Pharmacotherapy for Opioid Use Disorder

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Epidemic of opioid overdose deaths

Opioid-Related Deaths, Unintentional/Undetermined
Massachusetts: 2000-2014

Number of deaths

- 338 (2000)
- 468 (2001)
- 429 (2002)
- 549 (2003)
- 525 (2005)
- 615 (2006)
- 614 (2007)
- 561 (2008)
- 599 (2009)
- 526 (2010)
- 603 (2011)
- 668 (2012)
- 939 (2013)
- 1,047 (2014)
- 1,256 (2014)
129 x higher risk OD death after release
Figure. Mortality rate, by week since release, for overdose and all other (nonoverdose) causes of death.
Addiction & Incarceration

• 48% of federal prisoners incarcerated for drug offenses

• 85% substance-involved
  – 1.5 million meet DSM criteria for substance use disorder
  – 458,000 history of SUD, under the influence, or crime committed to obtain money to buy drugs

• In 2006, alcohol and other drugs were involved in:
  – 78% of violent crimes
  – 83% of property crimes
  – 77% of public order, immigration or weapons offenses and probation/parole violations

Mumola, CJ. US Dept. of Justice, 2006; Bureau of Justice Statistics, 2011
SUD Treatment Within Corrections

• Among state prisoners with a drug use disorder in 2004:
  – 0.8% received detoxification services
  – 0.3% received maintenance pharmacotherapy
  – 6.5% received counseling by a professional
  – 9.5% received treatment in a residential facility

Risk factors for overdose

• Reduced tolerance
• Mixing substances
• Using alone
• Lack of treatment

  – Treatment of opioid use disorder with opioid agonist medications reduces opioid overdose risk by almost 90%

United Nations Office on Drugs and Crime
https://www.unodc.org/docs/treatment/overdose.pdf
Addiction

“The question is frequently asked: Why does a man become a drug addict? The answer is that he usually does not intend to. [The drug] wins by default. I tried it as a matter of curiosity... I ended up hooked. You don’t decide to be an addict. One morning you wake up sick and you’re an addict.”

William S. Burroughs, *Junky* (1953)
Natural History of Opioid Use Disorder

Withdrawal

Tolerance & Physical Dependence

Acute use

Chronic use

Euphoria

Normal

Slide courtesy of Dan Alford, 2012
“When you can stop you don't want to, and when you want to stop, you can't.”

Addiction

- Primary, chronic brain disease characterized by compulsive drug seeking and use *despite harmful consequences*

- Involves cycles of relapse and remission

- 40-60% genetic

- Without treatment addiction is progressive and can result in disability or premature death

this is your brain on drugs.
Addiction Changes Brain Structure and Function

Decreased Heart Metabolism in Coronary Artery Disease

Healthy heart | Diseased Heart

Decreased Brain Metabolism in Addiction

Healthy Brain | Diseased Brain
Visualizing Recovery

BRAIN RECOVERY WITH PROLONGED ABSTINENCE

Healthy Person

METH Abuser
1 month abstinence

METH Abuser
14 months abstinence

A Treatable Disease

Why is addiction treatment evaluated differently? Both require ongoing care

Hypertension Treatment

Addiction Treatment

Pharmacological Treatments

• Full opioid agonist: methadone
• Partial opioid agonist: buprenorphine
• Opioid antagonist: naltrexone
“What it comes down to is that we take care of the pharmacological problems, leaving the addict, and everyone else, free to turn his attention to other problems. It does not strike me as relevant whether these patients get off Methadone. Some may want to and that’s fine. What is relevant is that a treatment can be developed so that the addict can become a socially useful citizen, happy in himself and in society.”
Medication Saves Lives

HIV-related deaths

- 1984: HIV discovered
- 1986: First NRTI (Retrovir) launched
- 1988: Impact of HAART
- 1990: First PI (Invirase) launched
- 1991: First NNRTI (Viramune) launched
- 1996: First NRTI+NRTI combination (Combivir) launched
- 1998: First PI (Invirase) launched
- 2002: First PI (Fuzeon) launched
- 2004: First NRTI+NRTI+ NNRTI combination (Atripla) launched

Nature Reviews | Drug Discovery
Maryland: 50% reduction in overdose death with opioid agonist treatment

France: 79% reduction in overdose death with opioid agonist treatment
Methadone Reduces Heroin Use

**Time Using Narcotics Daily**
- 70% before treatment
- 16% 1 year after treatment

**Percentage of Heroin Use Among New Admissions**
- 97% Pretreatment
- 67% Less Than 6 Months of Treatment
- 23% Average Stay 6 Months to 4.5 Years of Treatment
- 8% Long-Term Treatment 4.5 Years or More

N = 617
Methadone Reduces HIV Infection

HIV Infection by Methadone Treatment Status at Baseline

Opioid Agonist Therapy Reduces Death

Kimber J et al. BMJ 2010;341:bmj.c3172
Other Benefits of Opioid Agonist Tx

• Reduction in the use of illicit drugs
• Reduction in criminal activity
• Reduction in needle sharing
• Reduction in HIV infection rates and transmission
• Cost-effective
• Reduction in commercial sex work
• Reduction in the number of reports of multiple sex partners
• Improvements in social health and productivity
• Improvements in health conditions
• Retention in addiction treatment
• Reduction in suicide
• Reduction in lethal overdose

Rapid Return to Injection Drug Use Following Premature Termination of Methadone Maintenance Treatment

(N = 388 Male Patients)

Poor Outcomes Without Maintenance

**Treatment group:**
- Highly significant ASI reduction
- 75% negative tox screens
- 75% retained in treatment
- No deaths

**Control group:**
- 0% retained in treatment
- **20% died**
Relapse Common Following Taper

Risk of Death 10x Higher on Waiting List

Antagonist therapy: Naltrexone
Cost Savings of Treatment

• Methadone maintenance patients health care costs 50%-62% lower than those not on MMT
• Adherence to buprenorphine associated with lower outpatient, inpatient, ED, and total healthcare costs
• Buprenorphine treatment significantly reduces total healthcare costs compared to no treatment ($13,578 vs $31,055)

The effectiveness of opioid maintenance treatment in prison settings: a systematic review

Dagmar Hedrich¹, Paula Alves¹,², Michael Farrell³, Heino Stöver⁴, Lars Møller⁵ & Soraya Mayet⁶

- 21 studies, 6 experimental, 15 observational
- Treatment during incarceration → reduced heroin use, injection, and syringe sharing during incarceration
- Pre-release treatment → increased treatment entry, retention, & reduced post-release heroin use
A randomized clinical trial of methadone maintenance for prisoners: findings at 6 months post-release

Michael S. Gordon¹, Timothy W. Kinlock¹,², Robert P. Schwartz¹,³ & Kevin E. O’Grady⁴

• Compared counseling alone to counseling + passive referral to methadone OR counseling + initiation of methadone during incarceration

• Counseling + methadone initiation significantly increased treatment retention (P = 0.0001), decreased opioid-positive toxicology (P = 0.002), and reduced days of involvement in self-reported heroin use and criminal activity
Engagement with opioid maintenance treatment and reductions in crime: a longitudinal national cohort study

Anne Bukten¹, Svetlana Skurtveit¹,², Michael Gossop³, Helge Waal¹, Per Stangeland¹, Ingrid Havnes¹,⁴ & Thomas Clausen¹

- Looked at rates of crime prior during between and after treatment with methadone
- Community population, lots of involvement with CJS
  - 3221 participants, 4222 convictions
- Methadone treatment reduced crime by more than half
- Those in continuous treatment, 2/3 reduction
• Compared buprenorphine to methadone
• Post-release treatment retention higher in buprenorphine group (48% vs. 14%, p < .001)
• Prior to release, buprenorphine patients more likely to plan to continue treatment in community (93% vs. 44%, p < .001)
• No post-release differences in self-reported relapse to illicit opioid use, self-reported re-arrests, self-reported severity of crime or re-incarceration in jail
• Limitation: low methadone dosages in trial (30 mg/day on average)
A Randomized Trial of Oral Naltrexone for Treating Opioid-Dependent Offenders

Donna M. Covello, PhD\textsuperscript{1}, James W. Cornish, MD\textsuperscript{1,2}, Kevin G. Lynch, PhD\textsuperscript{1}, Arthur I. Alterman, PhD\textsuperscript{1}, and Charles P. O'Brien, MD, PhD\textsuperscript{1,2}

- 111 individuals under correctional supervision in the community in outpatient counseling +/− naltrexone
- Only 32% NTX and 29% of controls completed 6 months of treatment
- Slightly more negative opioid tox screens in those retained on NTX
40% completed all 6 injections
Overall follow-up across sites was 66%
Study retention much better in completers
Opioid use and incarceration much lower among treatment completers
  • 4% of completers with opioid positive tox vs 44% of the non-completers
  • 50% of non-completers re-incarcerated vs 15% completers
Patient Selection

• All patients with opioid use disorder should be offered pharmacotherapy

• Choice of treatment should be based on:
  – Assessment of treatment needs
  – Prior treatment history
  – Evidence-based evaluation
  – Patient acceptance
  – Treatment availability

• Pros and cons exist for each type of treatment
  – Methadone vs buprenorphine vs naltrexone
WHO Guidelines

• “Of all the treatments, opioid agonist maintenance treatment, combined with psychosocial assistance is most effective... psychosocial services should be made available to all patients, although those who do not take up the offer should not be denied effective pharmacological treatment.”

Long-Term Outcomes

• At Month 42:
  – 32% abstinent from opioids and not on agonist therapy
  – 30% in remission on opioid agonist therapy
  – 7.5% using illicit opioids while on agonist therapy
  – 31% relapsed to opioid use not on agonist therapy

• Medical management vs MM + counseling not associated with abstinence

• Engagement in agonist therapy significantly associated with abstinence
  – 80% on treatment were abstinent at month 42

Integrating Pharmacotherapy into Drug Court

- Drug Court could be ideal setting for pharmacotherapy
  - Monitored, structured treatment, team-based care

- Considerations:
  - Clinician assessment and treatment plan
  - Ongoing monitoring and evaluation
  - Close communication with prescribing physician

- Relapse indicates need for treatment re-evaluation, not punishment
Questions?

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