Treatment of opioid use disorders

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Disclosures

• I have no financial conflicts to disclose
• I will review evidence based off-label use of medications
Outline
Outline

- Epidemiology
- Neurobiology
- Preventive efforts
- Treatment
- Longitudinal outcomes
- Conclusions
Epidemiology

NSDUH, 2014
Drug overdose deaths involving opioids by type of opioid
United States, 2000–2014

CDC, 2016
Prescription Opioids and Heroin use during the Previous Year

Comptom, 2016
Prescription Opioids and Heroin Drug Poisoning

Comptom, 2016
Opioid-Related Deaths, Unintentional/Undetermined
Massachusetts: 2000-2014

Number of deaths:

<table>
<thead>
<tr>
<th>Year</th>
<th>Confirmed</th>
<th>Estimated</th>
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<tbody>
<tr>
<td>2000</td>
<td>338</td>
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<tr>
<td>2001</td>
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<td>2002</td>
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<td>2003</td>
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<tr>
<td>2005</td>
<td>525</td>
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<tr>
<td>2006</td>
<td>615</td>
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<tr>
<td>2007</td>
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<tr>
<td>2008</td>
<td>561</td>
<td></td>
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<td>2009</td>
<td>599</td>
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<tr>
<td>2010</td>
<td>526</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>603</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>668</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>910</td>
<td>939</td>
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<tr>
<td>2014</td>
<td>1,047</td>
<td>1,256</td>
</tr>
</tbody>
</table>

Massachusetts Department of Public Health, 2015
Source Where Pain Killers Were Obtained
Age 12 or Older: 2010-2011

Note: The percentages do not add to 100 percent due to rounding.

1 The Other category includes the sources "Wrote Fake Prescription," "Stole from Doctor's Office/Clinic/Hospital/Pharmacy," and "Some Other Way."
Neurobiology
Substance use disorders (DSM-5)

- **Neuroadaptation:**
  - Tolerance
  - Withdrawal

- **Cognitive distortion:**
  - Importance of substance use
  - Subjective awareness of decrease control
  - Craving or a strong desire or urge to use

- **Behavioral dyscontrol:**
  - Obtaining, using and recovering
  - Use despite knowledge of problems
  - Using more and longer than intended
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Preventive efforts
Preventive efforts

• Education of medical and nursing students on universal precautions with controlled substances

• Prescription guidelines for practicing physicians and dentists on safe pain management

• Prescription monitoring program (PMP)

• Safe storage of opioid analgesics (locked box)

• Appropriate disposal of unused opioid analgesics

• Naloxone rescue kits available (standing orders)
Treatment
The proportion of all clients receiving methadone was 22 to 25 percent between 2006 and 2010.

The proportion of clients receiving buprenorphine was 1 percent or less from 2006 to 2008, but increased to 2 percent in 2009 and 2010.
Substance Abuse Treatment Services

1. Detoxification / stabilization units
2. Inpatient acute hospitalization
3. Nonhospital residential rehabilitation
4. Partial day hospital / intensive outpatient program (IOP)
5. Outpatient treatment / office-based
Psychosocial treatments

1. Drug Counseling
2. Cognitive Behavioral Therapy
3. Relapse prevention
4. Mindfulness
5. Contingency Management
6. Twelve Steps facilitation
7. Motivational Enhancement Therapy
8. Self-help groups
Let's expand our view.
Use of Medications
Managed withdrawal

• In-patient stabilization units
• Reduce opioid withdrawal symptoms
• Transition off daily opioid use
• Evaluate and treat comorbid medical and psychiatric problems
• Usually 4-5 days → needs follow-up
Managed withdrawal

• Methadone
• Clonidine
• Buprenorphine
Medication assisted treatment (MAT)

- Outpatient settings
- Suppress opioid withdrawal symptoms
- Suppress craving for opioids
- Stop opioid use and relapse
- Adjust daily dose to avoid sedation
Medication assisted treatment (MAT)

- Naltrexone
- Methadone
- Buprenorphine + Naloxone
Naltrexone

- **Indications**: Severe opioid use disorder
- **Mechanism**: Opiate receptor antagonist
- **Efficacy**: Oral is good in high motivated.
- **Implementation**: 50-100 mg/per day; LFT’s
- **Side Effects**: nausea, headache, anxiety, OD
- **Compliance**: Improved with naltrexone depot (IM)

(Comer, 2006; Krupitsky, 2011)
Naltrexone Depot

Krupitsky, 2011
Methadone

- **Indications:** Severe opiate use disorder
- **Mechanism:** Full opiate receptor agonist.
- **Efficacy:** 70-80% retention in OTP.
- **Implementation:** Start at 25-30mg and built-up dose until opiate free urines.
- **Side effects:** sedation
- **Interactions:** benzodiazepine – alcohol.
Methadone

- Age >18 or 2 documented failures of detox.
- One year history of severe opiate use disorder
- Exceptions:
  - Pregnancy
  - Release from prison
  - History of previous treatment.
Methadone dose: illicit opioid use

Strain, 1999
Buprenorphine

- Partial opiate receptor agonist
- Combination tablet /film 4:1 (Bup/naloxone)
- Sublingual administration
- High affinity and slow dissociation
- Office based opiate use treatment
- Death associated with IV use and with benzodiazepines
Buprenorphine, Methadone, LAAM: Opioid Urines

Mean % Negative

Study Week

All Subjects

Lo Meth

Bup

Hi Meth

LAAM

19%

49%

40%

39%

19%

Johnson, 2000
Treatment of opioid dependent youth

Woody, 2008

Detox indicates detoxification group. Error bars indicate 95% confidence intervals.

*12-Week buprenorphine-naloxone group.
Buprenorphine with Memantine for young adults

Figure 2

Mean Proportion of Opioid Use

- Placebo
- Mem 15mg
- Mem 30mg

Weeks

Gonzalez, 2015
Buprenorphine and Memantine for young adults

Figure 4

Gonzalez, 2015
Long-term outcomes
Long-term outcomes

- Reduction of mortality compared to untreated controls (Gronbladh, 1990)
- Decrease IVDU from 81% to 29% vs 82% at 1 year of those who left treatment (Ball and Ross, 1991)
- HIV seroconversion: methadone 3.5% vs active IVDU 22%
Prevalence of past month heroin use, heroin dependence and other drug use across the 11-year follow-up period

Teesson, 2015
## Comorbid disorders impact

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Odds Ratio (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Major Depression *</td>
<td>1.96 (1.50 – 2.55)</td>
</tr>
<tr>
<td>Antisocial Personality</td>
<td>1.02 (0.70 – 1.32)</td>
</tr>
<tr>
<td>Borderline Personality</td>
<td>1.16 (0.91 – 1.48)</td>
</tr>
<tr>
<td>PTSD</td>
<td>0.81 (0.63 – 1.05)</td>
</tr>
</tbody>
</table>

Teesson, 2015
# Treatment effect

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Effect Size</th>
<th>95% CI</th>
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</thead>
<tbody>
<tr>
<td>MAT</td>
<td>1.11</td>
<td>(0.90 – 1.38)</td>
</tr>
<tr>
<td>Detoxification *</td>
<td>1.52</td>
<td>(1.20 – 1.92)</td>
</tr>
<tr>
<td>Residential Rehab *</td>
<td>0.59</td>
<td>(0.46 – 0.76)</td>
</tr>
</tbody>
</table>

*Teesson, 2015*
Conclusion

- Current opioid use epidemic is responsibility of all to help reduce.
- Education and change in prescription practices are key elements in prevention.
- Reduction of diversion and appropriate disposal is important.
- Medication-assisted treatments are effective.
- There is still need to develop effective short-term treatments.