PERINATAL OPIOID USE DISORDER

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DISCLOSURES

- I receive clinical trial support from Neuronetics.
- I have received clinical trial support from Sage Therapeutics.
- Neither will be discussed today.

OBJECTIVES

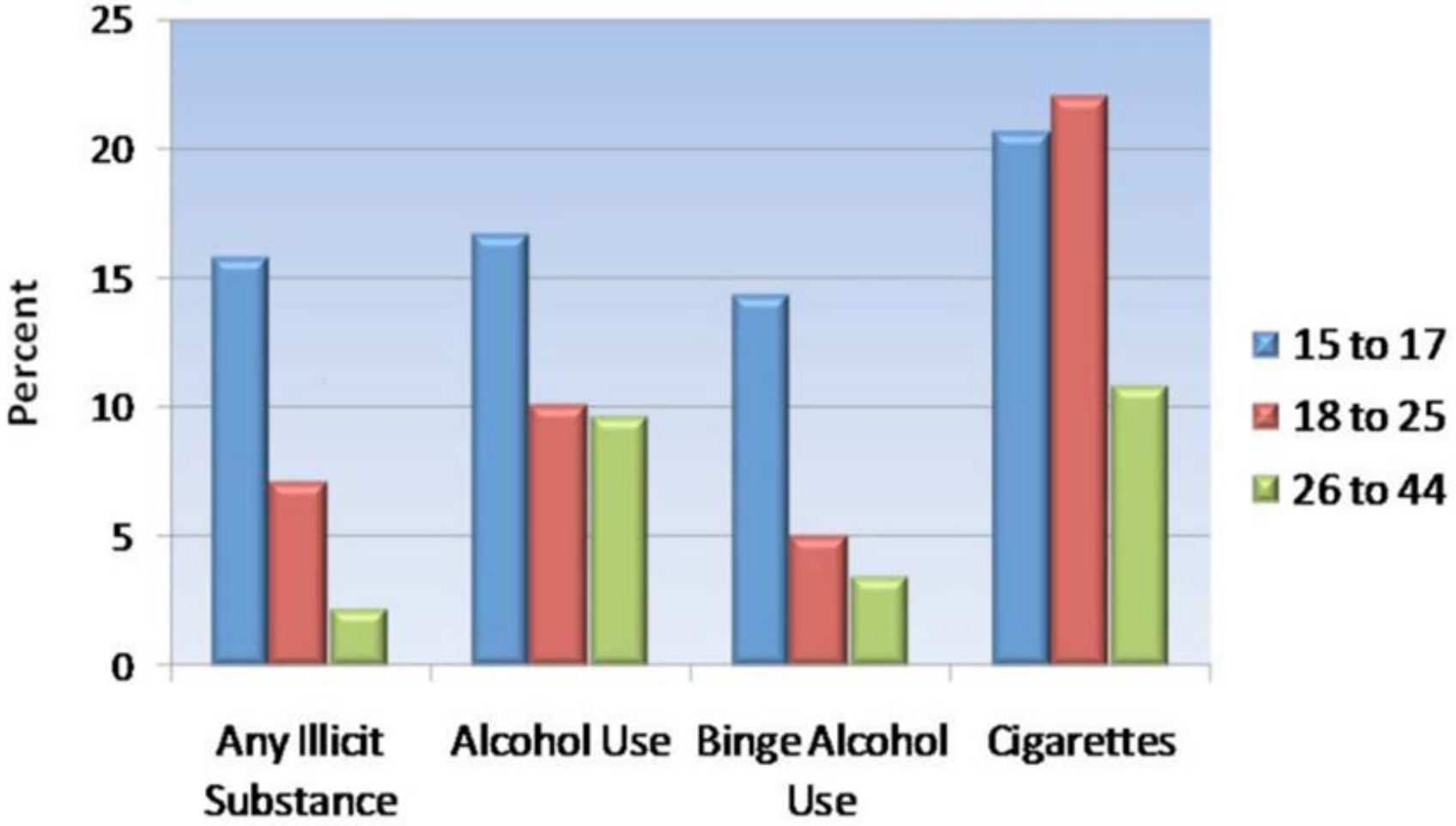
1. Define the impact of opioid use disorder during pregnancy
2. Explore the obstetrical and neonatal complications of maternal opioid use disorder
3. Discuss treatment options for perinatal opioid use disorder

SUBSTANCE USE DURING PREGNANCY

- An average of 4 million pregnancies annually in the United States
- Up to 27.5% of pregnant women reports licit use within the past 30 days
  - ~1.1 million per year
- Up to 5% of pregnant women report illicit drug use within the past 30 days
  - ~200,000 per year

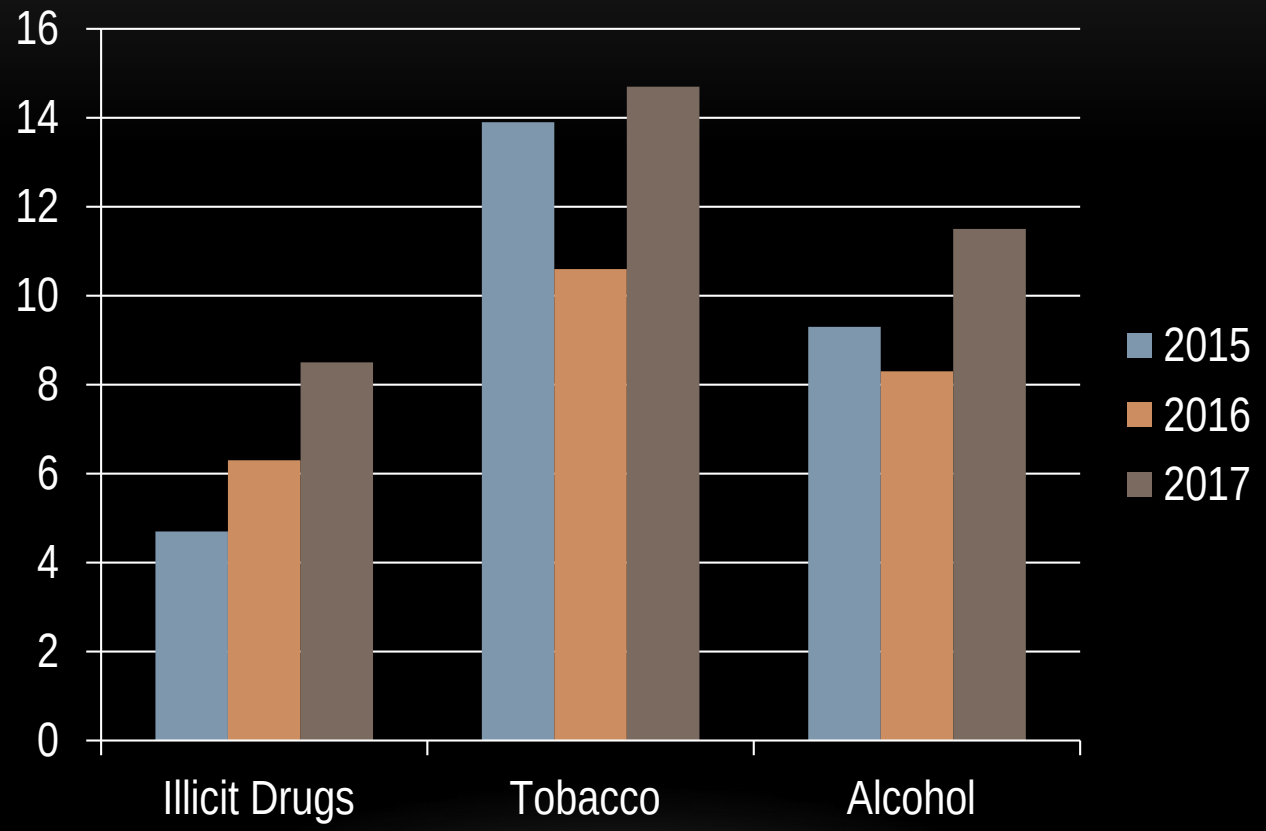
Current Substance Use Among Pregnant Women

Aged 15-44, by Age, 2008-2009 Combined

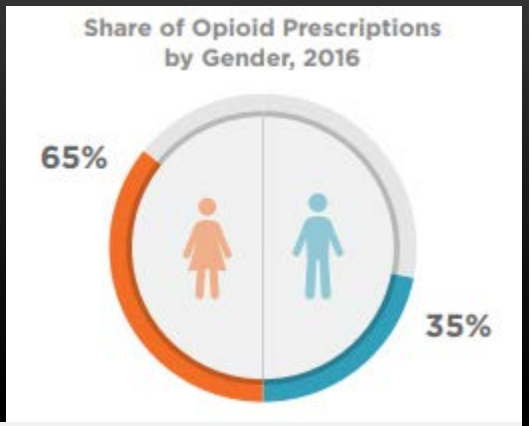


Source: SAMHSA, NSDUH, 2010

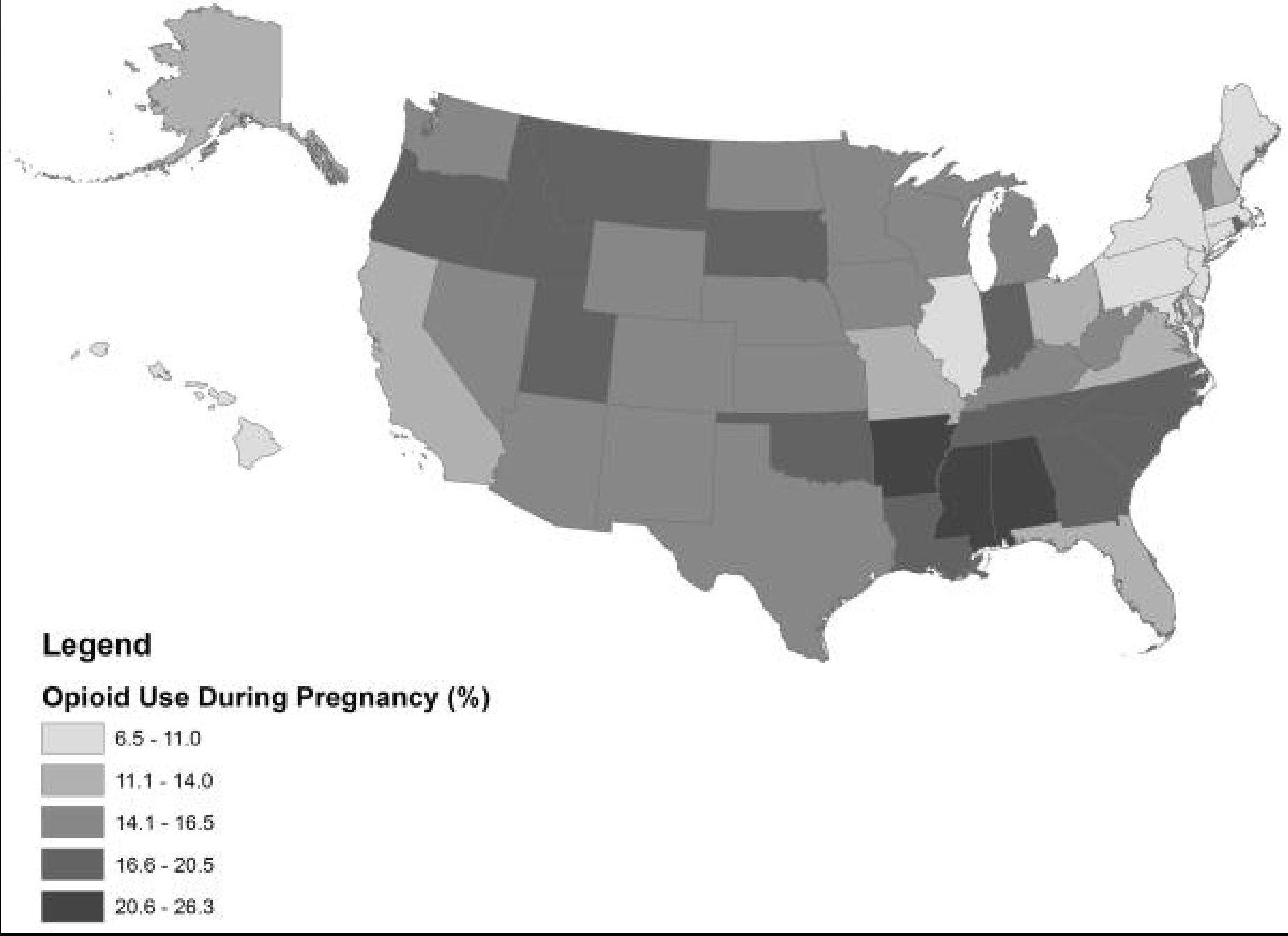
SUBSTANCE USE IN PAST MONTH AMONG PREGNANT WOMEN AGED 15-44



OPIOID EPIDEMIC AND WOMEN



Women 40-59 years old received the greatest number of opioid prescriptions overall, almost twice as many as their male counterparts. This age group also includes the female demographic (ages 45-54) most at risk of dying from an overdose of prescription opioids.[ix]


Legend
Opioid Use During Pregnancy (%)
6.5 - 11.0
11.1 - 14.0
14.1 - 16.5
16.6 - 20.5
20.6 - 26.3

NAS CASES PER 1000 DELIVERY HOSPITALIZATIONS IN THE UNITED STATES

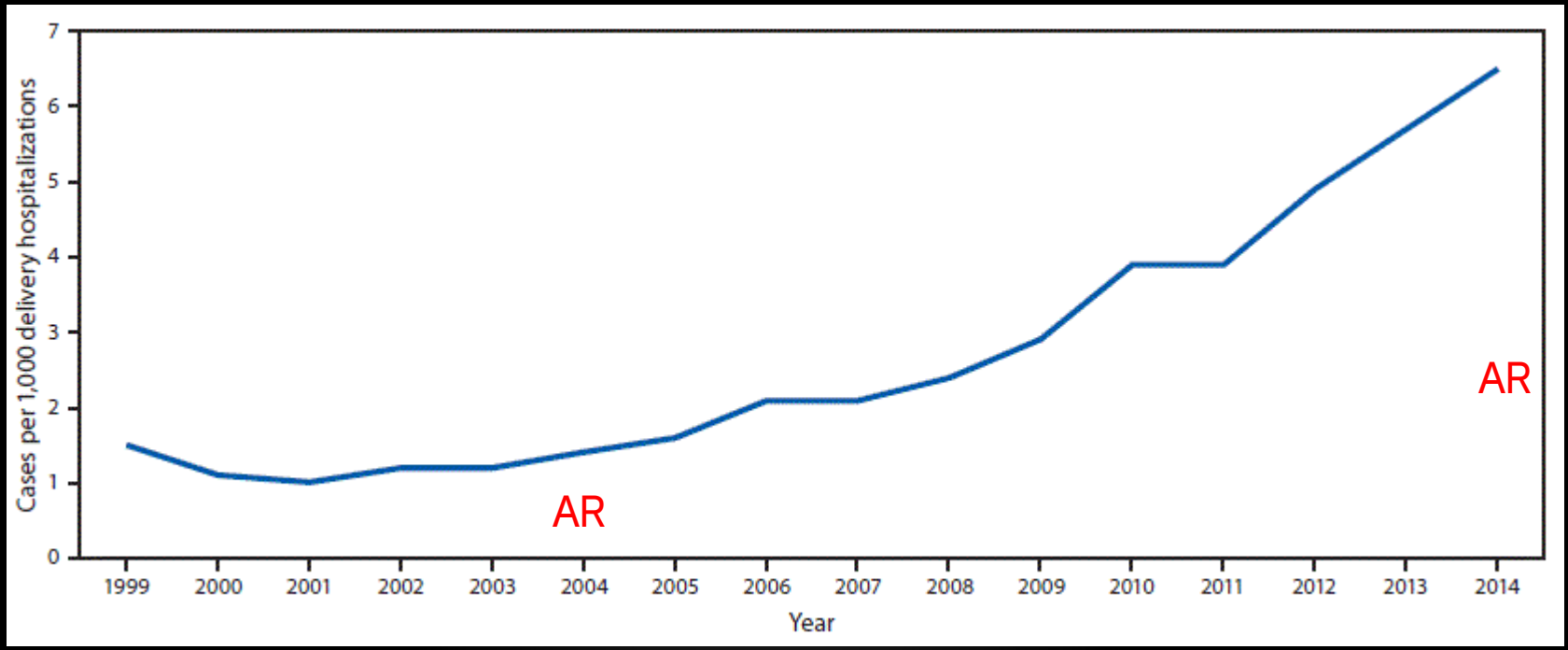


Table III. Adverse Effects of Exposure during Pregnancy

	Tobacco	Alcohol	Benzodiazepines	Opioids	Amphetamines	Cannabis	Cocaine
Miscarriage	+			+	+	+	+
Teratogenic		+	+				
Fetal Morbidity		+	+		+	+	+
Perinatal Mortality	+	+	+	+			
IUGR	+	+					
PROM	+	+					
Preterm Delivery	+	+		+	+		
LBW	+	+		+	+	+	
Neonatal Resp.			+	+			
Neonatal Withdrawal		+	+	+			
Developmental Problems	+	+				+	+

RESEARCH LIMITATIONS

- Data is limited
  - Ethics
  - Legal

- Potential confounders:
  - Other exposures
  - Environment
  - Comorbid psychiatric illnesses
  - Comorbid mental illnesses

OPIOID USE & PERINATAL OUTCOMES

Obstetrical Outcomes

- Insufficient prenatal care
- Insufficient self care
  - Poor nutrition
  - Possible exposure to STDs, violence, and legal consequences
- Increased risk of:
  - Placental abruption
  - Preterm Labor

Neonatal Outcomes

- Inconsistent evidence of increased risk for birth defects
  - Cardiac defects
  - Neural tube defects
- Increased risk of:
  - Fetal growth restriction
  - Fetal death
- Neonatal Abstinence Syndrome (NAS)

OPIOID USE & INFANT/CHILD OUTCOMES

- Kaltenback K an Finnegan LP. "Developmental outcome of children born to methadone maintained women: A review of longitudinal studies" Neurobehav Toxicol Teratol 1984;6(4):271-275
  - No significant differences in cognitive development up to 5 years of age

- HEALthy Brain and Development (HBCD) Study
  - Establish a large cohort of pregnant women significantly affected by the opioid crisis and follow them and their children for at least 10 years.
  - Help understand normative childhood brain development as well as the long-term impact of prenatal and postnatal opioid and other drug and environmental exposures.

HOW DO YOU DIAGNOSE?

- American College of Obstetrics and Gynecology guideline supports verbal, universal screening of all pregnant patients at initial visit

- SBIRT: Screening, Brief Intervention, and Referral to Treatment

- Screening
  - Validated verbal screening tools: 4Ps, NIDA Quick Screen, CRAFFT
- Brief Intervention
  - Providing feedback and advice on the impact of substance use on pregnancy
- Referral

SCREENING TOOLS

4 Ps

- **Parents**: Did any of your **parents** have a problem with alcohol or other drug use?
- **Partner**: Does your **partner** have a problem with alcohol or other drug use?
- **Past**: In the **past**, have you had difficulties in your life because of alcohol or other drugs, including prescription medications?
- **Present**: In the **past month**, have you drunk any alcohol or used other drugs?

CRAFFT (Under 26 y/o)

- C – Have you ever ridden in a CAR driven by someone (including yourself) who was high or had been using alcohol or drugs?
- R – Do you ever use alcohol or drugs to RELAX, fell better about yourself or fit in?
- A – Do you ever use alcohol or drugs while you are by yourself or ALONE?
- F – Do you ever FORGET things you did while using alcohol or drugs?
- F – Do your FAMILY or FRIENDS ever tell you that you should cut down on your drinking or drug use?
- T – Have you ever gotten in TROUBLE while you were using alcohol or drugs?

LEGAL ISSUES

- ACOG recommends advocacy for patients to decriminalize perinatal substance use in order to promote adequate recognition and treatment

- Nationally
  - Child abuse under civil child-welfare statutes (23 states and DOC)
  - Grounds for civil commitment (3 states)
  - Health care professionals must report suspected drug use (24 states and DOC)
  - Health care professionals must test if drug use is suspected (8 states)
- Arkansas
  - Child Maltreatment Act (i.e. Garrett's Law)
    - Arkansas code Annotated 12-18-101 et seq
    - Mandatory reporting if identified in mother at labor & delivery or if in the neonate
      - Division of Child and Family Services opens investigation

GARRETT'S LAW IN ARKANSAS

Number of reports has steadily increased from 2006 to present

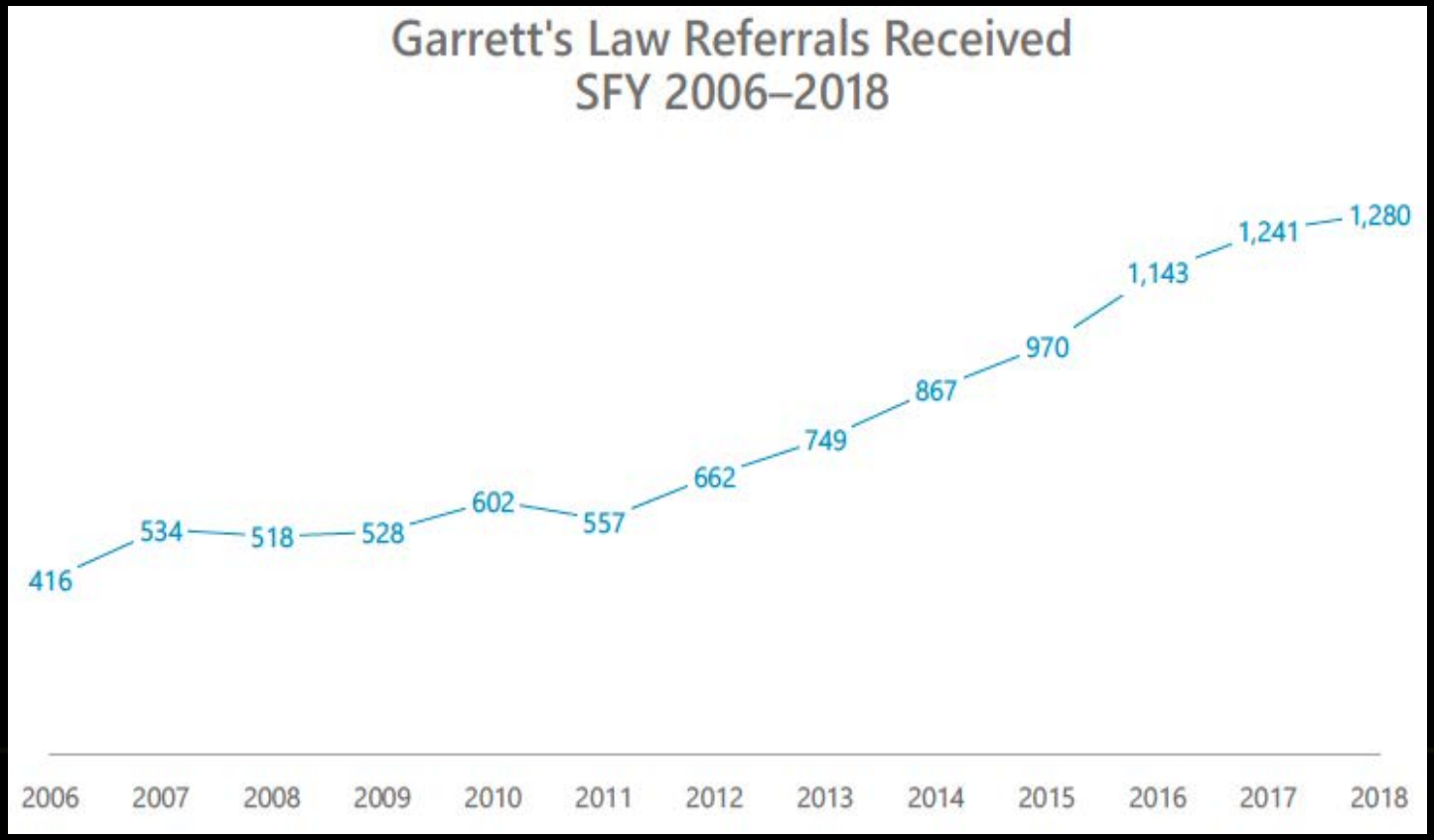


Table 2

Percentage of GL Reports in Which Drug Was Cited SFY 2015–2018

Type of Drug	SFY 2015	SFY 2016	SFY 2017	SFY 2018
Marijuana	65%	64%	66%	65%
Amphetamines/Methamphetamines	24%	26%	25%	26%
Opiates	19%	18%	18%	18%
Benzodiazepines	12%	10%	10%	10%
Cocaine	6%	6%	5%	4%
Barbiturates	1%	2%	1%	1%
Hallucinogens	1%	1%	1%	1%
Prescriptions	1%	1%	1%	<1%
Number of Drugs Cited*	**1,252**	**1,460**	**1,552**	**1,616**
Number of Reports	**970**	**1,143**	**1,241**	**1,280**

*Multiple drugs can be mentioned in a given report.

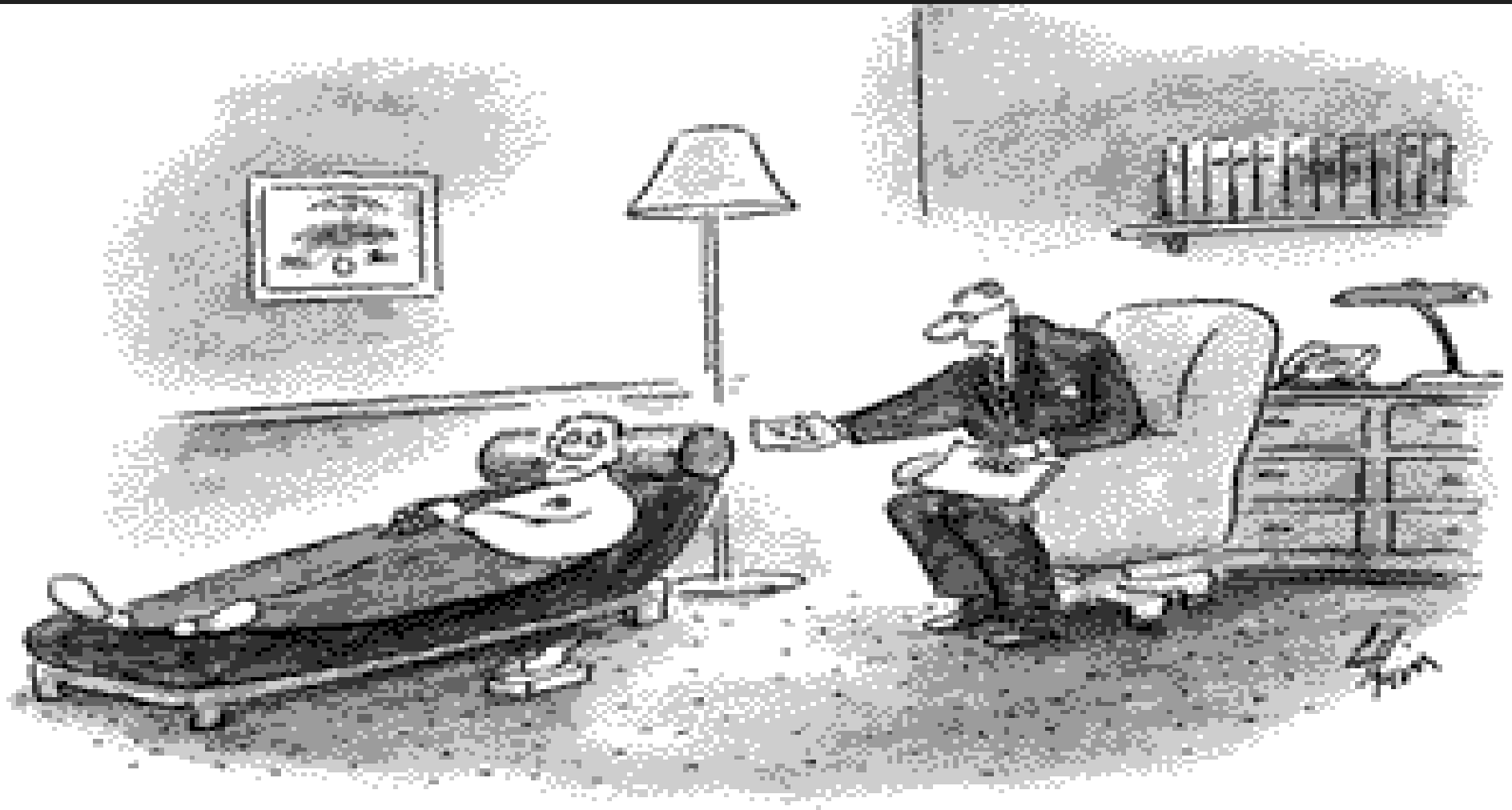
GENERAL TREATMENT OPTIONS FOR OUD

- Nothing
- Medically assisted detoxification
- Inpatient substance abuse rehabilitation
- Outpatient substance abuse rehabilitation
- Opioid agonist pharmacotherapy (Medication Assisted Treatment)
- Use alone or in combination
- Need to address any co-occurring neuropsychiatric illnesses
- Assessment and treatment of nicotine use disorder

- Medication assisted treatment during pregnancy is standard of care for anyone at risk of relapse
  - Detoxification alone results in increased risk for relapse, overdose, and adverse perinatal outcomes
- Goal = reduce risk of relapse and increased adherence to prenatal care
- "Neonatal abstinence syndrome is an expected and treatable condition"

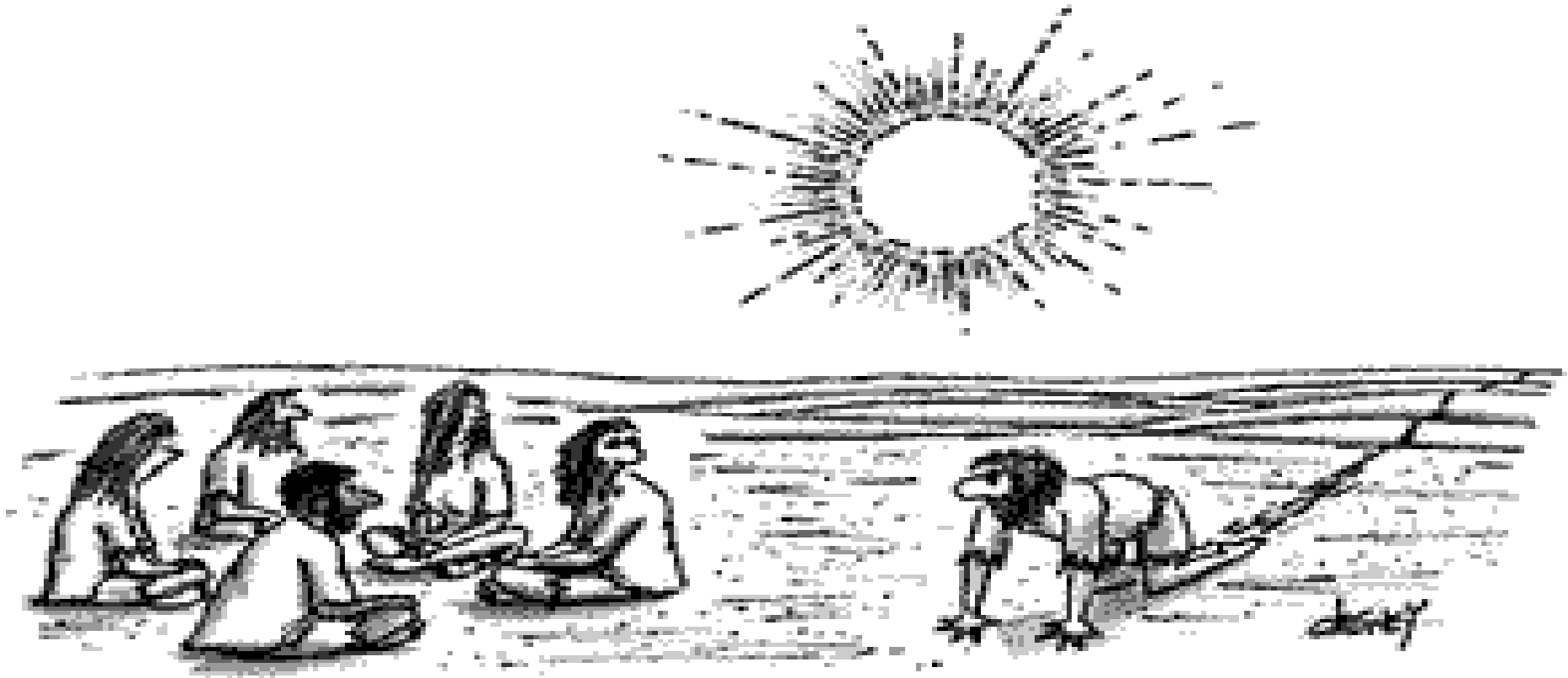
MEDICATION ASSISTED TREATMENT (MAT)

MEDICATION/PSYCHOSOCIAL



"I medicate first and ask questions later."

MEDICATION/PSYCHOSOCIAL



"Sorry, no water. We're just a support group."

MEDICATION ASSISTED TREATMENT

Opioid Agonist Therapy

- Methadone or Buprenorphine
- Prevents opioid withdrawal symptoms
- Reduce relapse
- Improves adherence to prenatal care

Counseling and Behavioral Therapy

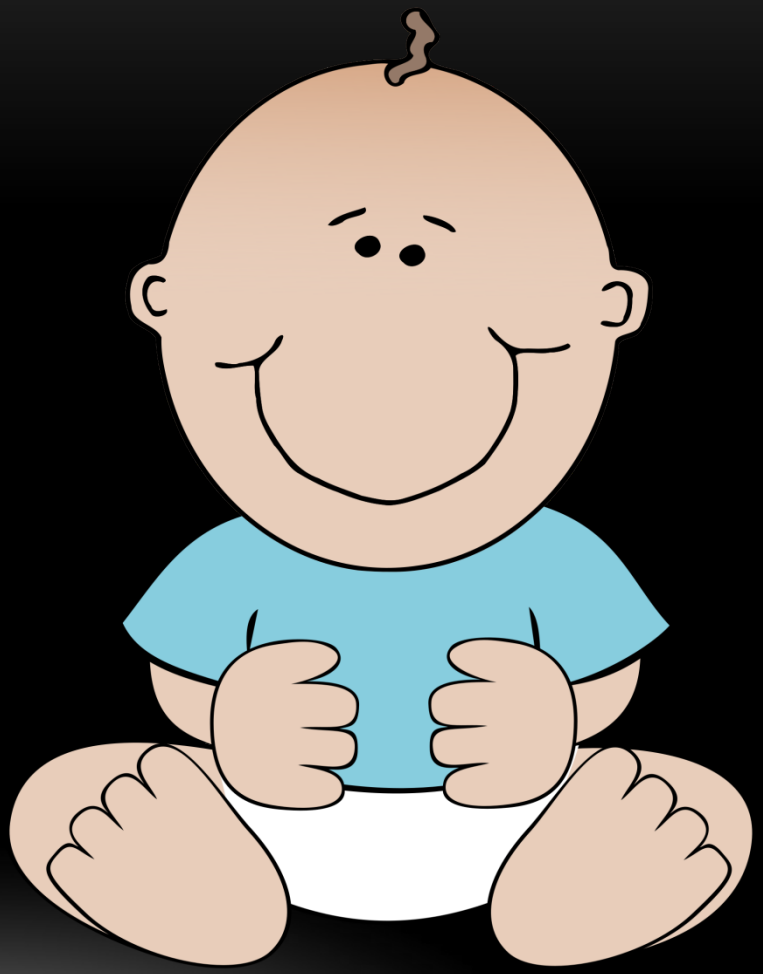
- Promotes relapse prevention and rehabilitation

NEONATAL ABSTINENCE SYNDROME (NAS)

- Treatable condition
- Most commonly referred to as the largest risk when discussing OUD and MAT during pregnancy
- At birth, all opioid-exposed neonates should be monitored for signs and symptoms of NAS
  - No guidelines exists
  - Finnegan scale, ESP
  - Similar ‘syndrome’ is seen with other exposures

NAS

- CNS disturbances
  - Tremors
  - Sneezing and/or yawning
  - Disturbed sleep
  - Excessive or high pitched crying
  - Seizures
- GI disturbances
  - Excessive sucking
  - Poor feeding and weight gain
  - Vomiting/Diarrhea
- Autonomic
  - Sweating
  - Low grade feer
  - Nasal suffiness



Drug	Signs	Onset	Duration
Alcohol	Hyperactivity, crying, irritability, poor suck, tremors, seizures; onset of signs at birth, poor sleeping pattern, hyperphagia, diaphoresis	3–12 h	18 mo
Barbiturates	Irritability, severe tremors, hyperacusis, excessive crying, vasomotor instability, diarrhea, restlessness, increased tone, hyperphagia, vomiting, disturbed sleep	1–14 d	4-6 mo
Caffeine	Jitteriness, vomiting, bradycardia, tachypnea	At birth	1-7 d
Chlordiazepoxide	Irritability, tremors; signs may start at 21 d	Days–weeks	9 mo
Clomipramine	Hypothermia, cyanosis, tremors; onset 12 h of age		4 d
Diazepam	Hypotonia, poor suck, hypothermia, apnea, hypertonia, hyperreflexia, tremors, vomiting, hyperactivity, tachypnea (mother receiving multiple drug therapy)	Hours–weeks	0–66 d
Hydroxyzine	Tremors, irritability, hyperactivity, jitteriness, shrill cry, myoclonic jerks, hypotonia, increased respiratory and heart rates, feeding problems, clonic movements (mother receiving multiple drug therapy)		5 wk
SSRIs	Crying, irritability, tremors, poor suck, feeding difficulty, hypertonia, tachypnea, sleep disturbance, hypoglycemia, seizures	Hours–days	1–4 wk

Figure 2. Neonatal abstinence syndrome diagnoses per 1,000 hospital births, Arkansas residents, 2010 - 2014*

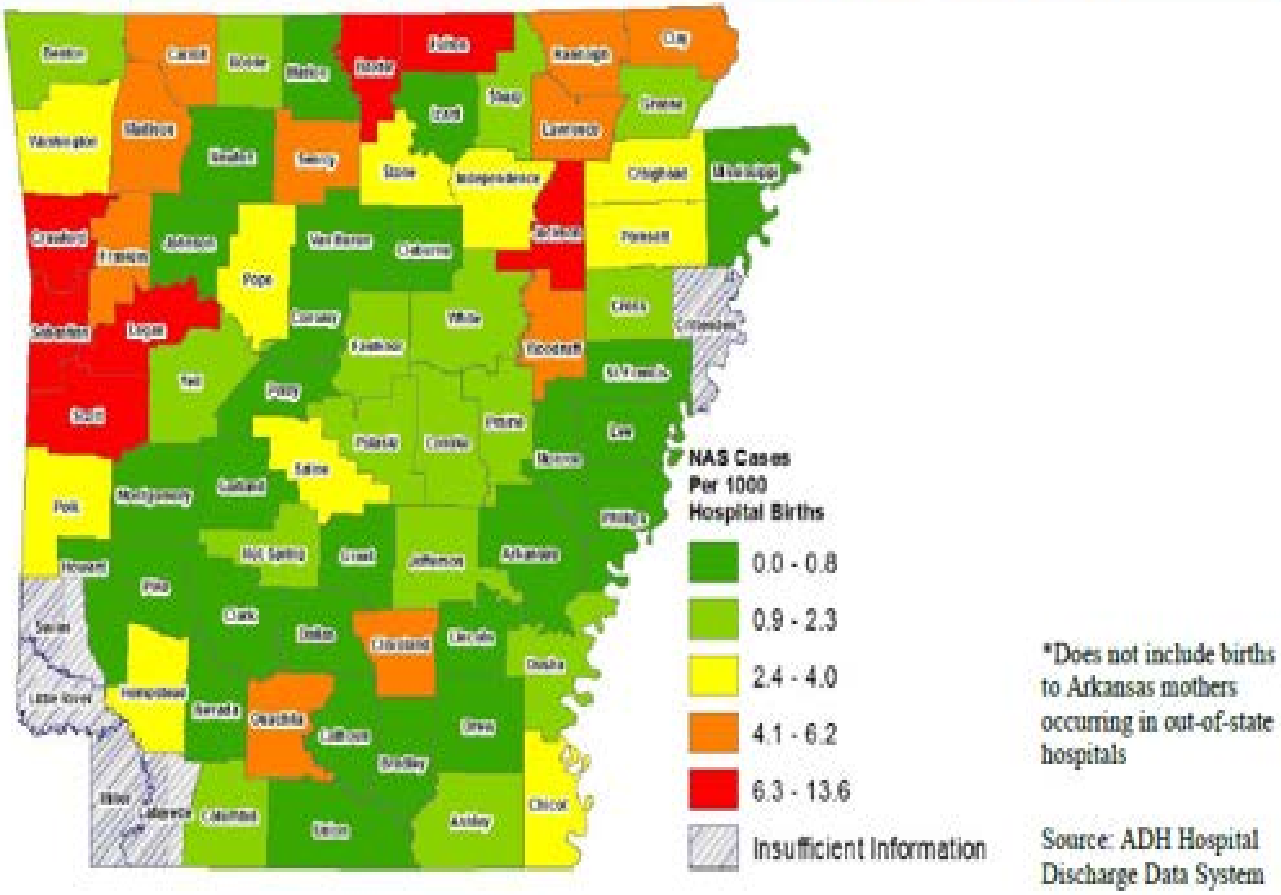


Table 1. Neonatal abstinence syndrome diagnoses: Demographic characteristics and insurance, Arkansas residents, 2014*

		Number	Percent**	Rate per 1,000
Race***	White	100	91.7%	4.1
	Non-white	9	8.3%	1.1
Ethnicity	Hispanic	12	11.0%	2.5
	Non-Hispanic	95	87.2%	3.4
Insurance	Medicaid	83	76.2%	4.7
	Private	15	14.8	1.5
	Other or unknown	11	10.1	2.1

*Totals vary due to missing values.
**Percentages may not add up to 100 due to missing values.
***Non-whites merged into a single category to ensure confidentiality.

Source: ADH Hospital Discharge Data System

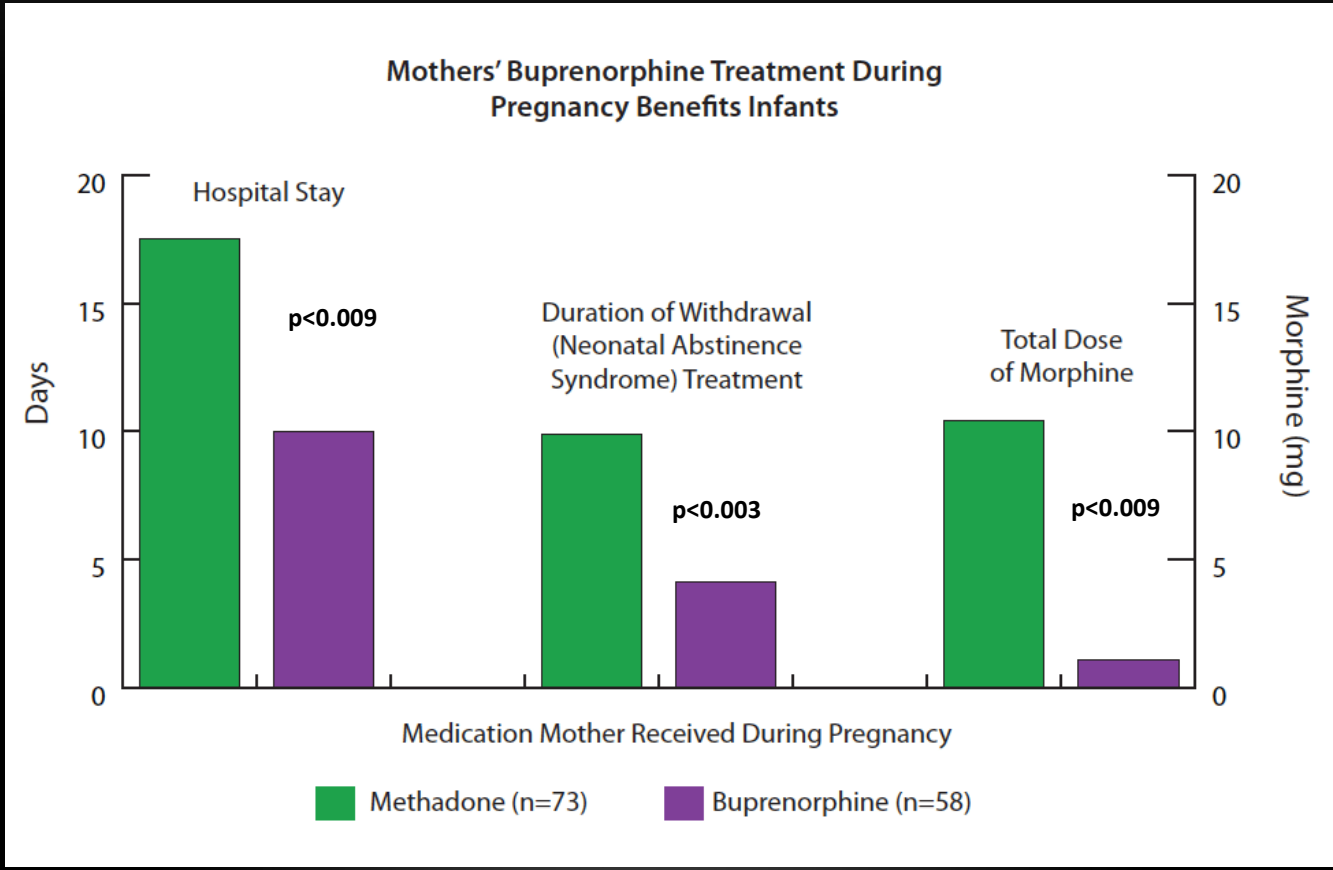
Aram J, et al., (2019) *Journal of the Arkansas Medical Society*

MOTHER STUDY

- MOTHER Study (Jones, et al, 2010) is largest RCT to date

- Randomization of 175 pregnant women with opioid dependence to methadone or buprenorphine
  - Double blind, double-dummy study
  - Primary outcomes: number of neonates requiring treatment for NAS, peak NAS score, total amount of morphine needed, length of hospital stay, and neonatal head circumference
  - Women were similar on all baseline characteristics

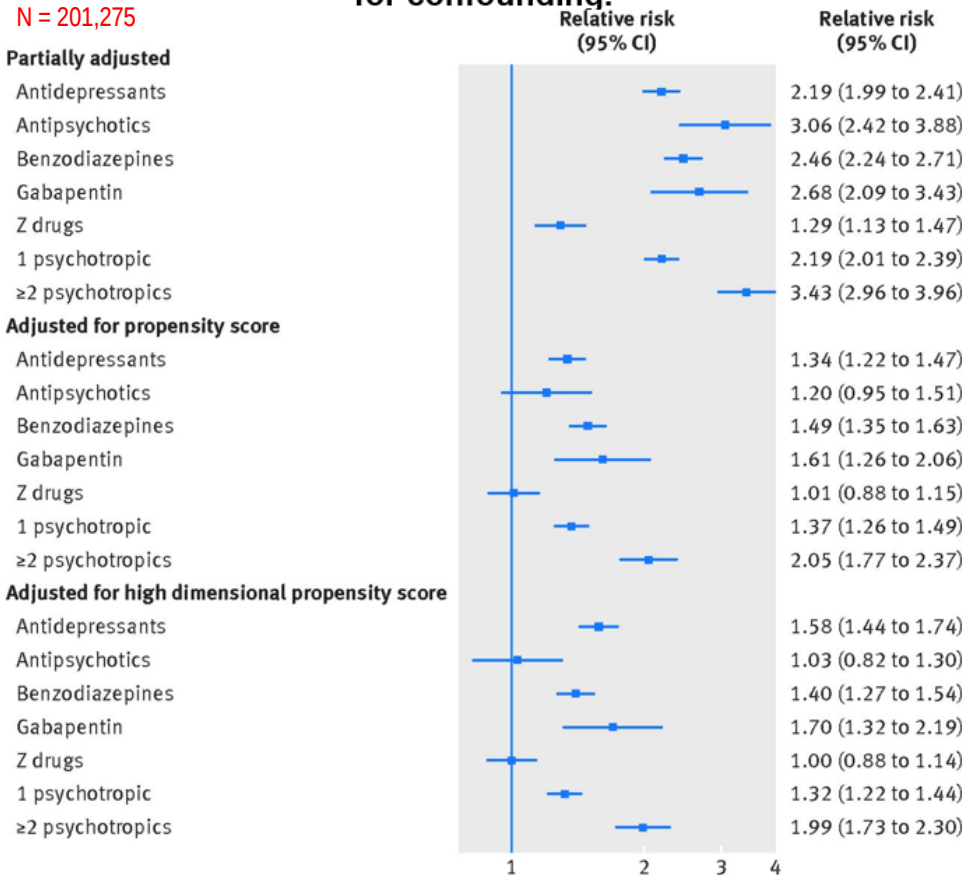
MOTHER STUDY, CONTINUED



OTHER FACTORS

- Boys have slightly higher rates of NAS diagnosis (55%) (Patrick et al 2012 JAMA)
- Variants in the OPRM1 and COMT genes have been associated with less severe NAS (Wachman et al 2013 JAMA)
- Breastfeeding decreases severity
- Early preterm infants (<34 weeks EGA) are at low risk
  - Developmental immaturity of CNS, lower fat deposits of drug, difficulty in clinical evaluation
- Incidence and duration does NOT depend on maternal dose
- Incidence and severity are associated with maternal tobacco use

Fig 2 Adjusted relative risk of neonatal drug withdrawal according to maternal exposure to psychotropic medications in addition to prescription opioids, according to level of adjustment for confounding.



Krista F Huybrechts et al. BMJ 2017;358:bmj.j3326

Drug and Alcohol Dependence
Volume 192, 1 November 2018, Pages 45-50

Full length article

Impact of psychiatric medication co-exposure on Neonatal Abstinence Syndrome severity

Elisha M. Wachman [a], A. Hutcheson Warden [b], Zoe Thomas [c], Jo Ann Thomas-Lewis [d], Hira Shrestha [a], F.N.U. Nikita [e], Daniel Shaw [f], Kelley Saia [b], Davida M. Schiff [g]

Retrospective study (n = 744)

Exposed to methadone or buprenorphine during third trimester

54% of mothers were on ≥ 1 psychotropic

32% of mothers were on ≥ 2 psychotropics

Table 4. Regression models for association of polypharmacy and individual psychiatric medication with NAS outcomes.

Psychiatric medication(s)	LOS (days)	Opioid treatment days	Medication treatment	Adjunctive medication
	MD (95% CI)	MD (95% CI)	aOR (95% CI)	aOR (95% CI)
Polypharmacy[a]	**4.31 (2.55, 6.06)**	**3.98 (2.24, 5.72)**	**1.87 (1.04, 3.38)**	**2.49 (1.57, 3.95)**
SSRIs[b]	0.59 (-1.46, 2.64)	0.91 (-1.14, 2.97)	0.93 (0.47, 1.85)	0.95 (0.55, 1.66)
Benzodiazepines[b]	**4.94 (2.86, 7.03)**	**4.68 (2.61, 6.75)**	1.68 (0.78, 3.65)	**2.57 (1.49, 4.42)**
Clonidine[b]	1.52 (-0.78, 3.83)	0.96 (-1.31, 3.23)	1.55 (0.66, 3.65)	1.26 (0.68, 2.32)
Gabapentin[b]	**2.79 (0.54, 5.03)**	1.07 (-1.12, 3.27)	**2.96 (1.18, 7.42)**	**1.92 (1.05, 3.53)**

Abbreviation: MD = Mean difference; aOR = adjusted odds ratio; LOS = length of hospital stay; SSRI = selective serotonin re-uptake inhibitor.

The bolded values are those results that were statistically significant with $p < 0.05$.

THE ROANOKE TIMES
Monday, September 20, 2004

STEPHANIE KLEIN-DAVIS | The Roanoke Times

, 35, a Bullitt Avenue resident, worries about the effect on her unborn child from the sound of jackhammers.

BREASTFEEDING

- Breastfeeding should be encouraged in the following scenario:
  - Stable on opioid agonists
  - Not using other illicit drugs
  - No other contraindications (e.g., HIV).
- Breastfeeding should be suspended if relapse occurs
- To feed the baby is best

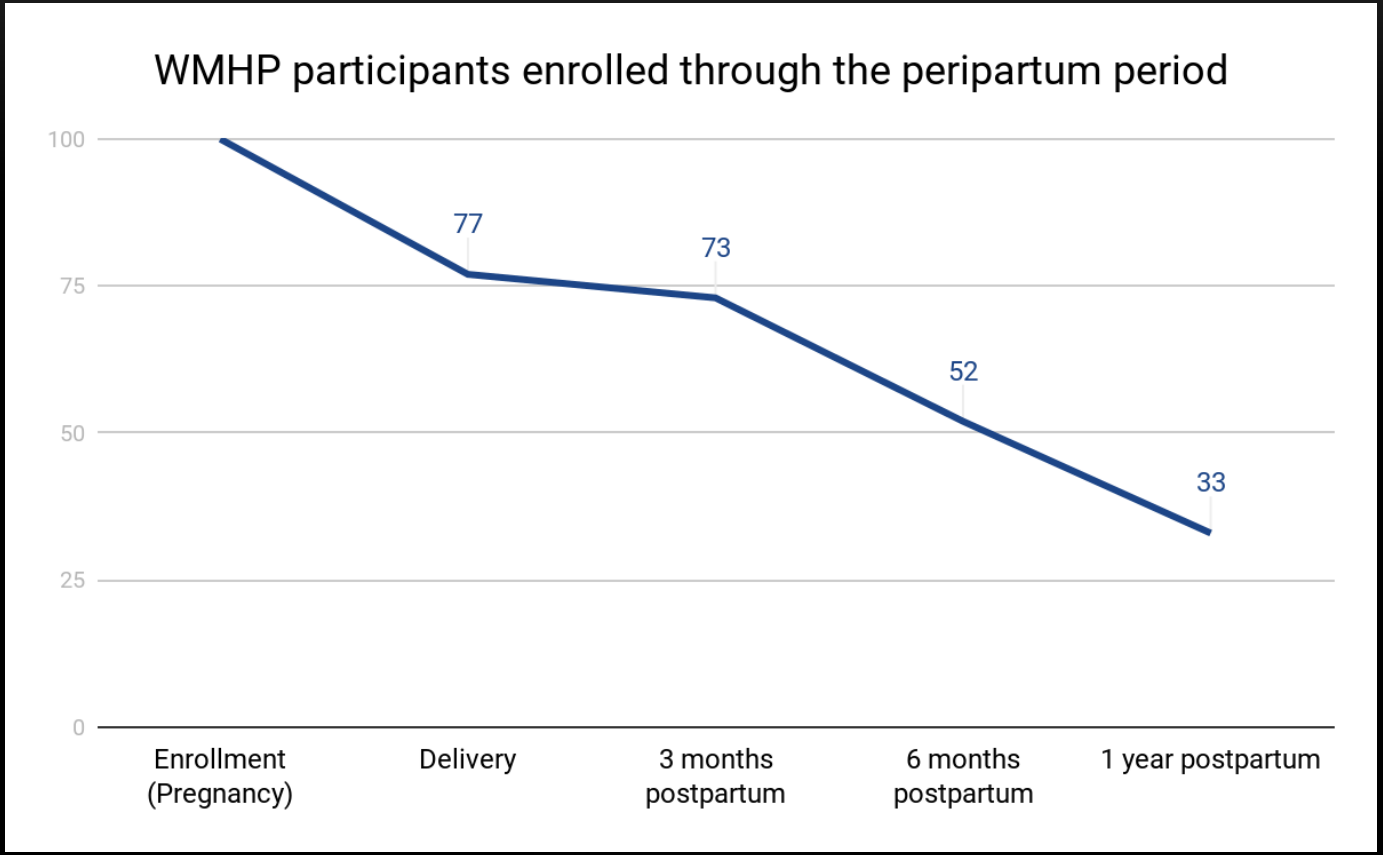
POSTPARTUM PERIOD

- Rate of Pregnancy
  - General population: 1.5 pregnancies in lifetime
  - SUD population: 4 pregnancies in lifetime

- Unintended pregnancy rates:
  - General population: 50%
  - SUD population: 80%

- Use of contraception
  - Lower rates of prescription contraception use
  - Similar rates of adherence
  - Long acting reversible contraceptives (e.g., IUDs, implants)

RETENTION IN TREATMENT



Postpartum Retention

Variable	Retention	Dropout	p value
Breastfeeding	66%	35%	0.044
Number of positive benzodiazepine drug results	1.90	4.44	0.038
Positive BZD drug result at delivery	18.4%	50%	0.014
Mean COWS score at visit prior to delivery	3.09	5.29	0.037

COWS -- Clinical Opioid Withdrawal Scale

WOMEN'S MENTAL HEALTH PROGRAM

Psychiatrists

Shona Ray-Griffith, MD

Jessica L. Coker, MD

Hannah Williams, MD

Program Manager

Bettina Knight, RN

Research Assistants

Amber Thomas

Caroline Brown

Therapist

Michael Cucciare, PhD

Psychology Intern

Peer Support Specialists/Certified Alcohol and Drug Counselor

Tojuana Greenlaw

WMHP – WHAT?

- Evaluate and manage neuropsychiatric illnesses during the perinatal period
  - Preexisting conditions (e.g., bipolar disorder, anxiety disorders, chronic pain, etc.) during pregnancy
  - New onset of depression/anxiety during pregnancy
  - Postpartum depression
- Evaluate and manage substance use disorders during the perinatal period
  - Inpatient detoxification available during pregnancy
  - Medication assisted treatment with buprenorphine
- Preconception consultation for medications

WMHP – HOW?

Contact Us/Referrals:

(501)526-8201

Patients must contact for an appointment

(not parents or other representatives)

All insurances accepted

ANGELS Hotline (24/7 Consultation):

501-526-7425 or 866-273-3835

angels.uams.edu

UAMS ADDICTION MEDICINE FELLOWSHIP

- Tentative start date: July 2020
- 1 year fellowship
- Addiction subspecialty for primary care doctors and psychiatry
- Focuses on prevention and treatment of, and the recovery from, opioid and substance use disorders

- Loan Repayment Program (LRP) Opportunities
  - Health Resources and Services Administration (HRSA)
    - National Health Service Corps LRP
    - Substance Use Disorder Workforce LRP

QUESTIONS?

Thank you!