Opioid Crisis: The challenges and opportunities to change the course of the epidemic

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Outline

- Historical aspects
- Current state of heroin addiction
- Current state of prescription opioid addiction (POA)
- Opioid OD deaths
- Management of opioid addiction
- Challenges
The MRI shows that your brain has been hijacked by dopamine pirates.

You are now under the full control of social media corporations, gambling casinos, and Big Pharma.

Are you writing me a prescription?

No, I'm buying stock in those companies.
Historical aspects
HEROIN

“It’s not hypnotic and there is no danger in acquiring a habit!”

– Boston Medical and Surgical Journal 1900
COUGH

The Problem Has Been Solved By
the pharmaceutical compound known as
Glyco-Heroin Smith

BAYER PHARMACEUTICAL PRODUCTS.

We are now sending to Physicians throughout the United States literature and samples of

ASPIRIN

The substitute for the Salicylates, agreeable of taste, free from unpleasant after-effects.

HEROIN

The Sedative for Coughs,
HEROIN HYDROCHLORIDE
Its water-soluble salt.
You will have call for them. Order a supply from your jobber.

BAYER PHARMACEUTICAL PRODUCTS.

Send for samples and Literature to

FARBENFABRIKEN OF ELBERFELD CO.
40 Stone Street, New York.
Opioid epidemics in modern US history

- First epidemic was early 1900s
  - Opioid maintenance started with Morphine clinics
- Second epidemic was post WW II
  - First methadone clinic opened in NY City in 1972
- This is our third opioid epidemic
Current state of heroin addiction
Scope of Heroin Use in the US (National Survey of Drug Use and Health, NSDUH)

- NSDUH: Past year heroin use
  - 2016: 948,000
  - 2014: 914,000
  - 2012: 669,000
  - 2007: 373,000

- NSDUH: Past month heroin use
  - 2016: 474,000
  - 2015: 591,000
  - 2014: 435,000
  - 2012: 335,000
  - 2007: 161,000
This increase has been seen in:

- Men
- Non-Hispanic whites
- Ages 18-25 years
- Living in the North East
- Suburban and rural communities
- Household income less than $20,000 per annum
- People addicted to prescription opioid drugs/cocaine/alcohol/marijuana
- People without insurance
# Heroin Use Has INCREASED Among Most Demographic Groups

<table>
<thead>
<tr>
<th></th>
<th>2002-2004*</th>
<th>2011-2013*</th>
<th>% CHANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SEX</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.4</td>
<td>3.6</td>
<td>50%</td>
</tr>
<tr>
<td>Female</td>
<td>0.8</td>
<td>1.6</td>
<td>100%</td>
</tr>
<tr>
<td><strong>AGE, YEARS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-17</td>
<td>1.8</td>
<td>1.6</td>
<td>--</td>
</tr>
<tr>
<td>18-25</td>
<td>3.5</td>
<td>7.3</td>
<td>109%</td>
</tr>
<tr>
<td>26 or older</td>
<td>1.2</td>
<td>1.9</td>
<td>58%</td>
</tr>
<tr>
<td><strong>RACE/ETHNICITY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>1.4</td>
<td>3</td>
<td>114%</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>1.7</td>
<td>--</td>
</tr>
<tr>
<td><strong>ANNUAL HOUSEHOLD INCOME</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than $20,000</td>
<td>3.4</td>
<td>5.5</td>
<td>62%</td>
</tr>
<tr>
<td>$20,000-$49,999</td>
<td>1.3</td>
<td>2.3</td>
<td>77%</td>
</tr>
<tr>
<td>$50,000 or more</td>
<td>1</td>
<td>1.6</td>
<td>60%</td>
</tr>
<tr>
<td><strong>HEALTH INSURANCE COVERAGE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>4.2</td>
<td>6.7</td>
<td>60%</td>
</tr>
<tr>
<td>Medicaid</td>
<td>4.3</td>
<td>4.7</td>
<td>--</td>
</tr>
<tr>
<td>Private or other</td>
<td>0.8</td>
<td>1.3</td>
<td>63%</td>
</tr>
</tbody>
</table>
Current state of prescription opioid addiction (POA)
11.5 Million People Misused Prescription Opioid Medication (2016)

<table>
<thead>
<tr>
<th>Number of People (in Thousands)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>11,517 (12 or Older)</td>
<td>4.3</td>
</tr>
<tr>
<td>881 (12 to 17)</td>
<td>3.5</td>
</tr>
<tr>
<td>2,454 (18 to 25)</td>
<td>7.1</td>
</tr>
<tr>
<td>8,181 (26 or Older)</td>
<td>3.9</td>
</tr>
</tbody>
</table>
1.8 Million People With Prescription Opioid Addiction (2016)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number of People (in Thousands)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 or Older</td>
<td>1,753</td>
<td>0.7</td>
</tr>
<tr>
<td>12 to 17</td>
<td>152</td>
<td>0.6</td>
</tr>
<tr>
<td>18 to 25</td>
<td>291</td>
<td>0.8</td>
</tr>
<tr>
<td>26 or Older</td>
<td>1,310</td>
<td>0.6</td>
</tr>
</tbody>
</table>
Some states have more painkiller prescriptions per person than others.

Number of painkiller prescriptions per 100 people:
- 52-71
- 72-82.1
- 82.2-95
- 96-143

The amount of opioids prescribed per person varied widely among counties in 2015.
Fentanyl encounters

- The number of fentanyl encounters more than doubled in the US from 5,343 in 2014 to 13,882 in 2015.
- Extremely high rates were found in Ohio, Massachusetts and New Hampshire.
- The steady increase in fentanyl encounters from 2013 to 2015 indicates that the supply of illicitly made fentanyl continues to increase primarily east of the Mississippi river with small increases west of the Mississippi.
- Research chemical U-47700 (unscheduled synthetic opioid) found in counterfeit oxycodone pills.
- Other synthetic opioids in the market: acetylfentanyl, carfentanil, butyrfentanyl (alveolar hemorrhages), W-18, MT-45 (ototoxic) and AH-7921.
Number of Reported Law Enforcement Encounters Testing Positive for Fentanyl in the US: 2010 - 2015
Opioid OD deaths
Opioid OD deaths

- Opioids were involved in 42,249 deaths in 2016 (Total drug ODs 64,000)
- Heroin was involved in 15,446 deaths in 2016
- Opioid overdose deaths were five times higher in 2016 than 1999
- In 2016, states with the highest rates of death due to drug overdose
  - West Virginia (52.0 per 100,000)
  - Ohio (39.1 per 100,000)
  - New Hampshire (39.0 per 100,000)
  - Pennsylvania (37.9 per 100,000)
  - Kentucky (33.5 per 100,000)
3 Waves of the Rise in Opioid Overdose Deaths

Wave 1: Rise in Prescription Opioid Overdose Deaths
Wave 2: Rise in Heroin Overdose Deaths
Wave 3: Rise in Synthetic Opioid Overdose Deaths

Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2016

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


Source: NCHS, National Vital Statistics System, Mortality
Percent distribution of drug overdose deaths for adolescents aged 15–19, by intent and sex: United States, 2015

Source: NCHS, National Vital Statistics System, Mortality
A MOTHER'S KISS

Is Not Half So Soothing to Baby as

Mrs. Winslow's Soothing Syrup

As Millions of Mothers Will Tell You.

It Soothes the Child.
It Softens the Gums.
It Allays all Pain.
It Cures Wind Colic.
It is the Best Remedy for Diarrhoea.

It is absolutely harmless and for over sixty years has proved the best remedy for children while teething.

BE SURE YOU ASK FOR
MRS. WINSLOW'S SOOTHING SYRUP
AND TAKE NO OTHER.
Management of Opioid use disorders (OUD)

- Opioid withdrawal treatment (OWT)
- Opioid maintenance treatment (OMT)
  - Dispensing and/or prescribing of a full or a partial mu agonist on a long term basis
OWT

- Extremely high relapse rates > 90%
- High risk for OD upon relapse
- Abstinence based approach is not the best treatment for opioid addiction
- *Treatment outcomes for behavioral interventions alone for opioid use disorders are dismal*
- *Outcomes for better for medication without behavioral interventions, but best for both combined*
Goals of OMT

- Eliminate or reduce illicit opioid use
- Eliminate drug cravings and withdrawal symptoms
- Decrease HIV/Hepatitis seroconversion
- Decrease in criminal behavior
- Improve social and occupational functioning & normalize brain functioning
FDA approved treatments

- **Methadone** (Liquid 10mg/ml)

- **Buprenorphine/Naloxone** (BUP-NX): sublingual films/tablets, buccal film

- **Buprenorphine**: sublingual tablets, XR SQ monthly preparation

- **Naltrexone**: tablets, IM monthly injection
Naltrexone

- Orally active opioid antagonist
- Half life 10-12 hours
- Approved in 1984 for OUD
- Poor compliance with PO Naltrexone for heroin addiction
- In 2010 FDA approved the extended-release Naltrexone (XR-NTX) 380mg monthly IM
- Two recent studies showed that both XR-NTX and BUP-NX were equally safe and effective
Comparative effectiveness of XR-NTX versus BUP-NX for opioid addiction

**XBOT (Clinical Trials Network)**

- 570 participants, 24 week open label randomized control trial
- n= 283 for XT-NTX
- n= 287 for BUP-NX
- Substantial induction hurdle
  - 72% of XR-NTX successfully initiated compared to 94% for BUP-NX
- Once initiated, both equally safe and effective

**Norwegian Study**

- 159 participants, 12 week open label randomized control
- n= 80 for XT-NTX
- n=79 for BUP-NX
- XR-NTX was noninferior to BUP-NX as regards to
  - Retention
  - Number of opioid negative drug tests
**Methadone**

- Full mu agonist
- NMDA antagonist and is an SNRI
- Oral bioavailability 80%
- $T_{1/2}$ 24 hrs, metabolized by CYP450 3A4, also 1A2 & 2D6
- Biphasic elimination alpha 8-12 hours and beta elimination 30-60 hours
- Induction does not require patient to be in withdrawal
- Approved for opioid addiction (liquid/wafer) and analgesia (tablets)
- Dose range 60-120mg

**Buprenorphine**

- Partial mu agonist
- Weak kappa antagonist
- S/L bioavailability 55%
- $T_{1/2}$ 37hrs, metabolized by CYP450 3A4
- Induction requires patients to be in withdrawal
- Tablets/Film approved for opioid addiction, patch approved for pain (Butrans)
- Dose range 8-16mg
<table>
<thead>
<tr>
<th><strong>Methadone</strong></th>
<th><strong>Buprenorphine</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Schedule II</td>
<td>▪ Schedule III</td>
</tr>
<tr>
<td>▪ Dispensed for addiction treatment, prescribed for pain</td>
<td>▪ Prescribed to treat opioid addiction</td>
</tr>
<tr>
<td>▪ Approved in pregnancy</td>
<td>▪ Studied in pregnancy (MOTHER Study)</td>
</tr>
<tr>
<td>▪ May prolong QTc</td>
<td>▪ No cardiotoxicity</td>
</tr>
<tr>
<td>▪ Limited to people in large metropolitan areas</td>
<td>▪ Has increased access to care</td>
</tr>
<tr>
<td>▪ <em>Highly stigmatized treatment</em></td>
<td>▪ <em>Less Stigma associated</em></td>
</tr>
</tbody>
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Buprenorphine XR preparations

- In November 2017 FDA approved Sublocade, the first once-monthly injectable buprenorphine for the treatment of moderate-to-severe OUD
  - Indicted for patients stable on sublingual buprenorphine for at least 7 days
- FDA’s Psychopharmacologic Drugs Advisory Committee recommended approval of CAM2038, an investigational buprenorphine weekly and monthly depot injection for the treatment of adults with OUD on November 1, 2017
Methadone Study: 18 Month Follow Up Of HIV- Subjects

Out of treatment: 22%
In-Treatment: 3.5%

(Metzger et al 1993)
Buprenorphine vs. Placebo for Heroin Dependence

4 Subjects in Control Group Died

Kakko, Lancet 2003
Challenges

• Addiction still seen as “moral failing”
• We continue to blame and shame our patients
• **Stigma** persist against patients as well as approved treatments
  ➢ Families/Friends/ 12 Step Sponsor
  ➢ Providers
• **Access**
  - Providers
    - 49,000 waived physicians
    - 48.1% of waived physicians were prescribing to 5 patients or fewer (Sigmon, 2015)
  - Psychosocial treatment
  - Pharmacological treatment
• Number of children in the Foster Care system
• Patients with chronic pain syndromes
Number of Opioid treatment Programs (OTP) Patients Receiving Methadone: 2003 to 2015

Source: SAMHSA National Survey of Substance Abuse Treatment Facilities (N-SSATS), 2003 to 2015
Note: Patient counts were not collected in 2014; patient counts for 2014 are estimated
Number and Percentage of Opioid Treatment Programs (OTPs) Providing Buprenorphine and Extended Release Naltrexone: 2003 to 2015

Source: SAMHSA National Survey of Substance Abuse Treatment Facilities (N-SSATS), 2003 to 2015
Note: The first year Extended Release Naltrexone data were collected was 2013