NIH’s Efforts to Reduce the Opioid Epidemic

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@NIDAnews
Prescription Drug Misuse/Abuse is a Major Problem in the US

Current Drug Use Rates in Persons Ages 12+

- Any Illicit Drug: 27.1
- Marijuana: 22.2
- Psychotherapeutics: 6.4
- Cocaine: 1.9
- Hallucinogens: 1.2
- Inhalants: 0.5
- Heroin: 0.3

Past Year Nonmedical Use of Psychotherapeutic Drugs Persons Ages 12+

- Inhalants: 2004: 0.6, 2005: 0.3, 2006: 0.4, 2007: 0.3, 2008: 0.2, 2009: 0.3, 2010: 0.2, 2011: 0.2, 2012: 0.3

Opioid Prescriptions have started to Decrease but Opioids Fatalities are still Increasing

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

2015 Overdose Deaths:
- Any Drug: 52,404
- Any Opioid: 33,091

Opioid OD Deaths US, 2000-2015

Source: IMS Health, U.S. Outpatient Retail Setting
Heroin Price Has Decreased in Recent Years

"Retail" Price Per PureGram

- $3,500
- $3,000
- $2,500
- $2,000
- $1,500
- $1,000
- $500
- $-


Emerging Illicit Synthetic Opioids

- Increasing reports of fentanyl laced-heroin and prescription pills
- Other synthetic opioids emerging i.e., Carfentanil

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

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

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

Knowledge of Pain Pathways – New Biomarkers for Pain?

New study assess glial role in human pain

- Patients with low back pain (LBP) versus controls
  - Uses PET to detect levels of glial protein (TSPO)
  - Demonstrates role of glial activation in human pain
  - Possible biomarker
  - May suggest new treatments for chronic pain

Loggia et al., Brain 2015;138.
Limiting Abuse by Predicting Addiction

- **OPRM1** encodes for the target of opioids
- Can variants predict likelihood addiction?
- **OPRM1** variant
  - Affects receptor levels in brain
  - Associated with increased risk for addiction, overdose severity

Hancock et al., Biol Psychiatry 2015; 78.
Peciña et al., Neuropsychopharmacology 2015; 40.
User Friendly Naloxone

- Naloxone Px increased 3.5X in past year
- NARCAN® Nasal Spray is the most prescribed naloxone
- 900,000 NARCAN® Nasal Spray doses distributed since launch in 2/16

Opioid Overdose Reversal By Narcan® Nasal Spray

N=245

Avetian GE et al., Current Medial Research and Opinion, 23 May 2017.
Overdose Treatment: Saving Lives for Future Recovery

• New stronger, longer acting formulations to address more potent opioids (e.g. fentanyl)

• Stimulation devices to prevent respiratory depression

• Overdose detection and alert technologies

• Post-overdose interventions to ensure engagement in treatment

An early prototype of a device students at the University of British Columbia have created to detect drug overdoses. (THE CANADIAN PRESS/HO-Courtesy of Sampath Satti)
Medications Assisted Therapies for OUD

**Effect**

- **Agonist**
  - (Methadone: Daily Dosing)

- **Partial Agonist**
  - (Buprenorphine: 3-4X week)

- **Antagonist**
  - (Naltrexone: ER 1 month)

**Log Dose**

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

- And INCREASES
  - Social functioning
  - Retention in treatment
  - Outcomes in NAS

**MAT** is highly underutilized
Emergency Department-Initiated Buprenorphine

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

D’Onofrio G et al., JAMA April 28, 2015.

Abstinence from Illicit Opioids over 12 Weeks with Interim Buprenorphine

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)

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


*Lee et al. NEJM March 31, 2016.*
Extended Release Formulations

**PROBUPHINE®**

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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<tr>
<td>100%</td>
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<tr>
<td>0%</td>
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**Placebo: N=124**

**XR-NTX: N=126**

*Krupitzky et al., Lancet 2011*

**FDA approval – May 26, 2016**
Innovative Opioid Addiction Treatments: Fentanyl Vaccine

• 2016: First vaccine for fentanyl and fentanyl analogs reported in a mouse model

• Successfully stimulated antibody production

• Reduced fentanyl reaching the brain

• Reduced analgesia and protected against overdose

Cutting Edge Science Meeting Series
to End the Opioid Crisis

1. Medications Development for Opioid Use Disorders and for Overdose Prevention and Reversal -- June 5, 2017

2. Development of Safe, Effective, Non-Addictive Pain Treatments -- June 16, 2017

3. Understanding the Neurobiological Mechanisms of Pain -- July 7, 2017
**Education**

**PAIN**
NIH Pain Consortium Centers of Excellence in Pain Education

**SUD**

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

Goal:
Improve pain treatment through education
## Scientific Strategies for Combating the Opioid Epidemic

### Short-term Strategies

- **Overdose Prevention & Reversal**
  - Stronger opioid antagonist formulations
  - Novel medications (e.g., 5-HT1A agonists, ampakines)
  - Phrenic-nerve stimulation devices
  - Technologies to detect overdose & alert help or autoinject naloxone

- **Treatment of Opioid-Use Disorders**
  - New formulations of existing medications
  - Repurposing approved therapies (e.g., lorcaserin)
  - Novel medications targeting neurobiology (e.g., lofexidine)
  - *Vaccines and monoclonal antibodies
  - Brain-stimulation technologies

- **Treatment of Chronic Pain**
  - Opioid formulations with abuse-deterrent properties
  - MOR-biased agonists
  - Cannabinoids
  - Novel or repurposed medications targeting pathophysiology (e.g., sodium-channel blockers)
  - Monoclonal antibodies
  - Brain-stimulation technologies
  - *Gene therapies
  - *Progenitor cell therapies
  - Precision medicine
  - Biomarkers

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Adapted from Volkow & Collins, NEJM, 2017.