Innovative Research and the Opioid Epidemic: Are We Closer to Finding Solutions?

October 13, 2017
2:00 - 3:00 p.m. ET
Webinar
The Role of Research in Finding Solutions to the Opioid Epidemic

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Director
National Institute on Drug Abuse
@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

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

IMS's Source Prescription Audit (SPA) &...

IMS Health, U.S. Outpatient Retail Setting
Estimate of Total U.S. Drug Deaths in 2016

Fentanyl-Related Deaths Surpassed Heroin or Rx Opioids in 2016

Graphs from NY Times Article based on CDC MMWR Report 2017
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
Non-pharmacological treatment
Neural stimulation;
Surgical interventions;
Meditation

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

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

Women suffer more pain in many categories and are prescribed more Opioids

Rates of U.S. Adults > 18 and Older Reporting Pain, 2015

Opioid Prescriptions U.S. Retail Pharmacies, 2002-2013

Source: IMS Health, National Prescription Audit
The Changing Face of Heroin Use in the US

Deaths Involving Natural and Semi-Synthetic Opioids

Cicero TJ et al., JAMA Psychiatry 2014.

Rudd RA et al., MMWR Morb Mortal Wkly Rep 2016
Medication Assisted Treatment (MAT)

Opioid Effect

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
Extended Release Formulations

**Vivitrol®**
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>20%</td>
<td>80%</td>
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<tr>
<td>80%</td>
<td>40%</td>
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<td>40%</td>
<td>0%</td>
<td>20%</td>
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</tbody>
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Placebo: N=124
XR-NTX: N=126
Krupitzky et al., Lancet 2011

**PROBUPHINE®**

![Graph showing the percentage of opioid-negative urine tests over weeks](image)

**Opportunities for Partnership in the Development of Longer Acting Formulations and/or Drug Combinations to Improve Treatment Compliance and Retention**

Rosenthal et al., Addiction 2013:105.

FDA approval – May 26, 2016
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.*
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 (ie ADHD, depression)

Diagram: Koob GF, Volkow ND. Neuropsychopharmacol Rev, 2010
Monoclonal Antibodies and Vaccines to Treat OUD and Prevent Overdose

- Heroin vaccine validated in primate model in 2017
- First vaccine for fentanyl and fentanyl analogs reported in a mouse model in 2016
- Reduces drug reaching the brain
- Protect high-risk individuals against overdose

Goal: Improve pain treatment through education

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

NIH Pain Consortium Centers of Excellence in Pain Education

SUD

Education
Addressing The Epidemic
A Public Health Research & Practice Approach
The Public Health Issues

• Scope of the epidemic
• How we got here?
• What can we do?
• What are some research & development needs?
Scope of the Epidemic
Opioid Drug Use & Addiction
A Major Public Health Problem

• Over 2.5 million Americans have a “Substance Use Disorder” with opioid / heroin
  – 91 Overdose deaths / day
  – 1,000 Emergency Department visits / day

• Drug overdoses have risen dramatically since 1999

• Poisonings are now the leading cause of preventable death from injury (Opioids are the major factor)

• Opioids are also now a major gateway to heroin use
Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2015

- Any Opioid
- Heroin
- Natural & Semi-Synthetic Opioids
  (e.g., fentanyl, tramadol)
- Other Synthetic Opioids
- Methadone

Demographics of Use

- Older adults (aged 40 years and older) are more likely to use prescription opioids than adults aged 20 – 39.
- More women than men
- Non-Hispanic whites more likely to use than Hispanics
- There are no significant differences in use between non-Hispanic whites and non-Hispanic blacks
- 75% are in the work place
- 7 / 10 companies report an impact on the workplace (Cost $13,000 per employee)
Variability Based On Location

Some states have more opioid prescriptions per person than others.

Number of opioid prescriptions per 100 people

- 52-71
- 72-82.1
- 82.2-95
- 96-143

How Did We Get Here?
How Did We Get Here?

- Pain as the 5th vital sign
- Underappreciation of addictive potential of opioids
- Aggressive marketing by pharma
- Use of opioids for chronic pain
- Over prescribing for many pain conditions
- Prescribing amounts excessive & “just in case” prescriptions
- Pass around market & recreational use
- Illegal markets
- Cheap heroin
Sources of Prescription Opioids Among Past-Year Non-Medical Users

- Given by a friend or relative for free
- Prescribed by ≥1 physicians
- Stolen from a friend or relative
- Bought from a friend or relative
- Bought from a drug dealer or other stranger
- Other

Percent of Users

Number of Days of Past-Year Non-Medical Use

Any | 1-29 | 30-99 | 100-199 | 200-365

a Obtained from the US National Survey on Drug Use and Health, 2008 through 2011.5
b Estimate is statistically significantly different from that for highest-frequency users (200-365 days) (P<.05).
c Includes written fake prescriptions and those opioids stolen from a physician’s office, clinic, hospital, or pharmacy; purchases on the Internet; and obtained some other way.

What Can We Do?
Prevention

• Improve surveillance systems
  – Drug availability overall
  – Legal & illegal drug use
  – Morbidity & mortality from drugs
    • Single, polypharmacy & with other conditions e.g. injury, chronic diseases
  – Improve death reporting on death certificates of drugs
Prevention

- Optimize access to pharmacotherapy for pain
  - Improve provider understanding of the management of pain (short & long term)
  - Reduce inappropriate prescribing of opioids (conditions & amounts)
  - Prescribing guidelines (CDC, others)
Prevention

- Reduce access to illegal opioids & address abuse
  - Provider education, training & prescribing policies
  - Patient & Consumer education
  - Reduce availability of unused medications
  - Enhanced enforcement of illegal activity by providers, pharmacists, law enforcement & regulatory authorities
Prevention

• Reduce access to illegal opioids & address abuse
  – Prescription drug monitoring programs at the state level
  – Insurance drug assistance programs, utilization review & prior authorization programs
  – Employer engagement with workman’s compensation programs
Treatment

- Expand treatment for evidenced based substance abuse overall
  - Especially for Medication-Assisted Treatment (MAT)
- Expand access and use of naloxone
  - A antidote to reverse opioid overdose
What Are Some Research & Development Needs?
Research & Development Needs

1. FDA needs to development of a formal method to incorporate the broader public health impact of opioid abuse in future FDA approval decisions regarding opioids

2. Develop more non-opioid pain medicines for severe pain

3. Develop abuse-deterrent opioids

4. Incorporate more prevention strategies into safe opioid prescribing, including modification of the standard opioid indication statements

5. Develop more medicines for medication assisted treatment

6. Develop more therapies for opioid overdose

Adopted from National Academies of Science, Engineering & Medicine Opioid Abuse Report, 2017
APHA is a global community of public health professionals and the collective voice for the health of the public. APHA is the only organization that combines 140 years of perspective, a broad-based constituency and the ability to influence federal policy to advocate for and improve the public’s health.

- Founded – April 18, 1872
- 501C(3) & Nonpartisan
- Over 50,000 individual & affiliate members
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Jeffrey Bratberg, PharmD
Clinical Professor,
University of Rhode Island
College of Pharmacy
AACP Vital Statistics

- 142 member schools and colleges of pharmacy are centers of academic excellence, scientific research, and innovation
- 6500+ faculty
- 63000+ students
AACP Mission

“The mission of AACP is to advance pharmacy education, research, scholarship, practice and service, in partnership with members and stakeholders, to improve health for all.”
OUD Practice

- Existing Harm Reduction
  - Syringes + supplies
  - Syringe disposal
  - Lockbox
  - Drug disposal

- Emerging Harm Reduction
  - Drug testing (i.e. fentanyl strips)
  - Supervised injection facility
  - Supervised observation facility

Pharmacists Help People
Live Healthier, Better Lives
OUD Practice

- Pharmacists = Medication safety specialists
  - Non-opioid or non-pharmacologic treatments
  - Lowest opioid dose, shortest duration
  - Co-prescribe naloxone (OEND)
  - Screening/referral (i.e. SBIRT)

- Disease state management
  - Motivational interviewing
  - Buprenorphine +/- naloxone, naltrexone
  - Across spectrum of care & at care transitions

Pharmacists Help People Live Healthier, Better Lives
OUD Service

- Government Task Forces
- Association Special Interest Groups
- Health department collaborations
- Hospital teams and protocols
- Community, family, teacher, teen & provider education
- Remove access barriers / Enhance info. sharing
OUD Education

- Reduce disease and treatment stigma
- Balance supply and demand solutions
- Interprofessional education and practice
- Achieve interprofessional competencies
- Integrated didactic / experiential curricula
- Reduce disparities via public health approach
- Advocacy and leadership
OUD Research

- New medication development
  - Pain – opioids, other
  - OUD – new drugs, new formulations
- Examine prescribing behaviors
  - Opioids, combinations
  - Naloxone
  - Buprenorphine, naltrexone
OUD Research

- Education retention / best practices / stigma
- Pharmacoeconomics
- Pharmacogenomics
- Secondary school OUD education delivery
- Pharmacy-based academic detailing, surveys
- Pharmacist managed buprenorphine
- How to communicate/screen for risk/refer
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