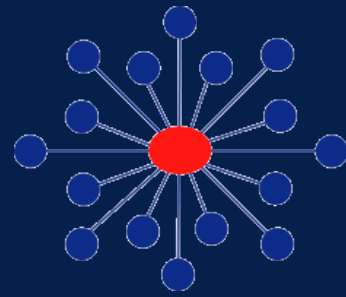


Medication Treatment for Opioid-dependent Expecting Mothers (MOMs; CTN-0080): A Randomized Trial Evaluating Extending Release and Sublingual Buprenorphine in Pregnancy through 12-months Postpartum



Michelle Lofwall, MD, DFAPA, DFASAM

American Society of Addiction Medicine
April 24, 2026



Medication Treatment for Opioid-dependent Expecting Mothers (MOMs; CTN-0080)

April 24 Concurrent sessions #2 10:45 – 12:00

Michelle Lofwall, MD, DFAPA, DFASAM

Last 3 years:

- ☀ Research consultant to Braeburn Pharmaceuticals and Berkshire Biomedical
- ☀ Honorarium from Camurus for research talk

Background and Rationale

Limitations of Sublingual Buprenorphine (BUP-SL)

- ☀ BUP-SL has challenges including risk of misuse¹, poor adherence² and daily peak-trough cycle impacting the infant³ and pregnant person⁴

Potential Advantages of Extended-Release (BUP-XR)

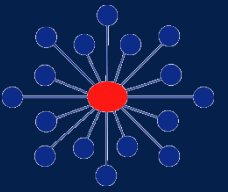
- ☀ BUP-XR eliminates misuse/diversion⁵ and avoids daily peak/trough cycle⁶

Potential Disadvantage of Extended-Release (BUP-XR)

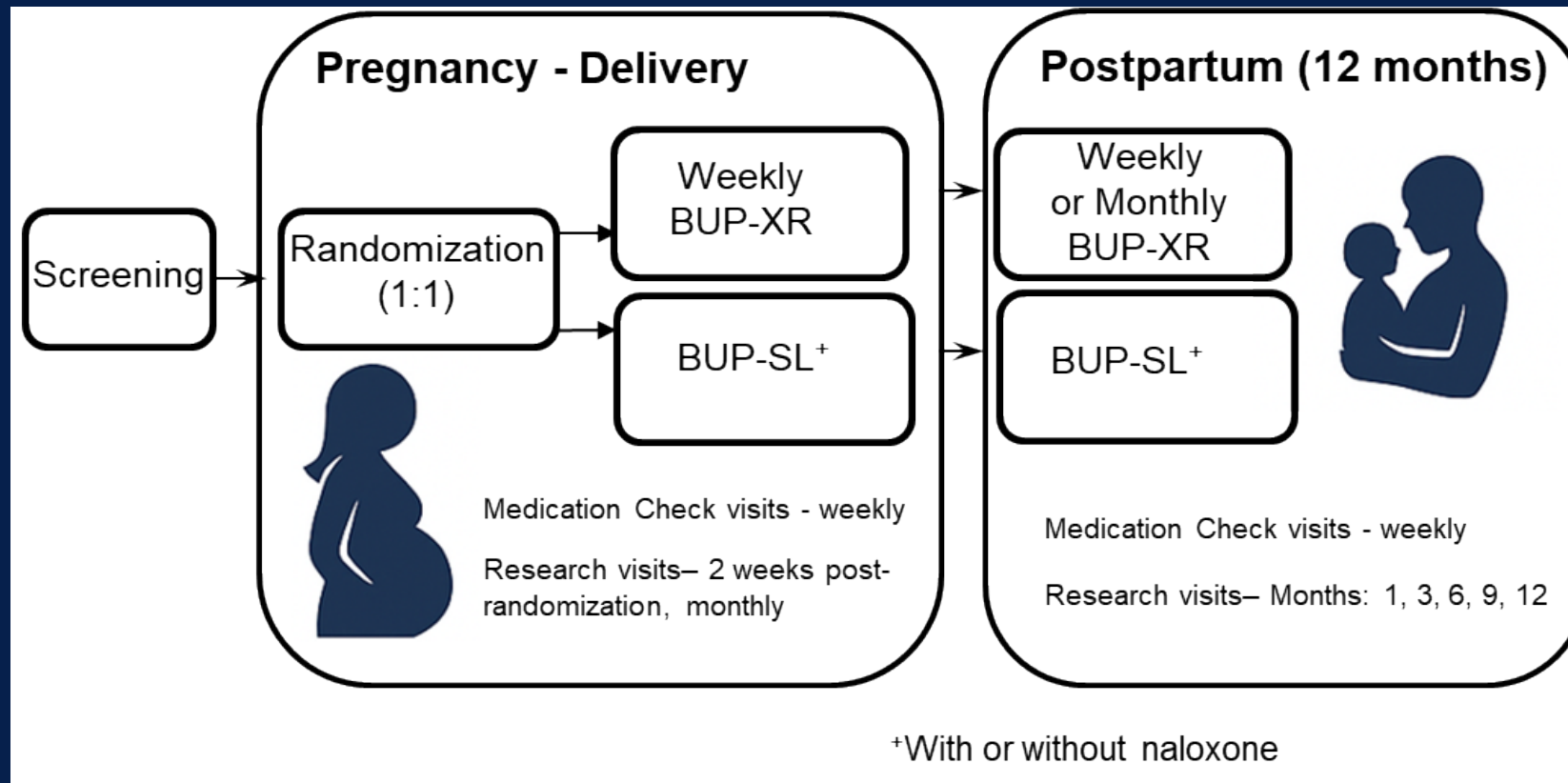
- ☀ Greater BUP exposure for the fetus given the higher area under the curve for BUP-XR⁷

Study Design

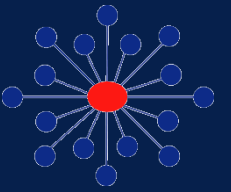
- ☀ Two-arm, open-label, non-inferiority, pragmatic randomized multisite trial
- ☀ Randomized 1:1 to:
 - BUP-XR (CAM2038/Brixadi[®]): weekly while pregnant and breastfeeding, monthly optional if not breastfeeding
 - BUP-SL (with or without naloxone based on site preference)
- ☀ All study medication free and dispensed from sites
- ☀ Stratified at time of enrollment by:
 - ☀ -Site,
 - ☀ -Estimated Gestational Age (EGA; 6-18 vs. 19-30 weeks),
 - ☀ -Receiving BUP-SL treatment at randomization (yes/no)
- ☀ Active treatment phase: pregnancy through 12 months postpartum



Study Schema and Dosing

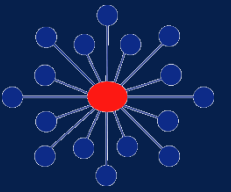


Target dose: BUP-SL-16 mg daily (BUP-XR 24 mg weekly) with individualized dosing determined by the prescribing clinician



Study Sites

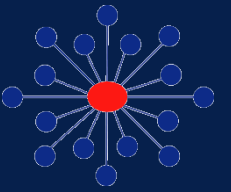
- ☀ Requirements: Employ recommended model of close collaboration between prenatal care and addiction treatment providers⁸
- ☀ Most sites were specialty obstetrics & gynecology programs providing OUD services (n = 9, 69.2%), and were affiliated with an academic institution (n = 11, 84.6%)⁹
- ☀ Ultimately, 13 sites in 12 states (CA, FL, MA, NM, OH, OR, PA, SC, TN, UT, WA, WV); one site screened but did not randomize a participant



Eligibility: Primary Inclusion Criteria

Potential participants must:

- be 18-41 years old
- be pregnant with single fetus at an EGA of 6 - 30 weeks
- meet DSM-5 criteria for moderate/severe OUD and be a good candidate for BUP maintenance and/or be currently prescribed BUP for the treatment of OUD
- be enrolled in outpatient addiction treatment at a participating site
- plan to deliver at a hospital that: 1) offers rooming-in for mom and infant during observation for neonatal opioid withdrawal syndrome (NOWS); 2) has a written protocol for NOWS management, and 3) does not send infants home on opioids for NOWS management



Study Eligibility: Primary Exclusion Criteria

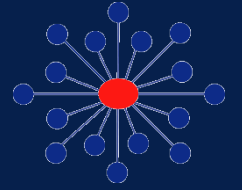
Potential participants must not:

- require medically-managed withdrawal from alcohol or other sedative/hypnotics
- have a psychiatric or medical condition that would make study participation and compliance unsafe or difficult
- be incarcerated or in any inpatient overnight facility as required by a court of law or have pending legal action or another situation that could prevent study activity participation
- be receiving methadone or naltrexone treatment
- be in or planning for treatment beyond clinically managed low-intensity residential services

Primary and Key Secondary Outcome Measures

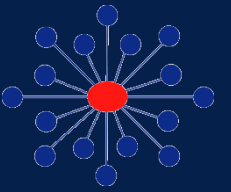
- ☀ Primary: Proportion of illicit opioid-negative urine drug screens (*fentanyl, morphine, codeine, ethylmorphine, heroin, hydrocodone, hydromorphone, methadone, and oxycodone*) during pregnancy; missing results imputed as positive ¹⁰
- ☀ Maternal Key Secondary: Proportion of illicit opioid-negative urine drug screens postpartum; missing results imputed as positive
- ☀ Infant Key Secondary:
 1. Treated for NOWS with opioids (yes/no)
 2. In treated infants, number of days of opioid treatment

Secondary Outcome Measures: Maternal



- ☀ All assessments except the Adequacy of Prenatal Care Utilization (APNCU) index¹¹ were analyzed separately for the pregnancy and postpartum phases
- ☀ BUP Adherence (% of expected treatment days)
 - a) BUP-XR: receiving weekly (=7 days adherent) or monthly (=28 days adherent) injection
 - b) BUP-SL: self-report of taking the prescribed SL dose, not disconfirmed by urine tests
- ☀ Drug and Alcohol Abstinence – based on urine tests that measured opioid and non-opioids including:
 - ☀ Cocaine, methamphetamine, amphetamine, marijuana, benzodiazepines, barbiturates, phencyclidine (PCP), methylenedioxymethamphetamine (MDMA, Ecstasy), and ethyl glucuronide

Secondary Outcome Measures: Maternal (cont'd)



- Collected at the research visits
 - Opioid craving was assessed with the Opioid Craving Scale¹²
 - Opioid withdrawal symptoms were assessed with the Short Opiate Withdrawal Scale (SOWS)-Gossop¹³



Secondary Outcome Measures: Infants

Extracted from the medical record:

- ☀ Three additional NOWS-related outcomes:
 - ☀ Infant hospital length of stay defined as the infant's age, in days, at discharge
 - ☀ For infants for whom Modified Finnegan scoring was used, peak score
 - ☀ For infants treated with morphine, total morphine for NOWS in mg
- ☀ Hospital discharge outcomes:
 - ☀ Maternal custody (yes/no)
 - ☀ Open case with child protective services (CPS; yes/no)
- ☀ Infant Development: The 12-month version of the Ages and Stages Questionnaire, third edition (ASQ-3)¹⁴ was used to screen for developmental delays in the infants (yes/no)

Safety Measures: Maternal

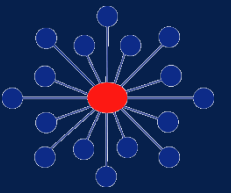
- ☀ Adverse Events (AEs) and Serious AEs (SAEs)
- ☀ Injection site reactions-injection (BUP-XR)
- ☀ Opioid overdoses—self-report of not able to respond to others or breathe adequately, resulting in naloxone rescue and/or emergency medical care/hospitalization ¹⁵
- ☀ Hospital Anxiety and Depression Scale (HADS) ¹⁶: Total scores



Safety Measures: Maternal (cont'd)

- ☀ Medical records (binary outcomes):
 - ☀ Primary C-section
 - ☀ Abnormal fetal presentation at delivery
 - ☀ Medical complications during labor
 - ☀ Pain medication (opioid, non-opioid) during labor or delivery, postpartum, prescribed at the time of discharge





Safety Measures: Infants

- ☀ Assessed weekly:
 - ☀ SAEs
 - ☀ Infant Sedation assessed by mother self-report of the infant: not waking up for feeding, having difficulty breathing (other than a stuffy nose), and/or feeling limp when held
- ☀ Medical records:
 - ☀ Live birth (yes/no)
 - ☀ EGA at delivery
 - ☀ Head circumference in centimeters
 - ☀ Weight at birth in grams
 - ☀ Length at birth in centimeters



Safety Measures: Infants (cont'd)

- ☀ Medical records (continued):
 - ☀ Apgar score at 1 and 5 minutes
 - ☀ Abnormal conditions (yes/no)
 - ☀ Interventions for abnormal conditions (yes/no)
 - ☀ Preterm (EGA < 37 wks.) (yes / no)
 - ☀ Infant discharged alive (yes / no)



BUP-XR Medication Supply Disruption

- December 20, 2021 to May 10, 2022
- Study BUP-SL offered to impacted participants
- Two BUP-XR participants in the pregnancy phase, 14 in the postpartum phase



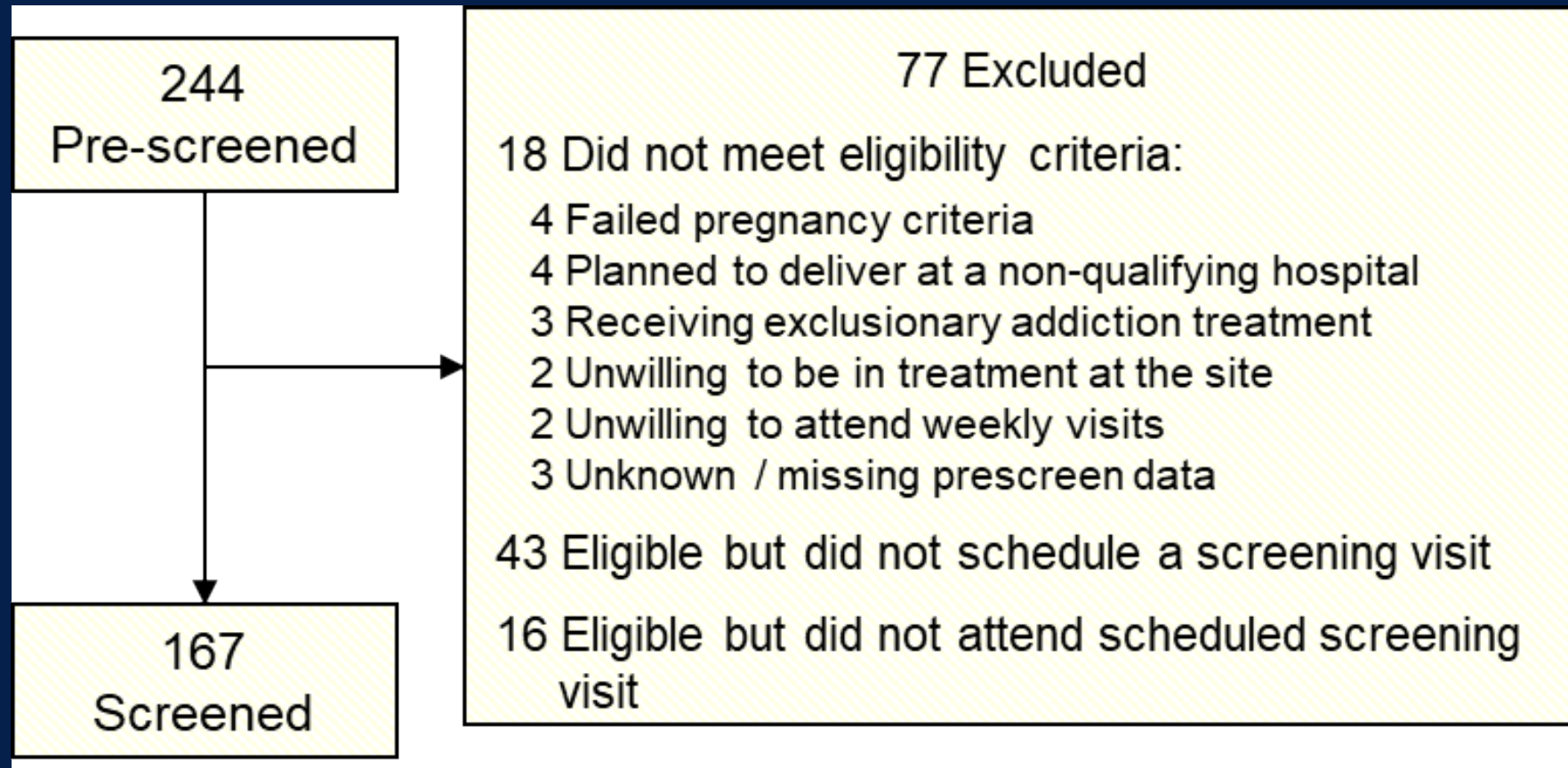
Primary and Maternal Key Secondary Analyses (illicit opioid use)

- ☀ Main analyses truncated BUP-XR participant data at the point where the disruption happened. Mixed-model regressions conducted with treatment cohort as the covariate of interest. Random variables included site and whether baseline EGA was less than 19 weeks (yes / no). If non-inferiority found, superiority tested planned a priori
- ☀ Alpha level: Primary outcome- alpha 0.05 (0.025 for superiority), maternal key secondary outcome was one of three secondary outcomes – alpha was 0.0167 (0.05/3)
- ☀ Sensitivity analyses: Included data post-medication disruption for impacted BUP-XR participants and tested the impact of including two baseline covariates: 1) the use of other substances as measured by UDSs and 2) the route of illicit opioid use (intravenous vs no intravenous use)

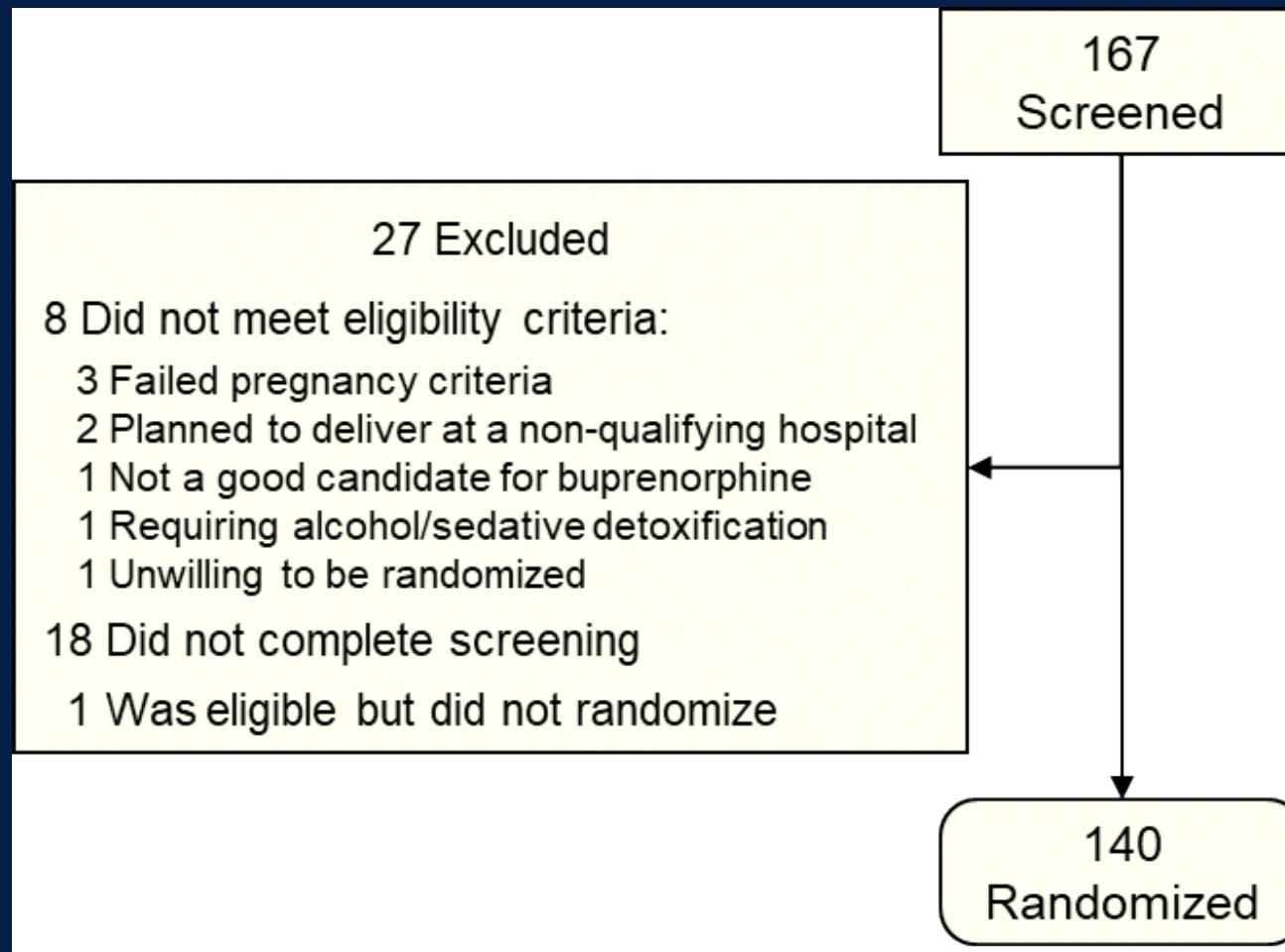
Results

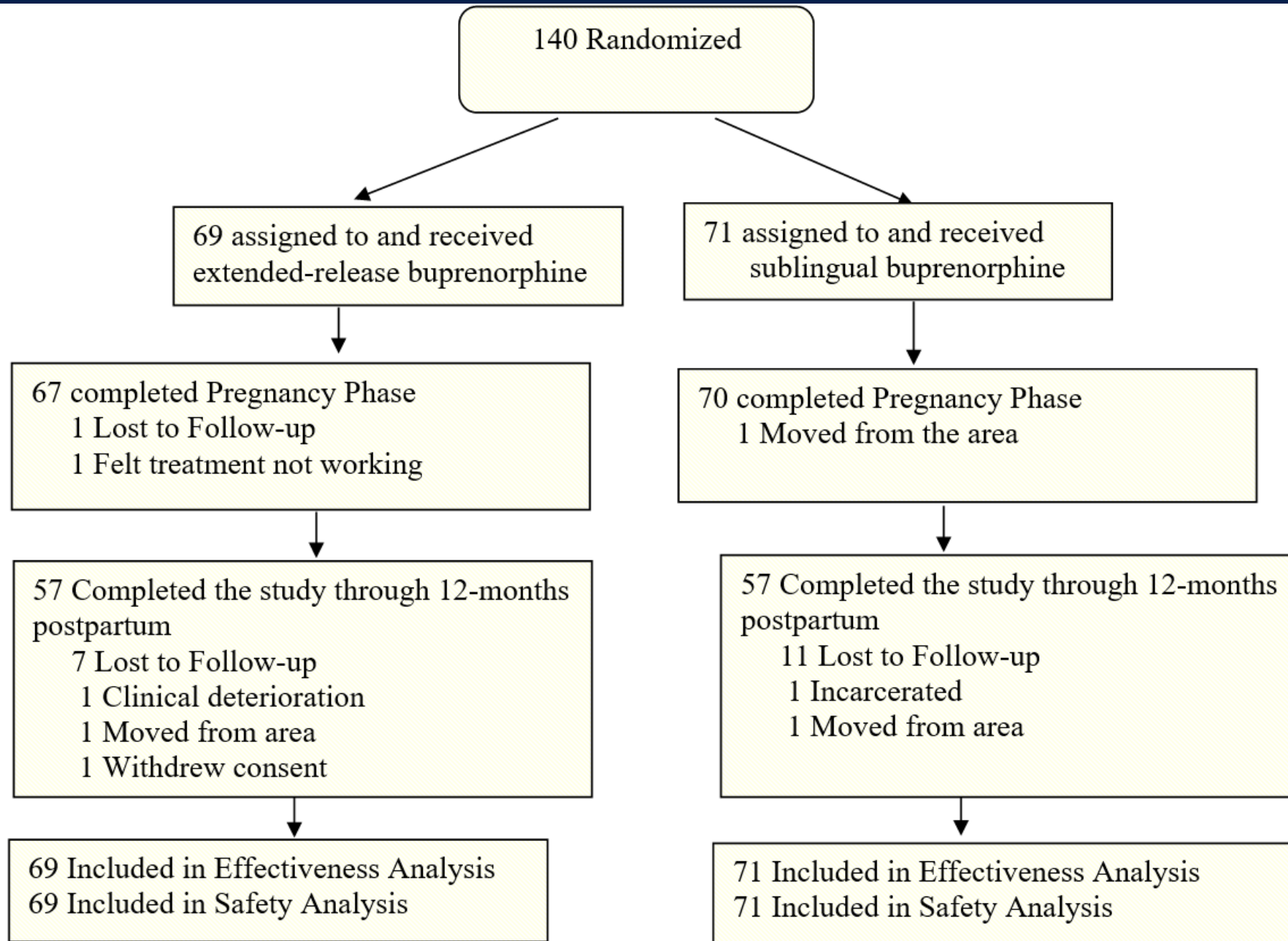


Flow of Participants Through Pre-screen



Flow of Participants Through Screening



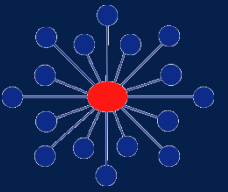


Sample Characteristics

	Total (N=140)
Age, yr	31.2 (4.6)
Hispanic or Latina ethnicity,	7%
Race	
White	83%
Black	7%
Other	10%
EGA of fetus, weeks (SD)	21.1 (6.5)
High school diploma, GED, or less	56%
Employed	34%
Married	15%
Taking BUP-SL at randomization	99%
Median days on BUP-SL	67.0

DSM-5 Other SUDs (past 12 months)

	Total (N=140)
Other DSM-5 SUDs (past 12 months)	
Cannabis	58%
Amphetamine	46%
Cocaine	26%
Sedatives	20%
Alcohol	19%



Substance use at baseline

	Total (N=140)
Substances for which UDS was positive for $\geq 5\%$ of participants	
Cotinine	85%
Marijuana	17%
Amphetamine	14%
Methamphetamine	11%
Fentanyl	9%
Cocaine	5%
Benzodiazepines	4%
Opiates	4%
Alcohol	4%
Injection illicit opioid use at baseline	7%

Effectiveness Outcomes



Primary and Maternal Key Secondary

Outcome	BUP-XR (N=69)	BUP-SL (N=71)	Effect Size	Superiority test
Illicit opioid-negative urine samples-Pregnancy	82.5% ± 4.2%	72.6% ± 4.2%	9.8% (1.7%, 18.0%)	p=0.009
Illicit opioid-negative urine samples-Postpartum*	60.2% ± 4.2%	59.5% ± 4.1%	0.6% (-12.7%, 14.0%)	p=0.45

- *Sample size post-partum: BUP-XR=67; BUP=69
- Sensitivity analyses produced comparable results

Maternal Secondary Outcomes: Pregnancy

- No significant group differences at the pre-established alpha level (0.0033)

Outcome	BUP-XR (N=69)	BUP-SL (N=71)	P Value
BUP Adherence	84.4% ± 3.1%	84.9% ± 3.0%	0.91
Drug and alcohol abstinence ¹	58.8% ± 3.4%	52.2% ± 3.4%	0.36
Opioid craving scale ²	1.9 ± 0.2	2.5 ± 0.2	0.31
Short Opiate Withdrawal Scale ²	5.6 ± 0.5	6.2 ± 0.5	0.14
Adequacy of Prenatal Care ³			0.045
Inadequate	36.7% ± 8.9%	19.4% ± 6.7%	
Intermediate	13.3% ± 6.3%	16.7% ± 6.3%	
Adequate	23.3% ± 7.9%	13.9% ± 5.8%	
Adequate Plus	26.7% ± 8.2%	50.0% ± 8.5%	

¹Excluding cotinine; ²BUP-XR n=67; BUP-SL n=70; ³BUP-XR n=30; BUP-SL n=36

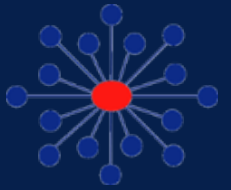
Maternal Secondary Outcomes: Postpartum

- No significant group differences at the pre-established alpha level (0.0033)

Outcome	BUP-XR (N=67)	BUP-SL (N=70)	P Value
BUP Adherence	69.3% ± 4.3%	75.5% ± 4.2%	0.30
Drug and alcohol abstinence ¹	34.7% ± 3.3%	35.0% ± 3.2%	0.77
Opioid craving scale ²	1.5 ± 0.2	1.7 ± 0.2	0.82
Short Opiate Withdrawal Scale ²	4.1 ± 0.5	5.3 ± 0.5	0.009

¹Excluding cotinine; ²BUP-XR n=66; BUP-SL n=67

Infant Key Secondary Outcomes



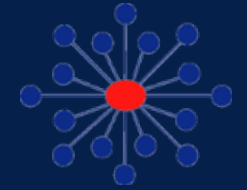
- **No significant group differences at the pre-established alpha level (0.0167)**

Outcome	BUP-XR (N=65 ¹)	BUP-SL (N=68)	P Value
Opioid treatment for NOWS	30.2% ± 5.8%	26.5% ± 5.4%	0.64
Days of opioid treatment ²	10.9 ± 2.2	14.8 ± 3.0	0.28

¹Main analysis excludes 2 infants impacted by medication disruption; ²BUP-XR n=19; BUP-SL n=18

- Sensitivity analyses produced comparable results

Infant Secondary Outcomes



- **No significant group differences at the pre-established alpha level (0.0033)**

Outcome	BUP-XR (N=66)	BUP-SL (N=69)	P Value
Total amount of morphine for NOWS-mg ¹	10.0 ± 3.7	10.4 ± 3.2	0.86
Hospital length of stay ²	8.5 ± 0.9	9.5 ± 1.0	0.54
Finnegan-Modified peak score ³	10.4 ± 0.8	10.0 ± 0.9	0.45
Maternal custody ⁴	90.9% ± 3.5%	89.7% ± 3.7%	0.81
Case with child protective services ⁵	32.8% ± 5.9%	38.8% ± 6.0%	0.48
Developmental delay at 12 months ⁶	17.3% ± 5.2%	15.4% ± 5.0%	0.79

¹Includes neonates treated with morphine who had total dose data (BUP-XR n=11; BUP-SL n=13); ²(BUP-XR n=65; BUP-SL n=67);

³Includes neonates scored using the Finnegan modified version (BUP-XR n=22; BUP-SL n=23); ⁴ BUP-XR n=66; BUP-SL n=68;

⁵BUP-XR n=64; BUP-SL n=67; ⁶Assessed among infants with a 12-month ASQ-3 (BUP-XR n=52; BUP-SL n=52)

Safety Outcomes



Serious Adverse Events (SAEs)

Outcome	Pregnancy		Postpartum		Infants	
	XR (N=69)	SL (N=71)	XR (N=67)	SL (N=70)	XR (N=67)	SL (N=70)
Any SAE	6 (8.7%)¹	19 (26.8%)¹	4 (6.0%)²	13 (18.6%)²	9 (13.4%)	11 (15.7%)
Medication-related SAE	-	1 (1.4%)	-	-	-	1 (1.4%)
Type of Serious Event— no. (%)						
Congenital anomaly/birth defect	-	-	-	-	5 (7.5%)	4 (5.7%)
Persistent/significant disability	-	-	-	-	-	-
Death	-	-	-	-	-	1 (1.4%)
Initial or prolonged hospitalization	6 (8.7%)¹	19 (26.8%)¹	4 (6.0%)	11 (15.7%)	6 (9.0%)	6 (8.6%)
Life threatening	-	-	-	2 (2.9%)	-	-
Important medical event	-	-	-	1 (1.4%)	-	-
System Organ Class (MedDRA v27.1)						
Congenital/genetic disorders	-	-	-	-	3 (4.5%)	3 (4.3%)
Pregnancy/perinatal	4 (5.8%)	8 (11.3%)	-	4 (5.7%)	-	1 (1.4%)
Psychiatric disorders	1 (1.4%)	6 (8.5%)	3 (4.5%)	4 (5.7%)	-	-

¹p<0.01; ²p<0.05

Nonserious Adverse Events (AEs)

Outcome	Pregnancy		Postpartum	
	XR (N=69)	SL (N=71)	XR (N=67)	SL (N=70)
Any Nonserious AEs	44 (63.8%)	47 (66.2%)	37 (55.2%)	45 (64.3%)
Medication-related AEs	18 (26.1%)¹	5 (7.0%)¹	2 (3.0%)	3 (4.3%)
Mild severity	22	6		
Moderate severity	6	2		
Severe severity	0	0		
Maximum Severity for any AE				
Mild	21 (47.7%)	16 (34.0%)	13 (35.1%)	11 (24.4%)
Moderate	17 (38.6%)	17 (36.2%)	18 (48.6%)	23 (51.1%)
Severe	6 (13.6%)	14 (29.8%)	6 (16.2%)	11 (24.4%)
System Organ Class (MedDRA v27.1)				
Gastrointestinal disorders	21 (30.4%)	16 (22.5%)	11 (16.4%)	13 (18.6%)
Infections and infestations	13 (18.8%)	20 (28.2%)	22 (32.8%)	27 (38.6%)
Pregnancy/perinatal	11 (15.9%)	20 (28.2%)	1 (1.5%)	5 (7.1%)

¹p<0.01

Maternal Safety Outcomes: Pregnancy/ Delivery

- No significant group differences at the pre-established alpha level (0.05)

Outcome	BUP-XR (N=69)	BUP-SL (N=71)	P Value
Opioid Overdose ¹	0.0% ± 0.0%	1.4% ± 1.4%	-
HADS Depression total score ¹	4.1 ± 0.3	5.0 ± 0.3	0.19
HADS Anxiety total score ¹	7.0 ± 0.4	7.3 ± 0.3	0.47
Primary C-section ²	22.7% ± 5.2%	20.0% ± 4.8%	0.70
Abnormal fetal presentation ³	15.4% ± 4.5%	18.6% ± 4.6%	0.62
Medical complications during labor ²	22.7% ± 5.2%	32.9% ± 5.6%	0.19
Pain medication receipt			
During labor or delivery ⁴	53.1% ± 6.2%	55.4% ± 6.2%	0.80
Opioid	46.9% ± 6.2%	49.2% ± 6.2%	0.79
Non-opioid	23.4% ± 5.3%	27.7% ± 5.6%	0.58
Other	0.0% ± 0.0%	3.1% ± 2.1%	-

¹BUP-XR n=67; BUP-SL n=70; ²BUP-XR n=66; BUP-SL n=70; ³BUP-XR n=65; BUP-SL n=70;

⁴BUP-XR n=64; BUP-SL n=65;

Maternal Safety Outcomes: Postpartum

Outcome	BUP-XR (N=67)	BUP-SL (N=69)	P Value
Pain medicine post-delivery in hospital¹	85.7% ± 4.4%	98.5% ± 1.5%	0.03
Opioid	30.2% ± 5.8%	50.0% ± 6.2%	0.02
Non-opioid	82.5% ± 4.8%	92.4% ± 3.3%	0.10
Other	12.7% ± 4.2%	6.1% ± 2.9%	0.20
Pain medicine at time of discharge¹	85.7% ± 4.4%	90.9% ± 3.5%	0.36
Opioid	20.6% ± 5.1%	25.8% ± 5.4%	0.49
Non-opioid	82.5% ± 4.8%	83.3% ± 4.6%	0.90
Other	9.5% ± 3.7%	4.5% ± 2.6%	0.28
Opioid Overdose² – no. (%)	4.5% ± 2.6%	0.0% ± 0.0%	-
HADS Depression total score²	3.5 ± 0.3	4.3 ± 0.3	0.09
HADS Anxiety total score²	5.8 ± 0.4	6.8 ± 0.4	0.04

¹BUP-XR n=63; BUP-SL n=66; ²BUP-XR n=66; BUP-SL n=67

Infant Safety Outcomes

Outcome	BUP-XR (N=66)	BUP-SL (N=69)	P Value
Live birth– no. (%)	100%	100%	-
Infant discharged alive – no. (%)	100%	100%	-
Head circumference ¹ -cm	34.0 ± 0.2	33.4 ± 0.2	0.049
Weight at birth ² - g	3163.4 ± 71.1	3005.7 ± 69.0	0.11
Length at birth ³ - cm	49.4 ± 0.4	48.9 ± 0.3	0.39
Gestational age at delivery – weeks	38.2 ± 0.2	37.7 ± 0.2	0.13
Apgar score ⁴ - 1 min	7.5 ± 0.2	7.7 ± 0.2	0.28
Apgar score ⁴ - 5 min	8.5 ± 0.1	8.7 ± 0.1	0.20
Abnormal conditions ² -no. (%)	47.7% ± 6.2%	39.1% ± 5.9%	0.32
Intervention for abnormal condition ² -no. (%)	52.3% ± 6.2%	43.5% ± 6.0%	0.31
Preterm, <37 wk – no. (%) ³	12.1% ± 4.0%	21.7% ± 5.0%	0.14
Infant Sedation ⁵ -no. (%)	32.3% ± 6.7%	25.7% ± 6.2%	0.57
Did not wake up for feeding	13.7% ± 4.8%	3.8% ± 2.7%	0.10
Any difficulty breathing	23.5% ± 5.9%	15.4% ± 5.0%	0.30
Felt limp when held	13.7% ± 4.8%	17.3% ± 5.2%	0.62

¹BUP-XR n=61; BUP-SL n=67333333; ²BUP-XR n=65; BUP-SL n=69; ³BUP-XR n=63; BUP-SL n=67; ⁴BUP-XR n=64; BUP-SL n=69; ⁵For infants receiving breastmilk (BUP-XR n=51, BUP-SL n=52)

Discussion



Discussion: Pregnancy Effectiveness Results

- ✦ Significantly higher illicit opioid abstinence in the BUP-XR (82.5%) versus BUP-SL (72.6%), groups in context of similarly high rates of BUP adherence (~85%) suggests the higher BUP-XR abstinence rate is likely due to its pharmacokinetic advantages (e.g., no daily peak-trough)
- ✦ Notably, all but two participants were on BUP-SL at randomization; median of ~67 days
 - ✦ By comparison, 65% illicit opioid abstinence has been reported for pregnant participants started on BUP-SL¹⁷

Discussion of Infant Effectiveness Results

- ☀ No significant treatment group differences for infant effectiveness outcomes
- ☀ 28% of infants received opioid treatment for NOWS; 39-48% in past research¹⁸⁻²⁰
- ☀ 30 infants scored with Eat Sleep Console not significantly different than 105 infants scored with another (e.g., Finnegan) or unknown system (23.3% vs. 29.1%, $p=0.65$)
- ☀ Lower proportion of infants treated with opioids may reflect the high quality of the care provide by study sites and/or to the relative clinical stability of the sample

Discussion of Postpartum Effectiveness Results

No significant treatment group differences for postpartum effectiveness outcomes

- ☀ BUP-XR and BUP-SL participants had similar rates of illicit opioid abstinence postpartum (60.2%vs. 59.5%)

Postpartum-specific challenges influencing treatment retention and illicit opioid use:

- ☀ Demands of infant care²¹ (90% of sample had custody)
- ☀ Open CPS case (36% of the sample) can be a motivator for treatment discontinuation²²
- ☀ Approximately 35% discontinued medication postpartum compared to 10% during pregnancy

Discussion of Maternal Safety Results

Few significant treatment group differences:

- ☀ SAEs more frequent in BUP-SL participants during both pregnancy and postpartum but only 1 was treatment related;
- ☀ Medication-related AEs more common in BUP-XR during pregnancy; lack of treatment group differences in AEs (i.e., regardless of medication relatedness) and gastrointestinal AEs, which are prone to unreliable attribution to study medication, ²³ being attributed to BUP-XR at twice the rate of BUP-SL, suggest a potential bias in attributing AEs to the more novel medication
- ☀ Lower proportion of BUP-XR participants received opioid pain medicine during post-delivery and had lower postpartum anxiety scores; BUP-SL effective for pain ²⁴ and has anxiolytic effects²⁵; might be more pronounced for BUP-XR (more stable BUP levels and higher exposure)

Discussion of Infant Safety Results

Fetal growth restriction has been highlighted as a safety concern with methadone and BUP use during pregnancy²⁶

- ☀ The single significant treatment group difference: larger head circumference at birth in the BUP-XR group and the lack of difference for birth weight and length suggest BUP-XR did not increase the risk of fetal growth restriction
- ☀ The lack of adverse safety outcomes in the BUP-XR-, relative to BUP-SL-, exposed infants is consistent with research finding that higher doses of buprenorphine during pregnancy are not associated with adverse infant outcomes.²⁷

Strengths / Limitations

☀ Strengths:

- ☀ Randomized trial;
- ☀ Geographically diverse sites;
- ☀ Comprehensive effectiveness and safety assessments;
- ☀ Strong study completion rate

☀ Limitations:

- ☀ Adequately powered for the primary outcome but may have been underpowered for other outcomes;
- ☀ Many outcomes relied on medical records which were associated with missing data and are prone to other data quality issues;
- ☀ Limited racial and ethnic diversity of participant sample;
- ☀ Relative clinical stability of the sample

Conclusions

- ☀ The results from this landmark trial support the use of weekly BUP-XR for treating opioid use disorder in pregnant individuals



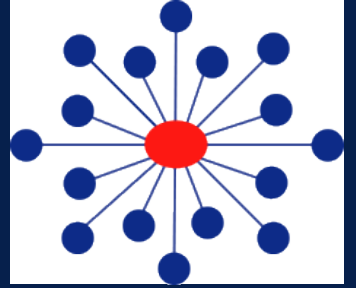
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Questions?



CTN-0080 MOMs



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Back-up slides



Infant Key Secondary Outcomes Analyses (NOWS treatment; days of opioid treatment)

- ☀ Main analyses excluded two infants whose mothers were impacted by the BUP-XR disruption during pregnancy. Regressions had treatment cohort as the covariate of interest and fixed effects of site and baseline EGA less than 19 weeks (yes / no) if significant. Alpha = 0.0167
- ☀ Sensitivity analyses: Included the two infants excluded in the main analysis; tested the impact of including covariates selected using Corrected Akaike Information Criterion (AIC-C):
 - ☀ Maternal-related covariates:
 - ☀ % cotinine-positive UDS
 - ☀ % non-nicotine-substance-positive UDS
 - ☀ Exposure to psychiatric medications (yes / no)
 - ☀ Infant-related covariates:
 - ☀ Breastfeeding while in hospital (yes / no)
 - ☀ Finnegan for scoring NOWS (yes / no)
 - ☀ Eat-Sleep-Console (yes / no)
 - ☀ Hospital-related covariates:
 - ☀ Minimum days of observation for NOWS / NAS

Secondary/Safety Outcomes Analyses

- ☀ Main analyses: Included all data (i.e., ignoring medication disruption). Regressions had treatment cohort as the covariate of interest and fixed effects of site and whether baseline EGA was less than 19 weeks (yes / no) if significant. Baseline value included as a covariate.
- ☀ Alpha: 0.0033 (0.05/15) for secondary outcomes, 0.05 for safety outcomes
- ☀ Sensitivity analyses: For infant NOWS-related outcomes, tested the impact of including maternal-related, infant-related, and hospital-related covariates selected using AIC-C

Medication Dose: BUP-XR

	Pregnancy ¹	Postpartum ²
Weekly medication		42%
8 mg dose	3%	16%
16 mg dose	12%	8%
24 mg ³ dose	26%	32%
32 mg dose	59%	44%
Monthly medication		58%
64 mg dose		9%
96 mg ³ dose		26%
128 mg dose		65%
Discontinuation	12%	37%

¹Reflects the dose closest to delivery or last dose before medication disruption for impacted participants; ² Dosing reflects the last postpartum dose or last dose before medication disruption for impacted participants; ³equivalent to 12-16 mg of BUP-SL

Medication Dosing: BUP-SL

	Pregnancy ¹	Postpartum ²
Mono product ³	69%	43%
Total daily dose mean (SD)	18.8 (6.7)	18.2 (6.8)
Dosing > 1x Daily	86%	83%
Discontinuation	9%	33%

¹Dosing reflects the dosing closest to delivery; ² Dosing reflects the last postpartum dose;

³buprenorphine only

Injection Site Examinations (BUP-XR)

- ☀ Reactions were reported in 14.6% of 2,384 injection sites examined
- ☀ 726 total symptoms documented, most prevalent:
 - ☀ Induration (24%)
 - ☀ Itching (17%)
 - ☀ Tenderness (16%)
- ☀ Severity:
 - ☀ Mild (78%)
 - ☀ Moderate (21%)
 - ☀ Severe (<1%)