OPIOID UPDATE

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@NIDAnews
Overdose Death Rates

1999

2015

Designed by L. Rossen, B. Bastian & Y. Chong. SOURCE: CDC/NCHS, National Vital Statistics System
Analgesic Mechanisms of Mu Opiate Drugs (Heroin, Vicodin, Morphine)
Opioid Prescriptions 1991-2011

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

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

IMS Health, U.S. Outpatient Retail Setting
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
Biased Mu-Opioid Receptor Ligands: A Promising New Generation Of Pain Therapeutics

Biomarkers for Personalized Treatment
Imaging + Genetics → Addiction Prediction

• *OPRM1* encodes for target of opioids — and varies from person to person
  — Can variants predict likelihood of addiction?

• *OPRM1* variant
  — Affects specific receptor levels in brain
  — Associated with increased risk for addiction, overdose severity

• Highlights *precise, personalized* nature of addiction....

Hancock et al., *Biol Psychiatry* 2015; 78
Manini et al., *J Med Toxicol* 2013; 9
Estimate of Total U.S. Drug Deaths in 2016

- Total U.S. drug deaths
  - 20,000
  - 40,000
  - 60,000 deaths per year

Fentanyl-Related Deaths Surpassed Heroin or Rx Opioids in 2016

- Around 64,000 people died from drug overdoses in the U.S. in 2016
  - Peak car crash deaths (1972)
  - Peak H.I.V. deaths (1995)
  - Peak gun deaths (1993)

- Drugs involved in U.S. overdose deaths, 2000 to 2016
  - 20,100 Fentanyl and fentanyl analogues
  - 15,400 Heroin
  - 14,400 Prescription opioids
  - 10,600 Cocaine
  - 7,660 Methamphetamine
  - 3,280 Methadone

Graphs from NY Times Article based on CDC MMWR Report 2017
NALOXONE REQUIRES FAST AND EFFICIENT DELIVERY as achieved with iv injection but few know how to inject

Receptor occupancy by INTRANASAL equivalent to INTRAVENOUS Naloxone

Intranasal naloxone reaches blood as fast as Intramuscular naloxone and achieves higher levels
Medication Assisted Treatment (MAT)

Opioid Effect vs. Log Dose

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

But MAT is highly underutilized!
Relapse rates are very high!

OUD Cascade of Care in USA

Current estimates
Treatment gap
90% goal

Williams AR, Nunes E, Olfson M. 
Health Affairs Blog, 2017
New and Innovative Opioid Addiction Treatments

- Improved opioid based medications
- New non-opioid based medications
- Biologics (e.g., vaccines, antibodies)
- Non-pharmacological treatments

Extended Release Medications Improve Compliance

Probuphine

Probuphine is designed to release sustained therapeutic drug levels in patients with opioid addiction for up to six months.

% of urines negative (out of 72) for opioids across weeks 1-24

Rosenthal et al., Addiction 2013;105.

FDA approval – May 26, 2016
Target Selection on the Basis of the Neurocircuitry of Addiction

- Targets to interfere with drug reward
- Targets to reduce stress-induced drug seeking and to improve mood
- Targets to reduce cue-induced drug seeking and to improve executive function

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
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

Bremer et al, 2016; Janda and Treweek, 2012
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

Participants: parolees/probationers with opioid addiction received either
- Monthly ER naltrexone for 6 months
- Community treatment, including methadone or Suboxone (encouraged)


Treatments in Criminal Justice: Use of ER naltrexone

Comparative Effectiveness: Bup-NX vs ER Naltrexone

Lee et al. NEJM March 31, 2016.
NIH Public Private Partnership to Address Opioid Crisis

**Focus Area A:**
*Enhance the range of medication options to treat opioid use disorder and prevent/reverse overdoses.*

- Develop new formulations and combinations of medications to treat opioid use disorder and to prevent overdoses

- Develop more potent or longer lasting opioid antagonists to reverse overdoses from fentanyl or its derivatives.

- Develop and validate alternative endpoint other than abstinence that are acceptable to FDA for approval of OUD medications
NIH Public Private Partnership to Address Opioid Crisis

**Focus Area B:**

**Pain**

- Establish data sharing collaborative between industry groups
  - NIH to serve as a neutral broker
- Determine objective measures to understand, predict responses to pain
  - Biomarkers for pain – and a “Pain-ometer”
- Clinical trial network to accelerate trials on common and rare pain syndromes and to evaluate biomarkers