

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Jones HE, Kaltenbach K, Heil SH, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. *N Engl J Med* 2010;363:2320-31.

Appendix Figure 1. MOTHER Assessment Measures and Data Collection Schedule

Measures	Screening	Before/After Morphine Dosing	Pre-Delivery: Weekly	Pre-Delivery: Every 30 Days	Post-Delivery
Demographics	✓				
Medical history	✓				
Psychiatric assessment MINI ⁴⁶	✓				
Addiction Severity Index ⁴⁷	✓			✓	✓
Nicotine dependence ^{48,49}	✓				
Adjective Checklist ^{17,26}	✓	✓(On Day 3–4 after dosing)	✓		
Global Assessment ^{17,26}	✓	✓(On Day 3–4 after dosing)	✓		
Drug Dose Adequacy ^{17,26}	✓	✓(On Day 3–4 after dosing)	✓		
HIV Risk Behaviors ⁵⁰	✓	✓(On Day 3–4 after dosing)		✓	
OB visit	✓	✓ (or as scheduled by OB)		✓ or as needed weekly	
Concomitant medications ²⁵	✓		✓		✓
Clinical Institute Narcotic Assessment ⁵¹	✓	✓ (every 6 hours while awake during induction and continued until 72 hours post-receipt of the first dose of double-blind study medication)			
Adverse events ²⁶	✓		✓	weekly	Until study discharge
Urine drug screening results	✓		✓		
Blinding questionnaire ²⁶			EGA weeks 2, 35 (participant and staff)		✓once for NAS Raters
Safety blood sample	✓			EGA weeks 9,13,17,21,25, 29, 33, 37,and post-partum	✓
Biophysical Profile (Pre-dosing)		EGA week 32			
Biophysical Profile (Post-dosing)		✓(before dosing)			
Maternal and infant delivery information (e.g., birth weight)		✓(2 hours after dosing)			✓
Neonatal abstinence syndrome (NAS) ^{26,35-37}					✓ (every 3-4 hrs in hospital; twice daily for non-hospitalized neonates)
Nursery environment					✓ (at each NAS assessment)

Appendix Figure 1 REFERENCES

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Appendix Figure 2. Maternal Opioid Treatment: Human Experimental Research (MOTHER) Neonatal Abstinence Measure

PATIENT ID# _____		Morphine Maintenance							
Dose given q 3-4 hrs with feeds; do not exceed 4 hrs between doses		<ul style="list-style-type: none"> • Maintain dose if score 0-8 • Increase dose by 0.02 if score is 9-12 (rescore before dosing) • Increase dose by 0.04 if score 13-16 • Increase score by 0.06 if score 17-20 							
SCORE Morphine (0.04mg/0.1ml) DOSE FOR INITIATION 0-8 0 9-12 0.04 mg/dose 13-16 0.08 mg/dose 17-20 0.12 mg/dose 21-24 0.16 mg/dose 25 or above 0.20mg/dose									
Morphine Initiation:		Weaning Instructions:							
<ul style="list-style-type: none"> • If neonate scores 9-12 re-score after feeding or within the hour and if re-score is 9-12 start treatment based on highest score. If re-score is 0-8, do not initiate treatment. • If initial score is 13 or greater, start treatment immediately without reassessment. 		<ul style="list-style-type: none"> • Maintain on dose 48 hrs before starting weaning • Wean 0.02 mg morphine every day for a score is 0-8 • Defer wean for score e 9-12 							
Timing of Scoring: Hospitalized infants scored every 3-4 hrs before feeds. Reassessment Occurs immediately after feeds or within 1 hour.		Re-escalation							
Discharged (e.g., in GCRC) infants scored twice a day scores must be separated by 8 hrs)		<ul style="list-style-type: none"> • If neonate scores 9-12 re-score as described for initiation , • If second score is in 9-12 increase morphine 0.01 mg q3-4 hrs • If 2 consecutive scores 13-16, increase 0.02 mg q3-4 hrs • If 2 consecutive scores in 17-20, increase 0.04 mg q3-4 hrs etc 							
NOTE: Discharged infants are to be admitted to hospital if the infant receives a single score of 9 or more									
SIGNS AND SYMPTOMS	Score	Date/time	Date/time	Date/time	Date/time	Date/time	Date/time	Date/time	Date/time
Please note presence (pr) or absence (ab) of items where indicated. Include observations for the past 4 hour period.									
Crying: excessive high pitched	2								
Crying: Continuous high pitched	3								
Sleeps < 1 hour after feeding	3								
Sleeps < 2 hours after feeding	2								
Sleeps < 3 hours after feeding	1								
Hyperactive Moro Reflex	1								
Markedly Hyperactive Moro Reflex	2								
Mild Tremors: Disturbed	1								
Moderate-Severe Tremors: Disturbed	2								
Mild Tremors: Undisturbed	1								
Moderate-Severe Tremors: Undisturbed	2								
Myoclonic jerks	present/absent	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab
Increased Muscle Tone	1-2								
Excoriation (indicate specific area):	1 - 2								
Mottling	present/absent	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab
Generalized Seizure (or convulsion)	8								
Convulsions	present/absent	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab
Fever ≥ 37.3 C (99.2 F)	1								
Fever >38.4 (101.2 F)	present/absent	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab
Frequent Yawning (4 or more successive times)	1								
Sweating	1								
Nasal Stuffiness	1								
Sneezing (4 or more successive times)	1								
Tachypnea (Respiratory Rate> 60/min)	2								
Retractions	present/absent	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab
Nasal flaring	present/absent	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab
Poor Feeding	2								
Excessive sucking	present/absent	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab
Vomiting (or regurgitation)	2								
Projectile vomiting	present/absent	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab
Loose Stools	2								
Watery Stools	present/absent	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab	<input type="checkbox"/> pr <input type="checkbox"/> ab
Failure to Thrive (Current weight ≥ 10% below birth weight) 90% BWT=_____	2 (record weight in score box 1 x day)								
Excessive Irritability	1 - 3								
TOTAL SCORE									
CURRENT MORPHINE DOSE	Dose in mg _____ Time Given _____								
STATUS OF TREATMENT*	N, I, M, W, R								
INITIALS of SCORER									

Note: Code Status of Treatment as follows: N="No treatment", I="Initiation", M="Maintenance", W="Weaning", R=" Re-Escalation"

MOTHER NAS SCORING

The MOTHER NAS scoring instrument is a revision of the Finnegan scoring system for the Neonatal Abstinence Syndrome.

Following are the operation definitions of scores:

<i>Criteria</i>	<i>Operational Definition</i>
Crying	
Crying=0	Non-high pitched and /or crying stops with caretaker or self soothing
Crying: Excessive high pitched =2	High pitched cry more than 15 seconds or intermittently up to 5 minutes
Crying: Continuous high pitched =3	High pitched cry more than 15 seconds and intermittently more than 5 minutes
Sleeping	
Sleeping 3+ hours after feeding=0	Use the longest single continuous time sleeping since last feeding
Sleeping <3 hours after feeding=1	Use the longest single continuous time sleeping since last feeding
Sleeping <2 hours after feeding=2	Use the longest single continuous time sleeping since last feeding
Sleeping <1 hour after feeding=3	Use the longest single continuous time sleeping since last feeding
Moro Reflex	
Hyperactive Moro=0	Arms return to chest within 1 to 2 seconds after extension
Hyperactive Moro=1	Arms stay up 3-4 seconds and / or pronounced jitteriness of the hands during or at the end of the Moro reflex
Markedly Hyperactive Moro=2	Arms stay up 5 seconds or more. Jitteriness may or may not be noted
Tremors Disturbed	
Mild Tremors: Disturbed=0	No tremors when disturbed.
Mild Tremors: Disturbed=1	Hands or feet only. Tremors last for up to 3 seconds
Moderate-Severe Tremors: Disturbed=2	Arms or legs. Tremors last for more than 3 seconds
Tremors Undisturbed	
Mild Tremors: Undisturbed=0	No tremors undisturbed. If the infant is asleep, a few jerking movements of the extremities may be present.
Mild Tremors: Undisturbed=1	Hands or feet only. Tremors last for up to 3 seconds
Moderate-Severe Tremors: Undisturbed=2	Arms or legs. Tremors last for more than 3 seconds

MOTHER NAS SCORING

Criteria

Operational Definition

Criteria	Operational Definition
Myoclonic Jerks	
Myoclonic Jerks (present or absent)	Infant must be awake when involuntary spasms or twitching of muscle in face or extremities are observed
Increased Muscle Tone	
Increased muscle tone=0	Some resistance to extension or flexion but slight flexion or extension is possible and the extremity returns spontaneously to its prior position
Increased muscle tone=1	Difficult to straighten or bend the arms but is possible AND head lag is present
Increased muscle tone=2	No head lag noted and / or arms or legs won't straighten or bend
Excoriation	
Excoriation=0	No excoriation present
Excoriation=1	Skin is red but intact or healing and no longer broken (indicate specific area)
Excoriation=2	Skin is broken (indicate specific area)
Mottling	
Mottling (present or absent)	Make sure infant is not chilled when evaluated. The presence of mottling is defined by the identification of marbling or discoloration on chest, trunk, arms or legs.
Generalized Seizure (or convulsion)	
Generalized Seizure (or convulsion)=0	No seizure or convulsion present
Generalized Seizure (or convulsion)=8	Eye staring, rapid involuntary movements of the eyes, chewing, back arching, fist clenching, etc.
Convulsion	
Convulsions (present or absent)	The presence of convulsions is defined by the jerking or tonic clonic movements, present in conjunction with or in the absence of seizure.
Fever	
Fever=0	Temperature < or = 37.2 C (99.1 F)
Fever > 37.3 C (99.2 F)=1	Temperature ≥ 37.3 C (99.2 F)
Fever > 38.4 C (101.2 F) (present or absent)	Temperature >38.4 C (101.2 F)
Yawning	
Yawning=0	Infant yawns 3 times or less in succession
Yawning=1	Infant yawns 4 or more times in succession. This may have occurred at any point within the 3-4 hour period prior to assessment.
Sweating	
Sweating=0	Wetness due to sweat may be present on back of neck due to overheating
Sweating=1	Wetness is felt on the infant's forehead or upper lip

MOTHER NAS SCORING

Criteria

Operational Definition

Nasal Stuffiness	
Nasal Stuffiness=0	No nasal noise
Nasal Stuffiness=1	Any nasal noise – may or may not have a runny nose
Sneezing	
Sneezing=0	Sneezing occurs 3 times or less in succession
Sneezing=1	Sneezing occurs 4 or more successive times
Tachypnea	
Tachypnea=0	Respiratory rate \leq 60 minute. Infant must be at rest, respirations must be counted for a full minute.
Tachypnea=2	Respiratory rate $>$ 60 minute. Infant must be at rest, respirations must be counted for a full minute.
Retractions	
Retractions (present or absent)	Retractions occur due to the use of intercostals muscles to assist respiration.
Nasal Flaring	
Nasal Flaring (present or absent)	Outward spreading of the nostrils during breathing.
Poor Feeding	
Poor Feeding=0	Feeding occurs smoothly, takes less than 20 minutes.
Poor Feeding=2	Feeding takes more than 20 minutes and any one or more of the following: Excessive sucking prior to feeding but infrequent sucking during feeding. Takes a small amount of formula/breast milk or loses formula/breast milk out sides of mouth. Uncoordinated suck-swallow mechanism. Continuously gulps formula/breast milk but stops frequently to breathe, burp or spit up. Places tongue above or to the side of nipple.
Excessive Sucking	
Excessive Sucking (If present, may score 2 from above and present, or Present with no score, or absent)	Four or more times in 3 to 4 hour assessment period infant displays increased rooting (turns head to one side in search of food) while displaying rapid swiping movements with the hand across the mouth in an attempt to such on fist, hands or pacifier. May occur prior to or after feeding.
Vomiting	
Vomiting (or regurgitation)=0	No vomit or regurgitation associated with burping.
Vomiting (or regurgitation)=2	Vomits whole feeding or vomits 2 or more times during feed but not associated with burping or large amounts during burping.

MOTHER NAS SCORING

Criteria

Operational Definition

Criteria	Operational Definition
Projectile Vomiting	
Projectile Vomiting (If present, score 2 above and pick present, or absent if absent)	Forceful ejection of stomach contents from mouth during or immediately after feeding.
Loose Stools	
Loose Stools=0	Normal stool.
Loose Stools=2	Stool is half liquid / half solid – may or may not leave water ring in diaper.
Watery Stools	
Watery Stools (present or absent)	Soft mushy, liquid or had stool that is accompanied by a water ring on the diaper.
Failure to Thrive	Current weight divided by Birth Weight = ____%. Record birth weight in score sheet box at admission and then in the score sheet box once a day.
Failure to Thrive=0	Current weight is 91% to 100% or more of birth weight.
Failure to Thrive=2	Current weight is 90% of birth weight or less.
Excessive Irritability	
Excessive Irritability=0	Not sensitive to sound, light or touch. Can achieve calm or relaxed state by self. Able to be consoled by caretaker.
Excessive Irritability=1	Consoling calms infant in 5 minutes or less. Sensitive or aversive to sound, light or touch. Cannot achieve calm or relaxed state by self.
Excessive Irritability=2	Consoling calms infant in 6-15 minutes. Sensitive or aversive to sound, light or touch. Cannot achieve calm or relaxed state by self.
Excessive Irritability=3	Consoling takes 15 or more minutes or is unsuccessful. Sensitive or aversive to sound, light or touch. Cannot achieve calm or relaxed state by self.

Appendix Table 1. Primary and Secondary Outcomes in the Methadone and Buprenorphine Groups Adjusted for Covariates

Outcome Measure	Methadone	Buprenorphine	Odds Ratio (<i>Confidence Interval</i>)	P
<i><u>Primary Outcomes</u></i>				
Treated for NAS [Yes]			.7 (.24, 2.1)	.43
NAS peak score	13.6 (.7)	12.0 (.7)		.07
Total amount of morphine for NAS (mg)	10.3 (2.5)	1.1 (.6)		<.001
Days of infant hospital stay	16.9 (1.7)	2.4 (.1)		<.002
Head circumference (cm)	33.4 (.2)	33.6 (.3)		.37
<i><u>Secondary Neonatal Outcomes</u></i>				
Days medicated for NAS	11.0 (2.2)	4.3 (1.1)		<.002
Birthweight (gm)	2980.7 (50.0)	2995.6 (55.9)		.83
Infant length (cm)	48.5 (.5)	49.7 (.5)		.09
Pre-term (<37 weeks) birth [Yes]			.4 (.1, 2.8)	.16
Gestational age at delivery (weeks)	37.9 (.3)	38.8 (.3)		.011
Apgar score at 1 minute	8.0 (.2)	7.9 (.2)		.65
Apgar score at 5 minutes	8.9 (.1)	8.9 (.1)		.69
<i><u>Secondary Maternal Outcomes</u></i>				
Cesarean section [Yes]			.6 (.2, 2.1)	.22
Maternal weight gain (kg)	8.6 (.8)	7.9 (.9)		.57
Non-normal presentation [Yes]			.2 (.0, 2.2)	.056
Analgesia during delivery [Yes]			1.1 (.2, 5.1)	.90
Drug screen at delivery [Positive]			2.0 (.2, 17.2)	.33
Medical complications at delivery [Yes]			.4 (.1, 1.2)	.012
Study discontinuance [Yes]			3.1(.9, 11.3)	.009
Amount of voucher money earned for drug-negative tests (US \$)	1195.14 (63.83)	1167.32 (64.70)		.51
Number of prenatal obstetrical visits	8.5 (.3)	8.6 (.3)		.91

Notes. Estimates are n (%) or Mean (SE). Based on the α level chosen for the tests of significance (see article), 99.09% confidence intervals were used for the primary outcome measures, and 99.6825% confidence intervals for the secondary neonatal and maternal outcome measures. Estimates represent the medication effect in a statistical model adjusting for site and the covariates. Means and standard errors are the model-derived exponentiated estimated model means for the Poisson-distributed outcome measures and the model-derived least squares means for the normally-distributed outcome measures, while odds ratios were estimated for a logistic regression analysis in which the methadone group served as the reference category and the likelihood of the outcome enclosed in [brackets] was modeled. Covariates for the neonatal outcomes were: number of days of study medication; average daily number of cigarettes smoked during study enrollment; percent of cocaine-positive urine tests; exposure (yes *v.* no) to serotonin specific reuptake inhibitor (SSRI) medications during study enrollment; number of prenatal obstetrical visits during study enrollment; and estimated gestational age at delivery (except when estimated gestational age at delivery was the outcome measure). Maternal urine screening test results (positive *v.* negative) for opioids, benzodiazepines, cocaine, and marijuana in the 28 days prior to delivery were included as additional covariates for treated for NAS, peak score on the MOTHER NAS scale during the assessment period, and days medicated for NAS. With the exception of discontinued from the study, covariates for the maternal outcomes were: number of days of study medication; number of prior drug treatments; baseline self-report of methadone use within the last 48 hours; and percent of cocaine-positive urine tests (except for urine drug screening results at delivery). Body mass index served as an additional covariate for cesarean section (yes *v.* no), maternal weight gain, non-normal presentation (yes *v.* no), and anesthesia during

delivery, while last morphine dose in milligrams prior to randomization served as an additional covariate for urine drug screening results at delivery (positive v. negative), medical complications at delivery (yes v. no), amount of drug-abstinent-contingent voucher money earned, and number of prenatal obstetrical visits attended. Number of prior drug treatments, baseline self-report of methadone use within the last 48 hours, any cocaine use (yes v. no) within 30 days of study entry, and last morphine dose in milligrams prior to randomization served as covariates for discontinued from the study (completer v. non-completer), for which $N=175$.

Appendix Table 2. Selected Neonatal Outcomes for Neonates of Non-Completers

	Methadone		Buprenorphine	
	<i>n</i> or <i>n/n</i>	% or Mean (<i>SD</i>)	<i>n</i> or <i>n/n</i>	% or Mean (<i>SD</i>)
Treated for NAS	7/11	64%	9/16	56%
Birthweight (cm)	11	2632.4 (436.5)	18	2939.7 (469.7)
Gestational age at delivery (weeks)	11	36.8 (1.7)	18	37.8 (1.7)
Apgar score at 1 minute	11	7.2 (1.9)	16	8.3 (.9)
Apgar score at 5 minutes	11	8.7 (.5)	16	9.3 (.6)

Note. In order to provide a more complete summary of the impact of the two medications, efforts were made to collect data on the neonates of the 44 maternal non-completers. Four of these participants had been administratively discharged from their program due to rules violations (e.g., physical threats against staff) and so current information on their whereabouts was unobtainable. Two fetal deaths occurred in the methadone condition. It was possible to collect a limited amount of birth information on a portion of the remaining 38 neonates whose participant mothers were able to be located, provided consent, and gave birth in a local hospital. Considerable caution needs to be exercised in interpreting these data, as they were collected under non-standard conditions outside the control of the study investigators. Therefore, summary statistics are reported for descriptive purposes only and the two groups are not compared statistically.

Nonetheless, two points merit mention. First, the birth outcomes of these neonates suggest they were, on average, inferior to their counterparts in their respective Medication Condition (Table 3), as evidenced in their slightly lower birthweights, gestational age at delivery, and Apgar scores at 1 minute. Second, the outcomes for the neonates in the buprenorphine condition are, in each case, superior to the corresponding outcomes of the neonates in the methadone condition.

Appendix Table 3. Percentage of Urine-Positive Screening Test Results
During Study Enrollment and in the Last 4 Weeks Prior to Delivery (N=131)

	Methadone	Burprenorphine
<i><u>During Study Enrollment</u></i>		
Opioid-positive	23%	33%
Cocaine-positive	16%	21%
Benzodiazepine-positive	7%	9%
Marijuana-positive	15%	17%
<i><u>Last 4 Weeks Prior to Delivery</u></i>		
Opioid-positive	6%	11%
Cocaine-positive	0%	0%
Benzodiazepine-positive	1%	5%
Marijuana-positive	10%	11%

Notes. All Ps > .2 associated with Fisher exact tests for all variables (except for cocaine-positive in the last 4 weeks prior to delivery, which can't be tested due to no variability. Drug-positive rates for 5 other illicit substances (e.g., amphetamines) for which testing was conducted were substantially lower than the rates for opioids, cocaine, benzodiazepines, and marijuana.

Medication Dosage

The average doses of methadone and buprenorphine at delivery were 78.2 mg and 16.2 mg respectively. Similar numbers of medication dose increases were provided for methadone (.1, 1.2, and 1.5) and buprenorphine (.1, 1.3, and 1.2) during the first, second, and third trimesters, respectively.

Blinding

Only 24.7% of the participants in the methadone condition and 51.7% of the participants in the buprenorphine condition consistently correctly identified their blind medication, with the frequency of guessing correctly less than expected chance levels in the methadone condition, $P < .001$, not different than chance in the buprenorphine condition, $P = .79$, and inferior in the methadone condition relative to the buprenorphine condition, $P = .0014$. These results are likely due to the fact that most participants guess they are receiving the more novel medication¹. NAS raters were unable to guess the Medication Condition of either the methadone, $P = .08$, or buprenorphine participants, $P = .43$, nor did their relative frequency of guessing correctly differ by medication condition, $P = .56$. Results demonstrate successful study blinding procedures.

1. Jones HE, et al. Buprenorphine versus methadone in the treatment of pregnant opioid-dependent patients: Effects on the neonatal abstinence syndrome. *Drug Alcohol Depend* 2005;79:1-10.