **and**
    - dose does not exceed 1,800 mcg/day.

Buprenex (buprenorphine injection)

- Documentation of the following is required:
    - appropriate diagnosis; **and**
    - clinical rationale why oral pain medications cannot be used; **and**
    - adverse reaction or contraindication to fentanyl transdermal that cannot be expected or managed as a part of opioid therapy; **and**
    - adverse reaction or contraindication to buprenorphine transdermal.

butorphanol nasal spray

- Documentation of the following is required:
    - diagnosis of acute pain; **and**
    - quantity is ≤ two canisters/month; **and**
    - medical records documenting one of the following:
        - adverse reaction or contraindication to all other generic short-acting opioids: codeine, hydromorphone, morphine, and oxycodone; **or**
        - medical necessity for nasal spray formulation and adverse reaction or contraindication to both morphine immediate-release solution and oxycodone immediate-release solution.

codeine products for members < 12 years old

- Documentation of one of the following is required:
    - CYP2D6 genotyping confirms member is not an ultra-rapid CYP2D6 metabolizer; **or**
    - member has previously utilized a codeine-containing product without adverse effect that prevents repeat use.

dihydrocodeine/acetaminophen/caffeine, dihydrocodeine/aspirin/caffeine,hydrocodone/acetaminophen 300mg, hydrocodone 2.5 mg, 5 mg, 10 mg/ibuprofen, oxycodone/acetaminophen 300 mg, oxycodone/ibuprofen, Xartemis XR (oxycodone/acetaminophen extended-release)

Please refer to table in Section I. Prior-Authorization Requirements: Clinical Notes above for hydrocodone/acetaminophen and oxycodone/acetaminophen strengths that do not require PA within dose limits.

- For strengths and formulations that require PA, documentation of the following is required:
    - appropriate diagnosis; **and**
    - medical records documenting an inadequate response, adverse reaction, or contraindication to all of the following:
        - codeine/acetaminophen; **and**
        - hydrocodone/acetaminophen; **and**
        - hydrocodone/ibuprofen; **and**

        - oxycodone/acetaminophen.

fentanyl 37.5 mcg/hr, 62.5 mcg/hr, 87.5 mcg/hr transdermal system

- Documentation of the following is required:
    - clinical rationale why two patches cannot be combined to obtain the equivalent strength requested.

fentanyl transmucosal system (Actiq)

- Documentation of the following is required:
    - indication of breakthrough cancer pain; **and**
    - adverse reaction or contraindication to all of the following:
        - hydromorphone immediate-release; **and**
        - morphine immediate-release; **and**
        - oxycodone immediate-release; **and**
    - member is maintained on a long-acting opioid regimen; **and**
    - prescriber is an oncologist or pain specialist.

levorphanol tablet

- Documentation of the following is required:
    - adverse reaction or contraindication to all of the following that cannot be expected or managed as a part of opioid therapy:
        - fentanyl transdermal; **and**
        - morphine extended-release; **and**
        - oxycodone extended-release tablet (requires PA - see criteria below); **and**
    - clinical rationale for use of the requested agent over all other long-acting opioids.

meperidine

- Documentation of the following is required:
    - appropriate diagnosis; **and**
    - allergy to morphine; **and**
    - member has not used morphine derivatives since documented date of morphine allergy.

methadone injection, Opana injection (oxymorphone injection)

- Documentation of the following is required:
    - appropriate diagnosis; **and**
    - clinical rationale for use over oral formulations of the same product.

methadone tablet

- Documentation of the following is required:

- appropriate diagnosis; **and**
- member is not opioid naive; **and**
- baseline ECG showing normal QTc interval; **and**
- one of the following:
  - adverse reaction or contraindication to long-acting morphine sulfate and fentanyl transdermal that cannot be expected or managed as a part of opioid therapy; **or**
  - clinical rationale for the use of oral methadone over other long-acting opioids.

morphine extended-release capsules (Kadian, generics)

- Documentation of the following is required:
  - appropriate diagnosis; **and**
  - clinical rationale for use in place of long-acting generic morphine tablets.

Nucynta (tapentadol), Opana IR (oxymorphone immediate-release)

- Documentation of the following is required:
  - appropriate diagnosis; **and**
  - adverse reaction or contraindication to all of the following:
    - hydromorphone immediate-release; **and**
    - morphine immediate-release; **and**
    - oxycodone immediate-release.

opioid powders

- Documentation of the following is required:
  - appropriate diagnosis; **and**
  - clinical rationale why other commercially available alternatives cannot be used.

Oxaydo (oxycodone immediate-release)

- Documentation of the following is required:
  - clinical rationale as to why the generically available 5 mg tablets cannot be used.

oxycodone extended-release tablet

- Documentation of the following is required:
  - appropriate diagnosis; **and**
  - adverse reaction or contraindication to long-acting morphine sulfate or fentanyl transdermal that cannot be expected or managed as a part of opioid therapy.

pentazocine/naloxone

- Documentation of the following is required:

- appropriate diagnosis; **and**
- adverse reaction or contraindication to all of the following:
  - one nonsteroidal anti-inflammatory drug (NSAID); **and**
  - hydromorphone immediate-release; **and**
  - morphine immediate-release; **and**
  - oxycodone immediate-release; **and**
  - tramadol; **and**
- dose does not exceed 600 mg/day of pentazocine.

Prialt (ziconotide intrathecal injection)

- Documentation of the following is required:
  - appropriate diagnosis; **and**
  - member is intolerant or refractory to other treatments such as systemic analgesics and adjunctive therapy; **and**
  - member is intolerant or refractory to intrathecal morphine.

tramadol/acetaminophen

- Documentation of the following is required:
  - appropriate diagnosis; **and**
  - clinical rationale for use of the combination product over the commercially available separate agents.

tramadol extended-release capsule, tablet

- Documentation of the following is required:
  - appropriate diagnosis; **and**
  - medical records documenting an inadequate response or adverse reaction to generic tramadol immediate-release; **and**
  - clinical rationale for use of an extended-release formulation.

tramadol products for members < 12 years old

- Documentation of the following is required:
  - individual drug PA criteria must be met first where applicable; **and**
  - one of the following:
    - CYP2D6 genotyping confirms member is not an ultra-rapid CYP2D6 metabolizer; **or**
    - member has previously utilized a tramadol-containing product without adverse effect that prevents repeat use.

In addition to individual drug PA criteria above, some opioids are subject to additional Duplicate Therapy, High Dose, High Dose Short-Acting Monotherapy, and Quantity Limit restrictions.

Duplicate Therapy

The following opioids require PA if there is concurrent use of two long-acting or two short-acting opioids for at least 60 days out of any 180-day period:

Long-acting	**Short-acting**
Arymo ER (morphine extended-release tablet)	Abstral, Actiq, Fentora, Lazanda, Subsys (fentanyl immediate-release)
Belbuca (buprenorphine buccal film)	Buprenex (buprenorphine injection)
Butrans (buprenorphine transdermal)	butorphanol nasal spray
Dolophine, Methadose (methadone)	codeine
Duragesic (fentanyl transdermal system)	Demerol (meperidine)
Embeda (morphine/naltrexone)	dihydrocodeine/acetaminophen/caffeine
Exalgo (hydromorphone extended-release)	Dilaudid (hydromorphone)
Hysingla ER (hydrocodone extended-release tablet)	hydrocodone/acetaminophen
Kadian (morphine extended-release capsule)	hydrocodone/ibuprofen
levorphanol tablet	MSIR (morphine immediate-release)
Morphabond ER (morphine extended-release tablet)	Nucynta (tapentadol)
morphine extended-release capsule	Opana IR (oxymorphone immediate-release)
MS Contin (morphine controlled-release)	Oxaydo (oxycodone immediate-release)
Nucynta ER (tapentadol extended-release)	oxycodone/aspirin
Opana ER (oxymorphone extended-release)	oxycodone/ibuprofen

Oxycontin (oxycodone extended-release tablet)	Percocet, Xartemis XR (oxycodone/acetaminophen)
oxymorphone extended-release	Prialt (ziconotide)
Xtampza (oxycodone extended-release capsule)	Synalgos-DC (dihydrocodeine/aspirin/caffeine)
Zohydro ER (hydrocodone extended-release capsule)	Tylenol/Codeine (acetaminophen/codeine)

- If PA is required for duplicate therapy, documentation of the following is required:
  - appropriate diagnosis; **and**
  - individual drug PA criteria must be met first where applicable; **and**
  - clinical rationale for not maximizing opioid monotherapy.

High-Dose

The following opioids and analgesics require PA for high-dose if used at doses exceeding the limits listed below:

Long-acting		**Short-acting**	
Arymo ER (morphine extended-release tablet)	> 120 mg/day	acetaminophen products	> 4 grams/day
Belbuca (buprenorphine buccal film)	> 1,800 mcg/day	acetaminophen with codeine products	> 4 grams acetaminophen/day > 360 mg codeine/day
Butrans (buprenorphine transdermal system)	> 20 mcg/hr	codeine products	> 360 mg/day
Dolophine, Methadose (methadone)	> 30 mg/day	Dilaudid (hydromorphone)	> 32 mg/day
Duragesic (fentanyl transdermal system)	> 50 mcg/hr	hydrocodone/acetaminophen	> 80 mg/day
Embeda (morphine/naltrexone)	> 120/4.8 mg/day	hydrocodone/ibuprofen	> 80 mg hydrocodone/day

			> 3.2 grams ibuprofen/day
Exalgo (hydromorphone extended-release)	> 32 mg/day	morphine immediate-release	> 120 mg/day
Hysingla ER (hydrocodone extended-release tablet)	> 80 mg/day	Opana (oxymorphone immediate-release)	> 40 mg/day
Kadian (morphine extended-release capsule)	> 120 mg/day	Oxaydo (oxycodone immediate-release)	> 80 mg/day
levorphanol tablet	> 4 mg/day	oxycodone/acetaminophen	> 80 mg/day
Morphabond ER (morphine extended-release tablet)	> 120 mg/day	oxycodone/aspirin	>4 grams aspirin/day
morphine extended-release capsule	> 120 mg/day	oxycodone/ibuprofen	> 80 mg oxycodone/day > 3.2 grams ibuprofen/day
MS Contin (morphine controlled-release)	> 120 mg/day		
Opana ER (oxymorphone extended-release)	> 40 mg/day		
Oxycontin (oxycodone extended-release tablet)	> 80 mg/day		
oxymorphone extended-release	> 40 mg/day		
Xtampza (oxycodone extended-release capsule)	> 72 mg/day		
Zohydro ER (hydrocodone extended-release capsule)	> 80 mg/day		

- If exceeding 4 grams/day of an acetaminophen- or aspirin-containing product, or 3.2 grams/day of an ibuprofen-containing product, documentation of the following is required:
    - appropriate diagnosis; **and**

- individual drug PA criteria must be met first, where applicable; **and**
- clinical rationale for utilizing greater than 4 grams of acetaminophen or aspirin, or greater than 3.2 grams of ibuprofen per day.

- If exceeding the above high-dose limits for other agents, documentation of the following is required:
  - appropriate diagnosis; **and**
  - individual drug PA criteria must be met first, where applicable; **and**
  - medical records documenting treatment plan, including clinical rationale for high-dose and titration of medication up to current dose; **and**
  - pain consult from a pain specialist or hematologist/oncologist supporting the high dose of opioid requested; **and**
  - signed and dated patient-prescriber agreement for opioid use.

High-Dose Short-Acting Monotherapy

The following opioids and analgesics require PA for monotherapy if used at doses exceeding the limits listed below:

Short-acting	
acetaminophen with codeine products	> 4 grams acetaminophen/day > 360 mg codeine/day
codeine products	> 360 mg/day
Dilaudid (hydromorphone)	> 32 mg/day
hydrocodone/acetaminophen	> 80 mg/day
hydrocodone/ibuprofen	> 80 mg/day hydrocodone >3.2 grams/day ibuprofen
morphine immediate-release	> 120 mg/day
Opana (oxymorphone immediate-release)	> 40 mg/day

Oxaydo (oxycodone immediate-release)	> 80 mg/day
oxycodone immediate-release	> 80 mg/day
oxycodone/acetaminophen	> 80 mg/day
oxycodone/aspirin	>4 grams/day aspirin
oxycodone/ibuprofen	> 80 mg/day oxycodone >3.2 grams/day ibuprofen

- If exceeding the above high-dose limits and using as monotherapy, documentation of the following is required:
  - individual drug PA criteria must be met first, where applicable; **and**
  - medical records documenting treatment plan, including clinical rationale for high-dose and titration of medication up to current dose; **and**
  - pain consult from a pain specialist supporting the high dose of opioid requested; **and**
  - clinical rationale for not utilizing a long-acting agent in a member requiring high-dose short-acting opioid therapy for the treatment of chronic pain; **and**
  - signed and dated patient-prescriber agreement for opioid use.

Quantity Limits

The following opioids require PA if used at the quantities listed below:

Long-acting	
Arymo ER (morphine extended-release tablet)	> 90 tablets/month
Butrans (buprenorphine transdermal system)	> 4 patches/28 days
Duragesic (fentanyl transdermal system)	> 10 patches/month
Embeda (morphine/naltrexone)	> 30 capsules/month
Exalgo (hydromorphone extended-release)	> 30 tablets/month

fentanyl 37.5, 62.5, 87.5 mcg/hr transdermal system	> 10 patches/month
Hysingla ER (hydrocodone extended-release tablet)	> 30 tablets/month
Kadian (morphine extended-release capsule)	> 30 capsules/month
levorphanol tablet	> 60 tablets/month
Morphabond ER (morphine extended-release tablet)	> 60 tablets/month
morphine extended-release capsule	> 30 capsules/month
Opana ER (oxymorphone extended-release)	> 60 tablets/month
Oxycontin (oxycodone extended-release tablet)	> 90 tablets/month
oxymorphone extended-release	> 60 tablets/month
Xtampza (oxycodone extended-release capsule)	> 60 capsules/month
Zohydro ER (hydrocodone extended-release capsule)	> 60 capsules/month

- If exceeding the above quantity limits, documentation of the following is required:
  - appropriate diagnosis; **and**
  - individual drug PA criteria must be met first, where applicable; **and**
  - requested dose cannot be obtained within the established quantity limits.

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Last updated 01/28/19

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Exhibit P

Massachusetts Department of Public Health

Findings of the Opioid Task Force and Department of Public Health Recommendations on Priorities for Investments in Prevention, Intervention, Treatment and Recovery

June 10, 2014

Executive Summary

In response to the growing opioid addiction epidemic in Massachusetts, and across the nation, Governor Patrick declared a public health emergency on March 27, 2014. The Governor directed the Department of Public Health (DPH) to take several actions to combat overdoses, stop the opioid epidemic from getting worse, help those already addicted to recover, and map a long-term solution to ending widespread opioid abuse in the Commonwealth. Per the Governor's directive, DPH utilized the Executive Committee of the Interagency Council on Substance Abuse and Prevention to create the Opioid Task Force (Task Force). This Task Force was charged with providing recommendations to strengthen the Commonwealth's opioid abuse prevention and treatment systems to reduce overdose events, prevent opioid misuse and addiction, increase the numbers of persons seeking treatment, and support persons recovering from addiction in our communities.

This report summarizes the findings of the Task Force and provides recommendations for strengthening our Commonwealth's ability to respond to the opioid crisis with a focus on prevention, intervention, treatment and recovery. These recommendations include, but are not limited to, the expansion of treatment beds; the formation of a centralized navigation system for patients, families, and first responders to locate treatment services; a public-facing dashboard that would help facilitate consumer choice of services; additional opioid prevention coalitions for support and education; more stringent safeguards for those opioids which are most frequently abused and misused; a meeting of New England governors to develop a regional response to the opioid epidemic; and the expansion of the use of injectable naltrexone for persons re-entering the community from correctional facilities.

Since the convening of this Task Force, the Massachusetts Legislature has also taken actions to address the opioid epidemic in Massachusetts. The recommendations included in this report complement the Legislature's proposals, and DPH looks forward to continuing to work closely with the Legislature on the important issue of opioid misuse, abuse and overdose.

Despite having one of the strongest treatment systems in the country as measured by the robust continuum of care offered and the presence of dedicated addiction treatment providers, there are still opportunities for improvement. DPH believes that with the policy recommendations made here, particularly with an emphasis on safe opioid prescribing, the Department will be able to help those struggling with addiction, their loved ones and communities.

Introduction

Massachusetts is experiencing an opioid addiction epidemic. From 2000 to 2012 the number of unintentional fatal opioid overdoses in Massachusetts increased by 90 percent.[1] In 2012, 668 Massachusetts residents died from unintentional opioid overdoses, a 10 percent increase over the previous year.[2] The Massachusetts State Police reported that in jurisdictions in which they respond to homicides at least 140 people died of suspected heroin overdoses between November 2013 and March 2014. Various communities in the Commonwealth have reported previously unseen spikes in both fatal and non-fatal opioid overdose in recent months. The Department of Public Health (DPH) Bureau of Substance Abuse Services (BSAS) data shows that in FY13 nearly half of all persons receiving treatment in the publicly funded system reported opioids as their primary or secondary drug of choice. In addition, approximately 40 percent of persons served in FY13 in the BSAS system were between the ages of 13 and 29.

Massachusetts is not alone in struggling with the devastating consequences of opioid misuse, abuse and addiction. In 2013, the U.S. Department of Health and Human Services deemed prescription-opioid overdose deaths an epidemic.[3] In the United States, deaths from

[1] Fatal Opioid-related Overdoses Among MA Residents, 2000-2013. Massachusetts Department of Public Health, March 2013. Available at: http://www.mass.gov/eohhs/docs/dph/substance-abuse/opioid/fatal-opioid-overdoses-2000-2013.docx. Accessed on June 5, 2014.
[2] Fatal Opioid-related Overdoses Among MA Residents, 2000-2013. Massachusetts Department of Public Health, March 2013. Available at: http://www.mass.gov/eohhs/docs/dph/substance-abuse/opioid/fatal-opioid-overdoses-2000-2013.docx. Accessed on June 5, 2014.
[3] Addressing prescription drug abuse in the United States: current activities and future opportunities. U. S. Department of Health and Human Services, 2013. Available at: http://www.cdc.gov/homeandrecreationalsafety/overdose/hhs_rx_abuse.html. Accessed on: June 9, 2014.

prescription opioid overdose quadrupled between 1999 and 2010.[4] People who are abusing opioids are also at high risk for, among other things, liver disease, Hepatitis C, and HIV infection.[5] Opioid addicted individuals live approximately 15 years less than people who do not have the disease.[6] Opioid addiction is a chronic disease, which like other chronic illnesses, cannot be cured but can be effectively treated and managed.[7]

On March 27, 2014, in response to the crisis of opioid abuse in the Commonwealth and after meeting individuals and families impacted by it, Governor Patrick declared a public health emergency and, among other actions, committed an additional $20 million in state funding to increase treatment and recovery services and directed the Commissioner of the Department of Public Health to establish an Opioid Task Force (Task Force) within the Interagency Council on Substance Abuse and Prevention (Council). The Task Force was charged with providing recommendations to reduce overdose events, prevent opioid misuse and addiction, increase the numbers of persons seeking addiction treatment, support persons recovering from addiction in our communities, and map a long term solution to address opioid abuse in the Commonwealth.

This report contains a description of the Task Force's methodology, an overview of substance abuse services offered by the Commonwealth, findings from the Task Force's deliberations, and actions recommended by DPH in response to the Task Force's work and findings.

Task Force Methodology

In addition to the Executive Committee of the Council, the membership of the Task Force included those struggling with addiction and their families, providers, insurers, first responders, public safety officials, local

[4] Jones CM, Mack KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. JAMA 2013; 209:657-659.
[5] Moore K and Dusheiko G. Opiate Abuse and Viral Replication in Hepatitis C. American Journal of Pathology November 2005;167(5):1189-1191.
[6] Smyth B, Fan J, Hser Y, Life Expectancy and Productivity Loss Among Narcotics Addicts Thirty-Three Years After Index Treatment. Journal of Addictive Diseases 2006; 25(4): 37-47.
[7] Kritz S, Chu M, John-Hull C, Madray C, Louie B, and Brown LS Jr., Opioid dependence as a chronic disease: the interrelationships between length of stay, methadone dose and age on treatment outcome at an urban opioid treatment program. J Addiction Dis. 2009, 28(1):53-6.

government representatives, the judiciary and legislators. A complete list of participants can be found in Appendix III. The mission of the Task Force was to develop recommendations to improve on the Commonwealth's current efforts to (1) prevent opioid abuse, addiction and overdose; (2) educate the public about opioid addiction and treatment options; (3) facilitate access to treatment though improved care coordination; (4) expand the current treatment system; (5) ensure access to the full continuum of treatment services by all insurers; (6) divert non-violent criminal offenders with substance use disorders to appropriate treatment; (7) assist persons with addictive disorders re-entering the community from correctional facilities to maintain opioid abstinence; and (8) expand community based recovery supports.

Given the urgency of the opioid epidemic and taking into consideration the 60-day time frame in which to consider and develop recommendations, the Task Force formed focus groups (Appendix V) to maximize stakeholder input and to allow for a comprehensive overview of the current system. A total of 19 focus groups and/or interviews were held with stakeholders from across the Commonwealth, including persons who were actively using opioids, persons in recovery, parents, prevention coalitions, law enforcement, members of the judiciary, state agency representatives, schools and colleges, behavioral health providers, pharmacists, hospitals, emergency room physicians, physicians specializing in addiction medicine, first responders and insurers. As previously noted, approximately 40 percent of persons served in FY13 in the BSAS system were between the ages of 13 and 29, so particular attention was given to this age group when discussing priorities.

The Task Force met as a committee of the whole three times. During the first meeting, the Task Force members discussed the opioid problem and its charge, agreed upon the focus group approach, and brainstormed potential investments. During the second meeting, members reviewed and commented on early findings and proposed recommendations from the initial focus groups, which can be found in Appendix IV. During the final meeting, the Task Force members reviewed a series of focus group recommendations and provided feedback to DPH on those

recommendations. Finally, DPH reviewed and prioritized those recommendations based on their ability to have a positive impact on the public health emergency in the short and long term.

Overview of Massachusetts Substance Abuse Services

Massachusetts has one of the strongest substance abuse treatment systems in the country.[8] The Bureau of Substance Abuse Services (BSAS) is the single state authority on substance abuse and provides a robust system that provides services across the full continuum of care. The BSAS is charged with licensing addiction treatment programs as defined in 105 CMR 164.012, licensing addiction counselors as defined in 105 CMR 168.000, and funding a continuum of prevention, intervention, treatment and recovery support services. The BSAS also sets policy in this area and serves as the payer of last resort for persons seeking treatment services who are either uninsured or underinsured. The types of services are summarized below.

Prevention

The BSAS prevention efforts include funding community based primary prevention campaigns across the state aimed at preventing the misuse and abuse of, and addiction to, alcohol and other drugs. Other BSAS prevention efforts include the development of print materials and media campaigns to educate various stakeholders about the consequences of underage drinking and the misuse of alcohol and other drugs, the dissemination of evidence based prevention practices and the expansion of education about addictive disorders in various training programs for health professionals, including physicians and allied health professionals.

[8] See, for example, treatment rates as documented in the National Survey of Substance Abuse Treatment Services (N-SSATS), 2011. Population: U.S. Census Bureau, Population Estimates, State population dataset - SCPRC-EST2009-18+POP-RES. From: The Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Available at: http://www.samhsa.gov/data/DASIS/2k11nssats/NSSATS2011Tbl6.33.htm. Accessed on: June 5, 2014.

Intervention

The BSAS intervention efforts include providing funding to groups that support and advocate for individuals and families dealing with addictive disorders such as the Massachusetts Organization for Addiction Recovery (MOAR) and Learn to Cope. The Massachusetts Overdose Education and Naloxone Distribution program is a model for the nation in terms of how to widely distribute naloxone (sometimes referred to as Narcan), a lifesaving medication that can reverse opioid overdose, to persons likely to witness an opioid overdose.

Treatment

The BSAS provides a full continuum of licensed treatment services in inpatient, residential and outpatient treatment settings. In FY13 there were approximately 40,000 enrollments to the BSAS-funded acute treatment services (ATS) or detoxification programs. The primary purpose of these programs is to medically treat withdrawal symptoms in persons dependent upon opioids, alcohol or other drugs. Specialized services are available to those under 18 through Youth Stabilization Programs. Detoxification services are paid for by commercial insurers, MassHealth and other public payers, and the BSAS. Typically, individuals remain in detox programs for 4-6 days. Best practice dictates that persons in these programs should continue in "step-down" treatment services in order to maximize their potential for continued abstinence from drugs of abuse. Focus groups that included active consumers, consumers in recovery and family members all emphasized this point.

There are a number of step-down services available, including Clinical Stabilization Service (CSS) programs which provide a range of services, including nursing, intensive education and counseling on the nature of addiction and its consequences, relapse prevention and aftercare planning for individuals beginning to engage in recovery. The usual length of inpatient stay in a CSS program is 10-14 days. These programs are paid for by MassHealth, the BSAS and some commercial insurers. Transitional Support Service (TSS) programs are another example of a short term

residential “step-down” service. The expected length of stay in these programs is up to 30 days. TSS services provide intensive care management services to prepare individuals for long-term residential rehabilitation or a return to the community. TSS services are solely funded with the BSAS dollars.

Residential rehabilitation treatment programs feature a planned program of substance abuse treatment within a 24-hour residential setting located in the community. These residential treatment programs serve individuals in the early stages of addiction recovery, where safe and stable living environments are essential to recovery. Residential rehabilitation facilities primarily serve adults, but there are some facilities that focus on youth or families. Individuals and families typically receive treatment in residential settings for 6-12 months while youth programs are generally 3 months in duration. Like TSS, residential rehabilitation is only funded by the BSAS.

Outpatient substance abuse treatment is also available across the state. Paid for to varying extents by commercial insurers, MassHealth and other public payers, and the BSAS, services may include individual, group and family counseling, intensive day treatment and educational services. A subset of outpatient programs focus on providing services to individuals dually diagnosed with substance abuse and mental health conditions, persons who have been convicted of driving under the influence of substances and/or adolescents.

Many opioid addicted people utilize outpatient medication assisted treatment (MAT) services. Opioid Treatment Programs (OTP) provide methadone dosing services in combination with an array of other services including counseling, drug screening and case management services. Buprenorphine, sometimes known as suboxone, is another example of MAT. Buprenorphine is available to patients in physician offices. This arrangement is called Office Based Opioid Treatment (OBOT). In order to prescribe buprenorphine, a physician must obtain a waiver from the Drug Enforcement Agency. Physicians are limited to providing OBOT to 30 individuals in the first year of receiving a waiver and up to 100 individuals thereafter. In 2012, injectable naltrexone, known as Vivitrol, was approved

for the treatment of opioid dependence. This medication can be prescribed by any qualified health professional, including mid-level practitioners, and is given in the form of an injection on a monthly basis in the prescriber's office. All of these medications are FDA approved for the treatment of opioid dependence and are shown to be effective in the scientific literature. Methadone treatment is primarily paid for by MassHealth and the BSAS, while buprenorphine and injectable naltrexone are paid for by MassHealth and the majority of commercial insurers.

Some persons suffering from opioid addiction do not see a need for treatment. When these persons pose a danger to themselves or others by virtue of their addictive behaviors, they may be involuntarily committed to treatment. Under Massachusetts General Law Chapter 123, Section 35 (Section 35), "any police officer, physician, spouse, blood relative, guardian or court official" can petition the court to commit a "person who he has reason to believe is an alcoholic or substance abuser" if that abuse "substantially injures his health or substantially interferes with his social or economic functioning, or… he has lost the power of self-control over the use of such controlled substances." After reviewing the evidence to determine if the person is an immediate risk to himself or others, a judge may commit a person to treatment for up to 90 days. There are specific treatment programs that focus on serving individuals who are committed to treatment through Section 35.

Recovery is an ongoing process. Today, the BSAS funds 7 Recovery Support Centers (RSC) across the state staffed primarily by peer members in recovery. RSCs offer a drug-free environment and a variety of activities including classes, leisure activities and support group meetings. The BSAS also supports Recovery High Schools which provide a structured school environment for high-school aged youth in recovery to maintain their recovery and complete their education. Case management services are provided to youth and adults in their homes to support their continued abstinence from substances in the community.

Task Force Findings with DPH Recommended Actions

Below are the findings of the Task Force and DPH recommended actions in the areas of prevention, intervention, treatment, and recovery. The list of recommended investments in order of priority can also be found in Appendix I and additional policy and regulatory recommendations in Appendix II.

When considering infrastructure investments, especially the addition of inpatient and residential treatment services, the current proposed expansion in the number of treatment beds was taken into account. For example, the Governor's FY15 budget already includes the addition of a new detoxification and clinical stabilization service and both the House and the Senate supported the addition of these 64 beds in their respective budget proposals. Furthermore, as of April 2014, DPH completed an expansion of 80 transitional support services beds and 200 long term residential beds for single adults. Additionally, the Governor's FY15 budget includes the addition of long term residential services under the trial court expansion budget, another initiative supported by the legislature. The Governor's current budget also calls for the expansion of 8 specialty courts to divert non-violent offenders.

PREVENTION

Finding: There is a need for increased education for youth and families about the dangers of drug use.

Task Force members emphasized the importance of ongoing education for children and parents about the dangers of drug use, the appropriate use of prescription pain medications and their potential addictive qualities. Focus groups also discussed the potential of leveraging community coalitions.

Prevention programs designed and tested to reduce risk and increase awareness can help people of various ages develop and apply the skills necessary to stop problem behaviors before, and after, they begin. Research has demonstrated that research-based drug abuse prevention programs are cost-effective. Each dollar invested in prevention saves up to

7 dollars in areas such as substance abuse treatment and criminal justice system costs, not to mention their wider impact on the trajectory of young lives and their families.[9]

Recommended Actions

- The Governor should convene a meeting of New England governors to discuss a collective response to the opioid epidemic impacting the region;

- Develop a statewide evidence-based public service campaign on the prevention of addictive disorders targeted at youth and parents;

- Add up to five new Opioid Overdose Prevention Coalitions in high need areas.

Finding: There is a need for increased education for prescribers to ensure safe and effective pain management

The diagnosis and treatment of pain is integral to the practice of medicine, and inappropriate treatment of pain, including both over-treatment and under-treatment, is an important problem. Providers must balance the legitimate needs of patients with pain against the dangers to the public of opioids circulating through communities. Prescribers reported that they would like enhanced education about the potential addictiveness of prescription pain medications, how to identify at risk individuals, how to identify potential opioid abuse, and how to effectively taper people off of prescription pain medications without leading to addiction.

Recommended Action

- Practitioners are already required by medical boards to complete training on pain management to renew their licenses. This training could be further enhanced, particularly around safe prescribing

[9] National Institute on Drug Abuse. Topics in Brief: Drug Abuse Prevention. Revised March 2007. Available at: http://www.drugabuse.gov/publications/topics-in-brief/drug-abuse-prevention. Accessed on: June 5, 2014.

practices and managing of medications to decrease the risk of addiction.

INTERVENTION

Finding: Opportunities exist to improve safe prescribing and dispensing of controlled substances.

Deaths from prescription opioid overdoses quadrupled from 1999 to 2010 and far exceed the combined toll of cocaine and heroin overdoses.[10] At the same time, prescription opioid pain medications serve an important and legitimate role in the treatment of pain. Safe prescribing and dispensing practices are needed to decrease the risk of misuse and abuse while allowing for the legitimate use of these important medications. Focus groups discussed the role of pharmacists in providing education to consumers at the time of dispensing, as well as potentially engaging with prescribers. Focus groups also discussed the utility and limitations of the Prescription Monitoring Program, and its role in preventing prescription drug misuse and abuse.

Recommended Actions

- Review and develop regulations to promote the safe prescribing and dispensing of controlled substances, including the funding of necessary infrastructure to support these activities;
- For those opioids which are most frequently abused and misused, DPH recommends that the DPH Drug Control Program propose regulations mandating all prescribers to utilize the PMP each time they issue a prescription for Schedule II or III drugs that have been determined by DPH to be commonly misused or abused and designated as a drug that needs additional safeguards;

[10] Jones CM, Mack KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. JAMA 2013;309:657-659.

- Task the various boards of registration, within and beyond DPH, with consideration of regulations to minimize diversion and misuse while ensuring safe prescribing and patient access to medication;

- Consider additional safe prescribing recommendations to be issued by the Joint Policy Working Group.

TREATMENT

Finding: There is a need for centralized treatment resources.

Task Force members discussed the challenges to accessing services in a timely manner, noting the importance of getting treatment within the window of opportunity when an individual is ready to accept it. Well-accepted models recognize that treatment needs to be matched to the patient's acceptance of it for the treatment to be most successful. Across the focus groups, there was not a clear understanding of how to access the treatment network in Massachusetts. Focus group participants described the burden of having to call multiple programs on an ongoing basis to find available services.

Recommended Actions

- Develop a central navigation system for adult services that can be accessed through an 800 number. The system would maintain a real time inventory of available substance abuse services across the continuum of care. Central navigation could be utilized to identify appropriate resources by consumers and their families, first responders, schools, and providers. When contacted, intake staff would work, if appropriate, with the caller to place the person needing services into the best available setting;

- Establish pilot regional walk-in centers that could coordinate with central navigation as needed. These centers could provide assessment, liaison with central intake to place the person in the best

treatment setting, daily clinically run group sessions, and emergency one-on-one counseling;

- Develop and implement a public facing dashboard to facilitate consumer choice by providing quality assessments and other information about treatment options.

Finding: Individuals and families report challenges in accessing services beyond simply knowing where they are.

Treatment is necessary to provide patients relief from physical withdrawal symptoms and to place patients on the road to recovery. Task Force members heard from several individuals struggling with addiction and their families who described difficulty in accessing treatment services. BSAS notes that approximately 40 percent of persons served in FY13 in the BSAS system were between the ages of 13 and 29, making this an important population to consider. In addition, 20 percent of 16 to 24 year olds served in the BSAS system in FY13 had children under six, highlighting the need for services for families with children.

<u>Recommended Actions</u>

- Add treatment programs with an emphasis on:
    - Community-based treatment programs for youth and young adults to provide home-based counseling services;
    - Residential treatment programs for populations in need, including adolescents and transitional age youth, families, single adults with children, Hispanics, and residents in currently geographically underserved areas such as Franklin County; and
    - Clinical Stabilization Services program for step down services.
- Add funding to allow community health centers to increase capacity to provide medication assisted treatment including injectable naltrexone to people in the community.

Finding: Providers and consumers express concerns about barriers to access

Even when treatment is available, individuals and families may still have trouble accessing that treatment. For example, providers and consumers that participated in our focus group expressed the belief that insurers are too restrictive in authorizing certain care. Other issues that potentially affect access include housing issues and physician reluctance to receive authority to prescribe buprenorphine due to real and/or perceived burdensome regulatory requirements. Stigma is also an important barrier to treatment. All of these factors can prevent individuals from obtaining the treatment they need as the first step to recovery.

Recommended Actions

- DPH and the Division of Insurance, in consultation with the Health Policy Commission, should conduct a comprehensive review of medical necessity criteria and utilization review guidelines for opioid abuse and addiction treatment developed by carriers and consult with clinical experts to develop minimum criteria for opioid abuse and addiction treatment services that will be considered medically necessary for all plans;
- The Interagency Council on Substance Abuse and Prevention should expand its review of substance abuse issues to review interagency regulatory and operational barriers to treatment, such as loss of foster care placement, long wait periods for insurance coverage, lack of drug-free shelters, and physician reluctance to receive authority to prescribe buprenorphine due to real and/or perceived burdensome regulatory requirements.

Finding: Correctional facilities are an important site of care for opioid addiction.

Task Force members noted the impact of opioid addiction on incarcerated individuals. Jails and prisons offer treatment for addiction on a voluntary

basis; however, in some facilities, individuals receive incentives to participate in treatment programs. Whether or not individuals have received treatment for their substance use while incarcerated, it is important to provide individuals support once they complete their sentences. Otherwise, without that support, they may relapse, and this relapse could cause them to engage in behaviors that potentially result in re-incarceration.

Recommended Actions

- Enhance the DOC's and Sheriff Offices' continuum of care by increasing the availability of treatment for offenders at designated DOC facilities. Specifically, DOC recommends implementing a basic substance abuse education/motivation enhancement program targeting offenders with substance abuse issues, and a graduate maintenance and aftercare program for offenders who have completed the residential substance abuse treatment program. Currently, the DOC provides substance abuse treatment for inmates who are nearing release, as research has indicated that offenders receive the maximum benefits of treatment prior to release when they are focused on reentering the community;

- Support the expansion of the use of injectable naltrexone for persons re-entering the community from correctional facilities by providing funding for supportive case management services to ensure participants comply with their post-release treatment plan and assist them in navigating access to other critical services.

RECOVERY

Finding: There is a need for peer support in the recovery process.

Research has shown that recovery is facilitated by social support. Peer recovery support services are designed and delivered by people who have experienced both substance use disorder and recovery. These services help people become and stay engaged in the recovery process and reduce

the likelihood of relapse. Because they are designed and delivered by peers who have been successful in the recovery process, they embody a powerful message of hope, as well as a wealth of experiential knowledge. The services can effectively extend the reach of treatment beyond the clinical setting into the everyday environment of those seeking to achieve or sustain recovery. Focus group participants emphasized that opioid addiction is a chronic disease and recovery is an ongoing process that requires ongoing supports. In addition, they emphasized the need to provide support services not just during normal business hours but on nights and weekends to provide safe, drug-free activities to support the recovery process.

Recommended Actions

- Develop a peer to peer support network by encouraging the hiring of recovering peers to speak with at-risk youth and other special high risk populations, participate in a speakers bureau, and meet with individuals at critical transition points such as in emergency rooms, time of arrest or when returning to the community.

Finding: There is a need for expanded recovery services across the state.

There are currently 7 Recovery Support Centers across the Commonwealth that operate 12 hours per day. People in recovery highlighted the value of these services and their desire to have increased access to them. Both the focus groups and Task Force recognized that there is a need for expanded recovery support services focused on creating healthy communities that assist individuals maintain abstinence from drugs and alcohol after formal treatment has completed.

Recommended Actions

- Augment the capacity of Recovery Support Centers by expanding the hours of currently existing centers to include nights and weekends and by adding new Recovery Support Centers;

- Add a Recovery High School in Worcester area;
- Add Learn to Cope chapters across the Commonwealth;
- DPH also recommends developing and implementing a voluntary accreditation program for Alcohol Drug-Free Living housing, also known as sober homes. These homes can provide affordable housing and are an important part of the continuum of recovery support in the community.

Conclusion

These recommendations are important steps towards addressing the Commonwealth's public health emergency. DPH appreciates the leadership of Governor Patrick and the commitment and hard work of Task Force members who contributed their time, ideas, and expertise to help the Commonwealth address the opioid epidemic.

Since the convening of the Task Force, the Massachusetts Legislature has taken steps to address the opioid epidemic in Massachusetts. The recommendations included in this report complement the Legislature's proposals and DPH looks forward to continuing to work closely with the Legislature on the important issue of opioid misuse, abuse, and overdose.

Despite having one of the strongest treatment systems in the country as measured by the robust continuum of care offered and the presence of dedicated addiction treatment providers, we still have opportunities for improvement. DPH believes that with Governor Patrick's leadership and the policy recommendations made here, particularly with an emphasis on safe opioid prescribing, we will be able to help those struggling with addiction, their loved ones and impacted communities.

Appendix I: DPH Recommended Investments in Priority Order

Recommendation	Funding Estimate	Annualized	Pending Legislative Action
Develop a central navigation system that could be accessed through an 800 number. The system would build upon existing information lines, other central navigation systems and be used by consumers, families, first responders, health care professionals and behavioral health providers to access information about treatment options including current availability.	$1,450,000	Yes	Proposed Senate budget includes language and funding for a central navigation system
Pilot regional centers that provide assessment, drop-in counseling and referral to treatment on demand leveraging existing treatment organizations.	$1,800,000	Yes	Senate budget proposes $10M Trust Fund to expand services.
Develop Prescription Monitoring Program infrastructure to support safe opioid prescribing practices and new regulations related to the Public Health Emergency and accelerated enrollment of prescribers.	$1,500,000	Yes	SB2142 provides DPH additional authorities to require PMP registration and consultations, as well as places limitations on the prescribing physician. In the budget, House and Senate proposed $3.7M for roll-out of full, mandatory use of the PMP by prescribers.
DPH and the DOI, in consultation with the Health Policy Commission to conduct a comprehensive review of medical necessity criteria and utilization review guidelines for opiate abuse and addiction treatment developed by carriers pursuant to sections 12 and 16 of chapter 1760. The agencies to consult with clinical experts to develop minimum criteria for opiate abuse and addiction treatment services that will be considered medically necessary for all plans.	$250,000	No	SB2142 directs the Center for Health Information and Analysis (CHIA) to review accessibility of substance abuse treatment and the adequacy of coverage; while the Health Policy Commission is to determine standards for evidence-based substance abuse treatment and to create a certification process for providers.
Enhance the DOC's continuum of care by increasing the availability of treatment for offenders at designated DOC facilities.	$2,000,000	Yes	

Recommendation	Funding Estimate	Annualized	Pending Legislative Action
Support the expansion of the use of injectable naltrexone for persons re-entering the community from correctional facilities.	$1,000,000	Yes	
Add funding to allow community health centers to increase capacity to provide medication assisted treatment including injectable naltrexone to people in the community.	$300,000	Yes	
Develop a statewide evidence-based public service campaign on the prevention of addictive disorders targeted at youth and parents.	$1,000,000	No	SB2142 requires distribution of educational information on family support services to families, upon admission to the program. The Senate final budget proposes funding for a public education campaign.
Develop/implement voluntary accreditation for Alcohol and Drug-Free living homes.	$500,000	Yes, for at least 3 years	Senate and House proposed budgets include language and funding for voluntary accreditation for Alcohol and Drug-Free living homes.
Add five community based treatment programs for youth and young adults to provide home based counseling services using both evidence based treatment models.	$1,000,000	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Add two adolescent residential treatment programs for 13-17 year olds.	$855,125	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Add one residential treatment programs for 16-21 year olds.	$660,985	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Add one residential treatment program for 18-25 year olds.	$660,985	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Add one family residential treatment program.	$820,000	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Add two adult residential treatment programs prioritizing Hispanics and single adults with children.	$1,100,000	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Add one detoxification program in Franklin County.	$550,000	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Add one Clinical Stabilization Services Program.	$350,000	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Add five Opioid Overdose Prevention Coalitions in high need areas.	$500,000	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.

Recommendation	Funding Estimate	Annualized	Pending Legislative Action
Develop peer to peer support networks to meet with persons at critical transition points, such as in emergency rooms, at times of arrest, at times of program transition.	$500,000	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Expand the hours of currently existing Recovery Support Centers to cover nights and weekends.	$350,000	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Add three new Recovery Support Centers.	$1,050,000	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Add another Recovery High School in the Worcester area.	$500,000	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Add Learn to Cope Chapters across the state by adding program staff.	$300,000	Yes	As noted above, the Senate budget proposes a $10M trust fund to expand services.
Add a public facing dashboard to facilitate consumer choice and transparency, includes development of IT and data structures.	$1,000,000	No	Senate budget recommends a public facing dashboard.
TOTAL	$19,997,095		

Appendix II: Additional DPH Recommendations

DPH Policy and Regulatory Recommendations
DPH Drug Control Program will be proposing regulatory amendments to the PMP requiring all prescribers to utilize the PMP each time they issue a prescription for a Schedule II or III drug which has been determined by the Department to be commonly misused or abused and which has been designated as a drug that needs additional safeguards.
DPH suggests that the various boards of registration, within and beyond DPH, be tasked with consideration of regulations to minimize diversion and misuse while ensuring safe prescribing and patient access to medication
DPH recommends consideration of additional safe prescribing recommendations to be issued by the Joint Policy Working Group.

Appendix III: Task Force Members

Member	Affiliation
Dr. Thomas Amoroso	Medical Director, Tufts Health Plan
Cheryl Bartlett	Commissioner, Department of Public Health
Kim Bishop-Stevens	Coordinator, Substance Abuse Services, Department of Children and Families
Dr. Troy Brennan	Medical Director, CVS
Andrea Cabral	Secretary, Executive Office of Public Safety
Paula Carey	Chief Justice of the Trial Court
Paul Doherty	Parent, Learn to Cope
Ed Dolan	Commissioner of Probation
Chuck Farris	President and CEO, Spectrum Health Services
Peter Forbes	Commissioner, Department of Youth Services
Marcia Fowler	Commissioner, Department of Mental Health
Maryann Frangules	Executive Director, MA Coalition for Addiction Services
Dr. Barbara Herbert	Medical Director, St. Elizabeth's Comprehensive Addiction Program, Steward Health Care System
Tom Hoye	Mayor, Taunton
Hilary Jacobs	Director, Bureau of Substance Abuse Services, DPH
Paul Jeffrey	Pharmacy Director, MassHealth
Theodore Joubert	Chief, Fire Chiefs Association
Katie Joyce	Vice President for Policy and Domestic & International Government, Mass Life Sciences
Paul Kusiak	Parent
William Luzier	Executive Director, Interagency Council on Substance Abuse Services and Prevention
John McGahan	President, Gavin Foundation
Richard McKeon	Major, Division of Investigative Services
Rosemary Minehan	Judge, Plymouth District Court
Christopher Mitchell	Director of Program Services, DOC
Joseph Murphy	Commissioner, Massachusetts Division of Insurance

Member	Affiliation
Coleman Nee	Secretary, Department of Veterans' Services
Heidi Nelson	CEO, Duffy Health Center
Lora Pellegrini	President & CEO, Massachusetts Association of Health Plans
Dr. Debra Pinals	Assistant Commissioner, Forensic Mental Health Services, Department of Mental Health
John Polanowicz	Secretary, Executive Office of Health and Human Services
Domenic Sarno	Mayor, Springfield
David Seltz	Executive Director, Health Policy Commission
Luis Spencer	Commissioner, Department of Corrections
Martin Walsh	Mayor, Boston
Steven Walsh	Executive Director, Massachusetts Council of Community Hospitals
Steven Tolman	President, AFL-CIO

Appendix IV: Focus Group Feedback

Proposed Priorities and Funding Recommendations
(from Focus Groups with Task Force feedback included)
May 21, 2014

Focus Group Recommendations	Funding Estimate
DATA	
Develop and implement a public facing dashboard to facilitate consumer choice and improved performance management.	$1,000,000 Includes development of IT infrastructure
Increase capacity to allow for ongoing data analytics of service delivery system, including the supply and demand for services, program effectiveness, utilization patterns, provider service profiles, including results of injectable naltrexone (vivitrol) services	
POLICY/REGULATORY ACTION	
Develop and implement an accreditation program for Alcohol Drug-free Living housing, also known as sober homes. In developing program, be cognizant of sober homes as an important piece of the affordable housing.	$500,000

Focus Group Recommendations	Funding Estimate
Recommend initiatives to enhance the capabilities of clinicians to identify and treat patients with substance abuse issues or who are at risk for developing substance abuse issues. Such initiatives could include: • Enhancing the content of required CME course to include more on opiate addiction, including paths to addiction involving prescription drugs, and best practices on prescribing buprenorphine • Requiring all providers to complete the training by a specified date, and not wait until the time of license renewal. • Require Massachusetts medical schools and residency programs, nursing schools, and physician assistant training programs to increase training of physicians on pain management, including non-pharmaceutical management of pain, the use of pain medication and addiction medicine, training in SBIRT, screening pregnant women, safely weaning patients from pain medication, how to provide patient education and reduction in stigma Following training, provide support to providers of addiction services that are targeted at removing barriers to patient's receiving needed care.	Some funds may be needed to provide post training support
Review and develop regulations to promote the safe prescribing and dispensing of controlled substances.	N/A
Develop DOI and DPH regulations that require insurers to increase the medical management of opiate prescriptions by insurers (quantity limits, prior authorization, etc.), create physician prescription profiles, and use profiling information in making re-credentialing decisions.	N/A
Direct MassHealth and DPH to develop a pilot payment reform initiative based on an episodes of care model	$100,000 to develop the pilot (additional money needed to fund the pilot)

Focus Group Recommendations	Funding Estimate
DPH and the DOI, in consultation with the Health Policy Commission to conduct a comprehensive review of medical necessity criteria and utilization review guidelines for opiate abuse and addiction treatment developed by carriers pursuant to sections 12 and 16 of chapter 1760. The agencies to consult with clinical experts to develop minimum criteria for opiate abuse and addiction treatment services that will be considered medically necessary for all plans. DPH and DOI, in consultation with public and private payers to address barriers to accessing medication-assisted treatment.	$250,000
Provide PMP data downloads to insurers to enable them to obtain a complete prescribing profile of patients and physicians. Provide access to PMP data by health plan physicians and pharmacists to enable insurers to review patient-specific prescription histories.	$200,000
Hold a series of facilitated stakeholder forums to review and discuss evidence based research regarding most effective treatment approaches. Aim to develop a shared understanding of best treatment and care management practices and how persons seeking care can have that care covered by a combination of insurance and BSAS-funded services. Participants would include providers, insurers, state officials, first responders, consumers and family members. The sessions would be professional facilitated to assure that all parties are heard and the consensus goals are achieved.	$10,000 per session (recommend up to 10 sessions)
Develop statewide strategy for safely disposing of needles by providing locked needle disposal boxes in public areas throughout the state	N/A
Consider adoption of the Model Drug Dealer Act which allows family members to bring a civil lawsuit against a dealer if he/she sells drugs that lead to a fatal overdose.	N/A

Focus Group Recommendations	Funding Estimate
Charge Interagency Task Force on Substance Abuse and Prevention to review interagency regulatory and operational barriers to treatment. Examples of potential areas of review include: • Loss of foster care placement for a child who seeks residential treatment; • Long wait periods for insurance coverage; • Lack of drug-free shelters; • Physician reluctance to receive authority to prescribe buprenorphine due to real and/or perceived burdensome regulatory requirements.	N/A
PREVENTION	
Develop a sustained, state-wide, evidence-based public service campaign to educate youth and parents about dangers of addiction. In addition, the campaign may provide information on Massachusetts' Good Samaritan Law. Involve public figures who are role models for youth.	$1,000,000
Develop peer-to-peer support network by hiring recovering peers to: • Speak with at-risk youth and other special high risk populations • Participate in a speakers' bureau • Meet with individuals at critical transition points, such as in emergency rooms, at time of arrest, or when returning to the community	$400,000
Add five new Opioid Prevention coalitions in high need cities.	$100,000 per coalition
INTERVENTION	

Focus Group Recommendations	Funding Estimate
Develop a central navigation system for adult services that can be accessed through an 800 number. The system would maintain a real time inventory of available substance abuse services across the continuum of care. Central navigation could be utilized to identify appropriate resources by consumers and their families, first responders, schools, and providers. When contacted, intake staff would work, if appropriate, with the caller to place the person needing services in the best available setting. In addition, intake staff could direct uninsured individuals to assistance in applying for MassHealth benefits. The central navigation system should include resources available from both public and private payers and should be designed to gain efficiencies by building on existing resource programs.	$1,450,000
Pilot regional walk in centers that provide: • Assessment • Liaison with central intake to place person in best treatment setting • Daily open clinically run group sessions • Emergency 1 on 1 counseling The walk in centers would also coordinate with Central Navigation as needed. Where possible, leverage existing organizations to pilot walk-in center model.	$600,000 per site cost
Establish a state-wide, community-based care management service that supports consumers and families receiving services: • At times of transitions of care from one type of service provide to another (e.g., initial entry into the system, from detox to CSS, to TSS to residential programs, from jails/prisons to community) • When the person is living and receiving services in the community Care management services would be provided by both clinical care managers and peer navigators, working collaboratively on shared caseloads. The Care Management program should be designed to gain efficiencies by building on existing programs offered by other state agencies and insurers.	$10,000,000 (estimated based on cost of providing to Section 35 clients - $1M for 5,000 clients; assuming would interact with 50,000 clients)

Focus Group Recommendations	Funding Estimate
To increase early identification, develop and implement a widespread education and training program to allow nurses and other professionals to identify high risk individuals at as many interaction points as possible (e.g., schools, courts, MH clinics, CBHI providers). The training should include both information on how to identify potential opioid abuse and information on where and how to refer individuals and their families for assistance and/or treatment services.	$25,000 per regional training
Work with colleges to develop capacity to identify and treat at risk college students	$150,000
Share funding with cities and towns on a regional basis to fund at least one substance abuse counselor in each District Attorney's office to work with courts, first responders, and community and school organizations.	$40,000 per site
Expand the number of Drug Courts throughout the Commonwealth	$350,000 per court
Provide education, training and resource materials to First Responders to allow for them to provide hands on assistance in directing individuals to treatment, as appropriate.	TBD
TREATMENT	
Fund injectable naltrexone (Vivitrol), which reduces opioid cravings, for incarcerated people (in prisons and jails) who are returning citizens and work with public and private payers to reduce barriers to benefit coverage for medication-assisted treatments. Provide transition of care services to assure that returning citizens are linked up to appropriate services and MassHealth care management support services to assure on-going treatment and patient engagement.	$147,000 per site
Establish Opiate Treatment Programs in Correctional Facilities (e.g., jails and prisons)	$75,000 per site

Focus Group Recommendations	Funding Estimate
Enhance the DOC's continuum of care and improve post release linkages to community based services through the implementation of the following initiatives: • Improve the identification of offenders with substance abuse issues by adding a substance abuse specific assessment instrument at the Department's reception centers • Increase the availability of treatment for offenders with substance abuse issues by adding basic substance abuse education and motivational enhancement programs at designated DOC institutions. • Enhance the residential substance abuse treatment program by adding a graduate maintenance, aftercare and post release mentoring component • Increase salaries of substance abuse treatment staff to maximize the recruitment and retention of the most competent staff	$2,000,000
Selectively add residential beds for particularly vulnerable populations who are underserved, including women, single parents with children and Hispanics, and 18-25 year olds.	$504,000 per contract for adults $735,000 per contract for transitional age youth and young adults
Work with MassHealth and commercial insurers to increase capacity for outpatient services including, for example: • Intensive Outpatient Programs • Group visits at walk-in centers • Family-based programs • Youth programs, which will allow for diversion from DYS	N/A
Add medication-assisted treatment service sites, including expanding treatment at CHCs, to the extent possible under the law.	$100,000 per OBOT or injectable naltrexone; $300,000 per Methadone site
Add one detoxification program in Franklin County	$550,000
Add one CSS program, location to be determined	$350,000

Focus Group Recommendations	Funding Estimate
Provide technical assistance to pharmacies to encourage them to stock and dispense Naloxone Provide technical assistance and training to assure availability of Naloxone through first responders. Provide funding to assist first responders in replacing Naloxone supply.	N/A (TBD)
RECOVERY SUPPORTS	
Expand the number of recovery support centers (RSC) and expand access to RSC on nights and weekends.	$350,00 per new site (assuming expanded hours) $50,000 for current sites to expand hours
Provide drug free housing and programing 24/7	TBD
Add an additional recovery high school in Worcester County.	$500,000 per high school
Add support groups, such as Learn to Cope, in areas of state with need and no existing program.	$300,000

Appendix V- Focus Group Meetings

Focus Groups	
Organization	**Meeting Dates**
Active Consumers	May 14 (10:00AM) at Project AHOPE
Consumers in Recovery	April 17 (11:00AM) MOAR meeting (Lawrence) May 7 (10:00AM) at StepRox (Roxbury)
Family Members (Learn to Cope)	May 8 (7:00PM), Quincy
Health Insurers	April 23 (10:00AM) Attended meeting at MAHP April 25 (1:00PM) Attended BCBSMA meeting
Colleges	April 24 (1:00PM) Conducted call with Diane Fedorchak from UMASS Amherst
Mass Medical Society/Addictive Physicians	May 12 (6:00PM) at MMS offices in Waltham
ER doctors	April 24 (10:00AM) Call held with ER doctors from Sturdy Hospital
MA Hospital Association	April 30 Call held with MHA staff
Pharmacists	April 23 (1:00PM) Meeting held
BH providers	April 28 (12:30PM) Meeting held at Framingham Public Library
Judiciary	April 28 (10:00AM) Phone meeting held with Judges Carey and Minehan
Law Enforcement – Police/Fire	April 25 (10:00AM) Meeting held with firefighters in North Attleboro. May 12 Meeting held with police chiefs in Norwood
Interagency Workgroup on Youth (Jen Tracey)	May 14 (1:00PM)
Prevention Coalitions	May 12
Full Interagency Council	April 16 (9:45AM)
BSAS Consumer Advisory Council	April 16 (5:30PM)

Exhibit Q

PROP
PHYSICIANS FOR RESPONSIBLE OPIOID PRESCRIBING

2012 JUL 25 P 1:48

July 25, 2012

Dockets Management Branch
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville MD 20852

The undersigned clinicians, researchers and health officials from fields that include Pain, Addiction, Primary Care, Internal Medicine, Anesthesiology, Psychiatry, Neurology, Emergency Medicine, Toxicology, Rheumatology, and Pubic Health submit this petition under Section 21 CFR 10.20 and 21 CFR 10.30 and other pertinent sections of the Federal Food, Drug and Cosmetic Act or any other statutory provision which authority has been delegated to the FDA Commissioner to regulate labeling of opioid analgesics.

At present, the FDA-approved indication for nearly all instant-release opioid analgesics is "moderate to severe pain". For extended-release opioids, the indication is for "moderate to severe pain when a continuous, around-the clock analgesic is needed for an extended period of time." These overly broad indications imply a determination by FDA that they are safe and effective for long-term use. As outlined below, an increasing body of medical literature suggests that long-term use of opioids may be neither safe nor effective for many patients, especially when prescribed in high doses.

Unfortunately, many clinicians are under the false impression that chronic opioid therapy (COT) is an evidence-based treatment for chronic non-cancer pain (CNCP) and that dose-related toxicities can be avoided by slow upward titration. These misperceptions lead to over-prescribing and high dose prescribing. By implementing the label changes proposed in this petition, FDA has an opportunity to reduce harm caused to chronic pain patients as well as societal harm caused by diversion of prescribed opioids. In addition, FDA will be able to reinforce adherence to dosing limits that have been recommended by the United States Centers for Disease Control[1], the state of Washington[2] and the New York City Department of Health and Mental Hygiene[3].

The Federal Food, Drug and Cosmetic Act established that a drug intended to treat a condition must be proven safe and effective for use as labeled.[4]The current label on opioid analgesics does not comply with this law. By taking the actions requested in this petition, FDA will be able to exercise its regulatory responsibility over opioid manufacturers by prohibiting the marketing of opioids for conditions in which their use has not been proven safe and effective.

FDA-2012-P-0818

CP

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2012-6360

SPECIFIC ACTIONS REQUESTED FOR CHANGES TO OPIOID ANALGESIC LABELS:

1. Strike the term "moderate" from the indication for non-cancer pain.
2. Add a maximum daily dose, equivalent to 100 milligrams of morphine for non-cancer pain.
3. Add a maximum duration of 90-days for continuous (daily) use for non-cancer pain.

STATEMENTS OF SCIENTIFIC BASIS FOR PETITION:

1. Over the past decade, a four-fold increase in prescribing of opioid analgesics has been associated with a four-fold increase in opioid related overdose deaths and a six-fold increase in individuals seeking treatment for addiction to opioid analgesics.[5]

2. Prescribing of opioids increased over the past 15 years in response to a campaign that minimized risks of long-term use for CNCP and exaggerated benefits.[6,7,8]

3. Long-term safety and effectiveness of managing CNCP with opioids has not been established.[9]

4. Recent surveys of CNCP patients receiving COT have shown that many continue to experience significant chronic pain and dysfunction.[10,11]

5. Recent surveys using DSM criteria found high rates of addiction in CNCP patients receiving COT.[12,13]

6. A large sample of medical and pharmacy claims records found that two-thirds of patients who took opioids on a daily basis for 90 days were still taking opioids five years later.[14]

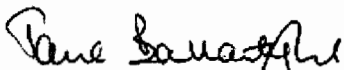
7. Patients with mental health and substance abuse co-morbidities are more likely to receive COT than patients who lack these risk factors, a phenomenon referred to as *adverse selection.*[15]

8. Three large observational studies published in 2010 and 2011 found dose-related overdose risk in CNCP patients on COT.[16,17,18]

9. COT at high doses is associated with increased risk of overdose death[18], emergency room visits[19] and fractures in the elderly[20].

There is no environmental impact associated with this Citizen's Petition and we wish to be excluded under 21 CFR Sec. 25.24.

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petition which are unfavorable to the petition (21 CFR Sec.10.30b).



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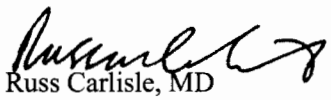

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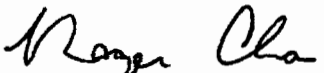

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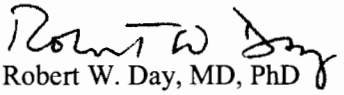

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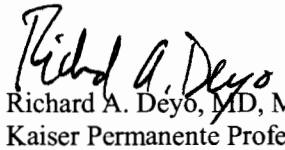

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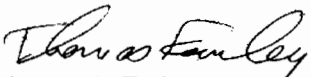

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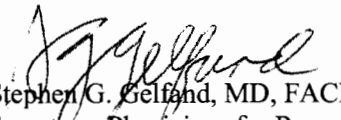

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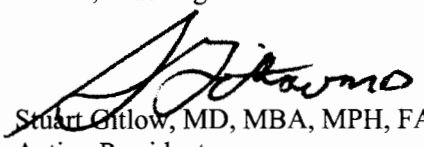

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9

28

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519

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