Improving Outcomes and Mortality from Fentanyl – MOUD split dose, Toxicology, Breastfeeding: Breastfeeding Considerations

Elisha Wachman, MD
Professor of Pediatrics, BU Chobanian & Avedisian School of Medicine
Neonatologist, Boston Medical Center, Boston MA

ASAM Annual Conference – April 5, 2024, Dallas, TX

Disclosure Information

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April 5, 2024

Elisha Wachman, MD

- No conflicts of interest to disclose

Learning Objectives

- Review the 2023 Academy of Breastfeeding Medicine guidelines for breastfeeding in the setting of non-prescribed opioid use
- Pharmacokinetics of opioids in breastmilk
- Considerations for initiation of breastfeeding in the setting of non-prescribed opioid use

Breastfeeding Benefits in Substance-Exposed Parent-Infant Dyads

- **Known health benefits for the dyad**
- **Reduces** severity of neonatal-opioid withdrawal syndrome
- May help birthing-individuals **bond** with their infant

Welle-Strand GK et al, 2013, Holmes AP et al, 2017, Liangliang C et al, 2022

Potential Harms of Breastfeeding in Substance-Exposed Parent-Infant Dyads

- **Reduced parental ability to respond to infant feeding cues**

- **Infant substance exposure through breast milk risking**:
  - Acute toxicity
  - Reduced breastfeeding ability
  - Potential alterations in infant brain development

Facilitators to Breastfeeding in Individuals with SUD

- **Comprehensive prenatal and addiction care**
  - Individuals with SUD have high rates of co-occurring mental illness, trauma, and structural inequities
- **Engagement with prenatal care**:
  - Improves paternal and neonatal outcomes
  - Reduces likelihood of active substance use at delivery
  - Can support a shared-decision making process

Choi S et al, 2021, Stulac S et al, 2019

Barriers to Breastfeeding

- **Barriers to prenatal and addiction treatment**
- **Punitive laws that criminalize substance use during pregnancy or mandate reporting to child services**
  - Deter pregnant individuals from seeking care and MOUD
- **Stigma & lack of support**
- **Varying provider recommendations**
- **Other medications**
- **Infant factors – NOWS, weight loss, parental-infant separation in the hospital**

Burns L et al, 2007 Hui K et al, 2017, Harp KLH & Bunting AM, 2020

ABM 2023 guidelines revision

BREASTFEEDING MEDICINE
Volume 18, Number 10, 2023

DOI: 10.1089/bfm.2023.29256.abm

ABM Protocol

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Academy of Breastfeeding Medicine Clinical Protocol #21: Breastfeeding in the Setting of Substance Use and Substance Use Disorder (Revised 2023)

Miriam Harris,[1,2] Davida M. Schiff,[3,4] Kelley Saia,[2,5] Serra Muftu,[3,4] Katherine R. Standish,[6] and Elisha M. Wachman[2,7]

Relative Infant Dose (RID)

- **Commonly used tool to estimate infant drug exposure**
- **RID % = Infant daily dose via breastmilk (mg/kg/day) / maternal dose (mg/kg/day) x 100**
  - **RID < 10% generally safe**
  - **RID > 25% should be avoided**
- **<u>Dependent on</u>:**
  - Drug pharmacology
  - Amount and timing of lactating individual's exposure
  - Lactating individual and infant metabolism
  - Infant gastric absorption

Harris M, et al, *Breastfeeding Med,* 2023

Non-Prescribed Opioids

- Little known about non-prescribed opioids
- Data on pharmacokinetics of prescribed opioids which can help to inform risk-benefit assessments
- Short-acting prescribed: RIDs low (1-5%), breastfeeding typically safe, dependent on total daily dose
- Risk for infant sedation, withdrawal, and respiratory depression with higher doses
- Impact on long-term infant outcomes via breastmilk exposure is unknown

Harris M, et al, *Breastfeeding Med,* 2023

Short Acting Prescribed Opioids

- Codeine: L4
  - Amount in milk is dependent on dose and maternal metabolism
  - Ultra-rapid CYP2D6 metabolizers
  - Infant apnea and somnolence; 1 case of neonatal death
- Morphine: L3
  - No reported adverse pediatric effects, but concerns given codeine adverse effects
- Oxycodone: L3
  - Sedation reported in up to 20% infants with doses >30mg/day
- Hydromorphone: L3
  - Sedation and apnea possible, especially with doses >30mg/day

Hale's Medications in Mother's Milk, 2021

Opioid Pharmacokinetics

Opioid	Peak drug effect	Drug half-life	RID(%)
Morphine	0.5 – 1 hour	2 – 4 hours	3.0%
Codeine	1 – 1.5 hours	3 hours	0.6 – 8.1%
Oxycodone	0.5 – 2 hours	3 – 4 hours	1.0 – 4.6%
Tramadol	2 – 3 hours	6 – 7.5 hours	2.9%

Hales, 2021; Lexicomp, 2022

Harris M, et al, *Breastfeeding Med,* 2023

Recommendations

- Non-prescribed fentanyl
- Non-prescribed heroin
- Unknown exposure dose

Substance	Recommendations	Strength	Evidence level
Non-prescribed opioids	Breastfeeding should be avoided during use of non-prescribed opioids	B	2

Harris M, et al, *Breastfeeding Med,* 2023

OUD Treatments

- Medication for opioid use disorder (MOUD) universally accepted as standard of care for OUD
- AAP, ACOG, and ABM all support breastfeeding in stable lactating individuals with OUD on MOUD
- Reduced severity of NOWS with breastfeeding

Wojnar-Horton RE, 1997; Jansson LM, 2008

OUD treatments

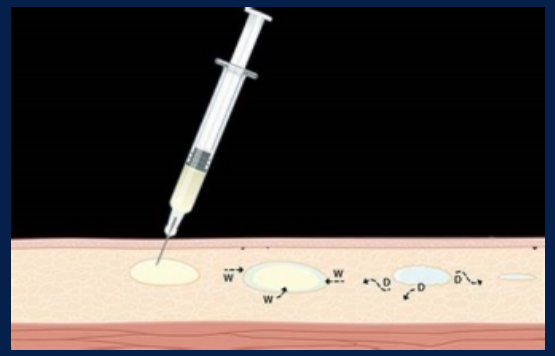
- **Methadone:**
  - Best studied among lactating individuals
  - Concentrations in breastmilk are low, RID 3%
  - Encourage regardless of dose
  - Long-term effects poorly understood but benefits outweigh the risks
- **Buprenorphine (sublingual formulations):**
  - Less studied but data suggest minimal concentrations in breastmilk
  - Few harms regardless of maternal dose
  - Long-term safety data is lacking

Illet KF, 2012; Jansson LM, 2016

Harris M, et al, *Breastfeeding Med,* 2023

Emerging Treatment: XR BUP

- **<u>Long-acting buprenorphine formulations:</u>**
  - Weekly and monthly formulations
  - No studies in lactation
  - Concerns about preservative **N-Methyl-2-pyurrolidone (NMP)** in monthly formulations



Harris M, et al, *Breastfeeding Med,* 2023

Emerging Treatment: Naltrexone

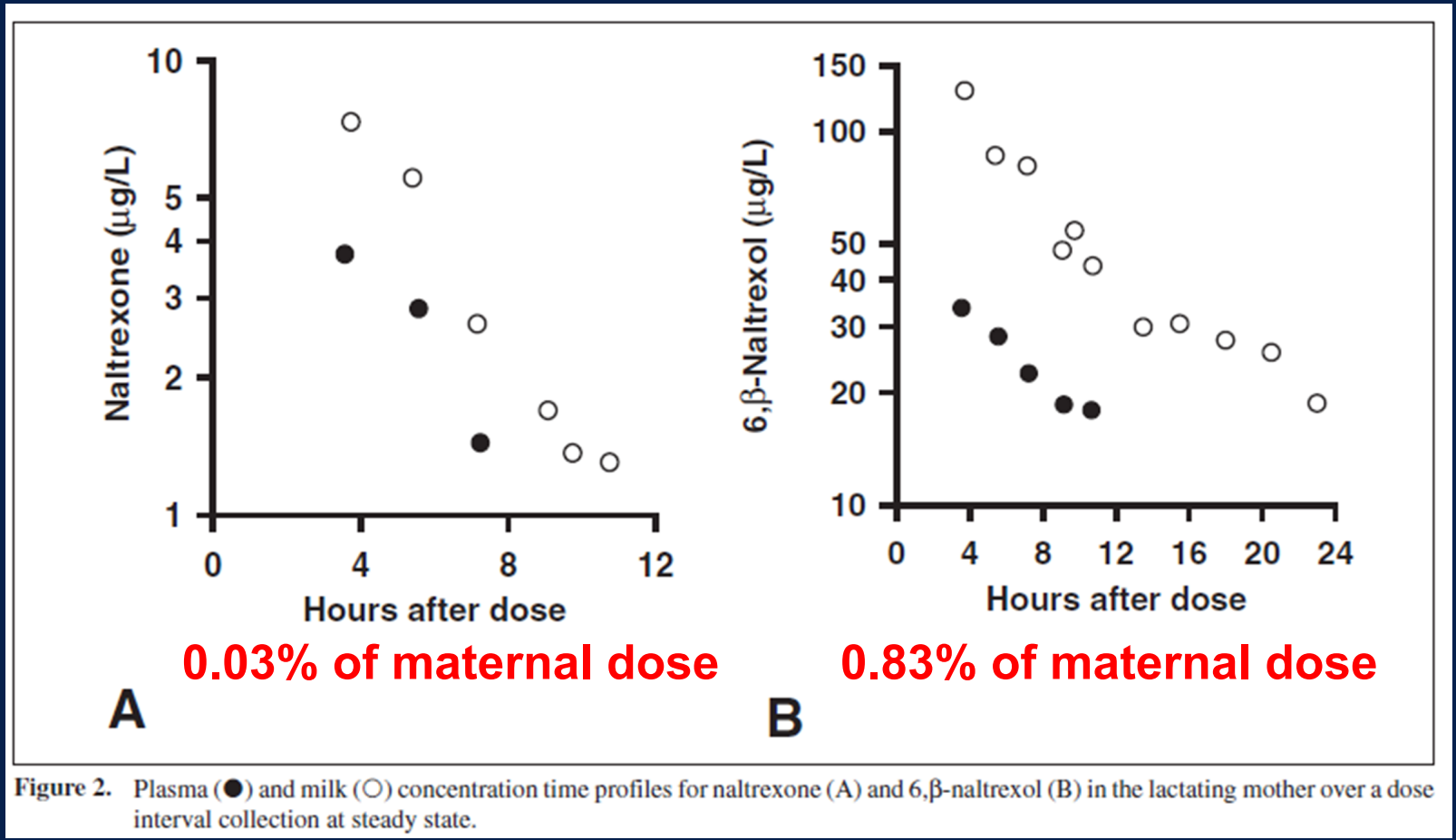


Figure 2. Plasma (●) and milk (○) concentration time profiles for naltrexone (A) and 6,β-naltrexol (B) in the lactating mother over a dose interval collection at steady state.

One mother with 6-week old infant; Oral NTX 50mg/day

Chan CF, et al, *J Hum Lact,* 2004

Timing of non-prescribed use during pregnancy and breastfeeding

- A single-site 2020 retrospective cohort study of 503 individuals receiving OUD treatment found that urine toxicology testing at delivery had the strongest association (aOR 3.72) with ongoing non-prescribed use postpartum

	90-30d before delivery	Within 30d of delivery	At delivery
Sensitivity	44%	26%	27%
Specificity	74%	79%	93%
PPV	36%	36%	56%
NPV	80%	86%	78%
Chi-Squared Test	P =0.033	P=0.006	P<0.001

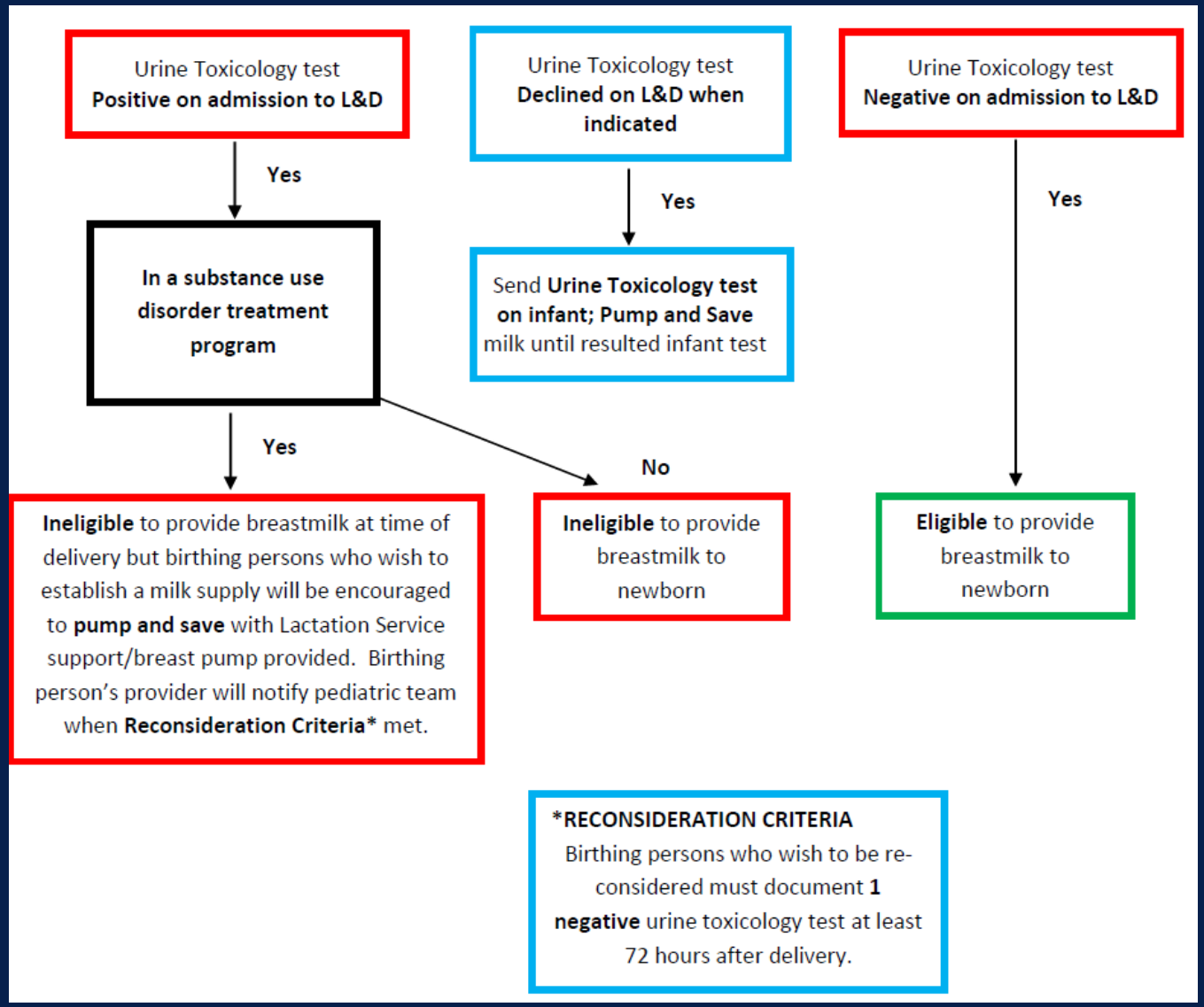
Harris et al, 2020

Breastfeeding initiation

- Individuals motivated to breastfeed with recent non-prescribed substance can be supported in pumping to establish a milk supply
- Multi-disciplinary approaches can support decisions on when to start breastfeeding
- Before breastfeeding sufficient time should pass to allow for substance clearance from breast milk

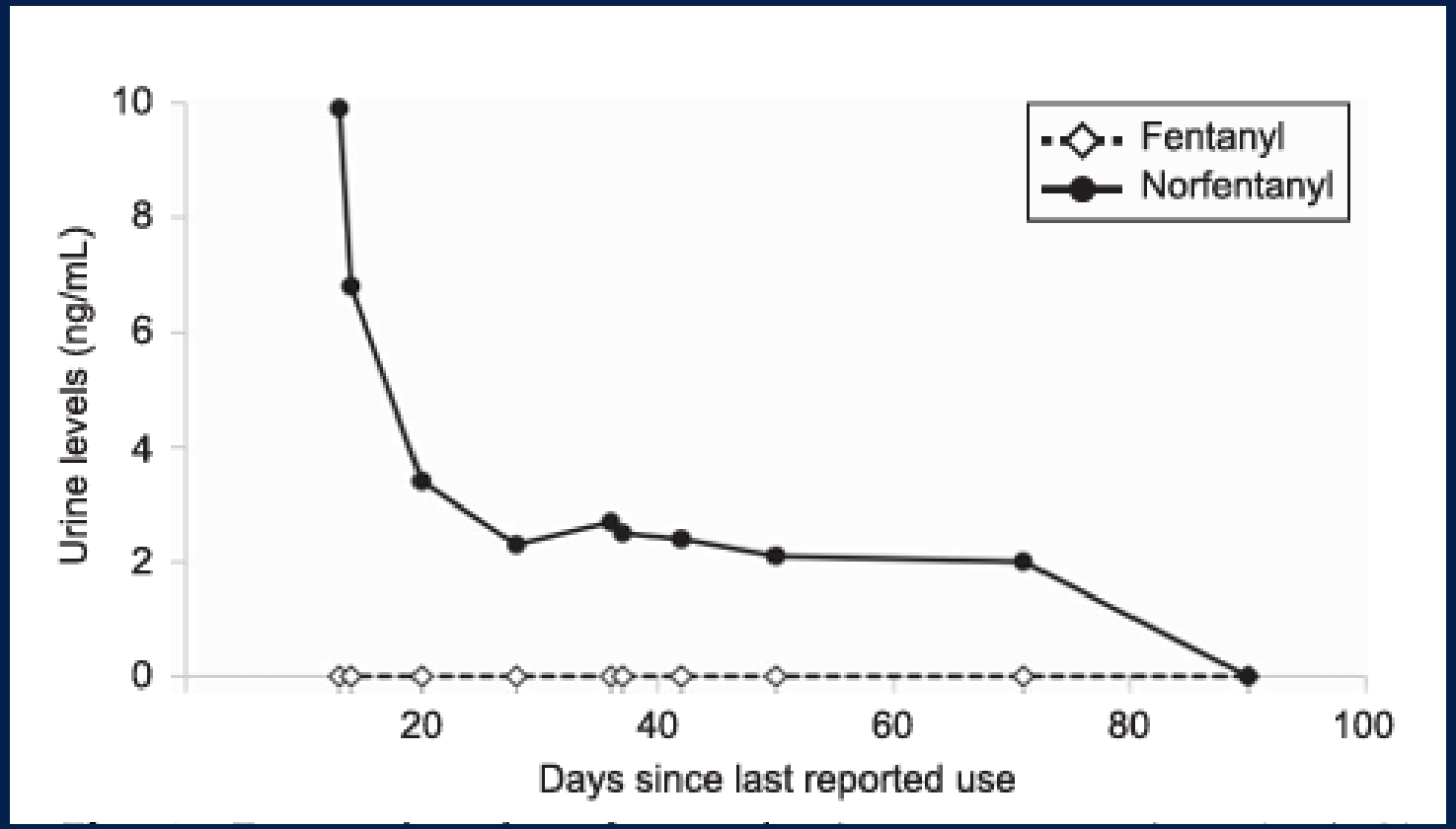
Harris M, et al, *Breastfeeding Med,* 2023

Sample practice guidelines



Fentanyl Clearance

- P450 CYP34A -> slow tissue release
- Genetics, BMI, hepatic, renal, medication factors
- Pregnancy factors
- Rates of nor-fentanyl decrease steadily out to **70 days** after last use



Wanar A, et al, *Obstet Gynecol*, 2020

General Recommendations

Recommendation	Recommendation strength	Evidence level
Individuals with SUD should engage in multidisciplinary prenatal & postpartum SUD care.	B	2
Individuals who discontinue non-prescribed substance use by the delivery hospitalization can be supported in breastfeeding initiation provided appropriate safeguards & follow-up are in place.	B	2

Harris M, et al, *Breastfeeding Med,* 2023

Final Takeaways

- Modification of breastfeeding recommendations in the setting of non-prescribed opioid use
- Support of individuals who wish to breastfeed
- Focus on pharmacokinetics and delivery time point
- Need for continued research in this area

Acknowledgements

- ABM co-authors: Miriam Harris, MD; Davida Schiff, MD; Kelley Saia, MD; Katherine Standish, MD; Serra Muftu

- Boston Medical Center perinatal substance use committee / Project RESPECT program

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