

SUBSTANCE USE DISORDERS IN PREGNANCY

LAUREN AUGELLO, MD
PSYCHIATRY ADDICTIONS FELLOW
UNIVERSITY OF WASHINGTON









GENERAL DISCLOSURES

The University of Washington School of Medicine also gratefully acknowledges receipt of educational grant support for this activity from the Washington State Legislature through the Safety-Net Hospital Assessment, working to expand access to psychiatric services throughout Washington State.



SPEAKER DISCLOSURES

✓ No conflicts of interest



OBJECTIVES

- Understand scope and impact of substance use in pregnancy
- Gain a basic understanding of maternal and fetal effects for most common substances
- Review recommendations for screening, intervening and referring



Los Angeles Times

Mother Convicted as Drug Deliverer After Cocaine Is Found in Newborns

July 14, 1989 | From Associated Press

SANFORD, Fla. — An addict who gave birth to two children with traces of cocaine in their systems was convicted of drug delivery Thursday under a law routinely used against drug dealers.

"A derivative of cocaine which the defendant had introduced into her body passed into theirs" through the umbilical cord, Circuit Judge O. H. Eaton Jr. ruled in the non-jury trial.

Jennifer Clarise Johnson, 23, faces up to 30 years in prison, but prosecutor Jeff Deen said he would recommend that she continue in a drug-treatment program and receive a long period of probation.

Deen said the verdict is "a new tool for prosecutors to put a stop to this great problem in this state and in the nation."





Born into suffering: More babies arrive dependent on drugs

Laura Ungar, USA TODAY

Published 10:27 a.m. ET July 8, 2015 | Updated 7:10 p.m. ET July 8, 2015



(Photo: Alton Strupp, The Courier-Journal)



LOUISVILLE, Ky. — Shortly after he was born, tremors wracked Leopoldo Bautista's tiny body as he suffered through the pain of drug withdrawal — pain his mother understands.

Samantha Adams is being treated with methadone for a heroin addiction, and she passed the

methadone into Leopoldo's system. Sitting vigil with him at Norton Hospital, she tears up as she describes the 10-day-old "going through what I'd been through."

Being born into suffering is becoming ever more common as research shows a continuing surge in drug-dependent infants amid a national epidemic of pain pill and now heroin abuse, with no end in sight.



ACCESS TO CARE

- Research demonstrates that punitive policies applied to substance use do not improve outcomes
- Improved outcomes are associated with public health models that emphasize harm reduction and access to treatment



ACCESS TO CARE

Early prenatal care is recommended for the best possible maternal and infant outcomes (CDC, 2011).



ACCESS TO CARE

- National Survey: Abstinence rate of 57%
- Prospective Study: Abstinence rate of 96% of heavy drinkers, 78% of cannabis users, 73% of cocaine users and 32% of cigarette smokers
- Precipitous rates of relapse following delivery



EPIDEMIOLOGY

5.9% of pregnant women use **illicit drugs**, **8.5%** drink **alcohol** and **15.9%** smoke **cigarettes**, resulting in over **380,000** offspring exposed to illicit substances, over **550,000** exposed to alcohol and over **one million** exposed to tobacco in utero.



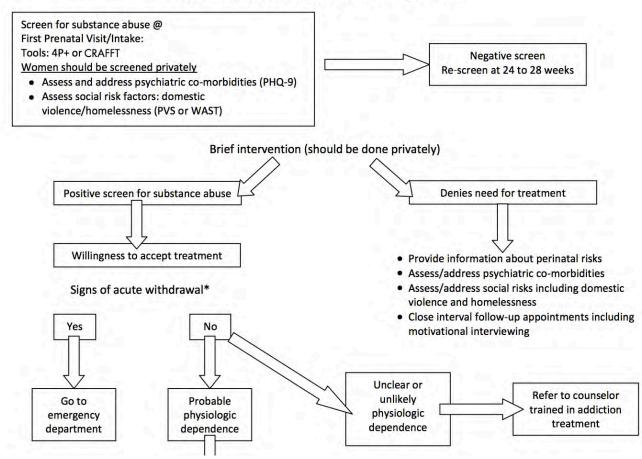
UNIQUE CONSIDERATIONS

- Impact varies and is complicated by:
 - drug, point of exposure and extent of use
 - polysubstance use
 - comorbid and undertreated psychiatric and medical conditions
 - lack of prenatal care
 - Poverty
 - Interpersonal violence
 - Impaired maternal-infant and bonding
- Limited research



APPROACH

Screening and Brief Intervention Algorithm**



APPROACH

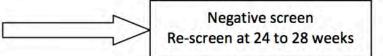
Screen for substance abuse @

First Prenatal Visit/Intake:

Tools: 4P+ or CRAFFT

Women should be screened privately

- Assess and address psychiatric co-morbidities (PHQ-9)
- Assess social risk factors: domestic violence/homelessness (PVS or WAST)





SCREENING

Screen	Sens (%)/Spec(%)	Substance	Cost	
AUDIT-C	67-95/85	Alcohol	Free	
CRAFFT (15-24 yo)	76/94	Alcohol and drug	Free	
4P's Plus	87/76	All	Permission	
T-ACE	69-88/1-89	Heavy alcohol	Free	
TICS	80/80	Alcohol and drug	Free	
TWEAK	71-91/73-83	Heavy alcohol	Free	



SCREENING

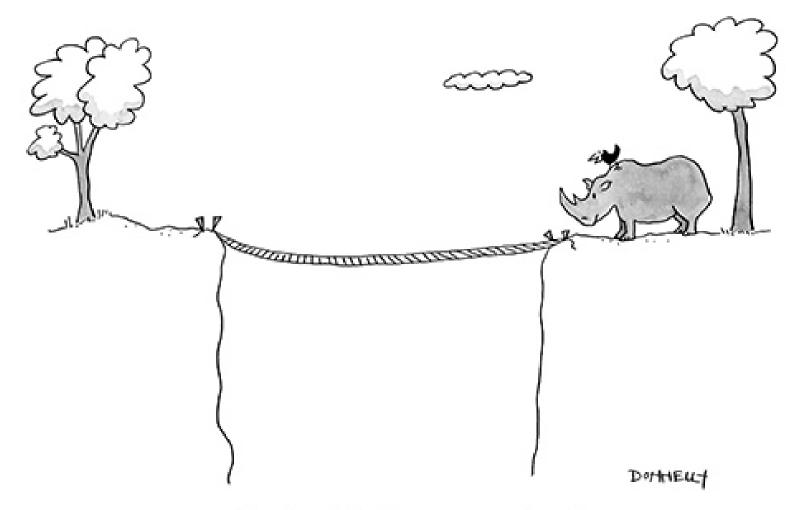
- Assess: Readiness to change
- Advise: fill in knowledge gaps for all pts
- Assist and Arrange: if ready, refer



SCREENING

Drug toxicology is NOT recommended for universal screening because it has limitations and should only be considered if there is a clinical indication and with consent.





"Go ahead. Nothing to worry about."



TOBACCO: INTRODUCTION

- Remains one the most prevalent and preventable causes of infant morbidity and mortality in the US
- Almost ½ quit during pregnancy and close to 80% relapse following delivery
- Smokers have the lowest abstinence rates when compared with other substances



TOBACCO: PATHOPHYSIOLOGY

- Nicotine easily crosses the placenta
- Amniotic fluid nicotine levels are severely elevated
- Increases placental resistance and toxin exposure
 impaired fetal oxygenation



TOBACCO: ADVERSE EFFECTS

PREGNANCY

- Early Pregnancy Loss/IUFD
- Ectopic Pregnancy
- Preterm Delivery
- Low Birth Weight/SGA
- PROM
- Placental abruption/Previa
- Antenatal depressive symptomatology in the mother

POSTNATAL

- SIDS
- NFC
- Childhood Asthmas/Obesity/Increased risk for Respiratory Infections and Otitis Media
- Associations with poor academic outcomes/ADHD/substance use/antisocial behaviors (studies have mixed results; many confounders)
- Altered maternal/fetal attachment (confounders)



TOBACCO: INTERVENTIONS

- Early identification and counseling
- Contingency management
 - Cochrane review: CM superior to other interventions
- NRT +/- Bupropion
 - NRT increases abstinence rates in late pregnancy by 40%



CONTINGENCY MANAGEMENT



The Center

Program Reviews

Eye on Innovation

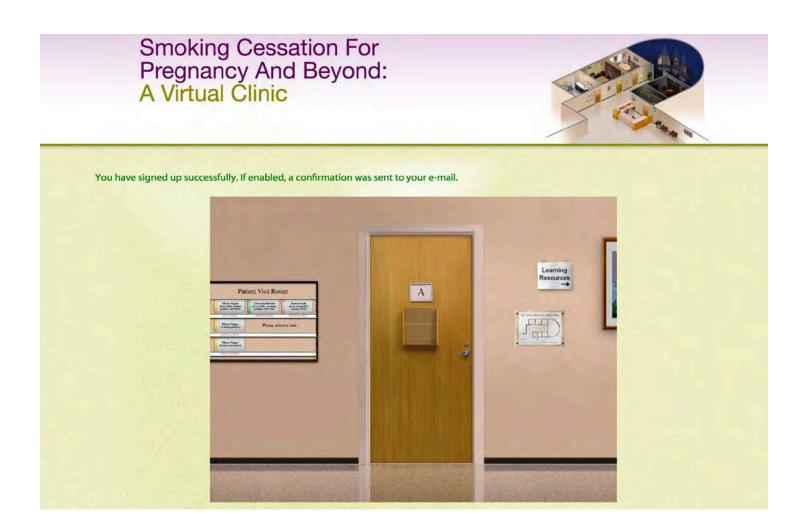
Resources

PROGRAM REVIEWS

Motive8: Online contingency management for smoking cessation



TOBACCO: INTERVENTIONS





ALCOHOL: EPIDEMIOLOGY

"CDC to Women: Protect Your Womb From the Devil Drink," sneered The Atlantic. Slate wondered: "CDC Says Women Shouldn't Drink Unless They're On Birth Control. Is It Drunk?!?"

<u>Jezebel</u>, <u>Elle</u> and <u>USA Today</u> all expressed (righteous) outrage at the idea that a government agency should suggest an entire population of adult women stop drinking because of theoretical fetuses.



ALCOHOL: EPIDEMIOLOGY

- Approximately 3.3 million U.S. women aged 15-44 years who were not pregnant and not sterile were at risk for an alcohol-exposed pregnancy during 2011–2013.
- A developing baby can be exposed to alcohol before a woman knows she is pregnant.



ALCOHOL: EPIDEMIOLOGY

- Prenatal alcohol exposure is the leading preventable cause of birth defects and neurodevelopmental in the US.
- Binge drinking is clearly associated with harmful effects in pregnancy.
- Studies on light and moderate drinking have inconsistent findings.

©2017 University of Washington

ALCOHOL: PATHOPHYSIOLOGY

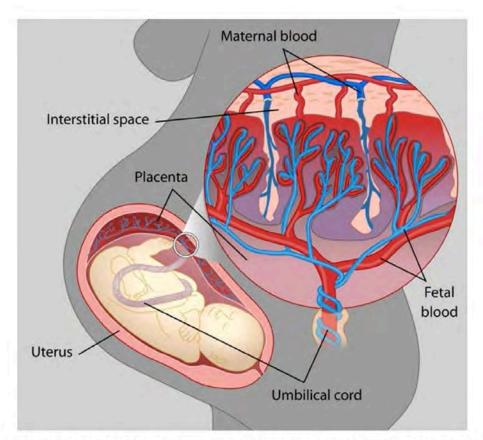


Figure 5.5 In the placenta alcohol follows nutrients across the interstitial space from the maternal to the fetal blood supply. The baby gets as much alcohol as the mother gets.



Alcohol use during pregnancy can lead to lifelong effects.

Up to 1 in 20 US school children may have FASDs.



People with FASDs can experience a mix of the following problems:

Physical issues

 low birth weight and growth



- · problems with heart, kidneys, and other organs
- damage to parts of the brain .

Which leads to ...

Behavioral and intellectual disabilities



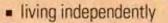
- learning disabilities and low IQ
- hyperactivity
- difficulty with attention
- poor ability to communicate in social situations
- poor reasoning and judgment skills



These can lead to...

Lifelong issues with

 school and social skills



- mental health
- substance use
- keeping a job
- trouble with the law



Drinking while pregnant costs the US \$5.5 billion (2010).













SOURCES: CDC Vital Signs, February 2016. American Journal of Preventive Medicine, November 2015.

ALCOHOL: FASD

	Four Diagnoses under	the Umbre	lla of FASD			
Diagnosis		Growth	FAS Face	Brain		Alcohol
1. FAS	Fetal Alcohol Syndrome	al Alcohol Syndrome growth face severe				
2. PFAS	PFAS Partial FAS		face	severe		alc
3. SE/AE*	Static Encephalopathy / Alc Exposed	Exposed severe			alc	
4. ND/AE	Neurobehavioral Disorder / Alc Exposed			1	moderate	alc

Also referred to as:

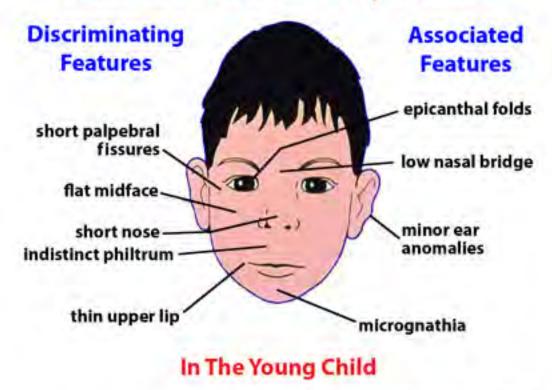
- Alcohol Related Neurodevelopmental Disorder (ARND) or
- Neurodevelopmental Disorder Prenatal Alcohol Exposed (ND-PAE)

https://depts.washington.edu/fasdpn/htmls/fasd-fas.htm



ALCOHOL: FAS

Faces in Fetal Alcohol Syndrome



Streissguth, 1994

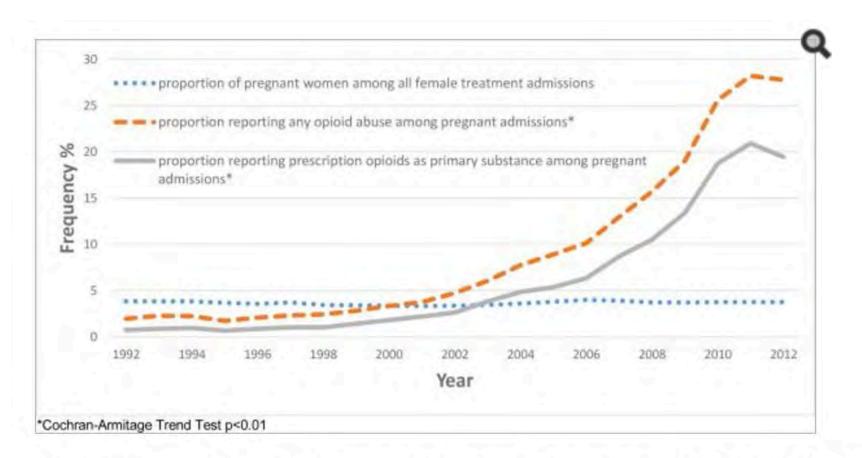


ALCOHOL: INTERVENTIONS

- Behavioral Intervention
 - No evidence supporting one intervention over another
- Medication Assisted Treatment
 - Naltrexone (?), disulfiram (no?), acamprosate (no?)
- Referral to a higher level of care as indicated
 - Medically supervised withdrawal
 - Residential treatment



OPIOIDS: EPIDEMIOLOGY



Pregnancy and prescription opioid abuse among substance abuse treatment admissions, TEDS-A 1992-2012

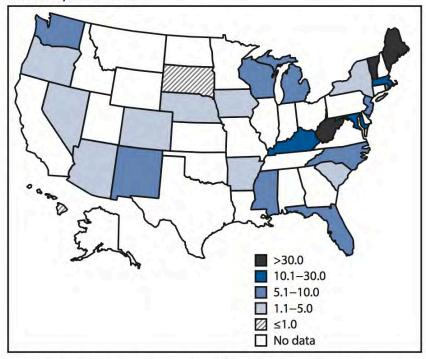
OPIOIDS: ADVERSE EFFECTS

- Placental Abruption
- IUFD
- Intraamniotic infection
- IUGR
- Fetal passage of meconium
- Preeclampsia
- Premature labor and delivery
- Premature rupture of membranes
- Placental insufficiency
- Miscarriage
- Postpartum hemorrhage
- Septic thrombophlebitis
- Mixed data on teratogenecity



OPIOIDS: NAS

FIGURE. Neonatal abstinence syndrome (NAS) incidence rate* — 25 states, 2012–2013[†]



Source: State Inpatient Databases, Healthcare Cost and Utilization Project.



^{*} NAS cases per 1,000 hospital births.

[†] Incidence rates reported are for 2013, except for four states (Maine, Maryland, Massachusetts, and Rhode Island) for which 2013 data were not available; 2012 data are reported for these states.

OPIOIDS: NAS

- Clinical diagnosis:
 - –hx of maternal opioid use
 - –positive tox screen
 - –neonatal findings c/w NAS
- Varies widely in presentation
- Potentiated by other substances
- No known long-term adverse effects



OPIOIDS: INTERVENTIONS



COMMITTEE OPINION



Number 524 • May 2012

Committee on Health Care for Underserved Women and the American Society of Addiction Medicine

This information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

ABSTRACT: Opioid use in pregnancy is not uncommon, and the use of illicit opioids during pregnancy is associated with an increased risk of adverse outcomes. The current standard of care for pregnant women with opioid dependence is referral for opioid-assisted therapy with methadone, but emerging evidence suggests that buprenorphine also should be considered. Medically supervised tapered doses of opioids during pregnancy often result in relapse to former use. Abrupt discontinuation of opioids in an opioid-dependent pregnant woman can result in preterm labor, fetal distress, or fetal demise. During the intrapartum and postpartum period, special considerations are needed for women who are opioid dependent to ensure appropriate pain management, to prevent postpartum relapse and a risk of overdose, and to ensure adequate contraception to prevent unintended pregnancies. Patient stabilization with opioid-assisted therapy is compatible with breastfeeding. Neonatal abstinence syndrome is an expected and treatable condition that follows prenatal exposure to opioid agonists.



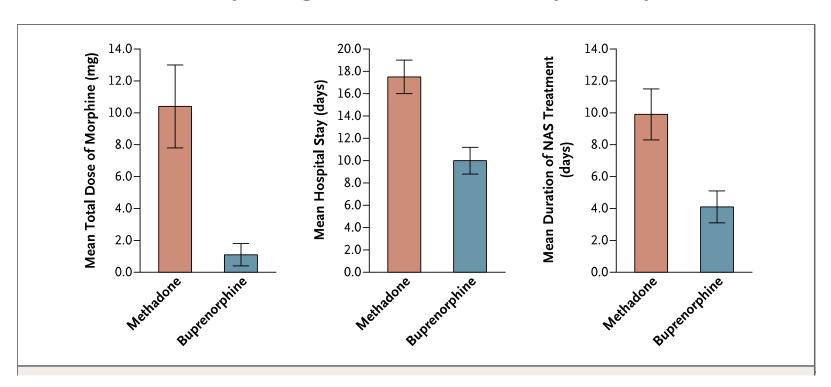
- Medically supervised withdrawal can be safely performed, but it presents a high risk for relapse (41 to 96%)
 - Placental abruption, PTL, meconium, growth delay, fetal death
 - Poor prenatal care



- Reduces risk of illicit opiate use and other drugs diminishing risk of transmission of infectious diseases
- Prevents fluctuation in maternal drug level over the course of the day thus avoiding fetal distress
- Improves participation in prenatal care
- Improves maternal nutrition and infant birth weight
- Reduces obstetric complications (IUFD, PTL etc)
- Removes opiate-dependent woman from high-risk environment

©2017 University of Washington

Outcomes comparing methadone to buprenorphine



Methadone



Most evidence in pregnancy

Daily observed dosing

No diversion potential

No ceiling effect

Longer NAS hospital stay

Buprenorphine



Office based therapy

Diversion potential

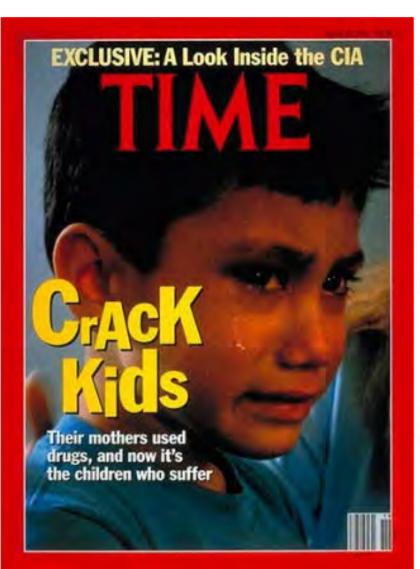
Need to be in withdrawal to start

Ceiling effect

Shorter NAS hospital stay



COCAINE



The New Hork Times
Revisiting the 'Crack Babies'
Epidemic That Was Not





COCAINE: ADVERSE EFFECTS

- PROM
- Placental abruption
- Preterm birth (OR = 3.38; 95% CI: 2.72–4.21)
- Low birth weight (OR = 3.66; 95% CI: 2.90– 4.63)
- **SGA** (OR = 3.23; 95% CI: 2.43–4.30)

COCAINE: INTERVENTIONS

- CBT, MI and CM
- No evidence-based pharmacologic treatments



CANNABIS: EPIDEMIOLOGY

- Most commonly used illicit substance in pregnancy and lactation
- Prevalence ranges from 10% to 43%



CANNABIS: PATHOPHYSIOLOGY

- δ -9-tetrahydrocannabinol (THC) crosses the placenta, but its major metabolite does not
- Fetal THC concentrations are lower than maternal
- Produces 5x the amount of CO as cigarette smoke

CANNABIS: ADVERSE EFFECTS



Pregnant Women Turn to Marijuana, Perhaps Harming Infants

More expectant mothers are using marijuana, believing it safe. But research suggests it may hurt brain development and reduce birth weight.

NYTIMES.COM



CANNABIS: ADVERSE EFFECTS

- LBW*
- PTL*
- SGA*
- Fetal brain growth
- Poor attention and executive functioning
- Lower academic achievement
- Increased behavioral problems



CANNABIS: INTERVENTIONS

- CBT, MI, CM?
 - Brief Marijuana Dependence Counseling by SAMSHA
- No evidence-based pharmacologic treatments



BREASTFEEDING

- Illicit substances including marijuana, heroin, cocaine and methamphetamine: contraindicated in breastfeeding according to the AAP.
- Nicotine and alcohol: benefits outweigh risks with limited use
- Methadone: encouraged

SUMMARY

- Screen all pts for substance use in pregnancy and screen more than once
- Fill in gaps in knowledge around substance use in pregnancy
- Weigh the r/b of various treatments with the risks of continued substance use in pregnancy
- Refer to a higher level of care as indicated



The New York Times

July 24, 1992

Mother Cleared of Passing Drug to Babies

By TAMAR LEWIN

Correction Appended

The Supreme Court of Florida yesterday overturned the conviction of Jennifer Clarice Johnson, the first woman in the nation convicted of delivering drugs to her newborn infants through the umbilical cord in the seconds after their births.

Ms. Johnson, 26 years old, of Altamonte Springs, was charged and found guilty under laws intended to apply to drug traffickers. About 160 such criminal cases have been brought nationwide.

"It's a great victory for public health, for women and newborns and common sense," said Lynn Paltrow, litigation director of the Center for Reproductive Law and Policy, which provided legal representation for Ms. Johnson. "It's the first Supreme Court in any state to address a conviction of a pregnant woman for giving birth to a substance-exposed newborn. It's significant both because it's a unanimous decision and because now all the courts that have ruled on these cases say they're illegal, unconstitutional or both."



RESOURCES

- See email attachment for more information:
 - Swedish OB Outreach Clinic
 - 26 day inpatient "Chemically Using Pregnant Women" programs
 - Outpatient Treatment Programs
 - 6 month residential treatment programs for pregnant and parenting women
 - Parent-Child Assistance Program (PCAP)
 - MOMs Plus Case Management
 - Nurse-Family Partnership
 - Maternity Support Services and Infant Case Management



SPECIAL THANKS TO

Drs. Duncan, Sapienza and Peterson



- Abrams RM, Cook CE, Davis KH, Niederreither K, Jaeger MJ, Szeto HH. Plasma delta-9-tetrahydrocannabinol in pregnant sheep and fetus after inhalation of smoke from a marijuana cigarette. Alcohol Drug Res. 1985-1986;6(5):361–369
- ACOG Committee on Health Care for Underserved Women, American Society of Addiction Medicine. ACOG Committee Opinion No. 524: Opioid abuse, dependence, and addiction in pregnancy. Obstet Gynecol 2012; 119:1070.
- Addis A, Moretti ME, Ahmed Syed F, Einarson TR, Koren G. Fetal effects of cocaine: an updated meta-analysis. Reprod Toxicol. 2001; 15:341–69.
- Administration SAaMHS. The National Survey on Drug Use and Health Report: Substane use among womend urign pregnancy and following childbirth. Office of Applied Studies SAaMHSA. , editor. Rockville: p. MD2009
- Alcohol and Pregnancy. Centers for Disease Control and Prevention. https://www.cdc.gov/vitalsigns/fasd/. Published February 2, 2016. Accessed March 26, 2017.
- Angelotta, J. W., & Friedman, R. A. (2016). A Moral or Medical Problem? The Relationship between Legal Penalties and Treatment Practices for Opioid Use Disorders in Pregnant Women. Women's Health Issues, 1–7.
- Bailey JR, Cunny HC, Paule MG, Slikker W Jr. Fetal disposition of delta 9-tetrahydrocannabinol (THC) during late pregnancy in the rhesus monkey. Toxicol Appl Pharmacol.1987;90(2):315–321
- Bandstra ES, Vogel AL, Morrow CE, Xue L, Anthony JC. Severity of prenatal cocaine exposure and child language functioning through age seven years: a longitudinal latent growth curve analysis. Subst Use Misuse. 2004; 39:25–59.
- Bartu AE, llett KF, Hackett LP, et al. Buprenorphine exposure in infants of opioid-dependent mothers at birth. Aust N Z J Obstet Gynaecol 2012; 52:342.
- Behnke, M., & Smith, V. C. (2013). Prenatal Substance Abuse: Short- and Long-term Effects on the Exposed Fetus. Pediatrics, 131(3), e1009–e1024.
- Bell J, Towers CV, Hennessy MD, et al. Detoxification from opiate drugs during pregnancy. Am J Obstet Gynecol 2016; 215:374.e1.
- Benningfield MM, Arria AM, Kaltenbach K, et al. Co-occurring psychiatric symptoms are associated with increased psychological, social, and medical impairment in opioid dependent pregnant women. Am J Addict. 2010; 19:416–21.
- Biederman J, Martelon M, Woodworth KY, Spencer TJ, Faraone SV. Is Maternal Smoking During Pregnancy a Risk Factor for Cigarette Smoking in Offspring? A Longitudinal Controlled Study of ADHD Children Grown Up. J Atten Disord. 2014
- Bio LL, Siu A, Poon CY. Update on the pharmacologic management of neonatal abstinence syndrome. J Perinatol 2011; 31:692.
- Bishop, Darla; Borkowski, Liz; Couillard, Megan; Allina, Amy; Baruch, Susanna; and Wood, Susan, "Pregnant Women and Substance Use: Overview of Research & Policy in the United States" (2017). Jacobs Institute of Women's Health. Paper 5. http://hsrc.himmelfarb.gwu.edu/sphhs.centers jacobs/5



- Burd L, Blair J, Dropps K. Prenatal alcohol exposure, blood alcohol concentrations and alcohol elimination rates for the mother, fetus and newborn. J Perinatol 2012; 32:652.
- Carroll KM, Nich C, Lapaglia DM, Peters EN, Easton CJ, Petry NM. Combining cognitive behavioral therapy and contingency management to enhance their effects in treating cannabis dependence: less can be more, more or less. Addiction. 2012; 107:1650–9.
- Chamberlain C, O'Mara-Eves A, Oliver S, et al.: Psychosocial interventions for supporting women to stop smoking in pregnancy. Cochrane Database Syst Rev. 2013; 10: CD001055.
- Chang G, Goetz MA, Wilkins-Haug L, Berman S. A brief intervention for prenatal alcohol use: an in-depth look. J Subst Abuse Treat 2000;18:365–9.
- Chaplin TM, Freiburger MB, Mayes LC, Sinha R. Prenatal cocaine exposure, gender, and adolescent stress response: a prospective longitudinal study. Neurotoxicol Teratol. 2010; 32:595–604
- Chasnoff IJ, Wells AM, McGourty RF, Bailey LK. Validation of the 4P's plus screen for substance use in pregnancy validation of the 4P's plus. Journal of Perinatology: Official Journal of the California Perinatal Association. 2007;27(12):744–748.
- Coleman T, Cooper S, Thornton JG, et al.: A randomized trial of nicotine- replacement therapy patches in pregnancy. N Engl J Med. 2012; 366(9): 808–818.
- Colman GJ, Joyce T. Trends in smoking before, during, and after pregnancy in ten states. Am J Prev Med. 2003; 24:29–35.
- Compton WM, Thomas YF, Stinson FS, et al.: Prevalence, correlates, disability,
- and comorbidity of DSM-IV drug abuse and dependence in the United States: results from the national epidemiologic survey on alcohol and related conditions. Arch Gen Psychiatry. 2007; 64(5): 566–576.
- Concheiro M, Jones HE, Johnson RE, et al. Preliminary buprenorphine sublingual tablet pharmacokinetic data in plasma, oral fluid, and sweat during treatment of opioid-dependent pregnant women. Ther Drug Monit 2011; 33:619.
- Cooper S, Lewis S, Thornton JG, et al.: The SNAP trial: a randomised placebo-controlled trial of nicotine replacement therapy in pregnancy--clinical effectiveness and safety until 2 years after delivery, with economic evaluation. Health Technol Assess. 2014; 18(54): 1–128.
- Copeland J, Swift W, Roffman R, Stephens R. A randomized controlled trial of brief cognitive- behavioral interventions for cannabis use disorder. J Subst Abuse Treat. 2001; 21:55–64. discussion 5-6.
- Cnattingius S. The epidemiology of smoking during pregnancy: smoking prevalence, maternal characteristics, and pregnancy outcomes. Nicotine Tob Res. 2004; 6(Suppl 2):S125–40.
- Dalterio SL. Cannabinoid exposure: effects on development. Neurobehav Toxicol Teratol.1986;8
- Desai RJ, Hernandez-Diaz S, Bateman BT, et al.: Increase in prescription opioid use during pregnancy among Medicaid-enrolled women. Obstet Gynecol. 2014; 123(5): 997–1002.4):345–352

- DiFranza JR, Aligne CA, Weitzman M. Prenatal and postnatal environmental tobacco smoke exposure and children's health. Pediatrics. 2004; 113:1007–15.
- Doberczak TM, Kandall SR, Wilets I. Neonatal opiate abstinence syndrome in term and preterm infants. J Pediatr 1991; 118:933.
- El-Mohandes A, Herman AA, Nabil El-Khorazaty M, et al. Prenatal care reduces the impact of illicit drug use on perinatal outcomes. J Perinatol 2003; 23:354.
- El-Mohandes AA, Windsor R, Tan S, et al.: A randomized clinical trial of trans-dermal nicotine replacement in pregnant African-American smokers. Matern Child Health J. 2013; 17(5): 897–906.
- Essex HN, Parrott S, Wu Q, et al.: Cost-Effectiveness of Nicotine Patches for Smoking Cessation in Pregnancy: A Placebo Randomized Controlled Trial (SNAP). Nicotine Tob Res. 2015. 17(6): 636–42.
- Fisher SE, Atkinson M, Chang B. Effect of delta-9-tetrahydrocannabinol on the in vitro uptake of alpha-amino isobutyric acid by term human placental slices. Pediatr Res.1987;21(1):104–107
- Forray A. Substance use during pregnancy. F1000Research. 2016;5:F1000 Faculty Rev-887. doi:10.12688/f1000research.7645.1.
- Forray A, Merry B, Lin H, et al.: Perinatal substance use: a prospective evaluation of abstinence and relapse. Drug Alcohol Depend. 2015; 150: 147–155.
- Frank DA, Augustyn M, Knight WG, Pell T, Zuckerman B. Growth, development, and behavior in early childhood following prenatal cocaine exposure: a systematic review. JAMA. 2001; 285:1613–25.
- Fricker HS, Segal S. Narcotic addiction, pregnancy, and the newborn. Am J Dis Child 1978; 132:360.
- Gouin K, Murphy K, Shah PS. Effects of cocaine use during pregnancy on low birthweight and preterm birth: systematic review and metaanalyses. Am J Obstet Gynecol. 2011; 204:340.e1

 .e12.
- Havens JR, Simmons LA, Shannon LM, Hansen WF. Factors associated with substance use during pregnancy: results from a national sample. Drug Alcohol Depend. 2009; 99:89–95.
- Hayes MJ, Brown MS: Epidemic of prescription opiate abuse and neonatal abstinence. JAMA. 2012; 307(18): 1974–1975.
- Hendrée E. Jones, Ph.D., Karol Kaltenbach, Ph.D., Sarah H. Heil, Ph.D., Susan M. Stine, M.D., Ph.D., Mara G. Coyle, M.D., Amelia M. Arria, Ph.D., Kevin E. O'Grady, Ph.D., Peter Selby, M.B., B.S., Peter R. Martin, M.D., and Gabriele Fischer, M.D. Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure N Engl J Med 2010; 363:2320-2331
- Henderson J, Gray R, Brocklehurst P. Systematic review of effects of low-moderate prenatal alcohol exposure on pregnancy outcome. BJOG 2007; 114:243.
- Higgins ST, Bernstein IM, Washio Y, et al.: Effects of smoking cessation with voucher-based contingency management on birth outcomes. Addiction. 2010; 105(11): 2023–2030.
- Hoch E, Bühringer G, Pixa A, et al. CANDIS treatment program for cannabis use disorders: Findings from a randomized multi-site translational trial. Drug Alcohol Depend. 2014; 134:185–93.



- Hoch E, Noack R, Henker J, et al. Efficacy of a targeted cognitive-behavioral treatment program for cannabis use disorders (CANDIS). Eur Neuropsychopharmacol. 2012; 22:267–80.
- Holbrook, B. D. (2016), The effects of nicotine on human fetal development. Birth Defect Res C, 108: 181–192. doi:10.1002/bdrc.21128
- Hudak ML, Tan RC, COMMITTEE ON DRUGS, et al. Neonatal drug withdrawal. Pediatrics 2012; 129:e540.
- Hutchings DE, Martin BR, Gamagaris Z, Miller N, Fico T. Plasma concentrations of delta-9-tetrahydrocannabinol in dams and fetuses following acute or multiple prenatal dosing in rats. Life Sci.1989;44(11):697–701
- Hull L, May J, Farrell-Moore D, Svikis DS. Treatment of cocaine abuse during pregnancy: translating research to clinical practice. Curr Psychiatry Rep. 2010; 12:454–61.
- Ier no D, Mantzari E, Hirst J, et al.: Financial incentives for smoking cessation in pregnancy: a single-arm intervention study assessing cessation and gaming. Addiction. 2015; 110(4): 680–688.
- Janisse JJ, Bailey BA, Ager J, Sokol RJ. Alcohol, Tobacco, Cocaine, and Marijuana Use: Relative Contributions to Preterm Delivery and Fetal Growth Restriction. Substance Abuse. 2013; 35:60–7.
- Jansson LM, Velez M. Neonatal abstinence syndrome. Curr Opin Pediatr 2012; 24:252.
- Jaques SC, Kingsbury A, Henshcke P, et al. Cannabis, the pregnant woman and her child: weeding out the myths. J Perinatol. 2014; 34:417–24.
- Jones HE, Johnson RE, Jasinski DR, Milio L. Randomized controlled study transitioning opioid-dependent pregnant women from short-acting morphine to buprenorphine or methadone.
 Drug Alcohol Depend 2005; 78:33.
- Jones HE, O'Grady KE, Malfi D, Tuten M. Methadone maintenance vs. methadone taper during pregnancy: maternal and neonatal outcomes. Am J Addict 2008; 17:372.
- Higgins ST, Washio Y, Heil SH, et al.: Financial incentives for smoking cessation
- among pregnant and newly postpartum women. Prev Med. 2012; 55(Suppl): S33–S40.
- Horne AW, Brown JK, Nio-Kobayashi J, et al. The association between smoking and ectopic pregnancy: why nicotine is BAD for your fallopian tube. PLoS One. 2014; 9:e89400.
- Kacinko SL, Jones HE, Johnson RE, et al. Urinary excretion of buprenorphine, norbuprenorphine, buprenorphine-glucuronide, and norbuprenorphine-glucuronide in pregnant women receiving buprenorphine maintenance treatment. Clin Chem 2009; 55:1177.
- Kaltenbach K, Berghella V, Finnegan L. Opioid dependence during pregnancy. Effects and management. Obstet Gynecol Clin North Am 1998; 25:139.
- Ko JY, Farr SL, Tong VT, Creanga AA, Callaghan WM. Prevalence and patterns of marijuana use among pregnant and nonpregnant women of reproductive age. Am J Obstet Gynecol. 2015

- Koren G, Nulman I, Chudley AE, Loocke C. Fetal alcohol spectrum disorder. CMAJ 2003; 169:1181.
- Lam SK, To WK, Duthie SJ, Ma HK. Narcotic addiction in pregnancy with adverse maternal and perinatal outcome. Aust N Z J Obstet Gynaecol 1992; 32:216.
- Lewin T. Mother Cleared of Passing Drug to Babies. New York Times. http://www.nytimes.com/1992/07/24/news/mother-cleared-of-passing-drug-to-babies.html. Published July 24, 1992. Accessed March 21, 2017.
- Levitt C, Shaw E, Wong S, et al.: Systematic review of the literature on postpartum care: effectiveness of interventions for smoking relapse prevention, cessation, and reduction in postpartum women. Birth. 2007; 34(4): 341–347.
- Liu AJ, Jones MP, Murray H, et al. Perinatal risk factors for the neonatal abstinence syndrome in infants born to women on methadone maintenance therapy. Aust N Z J Obstet Gynaecol 2010; 50:253.
- Lotfipour S, Ferguson E, Leonard G, et al. Maternal cigarette smoking during pregnancy predicts drug use via externalizing behavior in two community-based samples of adolescents. Addiction. 2014; 109:1718–29.
- Ludlow JP, Evans SF, Hulse G. Obstetric and perinatal outcomes in pregnancies associated with illicit substance abuse. Aust N Z J Obstet Gynaecol. 2004; 44:302–6.
- Magee SR, Bublitz MH, Orazine C, et al. The relationship between maternal-fetal attachment and cigarette smoking over pregnancy. Matern Child Health J. 2014; 18:1017–22.
- Mamun AA, Najman JM. Birth outcomes associated with cannabis use before and during pregnancy. Pediatric ReseaRch. 2012; 71
- Mark K, Desai A, Terplan M. Marijuana use and pregnancy: prevalence, associated characteristics, and birth outcomes. Arch Womens Ment Health. 2015
- Martin CE, Longinaker N, Mark K, Chisolm MS, Terplan M. Recent trends in treatment admissions for marijuana use during pregnancy. J Addict Med. 2015; 9:99–104.
- Maas U, Kattner E, Weingart-Jesse B, et al. Infrequent neonatal opiate withdrawal following maternal methadone detoxification during pregnancy. J Perinat Med 1990; 18:111.
- Maeda A, Bateman BT, Clancy CR, et al. Opioid abuse and dependence during pregnancy: temporal trends and obstetrical outcomes. Anesthesiology 2014; 121:1158.
- Maritz GS. Perinatal exposure to nicotine and implications for subsequent obstructive lung disease. Paediatr Respir Rev. 2013; 14:3–8.
- Martin CE, Longinaker N, Terplan M. Recent trends in treatment admissions for prescription opioid abuse during pregnancy. Journal of substance abuse treatment. 2015;48(1):37-42. doi:10.1016/j.jsat.2014.07.007.
- Maternal and Infant Health. Centers for Disease Control and Prevention. https://www.cdc.gov/reproductivehealth/maternalinfanthealth/. Published January 12, 2017. Accessed March 26, 2017.
- Metz TD, Stickrath EH. Marijuana use in pregnancy and lactation: a review of the evidence. Am J Obstet Gynecol. 2015



- Morgan B, Brake SC, Hutchings DE, Miller N, Gamagaris Z. Delta-9-tetrahydrocannabinol during pregnancy in the rat: effects on development of RNA, DNA, and protein in offspring brain. Pharmacol Biochem Behav. 1988;31(2):365–369
- Murthy NV, Melville GN, Wynter HH. Contractile responses of uterine smooth muscle to acetylcholine and marihuana extract. Int J Gynaecol Obstet. 1983;21(3):223–226
- Nanovskaya T, Deshmukh S, Brooks M, Ahmed MS. Transplacental transfer and metabolism of buprenorphine. J Pharmacol Exp Ther 2002; 300:26.
- New white paper on pregnant women and substance use provides overview of research and policy. Milken Institute School of Public Health. http://publichealth.gwu.edu/content/new-white-paper-pregnant-women-and-substance-use-provides-overview-research-and-policy. Accessed March 26, 2017.
- Nicotine replacement therapy effect on pregnancy outcomes. Forinash AB, et al Ann Pharmacother, 2010 Nov: 44 (11)
- Oncken CA, Kranzler HR: What do we know about the role of pharmacotherapy for smoking cessation before or during pregnancy? Nicotine Tob Res. 2009; 11(11): 1265–1273.
- Ostrea EM Jr, Brady MJ, Parks PM, et al. Drug screening of meconium in infants of drug-dependent mothers: an alternative to urine testing. J Pediatr 1989; 115:474.
- Passey ME, Sanson-Fisher RW, D'Este CA, et al.: Tobacco, alcohol and cannabis use during pregnancy: clustering of risks. Drug Alcohol Depend. 2014; 134: 44–50.
- Patrick SW, Dudley J, Martin PR, et al. Prescription opioid epidemic and infant outcomes. Pediatrics 2015; 135:842.
- Patrick SW, Schumacher RE, Benneyworth BD, Krans EE, McAllister JM, Davis MM. Neonatal abstinence syndrome and associated health care expenditures: United States, 2000-2009. JAMA. 2012; 307:1934–40. [PubMed: 22546608] Informative study on neonatal abstinence syndrome and the healtcare costs of opioid use in pregnancy.
- Patrick SW, Schumacher RE, Benneyworth BD, et al.: Neonatal abstinence syndrome and associated health care expenditures: United States, 2000–2009. JAMA. 2012; 307(18): 1934–1940.
- Petry NM. Contingency management: what it is and why psychiatrists should want to use it. The Psychiatrist. 2011;35(5):161-163. doi:10.1192/pb.bp.110.031831.
- Pharmacological interventions for promoting smoking cessation during pregnancy. Coleman T et al Cochrane Database Syst Rev. 2015 Dec 22;(12)
- Pineles BL, Park E, Samet JM. Systematic review and meta-analysis of miscarriage and maternal exposure to tobacco smoke during pregnancy. Am J Epidemiol. 2014; 179:807–23.
- Press FA. Mother Convicted as Drug Deliverer After Cocaine Is Found in Newborns. Los Angeles Times. http://articles.latimes.com/1989-07-14/news/mn-3733_1_umbilical-cord. Published July 14, 1989. Accessed March 26, 2017.
- Ratner PA. Johnson JL. Bottorff JL. Smoking relapse and early weaning among postpartum women; is there an association? Birth, 1999; 26:76–82.
- Rickman R. Crack Kids. Time. May 1991.



- Rickman R. Crack Kids. Time. May 1991.
- Rodríguez de Fonseca F, Cebeira M, Fernández-Ruiz JJ, Navarro M, Ramos JA. Effects of pre- and perinatal exposure to hashish extracts on the ontogeny of brain dopaminergic neurons. Neuroscience. 1991;43(2-3):713–723
- Saint Louis C. Pregnant Women Turn to Marijuana, Perhaps Harming Infants. New York Times. https://www.nytimes.com/2017/02/02/health/marijuana-and-pregnancy.html. Published February 2, 2017. Accessed March 21, 2017.
- Salihu HM, Wilson RE. Epidemiology of prenatal smoking and perinatal outcomes. Early human development. 2007; 83:713–20
- Schempf, A. H., & Strobino, D. M. (2009). Drug use and limited prenatal care: an examination of responsible barriers. American Journal of Obstetrics and Gynecology, 200(4), 412.e1–412.e10.
- Schottenfeld RS, Moore B, Pantalon MV. Contingency management with community reinforcement approach or twelve-step facilitation drug counseling for cocaine dependent pregnant women or women with young children. Drug Alcohol Depend. 2011; 118:48–55.
- Seligman NS, Almario CV, Hayes EJ, et al. Relationship between maternal methadone dose at delivery and neonatal abstinence syndrome. J Pediatr 2010; 157:428.
- Smoking Cessation ForPregnancy And Beyond: A Virtual Clinic. Smoking and Pregnancy: Home. https://www.smokingcessationandpregnancy.org/. Accessed March 26, 2017.
- Stade BC, Bailey C, Dzendoletas D, Sgro M, Dowswell T, Bennett D. Psychological and/or educational interventions for reducing alcohol consumption in pregnant women and women planning pregnancy. Cochrane Database Syst Rev 2009;(2): CD004228.
- Stephens RS. Roffman RA. Simpson EE. Treating adult marijuana dependence; a test of the relapse prevention model, J Consult Clin Psychol, 1994; 62:92–9.
- Substance Use Disorders During Pregnancy: Guidelines for Screening & Management. http://here.doh.wa.gov/materials/guidelines-substance-abuse-pregnancy/13_PregSubs_E16L.pdf. http://here.doh.wa.gov/materials/guidelines-substance-abuse-pregnancy/13_PregSubs_E16L.pdf. Published 2016. Accessed March 21, 2017.
- Sweeney PJ, Schwartz RM, Mattis NG, Vohr B. The effect of integrating substance abuse treatment with prenatal care on birth outcome. J Perinatol 2000; 20:219.
- Terplan M, Ramanadhan S, Locke A, Longinaker N, Lui S. Psychosocial interventions for pregnant women in outpatient illicit drug treatment programs compared to other interventions. Cochrane Database Syst Rev. 2015; 4:Cd006037.
- Vaz LR, Leonardi-Bee J, Aveyard P, et al. Factors associated with smoking cessation in early and late pregnancy in the smoking, nicotine, and pregnancy trial: a trial of nicotine replacement therapy. Nicotine Tob Res. 2014; 16:381–9.
- Ungar L. Born into suffering: More babies arrive dependent on drugs. USA Today. http://www.usatoday.com/story/news/nation/2015/07/08/babies-born-dependent-on-drugs-continue-to-rise/29212565/. Published July 8, 2015. Accessed March 26, 2017.
- United States Department of H, Human Services. Substance A, Mental Health Services Administration. Center for Behavioral Health S, Quality. National Survey on Drug Use and Health, 2012. Inter-university Consortium for Political and Social Research (ICPSR) [distributor]; 2013.
- Walters DE, Carr LA. Changes in brain catecholamine mechanisms following perinatal exposure to marihuana. Pharmacol Biochem Behav. 1986;25(4):763–768



- Walters DE, Carr LA. Perinatal exposure to cannabinoids alters neurochemical development in rat brain. Pharmacol Biochem Behav. 1988;29(1):213–216
- Warner TD, Roussos-Ross D, Behnke M. It's not your mother's marijuana: effects on maternal- fetal health and the developing child. Clin Perinatol. 2014; 41:877–94.
- Wendell AD. Overview and epidemiology of substance use in pregnancy. Clinic Obstet Gynecology 2013; 56:91-6.
- What is FASD? What is FASD? https://depts.washington.edu/fasdpn/htmls/fasd-fas.htm. Accessed March 21, 2017.
- WHO Recommendations for the Prevention and Management of Tobacco Use and Second-Hand Smoke Exposure in Pregnancy. Geneva: 2013.
- Williams JF, Smith VC, COMMITTEE ON SUBSTANCE ABUSE. Fetal Alcohol Spectrum Disorders. Pediatrics 2015; 136:e1395.
- Winerip M. Revisiting the 'Crack Babies' Epidemic That Was Not. New York Times. http://www.nytimes.com/2013/05/20/booming/revisiting-the-crack-babies-epidemic-that-was-not.html. Published May 30, 2013. Accessed March 21, 2017.
- Winhusen T, Kropp F, Babcock D, et al. Motivational enhancement therapy to improve treatment utilization and outcome in pregnant substance users. J Subst Abuse Treat 2008;35:161–73.
- Wong S, Ordean A, Kahan M, et al. Substance use in pregnancy. J Obstet Gynaecol Can 2011; 33:367.
- Yonkers KA, Forray A, Howell HB, et al. Motivational enhancement therapy coupled with cognitive behavioral therapy versus brief advice: a randomized trial for treatment of hazardous sub-stance use in pregnancy and after delivery. Gen Hosp Psychiatry 2012;34:439–49.

UW PACC
©2017 University of Washington