



Long-term Outcomes for Substance Exposed Infants

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Integrated Care for Women and Babies

Shared Learning Call

10/28/2024

Shout Outs!

- Laurie Halmo, MD
- Mishka Terplan, MD

Limitations

- Polysubstance use/exposures
- Lots of social confounders, particularly poverty
- Heterogeneous populations
 - Different substances/polysubstance use
 - Differences in dose
 - Differences in duration/timing of use
 - Differences in home and built environments
 - Differences in comorbid health concerns (mental health, nutritional status)

Nicotine

- Increased risk of overweight and obesity
- Increased risk of asthma
- Increased risk of ADHD
- Risk of decreased cognitive function and school performance
- Increased risk of nicotine dependence
- Some suggestion of increased risk of cancer
- Special limitations specific to nicotine exposure
 - Nicotine? PAHs? Vape juice? All kinds of other stuff? Postnatal SHS?

Alcohol

- Short term, but SIDS!
- Cognitive impairment (lower IQ)
- Specific cognitive skills may be impaired (e.g., fluency) even if global cognitive function (IQ) is within normal limits
- Difficulty with adaptive skills, social skills
- Increased risk of ADHD, ODD, depression, and other psychiatric comorbidities
- Increased risk of alcohol use disorder

Fetal Alcohol Spectrum Disorders (FASD)

Fetal Alcohol Syndrome (FAS)

- Central nervous system (CNS) problems, minor facial features, and growth problems
- Have trouble with learning, memory, attention span, communication, vision, or hearing
- Often have a hard time in school and trouble building relationships

Alcohol-Related Neurodevelopmental Disorder (ARND)

- Intellectual disabilities and problems with behavior and learning
- They might do poorly in school and have difficulties with math, memory, attention, judgment, and poor impulse control

Alcohol-Related Birth Defects (ARBD)

- Problems with the heart, kidneys, or bones or with hearing

Cannabis

- Increased risk of attention problems, reduced cognitive function and reduced academic performance
- Challenges with executive function
- Earlier initiation of cannabis use

Characteristics Associated With Cannabis Use Initiation by Late Childhood and Early Adolescence in the Adolescent Brain Cognitive Development (ABCD) Study

JAMA Pediatrics August 2023 Volume 177, Number 8

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David A. A. Baranger, PhD

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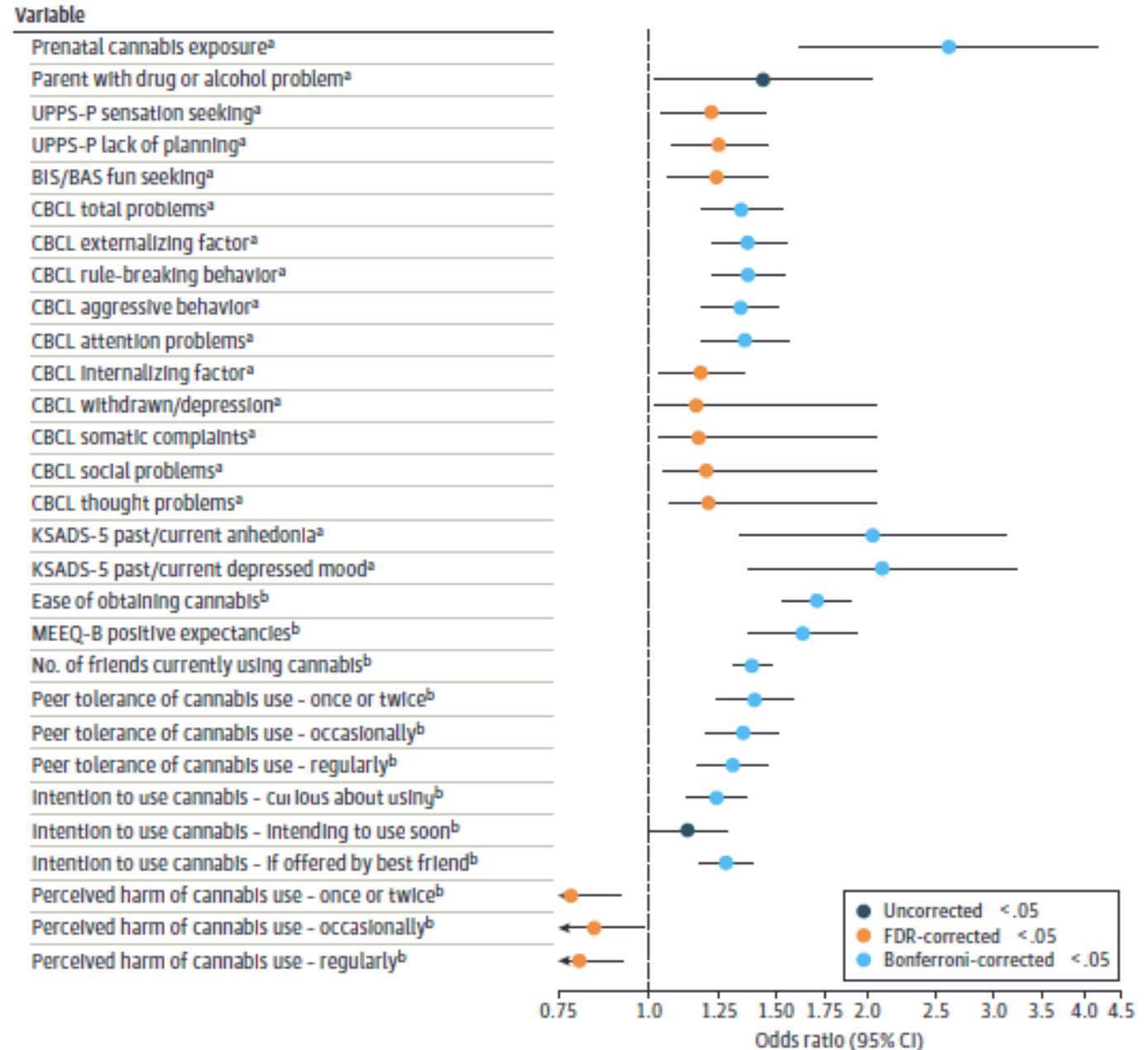
Cynthia Rogers, MD

Ryan Bogdan, PhD

Arpana Agrawal, PhD

“...prenatal cannabis exposure was associated with the largest risk for cannabis use initiation (OR, 2.60; 95% CI, 1.62-4.17); this association remained when additionally controlling for alcohol and tobacco use initiation, family or parent alcohol or drug problems, and prenatal alcohol and tobacco exposure (OR, 2.16; 95% CI, 1.17-3.97).”

Variables Associated With Cannabis Initiation as Children Enter Early Adolescence



Methamphetamine

- Heightened emotional reactivity
- Increased risk of anxiety and depression in toddler/early school years

Prenatal Methamphetamine Exposure and Childhood Behavior Problems at 3 and 5 Years of Age

LaGrasse et al

PEDIATRICS Volume 129, Number 4, April 2012

TABLE 4 Behavior Problems Scores According to Prenatal MA Exposure

Outcome	MA Exposure Group				Adjusted ^a					
	Age 3 Years		Age 5 Years		Exposure ^b		Age ^b		Interaction ^c	
	Exposed (n = 141)	Comparison (n = 147)	Exposed (n = 153)	Comparison (n = 151)	β (SE)	P	β (SE)	P	β (SE)	P
Externalizing	53.0 ± 1.9	52.0 ± 2.2	53.1 ± 2.0	49.6 ± 2.3	2.8 (2.0)	.150	-2.4 (0.8)	.003	2.5 (1.2)	.034
Attention problems	2.6 ± 0.4	2.6 ± 0.4	2.8 ± 0.4	2.7 ± 0.4	0.40 (0.4)	.278	0.01 (0.2)	.995	0.15 (0.2)	.552
Aggressive behavior	12.9 ± 1.3	11.8 ± 1.6	12.6 ± 1.4	10.0 ± 1.6	2.1 (1.4)	.123	-1.9 (0.6)	.002	1.5 (0.8)	.068
ADHD issues	5.3 ± 0.6	5.2 ± 0.6	5.5 ± 0.6	4.6 ± 0.6	0.62 (0.6)	.259	-0.61 (0.2)	.013	0.78 (0.4)	.029
Internalizing	50.9 ± 1.8	48.7 ± 2.2	54.2 ± 1.9	50.8 ± 2.2	3.5 (1.9)	.057	2.1 (0.8)	.007	1.1 (1.2)	.350
Emotionally reactive	3.2 ± 0.5	2.3 ± 0.6	3.7 ± 0.5	2.5 ± 0.6	1.4 (0.5)	.006	0.22 (0.2)	.318	0.29 (0.3)	.363
Anxious/depressed	2.8 ± 0.4	2.0 ± 0.5	3.4 ± 0.4	2.3 ± 0.5	1.0 (0.4)	.019	0.35 (0.2)	.010	0.28 (0.3)	.359
Somatic complaints	1.8 ± 0.3	1.8 ± 0.4	2.3 ± 0.4	2.3 ± 0.4	-0.06 (0.3)	.861	0.53 (0.2)	.002	-0.04 (0.2)	.883
Withdrawn	1.5 ± 0.4	1.4 ± 0.5	1.9 ± 0.4	1.7 ± 0.5	0.44 (0.4)	.273	0.37 (0.2)	.033	0.040 (0.2)	.866
Total problems	52.2 ± 1.8	51.1 ± 2.1	52.9 ± 1.8	50.2 ± 2.1	2.9 (1.8)	.119	-0.91 (0.8)	.227	1.63 (1.1)	.134

Data are presented as adjusted mean ± SE unless otherwise noted.

^a Adjusted analyses tested main effects of MA exposure and child age at assessment (3 vs 5 years) and the interaction of exposure and age, adjusted for prenatal exposure to alcohol, tobacco, and marijuana; birth weight; gender; SES; maternal age; single (no partner); caregiver change; domestic violence; postnatal use of MA; tobacco, alcohol, and marijuana exposure; caregiver psychological symptoms; the quality of the home; child abuse; and study site.

^b The reference group was the comparison group for analysis of exposure and 3 years for analysis of age.

^c A least squares mean procedure was applied to follow up a significant interaction.

Opioids

- Increased risk of ophthalmologic disorders
- Challenges with executive function
- Increased risk of mental health concerns in adolescence

HOT OFF THE PRESS!

First Trimester Use of Buprenorphine or Methadone and the Risk of Congenital Malformations

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Affiliations + expand



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- “Conclusions and relevance: In this cohort study, the risk of most malformations previously associated with opioid exposure was lower in buprenorphine-exposed infants compared with methadone-exposed infants, independent of measured confounders. Malformation risk is one factor that informs the individualized patient decision regarding medications for opioid use disorder in pregnancy.”
- Widely misinterpreted to mean that buprenorphine is “safer” in pregnancy than methadone
- In reality: neither buprenorphine or methadone was compared to control group. There is an irreducible minimum risk of congenital malformation in the general population. Neither group was compared to most important group: pregnant people with untreated OUD.
- Counseling patients: buprenorphine and methadone continue to demonstrate relative safety in pregnancy, and all people who are pregnant have some risk for congenital malformations. Help patients and providers avoid single-cause fallacy thinking.

Brief Report

A novel syndrome associated with prenatal fentanyl exposure

[Erin Wadman](#)¹, [Erica Fernandes](#)¹, [Candace Muss](#)¹, [Nina Powell-Hamilton](#)¹, [Monica H. Wojcik](#)^{2 3}, [Jill A. Madden](#)³, [Chrystalle Katte Carreon](#)⁴, [Robin D. Clark](#)⁵, [Annie Stenftenagel](#)⁶, [Kamal Chikalard](#)⁶, [Virginia Kimonis](#)⁶, [William Brucker](#)⁷, [Carolina Alves](#)⁸, [Karen W. Gripp](#)¹  



- Case series of 6 infants with physical exam findings concerning for SLOS (Smith-Lemli-Opitz syndrome); 4 additional infants added from other institutions
- Multiple and varied prenatal substance exposures, including illicitly manufactured fentanyl
- In reality: no previous literature demonstrating teratogenic risk of pharmaceutical fentanyl. Given the significant number of patients nationwide with prenatal IMF exposure, would expect additional case reports/series, which have failed to materialize.
- Counseling patients: clearly something significant happened to this small group of pregnant patients and their infants, however, this data is not enough to determine what or how, and is unlikely to be related to fentanyl exposure alone

Xylazine Use in Pregnancy: The Effects of the Fentanyl Adulterant Xylazine on Pregnant Patients and the Developing Fetus

Grace Noonan¹, Roopa Sethi^{1 2}

- Very little human data about xylazine in pregnancy
- Xylazine does appear to cross placenta. Assume xylazine also transmitted via lactation.
- Animal models demonstrate concern for decreased uterine blood flow, increased uterine vascular resistance, and decreased fetal growth.
- Counseling patients: consider growth ultrasound if known/consistent xylazine exposure during pregnancy

- Kratom is associated with opioid withdrawal in pregnant people and their infants (NOWS)
- Kratom use (lifetime) is relatively common among pregnant people with substance use (>30%)
- Kratom use during pregnancy and lactation is less common, but not absent (approx. 5%)
- Most people who used kratom during pregnancy report use for treatment of opioid withdrawal symptoms and stress.
- Need to ask specifically about kratom
- Counseling patients: education about NOWS, lactation safety, effective treatment options include buprenorphine



Clinical Rounds

Kratom (*Mitragyna speciosa*): A Case Review of Use Before and During Pregnancy

Mary Ann Faucher CNM, PhD, MPH ✉, Stephanie Morillos LCDC, RSPS, Polly Cordova CNM, DNP, Jessica McNeil-Santiel CNM, DNP, Nancy Onisko DO, Emily H. Adhikari MD, David B. Nelson MD

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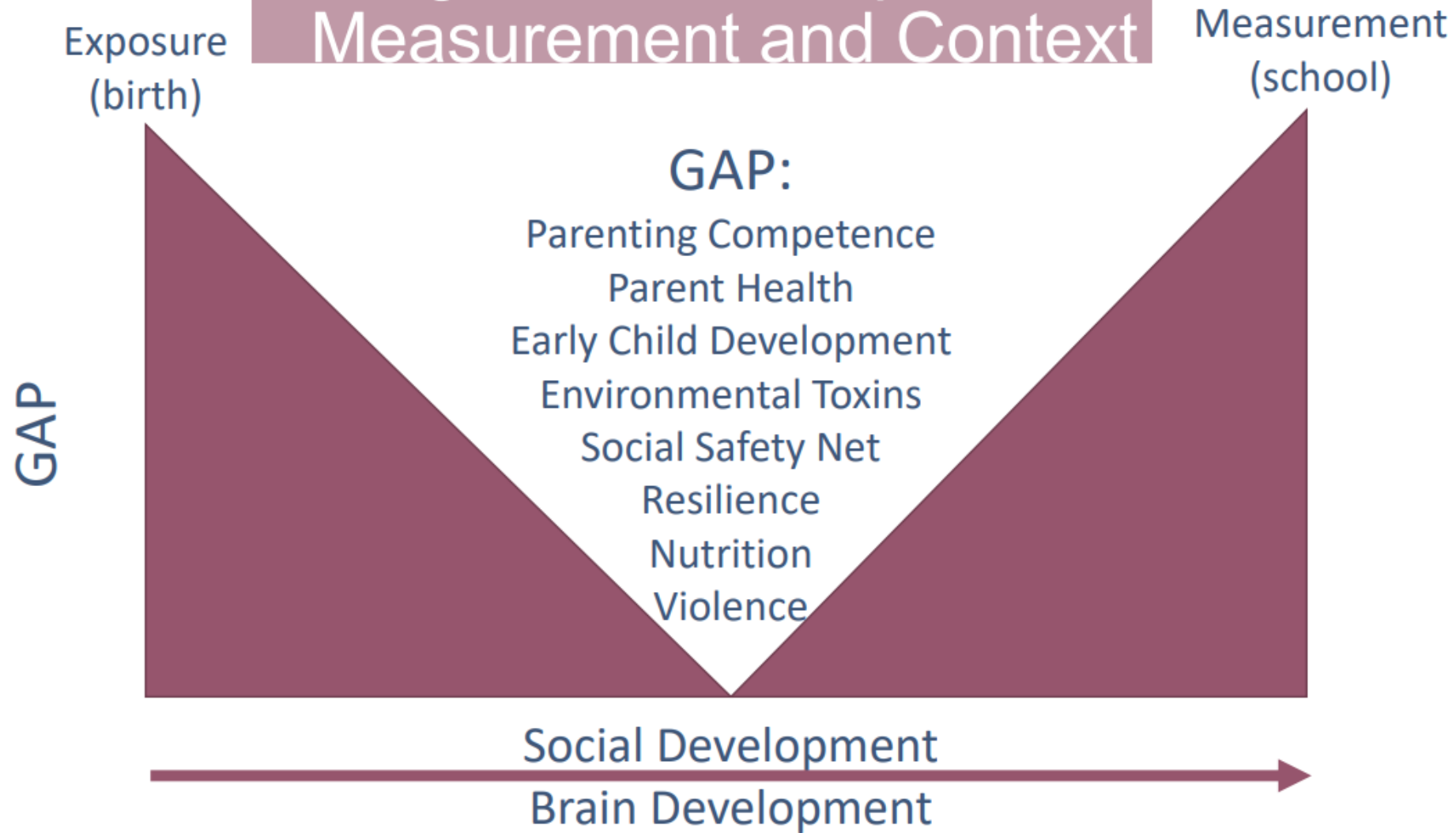
Kratom Use Among Pregnant and Lactating Individuals With Substance Use Disorder

Bowman, Justin BS; Lai, Miao BS; Charles, Jasmin E. PA-C; Gordon, Adam J. MD, MPH; Smid, Marcela C. MD, MA, I

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Drugs and Development: Measurement and Context



Intrauterine Exposure and the Care-Giving Environment

Children With In Utero Cocaine Exposure Do Not Differ From Control Subjects on Intelligence Testing

Hallam Hurt, MD; Elsa Malmud, PhD; Laura Betancourt; Leonard E. Braitman, PhD;
Nancy L. Brodsky, PhD; Joan Giannetta

Inner-city Achievers

Who Are They?

Hallam Hurt, MD; Elsa Malmud, PhD; Leonard E. Braitman, PhD; Laura M. Betancourt, BA;
Nancy L. Brodsky, PhD; Joan M. Giannetta, BA



Table 5. Home Observation for Measurement of the Environment*

Measurement	IQ \geq 90 (n=24)	IQ<90 (n=104)	P Value
Learning Stimulation	9 (5-11)	7 (1-11)	<.001
Language Stimulation	7 (6-7)	7 (4-7)	.03
Physical Environment	6 (5-7)	6 (0-7)	.25
Warmth and Affection	6 (2-7)	5 (0-7)	.01
Academic Stimulation	5 (4-5)	5 (1-5)	.006
Modeling	4 (2-5)	4 (0-5)	.05
Variety in Experience	8 (6-9)	7 (4-9)	<.001
Acceptance	4 (3-4)	4 (0-4)	.06
Total	48.5 (40-53)	43 (20-53)	<.001

* Values are expressed as median (range). See Caldwell and Bradley for more information on HOME.¹⁰

Practical strategies

- Optimize the post natal environment
- Maximize positive childhood experiences (the “antidote” to ACEs)
- Many thanks to Bird Gilmartin MD for her help on this section 😊

Practical strategies: in the office

1. Help families identify and strengthen safe, stable, nurturing relationships. Ask caregivers, “What does support look like for you? Who is supporting you? Who is supporting your child besides you?”
2. Help ensure infants are followed in a medical home
3. Routine screening labs for known neurotoxins/neurodevelopmental mediators (e.g., lead and hemoglobin screening)
4. Screen for caregiver mental health and substance use using a validated screening tool (i.e. EPDS, 5Ps, NIDA Quick Screen)
5. Developmental screening for the child with a validated screening tool (e.g. ASQ, MCHAT)
6. For children in out-of-home placement (foster or kinship care), welcome and include biological parents and family members as much as possible.

Practical strategies: referrals

- Early Intervention (for <3 years old) or Child Find (for 2 years 11 months – 5 years)
- Resources to assist with housing, employment, childcare, food, and transportation as needed
- Services that strengthen the parent-child interaction (e.g., dyadic therapy modalities like child parent psychotherapy, parent child interaction therapy)

Practical strategies: harm reduction

- Safe sleep
- Safe and sober caretaking and driving
- Substances/medications up, away, and out of sight
- Lockboxes/lockbags
- Carry naloxone
- Know the Poison Control Number (1-800-222-1222)

Maximizing positive childhood experiences

- Read books every day
- Play – at least 10-15 minutes every day, face to face, no phones
- Name feelings – both yours and your child’s; encourage children to name their own feelings as they grow
- Teach a relaxation/regulation skill (belly breathing, guided imagery, emotion scales (red/yellow/green zone), progressive muscle tightening and relaxation etc)
- Help children create a physical ”safe space” at home (“cozy corner,” box, closet etc)
- Avoid multitasking with your child as much as possible. When your child is talking, stop, put your phone down and listen.
- Catch your child doing a good job and praise them for something specific and concrete
- Set expectations ahead of time, then stick to what you said