Opioid Overdose—An American Epidemic

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Disclosures

• Dr. Moberg has nothing to disclose.
Objectives

- How we got where we are
- Where are we
- Ideas to fix the problem
Most importantly
Raise consciousness

"It's not the world that needs to change
- it's our consciousness we must raise."

~ Rasheed Ogunlaru

spiritualanalog.com
It all began with opium

Papaver somniferum
Opium

12%

3%
Ancient history

The Goddess Ninshubur
prior to 2900 BCE

Sumer, 3400 BCE
*Hul gil* = joy plant

Genie with a poppy
Modern history

December 31, 1600 East India Company
1601 1st four ships sent to India to open up opium trade

Grew opium in Bengal (contributed to famine of 1770) and auctioned it in Calcutta with understanding it would be smuggled into China.

1838 Seizure of opium shipment
1839-1842: First Opium War
1856-1860: Second Opium War
More history

• Friedrich Sertturner isolated morphine in 1805—thought to cure opium addiction
Another step forward?

C. Adler Wright
1874
England

Felix Hoffman
1897
Germany
The law of (2) unintended consequences
The law of (2) unintended consequences

MORPHINE

DIACETYL-MORPHINE (1898)

CODEINE
Heroin

Illegal: 1924 (by Congress)

Heros
Greek

Heroisch
German
China White
Cold water soluble

Afghanistan brown heroin
Requires acidification for solubility
Heat stable

Colombian heroin
Cold water soluble

Black Tar
Hot water soluble
Heat stable
“simple”
Federal regulatory theme

Increased restrictions on physicians
Regulatory history

Webb unconstitutional—1925

technicality
A shift in perspective

1986

Portenoy and Foley. Pain. 25:171-186
Consequences

• Non-cancer patients are candidates for opioids for chronic pain.
• Aggressive campaign
  – Low rate of addiction (1%)
  – Overdoses extremely rare
  – Easy to discontinue
• Sales of opioids—$9 billion per year
• Federation of State Medical Boards suggested all medical boards discipline physicians who undertreat pain (1998)*
• American Pain Foundation and American Pain Society→ 5th vital sign (1999 and 2001)

Wall Street Journal, December 17, 2012
To the Editor:
Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients, Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

Jane Porter
Hershel Jick, M.D.
Boston Collaborative Drug Surveillance Program Boston University Medical Center, Waltham, MA 02154

NEJM. 1980. 302:123
"Did I teach about pain management, specifically about opioid therapy, in a way that reflects misinformation? Well, against the standards of 2012, I guess I did," Dr. Portenoy said in an interview with The Wall Street Journal. "We didn't know then what we know now."

"I gave innumerable lectures in the late 1980s and '90s about addiction that weren't true," Dr. Portenoy said in a 2010 videotaped interview with a fellow doctor.
A CONFLUENCE OF FACTORS

PAIN AS THE FIFTH VITAL SIGN
VA 1999
TJC 2001
The Joint Commission published a guide sponsored by Purdue Pharma. "Some clinicians have inaccurate and exaggerated concerns" about addiction, tolerance and risk of death, the guide said. "This attitude prevails despite the fact there is no evidence that addiction is a significant issue when persons are given opioids for pain control."

WSJ, December 17, 2012
Is it even right?

Mularski et al., 2006
Measuring Pain as the Fifth Vital Sign Does Not Improve Quality of Pain Management
J Gen Int Med
21: 607-612
AN EXPLOSION OF OPIOIDS

A CONFLUENCE OF FACTORS

AN EXPLOSION OF OPIOIDS
ESPECIALLY LONG ACTING
April 2001
The Oxycontin® story

• 1917—Oxycodone begun to be used clinically (US market 1939)
• 1995—FDA approves extended release oxycodone (Oxycontin®)
• 2007—Federal lawsuit*
• 2010—New Oxycontin® formulation introduced
• 2013—FDA forbids generics

$600 million in fines and other payments by company; $34.5 million by three executives for criminal charges (criminal and civil penalties)
“OxyContin is a powerful, long acting narcotic that provides relief of serious pain for up to 12 hours. Initially, Purdue Pharma contended that OxyContin, because of its time-release formulation, posed a lower threat of abuse and addiction to patients than do traditional, shorter-acting painkillers like Percocet or Vicodin.

“That claim became the linchpin of the most aggressive marketing campaign ever undertaken by a pharmaceutical company for a narcotic painkiller...

“Between 1995 and 2001 OxyContin produced $2.8 billion in revenue.

FDA bans generic version of OxyContin; patent protection until 2025

Reuters, April 17, 2013

Important lessons

• A misplaced reward (patent protection until 2025?)
• An unintended consequence
• Opioid overdose
The unintended consequence
NEJM July 12, 2012 (103 patients)

• Preference for old version was unanimous
• Preference for Oxycontin® decreased by 36%
• Use of other opioids increased
  – 20% to 32% (hydrocodone and high dose fentanyl)
  – Heroin use doubled
• 24% found a way to defeat the safety measures
• 66% switched (heroin most popular)
Do we really need another one?

Zohydro®

Scientific panel of FDA voted 11-2 against, December 2012

FDA approved October 2013

Marketed March 2014

IM naltrexone
A CONFLUENCE OF FACTORS

MANAGED CARE

PRIMARY CARE REIMBURSEMENT DECLINES
ADDITION TREATMENT REIMBURSEMENT DECLINES AND
MICROMANAGED
LIMITATIONS FOR PHYSICAL THERAPY, CBT, ETC.
A CONFLUENCE OF FACTORS

INADEQUATE TRAINING OF HEALTH CARE PROVIDERS IN PAIN AND ADDICTION

National Center on Addiction and Substance Abuse, 2012
A CONFLUENCE OF FACTORS

TMI
PARALYSIS OF ANALYSIS
Benefits to treat pain  Risk of adverse outcomes
Pain is Prevalent

Age adjusted rates of U.S. adults reporting pain in the last 3 months

Low Back: 25%
Neck: 20%
Knee: 15%
Headache: 10%
Shoulder: 7%
Finger: 5%
Hip: 2%

Pain is Increasing

Trends in pain prevalence, United States, 1999-2004

The Current State of Affairs

- >50% of regular prescription opioid users have LBP
- Factors associated with increased likelihood of opioid prescribing and adverse selection
  - Greater psychologic distress
  - Poorer health and unhealthy lifestyles
  - Use of sedative-hypnotics
  - Patients with addiction (including nicotine dependence)
- Effects on function not consistently demonstrated in randomized trials
  - Some observational studies suggest opioid use associated with poorer functional outcomes
- Opioid use in acute LBP associated with poorer functional outcomes and subsequent long-term use
- Data indicate use of opioids related in part to presence of psychosocial factors that put patients at increased use for adverse opioid-related drug events

Opioid prescribing

- Increased medical costs
- Increased disability
- Subsequent surgery
- Continued opioid use
- Lack of improvement in function or quality of life

Manchikanti, et al. 2012, Pain Physician
Hyperalgesia and Allodynia

![Graph showing Allodynia vs Hyperalgesia](image)
SO WHERE IS ALL THIS LEADING?
Disturbing statistics

- Increased prescribing resulted in 423% inflation-adjusted increase in expenditures for chronic back pain
- 1997-2007: opioid prescription increased by 700%; grams of methadone prescribed increased by over 1200%
- 2010: enough opioids sold to medicate every US adult with 5 mg hydrocodone every 4 hours for one month

Boyer, 2012
MMWR, 11/4/2011
More

• U.S. = 4.6% of World’s Population
  Uses 80% of Global Opioid Supply
  Uses 99% of world’s hydrocodone

International Narcotics Control Board Report, 2008
National Vital Statistics System
Mortality File

MMWR, January 1, 2016
The rate of overdose deaths in the U.S. involving opioids, both prescription painkillers and heroin, has surged in recent years.

National Vital Statistics System
Mortality File

MMWR, January 1, 2016 and
WSJ, May 12, 2016
The lines continue to go in the wrong direction

Rising Toll
Climbing rates of U.S. overdose deaths from opioid painkillers and heroin have pushed the total number of drug overdose deaths above those from traffic accidents.

*Includes hydrocodone, oxycodone, morphine, codeine and others
Source: Centers for Disease Control and Prevention

Mothers of Addicts Turn to New Networks, WSJ, March 30, 2016
Death rate from overdoses caused by a single prescription painkiller

Source: Substance Abuse and Mental Health Services Administration, Center for Behavioral Statistics and Quality, Drug Abuse Warning Network Medical Examiner Component, 2009.
Opioid Sales, Admissions for Opioid-Abuse Treatment, and Deaths Due to Opioid Overdose in the United States, 1999–2010.

And worse

Study: Long Acting Opioids vs. Tricyclic Antidepressants/Anticonvulsants

Ray et al, JAMA, June 14, 2016, pp 2415-2423
Details

- Retrospective cohort of Tennessee Medicaid patients—1999-2012
- Compare all cause mortality from the two groups
- The populations were matched; 22,912 in each group
- No hospice, palliative care or cancer
- Most common diagnoses: Back pain (75%), Other musculoskeletal pain (63%) and Abdominal pain (18%)
- Most common interventions
  - Morphine SR in study group
  - Gabapentin in control group
Continuing on

• Results
• All cause mortality was 1.67 times greater in the opioid group.
• The difference is attributable to out of hospital deaths not in hospital deaths
• Most common causes of death: Cardiovascular and Respiratory
THIS IS A BIGGER PROBLEM THAN ADDICTION OR OVERDOSE
First-Time Use of Specific Drugs Among Persons Age ≥ 12 (2011)

The total initiates of nonmedical Rx drug use (red bars) taken together greatly exceeds initiates of marijuana in 2010.

A Public Health Crisis

In 2008, there were 14,800 prescription painkiller deaths.4

For every 1 death there are...

- 10 treatment admissions for abuse9
- 32 emergency dept visits for misuse or abuse6
- 130 people who abuse or are dependent7
- 825 nonmedical users7

2. Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: volume 1: summary of national findings. Rockville, MD: Substance Abuse and Mental Health Services Administration, Office of Applied Studies; 2011.
So where does leave us and where do we go from here?

- A charismatic individual
- Regulatory bodies
- Medical boards
- The pharmaceutical industry
- Accrediting bodies
- The uncomfortable position of the physician
Poppy Tea
Opium Tea
This is an opioid and is addictive
Know what is on the street

DRUG OVERDOSE HEALTH ALERT: Fentanyl-Contaminated Street Norco
March 25, 2016

The Sacramento County Division of Public Health has received reports from local hospital emergency departments of at least 12 poisoning overdoses within the past 48 hours associated with ingestion of street Norco tablets that may be contaminated with fentanyl.

Deadly fentanyl-laced pills emerge in Central Florida, agents say
May 7, 2016

Oxycodone/acetaminophen
Alprazolam
LA oxycodone

Will County, Illinois
April 14, 2016
Heroin plus fentanyl
53 overdoses, 18 deaths

MMWR, 4/26/2016
Vo et al.
**Deadly Drug**

Fentanyl emerged as a major threat in 2014, sparking a sharp rise in fatal overdoses in many states, including New Hampshire.

**Fentanyl seizures reported by forensic labs in the U.S.**

<table>
<thead>
<tr>
<th>Year</th>
<th>Seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>100</td>
</tr>
<tr>
<td>2010</td>
<td>200</td>
</tr>
<tr>
<td>2011</td>
<td>300</td>
</tr>
<tr>
<td>2012</td>
<td>400</td>
</tr>
<tr>
<td>2013</td>
<td>500</td>
</tr>
<tr>
<td>2014</td>
<td>600</td>
</tr>
<tr>
<td>2015</td>
<td>700</td>
</tr>
</tbody>
</table>

**New Hampshire overdose deaths**

<table>
<thead>
<tr>
<th>Year</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>100</td>
</tr>
<tr>
<td>2012</td>
<td>200</td>
</tr>
<tr>
<td>2013</td>
<td>300</td>
</tr>
<tr>
<td>2014</td>
<td>400</td>
</tr>
<tr>
<td>2015</td>
<td>500</td>
</tr>
<tr>
<td>2016</td>
<td>600</td>
</tr>
</tbody>
</table>

*2015 figures are half-year
†Through May 2; figures may grow, due to cases still pending toxicology
Sources: Drug Enforcement Administration obtained via FOIA (seizures); New Hampshire’s Office of the Chief Medical Examiner (deaths)
U-47700—a derivative of AH-7921

Currently imported from China

Opioid
Scheduled in Ohio

AP, June 7, 2016
Know what is over the counter

Eggleston et al, 2016

Conditional risk

Peripheral μ opioid receptor agonism
Calcium channel blockade
Calmodulin inhibition
Reduced paracellular permeability
1-(4-Nitrophenylethyl)piperidylidene-2-(4-chlorophenyl)sulfonamide w-18

Developed at University of Alberta—1980s
First appeared in Europe in 2014
Police noted it in Canada—end of 2015

CBC News, Edmonton, 4/21/2016
What we know

• W-18 is a member of a series of drugs (1-32)
• Synthesized in 1981 at University of Alberta
• First detected in August 2015 in tablets that were sold as fentanyl (3 tablets)
• Discovered in a seizure of 4 kg of white powder that was 90% w-18 in December 2015
• 2016—2.5 lbs of powder discovered in possession of a man in Florida
• No relationship to JWH-018

Calgary Herald, June 1, 2016  Medscape, June 11, 2016
Washington Post, April 27, 2016
What we don’t know

- Will naloxone reverse its effects?
- Is it even an opioid?
- What is its real potency?
- 10,000 more toxic than morphine?

Calgary Herald, June 1, 2016
Canadian Press, June 12, 2016
Medscape, June 11, 2016
## Know conversions

### Reduce calculated equianalgesic dose by 25%-50%*

<table>
<thead>
<tr>
<th>Closer to 50% reduction if patient is</th>
<th>Closer to 25% reduction if patient is</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receiving a relatively high dose of current opioid regimen</td>
<td>Does not have these characteristics</td>
</tr>
<tr>
<td>Elderly or medically frail</td>
<td>Is switching to a different administration route of same drug</td>
</tr>
</tbody>
</table>

*75%-90% reduction for methadone

---

Calculate equianalgesic dose of new opioid from EDT
Consider a PPA

Reinforce expectations for appropriate & safe opioid use

- Obtain opioids from a single prescriber
- Fill opioid prescriptions at a designated pharmacy
- Safeguard opioids
  - Do not store in medicine cabinet
  - Keep locked (e.g., use a medication safe)
  - Do not share or sell medication
- Instructions for disposal when no longer needed
- Commitments to return for follow-up visits
- Comply w/ appropriate monitoring
  - E.g., random UDT & pill counts
- Frequency of prescriptions
- Enumerate behaviors that may lead to opioid discontinuation
- An exit strategy
Case: Henry

• This is a 39 year old man with history of chronic pain to the right hip s/p MVA in 2006. He has had a THR that became infected and required 2 revisions.

• He reports pain management with OxyContin 40mg BID “down from 80” and occasional diazepam.

• On addiction interview, he says “I was in the service. I have never used drugs!”
**TOXICOLOGY**

**01/23/09 0954**

**CLINICAL URINE DRUG ABUSE SCREEN**

**AMPHETAMINE**
NEUTRAL

**BARBITURATES**
NEUTRAL

**BENZODIAZEPINES GC/MS**
POSITIVE

**COCAINE**
NEGATIVE

**COCAINE GC/MS CONFIRM**

> 30 ng/mL

Cocaine performed by GC/MS as Benzoylecgonine.

**ETHANOL**
NEGATIVE

**OPIATES**

**TOTAL MORPHINE by GC/MS**
< 40000 ng/mL

**TOTAL CODEINE by GC/MS**
< 100 ng/mL

**TOTAL HYDROMORPHONE**
< 100 ng/mL

**BENZODIAZEPINES GC/MS CONFIRM**

< 40 ng/mL

Urine Nordiazepam

Nordiazepam may be present as a metabolite of chlordiazepoxide, clorazepate, diazepam, halazepam or prazepam.

Urine Oxazepam

Oxazepam may be present as a metabolite of chlordiazepoxide, clorazepate, diazepam, halazepam, prazepam or temazepam.

Urine Temazepam

< 40 ng/mL

Temazepam may be present as a metabolite of diazepam.

**CLINICAL URINE DRUG ABUSE SCREEN**

**TOTAL OXYCODONE by GC/MS**

< 100 ng/mL

**PHENCYCLIDINE**
NEGATIVE

**THC (CANNABIS)**
NEGATIVE

**CREATININE URINE RANDOM**

212 mg/dL

**ADULTERANTS**

NEGATIVE

**COMMENTS:**

ADULTERANTS TESTED FOR INCLUDE CHROMATES AND NITRITES.

01/23/09 0954
He states,

“Your lab screwed up. It’s not my urine. I’ll do another test right now.”
### TOXICOLOGY

**CASE: Henry, UDT**

<table>
<thead>
<tr>
<th>Substance</th>
<th>Screen</th>
<th>GC/MS Confirm</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMPHETAMINE</td>
<td>NEGATIVE</td>
<td><strong>POS</strong></td>
<td></td>
</tr>
<tr>
<td>BARBITURATES</td>
<td>NEGATIVE</td>
<td><strong>POS</strong></td>
<td></td>
</tr>
<tr>
<td>BENZODIAZEPINE</td>
<td>NEGATIVE</td>
<td><strong>POS</strong>&lt;sup&gt;<strong>Y</strong>&lt;/sup&gt;</td>
<td>441 ng/mL</td>
</tr>
<tr>
<td>BENZODIAZEPINES GC/MS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COCAINE GC/MS CONFIRM</td>
<td></td>
<td></td>
<td>30 ng/mL</td>
</tr>
<tr>
<td>ETHANOL</td>
<td></td>
<td><strong>POS</strong></td>
<td>&lt;40 ng/mL</td>
</tr>
<tr>
<td>BIBAZEPINES GC/MS CONFIRM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxazepam</td>
<td></td>
<td><strong>POS</strong></td>
<td>&lt;40 ng/mL</td>
</tr>
<tr>
<td>nordiazepam</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxazepam may be present as a metabolite of clordiazepoxide, clorazepate, diazepam, halazepam or prazepam.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxazepam</td>
<td></td>
<td><strong>POS</strong></td>
<td>&lt;40 ng/mL</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxazepam</td>
<td></td>
<td><strong>POS</strong></td>
<td>&lt;40 ng/mL</td>
</tr>
<tr>
<td>Temazepam</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temazepam may be present as a metabolite of diazepam.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPIATES</td>
<td></td>
<td><strong>POS</strong>&lt;sup&gt;<strong>Y</strong>&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>TOTAL MORPHINE by GC/MS</td>
<td></td>
<td><strong>POS</strong></td>
<td>&lt;100 ng/mL</td>
</tr>
<tr>
<td>TOTAL CODEINE by GC/MS</td>
<td></td>
<td><strong>POS</strong></td>
<td>&lt;100 ng/mL</td>
</tr>
<tr>
<td>TOTAL HYDROCODONE by GC/MS</td>
<td></td>
<td><strong>POS</strong></td>
<td>&lt;100 ng/mL</td>
</tr>
<tr>
<td>TOTAL HYDROMORPHINE by GC/MS</td>
<td></td>
<td><strong>POS</strong></td>
<td>&lt;100 ng/mL</td>
</tr>
<tr>
<td>TOTAL OXYCODONE by GC/MS</td>
<td></td>
<td><strong>POS</strong></td>
<td>&lt;100 ng/mL</td>
</tr>
<tr>
<td>PHENCYCLIDINE</td>
<td></td>
<td>NEGATIVE</td>
<td></td>
</tr>
<tr>
<td>THC (CANNABIS)</td>
<td></td>
<td>NEGATIVE</td>
<td></td>
</tr>
</tbody>
</table>

**02/04/09**

**0954**
Examples of Metabolism of Opioids

- Codeine → Morphine → 6-MAM* → Heroin
  
  - Hydrocodone → Hydromorphone
  
  - Oxycodone → Oxymorphone

Not comprehensive pathways, but may explain presence of apparently unprescribed drugs

- $t_{1/2} = 25-30$ min
- $t_{1/2} = 3-5$ min

*6-MAM = 6-monoacetylmorphine

• “OK, doc. I did use cocaine twice. Once on Jan 1 and once on Feb 1. No other times.”

Table 3. Detection time of drugs of misuse in urine

| Drug                                           | Cutoff level (ng/mL) | Detection time in urine
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine (multidrug misusers, dose unknown)</td>
<td>1000</td>
<td>Up to 5 days</td>
</tr>
<tr>
<td>THCCOOH after smoking 1 marijuana cigarette</td>
<td>50</td>
<td>2 to 4 days</td>
</tr>
<tr>
<td>Benzylecgonine after 20 mg IV cocaine</td>
<td>300</td>
<td>Up to 1.5 days</td>
</tr>
<tr>
<td>Benzylecgonine after street doses of cocaine</td>
<td>300</td>
<td>2 to 3 days; up to 1 week at higher doses</td>
</tr>
<tr>
<td>Morphine from low-dose heroin (3-12 mg)</td>
<td>300</td>
<td>1 to 1.5 days</td>
</tr>
</tbody>
</table>

THCCOOH = 9-carboxy-Δ9 tetrahydrocannabinol; IV = intravenous
*May not accurately reflect detection after extraordinarily high doses in chronic users; †Administered via different routes; ‡Up to 1 month with frequent use
Clinical Pearls

• You only get what you test for.
• Know where you can access the metabolic pathways.
• Know where you can access detection times.
• Urine drug tests don’t help if the patient is abusing what you are prescribing.
Illinois Prescription Monitoring Program (PMP)

Illinois retail pharmacies report Schedule II-V controlled substance prescriptions dispensed on a weekly basis.

Providers have 24/7 access to current or prospective patient’s prescription history.

Assist providers to:

- Prevent potential drug interactions or accidental overdose
- Detect & prevent misuse, abuse, & diversion of controlled substances
- Prescribers can view a history of prescriptions dispensed under their DEA #
- HIPAA & confidentiality & disclosure provisions of Illinois Law cover info contained in the PMP database

To register, visit www.ilpmp.org

Prescription Drug Monitoring Programs (PDMPs)

49 states & 1 territory have legislation authorizing a PDMP
43 states have an operational PDMP

Individual state laws determine

- Who has access to PDMP information
- Which drug schedules are monitored
- Which agency administers the PDMP
- Whether prescribers are required to register w/ the PDMP
- Whether prescribers are required to access PDMP information in certain circumstances
- Whether unsolicited PDMP reports are sent to prescribers

43 states have an operational PDMP
Treatment

• Abstinence based treatment
• 12 step support groups
• Medication assisted treatment
  – Agonist therapy
    • Methadone
    • Buprenorphine
  – Antagonist therapy
    • Naltrexone
Harm reduction

- Don’t use
- Don’t inject, use in other ways (snort, smoke, sniff, etc.)
- Use only sterile equipment for injecting and don’t share
- Re-use or share cleaned equipment
- Re-use or share uncleaned equipment
Opioid deaths—major trends

• Prescription opioids a bigger threat
  – Methadone a major player but...
  – Not methadone in treatment centers

• Naloxone distribution has made a positive impact on heroin related deaths
Know your risk factors

- Taking more than usual dose
- Intravenous use
- Resuming use at usual dose after prison or treatment center
- Combining with another drug (mostly sedatives)
- Body packing
- Deliberate self harm
- Longer use of opioids—tolerance to respiratory effects develops slower than euphoric effects
Naloxone is the antidote

- No debate regarding this in medical facilities or EMS systems
- Distribution to lay people
39 jurisdictions
μ opioid receptor
Administration methods

Intramuscular

Intranasal
Pharmacist dispensing
Reports

- Number of successful reversals
- Decreased use of drugs
- Intranasal administration is effective
Concerns

• Can lay people be taught to recognize an overdose and administer naloxone?
• Baltimore, San Francisco, Chicago, New York (2 sites), state of New Mexico
• Green et al. (2008). Addiction—answer: yes, just as well as medically trained personnel
Concerns
Enabling
Only live addicts can seek (and receive) treatment
No study of opioid therapy versus placebo, no opioid therapy, or non-opioid therapy for chronic pain evaluated long-term ($\geq 1$ year) outcomes related to pain, function, or quality of life. Most placebo-controlled randomized clinical trials were $\leq 6$ weeks in duration.
Summary of 2016 CDC guidelines

- **Non-pharmacologic and non-opioid treatments preferred.**
- Establish treatment goals
- Immediate release first
- Lowest dose preferable; caution when exceeding 50 Morphine Milligram Equivalents
- Avoid exceeding 90 MME
- For acute pain only prescribe what is expected
- Evaluate response to opioids one 1-4 weeks after initiation for chronic pain
- If benefits do not outweigh harms taper and discontinue

Frieden & Houry, NEJM, March 15, 2016
Summary continued

- Mitigate risk
  - Considering naloxone
  - Avoiding other sedatives concurrently
  - Prescription monitoring
  - Urine drug testing
  - Refer addicts for treatment

Frieden & Houry, NEJM, March 15, 2016
### Survey Says!

<table>
<thead>
<tr>
<th>Responses</th>
<th>All Physicians %</th>
<th>Nurses including Advanced Practice Nurses %</th>
<th>All respondents %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very likely</td>
<td>49</td>
<td>36</td>
<td>41</td>
</tr>
<tr>
<td>Somewhat likely</td>
<td>27</td>
<td>26</td>
<td>26</td>
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<tr>
<td>Not very likely</td>
<td>10</td>
<td>14</td>
<td>13</td>
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<tr>
<td>Not at all likely</td>
<td>8</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Uncertain</td>
<td>3</td>
<td>9</td>
<td>7</td>
</tr>
</tbody>
</table>

Clinician likelihood to incorporate CDC guidelines into their practice

Total = 483  
Physicians = 241  
Nurses including APNs = 94

Medscape survey published 4/13/2016
FDA panel recommendations that REMS* should be expanded

- Include immediate release opioids as well as ER/LA
- Mandatory
- Focus on pain management as opposed to medications
- Be tied to CDC guidelines

*Risk Evaluation and Mitigation Strategies Medscape, May 6, 2016
What is the goal?

• Improve functionality not reduce pain to zero
Effect of Mindfulness-Based Stress Reduction vs Cognitive Behavioral Therapy or Usual Care on Back Pain and Function Limitations in Adults with Chronic Low Back Pain—A Randomized Clinical Trial

Cherkin et al. JAMA. 2016;315(12):1240-1249

AT 26 WEEKS

CBT and MBSR were superior to UC but CBT and MBSR were equal to each other
Bohnert et al. A Pilot Randomized Clinical Trial of an Intervention to Reduce Overdose Risk Behaviors among Emergency Department Patients at risk for Prescription Opioid Overdose. Drug and Alcohol Dependence. 163(2016);40-7.

Brief encapsulation

• 204 self described non-medical prescription opioid use in past 3 months
• 2 groups
  – Enhanced Usual Care (EUC)
  – Motivational Interviewing + EUC
• EUC = brochures and didactic information
• Surveys at baseline and 6 months
Results

- 87% retention rate
- 40.5% vs. 14.7% decrease in opioid overdose risk behaviors
- 50% vs. 39.5% decrease in opioid use
Plans for the future

• Balance individual need with societal risk
• Meeting need for timely action
• Reviewing labeling and post-marketing surveillance requirements
• Prioritize abuse deterrent formulations and overdose treatments
• Address lack of opioid alternatives
• Create clear guidelines for opioid use
• Create guidelines for managing pain in children
• Develop a better evidence base

Califf et al., NEJM, 4/14/2016
How to treat pain?
Where is the burden of proof regarding chronic opioids?
Intervention Summary

• Understand that the burden of proof to prescribe opioids for chronic pain has shifted to those who encourage the practice.
• Know the limitations of your drug tests.
• Non-pharmacologic and non-opioid based pharmacologic interventions are the best places to start and there is a growing literature base to support this.
Summary

• Opioid overdose is a major public health crisis in the US.
• Prescription drugs are the major cause.
• Chronic pain is the driver for the prescription writing with little evidence that outcomes are improved.
• Non-pharmacologic and non-opioid treatments are the best places to start to treat chronic pain.
• If chronic opioids are necessary patient assessment and monitoring are critical.
• Harm reduction, although not ideal, saves lives.
• Community naloxone programs have been shown to save lives by reversing overdoses.
• Only live addicts can receive treatment.
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