Opioid Use Disorder: General Population and Pregnancy

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Objectives

- Define terms
- Opioids use disorder/epidemic
- Opioid use and tx during/after pregnancy
- Maternal screening
- Access to tx
- Disparities
Definitions

- DSM-5 - No longer uses the terms substance abuse and substance dependence

- DSM-5 - Substance Use Disorder (SUD): defined as mild, moderate, or severe to indicate the level of severity, which is determined by the number of diagnostic criteria met by an individual
  - Recurrent use of alcohol and/or drugs causes clinically and functionally significant impairment, such as health problems, disability, and failure to meet major responsibilities at work, school, or home

- Substance misuse
Opioid Use Disorder

- >2 symptoms (in same yr)
- Tolerance (defined by either)
  - ↑ amounts for same effect
  - ↓ effect with same amount
- Withdrawal (defined by either)
  - Withdrawal syndrome
  - Take drug to ↓ withdrawal

Larger amounts used/longer time using
Much time spent
Attempts cut down
Neglecting major roles
Important activities ↓
Interpersonal probs
Physical/psych probs
Hazardous use
Craving
Definitions

- Opioid term covers
  - Body’s opioids (e.g. beta-endorphin, dynorphin)
  - Opiates - from poppy plant (e.g. morphine, heroin)
  - Synthetics (e.g. fentanyl, buprenorphine (Subutex))
  - Prescription opioid pain meds
    - Examples include oxycodone (Oxycontin);
      hydrocodone (Vicodin); tramadol (Ultram)
- Narcotic - A legal term (not medical term
  Means illegal use of controlled psychoactive substance
Definitions

- **Medication assisted treatment (MAT)**
  - Treatment for opioid problem
  - Also includes using medication to improve outcomes

- **Maintenance treatment**
  - Treatment to maintain recovery
116 people died every day from opioid-related drug overdoses.

948,000 people used heroin.

15,469 deaths attributed to heroin overdose.

17,087 deaths attributed to overdosing on commonly prescribed prescriptions.

11.5 million people misused prescription opioids.

$504 billion in economic costs.

Sources:
1. National Survey on Drug Use and Health, 2016
2. Mortality in the United States, 2016 NCHS Data Brief No. 293, December 2017
3. CEA Report: The underestimated cost of the opioid crisis, 2017

Updated January 2018. For more information, visit: http://www.hhs.gov/opioids/
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

Opioids killed more than 42,000 people in 2016
- 1/2 involved Rx opioids
- Over 1,000 people treated in ED for misusing a prescription opioid every day
- 1 in 4 people with Rx opioids for LT NCP in primary care struggle with addiction
- Most common Rx drugs in ODD
  - Methadone, oxycodone, hydrocodone
6% of the US population is on chronic opioids

The US makes up 5% of the world's population

* AND *

80% of opioids are consumed in the US

DRUG OVERDOSES KILL MORE THAN CARS, GUNS, AND FALLING.

Falling: 28,360 deaths
Guns: 32,351 deaths
Traffic accidents: 33,692 deaths
Drug overdoses: 41,340 deaths
(16,917 from opioid pain medicine)

San Diego County Estimates

- In 2016
- OUD = ~6% (171,037) ages 12+
- 238 overdoses
- Assuming 20% with OUD seek tx, 18,119 to 25,476 without local access to opioid agonist tx
- No regulatory barriers to naltrexone and counseling tx, this snapshot focuses on agonists
San Diego County Measures

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>All opioid overdose deaths, 2016</td>
<td>238 deaths; 7.2 per 100,000 people</td>
</tr>
<tr>
<td>Buprenorphine prescriptions, 2016</td>
<td>43,067 prescriptions; 13.0 per 1,000 people</td>
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<tr>
<td>Methadone patients at OTPs, 2016</td>
<td>3,599 methadone patients at OTPs; 127.5 per 100,000 people</td>
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<tr>
<td>Buprenorphine-waivered prescribers, February 2018 estimate</td>
<td>322 prescribers with a 30-patient limit, 83 prescribers with a 100-patient limit, 12 prescribers with a 275-patient limit; up to 128 prescribers from out of county prescribe to patients in the county.</td>
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<tr>
<td>Estimated count and rate of OUD</td>
<td>171,037 people with OUD; 6.0 per 100 people</td>
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<td>Estimated number of people with OUD who could be treated, given current</td>
<td>Between 8,732 and 16,089 people could be treated given current buprenorphine and methadone treatment capacity, depending on how many patients each buprenorphine prescriber treats.</td>
</tr>
<tr>
<td>Estimated treatment gap, assuming 20% of people with OUD seek treatment</td>
<td>Between 18,119 and 25,476 people are likely to seek treatment but cannot get it, based on current opioid agonist treatment capacity.</td>
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<td>Count and percent of prescribers with a buprenorphine waiver</td>
<td>There are 19,307 prescribers in the county, and 2.2% have a buprenorphine waiver.</td>
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Illicit Opioid Use in Pregnancy

Possible Risks:

- Neonatal Abstinence Syndrome (NAS)
- Neural tube defects
- Congenital heart defects
- Gastrochisis
- Stillbirth
- Preterm delivery
Opioid Use in Pregnancy

- 2000 to 2009, significant increase in use or dependence from 1.19 to 5.63 per 1,000 hospital births\(^2\)
- 2000 to 2012, increased incidence of neonatal abstinence syndrome (NAS) from 1.2 to 5.8 per 1,000 hospital births per year\(^3\)

- Other Conditions:
  - Congenital malformations, low birthweight, prematurity, and adverse effects on development and growth\(^4\)
**Methadone:**
- Clinic-based
- Opioid agonist: Prevents withdrawal
- Cross tolerance with other opioids
- Better rates of retention in treatment

**Buprenorphine:**
- Office-based
- Partial opioid agonist: Reduces withdrawal risk and blocks other narcotics
- Better at prognosis for Neonatal Abstinence Syndrome (NAS)
Treatment Options for Pregnant Women

- Medical opioid withdrawal followed by inpatient or outpatient non-drug psychosocial treatments
  - HIGH relapse rates
  - Poor long term outcomes
  - Fetus experiences withdrawal
- MAT - now standard of care
  - Methadone:
    - Pros: Improve prenatal care, reduce fetal mortality, and improve fetal growth
    - Cons: Daily pick ups at clinic, stigma
Treatment Options for Pregnant Women

**MAT - Continued**

**Buprenorphine (Suboxone®, Subutex®),**
- **Pros:** up to 30-day prescription, private, less severe NAS?\(^6\)
- **Cons:** Do not know long term effects on fetus/neonate, possibly higher dropout rates\(^7\)

**Naltrexone (Vivitrol®)**
- Insufficient research on pregnant women
- Concern about opioid blockade on developing fetus
Breastfeeding

- Good to breast feed in general
- Breastfeeding on MAT can help ease NAS
- Pump and Dump doesn't really work
- Shouldn’t breastfeed if consistently using drugs/EtOH
The MOTHER Study

- Double-blind, randomized, prospective study
- Lead site: Johns Hopkins; 7 other sites
- Prenatal exposure to methadone (20 to 140 mg/d) or bup (sublingual, 2 to 32 mg/d)
- 96 children and their mothers
- Assessments at 3, 6, 12, 24, 36 months
The MOTHER Study and Associated Findings\textsuperscript{8-10}

- Methadone or buprenorphine before birth exhibit normal development in early childhood.
- Bup has no harmful effects relative to methadone.
- Children exposed to methadone vs. bup show no difference in development.
- The severity of NAS had no effect on early childhood growth and development.
- NAS occurs the same (a little less than 50%) for both bup and methadone.
- Bup associated NAS needs treatment with less morphine, has decreased length of stay in the hospital, and decreased duration of treatment.
The MOTHER Study

Secondary Outcomes
One of the seven neonatal secondary outcome measures differed significantly between groups: neonates exposed to buprenorphine spent, on average, 58% less time in the hospital receiving medication for NAS than did those exposed to methadone (4.1 days vs. 9.9 days, P<0.003125 in accordance with prespecified thresholds for significance). This difference remained significant in analyses adjusted for selected covariates (Table 1 in the Supplementary Appendix). There were no significant between-group differences in any of the nine maternal secondary outcomes (Table 2, and Table 1 in the Supplementary Appendix).

Subgroup Analyses
To address the possibility that differences in neonatal outcomes between the two groups might be explained by higher average levels of opioid dependence in women who completed methadone treatment than in those who completed buprenorphine treatment, we performed post hoc analyses that excluded the 25 participants whose methadone dose at delivery exceeded 100 mg. The between-group differences in the amount of morphine required for the treatment of NAS and the length of the hospital stay remained significant (P<0.001 and P=0.003, respectively). The difference in the secondary outcome of duration of hospitalization while infants were receiving medication was no longer significant (P=0.01).

Adverse Events
Assuming an alpha level of 0.05 (to maximize the detection of differences between medications with respect to adverse events), the methadone group had higher rates of nonserious maternal events overall (P=0.003) and of nonserious maternal cardiovascular events in particular (P=0.01). The two medication groups did not differ significantly with respect to any serious maternal or neonatal adverse events or any nonserious neonatal adverse events (Table 3).

Discussion
In this randomized, double-blind trial, infants who had prenatal exposure to buprenorphine required significantly less morphine for the treatment of NAS, a significantly shorter period of NAS treatment, and a significantly shorter hospital stay than did infants with prenatal exposure to methadone. The superiority of buprenorphine over methadone did not extend to differences in the number of neonates requiring NAS treatment, peak NAS score, head circumference, any other neonatal outcome, or any maternal outcome. Although buprenorphine was superior for two of the five primary outcomes among women who completed treatment, women who were taking buprenorphine were more likely to discontinue treatment. If patients with more severe

Figure 2. Mean Neonatal Morphine Dose, Length of Neonatal Hospital Stay, and Duration of Treatment for Neonatal Abstinence Syndrome.
Maternal Substance Use

- Seen in all socioeconomic classes, ages, and races
- Increased risk: younger, unmarried, lower educational achievement
- Polydrug use
  - Neonates with heavy alcohol exposure in utero ~2 times as likely to be exposed to opiates and 3.3 times as likely to be exposed to amphetamines as compared with neonates with no alcohol exposure
- National epidemic of underdiagnosed neonatal exposure to alcohol
  - 1st graders in 4 US communities = 1-5% children are affected
  - n= 222 children with fetal alcohol spectrum disorder (only 2 previously diagnosed)
Maternal Screening

- Fear of stigmatization and/or initiation of children’s protective services intervention
  - Good relationships
    - Non-judgmental approach
    - Open-ended questions
    - Adequate time to achieve trust and obtain a full history
Access to Screening and Treatment

- Criminalization of drug use while pregnant
  - 18 states = criminal child abuse charges in 2012\(^\text{16}\)
  - 100 women prosecuted for assault for illicit opioid use in Tennessee in 2014\(^\text{15}\)
- Prenatal child abuse laws (~24 states + DC)
- Fear = Poor prenatal care\(^\text{17}\)
“If I had known that you go to the doctor and get a positive drug screen, I would not have gone to the doctor. I’d let nobody know. Especially not the doctor. Especially not the people who say they want to help. I really wanted the help. But now I feel that my help is punishing me. It hurts and it’s scary as hell that I’ve got to walk around carrying this baby and not know if I’m going to get charged.”

- Nikki, pregnant woman at a residential drug treatment center in Birmingham, Alabama
Access to Screening and Treatment

- Underutilized MAT = 18 states child abuse laws = 33% vs. 51%\(^\text{18}\)
- Barriers:
  - Psychological, social, and financial problems = psychosocial stress, exposure to violence, and limited access to adequate screenings and treatment\(^\text{19}\)
  - Waiting lists, geographic access, insurance\(^\text{20}\)
  - Drug Addiction Treatment Act (DATA) waiver\(^\text{21}\)
    - Low confidence, lack of institutional support, reimbursement issues
Maternal Screening

- Optimal approach:
  - Universal maternal screening (validated tools)
    - Alcohol only:
      - AUDIT-C, CAGE, TWEAK, T-ACE (heavy alcohol)
    - Alcohol + other:
      - **4Ps Plus** (Parents, Partners, Past, Pregnancy)
    - Adolescents/young adults: CRAFT
  - Other: DAST, ASSIST
Disparities (Opioids)-Socioeconomic

- Lower SES = Reliance on Medicaid \(^22\)
- Medication/Treatments are expensive \(^23\)
  - Methadone daily visits: $126 per week or $6,552 per year
  - Bup twice-weekly visits: $115 per week or $5,980 per year
  - Naltrexone: $1,176.50 per month or $14,112 per year
    - Diabetes = $3,560 and Kidney Disease = $5,634
- Costs associated with untreated OUD \(^24-26\)
  - Criminal justice, treating babies born dependent on opioids, greater transmission of infectious diseases, treating overdoses, injuries associated with intoxication, lost productivity
“As a pediatrician, I have seen many women work hard during pregnancy to achieve recovery, and make strong commitments to parenting at the same time. These are some of the most amazing and heroic people I have encountered in my professional career. Pregnancy gives a specific and strong motivation to achieve recovery, and recovery can make possible attentive and supportive parenting -- with the right supports!”

- Steven H. Chapman M.D., Director of the Boyle Community Pediatrics Program, Children’s Hospital at Dartmouth-Hitchcock, and Director of Child Health, Center for Addiction, Recovery, Pregnancy and Parenting
QUESTIONS?
References


References

13. Shor, Heavy in utero ethanol exposure is associated with the use of other drugs of abuse in a high-risk population. Alcohol 2010; 44:623
EXTRA SLIDES
New hepatitis C infections triple due to opioid epidemic

By Susan Scutti, CNN
Updated 2:40 PM ET, Thu May 11, 2017

Hepatitis C rates nearly double in pregnant women amid opioid epidemic, CDC says

By GILLIAN MOHNEY
The rates of facilities were lower in Southern and Midwestern states
- Higher number of Black, rural, and/or uninsured
- Inconsistent findings
  - Jones et al., 2015
    - Blacks and Hispanics less likely to complete treatment
    - Native Americans less likely to complete treatment for alcohol
    - Unemployment and housing instability explained Blacks and Hispanics’ completion disparities

- Le Cook & Alegria, 2011
  - No difference in tx use among Whites, Blacks, and Hispanics
- Opioid death rates have **quadrupled** since 1999
  - CDC declared an **epidemic**
- Veterans are **twice** as likely to die from accidental overdose
- Veterans at highest risk:
  - MH diagnosis/PTSD
  - $\geq 100$mg MEDD + SUD

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**National Overdose Deaths**
Number of Deaths from Opioid Drugs

Source: National Center for Health Statistics, CDC Wonder

- VA PBM Naloxone Kits RFU, Sept 2014
Opioid Use Disorder and HIV / HCV

Injection drug use problems

HIV and HCV linked to injectable drug use

- Majority of injection drug users are addicted to heroin or other opiates
- 25% of new HIV cases in the U.S. secondary to injection drug use
- 50% of new HCV cases secondary to injection drug use
- Prevalence of HCV infection in opioid dependent patients range from 36%–95%

High risk practices of injectable drug users

- Sharing of needles and syringes
- Sharing of paraphernalia
- Sexual exposure

Management

HIV and HCV linked to injectable drug use

- Opioid Agonist Treatment to Decrease HIV / HCV Transmission in Injection Drug Users
- Routine HCV antibody testing
  - With HCV infection 3 – 5 times more common in the U.S. than HIV/AIDS—and more deadly—CDC recommends routine HCV antibody testing (screening) for all current or former injection drug users