Effects of Substance Use on Pregnancy and Infant Outcomes

Ariadna Forray, MD
April 10, 2025

ACCESS Mental Health for Moms

Prevalence of Substance Use in Pregnancy

- Legal substances are the *most problematic* in terms of effect and magnitude

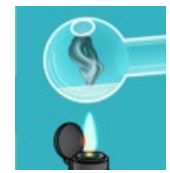
Alcohol (14%)*
*Among these 40% binge drink

Cigarettes (11%)

Prescription opiates (<2.5%)

- Illicit substances are less common

8%: Marijuana, Cocaine, Heroin, Amphetamines



Fosdin et al., MMWR, 2022;71(1):10-13
Drake et al, National Center for Health Statistics, 2018
National Survey on Drug Use and Health (NSDUH), 2021

ACCESS Mental Health CT

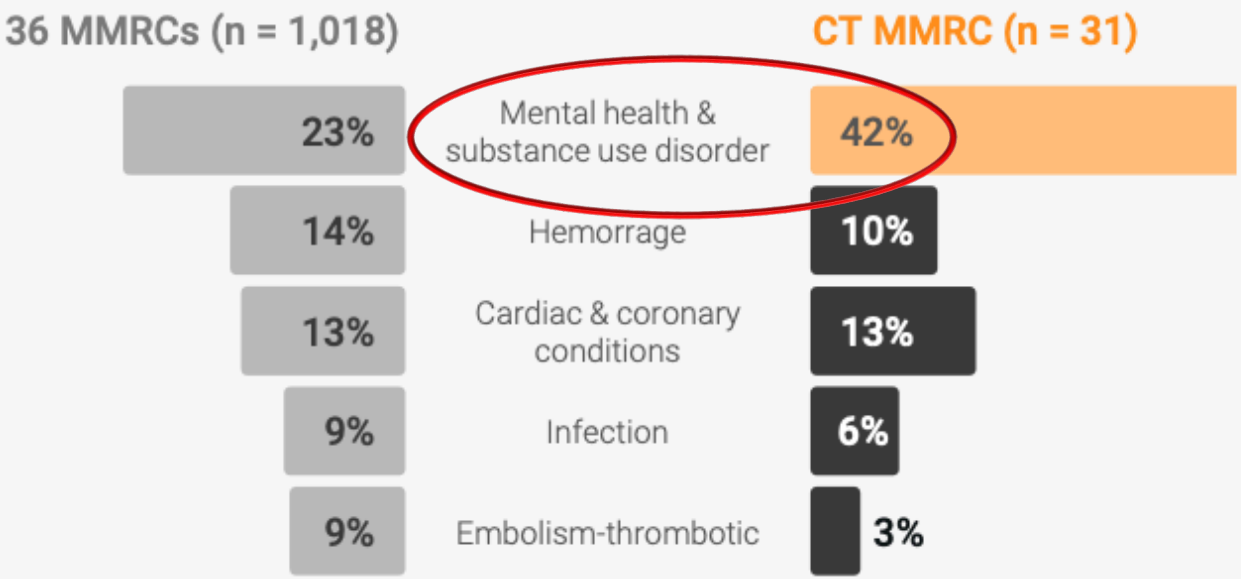
Caveats in Assessing the Effects of Substance Use In Pregnancy

- Delayed care or no prenatal care
- Co-occurring substance use is more the rule than the exception and one must account for multiple possible drug effects
- Those that are heavy users of a substance are more likely to use multiple substances
- Co-morbid psychiatric disorders
- Chaotic neonatal environment has a strong impact on child development

ACCESS Mental Health CT

Leading Underlying Causes of Pregnancy-related Deaths: 2015-2020

Mental health conditions, including substance use disorder, were the leading underlying causes of death both in Connecticut and in 36 US states that contributed data to the CDC's analysis of pregnancy-related deaths.



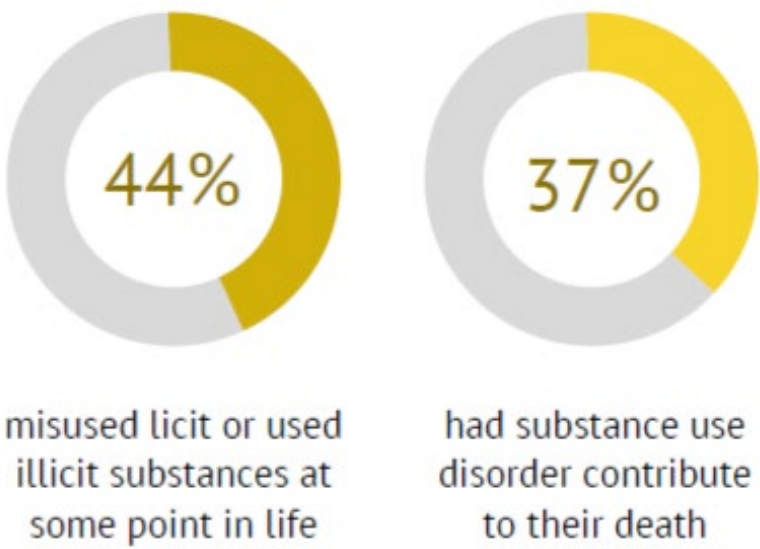
Data Sources: Connecticut Maternal Mortality Review Information Application (CT-MMRIA), 2015-2020 and data from Maternal Mortality Review Committees in 36 US states, 2017-2019.

ACCESS Mental Health CT

Mortality in Connecticut 2015-2017

Substance use

Among persons whose deaths were pregnancy-associated (n = 32):

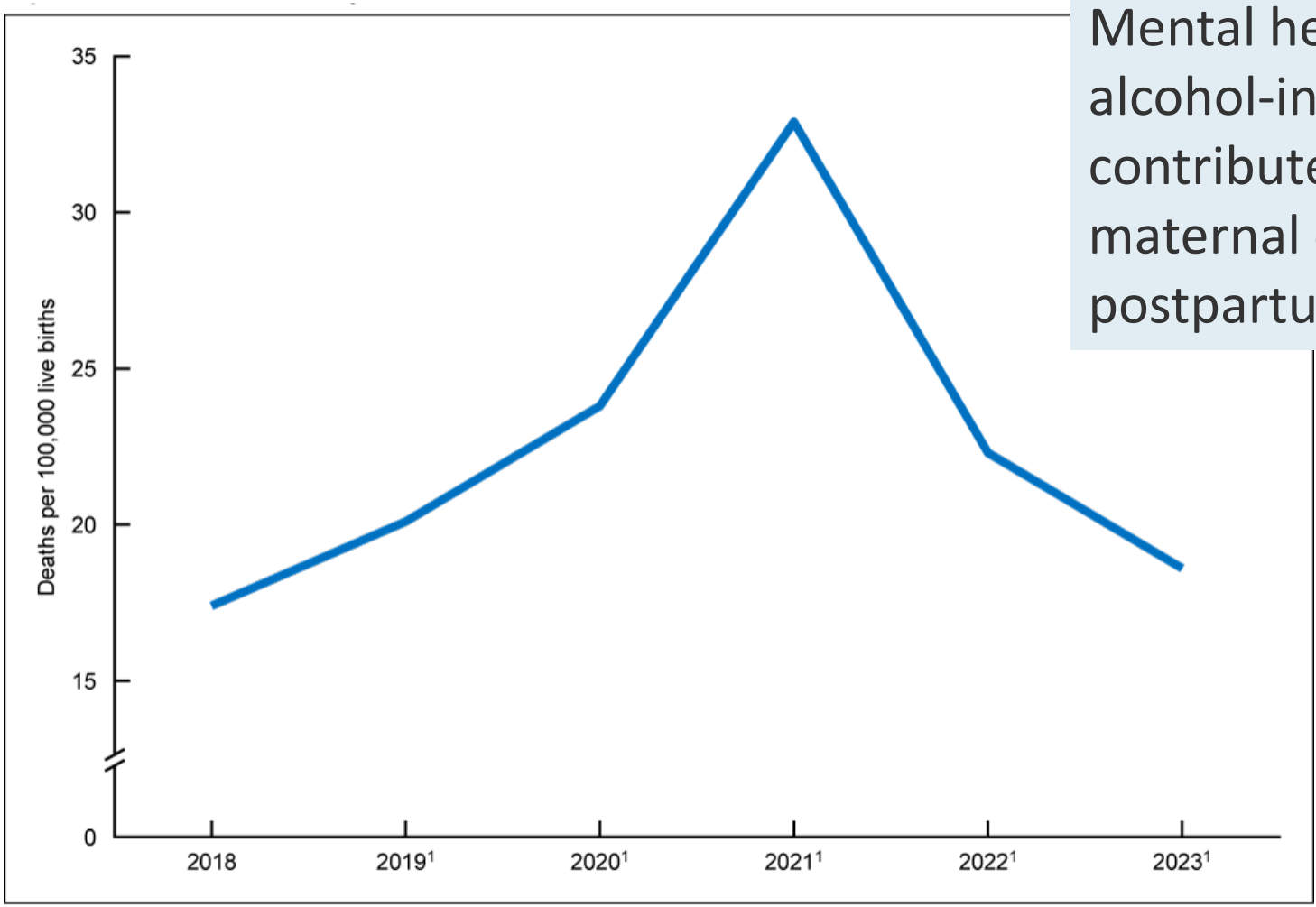


75% of these deaths occurred in the late postpartum period (43-365 days after delivery)

Pregnancy-Associated Deaths in CT, Data from CT MMRC, 2015-2019, DPH 2021

ACCESS Mental Health CT

Updated Maternal Mortality in US



[1]Statistically significant change in rate from previous year ($p < 0.05$).
SOURCE: National Center for Health Statistics, National Vital Statistics System, mortality data file.

Mental health and drug- and alcohol-induced death contributed to 21.2% of late maternal deaths in late postpartum period.

Hoyert DL. Maternal mortality rates in the United States, 2023. NCHS Health E-Stats. 2025. DOI: https://dx.doi.org/10.15620/cdc/174577.
Chen et al., JAMA Open Network, 2025; https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2832320

ACCESS Mental Health CT

Overview of Substance Use Effects on Pregnancy & Infant Outcomes

	Tobacco	Alcohol	Cannabis	Stimulants	Opiates
Pregnancy outcomes					
Preterm birth	✓	✓	✓	✓	✓
Small for gestational age	✓	✓	✓	✓	✓
Low birthweight	✓	✓	✓	✓	✓
Miscarriage/Spontaneous abortion	✓	✓		✓	
Placental abruption	✓			✓	✓
Premature rupture of membranes	✓			✓	
Ectopic pregnancy	✓				
Infant effects					
Cognitive deficits	✓	✓	✓	✓	✓
Teratogenicity		✓			
Infant mortality/Sudden Infant Death Syndrome	✓			✓	✓
Neonatal Withdrawal/Abstinence Syndrome		✓			✓
Behavioral Problems	✓	✓	✓	✓	✓

No Amount of Alcohol Use in Pregnancy is Considered Safe

Timing, dose and pattern of exposure are important

Early exposure is most associated with morphological abnormalities

Late exposure is most associated with growth deficits

Risk of central nervous system (CNS) deficits occurs across pregnancy

ACCESS Mental Health CT

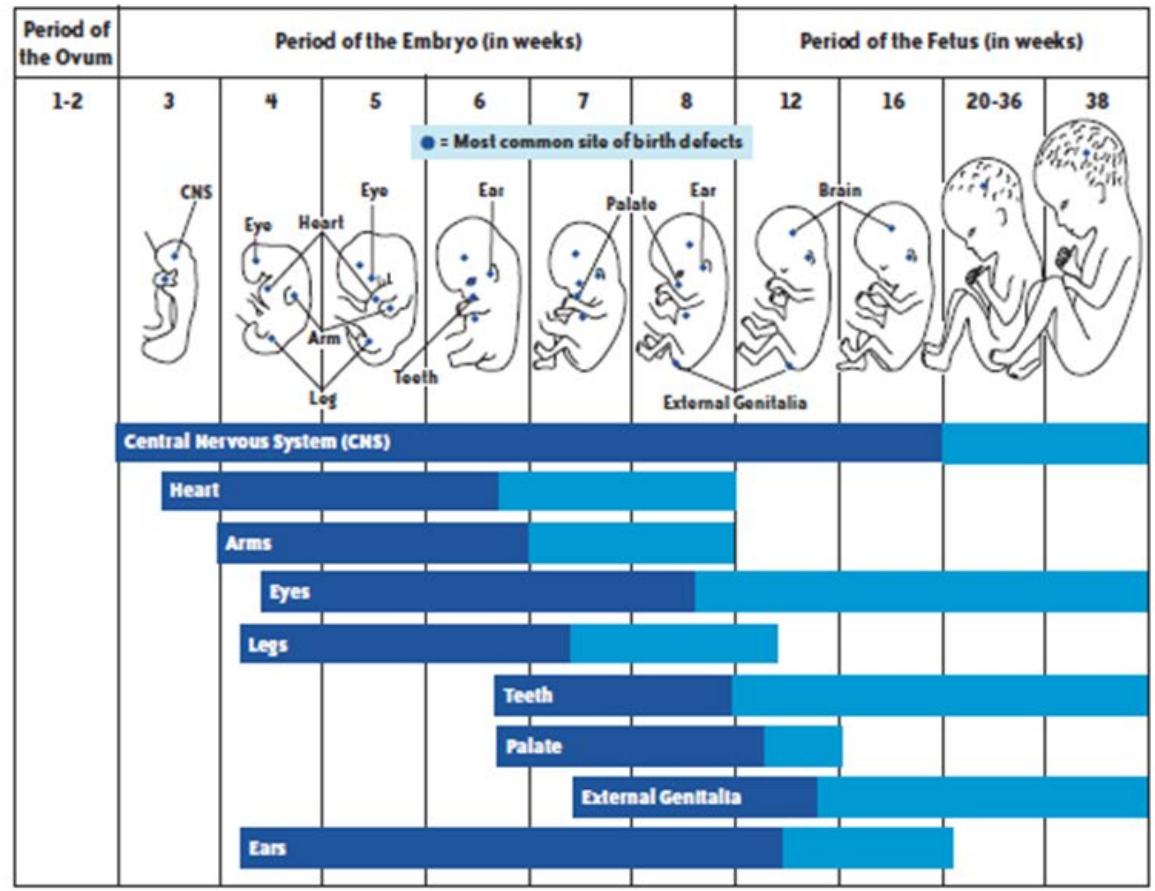
NO SAFE Time.

NO SAFE Amount.

NO SAFE Alcohol during Pregnancy.

PERIOD.

Fetal Development Chart



Vulnerability of the fetus to defects during different periods of development. The dark blue portion of the bars represents the most sensitive periods of development, during which teratogenic effects on the sites listed would result in major structural abnormalities in the child. The lighte blue portion of the bars represents periods of development during which physiological defects and minor structural abnormalities would occur.

SOURCE: Adapted from Moore 1993.

National Organization on Fetal Alcohol Syndrome

Helping children & families by advocating for the prevention and intervention of Fetal Alcohol Spectrum Disorders, the leading known cause of mental retardation & birth defects in the United States.

ACCESS Mental Health for Moms

Neonatal Alcohol Withdrawal

- Develops within 3-12 hours post delivery
- Characterized by:
  - Hyperactivity
  - Crying, irritability
  - poor suck
  - Hyperphagia
  - Diaphoresis
  - Abnormal sleep pattern
  - Tremors, seizures

Committee on Drugs, Pediatrics, 1998:101;1079-1086

ACCESS Mental Health CT

Fetal Alcohol Spectrum Disorders (FASD)

- Fetal alcohol syndrome (FAS)
- Partial fetal alcohol syndrome (pFAS)
- Alcohol-related neurodevelopmental disorder (ARND)
- Alcohol-related birth defects (ARBD)
- Neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE)

ACCESS Mental Health for Moms

Fetal Alcohol Syndrome (FAS)

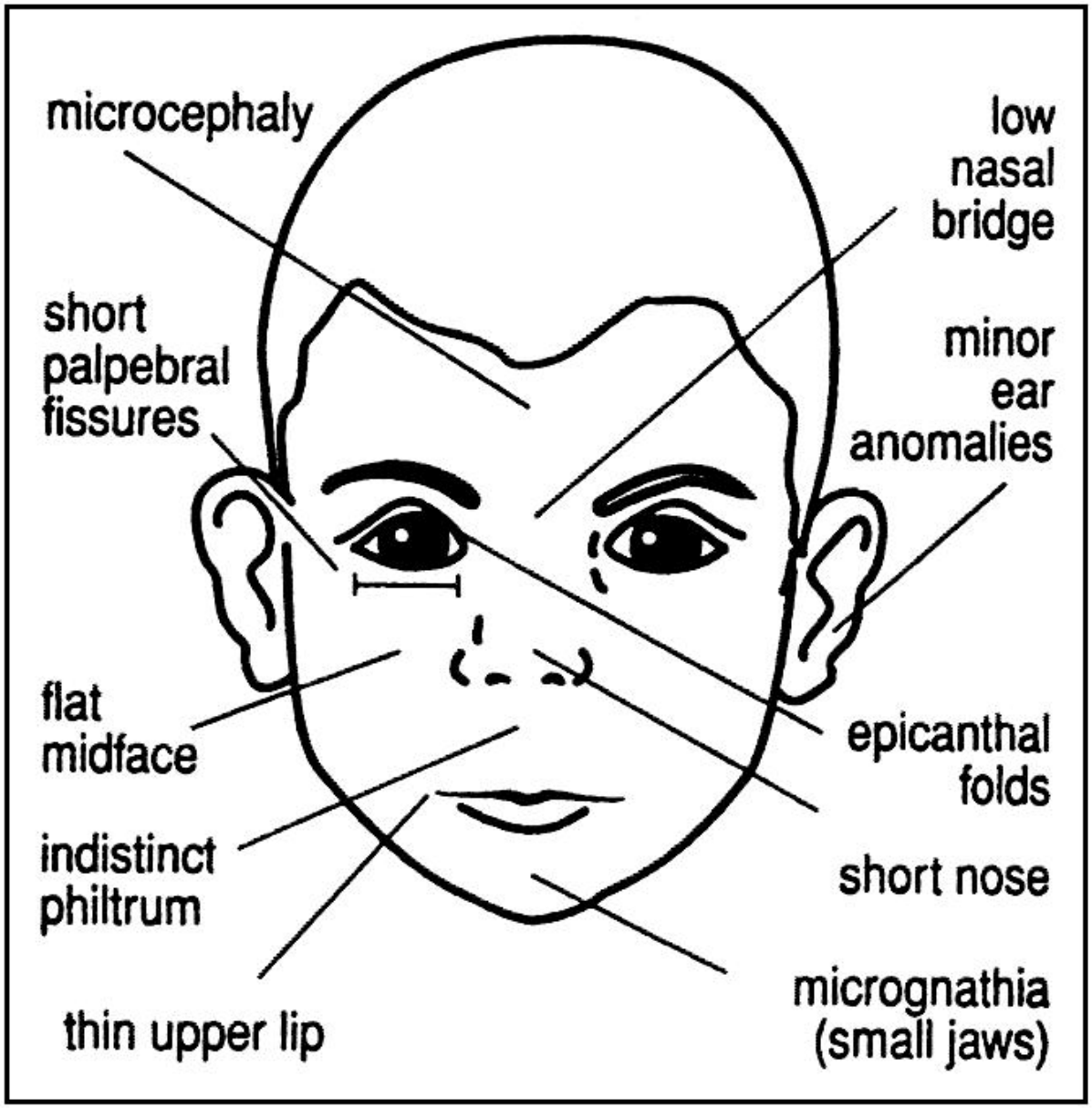
- The most serious end of the FASD spectrum
- Includes central nervous system (CNS) problems, minor facial features and growth problems
- Can also can have problems with learning, memory, attention span, communication, vision, or hearing

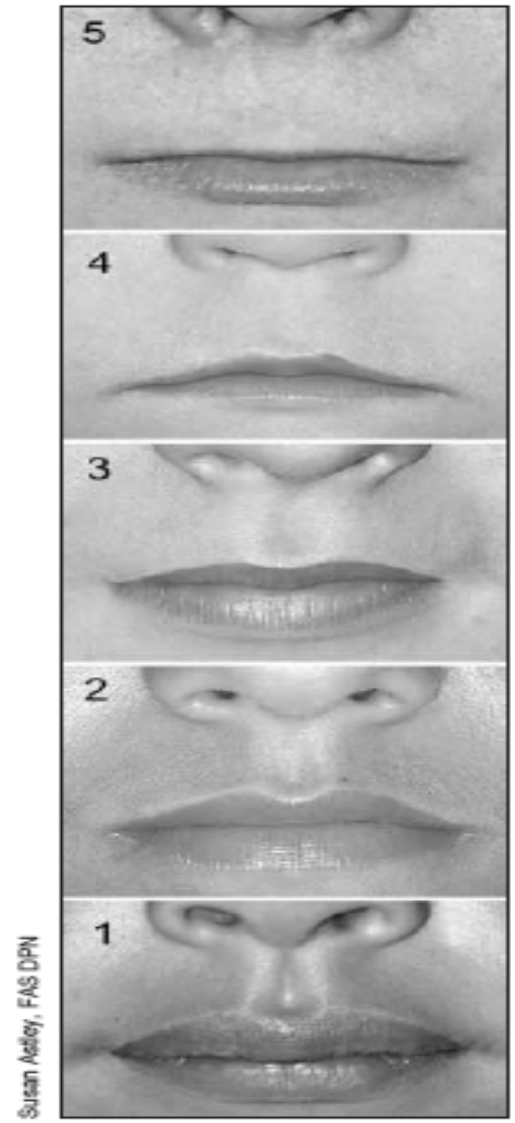
Partial FAS (pFAS)

- Does not meet the full diagnostic criteria for FAS and presents with some of the facial features, growth problem or CNS abnormalities

ACCESS Mental Health CT

FAS – Facial Features





Lip-philtrum guide. A 5-point pictorial scale

ACCESS Mental Health CT

Alcohol-Related Effects

- Alcohol-related birth defects (ARBD):
  - Congenital anomalies, including hearing problems, malformations and dysplasias involving heart, kidneys, or bones
- Alcohol-related neurodevelopmental disorder (ARND)
  - Evidence of neurodevelopmental abnormalities, such as intellectual disabilities and problems with behavior and learning
  - Might do poorly in school and have difficulties with math, memory, attention, judgment, and poor impulse control

ACCESS Mental Health CT

Neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE)

1. Difficulty with executive functioning and memory
2. Behavior problems, such as severe tantrums, irritability, and difficulty shifting attention from one task to another
3. Trouble with day-to-day living, which can include problems with bathing, dressing, and interacting with others

- The birthing parent must have consumed more than 13 alcoholic drinks per month of pregnancy or more than 2 alcoholic drinks in one sitting

ACCESS Mental Health CT

Long term Behavioral Consequences of Fetal Alcohol Syndrome/Effects

Among Adolescents and Adults:

- 61% had a disruption in school (suspended, expelled or dropped out)
- 60% had difficulty with the law
- 35% were incarcerated
- 23% were psychiatrically hospitalized
- 29% of adolescents and 46% of adults had problems with drugs or alcohol

Streissguth et al., Developmental and Behavioral Pediatrics, 2004:25;228-238

ACCESS Mental Health CT

Maternal-Fetal Risks Associated With Maternal Nicotine Use During Pregnancy

Preterm birth	OR 1.7-2.0
Placenta previa	OR 1.5-3.0
Placental abruption	OR 1.4-2.4
Fetal Growth Restriction	OR 2.2-2.4
SIDS	OR 2.0-3.0

Developmental effects:

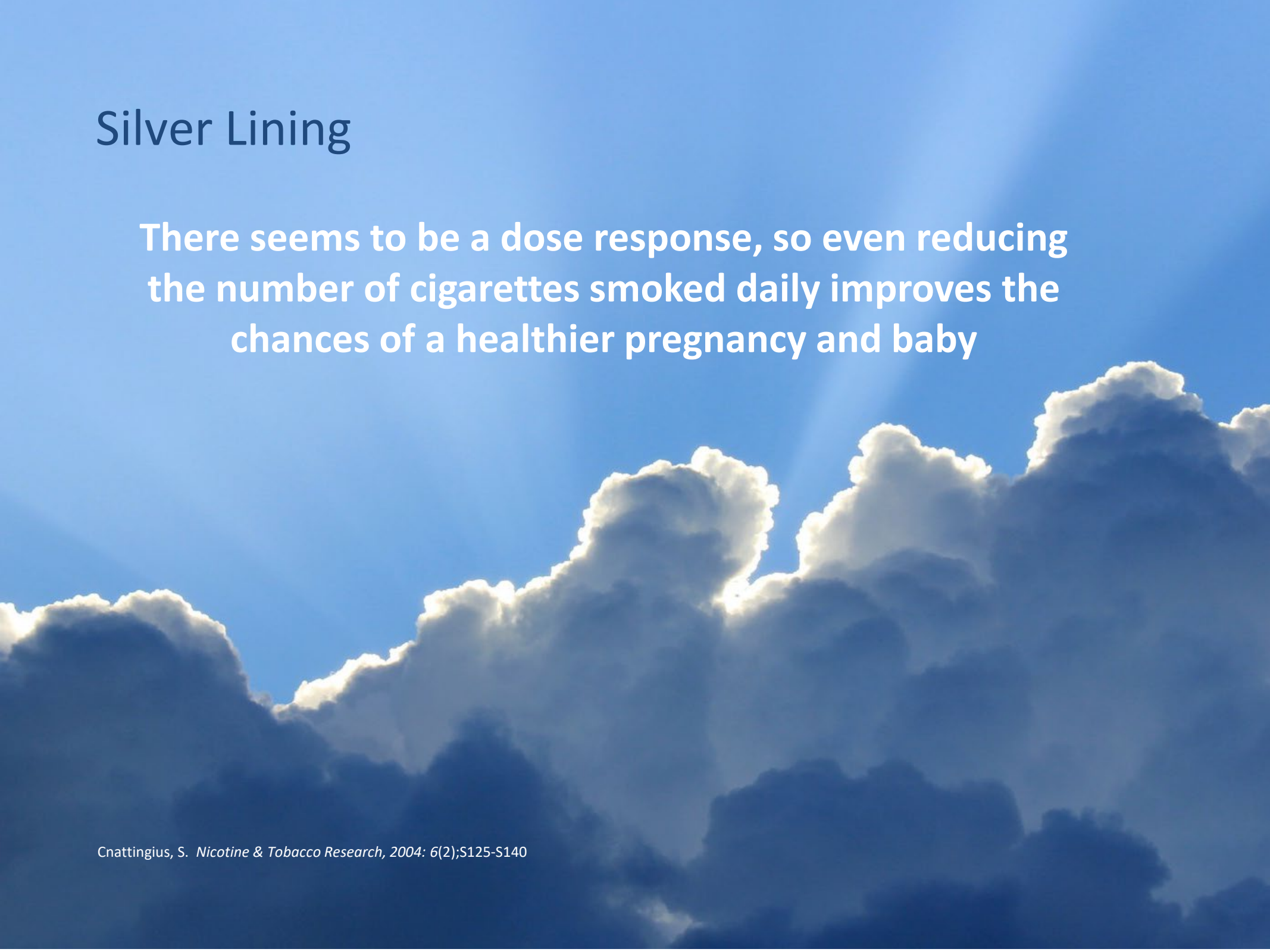
Increased risk of schizophrenia, externalizing and attention problems in offspring

Cnattingius, S. Nicotine & Tobacco Research, 2004
Ion & Bernal, Reprod Sci, 2015
Niemelä et al. Am J Psychiatry, 2016

ACCESS Mental Health for Moms

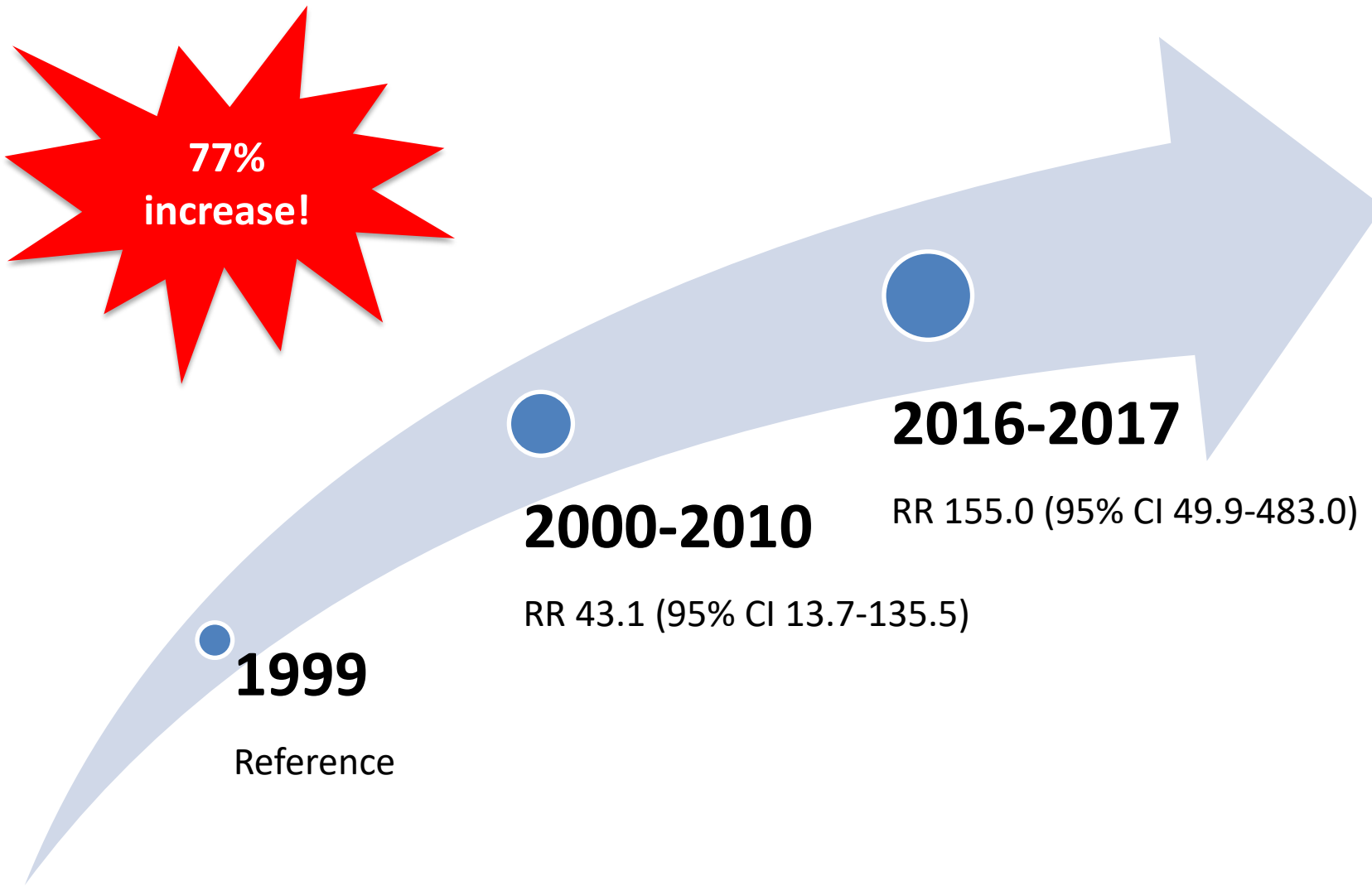
Silver Lining

There seems to be a dose response, so even reducing the number of cigarettes smoked daily improves the chances of a healthier pregnancy and baby



Cnattingius, S. *Nicotine & Tobacco Research, 2004: 6*(2);S125-S140

OUD-related Maternal Deaths 1999-2017



Mitra A et al., Obstet Gynecol. 2020;135:56S.

Associations between Opioid Use during Pregnancy and Maternal-Fetal Outcomes: 2007–2011

	Delivery Hospitalizations with Opioid Abuse or Dependence n (%)	Delivery Hospitalizations without Opioid Abuse or Dependence n (%)	Multivariable Odds Ratio* (95% CI)
Total	60,994	20,456,485	
Died during hospitalization	20 (0.03)	1,311 (0.006)	**4.6 (1.8–12.1)**
Cardiac arrest	24 (0.04)	1,873 (0.01)	**3.6 (1.4–9.1)**
Intrauterine growth restriction	4,157 (6.8)	431,032 (2.1)	**2.7 (2.4–2.9)**
Placental abruption	2,315 (3.8)	215,057 (1.1)	**2.4 (2.1–2.6)**
Length of stay >7 days	1,837 (3.0)	235,738 (1.2)	**2.2 (2.0–2.5)**
Preterm	10,538 (17.3)	1,506,941 (7.4)	**2.1 (2.0–2.3)**
Oligohydramnios	2,736 (4.5)	564,410 (2.8)	**1.7 (1.6–1.9)**
Transfusion	1,205 (2.0)	208,073 (1.0)	**1.7 (1.5–1.9)**
Stillbirth	727 (1.2)	124,607 (0.6)	**1.5 (1.3–1.8)**
Premature rupture of membranes	3,499 (5.7)	778,157 (3.8)	**1.4 (1.3–1.6)**
Cesarean delivery	22,130 (36.3)	6,768,679 (33.1)	**1.2 (1.1–1.3)**

Maeda et al., Anesthesiology, 121:1158-67; 2014

ACCESS Mental Health CT

Intrauterine Opiate Withdrawal

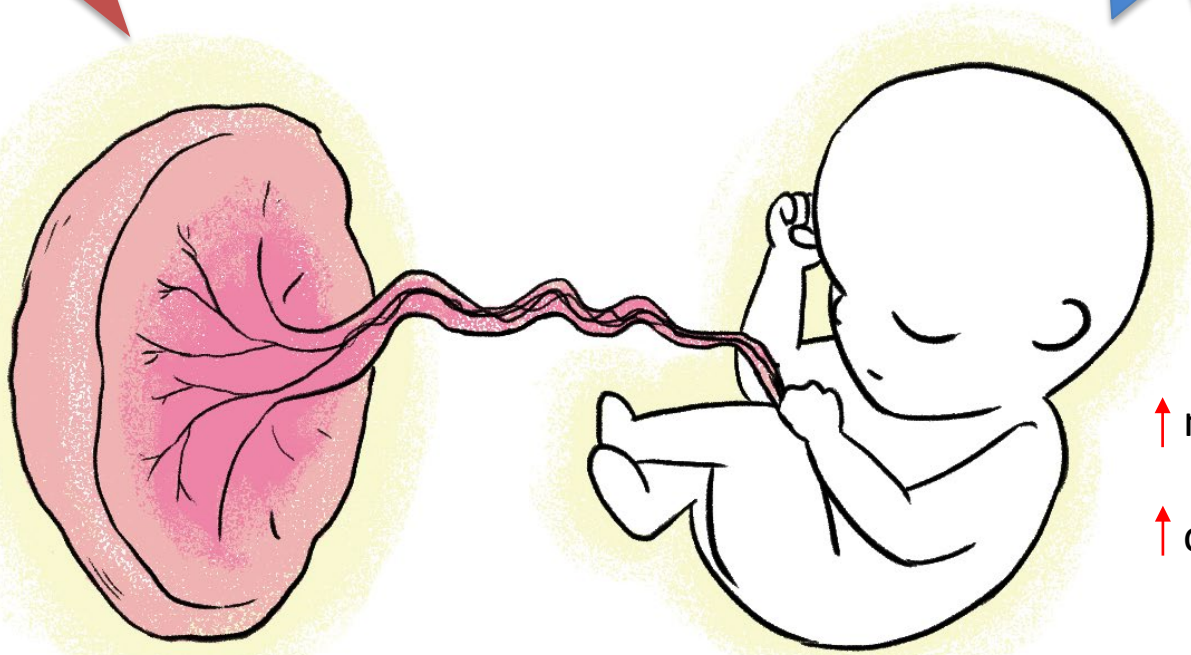
Acute maternal withdrawal

Acute fetal withdrawal

Catecholamine surge

↑ Uterine contractions

↓ Placental blood flow and O_2 supply



↑ motor activity

↑ oxygen demands

ACCESS Mental Health for Moms

McCarthy et al. Am J Obstet Gynecol. 2016

Neonatal Opioid Withdrawal Syndrome

Occurs in 45%-95% of exposed infants

Seizures

Hyperreflexia

Vomiting

Tremors

Irritability

Disorganized sleep

Increased sweating

Poor feeding and sucking

Loose stools and dehydration

Excessive or high-pitched crying

Yawning, stuffy nose, or sneezing

Patrick et al., JAMA, 2012
Committee on Drugs, Pediatrics, 1998;101:1079-1086
Ballard, J Perinat Neonat Nurs, 2002;15:76-85

ACCESS Mental Health for Moms

Opiate Use in Pregnancy

- Cigarette smoking in pregnant women with opioid use disorder is highly prevalent, 77% to 95%

ACCESS Mental Health CT

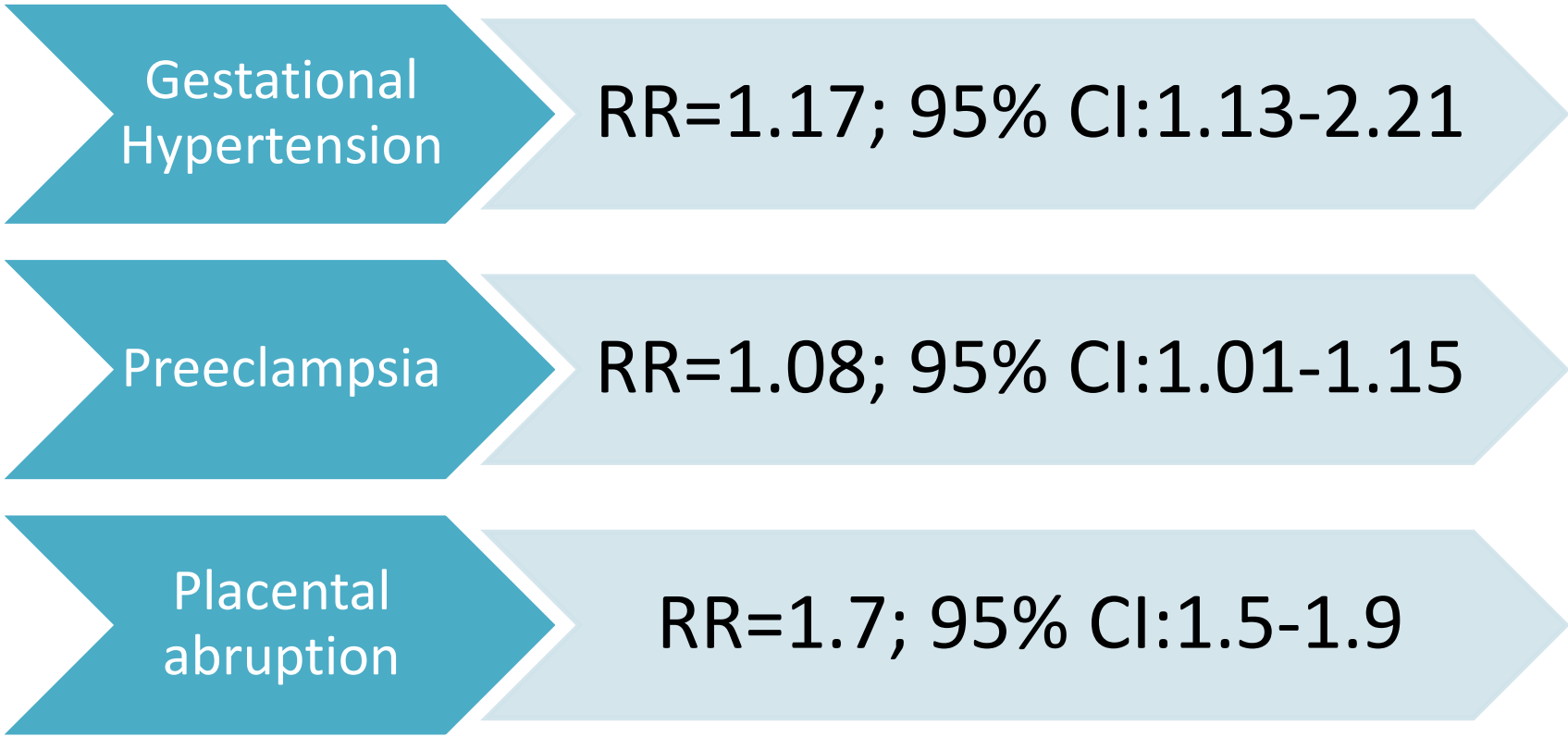
Neurodevelopmental Outcomes in Offspring Exposed to Opioids In Utero

- Findings limited by difficulties in following up cohorts and controlling for confounding factors
- Confounding factors: other substance use, poor prenatal care
- Most studies found no significant difference in cognitive development
- Chaotic neonatal environment has a strong impact on child development

Logan et al., Clin Obstet Gynecol. 2013:56(1):186-192

ACCESS Mental Health CT

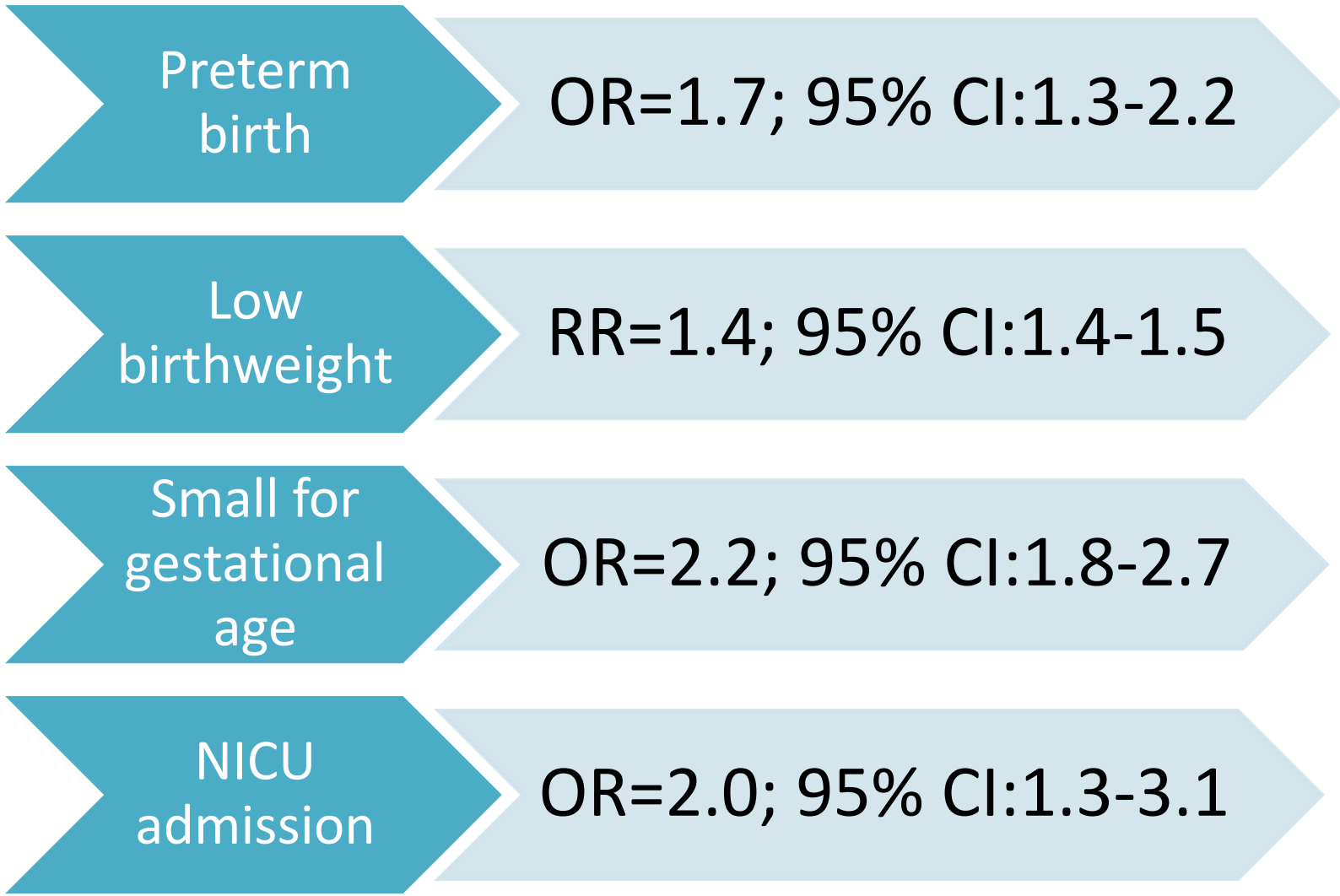
Cannabis Use and Maternal Outcomes



Corsi et al., JAMA. 2019;322(2):145-152
Young-Wolff et al., JAMA Internal Medicine, 2024

ACCESS Mental Health for Moms

Cannabis Use and Birth Outcomes



Mamun & Najman, Pediatric Reseach, 2012
Gunn J et al., BMJ Open. 2016;6:1-8
Corsi et al., JAMA. 2019;322(2):145-152

ACCESS Mental Health for Moms

Neonatal Outcomes and Cannabis Exposure in Pregnancy

TABLE 2
Odds ratios for associations between in utero cannabis exposure and neonatal outcomes, n = 364,924

Neonatal outcomes	Prevalence of neonatal outcomes by in utero cannabis exposure		Odds ratio (95% confidence interval) In utero cannabis exposure: yes vs no				
	Among exposed (n=22,624) % n/total	Among unexposed (n=342,300) % n/total	Model 1: unadjusted	Model 2: adjusted for sociodemographic characteristics[a]	Model 3: adjusted for covariates in previous model and exposure to other non-cannabis substance in utero[a]	Model 4: adjusted for covariates in previous model and prenatal care[a]	Model 5: adjusted for covariates in previous model and comorbidities[a]
Low birthweight	6.6% 1487/22,599	4.8% 16,419/341,928	1.40 (1.32–1.48)[b]	1.26 (1.19–1.34)[b]	1.19 (1.12–1.26)[b]	1.20 (1.12–1.27)[b]	1.20 (1.12–1.28)[b]
Small for gestational age	11.7% 2640/22,575	9.2% 31,488/341,671	1.30 (1.25–1.36)[b]	1.26 (1.20–1.32)[b]	1.24 (1.18–1.30)[b]	1.24 (1.18–1.30)[b]	1.24 (1.18–1.30)[b]
Early-moderate preterm birth (<34 wk)	2.1% 479/22,624	1.5% 5276/342,300	1.38 (1.26–1.52)[b]	1.16 (1.04–1.28)[b]	1.09 (0.98–1.21)	1.10 (0.99–1.22)	1.11 (1.00–1.23)[c]
Preterm birth (<37 wk)	7.9% 1794/22,624	6.6% 22,474/342,300	1.23 (1.16–1.29)[b]	1.12 (1.06–1.18)[b]	1.05 (0.99–1.11)	1.06 (1.00–1.12)[b]	1.06 (1.00–1.13)[b]
NICU admission	12.3% 2722/22,204	9.5% 31,867/336,408	1.34 (1.28–1.39)[b]	1.16 (1.11–1.22)[b]	1.06 (1.01–1.11)[b]	1.07 (1.02–1.12)[b]	1.06 (1.01–1.11)[b]
Respiratory support	2.7% 593/22,204	2.1% 6925/336,408	1.31 (1.20–1.42)[b]	1.13 (1.03–1.23)[b]	1.07 (0.97–1.17)	1.07 (0.98–1.18)	1.07 (0.97–1.18)

NICU, neonatal intensive care unit.

[a] The sociodemographic characteristics included were age categories, parity categories, race/ethnicity, Neighborhood Deprivation Index quartiles, and education. Other non-cannabis substance use included alcohol, opioid, stimulant, nicotine, and anxiety/sleep medications. Prenatal care included the Adequacy of Prenatal Care Utilization Index. Comorbidities included anemia 1 year before pregnancy, diabetes mellitus 2 years before pregnancy, prepregnancy body mass index category, asthma during pregnancy up to the first prenatal care visit, nausea and vomiting in pregnancy up to the first prenatal care visit, mood or anxiety diagnosis in pregnancy up to the first prenatal care visit, other mental health diagnosis in pregnancy up to the first prenatal care visit, depression medication in pregnancy up to the first prenatal care visit, gestational diabetes in pregnancy, and substance use diagnosis in pregnancy up to the first prenatal care visit; [b] $P<.05$; [c] $P=.055$.

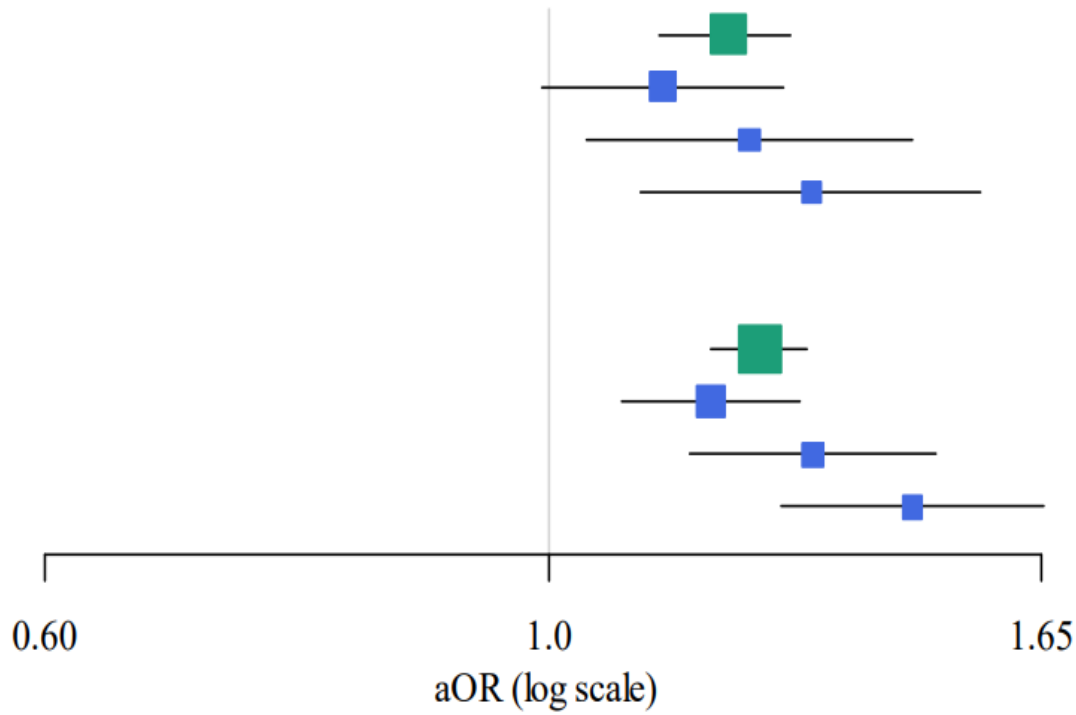
Avalos. In utero cannabis exposure and neonatal outcomes. Am J Obstet Gynecol 2024.

Avalos et al., AJOG, 2024

ACCESS Mental Health CT

Increase in adverse outcomes with increased frequency of cannabis use in pregnancy

	aOR (95% CI)
Low birth weight*	
Any cannabis use	1.20 (1.12-1.28)**
Monthly or less	1.12 (0.99-1.27)
Weekly	1.23 (1.04-1.45)**
Daily	1.31 (1.10-1.55)**
Small for gestational age*	
Any cannabis use	1.24 (1.18-1.30)**
Monthly or less	1.18 (1.08-1.29)**
Weekly	1.31 (1.15-1.48)**
Daily	1.45 (1.27-1.65)**



Avalos et al., AJOG, 2024

ACCESS Mental Health CT

Cognitive and Behavioral Effects of Heavy Prenatal Marijuana Use

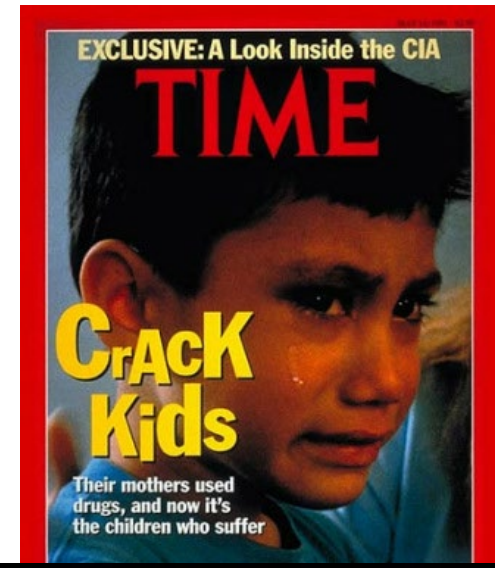
- Prenatal cannabis use during pregnancy associated with increased risk of attention, social and behavioral problems into early adolescence (ABCD study)
- Offspring exposed to 3 joints per week prenatally have an increased rate of externalizing behavioral problems and impulsivity
- Deficits in abstract and visual reasoning when assessed at age 3-4 and still present at age 9-12
- Increase addiction vulnerability in adulthood

Paul et al., JAMA Psychiatry, 2020
Goldschmidt et al., Neurotoxicology & Teratology, 2000;22:325-336
Huizink & Mulder Neurosci Biobehav Rev 2006;30:24-41
DiNieri et al., Biol Psychiatry. 2011;70(8):763-9

ACCESS Mental Health CT

Prenatal Cocaine Use

- Controversy about the magnitude of effects since the early descriptions of “crack babies”
- It is now thought that some of the deleterious effects are the consequences of poverty and other substance use
- Nonetheless, a number of deficits in offspring are specifically associated with prenatal cocaine use



ACCESS Mental Health CT

Cocaine Effects Immediately After Birth

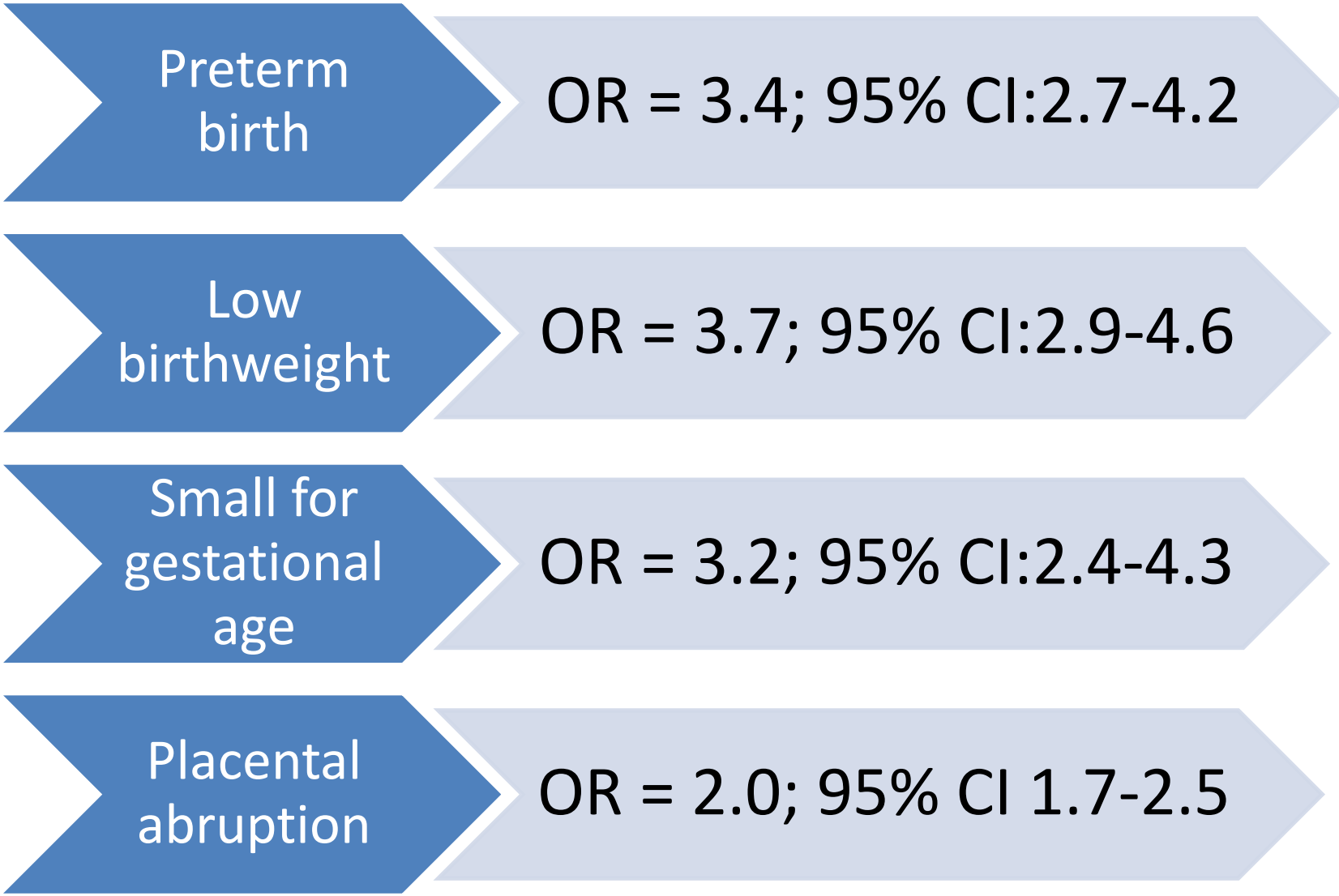
- Cocaine exposed neonates have lower arousability and are more excitable
  - Lower dosages are associated with lower arousability
  - Higher doses are associated with greater difficulties with excitability and non-optimal reflexes
- Frequently occur on postnatal days 2-3
- Additional effects include:

- Jitteriness
- Hyperactive Moro
- Excessive sucking
- Hypertonicity
- Abnormal EEG & Seizures
- Poor habituation
- Hyperreflexia
- Sleep disturbances

Committee on Drugs, Pediatrics, 1998;101:1079-1086
Chiriboga et al., Pediatrics, 1995;96:1070-1077

ACCESS Mental Health CT

Cocaine Use and Birth Outcomes



Gouin et al., Am J Obstet Gynecol, 2011;204(4):340.e1-e12
Dos Santos et al., Arch Gynecol Obstet, 2018 Sep;298(3):487-503

ACCESS Mental Health for Moms

Longer Term Effects of Prenatal Cocaine on Children

- Dose-related difficulties in attention control
- Diminished response inhibition
- Deficits in learning, among others
- Dose-related reductions in expressive language
- Generally, difficulties in the frontal-striatal system
- Effects may be influenced by postnatal environment

Morrow et al., J Pediatric Psychology, 2004
Mayes, Development and Psychopathology, 2005

Overview of Fetal Effects of Prenatal Substance Exposure

TABLE 2 Summary of Effects of Prenatal Drug Exposure

	Nicotine	Alcohol	Marijuana	Opiates	Cocaine	Methamphetamine
Short-term effects/birth outcome						
Fetal growth	Effect	Strong effect	No effect	Effect	Effect	Effect
Anomalies	No consensus on effect	Strong effect	No effect	No effect	No effect	No effect
Withdrawal	No effect	No effect	No effect	Strong effect	No effect	*
Neurobehavior	Effect	Effect	Effect	Effect	Effect	Effect
Long-term effects						
Growth	No consensus on effect	Strong effect	No effect	No effect	No consensus on effect	*
Behavior	Effect	Strong effect	Effect	Effect	Effect	*
Cognition	Effect	Strong effect	Effect	No consensus on effect	Effect	*
Language	Effect	Effect	No effect	*	Effect	*
Achievement	Effect	Strong effect	Effect	*	No consensus on effect	*

* Limited or no data available.

Behnke, M., Smith, V. C., & Committee on Substance Abuse. (2013). Prenatal substance abuse: short-and long-term effects on the exposed fetus. Pediatrics, 131(3),

ACCESS Mental Health CT

Thank you

ariadna.forray@yale.edu

ACCESS Mental Health CT