The Epidemic of Opioid Related Deaths: Strategies to Curtail it

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• The epidemic of opioid overdose deaths

• HHS Opioid initiative
  – Improve opioid prescribing
  – Wide distribute of Naloxone antidote
  – Expand MAT for OUD
Chronic Pain in the U.S.

- Chronic pain is extremely common, debilitating, and costly
  - Affects more than 100 million Americans
- Opioids are widely used for chronic pain
  - Opioid prescriptions have increased 3-fold over the last 20 years
  - Between 5 million and 8 million Americans use opioids for chronic pain management
- Mounting evidence suggests that it may be associated with important harms
  - In 2013, there were over 16,000 deaths due to prescription opioids
  - Harms include: overdose, abuse, addiction, sedation, impaired cognitive function, depression, constipation, and nausea
All Drug and Opioid Overdose Deaths: United States, 2000–2014

In 2014:

- About 4.3 million Americans used prescription opioids for non-medical reasons in last month
- About 2.3 million Americans abuse prescription opioids or heroin
- Over 165,000 Americans died from all prescription drug overdose from 1999 to 2014; in 2014,
  - 47,055 Americans died from all prescription drugs
  - 18,893 Americans died from prescription opioid pain relievers

Leading cause of accident death in the US

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Source Data retrieved from [http://wonder.cdc.gov/mcd.html](http://wonder.cdc.gov/mcd.html) by NIDA

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HIV/AIDS epidemic and opioids epidemic

• For opioids overdose death:
  – 10,574 deaths related to heroin
  – 18,893 deaths related to prescription opioids

• In 2013, 12,963 deaths (due to any cause) of Americans with diagnosed HIV infection ever classified as AIDS, 6,955 deaths were attributed directly to HIV.

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Opioid-involved drug overdose death rate (incidence) increase by type of opioid

Natural opiates:
- Codeine
- Morphine

Semi-synthetic opioids:
- Hydrocodone
- Oxycodone
- Heroin
- Hydromorphone
- Oxymorphone
- Buprenorphine

Synthetic opioids:
- Meperidine
- Fentanyl
- Methadone

Overdose Death Rates

1999

2014

Estimated Age-adjusted Death Rate per 100,000:
- 0.2
- 2.1-4
- 4.1-6
- 8.1-8
- 8.1-10
- 10.1-12
- 12.1-14
- 14.1-16
- 16.1-18
- 18.1-20
- >20

Year 2000

Year 2014

Designed by L. Rossen, B. Bastian & Y. Chong. SOURCE: CDC/NCHS, National Vital Statistics System
Number of Opioid Prescriptions per 100 Persons by State

States with overdose death rates >20 per 100,000 PY (2014):
- West Virginia (35.5)
- Ohio (24.6)
- Kentucky (24.7)
- Oklahoma (20.3)
- Pennsylvania (21.9)
- Delaware (20.9)
- Rhode Island (23.4)
- New Hampshire (26.2)
- New Mexico (27.3)
- Utah (22.4)
Relationship Between Opioid Prescribing and Drug Overdose Death Rates

Source: Death rate, 2008, CDC/NVSS. Opioid pain reliever sales rate, 2010, DEA’s ARCOS
Strategies to Curb the Escalating Prescription Opioid Overdose Fatality
Launched by Secretary Burwell
• Focused in three areas:
  – Improve opioid prescribing
  – Increase use of naloxone to reverse opioid overdose
  – Expand use of medication assisted treatment (MAT) to treat opioid use disorder (OUD)
• The epidemic of opioid overdose deaths

• HHS Opioid initiative
  – Improve opioid prescribing
  – Wide distribute of Naloxone antidote
  – Expand MAT for OUD
Goal: Improve pain treatment through education

Goal: Prevent SUD and improve outcomes in addiction through education of health care providers
• When to initiate or continue prescription opioid
• Selection of opioid, dose, duration, follow-up and discontinuation
• Assess risks and address harms
Prescription Drug Monitoring Program (PDMP)
• The epidemic of opioid overdose deaths

• **HHS Opioid initiative**
  – Improve opioid prescribing
  – *Wide distribute of Naloxone antidote*
  – Expand MAT for OUD
Receptor Receptor Receptor

Naltrexone
Naloxone

Signal Transduction
Partial Signal
No Signal

Effects
(pain relief, drowsiness, euphoria, respiratory suppression etc.)
Naloxone needs quickly reach peak blood concentration to reverse overdose

Source: http://www.micromedexsolutions.com/

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Take Home Message

• opioid overdose is a medical emergency and that fatalities are preventable if medical assistance is adequate and timely

• Naloxone is a specific antidote to reverse opioid overdose if applied adequately and timely
Naloxone Take Home Program

• Barriers:
  – Availability of naloxone
  – User friendliness of naloxone
  – Lack of training of proper administration of naloxone
  – Fear of civil liability and criminal sanctions

• Solutions
  – Increase accessibility
  – enacted

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911 Overdose “Good Samaritan” laws

• Many of these laws allow community members to seek or administer aid (e.g. Naloxone) to overdose victims without suffering legal repercussions regarding their own status of intoxication or possession of illicit substances.
State Laws Enabling Broader Access to Naloxone

Source: Public Health Law Research - phlr.org
**Expand Access to Intranasal Naloxone**

- As of 2013, 37.5% of organizations in the United States that distribute naloxone reported providing intranasal only; an additional 11.8% provide both i.n. and i.m. (Wheeler E, 2015, MMWR).
- In 2016, NIDA funded 9 grants to study the impact of co-prescription of naloxone with opioids in preventing opioid overdose death.
- Systematic review of 22 observational studies on take-home naloxone (THN), mainly in the U.S., revealed causal relationship between THN and reduced mortality (McDonald R 2016).
- Positive reversals of overdose were reported in 21 of 22 studies (McDonald R 2016).

In November of 2015, FDA approved first intranasal naloxone_ Narcan nasal spray (4 mg naloxone HCL in 0.1 ml), comparable or better than intramuscular naloxone.
• The epidemic of opioid overdose deaths

• **HHS Opioid initiative**
  - Improve opioid prescribing
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What is Opioid Use Disorder (OUD)?

• OUD is a subgroup of Substance Use Disorder (SUD)
• OUD involves misuse or abuse of prescription opioids or illicit heroin as “a problematic pattern of opioid use leading to clinically significant impairment or distress”, 2.5 million has OUD in the US in 2013
• OUD is a chronic brain disorder and can be managed effectively with behavior and pharmacological therapies (NIDA consensus panel.)
• OUD is associated with
  – Decreased quality of life
  – Increased morbidity and mortality
Past Year Opioid Use Disorders, 2003-14

Source: SAMHSA, NSDUH 2003-2014 PUF
Recent U.S. Health Care Reform Legislation

- Mandates that benefits for SUD/OUD measure up to medical and surgical benefits
  - Affordable Care Act (2010)
  - Children’s Health Insurance Program Reauthorization Act (2009)
  - Mental Health Parity and Addiction Act (2008)
- Requires essentially all health plans to offer, by 2014:
  - Prevention,
  - Early intervention, and
  - Treatment –for the full spectrum of “substance use disorders”
SUD care traditionally was separated from the main-stream medical care.


ACA Supports a chronic care model for all diseases (e.g., diabetes, hypertension, SUD), requires outcome measures include preventive care, treatment, continuous monitoring of recovery to minimize relapse.
Diagnostic Prevalence of SUD

<table>
<thead>
<tr>
<th>Use</th>
<th>Qualify!</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Serious Use</td>
<td>&quot;Harmful Use&quot;</td>
</tr>
<tr>
<td></td>
<td>~45,000,000</td>
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<tr>
<td>In Treatment ~ 2,300,000</td>
<td>~12% more</td>
</tr>
<tr>
<td></td>
<td>Qualify!</td>
</tr>
<tr>
<td>Little/No Use</td>
<td></td>
</tr>
</tbody>
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B. Tai 2013
US Health Reform
Affordable Care Act 2010

Very Frequent Use

Expanded Role
For Specialty Care

Very Rare Use

Major NEW Role
For Primary Care

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Care of Substance Use Disorders

- Very Frequent Use
- Chronic Care Model
- Office-Based PC Treatment
- Very Rare Use
- Prevention & Early Intervention

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What are the Effective Medications for OUD?

**Methadone**: agonist, oral

Only Opioid Treatment Programs (OTP) certified by SAMHSA may dispense

**Buprenorphine**: partial agonist, buccal or sublingual

prescribed by qualified physicians (30 patients in the first year, 100/year thereafter) by SAMHSA

**Naltrexone**: opioid antagonist, oral or intramuscular sustained formulation

Do not take until opioids are completely removed from the body

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Pharmacology of OUD Pharmacotherapies

Methadone, Buprenorphine of various dosage forms and naltrexone of various dosage forms are approved by FDA for OUD.
Agonist Medications Decrease Heroin OD

Agonist Treatment Reduced Heroin OD Deaths
Baltimore, Maryland, 1995-2009

Buprenorphine Reduced Heroin OD
France 1995-1999 (75% reduction)


CTN-0030: Treatment for Prescription Opioid Addiction with Buprenorphine

Phase 1: 4 days Detox
Phase 2: 12 weeks treatment

Tapering from bup/nx led to nearly universal relapse – whether initially or after a period of substantial improvement

Weiss, R. SAMHSA-NIDA/CCTN meeting, January 31st, 2012
Improving Treatments for OUD:
Implementing Medication-Assisted Treatment

- Emergency department-initiated buprenorphine
  - Reduced self-reported, illicit opioid use
  - Increased engagement in addiction treatment; decreased use of inpatient addiction treatment services
Expand access of MAT for OUD

• “… a broad population of physicians - not just addiction specialists – could treat OUD……”

• OTP – Opioid Treatment Program

• OBOT – Office Based Opioid Treatment
  – Primary care
  – HIV clinics
  – OB/GYN
  – ED
Medical Benefit for Chronic Diseases

**Diabetes**
- Physician visits
- Clinic visits
- Home health visits
- Insulin and 4 other meds
- Glucose tests, monitors, supplies
- HbA$_{1c}$, eye, foot exams 4x/year
- Smoking cessation
- Personal care visits
- Language interpreter

**SUD/OUD**
- Physician visits
- Clinic visits
- Home health visits
- MATs
- Lab tests, monitors, supplies
- Infectious diseases, mental health screen 4x/year
- Mental health counseling
- Language interpreter
“……we need to recognize that addiction is a disease. If we treat addiction like a crime then we're doing something that’s ineffective.

…. taking parity seriously so that mental health issues and addiction issues are treated as a disease in the same way that if somebody came in with a serious medical illness that it’s treated”
Thank you!!
What are the Barriers for delivering MAT?

<table>
<thead>
<tr>
<th>Barriers to Buprenorphine Prescribing</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insufficient nursing support</td>
<td>20%</td>
</tr>
<tr>
<td>Insufficient office support</td>
<td>19%</td>
</tr>
<tr>
<td>Payment issues</td>
<td>17%</td>
</tr>
<tr>
<td>Lack of institutional support</td>
<td>16%</td>
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<tr>
<td>Insufficient staff knowledge</td>
<td>12%</td>
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<tr>
<td>Pharmacy issues</td>
<td>8%</td>
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<tr>
<td>Low demand</td>
<td>7%</td>
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<tr>
<td>Office staff stigma</td>
<td>5%</td>
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<tr>
<td>Insufficient physician knowledge</td>
<td>3%</td>
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<tr>
<td>One or more barriers</td>
<td>55%</td>
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</tbody>
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References

Expand Access to Naloxone

• Life-saving and non-addictive drug (antagonist of opioid receptors) that can reverse the effects of an opioid overdose when administered in time.
• Intravenous and intramuscular injection form of naloxone have been used to reverse opioid overdose for long time by paramedic and ER
• Traditionally dispensed through community-based naloxone programs
• Widespread prescribing in outpatient, dispensed in retail pharmacies since 2013 due to the overdose deaths epidemic (Jones CM, 2016)
• In November of 2015, FDA approved first intranasal naloxone - Narcan nasal spray (4 mg naloxone HCL in 0.1 ml), comparable or better than intramuscular naloxone.