

# Methamphetamine in Pregnancy- 2022

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# Disclosure Information

## Marcela C Smid, MD

- ◆ Gilead Pharmaceuticals, Scientific Consultant
- ◆ NIH R21 R21 DSS10058068 PROMPT



# Disclosure Information

## Charles W Schauberger, MD

- ◆ No disclosures
- ◆ Just about all medications are off-label in pregnancy



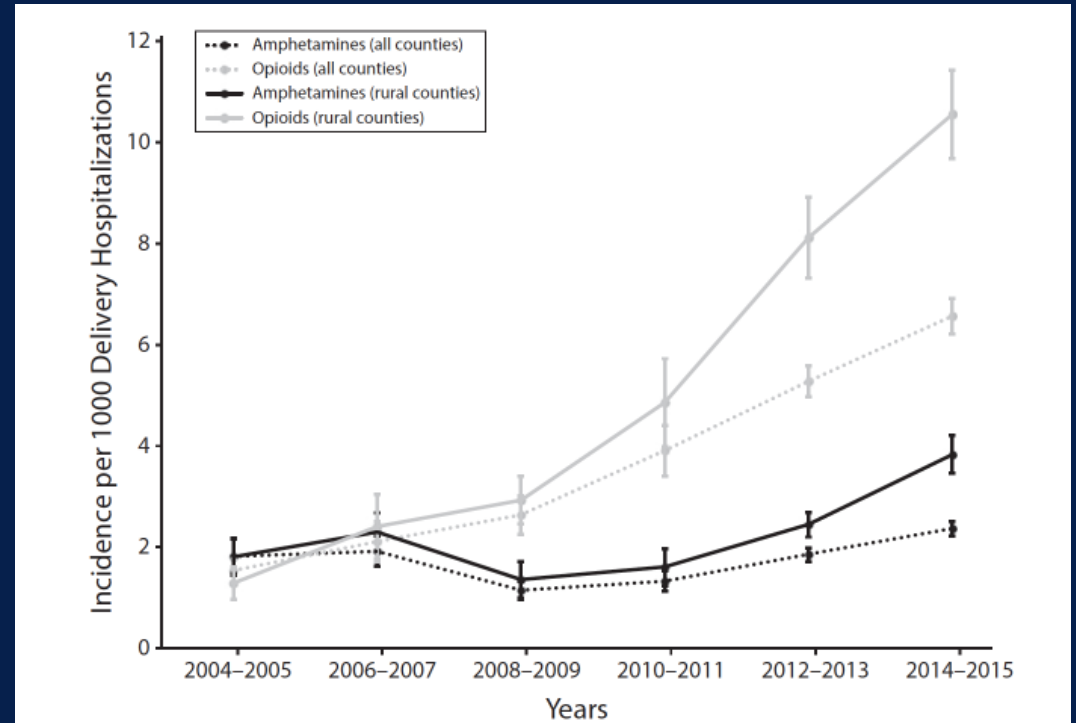
# Learning Objectives

Upon completion of this program, participants will be able to:

1. Describe maternal and perinatal outcomes associated with methamphetamine use in pregnancy
2. Discuss neonatal and child effect of methamphetamine exposure in pregnancy
3. Identify elements of prenatal and addiction care that may improve outcomes

# Pregnancy and Methamphetamine Use

- ◆ 1% of pregnancies affected by methamphetamine use. This translates to 37,000 mother-baby dyads/year
- But challenging patients to manage
- Amphetamines and opioid deliveries increased **disproportionately** in rural versus urban counties



Note. The sample size was n = 47 164 263. All data are survey-weighted and represented as rate per 1000 delivery hospitalizations. Whiskers indicate 95% confidence intervals.

FIGURE 1—National Trends in Amphetamine and Opioid Use Among Delivering Women: National Inpatient Sample, United States, 2004–2015

Amphetamine- and Opioid-Affected Births: Incidence, Outcomes, and Costs, United States, 2004–2015

Lindsay K. Admon, MD, MS; Gavin Barr, MD, PhD; Katy B. Kozhimannil, PhD, MPA; Caroline R. Richardson, MD; Vanessa K. Dalton, MD, MPH; and Tyler N. A. Winkelman, MD, MS

# Challenges of Prenatal Care

- No prenatal care, late onset of care, and infrequent visits
- Poor dating
- Hepatitis C in 19.2%, STI 23.6%
- Homelessness- 26.9%
- ◆ Incarceration- 26.2%
- ◆ More frequent antepartum admissions
- ◆ Use throughout the pregnancy

**Table 1. Maternal Demographics**

	Methamphetamine Users (n=276)	Control Patients (n=34,055)	<i>P</i> *
Age younger than 20 y	25 (9)	5,449 (16)	<.01
Obstetric visits fewer than 5	190 (69)	3,324 (10)	<.001
Hispanic ethnicity	152 (55)	24,179 (71)	<.001
Married	34 (12)	15,686 (46)	<.001

Data are n (%) unless otherwise specified.

\* *P* from  $\chi^2$  test.

# Obstetrical Outcomes

- Severe preeclampsia
- Preterm Labor
- IUGR
- Maternal cardiac problems/pulmonary edema
- Abruptio-more with cocaine

**Table 2. Perinatal Outcomes**

Perinatal Characteristics	Methamphetamine Users (n=273)	Control Patients (n=34,055)	P*
Preterm delivery	139 (52)	5,627 (17)	<.001
1-min Apgar score less than 4	16 (6)	665 (2)	<.001
5-min Apgar score less than 7	16 (6)	328 (1)	<.001
Cesarean delivery	79 (29)	7,730 (23)	<.02
Neonatal mortality	11 (4)	325 (1)	<.001
Maternal obstetric + intensive care unit admissions	6 (2)	95 (0.3)	<.001

Data are n (%) unless otherwise specified.

\* P from  $\chi^2$  test.

## Methamphetamine Use During Pregnancy Maternal and Neonatal Implications

Meadow M. Good, DO, Ido Solt, MD, Joann G. Acuna, MD, Siegfried Rotmensch, MD, and Matthew J. Kim, MD

# Congenital Anomalies

- Not good data – no clear constellation of symptoms like alcohol
- Prospective studies
  - Cleft palate
- Retrospective and case reports
  - NO association with cardiac defect, gastroschisis, limb reduction, open neural tube defect

## Prenatal Methamphetamine Exposure and Adverse Neonatal Outcomes: A Nationwide Cohort Study

Roman Gabrhelík<sup>a,b</sup> Svetlana Skurtveit<sup>c,d</sup> Blanka Nechanská<sup>a</sup> Marte Handal<sup>c</sup>  
Milada Mahic<sup>c</sup> Viktor Mravčík<sup>a,e</sup>

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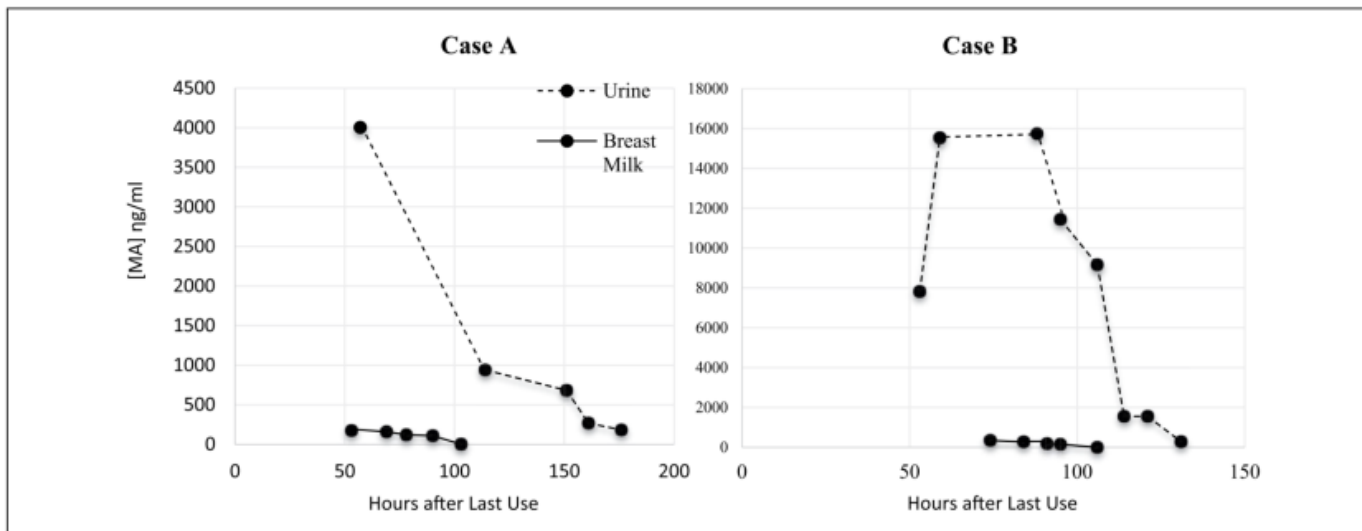
	Methamphetamine exposed versus Opioid exposed (ref.)			Methamphetamine exposed versus General population (ref.)			Opioids exposed versus General population (ref.)				
	<i>b</i>	95% CI	<i>p</i> value	<i>b</i>	95% CI	<i>p</i> value	<i>b</i>	95% CI	<i>p</i> value		
Malformation <sup>c</sup>											
Unadjusted			1.1	0.5 to 2.6	0.862	1.5	0.9 to 2.7	0.131	1.4	0.7 to 9.8	0.283
Adjusted <sup>d</sup>			1.1	0.4 to 2.7	0.918	1.4	0.8 to 2.4	0.288	1.2	0.6 to 2.4	0.533



# Lactation

- EXTREMELY Limited data
- Recommendation against breastfeeding during “active use” for infectious disease reasons. Less based on evidence of neonatal exposure through breastmilk.

**Figure 2.** Methamphetamine Concentrations ([MA]) in Urine and Breast Milk versus Hours after Last Methamphetamine Use for Cases A and B.



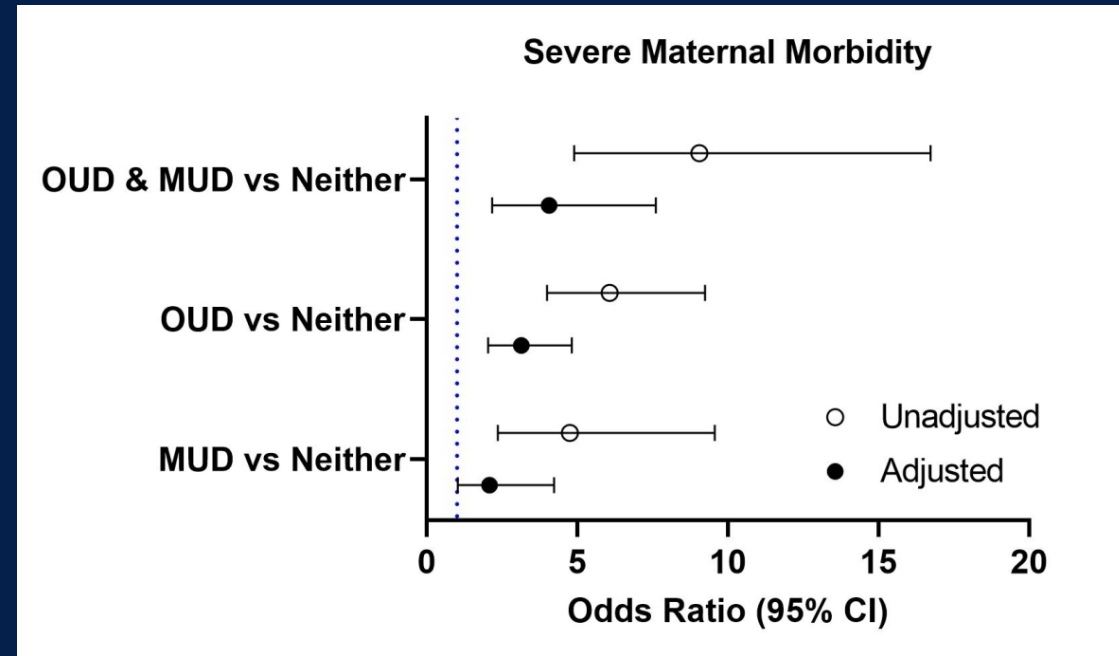
**Transfer of Methamphetamine (MA) into Breast Milk and Urine of Postpartum Women who Smoked MA Tablets during Pregnancy: Implications for Initiation of Breastfeeding**

Chulathida Chomchai, MD<sup>1</sup>, Summon Chomchai, MD, MPH<sup>2</sup>, and Ratchada Kitsommart, MD<sup>2</sup>

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# Severe Maternal Outcomes

- Racial and ethnic differences
  - More than 1:5 with MUD only Pacific Islander
  - 93% with OUD/MUD White
- Severe maternal morbidity and mortality (CDC criteria)
  - More than 1 in 5 women with co-occurring OUD/MUD
  - More than 1 in 10 with OUD or MUD
- This is a **LIFE THREATENING CONDITION for the dyad.**



- Smid et al Utah Population Database. Under review

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# Neonatal Outcomes

- Dyads with maternal OUD/MUD, OUD and MUD are at increased risk for neonatal abstinence syndrome, preterm birth and neonatal death.
- This is a **LIFE THREATENING CONDITION** for the dyad.

Neonatal Morbidity and Mortality					
NAS	22 (27.2)	61 (22.3)	15 (15.5)	783 (0.6)	<.001
Grade 3 or 4 IVH	0 (0.0)	0 (0.0)	1 (1.0)	127 (0.1)	0.026
NEC	0 (0.0)	0 (0.0)	0 (0.0)	60 (0.0)	0.977
Seizure	0 (0.0)	1 (0.4)	0 (0.0)	107 (0.1)	0.404
RDS	8 (9.9)	30 (10.9)	4 (4.1)	6496 (4.8)	<.001
HIE	0 (0.0)	1 (0.4)	1 (1.0)	167 (0.1)	0.052
PTB < 37w	4 (16.0)	9 (12.5)	8 (24.2)	5476 (10.2)	0.039
Gestational age mean (SD)	38.0 (3.7)	38.3 (2.6)	38.3 (3.2)	38.6 (2.1)	0.260
Neonatal death	1 (3.8)	1 (1.1)	2 (5.1)	586 (1.0)	0.038

Abbreviations: NAS neonatal abstinence syndrome; IVH intraventricular hemorrhage; NEC necrotizing enterocolitis; RDS respiratory distress syndrome; HIE hypoxic ischemic encephalopathy; PTB preterm birth; SD standard deviation; 5.7% of deliveries missing GA at delivery.

- Smid et al Utah Population Database. Under review

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# Child Effects

- Infant Development, Environment and Lifestyle study (IDEAL)
- 412 maternal-child pairs (204 methamphetamine exposed versus 208 unexposed pairs) from the United States and New Zealand.



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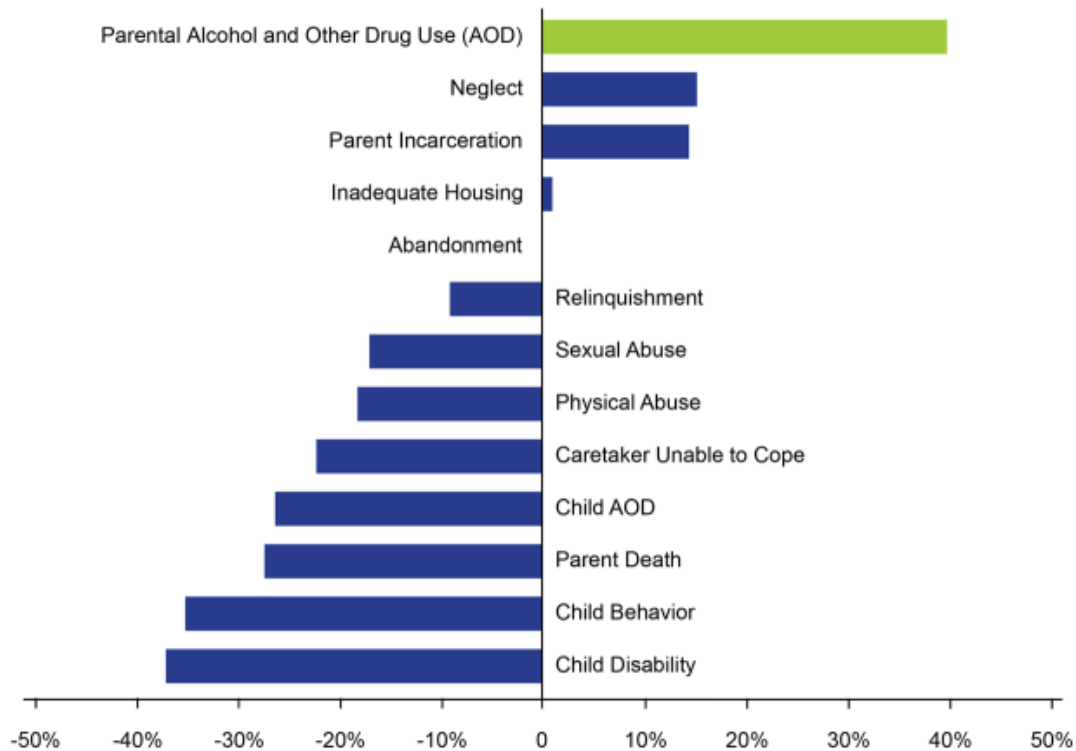
# Child Effects

- ◆ **At age 3 years**, neurodevelopmental outcomes correlated with **adverse social environments and *not* prenatal methamphetamine exposure.**
- ◆ **At age 3 and 5 years**, heavy prenatal methamphetamine exposure ( $\geq 3$  days per week), increased anxiety/depression and attention problems
- ◆ **At age 7.5 years** had poorer cognitive function on the Conner's Parent Rating Scale, but not behavioral problems



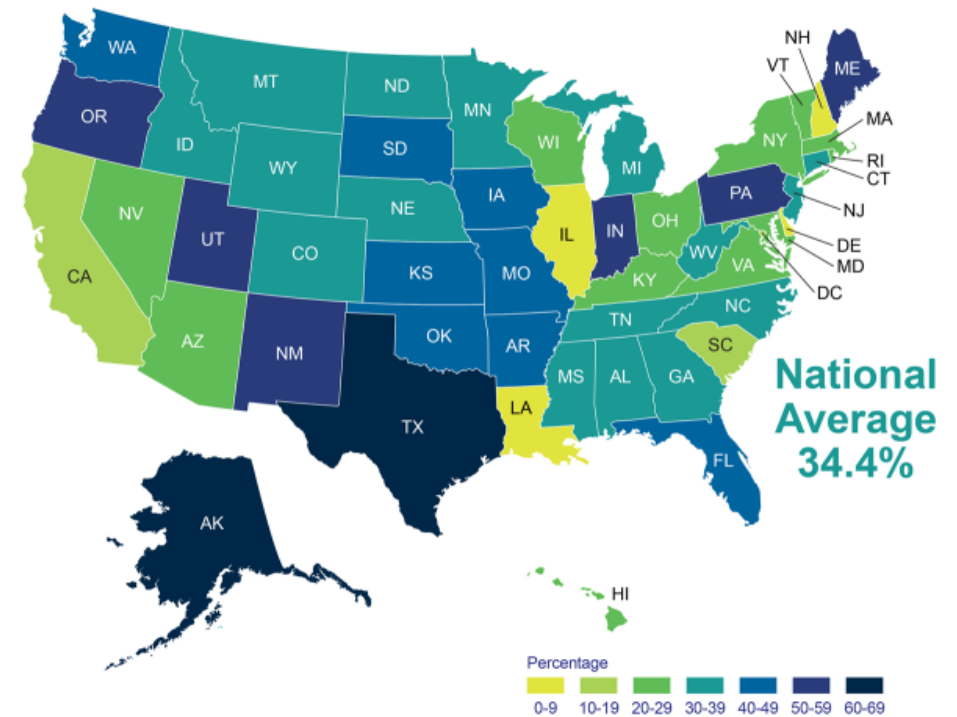
# Methamphetamines and Child Custody

Percentage Change in Reasons for Removal in the United States, 2009 to 2015



Source: AFCARS Data, 2010-2016

Parental Alcohol or Other Drug Use as Reason for Removal by State, 2015

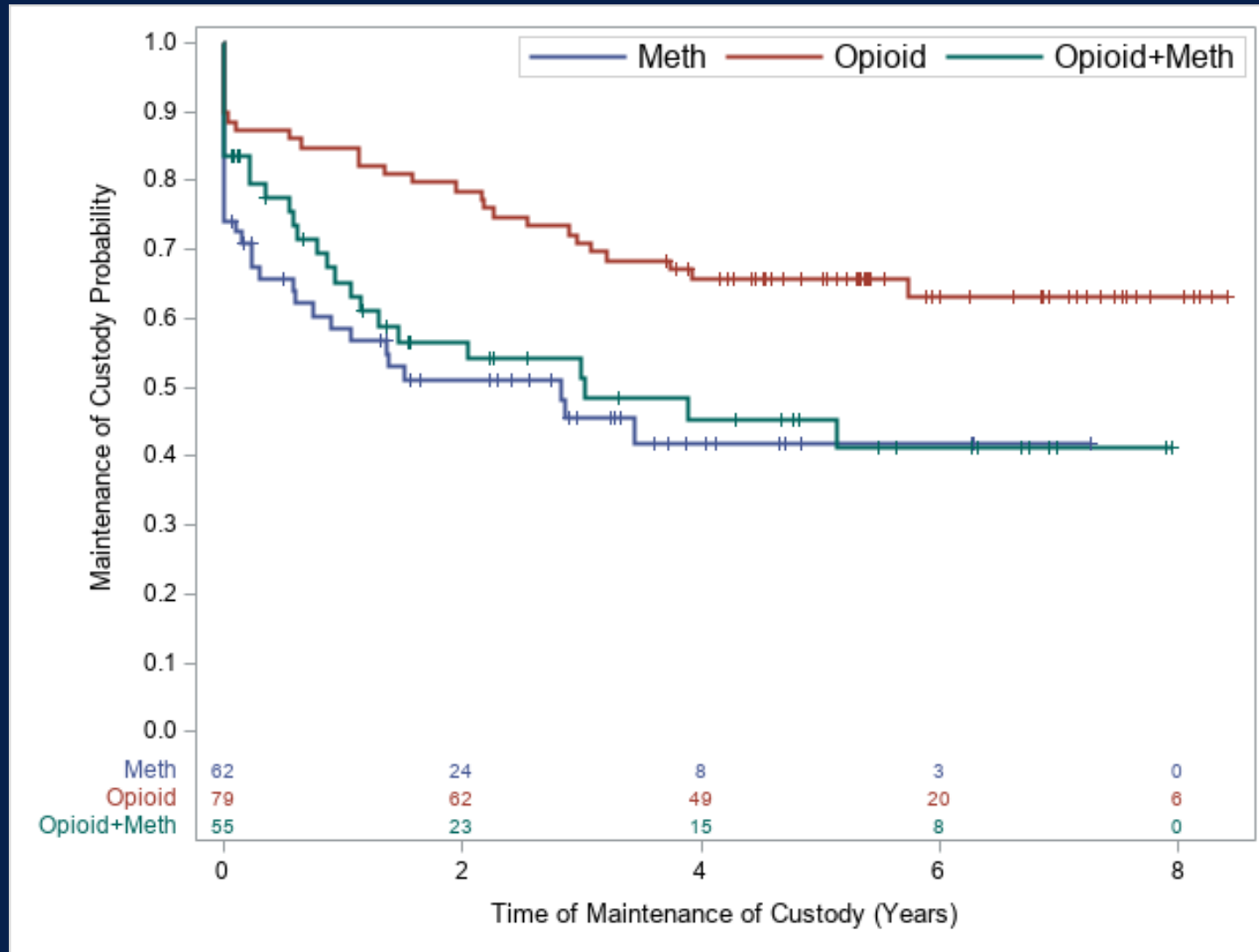


Note: Estimates are based on all children in out-of-home care at some point during Fiscal Year.

Source: AFCARS Data, 2016

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# Maintenance of Custody



P = 0.004

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# Methamphetamine Use Disorder and Treatment

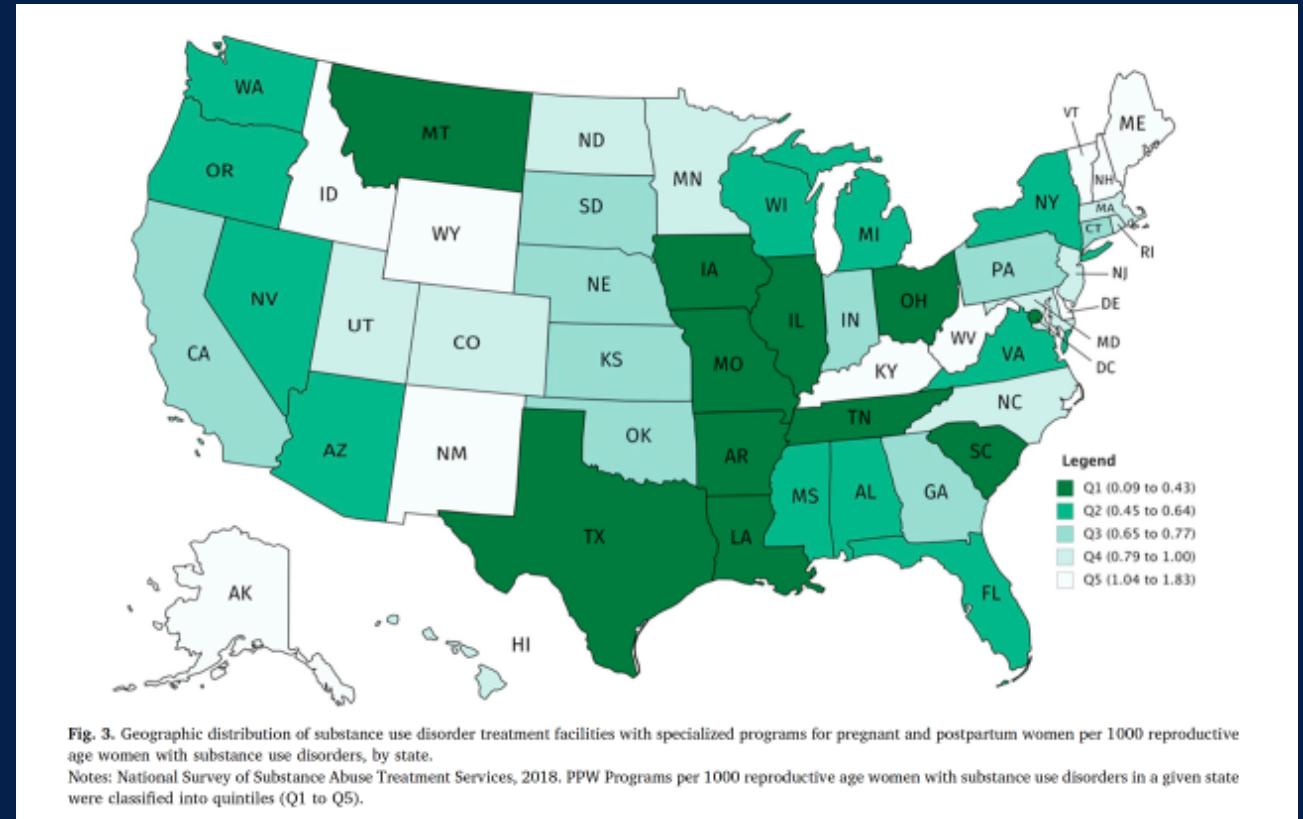


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# Methamphetamines and Treatment

- Women generally do better in women-specific treatment programs
- Pregnant and parenting women do best in specialized programs
- Incarceration is not treatment

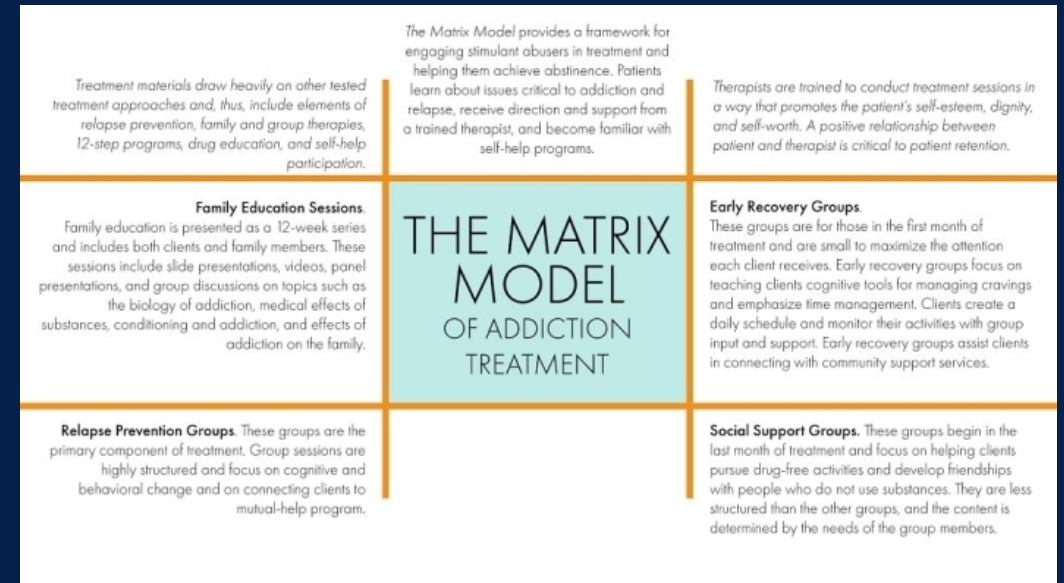


Substance use disorder treatment services for pregnant and postpartum women in residential and outpatient settings

Angélica Meinhofer<sup>a,\*</sup>, Jesse M. Hinde<sup>b</sup>, Mir M. Ali<sup>c</sup>

# Care Models

- ◆ Contingency management
  - ◆ Motivational incentives
- ◆ The Matrix Model
  - ◆ Manualized outpatient approach
- ◆ Cognitive-behavioral therapy (CBT)
- ◆ 12-Step facilitation therapy
- ◆ Mobile medical application: reSET<sup>®</sup>



## Contingency management for the treatment of methamphetamine use disorder: A systematic review

Hayley D. Brown, Anthony DeFulio \*

Western Michigan University, United States

## A multi-site comparison of psychosocial approaches for the treatment of methamphetamine dependence

Richard A. Rawson<sup>1</sup>, Patricia Marinelli-Casey<sup>1</sup>, M. Douglas Anglin<sup>1</sup>, Alice Dickow<sup>2</sup>, Yvonne Frazier<sup>3</sup>, Cheryl Gallagher<sup>4</sup>, Gantt P. Galloway<sup>5</sup>, James Herrell<sup>4</sup>, Alice Huber<sup>1</sup>, Michael J. McCann<sup>4</sup>, Jeanne Obert<sup>2</sup>, Susan Pennell<sup>3</sup>, Chris Reiber<sup>1</sup>, Denna Vandersloot<sup>9</sup>, Joan Zweben<sup>10</sup> and the Methamphetamine Treatment Project Corporate Authors\*

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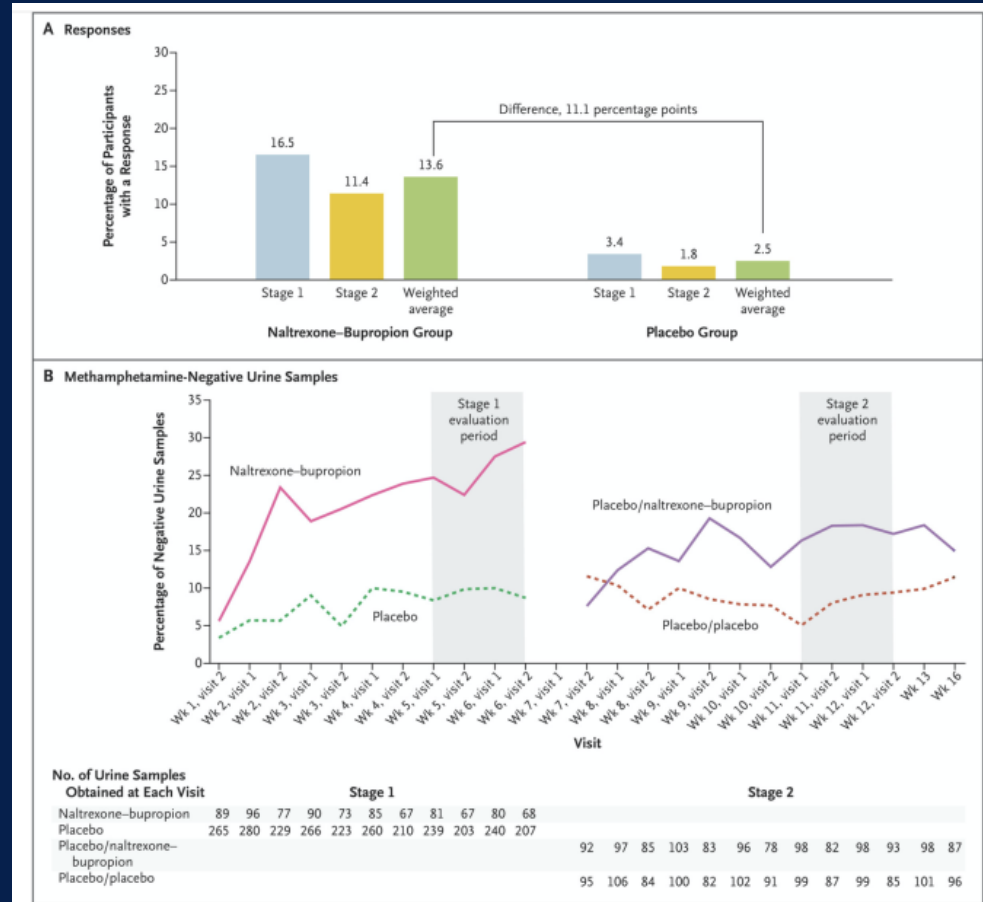
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# Medications for Methamphetamine Use Disorder

- Naltrexone 380 mg Q3 weeks
- Bupropion 150 mg XL daily
- Evidence-informed for pregnant individuals, not evidence based

Table 2. Primary and Secondary Outcomes in the Intention-to-Treat Population.<sup>a</sup>

Outcome	Stage 1		Stage 2		Treatment Effect Weighted Difference	95% CI
	Naltrexone–Bupropion (N=109)	Placebo (N=294)	Naltrexone–Bupropion (N=114)	Placebo (N=111)		
Primary outcome — no. of participants (%)†	18 (16.5)	10 (3.4)	13 (11.4)	2 (1.8)	11.1±2.5	—
Secondary outcomes						
Methamphetamine-negative urine samples — %‡	20.4±2.2	12.3±1.6	19.2±2.6	13.4±1.5	6.8±1.7	3.5 to 10.1
Change in methamphetamine craving according to visual analogue scale§	-30.0±3.2	-22.3±1.8	-31.8±3.2	-20.5±1.7	-9.7±2.1	-13.8 to -5.6
Change in score on PHQ-9 depression scale	-4.8±0.7	-3.3±0.3	-4.4±0.6	-3.7±0.4	-1.1±0.4	-1.9 to -0.2
Change in score on Treatment Effectiveness Assessment¶	6.5±1.5	2.2±1.0	6.2±1.5	2.5±1.1	4.0±0.9	2.3 to 5.7

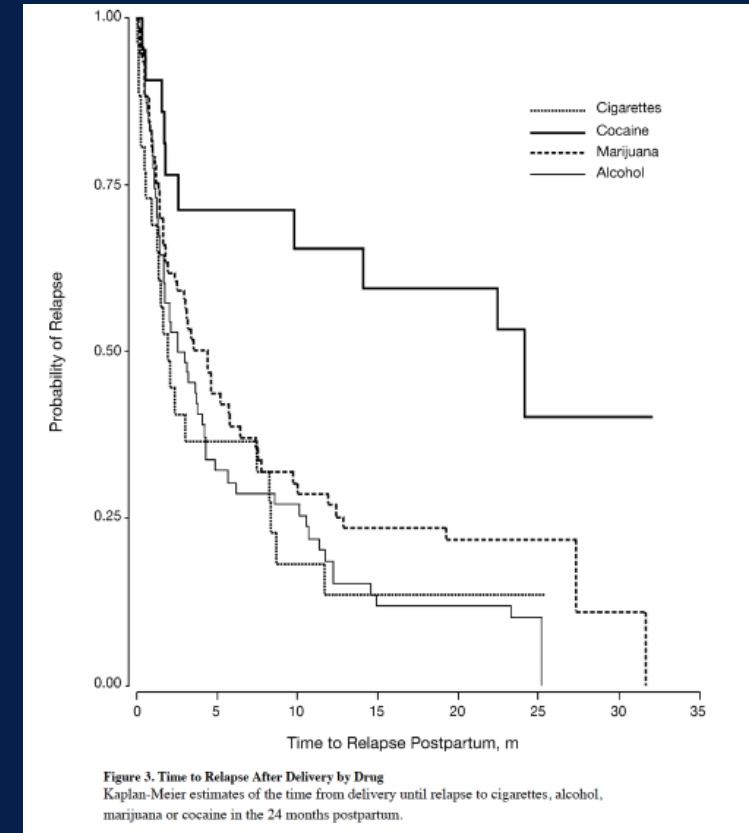
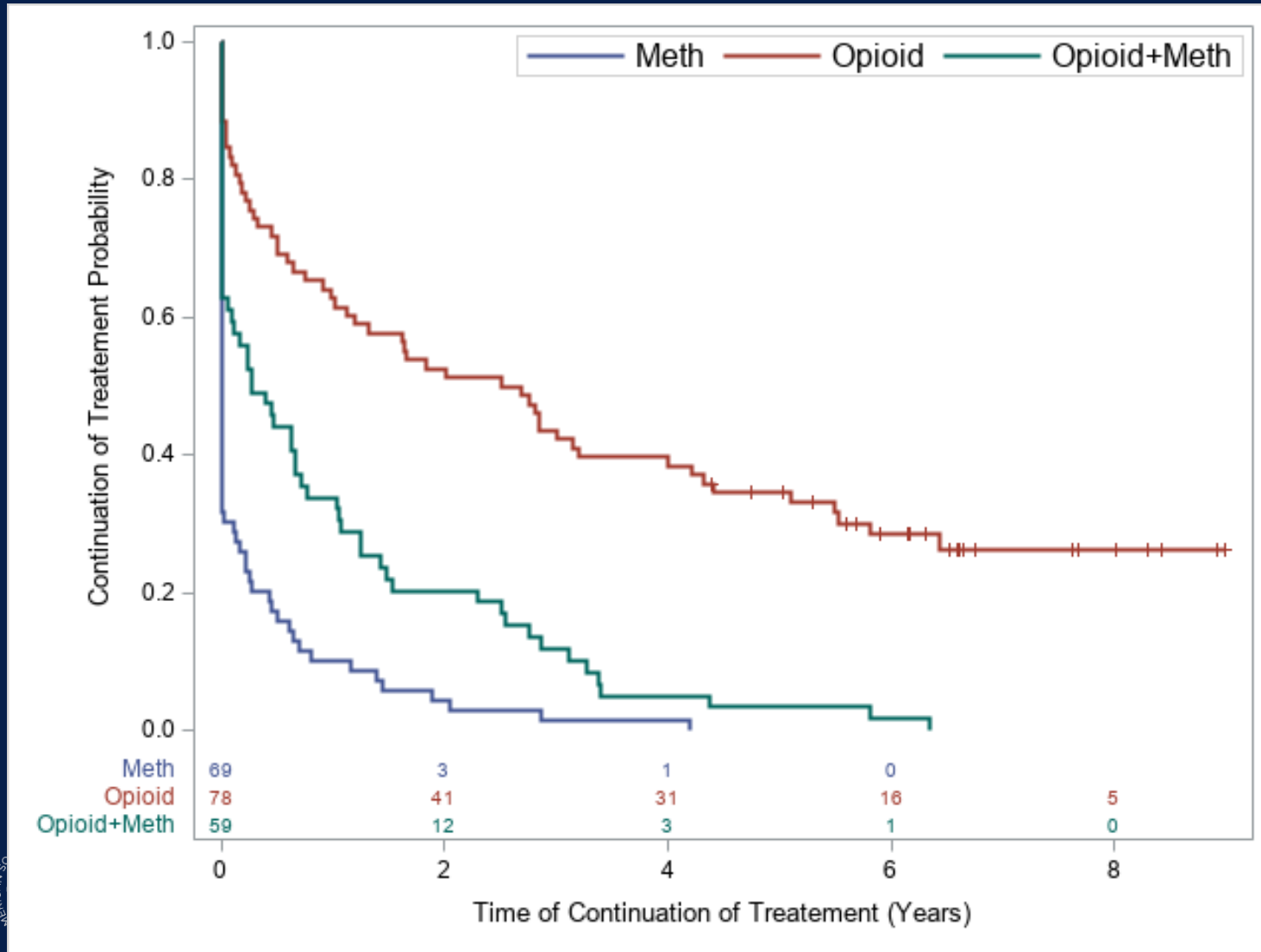


ORIGINAL ARTICLE

## Bupropion and Naltrexone in Methamphetamine Use Disorder

Madhukar H. Trivedi, M.D., Robrina Walker, Ph.D., Walter Ling, M.D., Adriane dela Cruz, M.D., Ph.D., Gaurav Sharma, Ph.D., Thomas Carmody, Ph.D., Udi E. Ghitza, Ph.D., Aimee Wahle, M.S., Mora Kim, M.P.H., Kathy Shores-Wilson, Ph.D., Steven Sparenborg, Ph.D., Phillip Coffin, M.D., M.I.A., et al.

# Continuation in Treatment



## Perinatal Substance Use: A Prospective Evaluation of Abstinence and Relapse

Ariadna Forray<sup>1</sup>, Brian Merry<sup>1</sup>, Haiqun Lin<sup>2</sup>, Jennifer Prah Ruger<sup>3</sup>, and Kimberly A. Yonkers<sup>1,2,4</sup>

P < 0.0001

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# Prevention Of Methamphetamine Use among Postpartum Women Trial (PROMPT)

- Up to 12 weeks postpartum
- **Intervention:** Micronized progesterone versus placebo
  - 200 mg twice daily
- **Feasibility:** 40 women
- **Safety:** maternal and neonatal outcomes
- **Primary efficacy outcome:** return to methamphetamine use



RECRUITMENT ONGOING at University of Utah



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# Final Takeaways/Summary

- Methamphetamine use disorder is **increasing**, particularly with co-occurring opioid use disorder.
- Methamphetamine associated with both adverse maternal and perinatal outcomes.
- Long term child outcomes are more strongly associated with adverse social settings than methamphetamine exposure.
- Treatment modalities are poorly studied in pregnant and postpartum women.

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