

# Use and Misuse of Opioids in Pregnancy

Presented by Dr. Jack Klein

Clinical Solution Consultant, Centene Corporation

Clinical Professor of OB/GYN at Washington University School of Medicine

100 million people in the US have chronic pain  
61.8 million people received one or more opioid RXs in 2016  
170,000 people used heroin for the first time in 2016 (75%  
abused Rx opioids first)  
2.1 million people in the US have SUD but only 20% are  
treated  
Half of the 2.6 million adults who have co-occurring mental  
illness and SUD did not receive mental health care or  
substance abuse treatment

- US has 5% of world population but, consumes 99% of hydrocodone and 81% of oxycodone.
- There are 115 deaths daily in the US from overdoses.
- There has been a 30% increase in ER visits for suspected overdoses.
- The average life expectancy in the US has gone down 2 years because of overdose deaths.
- Grandparents are now raising their grandchildren in increasing numbers.
- There are now more deaths annually from overdoses than automobile accidents.
- The 100 counties with the highest opioid related deaths have 7% of the population but 27% of all the opioid deaths.

# Definitions

- Use-Sporadic consumption of alcohol or drugs with no adverse consequences of that consumption
- Abuse- Although frequency may vary, some adverse consequences of that use are experienced by the user
- Physical dependence- A state of adaptation that is manifested by a substance class-specific withdrawal syndrome that can be produced by abrupt cessation or rapid dose reduction of a substance
- Psychological dependence- A subjective sense of a need for a specific psychoactive substance, either for its positive effect or to avoid negative effects associated with its abstinence
- Addiction- A primary chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads the individual to pathologically pursue reward and/or relief by substance abuse. It is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of one's behaviors and a dysfunctional emotional response. Relapse/remissions are common

# Opioid Treatment Facilities

- 60% of treatment facilities for SUD do not offer MAT
- 54% of opioid addiction centers do not offer MAT
- Only 7% of all MAT facilities offer all three recommended medications
- Only 20% of people with OUD are treated in the US
  
- In 2010, there were enough opioids prescribed to medicate every American around the clock for a month. 30% increase per decade
- This is 4 times the rate in Europe
- Women's death rate from overdose has increased 471% from 1999-2015
- Only 4% of US physicians are buprenorphine waivered

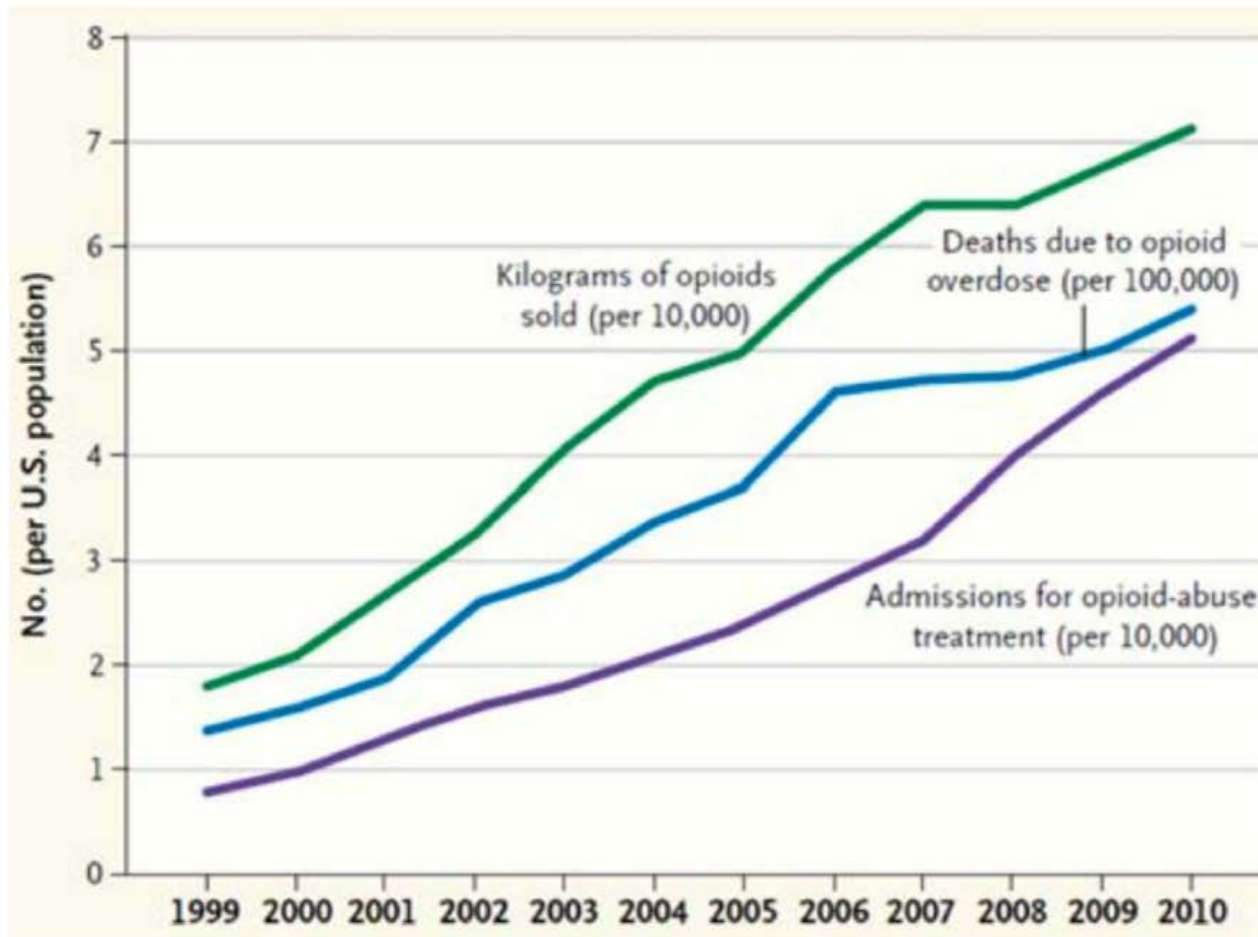
# Opioid Epidemic Pearls

- Opioid epidemic driven by making pain a vital sign
- Physicians were treating patients to alleviate pain
- Pharma told physicians that long acting opioids were not addictive
- More surgeries became outpatient procedures
- Most patients require 2-4 days of pain therapy.
- Each additional week of opioids increase dependence by 20%
- Every refill of a pain medication raises likelihood of OUD by 44%
- 53% of opioids are obtained from leftover pills from family or friends
- The pain trajectory is most important. Does the pain resolve or not

# Physiology of Addiction

- Long term treatment leads to tolerance, so higher doses needed
- Brains are rewired and structural and functional changes lower pain thresholds causing pain intolerance, brain fog and compromising impulse control
- Because of physiologic dependence, most patients live in an uncomfortable state of almost constant withdrawal
- Many chronic pain users are trying to avoid withdrawal symptoms
- People with OUD need a certain level of medication to feel normal
- They do not experience euphoria or get a high with chronic use

# Prescription opioids: 1999-2010



80% of the world's oral opioids are used in the US

CDC, MWR  
2011



# 2016 Opioid Addiction in the US

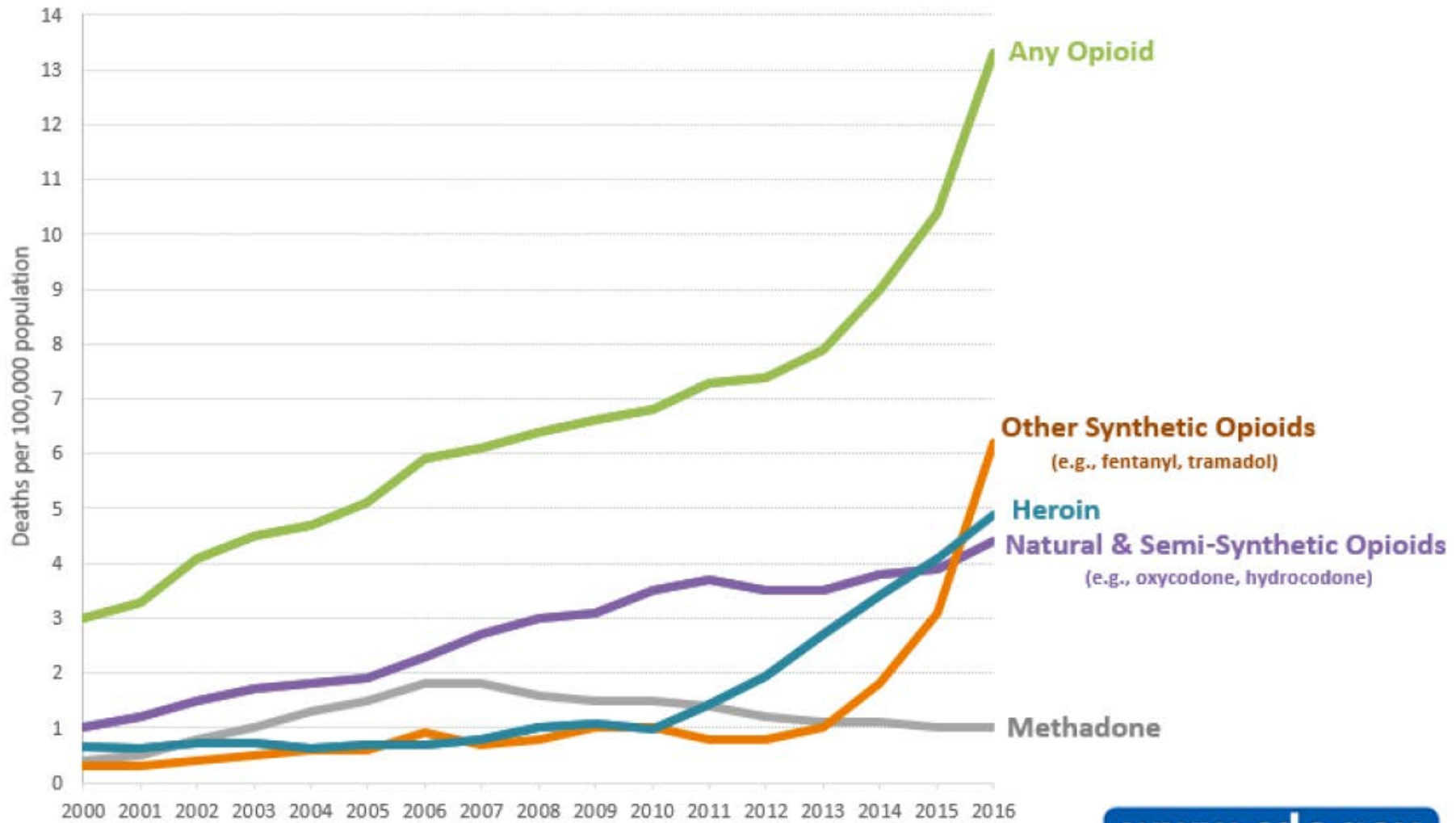
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- ▶ In 2015, of the 20.8 million Americans age 12 or older had a substance use disorder (7.8% of the population)
  - ▶ 2 million had a substance use disorder involving prescription pain relievers
  - ▶ 591,000 had a substance use disorder involving heroin

Center for Behavioral Health Statistics and Quality. (2016). Key substance use and mental health indicators in the United States: Results from the 2015 National Survey on Drug Use and Health Retrieved from <http://www.samhsa.gov/data/>

National Institute on Drug Abuse. (2014). Drug Facts: Heroin. Bethesda, MD: National Institute on Drug Abuse. Available at <http://www.drugabuse.gov/publications/drugfacts/heroin>.

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



SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2017. <https://wonder.cdc.gov/>.

[www.cdc.gov](http://www.cdc.gov)  
Your Source for Credible Health Information

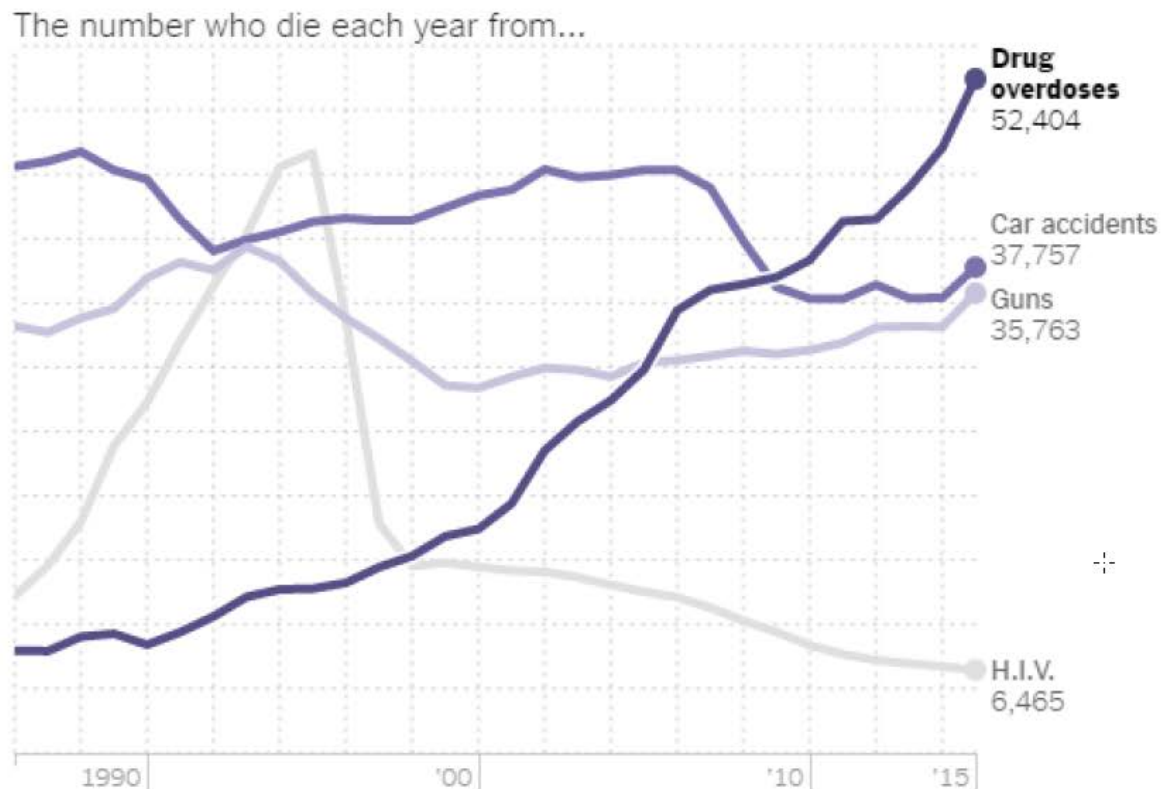
# Why are people dying?



Lethal doses



# Drug Overdose Death Rate in Comparison



The New York Times

By JOSH KATZ APRIL 14, 2017

Sources: [Centers for Disease Control and Prevention](#), National Center for Health Statistics.

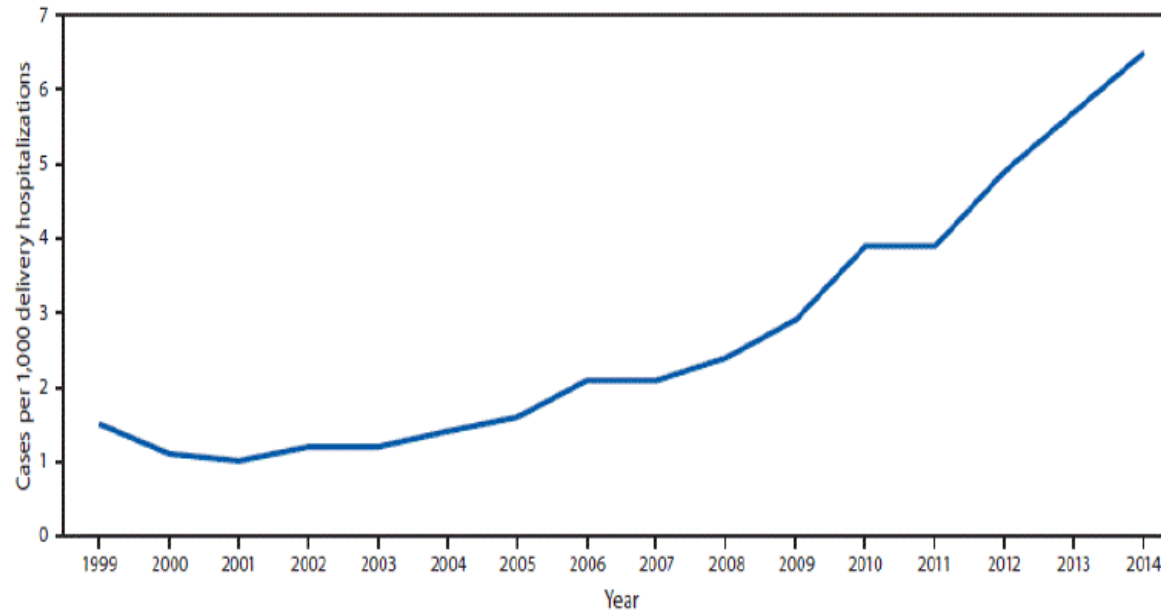
# Women and Opioids

- Women are more likely to suffer from chronic pain than men
- Women develop OUD at lower doses and over a shorter period of time while experiencing more cravings
- Women are more likely to be prescribed benzodiazepenes
- Women have a higher incidence of depression
- 80% of pregnancies in women with OUD are unplanned
- Pregnant women are more likely to make changes to improve the health of their baby

# Opioid Use Disorder at Delivery, 1999-2014

FIGURE 1. National prevalence of opioid use disorder per 1,000 delivery hospitalizations\* – National Inpatient Sample (NIS),<sup>†</sup> Healthcare Cost and Utilization Project (HCUP), United States, 1999-2014

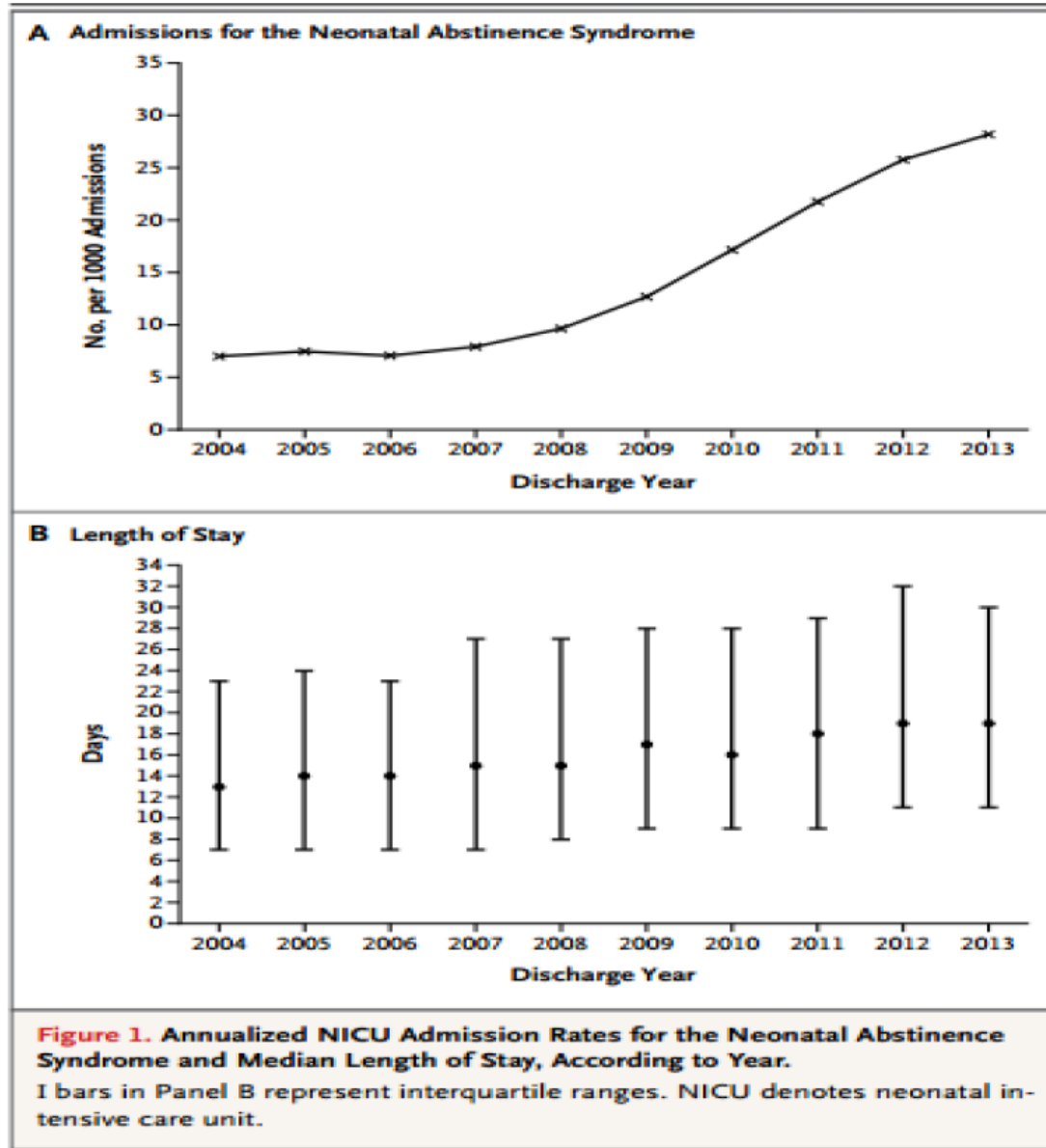
Return I



\* Prevalence numerator consisted of cases of opioid type dependence and nondependent opioid abuse based on *International Classification of Diseases, Ninth Revision* (ICD-9) codes (304.00-304.03, 304.70-304.73, 305.50-305.53), and denominator consisted of delivery hospitalization discharges.

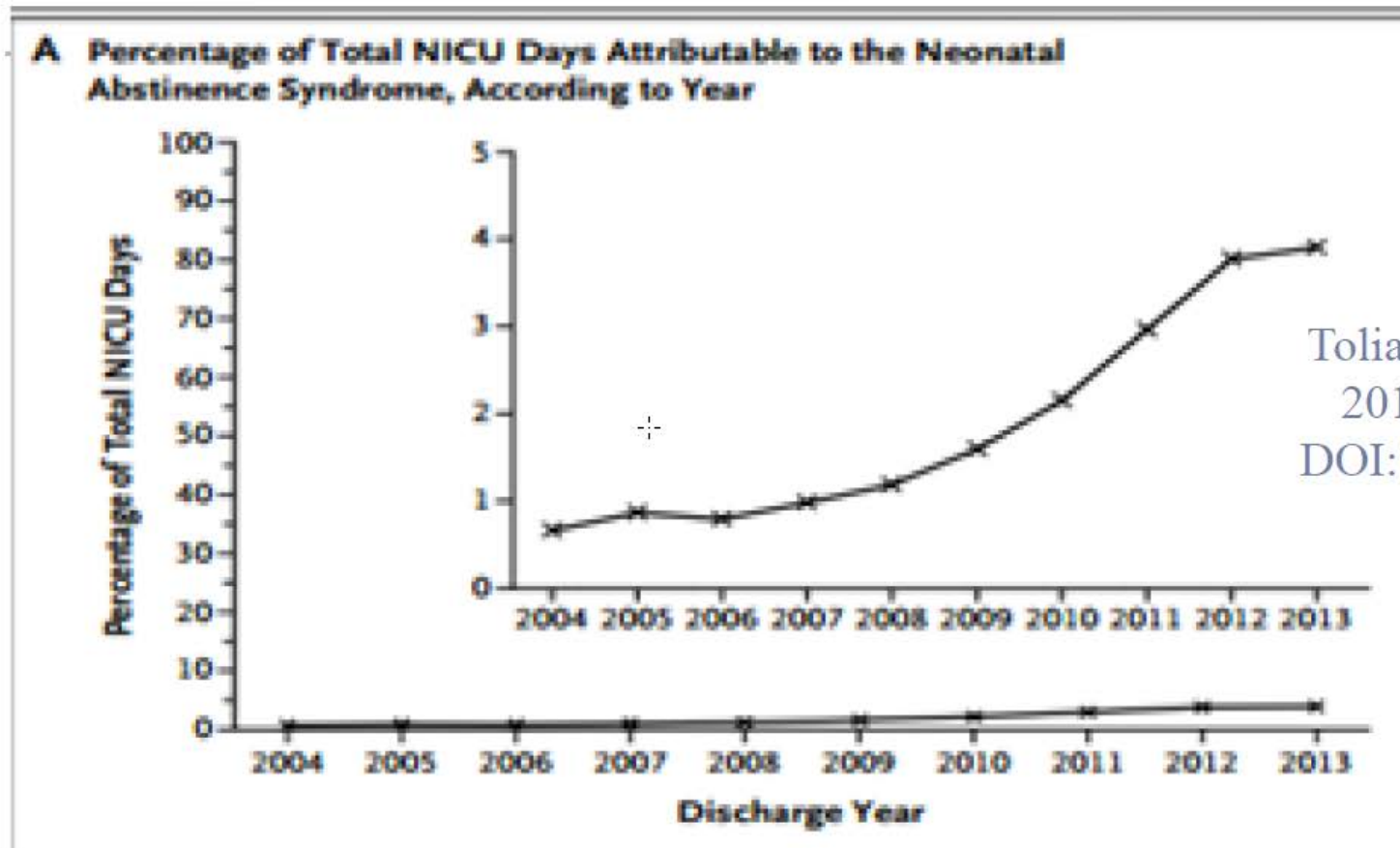
Haight SC, Ko JY, et al. *MMWR* August 10, 2018;67(31);845-9

# Increasing Incidence of NAS in US NICUs



Tolia VN, et al. NEJM  
2015;372;2118-26,  
DOI:10.1056/NEJMsal500439

# Increasing Incidence of NAS in U.S. NICUs



Tolia VN, et al. NEJM  
2015;372;2118-26,  
DOI:10.1056/NEJMsal  
500439



# Medical Problems Associated with Maternal Opioid Use (1)

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- ▶ STDs
- ▶ HIV
- ▶ Other infections
  - ▶ Endocarditis
  - ▶ Pneumonia
  - ▶ Cellulitis and abscesses
  - ▶ Sepsis
  - ▶ Tuberculosis
  - ▶ Urinary tract infections
  - ▶ Hepatitis (acute and chronic)
  - ▶ Osteomyelitis
- ▶ Abuse of other substances
- ▶ Mortality (OD, trauma)
  - ▶ More likely when combined with alcohol or sedative-hypnotics, benzodiazepines



ACOG, Committee Opinion 711. Obstet Gynecol, Aug 2017

## Medical Problems Associated with Maternal Opioid Use (2)

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- ▶ Anemia
- ▶ Thrombophlebitis and edema (swelling)
- ▶ Rh disease
- ▶ Nutritional deficiencies
- ▶ High risk behaviors to obtain drugs: theft, prostitution, violence with risk of being a victim of violence, or legal risk
- ▶ Mental Health Disorders
  - ▶ Depression and suicide
  - ▶ Coexisting psychiatric disease (anxiety, depression, bipolar, schizophrenia)

ACOG, Committee Opinion 711. Obstet Gynecol, Aug 2017

# Prenatal Opioid Abuse or Dependence and Obstetric Outcomes: 2007-2011 (Nationwide Inpatient Sample)

**Table 2.** Associations between Opioid Abuse or Dependence during Pregnancy and Obstetrical Outcomes: United States, 2007–2011

	Delivery Hospitalizations with Opioid Abuse or Dependence	Delivery Hospitalizations without Opioid Abuse or Dependence	Multivariable Odds Ratio* (95% CI)
	n (%)	n (%)	
Total	60,994	20,456,485	
Died during hospitalization	20 (0.03)	1,311 (0.006)	<b>4.6 (1.8–12.1)</b>
Cardiac arrest	24 (0.04)	1,873 (0.01)	<b>3.6 (1.4–9.1)</b>
Intrauterine growth restriction	4,157 (6.8)	431,032 (2.1)	<b>2.7 (2.4–2.9)</b>
Placental abruption	2,315 (3.8)	215,057 (1.1)	<b>2.4 (2.1–2.6)</b>
Length of stay >7 days	1,837 (3.0)	235,738 (1.2)	<b>2.2 (2.0–2.5)</b>
Preterm	10,538 (17.3)	1,506,941 (7.4)	<b>2.1 (2.0–2.3)</b>
Oligohydramnios	2,736 (4.5)	564,410 (2.8)	<b>1.7 (1.6–1.9)</b>
Transfusion	1,205 (2.0)	208,073 (1.0)	<b>1.7 (1.5–1.9)</b>
Stillbirth	727 (1.2)	124,607 (0.6)	<b>1.5 (1.3–1.8)</b>
Premature rupture of membranes	3,499 (5.7)	778,157 (3.8)	<b>1.4 (1.3–1.6)</b>
Cesarean delivery	22,130 (36.3)	6,768,679 (33.1)	<b>1.2 (1.1–1.3)</b>
Severe preeclampsia or eclampsia	722 (1.2)	289,668 (1.4)	<b>0.8 (0.7–0.9)</b>
Anesthesia complications	20 (0.03)	3,123 (0.02)	2.1 (0.8–5.3)
Cerebrovascular complications	37 (0.06)	5,079 (0.02)	2.0 (0.9–4.4)
Sepsis	273 (0.4)	79,169 (0.4)	1.3 (1.0–1.7)
Postpartum hemorrhage	1,866 (3.1)	589,811 (2.9)	1.1 (0.9–1.2)

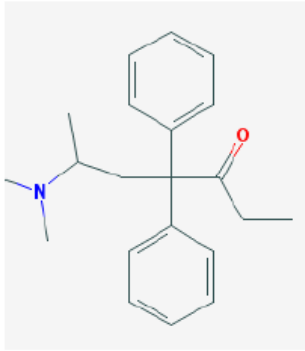
Statistically significant values are indicated in bold.

\* Adjusted for age group, race, primary payer, previous cesarean section, multiple gestation, and maternal preexisting conditions shown in table 1.

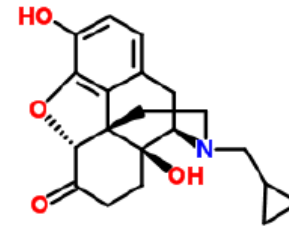
▶ Maeda A, et al. *Anesthesiology* 2014;121:1158-65

# Alternative Treatments for Narcotic Addiction

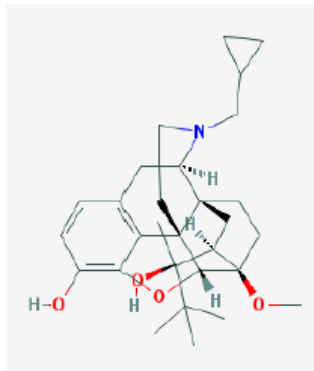
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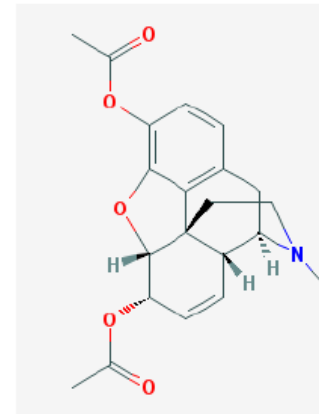
Methadone,  
Full agonist



Naltrexone,  
Opioid antagonist  
I



Buprenorphine  
,  
Partial agonist

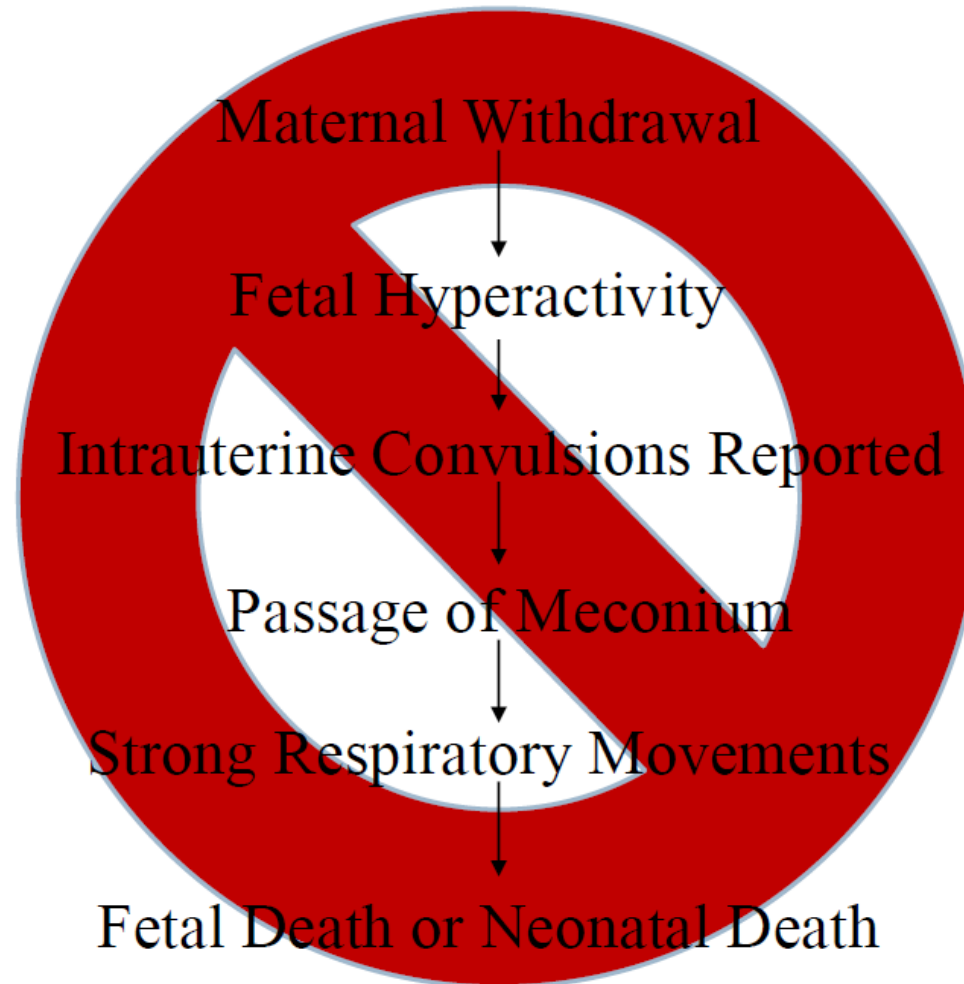


Heroin

Detox,  
of limited utility  
alone

# Fetal Withdrawal

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# Opioid Detoxification During Pregnancy

## A Systematic Review

*Mishka Terplan, MD, MPH, Hollis J. Laird, MPH, Dennis J. Hand, PhD, Tricia E. Wright, MD, MS, Ashish Premkumar, MD, Caitlin E. Martin, MD, MPH, Marjorie C. Meyer, MD, Hendrée E. Jones, PhD, and Elizabeth E. Krans, MD, MS*

**OBJECTIVE:** To systematically review maternal and neonatal outcomes associated with opioid detoxification during pregnancy.

**DATA SOURCES:** PubMed, PsycINFO, EMBASE, Cochrane, and ClinicalTrials.gov databases were searched from January 1, 1966, to September 1, 2016.

**METHODS OF STUDY SELECTION:** English-language studies that reported outcomes associated with opioid detoxification among pregnant women with opioid use disorder were included. Nonoriginal research articles (case reports, editorials, reviews) and studies that failed to report outcomes for detoxification participants were excluded. Bias was assessed using the Cochrane Collaboration's tool for assessing risk of bias and quality was

assessed using the U.S. Preventive Service Task Force Quality of Evidence scale.

**TABULATION, INTEGRATION, AND RESULTS:** Of 1,315 unique abstracts identified, 15 met criteria for inclusion and included 1,997 participants, of whom 1,126 underwent detoxification. Study quality ranged from fair to poor as a result of the lack of a randomized control or comparison arm and high risk of bias across all studies. Only nine studies had a comparison arm. Detoxification completion (9–100%) and illicit drug relapse (0–100%) rates varied widely across studies depending on whether data from participants who did not complete detoxification or who were lost to follow-up were included in analyses. The reported rate of fetal loss was similar among women who did (14 [1.2%]) and did not undergo detoxification (17 [2.0%]).

**CONCLUSIONS:** Evidence does not support detoxification as a recommended treatment intervention as a result of low detoxification completion rates, high rates of relapse, and limited data regarding the effect of detoxification on maternal and neonatal outcomes beyond delivery.

(*Obstet Gynecol* 2018;131:803–14)

DOI: 10.1097/AOG.0000000000002562

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*From the Departments of Obstetrics and Gynecology and Psychiatry, Virginia Commonwealth University, Richmond, Virginia; the Department of Obstetrics, Gynecology & Reproductive Sciences, Magee-Womens Research Institute, University of Pittsburgh, Pittsburgh, Pennsylvania; the Department of Obstetrics & Gynecology, Psychiatry & Human Behavior, Thomas Jefferson University, Philadelphia, Pennsylvania; the Department of Obstetrics, Gynecology, and Women's Health, University of Hawaii, Honolulu, Hawaii; the Department of Obstetrics and Gynecology, Northwestern University, Chicago, Illinois; the Department of Obstetrics and Gynecology, University of North Carolina, Chapel Hill, Chapel Hill, North Carolina; and the Department of Obstetrics, Gynecology & Reproductive Services, University of Vermont, Rutland, Vermont*

# Neonatal Abstinence Syndrome

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## ▶ Neurologic excitability

- ▶ Tremors
- ▶ Irritability
- ▶ Wakefulness
- ▶ High-pitched cry
- ▶ Increased tone
- ▶ Hyperactive reflexes
- ▶ Exaggerated Moro
- ▶ Seizures
- ▶ Increased sweating
- ▶ Frequent yawning and sneezing

## ▶ GI dysfunction

- ▶ Poor feeding
- ▶ Uncoordinated sucking
- ▶ Vomiting
- ▶ Diarrhea
- ▶ Dehydration
- ▶ Poor weight gain

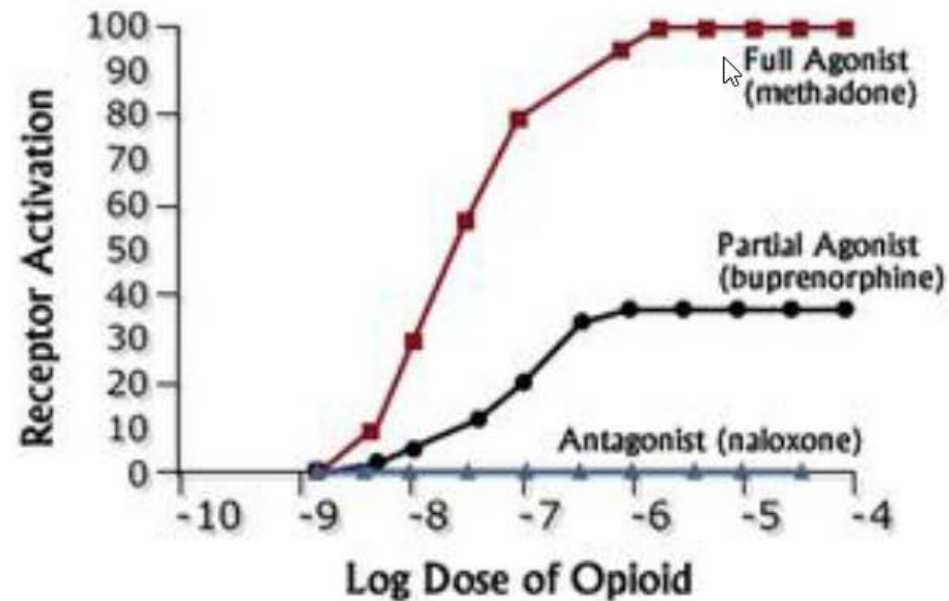
## ▶ Autonomic signs

- ▶ Increased sweating
- ▶ Nasal stuffiness
- ▶ Fever
- ▶ Mottling
- ▶ Temperature instability

Kocherlakota P. Neonatal Abstinence Syndrome. Pediatrics  
2014;134:e547-61

# Receptor Activation: Full Agonist, Partial Agonist, Antagonist

Receptor Activation:  
Full Agonist, Partial Agonist, Antagonist





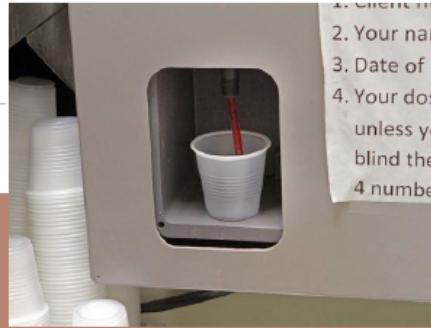
# Benefits of Medication for Opioid Use Disorder in Pregnancy (MOUD)

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- ▶ Decreases illegal opiate use and other drugs
- ▶ Slows the spread of HIV and other STDs
- ▶ Decreases spread of HCV
- ▶ Decreases crime
- ▶ Prevents fluctuation of maternal drug level over course of the day, decreases craving
- ▶ Reduces maternal mortality and severe morbidity
- ▶ May decrease risk of neonatal hypoxemia due to more stable intrauterine environment
- ▶ Improved birth weight compared to women on heroin
- ▶ Reduction in neonatal mortality compared to women on heroin
- ▶ Promotes retention in prenatal care

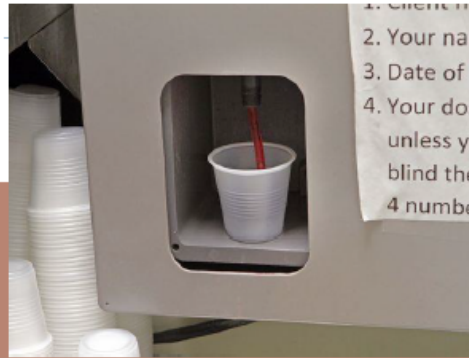
Therefore, narcotic replacement therapy with methadone (or buprenorphine) is the standard of care for pregnancy

# Methadone Vs Buprenorphine



	Methadone	Buprenorphine
Dosing	Daily	Once or twice daily
Route	Oral	Sublingual
Location	Federally licensed OTP	Office-based, by wavered physician or NP
Initiation	OTP or hospital <b>Withdrawal not necessary</b>	Office or hospital <b>Moderate withdrawal</b>
Retention	Greater (78%)	Lower (57.7%)
Diversion risk	++	+++
Risk of OD	++++	++ (especially with benzo)
Dose	60-150 mg	8-24 mg, ceiling effect
Convenience	Less	Much greater

# Methadone Vs Buprenorphine



**Methadone**

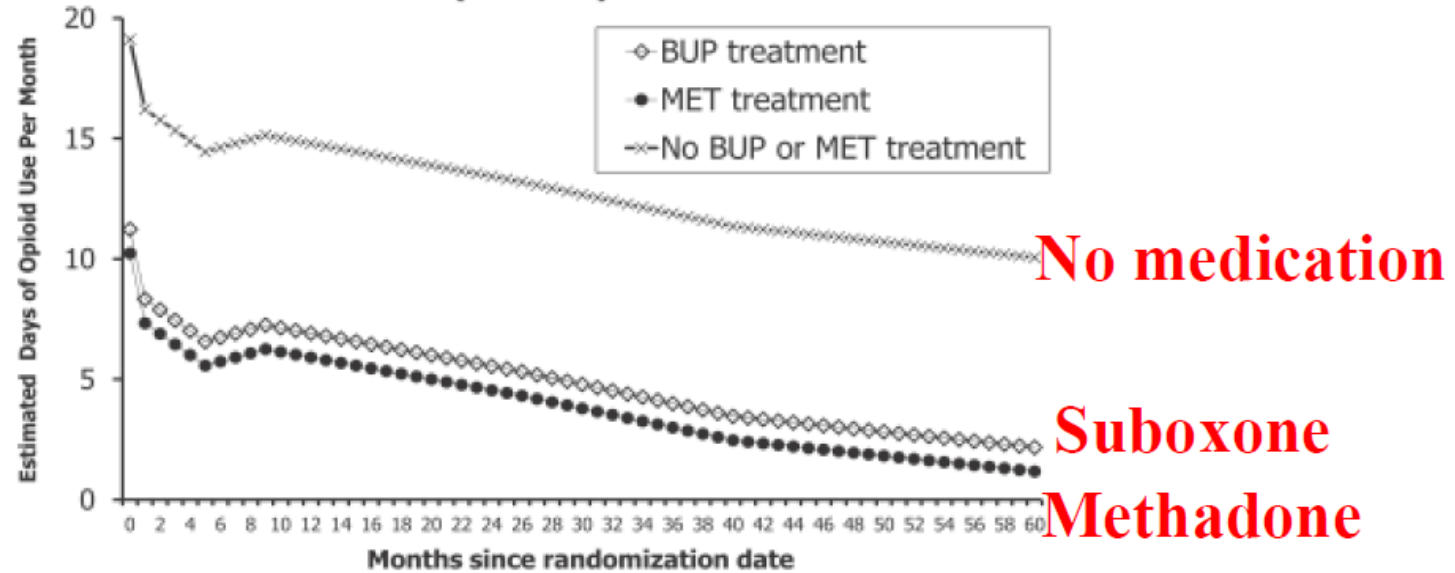


**Buprenorphine**

Counseling	On site	+/-
Treatment for Psych	No	+/-
Polysubstance Use	Preferred or for long-standing	May be better for newer users or prescription abuse
NAS	57%	47%
NAS treatment (d)	9.9 d	4.1 d
Breastfeeding safety	Safe	Safe
Neurodevelopmental outcome	Same as controls matched for age, race and SES	Limited data, appears safe

**Illicit Drug Use**

**Estimated Days of Opioid Use  
by the Types of Treatment Based on Model 4  
(N = 795)<sup>††</sup>**



<sup>††</sup>The number of participants in each type of treatment varied in each month and is therefore not indicated in the figure; on average over the follow-up period, each month there were about 14.2% of the participants in BUP treatment, 38.5% in MET treatment, and 46.9% in neither BUP nor MET treatment.

**Figure 4** Estimated days of opioid use by the types of treatment based on model 4 ( $n = 795$ )<sup>††</sup>. BUP:buprenorphine; MET:methadone.

Hser, Yih-Ing, et al. "Long-term outcomes after randomization to buprenorphine/naloxone versus methadone in a multi-site trial." *Addiction* (2016).

# Altered Pharmacokinetics of Methadone in Pregnancy

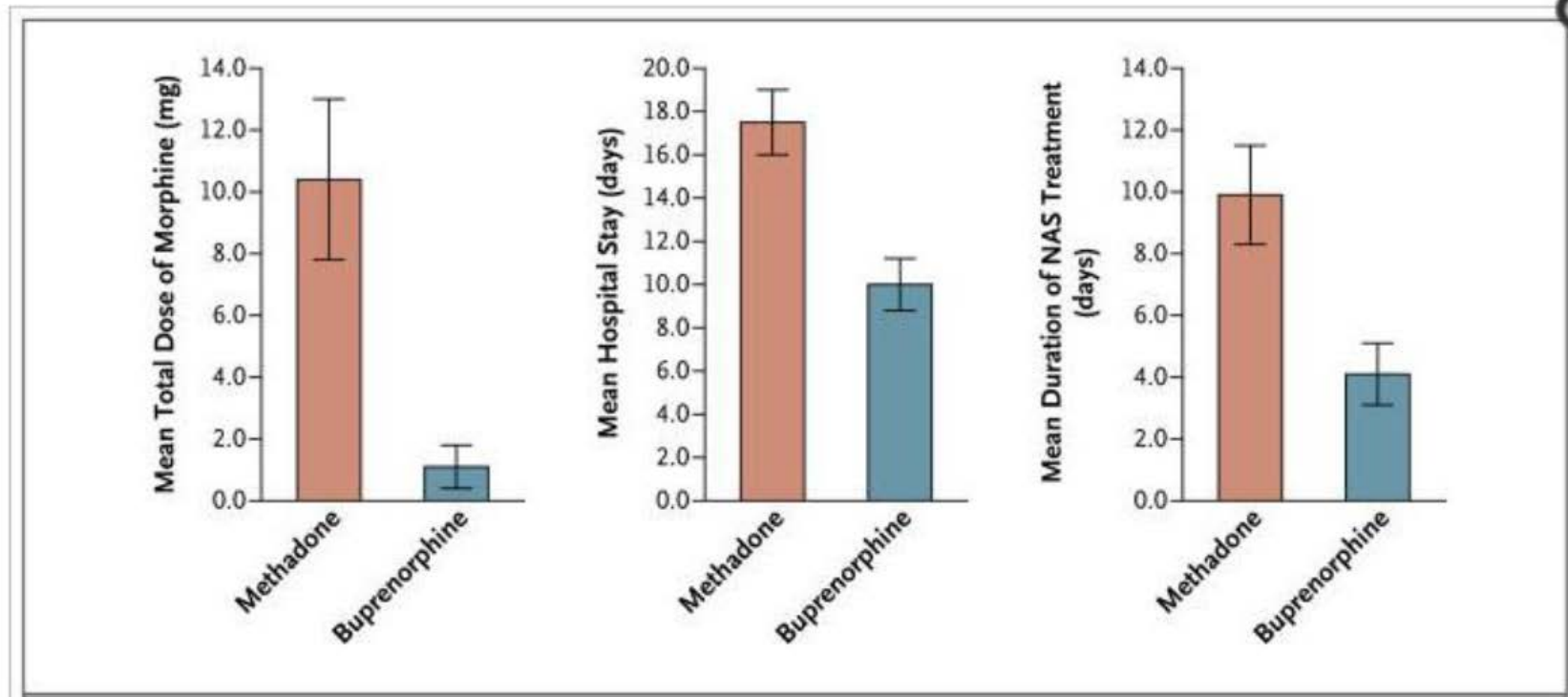
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- ▶ Increased plasma volume and volume of distribution
- ▶ Fraction of oral methadone absorbed is decreased
- ▶ Half-life decreased due to increased hepatic clearance
- ▶ Protein binding decreased
- ▶ High degree of individual variability in methadone metabolism in pregnancy
- ▶ Maternal symptoms predict serum trough more closely than dose

Drozdzick J, et al. AJOG 2002;187;1184-8

# Neonatal Abstinence After Methadone or Buprenorphine Exposure

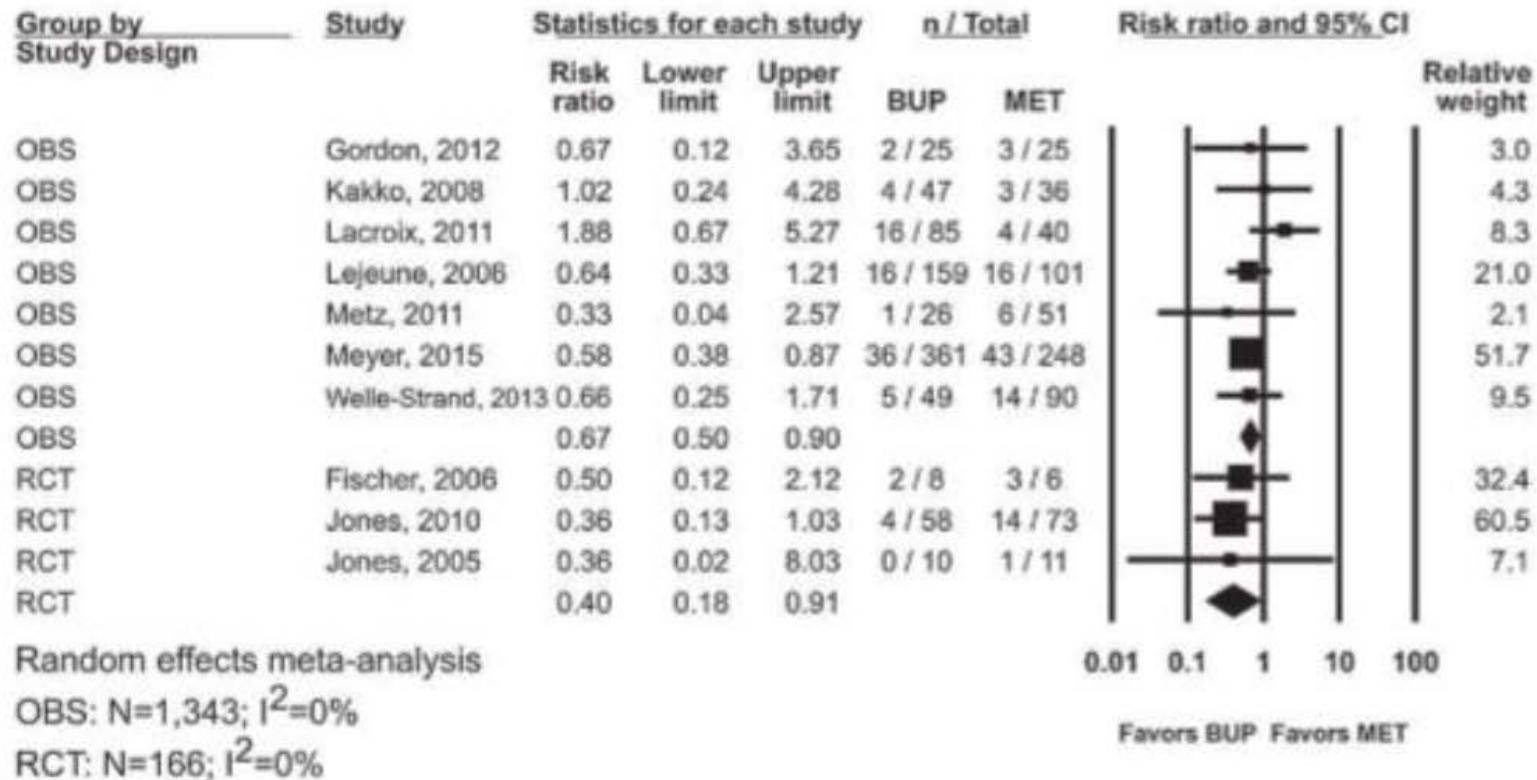
- ▶ Double Blind, multicenter RCT in 175 pregnant women



Jones HE, et al. NEJM 2010;363:2320-31

# Buprenorphine vs. Methadone, Meta-analysis

## Preterm birth



# Retrospective Methadone v. Buprenorphine: Newborn Outcomes

	Methadone (N=248)		Buprenorphine (n=361)		p
Infant Characteristics	n	M (SD) or (n%)	n	M (SD) or n (%)	
EGA at delivery	248	38.2 (2.5)	361	39.2 (2.2)	<0.001
Preterm (<37w)	248	43 (17%)	361	36 (10%)	<0.001
Birth weight (grams)	248	2899.7 (583.1)	361	3143.3 (578.9)	<0.001
HC (cm)	209	33.0 (2.0)	279	33.6 (2.1)	<0.001
Treated for NAS	245	106 (42%)	358	82 (23%)	<0.001
Days of NAS rx	106	133 ± 83	79	83 + 60	<0.001
LOS (d, EGA > 37w)	205	5.6 (2.8)	325	4.2 (12.6)	0.107
Breast Milk at discharge	247	156 (63%)	358	267 (75%)	0.003
Discharge to mother/family	248	237 (96%)	360	351 (98%)	0.189

► Meyer MC, et al. J Addict Med 2015;9:81-86



# Maternal Dose of MOUD

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- ▶ **Methadone**
  - ▶ Does NOT correlate with the degree of NAS
- ▶ **Buprenorphine**
  - ▶ Does NOT correlate with the degree of NAS

Cleary, et al. *Addiction* 2010;105(12);2017-84

# Opioid Use Disorder: Prenatal Care

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- ▶ Counseling (engagement in care)
- ▶ Identification and treatment of infectious diseases (HIV, HCV, STDs)
- ▶ Vaccinate for hepatitis A and B if serology negative
- ▶ Fetal well-being
  - ▶ Fetal growth
  - ▶ Non-stress testing when indicated
  - ▶ Investigate fetal morphology

# Opioid Use Disorder: Prenatal Care

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- ▶ Preterm labor prevention and education
- ▶ Neonatology (neonatal educator) consultation
- ▶ Lactation consultation
- ▶ Anesthesia consultation when indicated
- ▶ Identification and treatment of psychiatric comorbidities
- ▶ Drug interactions between buprenorphine, methadone and many other medications
- ▶ Urine Drug Screening

# Methadone Induction

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- ▶ 10-30 mg single initial dose (do not use scoring system to dose)
- ▶ Additional 5-10 mg if withdrawal symptoms reappear after 4 hours
- ▶ Max first day dose 40 mg
- ▶ After 40 mg reached, may treat symptoms
  - ▶ Clonidine 0.1 mg q 8 hr for anxiety
  - ▶ Loperamide (Immodium) 2-4 mg first dose
  - ▶ Ondansetron (Zofran) 4-8 mg q 8 hr prn
  - ▶ Diphenhydramine (Benadryl) 25 mg orally, q 6 hr prn (Use sparingly and not IV)



Baxter LE, et al. Safe Methadone Induction and Stabilization: Report of an Expert panel. J Addict Med 2013;7:377-386

# Methadone Induction

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- ▶ “start low, go slow”
- ▶ Risk of overdose
  - ▶ Single overdose in previously tolerant user who has been interrupted long enough to become intolerant
  - ▶ Accumulated toxicity with overly aggressive induction
  - ▶ Combining methadone with another drug: other opioids, sedative hypnotics or alcohol. Benzodiazepines most frequently reported in deaths with combined use.

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Baxter LE, et al. Safe Methadone Induction and Stabilization: Report of an Expert panel. J Addict Med 2013;7:377-386

# Methadone Stabilization

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- ▶ Maintenance in methadone program
- ▶ 60-150 mg/d generally adequate
- ▶ Least dose necessary to prevent withdrawal and relapse, but aim is not detoxification
- ▶ That dose is maintained, possibly increased if needed
- ▶ Over 100 mg/d dosing, trough testing valuable
- ▶ Consider twice daily dosing
- ▶ Multidisciplinary care

Baxter LE, et al. Safe Methadone Induction and Stabilization:  
Report of an Expert panel. J Addict Med 2013;7:377-386

# Buprenorphine Induction

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- ▶ Evaluate liver functions
- ▶ Consent process and treatment agreement
- ▶ Patient education
- ▶ Should be in mild to moderate withdrawal based on COWS, at least 7, > 12 preferable.
- ▶ There are no guidelines regarding the location of buprenorphine induction in pregnancy

# Buprenorphine Induction

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- ▶ To achieve moderate withdrawal, must be abstinent from opioid agonist to prevent precipitated withdrawal
  - ▶ Short-acting opioids (heroin, crushed oxycontin, percocet, vicodin, oxycodone) for 12 to 24 hours
  - ▶ Long acting opioids (oral oxycontin) for at least 24 hours
  - ▶ Methadone requires transition to short-acting narcotic or reduce to 20-30 mg daily for at least a week, then abstinent for 36 to 96 hours after last dose

BupPractice DATA Training 2013

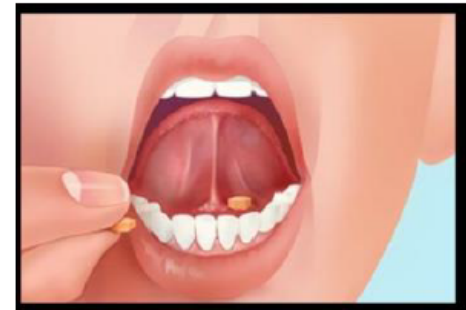
Clark N et al. Lintzeris, N et al. Presented at College on the Problems of Drug Dependence, 2006



# Buprenorphine Induction

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- ▶ Administer 4 mg dose SL and let dissolve completely, some give 2 mg
- ▶ Observe for 1-2 hours, give a second 2-4 mg dose if withdrawal symptoms reappear
- ▶ Total for first day should not exceed 8 mg (sometimes 12 mg)
- ▶ Day 2, dose depends on experience of day one. Begin 8-12 mg, can increase by 2 to 4 mg if withdrawal symptoms recur. Total daily dose should not exceed 16 mg.
- ▶ Most generally need 12 to 16 mg daily, ceiling effect seen between 10 to 16 mg.



BupPractice DATA 2000 Training, 2013

## Partial List of Meds Metabolized by Cytochrome P450 3A4

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### Inhibitors (may increase bup or methadone levels)

- ▶ Antihistamines
- ▶ Erythromycin
- ▶ Fluconazole
- ▶ Fluoxetine
- ▶ Metronidazole
- ▶ Omeprazol
- ▶ Paroxetine
- ▶ Most Protease Inhibitors


### Inducers (may decrease bup or methadone evels)

- ▶ Carbamazepine
- ▶ Dexamethasone
- ▶ Nevirapine
- ▶ Phenobarbital
- ▶ Phenytoin

*Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine (2007).  
"http://medicine.iupui.edu/clinpharm/ddis/clinical-table/" Accessed 2/26/15*

## Drug Interactions Between Methadone or Buprenorphine and Other Medications

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Medication	Methadone	Buprenorphine
AZT	Increase AZT, possible toxicity	No significant interaction
Darunavir	Possible Opiate withdrawal	
Nevirapine	Possible opiate withdrawal	May decrease levels
Fluconazole	Increased methadone	
Dextromethorphan	Delirium	
Carbamazepine Penytoin Phenobarbital	Opiate withdrawal	May decrease buprenorphine levels
St. John's Wort	Increased metabolism and elimination	Increased metabolism and elimination
Truvada	No interaction	No interaction

McCance-Katz EF, et al. Am J Addict 2010;19:4-16

# Methadone and Non-Stress Testing

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- ▶ Reduced baseline heart rate, variability, number of accelerations, FBMs and movements
- ▶ Higher number of nonreactive NSTs and longer time to reactivity
- ▶ No studies upon which to base recommendations for NSTs routinely
- ▶ Clearly indicated for additional indications (preeclampsia, IUGR)
- ▶ Best done before daily methadone dose or 4 hours after last dose

Jansson, et al. AJOG 2005;193:611-7

Anyaegbunam, et al. Gynecol Obstet Invest 1997;43:25-8

## Intrapartum Care on MAT

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- ▶ Ascertain fetal well-being
- ▶ Obtain urine toxicology prior to administration of medications
- ▶ Rapid HIV testing, if not already done
- ▶ HCV testing, if not already done
- ▶ **No Stadol (or Nubain)**
- ▶ Provide methadone or buprenorphine during labor
- ▶ Cesarean delivery for obstetric indications only
- ▶ Practice universal precautions
- ▶ For women on buprenorphine, specific pain management issues

# Anesthesia Considerations

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- ▶ **Buprenorphine** is partial mu agonist, with low intrinsic activity
- ▶ High receptor affinity, slow rates of dissociation.
  - ▶ Lower dose full agonists unlikely to provide pain relief
- ▶ Medication for MAT will not address labor pain
- ▶ Do not use partial agonist/antagonist such as Stadol or Nubain

# Anesthesia Considerations: Labor Analgesia

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- ▶ Neuraxial labor anesthesia preferred
  - ▶ Early
  - ▶ Some centers use Patient Controlled Epidural Analgesia
  - ▶ Nitrous oxide, if available
- ▶ For vaginal deliveries, epidural can be d/c after perineal repair I
  - ▶ For extensive 3<sup>rd</sup> or 4<sup>th</sup> degree repairs, epidural may be continued

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# Anesthesia Considerations: Cesarean

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- ▶ Preferred is spinal *or combined spinal- epidural*
  - ▶ Standard dosing for local anesthetic
  - ▶ General anesthesia only for usual obstetric and anesthesia considerations
- ▶ Post op
  - ▶ Pain management with consideration of whether treated with partial or full agonist for MAT
  - ▶ Continue MAT medication
  - ▶ Optimize non-narcotic medication
    - ▶ Ketorolac
    - ▶ IV acetaminophen
    - ▶ Sometimes gabapentin
    - ▶ Scheduled dosing

# Post-Cesarean Use of Narcotics for Pain Management

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- ▶ **Higher dose of narcotic generally needed**
  - ▶ Average 70% increase for methadone-maintained women
- ▶ **Hydromorphone and fentanyl have greater affinity for mu receptor**
- ▶ **After first 24 hr post-op, need for narcotic should decrease**
- ▶ **Consider dividing buprenorphine to lower dose, more frequently (i.e. q 6 hr)**
- ▶ **If had general, use hydromorphone PCA with continuous pulse-ox. If insufficient and needs fentanyl, requires ICU**
- ▶ **Transition to oxycodone when tolerating po**

Meyer M, et al Obstet Gynecol 2007;110:261-6

Jones HE, et al. Am J Drug Alcohol Abuse 2009;35:151-6

- ▶ Sens S, et al. Curr Pain Headache Rep 2016;6:20:16(1-8)

## Post-Partum

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- ▶ Encourage breastfeeding when appropriate
- ▶ Avoid narcotics for vaginal deliveries
- ▶ Pain management protocol for cesarean delivery
- ▶ Infants stay in the hospital for 5-7 days
- ▶ Rooming in (always)
- ▶ Upon maternal discharge, we provide courtesy room
- ▶ Consistency of care from antepartum to post-partum
  - ▶ MFM
  - ▶ WISH Social workers

# Mother-Infant Dyad

## The Substance Exposed Infant

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- ▶ Mother is the best treatment for baby whenever possible
- ▶ Non-pharmacologic treatment for NAS
  - ▶ Rooming in
  - ▶ Swaddling
  - ▶ Rocking
  - ▶ Low stimulation
  - ▶ Small and frequent feeds
  - ▶ Frequent burping
  - ▶ Skin-to-skin
- ▶ High calorie formulas or supplements

Holmes AV et al. Pediatrics 2016;137:e1-9  
Kocherlota. Pediatrics 2014;134:e547-61

# Mother-Infant Dyad

## The Substance Exposed Infant

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- ▶ **Finnegan scoring versus ESC**
  - ▶ Can the baby eat?
    - ▶ At least one ounce per feed
  - ▶ Can the baby sleep?
    - ▶ For at least an hour
  - ▶ Can the baby be consoled?
    - ▶ Within 10 minutes
- ▶ **ESC results in less use of morphine, decreased LOS and no adverse outcomes**
- ▶ **Yale study, decreased hospital costs for newborn from \$44,824 to \$10,289, and average LOS decreased from 22.4 to 5.9 d**

Grossman M, et al. Hospital Pediatrics 2018;8:1-6  
Grossman M, et al. Pediatrics 2017;139 (6):e20163360

# Breastfeeding and Methadone and Buprenorphine

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- ▶ AAP considers methadone and buprenorphine as compatible with breastfeeding regardless of dose
- ▶ 124 women receiving opioid maintenance
  - ▶ High initiation rates (77%)
  - ▶ But also high cessation rates
  - ▶ Breastfeeding reduced the need for withdrawal treatment in opioid-exposed infants on opioid maintenance therapy (53% vs 80%)
  - ▶ Infants on BMT and MMT who breastfed had shorter treatment for NAS

Welle-Strande, GK, et al. Acta Paediatrica 2013;102:1060-6

## Conclusions, Treatment Options for Opioid Addiction in Pregnancy

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- ▶ Opioid replacement medication discontinuation would be indicated rarely, if ever
- ▶ Methadone is the only FDA approved medication for narcotic replacement therapy in pregnancy, but buprenorphine is also excellent for a first line therapy
- ▶ Care for this population requires a multidisciplinary approach
- ▶ Breast-feeding should be encouraged in women abstinent from illicit opioids