The Opioid Epidemic:
How, Where, and What Can Be Done?

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse
@NIDAnews
Overdose Death Rates

1999

2016

Analgesic & **Reward** Mechanisms of Mu Opiate Drugs (Heroin, Vicodin, Morphine)

![Brain diagram showing analgesic and reward mechanisms](image)

- ACC (pain)
- Accumbens (reward)
- Thalamus (pain)
- PAG (pain)
Decreased Levels of DA D2 Receptors in Drug Addicted Individuals

Volkow et al., PNAS 2011
Opioid Prescriptions 1991-2011

IMS’s Source Prescription Audit (SPA) & Vector One®: National (VONA)

Opioid morphine milligram equivalents (MME) dispensed fell by over 15% from 2010-2015

IMS Health, U.S. Outpatient Retail Setting
1. Over prescription of opioid medications led to misuse
2. Addiction to prescription opioids led to heroin
3. Emergence of fentanyl(s), with higher potency and greater profitability in the black market than heroin.
NIH OPIOID RESEARCH INITIATIVE

Using Research to End the Opioid Crisis

PAIN MANAGEMENT
Safe, more effective strategies

OPIOID ADDICTION TREATMENT
New and innovative medications and technologies

OVERDOSE REVERSAL
Interventions to reduce mortality and link to treatment
Safe, More Effective Strategies for Pain Management

**Biased Mu-Opioid Receptor Ligands: New Generation Of Pain Therapeutics**

**Non-Opioid Analgesics**
- Cannabinoids;
- Inflammatory mediators;
- Ion channel blockers

**Targeted Opioid Analgesics**
- With reduced potential for addiction and overdose

**Biologics**
- E.g. antibodies that bind to pain producing cytokines

**Non-pharmacological treatment**
- Neural stimulation;
- Surgical interventions;
- Meditation

Medication Assisted Treatment (MAT)

Full Agonist
(Methadone: Daily Dosing)

Partial Agonist
(Buprenorphine: 3-4X week)

Antagonist
(Naltrexone: ER 1 month)

DECREASES:
• Opioid use
• Opioid-related overdose deaths
• Criminal activity
• Infectious disease transmission

INCREASES
• Social functioning
• Retention in treatment

MAT is highly underutilized!
Relapse rates are very high (50% in 6 months)

OUD Cascade of Care in USA

Williams AR, Nunes E, Olfson M. Health Affairs Blog, 2017
Expand access to MAT

Healthcare system
Criminal Justice system

Medication development

Extended release formulations
Drug combinations
New Targets, Vaccines others
Extended Release Formulations

- **Vivitrol®**

- **PROBUPHINE®**

  *FDA approval – May 26, 2016*

**IM Injection q 4 weeks for 24 weeks**

**Median % Opioid-Negative Urines**

<table>
<thead>
<tr>
<th>Percent of Weekly Urine Tests</th>
<th>PLACEBO</th>
<th>XR-NTX</th>
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<tbody>
<tr>
<td>100%</td>
<td></td>
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<tr>
<td>80%</td>
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<td>60%</td>
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<td>40%</td>
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<tr>
<td>20%</td>
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<tr>
<td>0%</td>
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</tbody>
</table>

*Placebo: N=124
XR-NTX: N=126*

*Krupitzky et al., Lancet 2011*

Opportunities for Partnership in the Development of Longer Acting Formulations and/or Drug Combinations to Improve Treatment Compliance and Retention
Improving Treatments for Addiction:  
**Naltrexone Trial in CJ Populations**

- **Participants**: parolees/probationers with opioid addiction – all *volunteers* – received either
  - Monthly injections of extended release naltrexone for 6 months
  - Community treatment, including methadone or Suboxone (encouraged)

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**Relapse Frequency**

- **Overdoses in 78 weeks:**
  - Control: 7
  - Naltrexone: 0

*Lee et al. NEJM March 31, 2016.*
Target Selection on the Basis of the Neurocircuitry of Addiction

Targets to interfere with drug reward

Targets to reduce cue-induced drug seeking and to improve executive function

Targets to reduce stress-induced drug seeking and to improve mood

Compounds targeted to neurocircuitry could be beneficial not just to addiction but also to diseases for which such circuits are disrupted (i.e., ADHD, depression)

Diagram: Koob GF, Volkow ND. Neuropsychopharmacol Rev, 2010
Immunotherapies for Opioid Use Disorder

Hwang et al., Efficacious Vaccine against Heroin Contaminated with Fentanyl. ACS Chem. Neurosci. 2018
Expand access to MAT

Healthcare system
Criminal Justice system

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The “Massachusetts Model” of Office Based Opioid Treatment (OBOT) with Buprenorphine

Collaborative care between nurse care managers and generalist physicians

**ER Admissions per OBOT Enrollment**

- Prior 6 Months
- Future 6 Months
- Future 7-12 Months

Implementing Buprenorphine Treatment in ED

- Reduced self-reported, illicit opioid use
- Increased engagement in addiction treatment; decreased use of inpatient addiction treatment services

**Self-Reported Illicit Opioid Use in the Past 7 Days**

- Baseline
- 30 days

**Source:** Office of Data Analytics and Decision Support, Bureau of Substance Abuse Services, MA Department of Public Health. 2014.

*D’Onofrio G et al., JAMA April 28, 2015.*
Opioid Medication Therapy (OMT) In Prison

Mortality Post Release

Survival Curve During the Year Following Release (Drug-Poisoning Mortality)

OMT resulted in a 75% reduction in mortality (85% reduction in overdoses) in the first month post release

OMT unexposed
OMT exposed

Days since prison release

Statewide Overdose Deaths

OD fatalities in those who had been incarcerated in 2017 decreased by 60% compared to 2016 (5.7% vs 14.5%)

179
1/1 to 6/30 2016

157
1/1 to 6/30 2017

12.5% decrease

Marsden J et al., Addiction 2017; 112:1408-1418.

Green TC and Clarke J. JAMA Psychiatry 2018;75(4).
**PAIN**

NIH Pain Consortium Centers of Excellence in Pain Education

**Goal:**
Improve pain treatment through education

**SUD**

Goal:
Prevent SUD and improve outcomes in addiction through education of health care providers