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Wisconsin Collaborative of Treatment Professionals
FOR EDUCATION AND CAPACITY TRAINING

Update on Neonatal Outcomes of Methamphetamine-Exposed Pregnancies

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Accreditation: CME

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Disclosures: Planners/Faculty

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*Ineligible companies are those whose primary business is producing, marketing, selling, reselling, or distributing healthcare products used by or on patients.

Objectives

- Describe short-term outcomes of infants exposed to methamphetamine *in utero*.
- Describe longer-term developmental outcomes of infants exposed to methamphetamine *in utero*.
- Describe two potential strategies to improve longer-term outcomes.

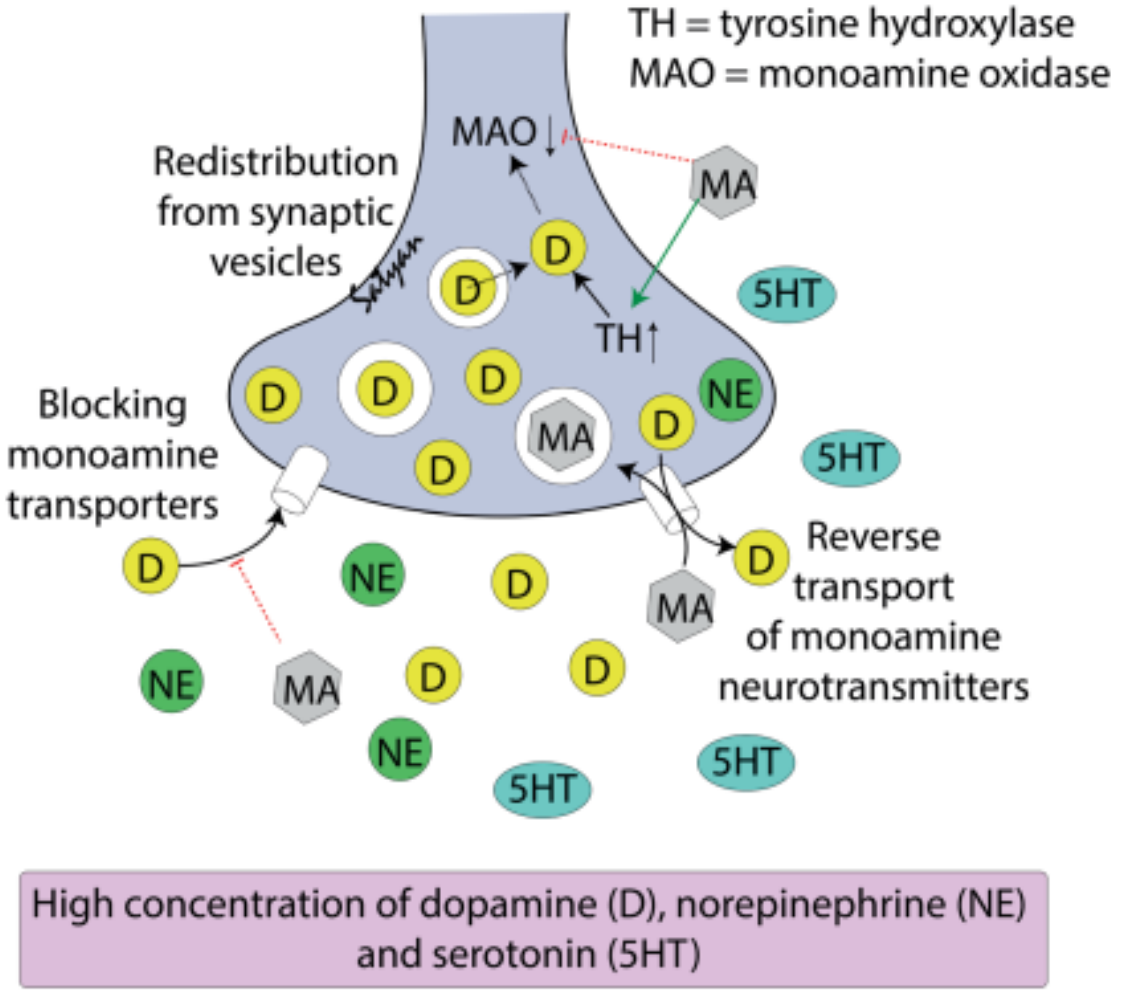
What do we know?

- PubMed

Pregnancy AND	Citations	5-year trend
Alcohol	31702	↑
Opioid	8638	↑
Tobacco	6657	↑↑↑
Cocaine	3014	↑
Cannabis OR marijuana	1863	↔
Methamphetamine	537	↑↑

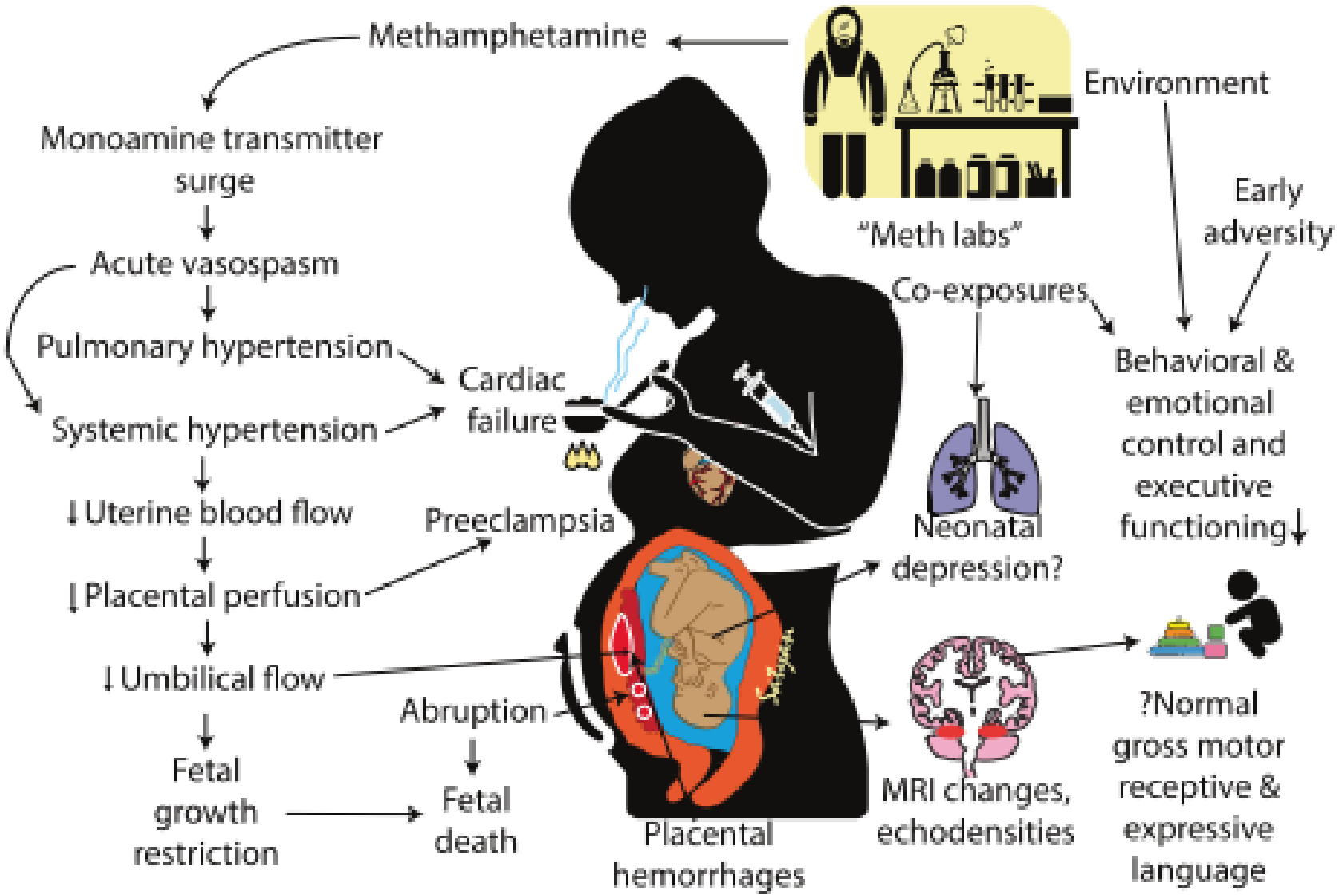
Methamphetamine

- Toxicity
  - Direct effects on neurotransmitter release and uptake
  - Indirect effects on cerebral hemodynamics
    - Cerebral blood flow
    - Perfusion pressure
    - Oxygenation
- Challenges
  - Small sample size in published studies
  - Potential confounding



Sankaran et al., 2022

Effects



Sankaran et al. J Perinatol, 2022

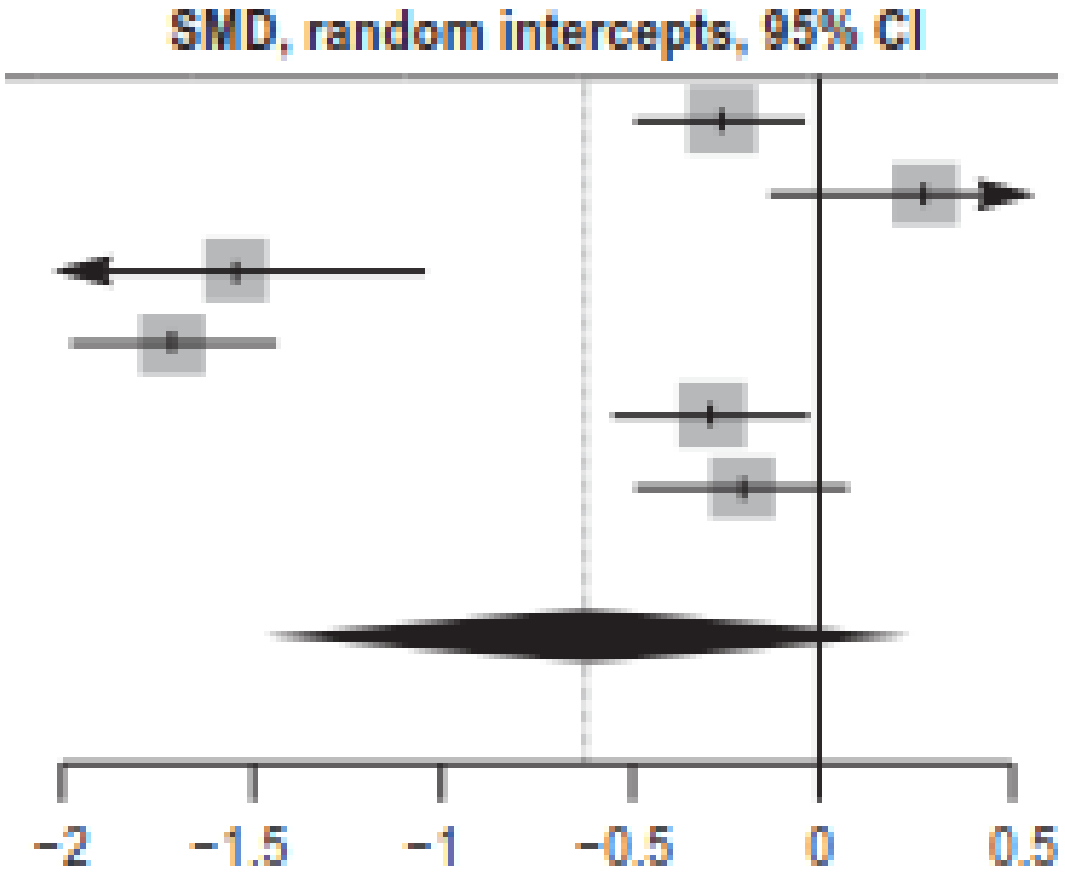
Teratogenicity

Teratogen: any substance, organism, or process that causes malformations in a fetus

- Animal studies: rats, mice, rabbits
- Early reports: higher prevalence of congenital malformations
- Subsequent case-control and prospective studies have not confirmed the findings
- Risk of teratogenicity: low

Garey et al., 2020; Smith and Santos, 2016; Dinger et al., 2017

Gestation



Gestational Age

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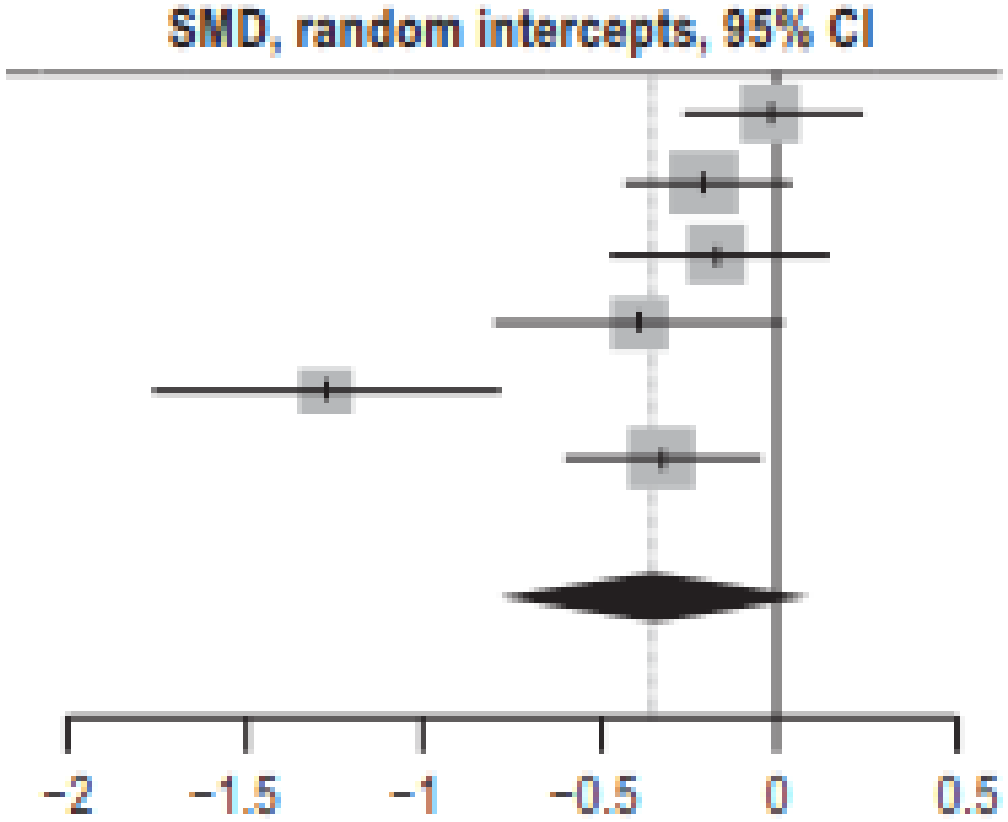
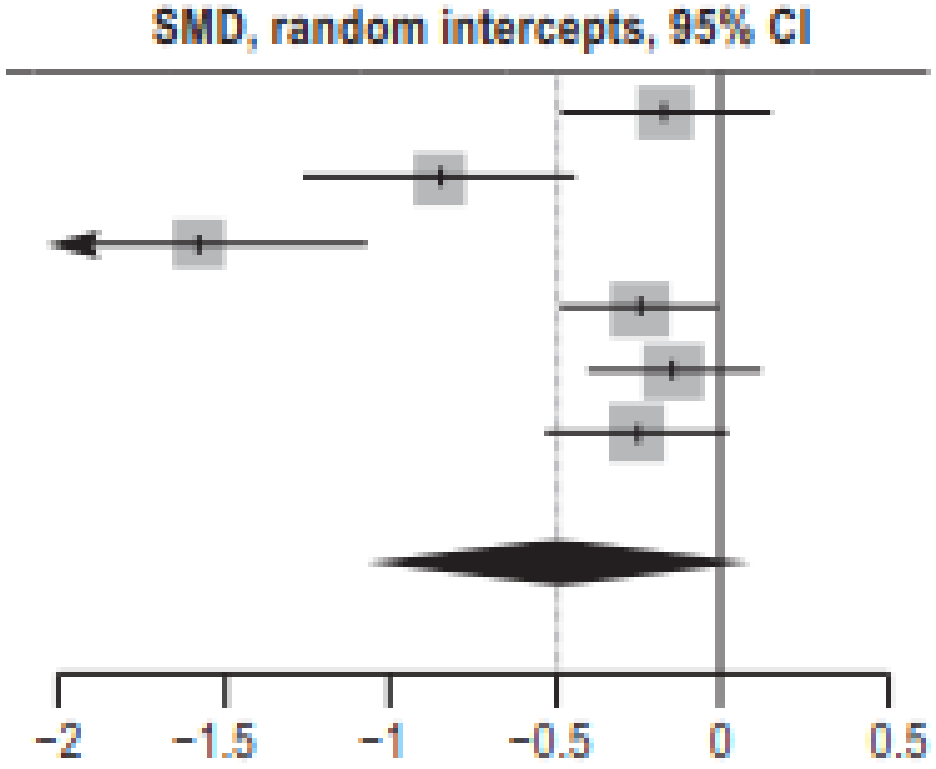
Harst et al., 2021

Fetal Growth and Gestation



Birth Weight



Head Circumference

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Harst et al., 2021

Withdrawal v Toxicity v Confounding

- Abnormal reflexes/poor quality movement
- Arousal/excitability
- Decreased ability to self-regulate
- Difficulty feeding
- Excessive sucking
- Extreme irritability
- Increased lethargy and hypotonicity
- Jitteriness
- Poor suck

Polysubstance use may be associated with other symptoms

Ackerman et al., 2021; Perez et al., 2021; Wells and Loshak, 2019

Development

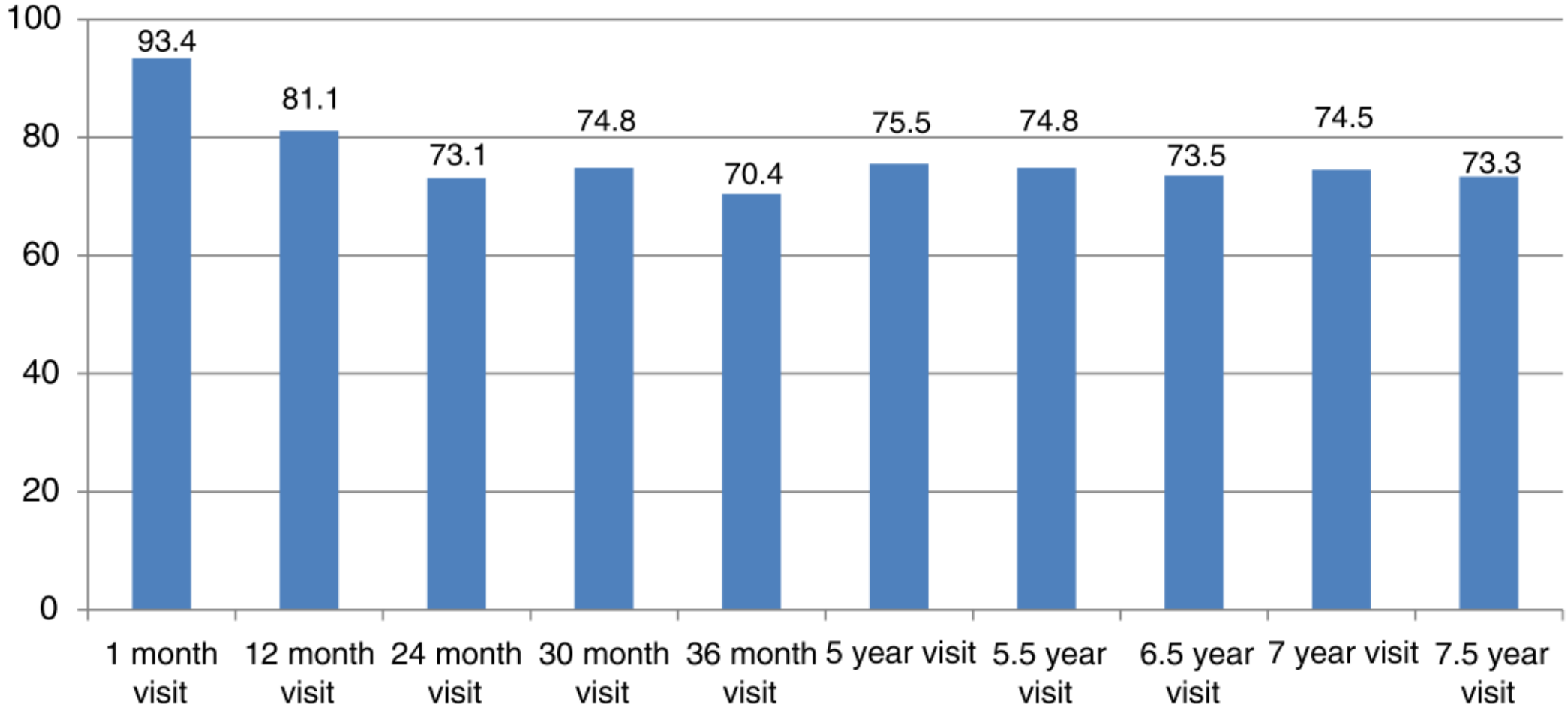
- Motor
- Cognitive
- Language and Communication
- Social and Emotional
- Physical

IDEAL Study

- Infant Development, Environment, and Lifestyle
- Recruitment from 4 sites over 2-year period
- Screened: 34,833
  - Eligible: 17,961
  - Consented: 3705
  - Longitudinal follow-up: 412
    - Exposed: 204
    - Matched comparisons: 208

Smith et al. Neurotoxicol Teratol, 2015

IDEAL Study



Smith et al. Neurotoxicol Teratol, 2015

Motor Development

	Exposed (N=160)	Comparison (N=168)	Adjusted P-value
Gross Motor Quotient	103.8 ± 5.79	103.64 ± 7.10	0.630
Stationary	10.70 ± 1.09	10.63 ± 1.29	0.412
Locomotion	10.97 ± 1.68	10.83 ± 2.00	0.763
Object manipulation	10.34 ± 1.33	10.48 ± 1.46	0.262
Fine Motor Quotient	104.94 ± 9.80	106.16 ± 10.46	0.240
Grasping	10.24 ± 1.89	10.61 ± 2.01	**0.027**
Visual-motor integration	10.34 ± 1.33	10.48 ± 1.46	0.761

Smith et al., 2011

Cognitive Development

	Exposed	Comparison	Adjusted P value
12 months	N=162	N=169	
MDI	94.23 ± 9.56	94.28 ± 10.64	0.785
24 months	N=147	N-=139	
MDI	84.51 ± 12.03	83.53 ± 13.36	0.216
36 months	N=135	N=141	
MDI	88.90 ± 11.11	87.76 ± 15.27	0.240

Smith et al., 2011

Cognitive Development

	Exposed (Mean, SD)	Control (Mean, SD)	p
Sequential processing			
Hand movements	7.04 (1.49)	10.64 (2.48)	<0.001
Simultaneous processing			
Conceptual thinking	5.33 (2.39)	9.50 (2.65)	0.005
Block counting	6.27 (3.38)	9.72 (1.97)	<0.001
Planning ability			
Story completion	4.96 (1.69)	8.23 (2.00)	<0.001
Learning ability			
Atlantis	5.65 (1.77)	8.82 (2.97)	<0.001
Atlantis delayed	6.74 (1.94	9.59 (2.48)	<0.001

Kwiatkowski et al., 2018

Language/Communication Development

- Search terms: *methamphetamine AND (language OR speech OR communication) AND development*: results 66 articles

- Derauf et al. 2011.

  Higher levels of environmental adversity were associated with compromised language development.
- Schreiter et al. 2019.

  Lower scores in language at 2 and 3 years age

Social and Emotional Development

	Age 3 Years		Age 5 Years		Exp Adj p	Age Adj p	Inter Adj p
	Exposed (n=141)	Comparison (n=147)	Exposed (n=153)	Comparison (n=151)			
Externalizing	53.0 ± 1.9	52.0 ± 2.2	53.1 ± 2.0	49.6 ± 2.3	0.150	0.003	**0.034**
Attention problems	2.6 ± 0.4	2.6 ± 0.4	2.8 ± 0.4	2.7 ± 0.4	0.278	0.995	0.552
Aggressive behav	12.9 ± 1.3	11.8 ±1.6	12.6 ± 1.4	10.0 ±1.6	0.123	**0.002**	0.068
ADHD issues	5.3 ± 0.6	5.2 ± 0.6	5.5 ± 0.6	4.6 ± 06	0.259	0.013	**0.029**
Internalizing	50.9 ± 1.8	48.7 ± 2.2	54.2 ± 1.9	50.8 ± 2.2	0.057	**0.007**	0.350
Emotionally reactive	3.2 ± 0.5	2.3 ± 0.6	3.7 ± 0.5	2.5 ± 0.6	**0.006**	0.318	0.363
Anxious/depressed	2.8 ± 0.4	2.0 ± 0.5	3.4 ± 0.4	2.3 ± 0.5	**0.019**	**0.010**	0.359
Withdrawn	1.5 ± 0.4	1.4 ± 0.5	1.9 ± 0.4	1.7 ± 0.5	0.273	**0.033**	0.866

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LaGasse et al., 2012

Physical Development

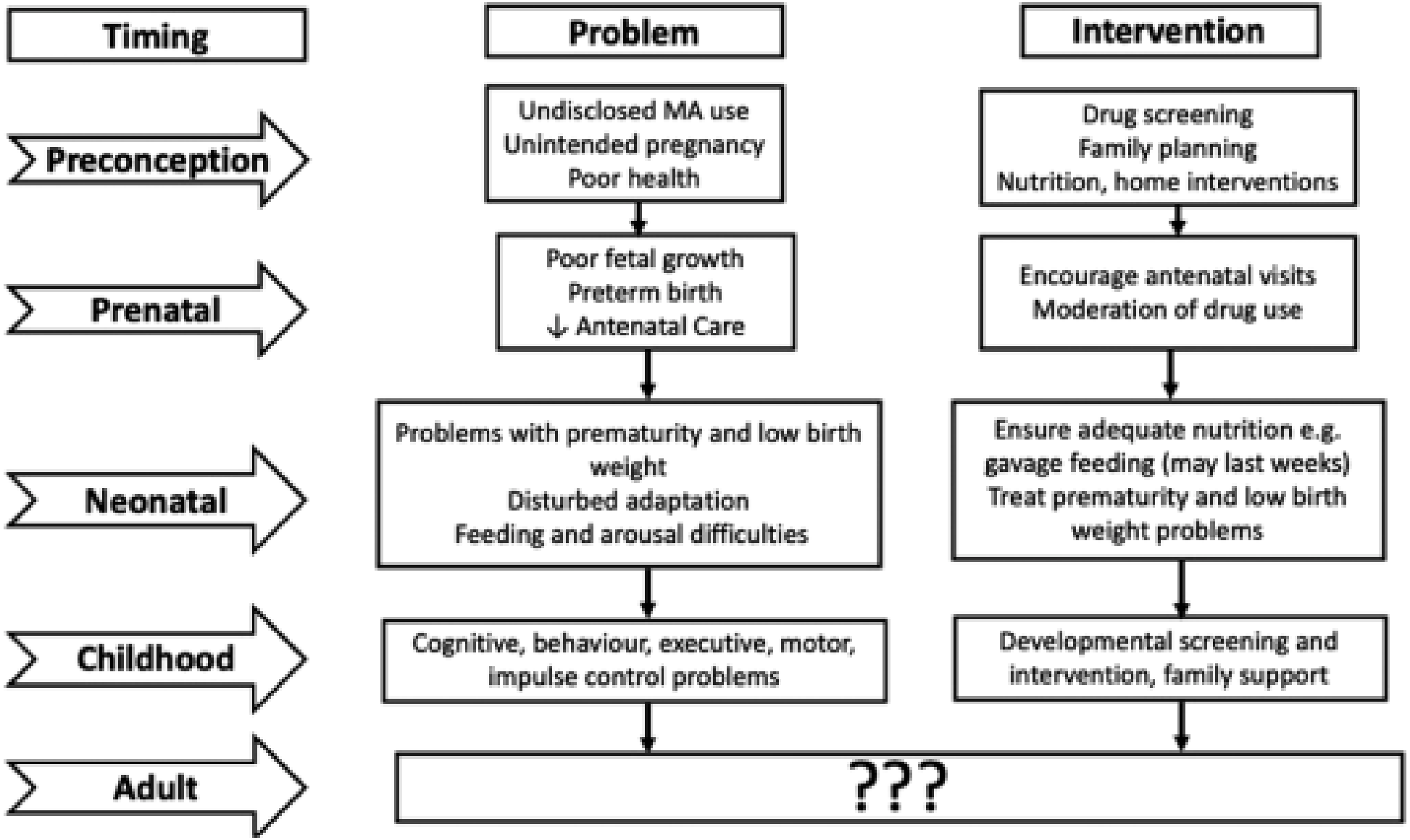
	N	MA exposed Mean (SD)	N	Not exposed Mean (SD)	p
Length (cm)					
1 year	93	74.75 (3.47)	100	75.42 (3.10)	0.160
2 years	99	86.68 (3.57)	99	87.37 (3.38)	0.162
3 years	82	95.34 (3.44)	85	96.8 (3.78)	**0.009**
Weight (kg)					
1 year	93	10.289 (1.287)	99	10.467 (1.208)	0.323
2 years	97	12.859 (1.639)	98	13.366 (1.699)	**0.035**
3 years	82	15.234 (2.140)	84	15.600 (2.375)	0.276
Head Circumference (cm)					
1 year	94	46.74 (1.36)	100	47.15 (1.40)	**0.036**
2 years	98	49.11 (1.29)	98	49.31 (1.49)	0.306
3 years	82	50.45 (1.29)	85	50.61 (1.38)	0.424

Wouldes et al., 2014

Confounding

A social environment characterized by quarrelling, violence, poverty, and low educational attainment of the primary caregivers was associated with a more pronounced manifestation of the effect of PME on behavioral development later in life, even after adjustment for socioeconomic status and educational attainment.

Harst et al., 2021



Perez et al., 2021

Thank you

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