Medication Treatment and Opioid Use Disorder

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Disclosures

• I have no disclosures or commercial interests to report
DRUG OVERDOSES NOW TAKE MORE LIVES EVERY YEAR THAN TRAFFIC ACCIDENTS

PRESIDENT OBAMA’S BUDGET CALLS FOR NEW $1.1 BILLION INVESTMENT TO EXPAND TREATMENT

Deaths per year

Drug Overdoses

Traffic Accidents

SOURCE: Centers for Disease Control and Prevention, National Center for Health Statistics (NCHS). Multiple Cause of Death 1999-2014 on CDC WONDER Online Database, released 2015.
Right now in Massachusetts, 5 people die every day are from drug overdose.

Number of drug overdose deaths has surpassed number of deaths at height of US AIDS epidemic.
Fentanyl present in 66% of overdose deaths

Opioid-related deaths in Massachusetts increased more than 350% from 2000 to 2015.
In MA 76% of opioid overdose deaths occurred in people under 50 years of age

In 2015, ~2/3 of people who died from opioids were younger than 45

Sent letter to over 2.3 million health care practitioners and public health leaders to seek help for the prescription opioid crisis. Calling for:

1. Education to treat pain safely and effectively
2. Screening for opioid use disorder & to provide/connect patients with tx
3. Viewing SUDs as chronic illness, *not moral failing*
“……we need to recognize that addiction is a disease. If we treat addiction like a crime then we're doing something that’s ……ineffective.

…. taking parity seriously so that mental health issues and addiction issues are treated as a disease in the same way that if somebody came in with a serious medical illness that it’s treated”
Opioid Initiative: HHS Actions to Address Opioid-Drug Related Overdoses and Death

• Announced March 26, 2015

• Initiative focuses on three priority areas:
  1. Improving opioid prescribing practices
     a. Improve clinical decision-making; reduce inappropriate prescribing
     b. Enhance prescription drug monitoring (PDMPs)
     c. Support data sharing to facilitate appropriate prescribing
  2. Expanding use of Naloxone to reduce overdose deaths
     a. Accelerate development of new naloxone formulations
     b. Disseminate best practice for naloxone distribution
     c. Expand utilization of naloxone
  3. Expanding use of Medication-Assisted Treatment (MAT)
     a. Support research on effective use and dissemination of MAT
     b. Increase access to clinically effective MAT strategies
The Treatment Gap

Only 1 in 10 people with a SUD receive any kind of specialty treatment

Heroin Overdose Death and OAT

Opioid agonist treatment following nonfatal opioid overdose

- 7,634 individuals who survived ambulance encounter for opioid-related overdose in 2013-2014
- Over median follow-up of 10 months 149 (2.0%) had fatal opioid overdose
  - Represents 6.8% of all fatal opioid overdoses
- ~ 5% of individuals received OAT each month
- 12 month cumulative incidence of fatal opioid overdose by OAT as time varying covariate:
  - 2.3% if NOT engaged in OAT
  - 1.1% if engaged in OAT
Addiction: Is A Disease....
Greater than 1 in 7: Substance Use Disorder

Evaluation of A Hypothetical Treatment

Just Like Hypertension, Addiction Is A Chronic Disease That Requires Continued Care—but the RESULTS are usually measured AFTER THE TREATMENT CONDITION HAS BEEN WITHDRAWN!

Alcohol misuse, illicit drug use, misuse of medications, and SUDs estimated to cost US >$400 billion annually due to:

- Lost workplace productivity
- Health care expenses
- Law enforcement/criminal justice costs
- Losses from motor vehicle crashes


Opioid Detoxification Outcomes

• Low rates of retention in treatment
• High rates of relapse post-treatment
  • < 50% abstinent at 6 months
  • < 15% abstinent at 12 months
• Increased rates of overdose due to decreased tolerance

O’Connor PG JAMA 2005
Mattick RP, Hall WD. Lancet 1996
Stimmel B et al. JAMA 1977
Reasons for Relapse

- **Protracted abstinence syndrome**
  - Secondary to derangement of endogenous opioid receptor system
- **Symptoms**
  - Generalized malaise, fatigue, insomnia
  - Poor tolerance to stress and pain
  - Opioid craving
- **Conditioned cues (triggers)**
- **Priming with small dose of drug**
What is the **gold standard** of care for people with Opioid Use Disorder?
Medications for addiction (i.e., methadone, buprenorphine and naltrexone) have...

- Demonstrated superiority over behavioral interventions
- Buprenorphine and methadone (to a lesser degree naltrexone) been shown to:
  - Reduce overdose rates
  - Increase retention in care
  - Reduce recidivism in incarcerated populations
  - Improve quality of life
  - Decrease depressive symptoms

## Evidence based Treatment: Opioid Use Disorder

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Methadone</th>
<th>Buprenorphine</th>
<th>Naltrexone</th>
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<tbody>
<tr>
<td><strong>Brand names</strong></td>
<td>Dolophine, Methadose</td>
<td>Subutex, Suboxone, Zubssolv</td>
<td>Depade, ReVia, Vivitrol</td>
</tr>
<tr>
<td><strong>Class</strong></td>
<td>Agonist (fully activates opioid receptors)</td>
<td>Partial agonist (activates opioid receptors but produces a diminished response even with full occupancy)</td>
<td>Antagonist (blocks the opioid receptors and interferes with the rewarding and analgesic effects of opioids)</td>
</tr>
<tr>
<td><strong>Use and effects</strong></td>
<td>Taken once per day orally to reduce opioid cravings and withdrawal symptoms</td>
<td>Taken orally or sublingually (usually once a day) to relieve opioid cravings and withdrawal symptoms</td>
<td>Taken orally or by injection to diminish the reinforcing effects of opioids (potentially extinguishing the association between conditioned stimuli and opioid use)</td>
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<tr>
<td><strong>Advantages</strong></td>
<td>High strength and efficacy as long as oral dosing (which slows brain uptake and reduces euphoria) is adhered to; excellent option for patients who have no response to other medications</td>
<td>Eligible to be prescribed by certified physicians, which eliminates the need to visit specialized treatment clinics and thus widens availability</td>
<td>Not addictive or sedating and does not result in physical dependence; a recently approved depot injection formulation, Vivitrol, eliminates need for daily dosing</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>Mostly available through approved outpatient treatment programs, which patients must visit daily</td>
<td>Subutex has measurable abuse liability; Suboxone diminishes this risk by including naloxone, an antagonist that induces withdrawal if the drug is injected</td>
<td>Poor patient compliance (but Vivitrol should improve compliance); initiation requires attaining prolonged (e.g., 7-day) abstinence, during which withdrawal, relapse, and early dropout may occur</td>
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Opioid Agonist Therapy (OAT)

- Normal
- Withdrawal
- Acute use
- Chronic use
- Tolerance and Physical Dependence

Euphoria

OAT
Medications for Opioid Use Disorders

- **Buprenorphine** – partial agonist, relieves cravings without “high” or dangerous side effects. Prescribed in office based settings.
  - **Suboxone** – combines buprenorphine with naloxone (antagonist) to ward off attempts to get high by injecting. If injected, the naloxone would induce withdrawal symptoms.
  - **Probuphine** – implant with continuous delivery for 6 months

- **Naltrexone** – antagonist, not addictive or sedating. Vivitrol is injectable long acting formulation, eliminating need for daily dosing. Should be used only after detox to avoid withdrawal symptoms

- **Methadone** – agonist, taken orally, reaches brain slowly, only available in approved outpatient programs, dispensed daily

https://www.drugabuse.gov/publications/research-reports/heroin/what-are-treatments-heroin-addiction
No opioid effect

Full MU Agonist:
Methadone

Partial MU Agonist:
Buprenorphine

Full MU Antagonist:
Naltrexone

• Naltrexone has the highest receptor BINDING AFFINITY, then buprenorphine, then methadone
Opioid Agonist Therapy Goals

- Alleviate physical withdrawal *(low doses)*
- “Narcotic blockade” *(higher doses)*
- Alleviate drug craving *(higher doses)*
- Normalized deranged brain changes
UMass Study Findings in Massachusetts

Studied 5,600 Mass Health Clients prescribed buprenorphine and methadone (2003-2007)

Overall Mass Health expenditures lower than for those with no treatment

Clients on Medications had significantly lower rates of relapse, hospitalizations and ED visits: no more costly than other treatments

Buprenorphine attracting younger and newer clients to treatment

73% Mortality in those not on medication

Buprenorphine and methadone maintenance markedly reduce risk of fatal overdose

In MA 2013-2014, engagement in opioid agonist treatment (OAT; i.e., buprenorphine or methadone) following nonfatal opioid-related overdose was found to be associated with a 50% decrease in risk of subsequent fatal opioid-overdose compared to those not on OAT.
Methadone Maintenance

• Evidence-based treatment using the medical model
• Includes interdisciplinary care, mandated counseling
• Includes behavioral interventions, testing
• Includes diversion control plans
Stigma and Misinformation

Truckers punch in at drug clinic before work

BIG DIG JUNKIES

HERALD EXCLUSIVE: PAGE 2

GETTING OUT: A U.S. Navy special forces helicopter carries a victim of Hurricane Katrina out of a facility in New Orleans on Wednesday. The man, who was rescued from a hole in the ground, died of injuries sustained in the storm.

KATRINA COVERAGE: PAGES 4-6, 25

Cape refugee plans on hold
Methadone Maintenance Treatment

• Increases overall survival
• Increases treatment retention
• Decreases illicit opioid use
• Decreases hepatitis and HIV seroconversion
• Decreases criminal activity
• Increases employment
• Improves birth outcomes
OUD Treatment Paradox

• >40 years of research support efficacy of methadone maintenance for OUD

• Methadone treatment programs, aka Opioid Treatment Programs (OTPs), must be certified by SAMHSA and registered by the U.S. Drug Enforcement Administration (DEA)
  • Predominantly outpatient programs that provide pharmacotherapy in combination with behavioral therapies
Dosing of Traditional Medications

• Methadone
  • The dose is increased until opioid craving, illicit opioid use, and withdrawal symptoms have abated, or, until excessive side-effects (i.e., sedation, constipation, etc.) require a reduction in dose
A New Law

Drug Addiction Treatment Act (DATA) 2000

• Amendment to the Controlled Substances Act
• Allows physician to prescribe narcotic drugs scheduled III, IV or V, FDA approved for opioid maintenance or detoxification treatment
  • Prior 10/2002 no drug existed
  • Methadone does not qualify Schedule II
Qualifying physician

• Has capacity to refer patients for appropriate counseling and ancillary services

• Year 1: Maximum 30 patients/provider

• After Year 1: May request approval to treat up to 100 patients*

*Recently amended with rule making
Waivered buprenorphine prescribers in the U.S.

Total number of prescribers: 36,714

22,954 Buprenorphine WAIVERED Physicians: 30 Patient LIMIT (67.2%)

Source: Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration. 2015.
11,186 Buprenorphine WAIVERED Physicians: 100 Patient LIMIT (32.8%)
July, 2016: HHS Rule to Increase Patient Limit to 275

- Current waiver to treat up to 100 patients, 1 year +

- Additional credentialing of board certification in addiction medicine or addiction psychiatry by ABMS, ABAM or AOA or practicing in a Qualified Practice Setting (QPS)

- Complete Request, Attest, Reaffirm Q 3 years

- SAMHSA approves or denies within 45 days
Comprehensive Addiction and Recovery Act, 2016

- Expand prevention, education
- Expand access to naloxone
- Strengthen Prescription Drug Monitoring Programs
- Expand evidence-based opioid use disorder treatment
- Expand Medication-Assisted Treatment
CARA: Authorizing NP’s and PA’s Prescribing

• Waivered to prescribe buprenorphine five year period expires 2021

• Newly waivered PAs and NPs, and physician to treat 30 patients in year one
  • May increase to 100 after one year with certain conditions

• NP and PA’s must complete 24 hours addition education with accredited, authorized providers
  • HHS secretary may waive/adjust requirements for those working in addiction

• Collaborative/supervised relationship required based on state law
  • If supervision required must be by a “qualified physician” One who could prescribe
CARA for NP’s and PA’s

• Complete 24 hours of training: Learning objectives
  • Proposed Learning Objectives for the Nurse Practitioner and Physician Assistant Waiver Training.pdf

• Supervised by or work in collaboration with a qualifying physician if required within state

• Approved through 2021, then re-evaluate
Office-Based Opioid Treatment
Buprenorphine

• Studies (RCT) show buprenorphine more effective than placebo and equally effective to moderate doses (80 mg) of methadone on primary outcomes of:
  • Abstinence from illicit opioid use
  • Retention in treatment
  • Decreased opioid craving

Johnson et al. NEJM 2000
Fudala PJ et al. NEJM 2003
Partial Agonist: Ceiling Effect

- **Full Agonist**: Maximum opioid agonist effect is never achieved.
- **Partial Agonist** (Buprenorphine): Increasing activity at increased doses.
- **Full Antagonist**: Opioid effect, sedation, respiratory depression.
Buprenorphine Efficacy

75% Retention
75% UTS negative in treatment
20% mortality in the placebo group

Opioid Agonist Therapy

- Methadone or Buprenorphine (Subutex)
- Reduces risk for overdose death by 70%
- Not recommended to wean off in pregnancy
- Stable dose of opioid for the fetus
- Decreased risk for fetal distress, preterm birth, growth restriction, and pregnancy loss
Neonatal Abstinence Syndrome

“Drug addicted newborns”

“Substance exposed newborns”
Feeding Method and NAS

Data from Tufts Medical Center & Affiliates and Eastern Maine Medical Center, PAS 2014
Extended Abstinence is Predictive of Sustained Recovery

After 5 years – if you are sober, you probably will stay that way.

It takes a year of abstinence before less than half relapse.

Dennis et al, Eval Rev, 2007

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<tr>
<th>Duration of Abstinence at Year 7</th>
<th>% Sustaining Abstinence through Year 8</th>
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<tbody>
<tr>
<td>1 to 12 months (n=157, OR=1.0)</td>
<td>0%</td>
</tr>
<tr>
<td>1 to 3 years (n=138, OR=3.4)</td>
<td>10%</td>
</tr>
<tr>
<td>3 to 5 years (n=59, OR=11.2)</td>
<td>20%</td>
</tr>
<tr>
<td>5+ years (n=96, OR=11.2)</td>
<td>86%</td>
</tr>
</tbody>
</table>
Present State: Opened Pandora’s Box

↓ Opioid analgesic prescribing
(i.e., person can no longer access drug of choice or treat pain through medical system)

✗ Medication Maintenance not rapidly expanded to meet demand for addiction treatment
(not possible due to resource constraints and fragmented addiction treatment system)

⬆ People driven to black market
many began to purchase drugs on street (often transitioning to heroin which has a much cheaper street value)
“Our lives begin to end the day we become silent about things that matter”

Martin Luther King Jr.
PCSS-MAT Mentoring Program

• PCSS-MAT Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid addiction.

• PCSS-MAT Mentors comprise a national network of trained providers with expertise in medication-assisted treatment, addictions and clinical education.

• Our 3-tiered mentoring approach allows every mentor/mentee relationship to be unique and catered to the specific needs of both parties.

• The mentoring program is available, at no cost to providers.

For more information on requesting or becoming a mentor visit: pcssmat.org/mentoring
PCSS-MAT is a collaborative effort led by American Academy of Addiction Psychiatry (AAAP) in partnership with: American College of Emergency Physicians (ACEP); American College of Physicians (ACP); American Osteopathic Academy of Addiction Medicine (AOAAM); American Psychiatric Association (APA); American Society of Addiction Medicine (ASAM); Association for Medical Education and Research in Substance Abuse (AMERSA); and the National Association of Drug Court Professionals (NADCP).

For More Information: www.pcssmat.org

Twitter: @PCSSProjects

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Discussion and Questions

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