Long Term Outcomes for Infants Prenatally Substance Exposed: Knowns, Unknowns, and Strategies for Intervention

Laurie Seidel Halmo, MD, FAAP
Assistant Professor of Pediatrics and Medical Toxicologist
University of Colorado School of Medicine
Volunteer Faculty, Rocky Mountain Poison and Drug Safety

Disclosures

- None

Learning Objectives

1) Summarize the data regarding long-term health and neurodevelopmental outcomes for infants prenatally exposed to nicotine, alcohol, cannabis, amphetamines and opioids
2) Describe the limitations of the data surrounding long-term outcomes for infants prenatally exposed to substances
3) List three recommendations you can employ to improve long-term outcomes for infants prenatally substance exposed

What I'm not going to talk about

- Mechanisms/animal/preclinical data
- Comprehensive reviews of anything
- Pregnancy/delivery/birth outcomes
- Imminent social outcomes (e.g., child welfare involvement)
- Cocaine, benzodiazepines, and many, many other medications and substances that pregnant people sometimes use or take

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Limitations

- Polysubstance use/exposures
- Lots of social confounders, particularly poverty
- Heterogeneous populations
  - Different substances/polysubstance use
  - Differences in dose
  - Differences in duration/timing of use
  - Differences in home and built environments
  - Differences in comorbid health concerns (mental health, nutritional status)

Learning Objectives

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Nicotine

- Increased risk of overweight and obesity
- Increased risk of asthma
- Increased risk of ADHD
- Risk of decreased cognitive function and school performance
- Increased risk of nicotine dependence
- Some suggestion of increased risk of cancer
- Special limitations specific to nicotine exposure
  - Nicotine? PAHs? Vape juice? All kinds of other stuff? Postnatal SHS?

Systematic review and meta-analysis of the association between maternal smoking in pregnancy and childhood overweight and obesity

Sarah Rayfield and Emma Plugge

J Epidemiol Community Health 2017;**71**:162–173.

39 studies in total
236,687 children
5 continents (North America, South America, Europe, Australia, Asia)

Systematic review and meta-analysis of the association between maternal smoking in pregnancy and childhood overweight and obesity

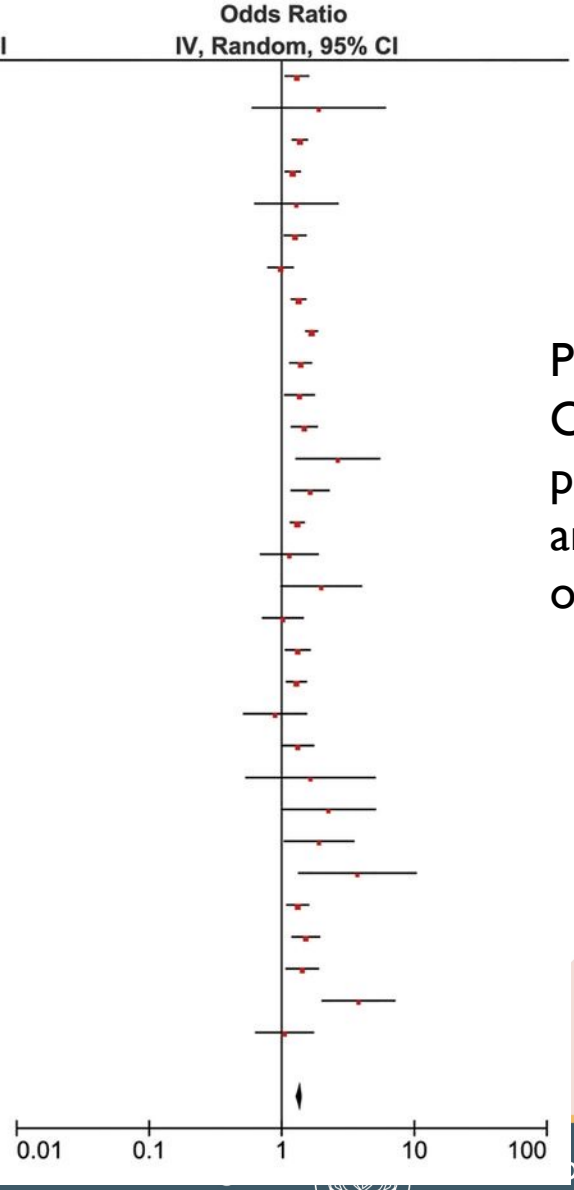
Sarah Rayfield and Emma Plugge

J Epidemiol Community Health 2017;**71**:162–173.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Al Mamum 2006 (Australia)	0.2624	0.109	4.6%	1.30 [1.05, 1.61]
Braun 2010 (USA)	0.6419	0.5951	0.3%	1.90 [0.59, 6.10]
Chen 2006 (USA) Female	0.3148	0.0719	6.4%	1.37 [1.19, 1.58]
Chen 2006 (USA) Male	0.1906	0.0724	6.4%	1.21 [1.05, 1.39]
Fasting 2009 (Norway)	0.2546	0.3738	0.7%	1.29 [0.62, 2.68]
Gorog 2011 (Europe)	0.2311	0.1028	4.9%	1.26 [1.03, 1.54]
Harris 2013 (USA)	-0.0202	0.1165	4.3%	0.98 [0.78, 1.23]
Hawkins 2009 (UK)	0.2927	0.0692	6.6%	1.34 [1.17, 1.53]
Kleiser 2009 (Germany)	0.5188	0.0578	7.2%	1.68 [1.50, 1.88]
Kuhle 2010 (Canada)	0.3293	0.1012	5.0%	1.39 [1.14, 1.69]
Laitinen 2012 (Finland)	0.3075	0.1369	3.6%	1.36 [1.04, 1.78]
Mangrio 2010 (Sweden)	0.392	0.1199	4.2%	1.48 [1.17, 1.87]
Mendez 2008 (Spain)	0.9746	0.3762	0.7%	2.65 [1.27, 5.54]
Messiah 2012 (USA)	0.4947	0.1726	2.7%	1.64 [1.17, 2.30]
Moller 2014 (Denmark)	0.27	0.0665	6.7%	1.31 [1.15, 1.49]
Moschonis 2008 (Greece)	0.131	0.2606	1.4%	1.14 [0.68, 1.90]
Olson 2009 (USA)	0.6861	0.3619	0.8%	1.99 [0.98, 4.04]
Pinot de Moira 2010 (UK) Offspring	0.0198	0.1848	2.4%	1.02 [0.71, 1.47]
Power 2002 (UK) Female	0.2776	0.1139	4.4%	1.32 [1.06, 1.65]
Power 2002 (UK) Male	0.2546	0.0937	5.3%	1.29 [1.07, 1.55]
Raum 2011 (Germany)	-0.1165	0.2841	1.2%	0.89 [0.51, 1.55]
Risvas 2011 (Finland)	0.2776	0.1468	3.3%	1.32 [0.99, 1.76]
Seach 2010 (Australia)	0.499	0.5775	0.3%	1.65 [0.53, 5.11]
Shi 2013 (Canada)	0.8109	0.4225	0.6%	2.25 [0.98, 5.15]
Suzuki 2009 (Japan)	0.6471	0.3151	1.0%	1.91 [1.03, 3.54]
Timmermans 2014 (Netherlands)	1.3137	0.5248	0.4%	3.72 [1.33, 10.41]
Toschke 2007 (Germany)	0.2776	0.1013	5.0%	1.32 [1.08, 1.61]
Von Kries 1999 (Germany)	0.4187	0.1271	3.9%	1.52 [1.18, 1.95]
Von Kries 2002 (Germany)	0.3577	0.148	3.3%	1.43 [1.07, 1.91]
Wideroe 2003 (Norway and Sweden)	1.335	0.3275	0.9%	3.80 [2.00, 7.22]
Yang 2013 (Belarus)	0.0488	0.2606	1.4%	1.05 [0.63, 1.75]
Total (95% CI)			**100.0%**	**1.37 [1.28, 1.46]**

Heterogeneity: Tau² = 0.01; Chi² = 54.88, df = 30 (P = 0.004); I² = 45%

Test for overall effect: Z = 9.34 (P < 0.00001)



Pooled adjusted OR for maternal prenatal smoking and childhood overweight

Systematic review and meta-analysis of the association between maternal smoking in pregnancy and childhood overweight and obesity

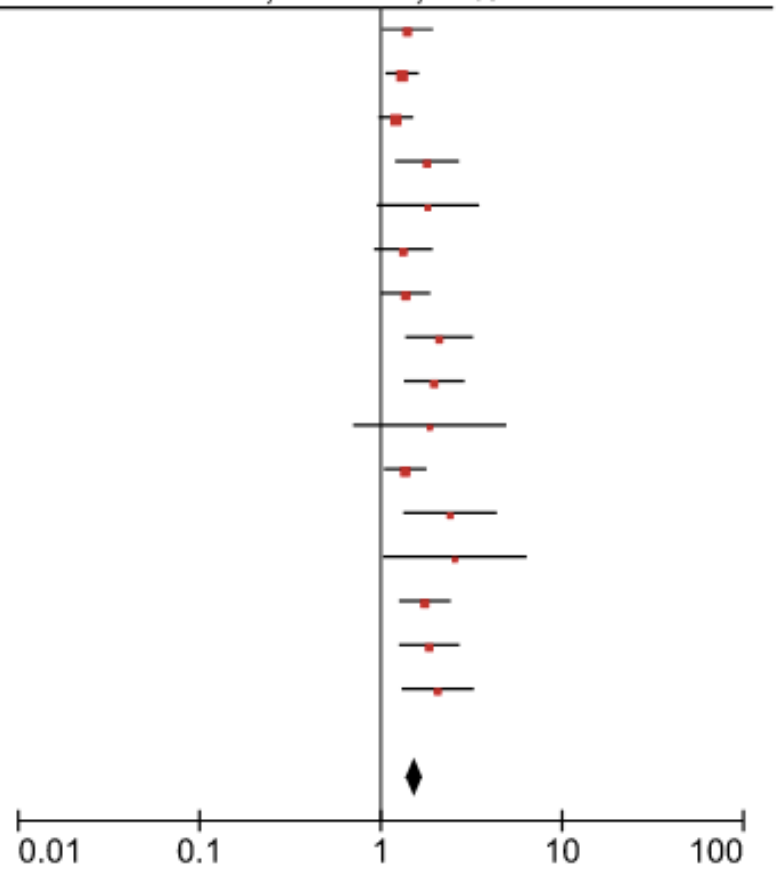
Sarah Rayfield and Emma Plugge

J Epidemiol Community Health 2017;**71**:162–173.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Al Mamum 2006 (Australia)	0.3365	0.1666	7.7%	1.40 [1.01, 1.94]
Chen 2006 (USA) Female	0.27	0.108	13.2%	1.31 [1.06, 1.62]
Chen 2006 (USA) Male	0.1906	0.113	12.6%	1.21 [0.97, 1.51]
Dubois 2006 (Canada)	0.5878	0.2069	5.5%	1.80 [1.20, 2.70]
Gorog 2011 (Europe)	0.5988	0.3317	2.4%	1.82 [0.95, 3.49]
Harris 2013 (USA)	0.2852	0.19	6.3%	1.33 [0.92, 1.93]
Kleiser 2009 (Germany)	0.3148	0.1606	8.1%	1.37 [1.00, 1.88]
Mangrio 2010 (Sweden)	0.7419	0.2197	5.0%	2.10 [1.37, 3.23]
Messiah 2012 (USA)	0.678	0.1966	6.0%	1.97 [1.34, 2.90]
Olson 2009 (USA)	0.6217	0.497	1.1%	1.86 [0.70, 4.93]
Salsberry 2007 (USA)	0.3097	0.138	9.9%	1.36 [1.04, 1.79]
Shi 2013 (Canada)	0.8796	0.3033	2.9%	2.41 [1.33, 4.37]
Suzuki 2009 (Japan)	0.94	0.4659	1.3%	2.56 [1.03, 6.38]
Toschke 2007 (Germany)	0.5596	0.1675	7.6%	1.75 [1.26, 2.43]
Von Kries 1999 (Germany)	0.6152	0.196	6.0%	1.85 [1.26, 2.72]
Von Kries 2002 (Germany)	0.7227	0.2342	4.5%	2.06 [1.30, 3.26]
Total (95% CI)			**100.0%**	**1.55 [1.40, 1.73]**

Heterogeneity: Tau² = 0.01; Chi² = 19.71, df = 15 (P = 0.18); I² = 24%

Test for overall effect: Z = 8.13 (P < 0.00001)



Pooled adjusted OR for maternal prenatal smoking and childhood obesity

Maternal smoking status before and during pregnancy and bronchial asthma at 3 years of age: a prospective cohort study

Sci Rep. 2023; 13: 3234.
PMID: 36828882

Kunio Miyake[1], Megumi Kushima[2], Ryoji Shinohara[2], Sayaka Horiuchi[2], Sanae Otawa[2], Yuka Akiyama[1], Tadao Ooka[1], Reiji Kojima[1], Hiroshi Yokomichi[1], Zentaro Yamagata[1,2] & The Japan Environment and Children's Study Group*

Prospective Japanese birth cohort study (no recall bias)
Self-administered questionnaires during pregnancy, at 1.5 years and 3 years of age
"Diagnosed with bronchial asthma by a doctor after the age of 2 years"
56,212 birthing parent-child dyads included without secondhand smoke exposure after birth

Maternal smoking status before and during pregnancy and bronchial asthma at 3 years of age: a prospective cohort study

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Adjusted for partner's smoking status before birth, frequency of second-hand smoke exposure during pregnancy, maternal history of bronchial asthma, maternal age at birth, pre-pregnancy body mass index, maternal educational level, child's sex, gestational age at birth, mode of delivery, childcare attendance at1 year of age, breastfeeding at 1 year of age, and older siblings.

N= 56,212 kids with no SHS exposure after birth	cOR (95% CI)	aOR (95% CI)
Maternal smoking status before birth		
Never	1.00	1.00
Quit before recognising current pregnancy	1.17 (1.08–1.26)	1.12 (1.03–1.22)
Quit after finding out current pregnancy	1.25 (1.12–1.39)	1.15 (1.02–1.30)
Still smoke (during pregnancy, but no SHS exposure after birth)	1.93 (1.60–2.32)	1.40 (1.12–1.74)

Sci Rep. 2023; 13: 3234.
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Maternal Smoking During Pregnancy and ADHD: Results From a Systematic Review and Meta-Analysis of Prospective Cohort Studies

Yan He[1], Jian Chen[1], Li-Hua Zhu[1], Ling-Ling Hua[1], and Fang-Fang Ke[1]

Journal of Attention Disorders
2020, Vol. 24(12) 1637–1647

12 prospective cohort studies (no recall bias)
17,034 pregnant individuals included

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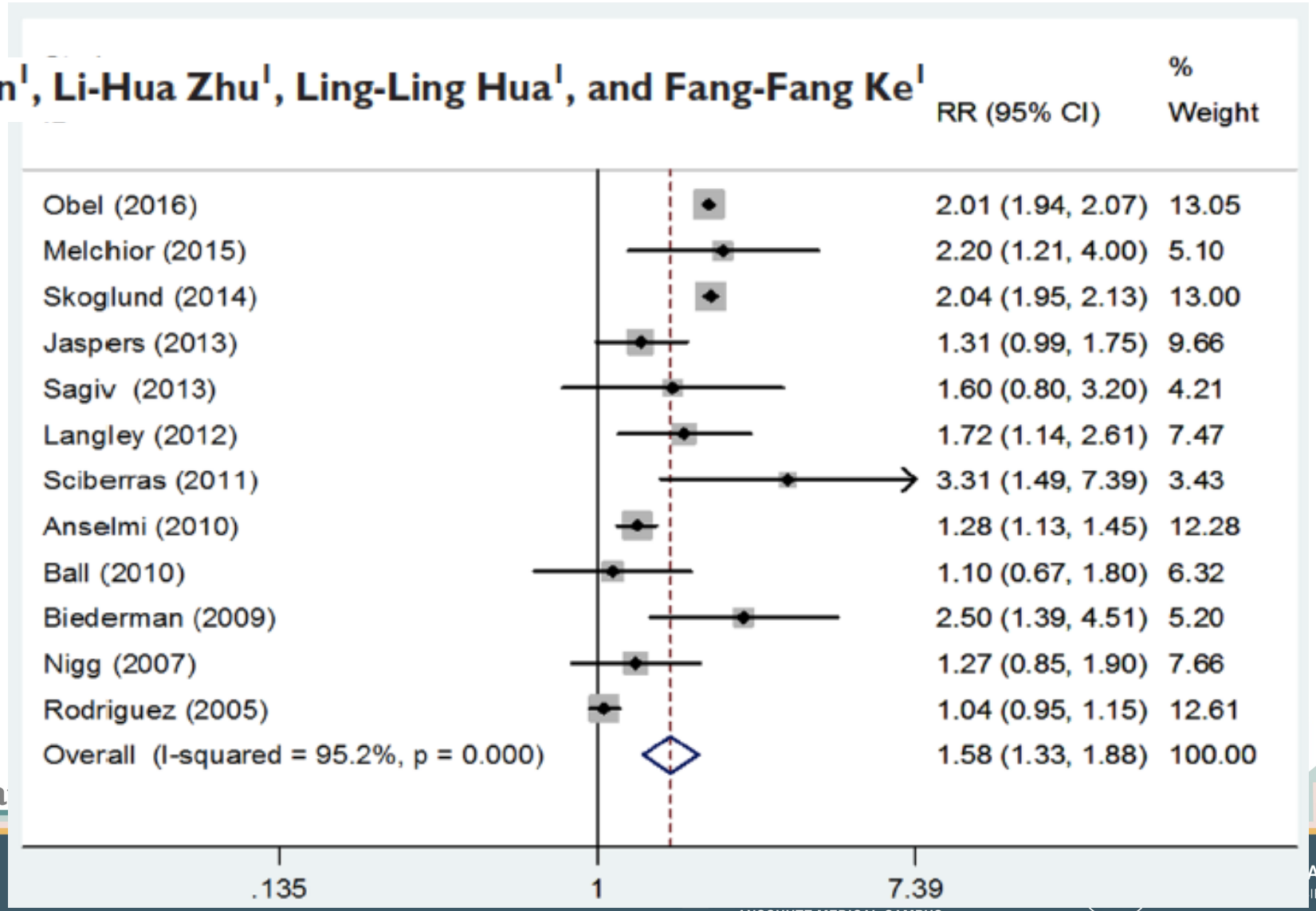
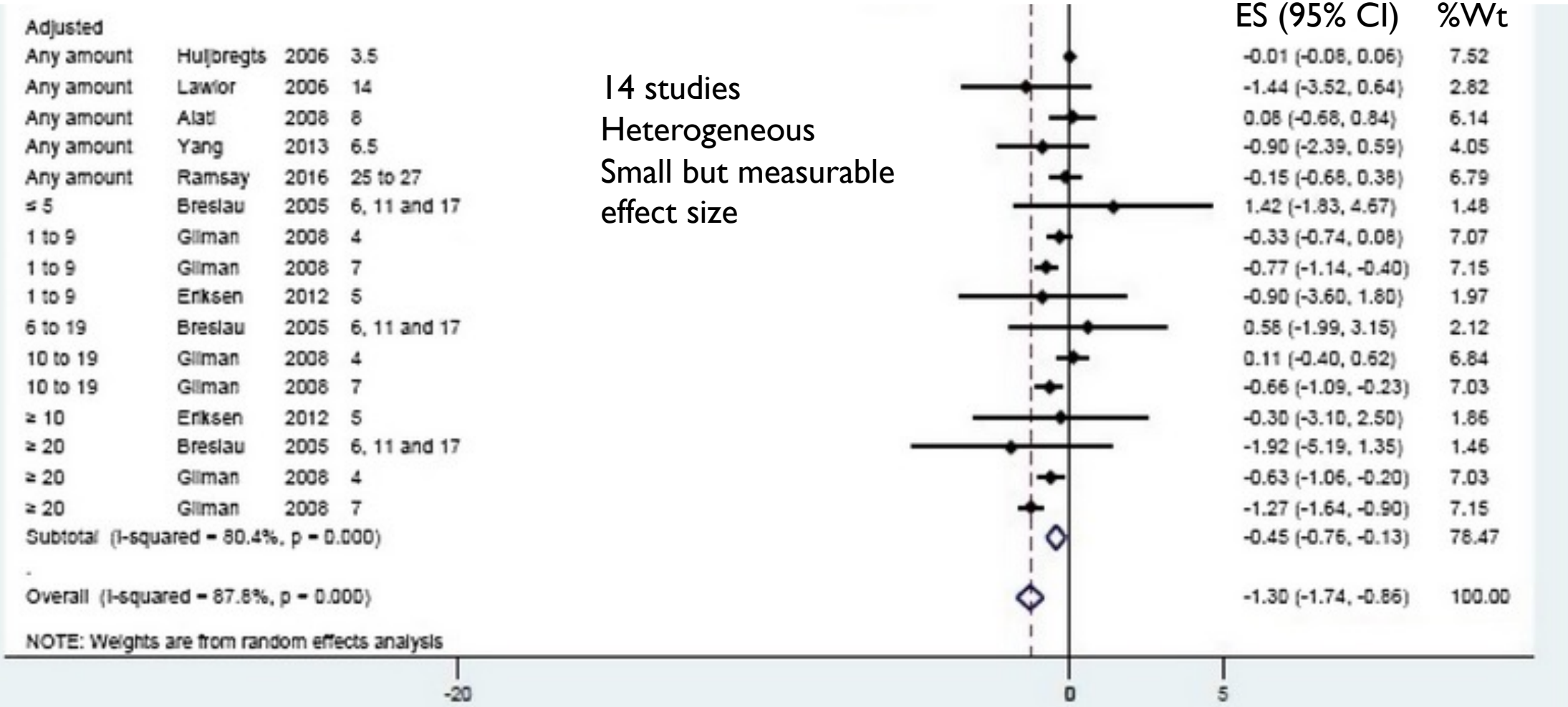


Maternal smoking during pregnancy and intelligence quotient in offspring: A systematic review and meta-analysis

Neurotoxicology 85 (2021) 99–114

Mariana Lima Corrêa [a,b,*], Pedro San Martin Soares [a], Bruna Gonçalves Cordeiro da Silva [a], Fernando Wehrmeister [a], Bernardo Lessa Horta [a], Ana Maria Baptista Menezes [a]



14 studies
Heterogeneous
Small but measurable effect size

Maternal smoking during pregnancy and poor academic performance in adolescent offspring: A registry data-based cohort study

Addictive Behaviors 123 (2021) 107072

Getinet Ayano [a,b,*], Kim Betts [a], Berihun Assefa Dachew [a], Rosa Alati [a,c]

3 linked databases in NSW, Australia
National Assessment Program for Literacy and Numeracy (NAPLAN)
>168,000 participants

Table 2
Association between perinatal maternal smoking during pregnancy with offspring academic performance at year 9 (aged 14 years).

Academic performance domains	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
	Model		Mode 2		Model 3	
Reading below benchmark	2.93 (2.80–3.06)	0.001	2.50 (2.38–2.62)	0.001	2.49 (2.37–2.62)	0.001
Spelling below benchmark	3.56 (3.40–3.71)	0.001	3.10 (2.97–3.25)	0.001	3.12 (2.98–3.26)	0.001
Numeracy below benchmark	2.83 (2.67–2.98)	0.001	2.41 (2.28–2.54)	0.001	2.43 (2.30–2.58)	0.001
Writing below benchmark	3.33 (3.19–3.48)	0.001	2.91 (2.78–3.03)	0.001	2.97 (2.84–3.11)	0.001
Any domain below the benchmark	3.26 (3.16–3.37)	0.001	2.83 (2.74–2.94)	0.001	2.87 (2.74–2.99)	0.001

Key:
Model 1 was unadjusted model (crude model)
Model 2 adjusted for maternal factors such as sociodemographic confounding variables such as maternal age at birth, marital status, educational status education, and occupational status, and clinical factors such as maternal prenatal and perinatal psychiatric admissions, maternal diabetes, and chronic hypertension
Model 3 further adjustment for child-related potential confounding variables such as birth weight, sex, and language spoken at home in the above model (model 2)

Prenatal Tobacco Exposure and the Risk of Tobacco Smoking and Dependence in Offspring: a Systematic Review and Meta-Analysis

Drug and Alcohol Dependence 227 (2021) 108993

Bereket Duko [a,b,*], Gavin Pereira [a,c], Robert J. Tait [d], Sylvester Dodzi Nyadanu [a], Kim Betts [a], Rosa Alati [a,e]

27 studies included (26 cohort studies, 1 case control study)
9 countries

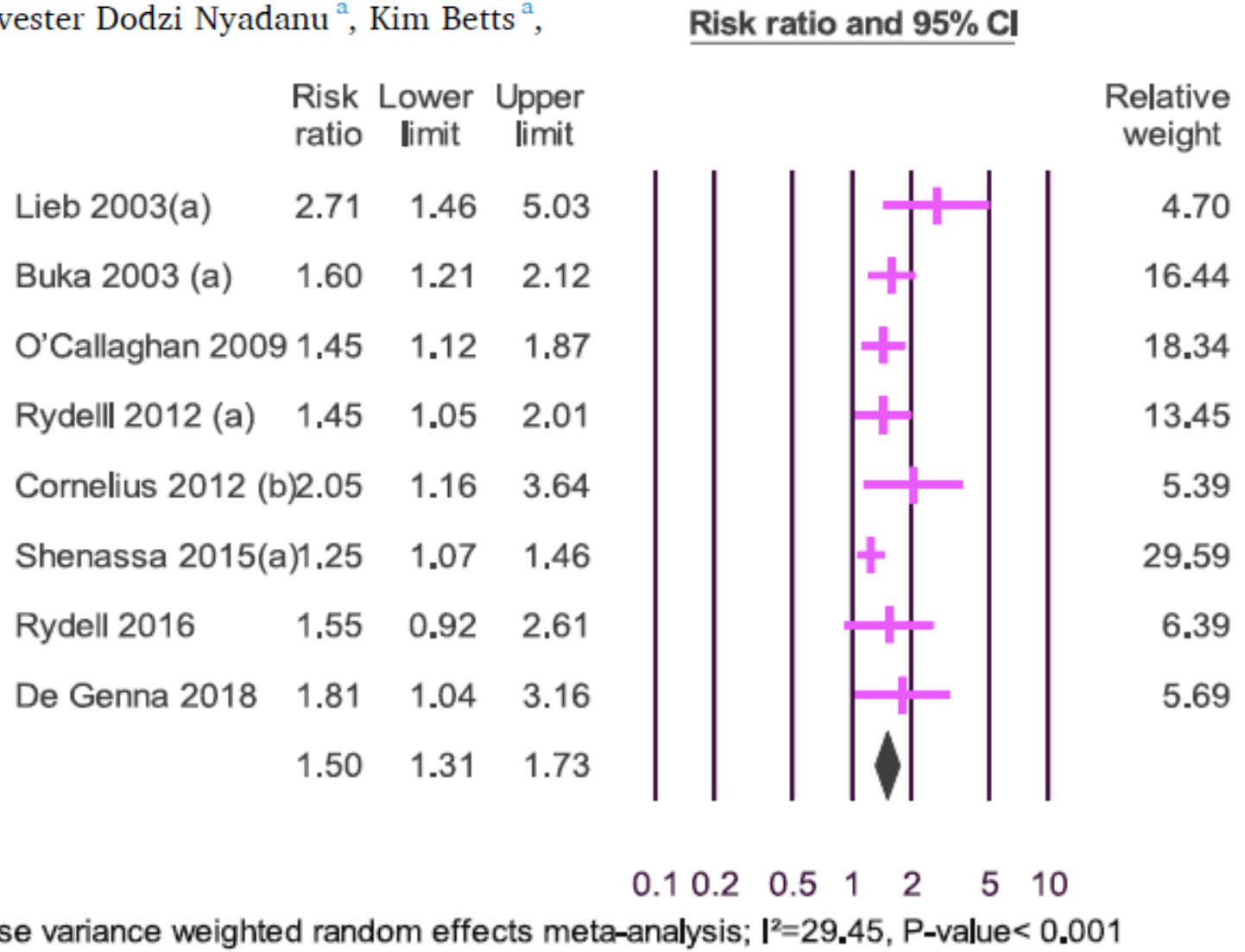


Fig. 3. The risk of tobacco dependence in offspring exposed to maternal prenatal tobacco smoking.

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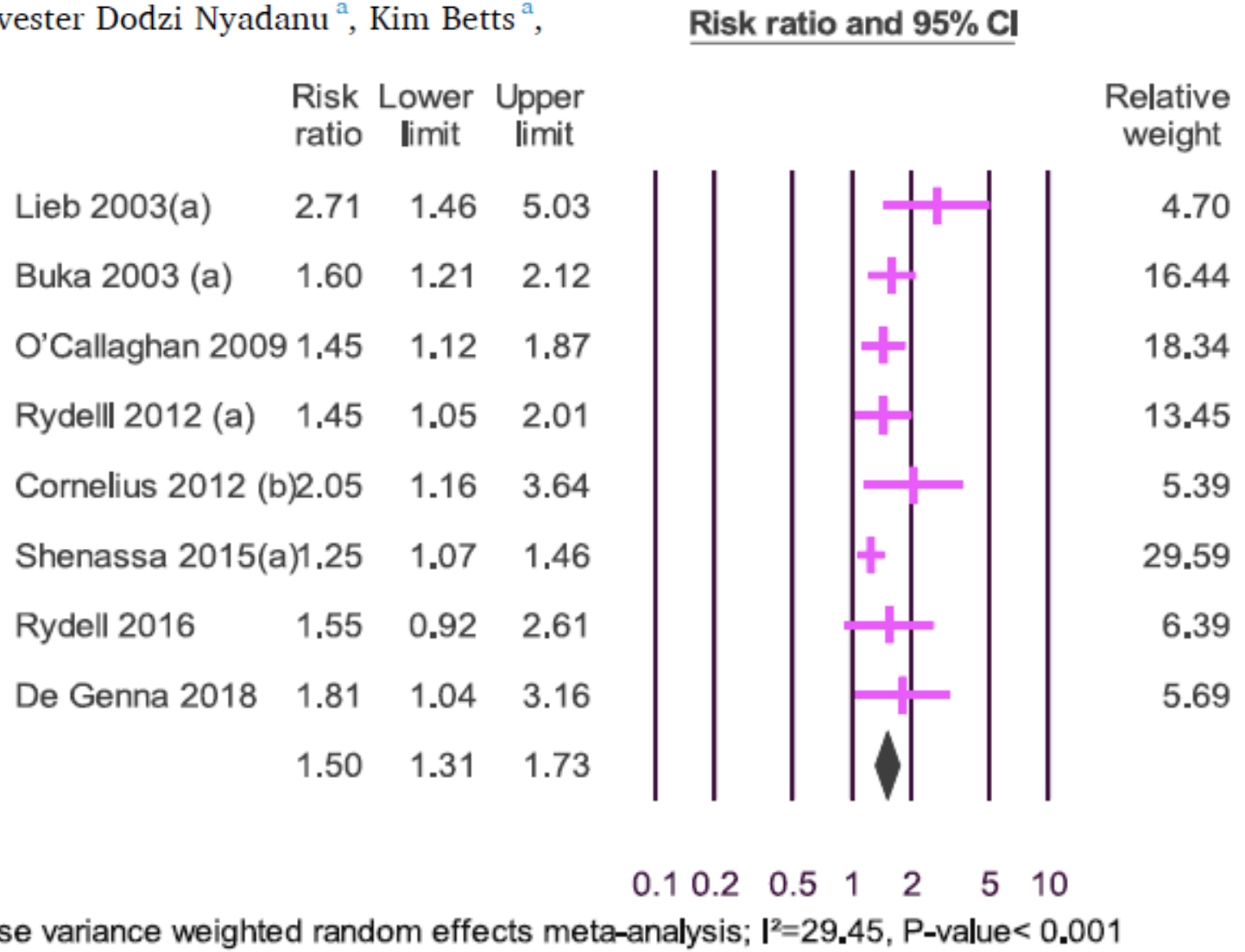
Also found significant increase in risk of:
- Current smoking [RR 1.70 (1.48, 1.95)
- Lifetime (ever) smoking [RR 1.21 (1.05, 1.38)
- Initiation/experimentation [RR 2.08 (1.18, 3.68)



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Also found significant increase in risk of:
- Current smoking [RR 1.70 (1.48, 1.95)
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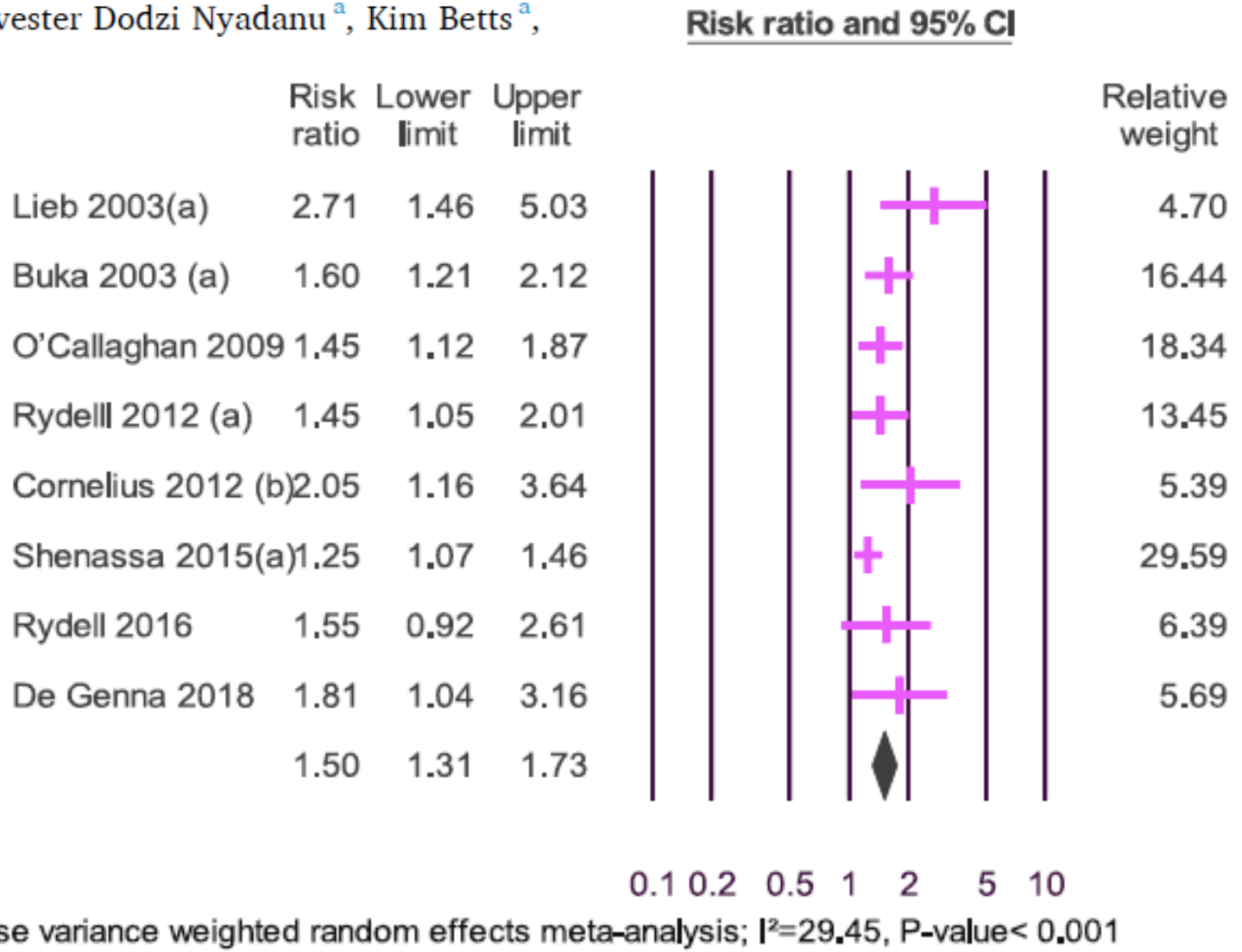
- Initiation/experimentation [RR 2.08 (1.18, 3.68)

Paternal smoking during pregnancy did NOT significantly increase risk of tobacco smoking in exposed offspring [RR 1.39 (0.93, 2.08)



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Nicotine and increased risk of cancer??

- "Maternal smoking during pregnancy is associated with increased long-term risk for benign but not malignant tumors….Despite this large population study with long follow-up, childhood malignancies are rare, and clarifying the possible association may require further studies." PMID 30513488

Nicotine and increased risk of cancer??

- "Maternal smoking during pregnancy is associated with increased long-term risk for benign but not malignant tumors….Despite this large population study with long follow-up, childhood malignancies are rare, and clarifying the possible association may require further studies." PMID 30513488
- "The summary odds ratio (OR) of childhood ALL associated with paternal smoking was 1.11 (95% Confidence Interval (CI): 1.05-1.18, I(2) = 18%) during any time period, 1.25 (95% CI: 1.08-1.46, I(2) = 53%) preconception; 1.24 (95% CI: 1.07-1.43, I(2) = 54%) during pregnancy, and 1.24 (95% CI: 0.96-1.60, I(2) = 64%) after birth" PMID 21765828

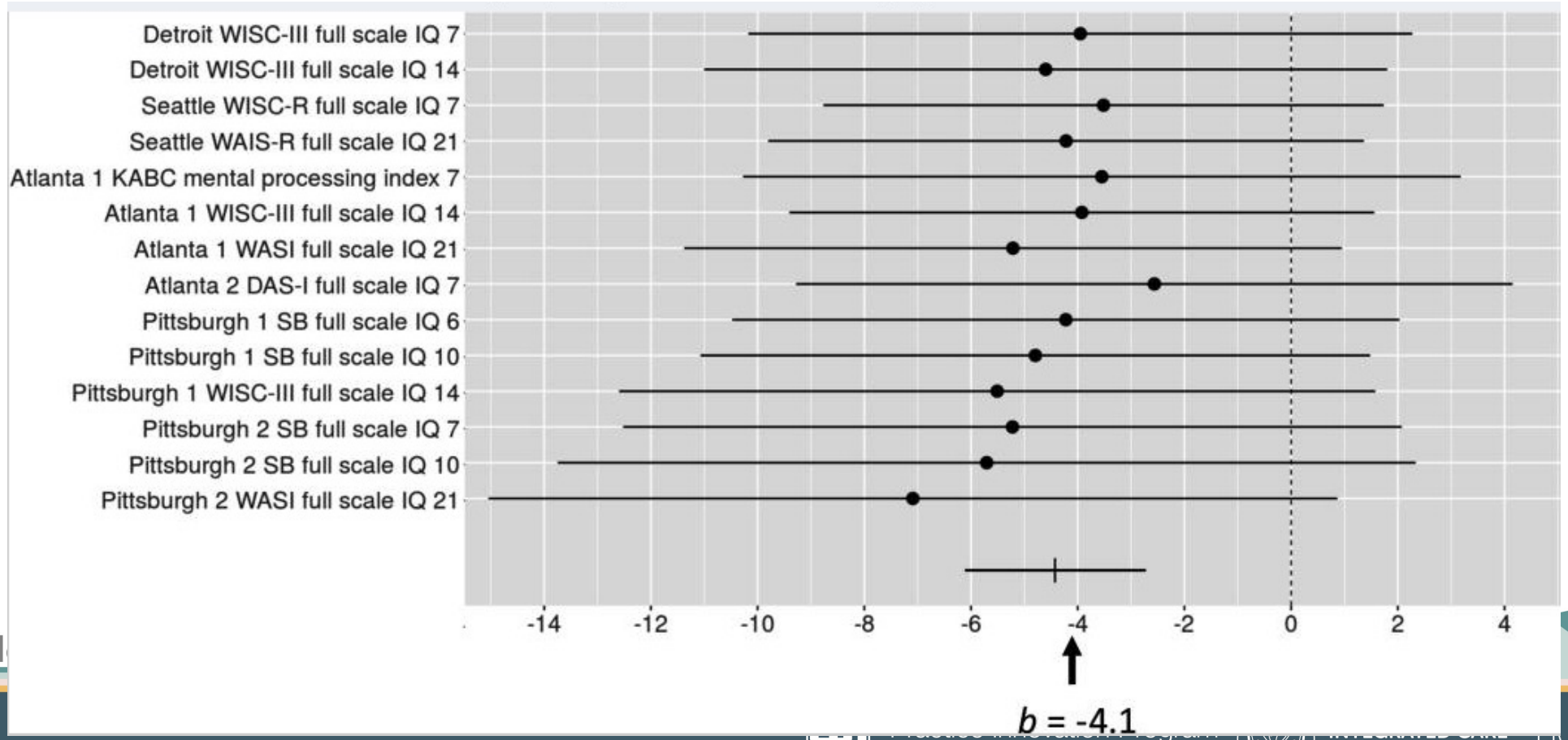
Alcohol

- Cognitive impairment (lower IQ)
- Specific cognitive skills may be impaired (e.g., fluency) even if global cognitive function (IQ) is within normal limits
- Difficulty with adaptive skills, social skills
- Increased risk of ADHD, ODD, depression, and other psychiatric comorbidities
- Increased risk of alcohol use disorder

Effects of prenatal alcohol exposure on cognitive and behavioral development: Findings from a hierarchical meta-analysis of data from six prospective longitudinal U.S. cohorts

Alcohol Clin Exp Res. 2021 Oct; 45(10): 2040–2058.

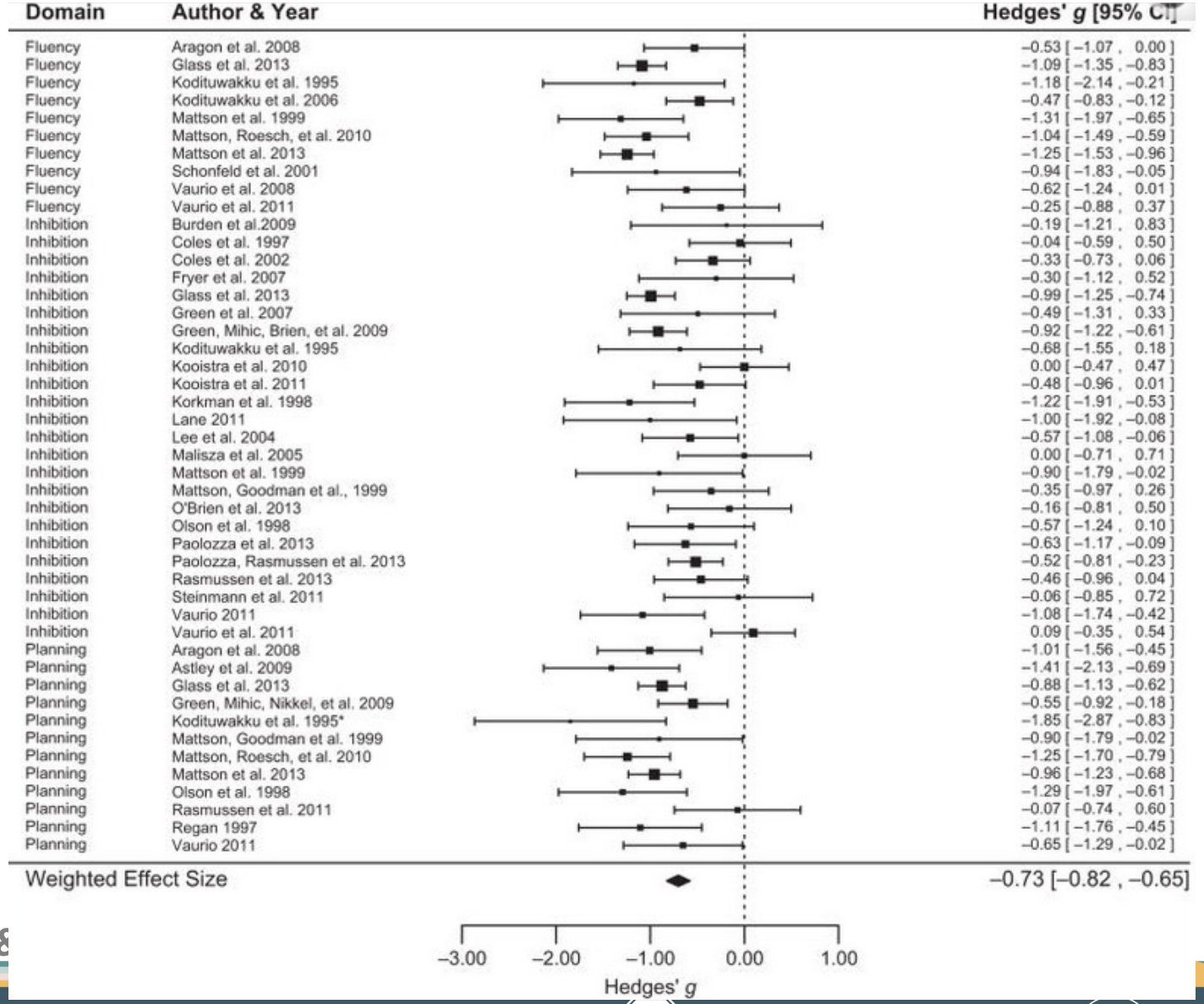
Joseph L. Jacobson,[1] Tugba Akkaya-Hocagil,[2] Louise M. Ryan,[3,4] Neil C. Dodge,[1] Gale A. Richardson,[5] Heather Carmichael Olson,[6] Claire D. Coles,[7] Nancy L. Day,[5] Richard J. Cook,[2] and Sandra W. Jacobson[1]



Research Review: Executive function deficits in fetal alcohol spectrum disorders and attention-deficit/hyperactivity disorder – a meta-analysis

J Child Psychol Psychiatry. 2016 Feb; 57(2): 116–131.

Danielle Kingdon, Christopher Cardoso, and Jennifer J. McGrath



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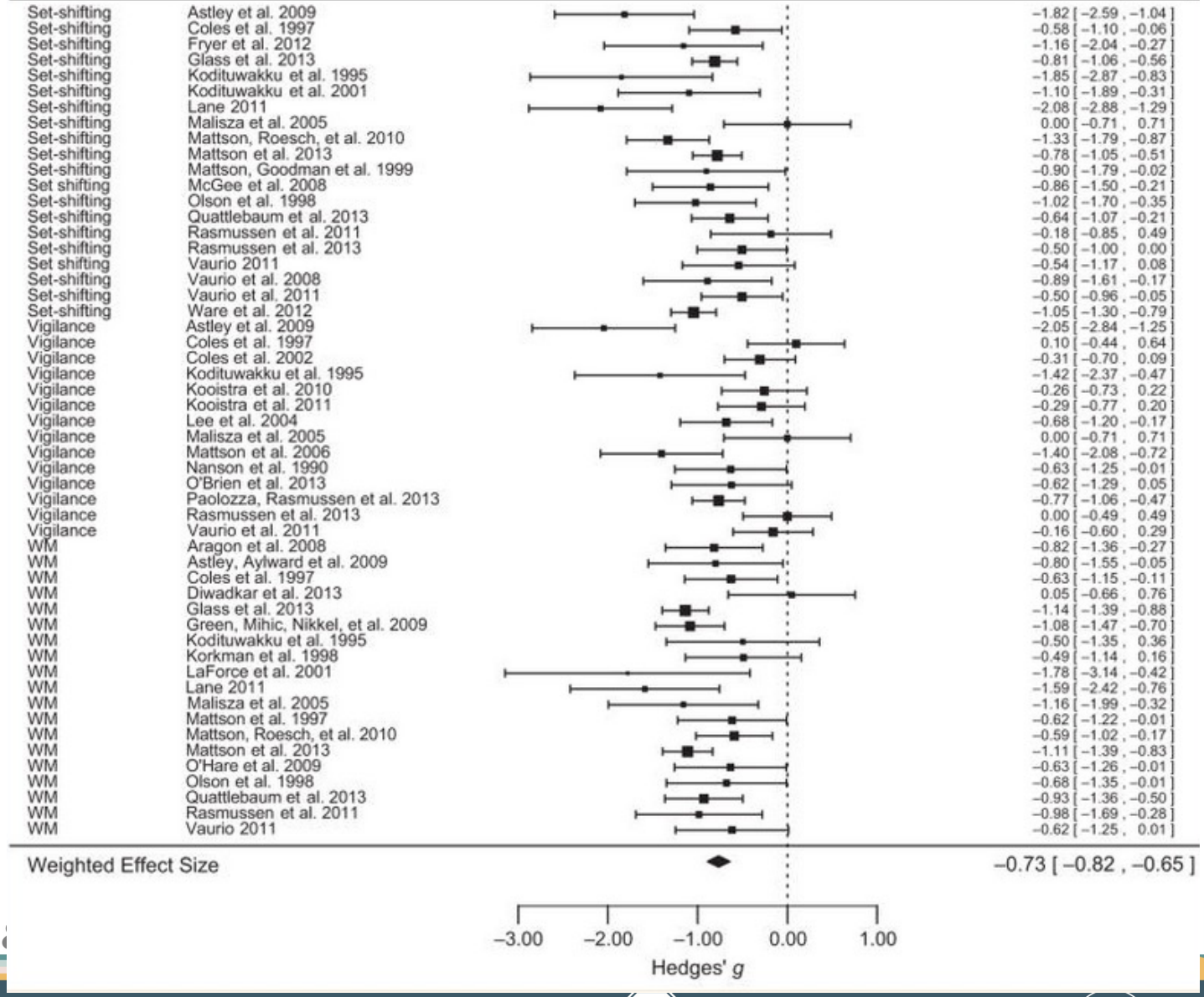


Relation Between Adaptive Function and IQ Among Youth with Histories of Heavy Prenatal Alcohol Exposure

Birth Defects Res. 2019 Jul 15; 111(12): 812–821.

Lauren R. Doyle,[a] Claire D. Coles,[b,c] Julie A. Kable,[c] Philip A. May,[d,e] Elizabeth R. Sowell,[f] Kenneth L. Jones,[g] Edward P. Riley,[a] Sarah N. Mattson,[a] and CIFASD

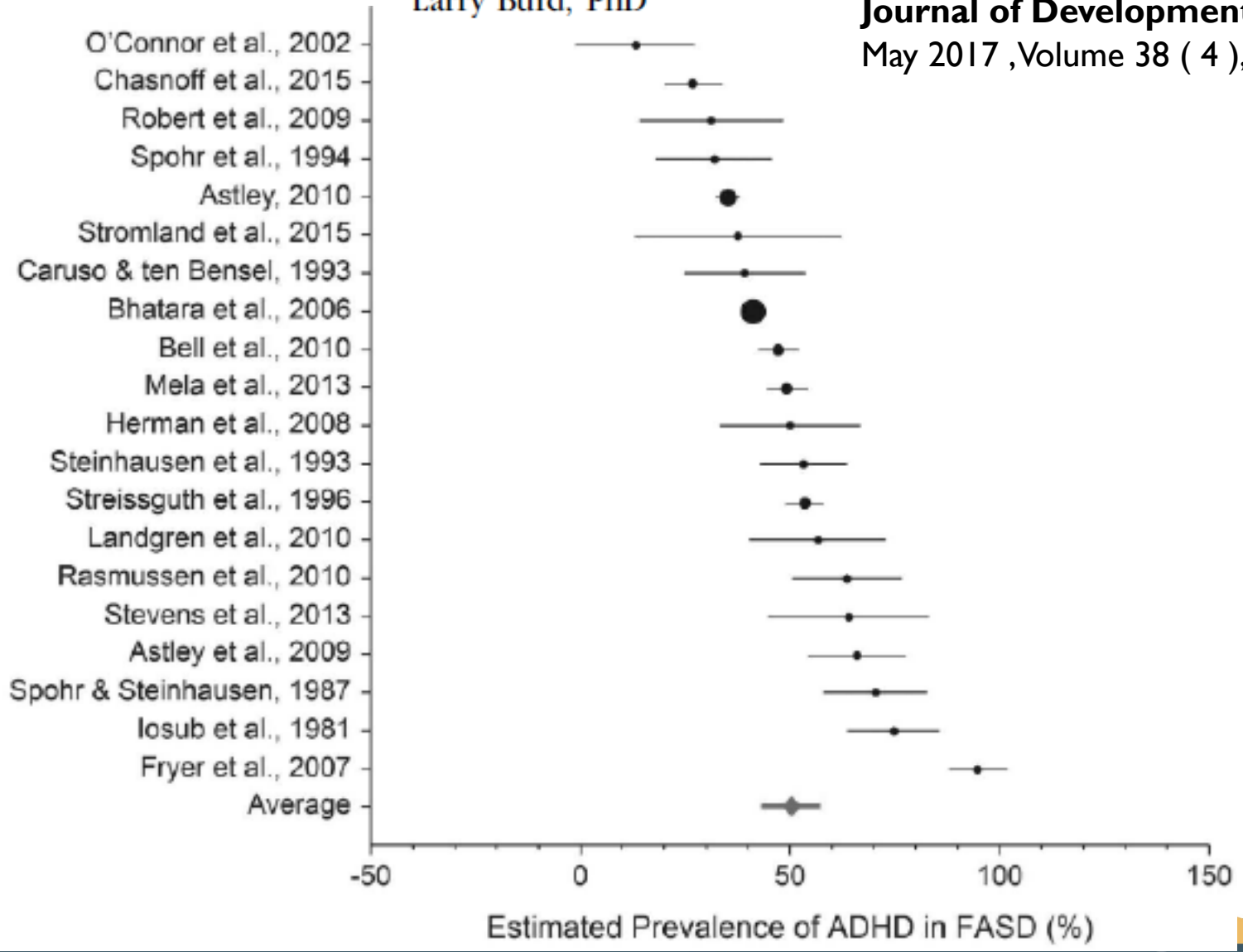
- N=437 (AE=163, CON=274) participants ages 8-16
- "Within the high IQ range, the correlation between FSIQ and Communication was significant in the CON group (r = .445; p < .001) but not in the AE group (r = −.005; p = .963) and average Communication scores were significantly higher (p = .018) in the CON group (M = 106.67) than the AE group (M = 92.26)."
- "Although higher intellectual functioning was associated with better adaptive function ability among controls, this was not found among the alcohol-exposed youth where a general dampening of adaptive ability was noted. Further, the differential relationship between IQ and adaptive function between groups appears to be driven by communication abilities."

Comorbid Mental Disorders in Fetal Alcohol Spectrum Disorders: A Systematic Review

Deland Weyrauch, BA, Megan Schwartz, BS, Brandon Hart, BS, Marilyn G. Klug, PhD, Larry Burd, PhD

Journal of Developmental & Behavioral Pediatrics
May 2017 ,Volume 38 (4), p 283 – 291

26 articles in total
5984 FASD cases



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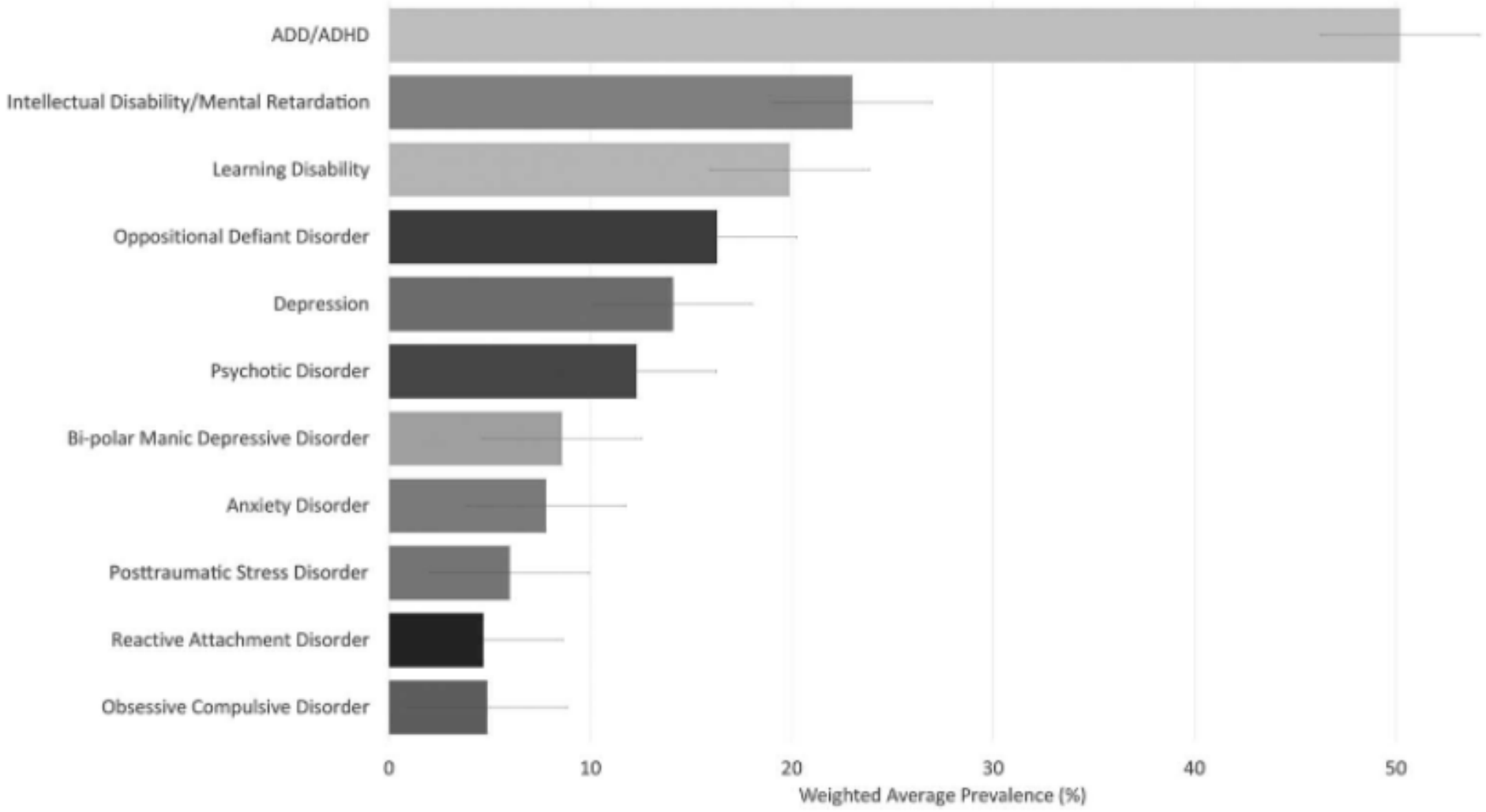

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Comorbidity	Weighted Prevalence from Studies: Average ( )	SE	LL	UL	Population Prevalence ( )	Difference ( )	Ratio	Z	
ADHD	50.2	3.5	43.4	57.1	5.0	45.2	10.0	12.947	.001
ID	23.0	3.8	15.6	30.3	1.0	22.0	23.0	5.821	.001
Learning disorder	19.9	4.2	11.6	28.2	10.0	9.9	2.0	2.337	.010
Oppositional defiant disorder	16.3	2.2	11.9	20.6	3.3	13.0	4.9	5.827	.001
Depression	14.1	3.7	6.9	21.3	3.5	10.6	4.0	2.893	.002
Psychotic Disorder	12.3	3.9	4.7	19.8	0.5	11.8	24.5	3.052	.001
Bipolar Disorder	8.6	3.4	2.0	15.2	2.7	5.9	3.2	1.765	.039
Anxiety disorder	7.8	2.0	3.9	11.8	0.7	7.1	11.2	3.527	.001
PTSD	6.0	1.0	4.0	8.0	4.0	2.0	1.5	1.919	.027
Obsessive compulsive disorder	4.9	3.0	−1.1	10.9	1.2	3.7	4.1	1.212	.113
Reactive attachment disorder	4.7	0.8	3.1	6.3	0.5	4.2	9.3	5.154	.001

In Utero Alcohol Exposure and Prediction of Alcohol Disorders in Early Adulthood

A Birth Cohort Study

Arch Gen Psychiatry. 2006;63:1009-1016

Rosa Alati, PhD; Abdullah Al Mamun, PhD; Gail M. Williams, PhD; Michael O'Callaghan, MD; Jake Moses Najman, PhD; William Bor, MD

Table 4. Multivariable Associations Between Maternal Alcohol Use Over Time and Onset of Alcohol Disorders at Age 21 Years*

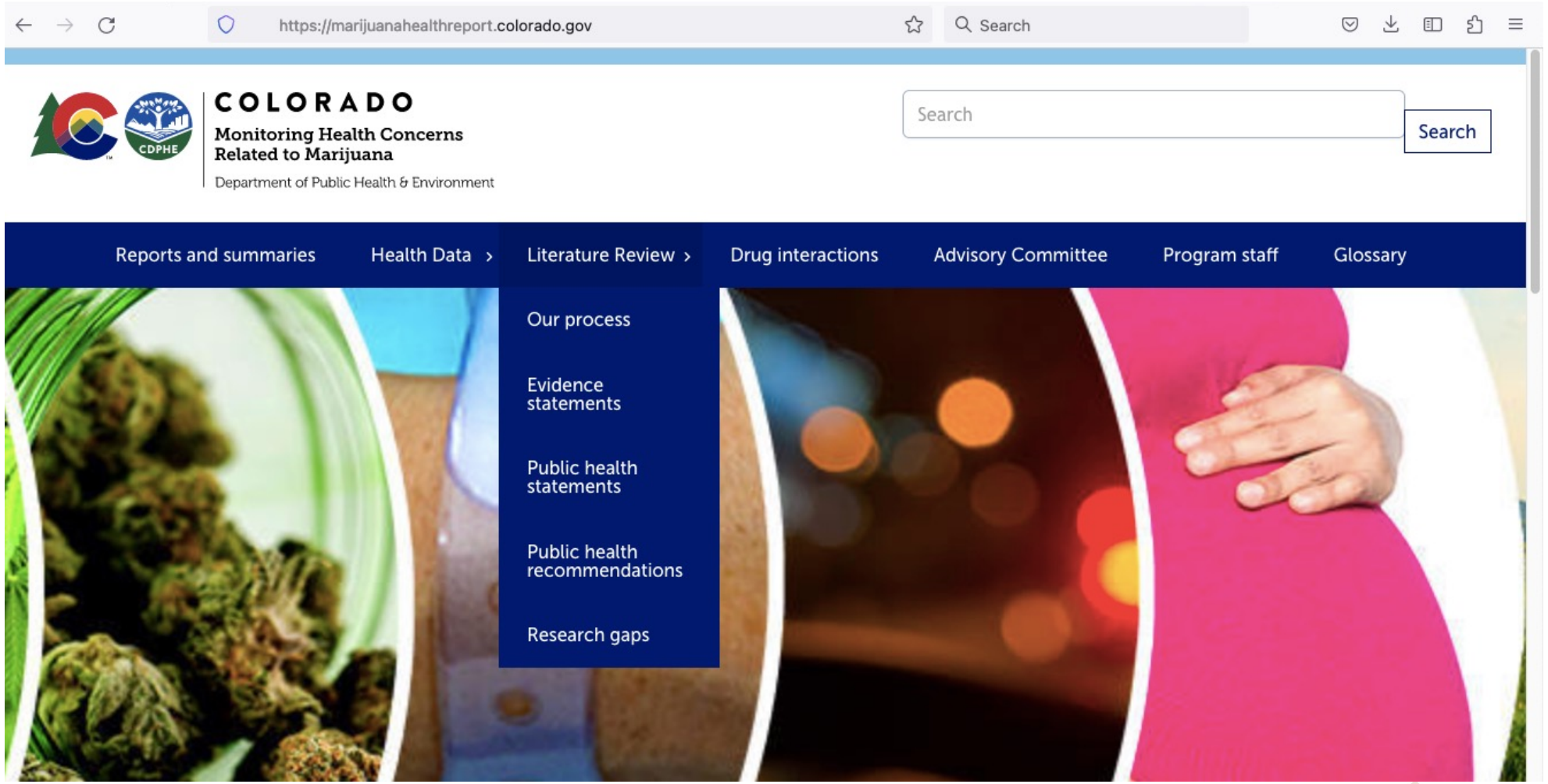
	% Reporting	Early Onset			Late Onset		
		Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Maternal alcohol use over time†							
≤2 Glasses	50.0	1	1	1	1	1	1
≥3 Glasses in early pregnancy	3.8	3.93 (2.21-6.97)	3.04 (1.68-5.50)	2.95 (1.62-5.36)	3.37 (1.80-6.28)	3.37 (1.78-6.37)	3.29 (1.74-6.24)
≥3 Glasses in late pregnancy	3.9	1.78 (0.93-3.41)	1.42 (0.73-2.75)	1.35 (0.69-2.63)	1.86 (0.95-3.62)	1.70 (0.86-3.38)	1.67 (0.84-3.31)
≥3 Glasses during both pregnancy periods	1.7	3.45 (1.50-7.95)	2.40 (0.91-6.34)	2.49 (1.06-5.85)	2.60 (1.00-6.74)	2.46 (0.93-6.53)	2.43 (0.91-6.44)
≥3 Glasses but not during pregnancy	40.7	1.20 (0.90-1.60)	0.94 (0.68-1.28)	0.94 (0.68-1.28)	1.57 (1.17-2.09)	1.55 (1.13-2.10)	1.52 (1.12-2.07)

*Of the 2555 offspring who completed the Composite International Diagnostic Interview–computerized version at age 21 years, 333 (13.0%) met *DSM-IV* criteria for early onset of an alcohol disorder (onset between ages 13 and 17 years) and 307 (12.0%) for late onset (onset between ages 18 and 21 years); 1915 (75.0%) met no criteria for a disorder. Data are expressed as odds ratio (95% confidence interval) unless otherwise indicated. Model 1 is adjusted for sex; model 2, for sex, smoking over time, birth weight, gestational age, maternal education, age, and marital status at the antenatal visit; and model 3, all items adjusted for in model 2 plus maternal anxiety at the 5-year follow-up and maternal depression and child behavior at the 14-year follow-up. The fully adjusted analysis was conducted on 2138 participants with complete data at all phases.

†No specific quantity of alcohol was mentioned in the questionnaire, but current guidelines estimate approximately 10 g per standard drink.

Cannabis

- Increased risk of attention problems, reduced cognitive function and reduced academic performance
- Challenges with executive function
- Earlier initiation of cannabis use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Advisory Committee
Program staff
Glossary
Our process
Evidence statements
Public health statements
Public health recommendations
Research gaps

Evidence statements

Cannabis evidence statements
Adolescents and young adults

COLORADO
Monitoring Health Concerns Related to Marijuana
Department of Public Health & Environment

The relationships between adolescent and young adult marijuana use and cognitive abilities, academic performance, mental health, and future substance use.

Findings

Adolescents and young adults who use marijuana are more likely to experience psychotic symptoms as adults (such as hallucinations, paranoia, and delusional beliefs), future psychotic disorders (such as schizophrenia) and suicidal thoughts or attempting suicide. Evidence shows that adolescents who use marijuana are more likely to not graduate high school or attain a college degree, can become addicted to marijuana, and that treatment for marijuana addiction can decrease use and dependence.

Research recommendations

Promote and develop public education for adolescents, young adults, parents and caregivers, using optimal methods including social media. Focus should be on accurate information regarding cannabis use disorder and treatment for it, as well as the risk of developing future mental health symptoms and disorders, especially when using high THC concentration products. It is important to improve data quality by systematically collecting information on the frequency, amount, THC content, and method of marijuana use/consumption in both public health surveillance and medical care settings.

Select health topic

- Adolescents & Young Adults
- Cancer
- Cardiovascular
- Dose and Drug Interactions
- Driving
- Gastrointestinal & Reproductive
- Injury
- Neurological, Cognitive & Mental Health
- Pregnancy & Breastfeeding
- Respiratory Effects
- Unintentional Exposures in Children

Evidence statements

Benefits of quitting	We found SUBSTANTIAL evidence that some adolescent and young adult marijuana users who receive treatment for cannabis use disorder (including cognitive behavioral therapy, motivational enhancement/interviewing, multidimensional family therapy, abstinence-based contingency management, and/or computerized interventions) can decrease their marijuana use and dependence

Effects of prenatal marijuana use on exposed offspring	We found MODERATE evidence that maternal marijuana use during pregnancy is associated with decreased academic ability of exposed offspring	
	We found MODERATE evidence that maternal use of marijuana during pregnancy is associated with attention problems in exposed offspring.	
	We found MODERATE evidence that maternal use of marijuana during pregnancy is associated with reduced cognitive function in exposed offspring	
	We found LIMITED evidence that maternal use of marijuana during pregnancy is associated with decreased growth in exposed offspring.	
	We found LIMITED evidence that maternal marijuana use during pregnancy is associated with behavior problems in exposed offspring.	
	We found MODERATE evidence that maternal use of marijuana during pregnancy is associated with decreased IQ scores in exposed offspring.	
	We found MIXED evidence for whether or not maternal use of marijuana during pregnancy is associated with newborn behavior issues.	
	We found a LIMITED body of research that failed to show association between maternal use of cannabis during and after pregnancy and SIDS.	
Mental health and substance use	We found LIMITED evidence that maternal use of marijuana during pregnancy is associated with increased depression symptoms in exposed offspring	

Substantial | Moderate | Limited | Mixed | Insufficient | Biological evidence | Case report/series | Drug interaction study

https://marijuanahealthreport.colorado.gov/literature-review/evidence-statements

marijuana health report colorado

4 scientific articles reviewed and rated

Found Association

3
Medium Quality

1
Low Quality

The following articles were reviewed, rated, and included in developing this statement.

Betts, K. S., et al., 2021, Prenatal cannabis use disorders and offspring primary and secondary educational outcomes

Fried, P. A., 1997, Reading and language in 9- to 12-year olds prenatally exposed to cigarettes and marijuana

Goldschmidt, L., 2004, Prenatal marijuana and alcohol exposure and academic achievement at age 10

Goldschmidt, L., 2012, School achievement in 14-year-old youths prenatally exposed to marijuana

Article review: None

None

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marijuana health report colorado

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Article review: Medium Quality

Betts, K. S., et al., 2021, Prenatal cannabis use disorders and offspring primary and secondary educational outcomes

Findings

- Prenatal cannabis use disorder was found to be associated with offspring not meeting national academic standards in spelling (OR 1.35; 95% CI 1.07 - 1.70), grammar (OR 1.40; 95% CI 1.17
- Prior to matching cases with controls, prenatal CUD exposure in offspring was associated to not meeting the national academic standards across all domains, reading, spelling, grammar, writing, and numeracy.
- "Our study clearly demonstrates that much of the observed association between prenatal CUD and offspring education performance is dependent upon comorbidities and socio-economic factors."

Strengths

- Controlled for many confounding factors; socioeconomic status, type of school, language background of student, maternal age at birth, number of previous pregnancies, prenatal smoking status, gestational diabetes, pre-existing diabetes, gestational hypertension, pre-existing hypertension, delivery method, resuscitation, and need for intensive care
- Educational outcomes measured at 3 times-points from early primary school to early high school
- Large sample size (N = 189,558)

Limitations

- Relied on ICD-10 codes to determine cannabis use disorder in mothers, providing no details about maternal cannabis use pattern (timing of use during pregnancy, frequency, type of product, amount used, etc)
- Outcome measures represent an extreme measure of educational outcome
- Findings only generalizable to mothers with cannabis use disorder diagnosis

Characteristics Associated With Cannabis Use Initiation by Late Childhood and Early Adolescence in the Adolescent Brain Cognitive Development (ABCD) Study

JAMA Pediatrics August 2023 Volume 177, Number 8

Alex P. Miller, PhD
David A. A. Baranger, PhD
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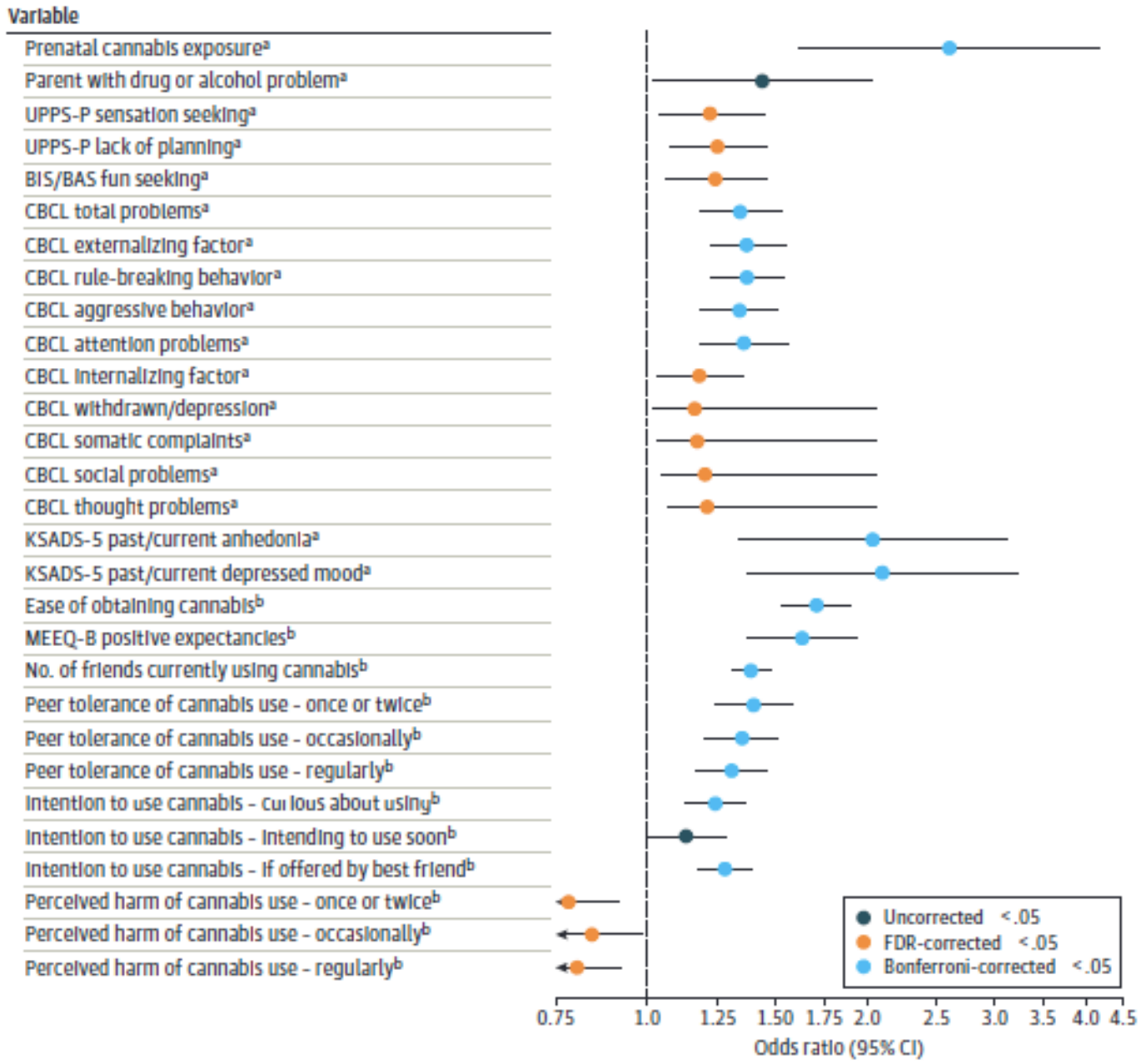
Alexander S. Hatoum, PhD
Cynthia Rogers, MD
Ryan Bogdan, PhD
Arpana Agrawal, PhD

Variables Associated With Cannabis Initiation as Children Enter Early Adolescence



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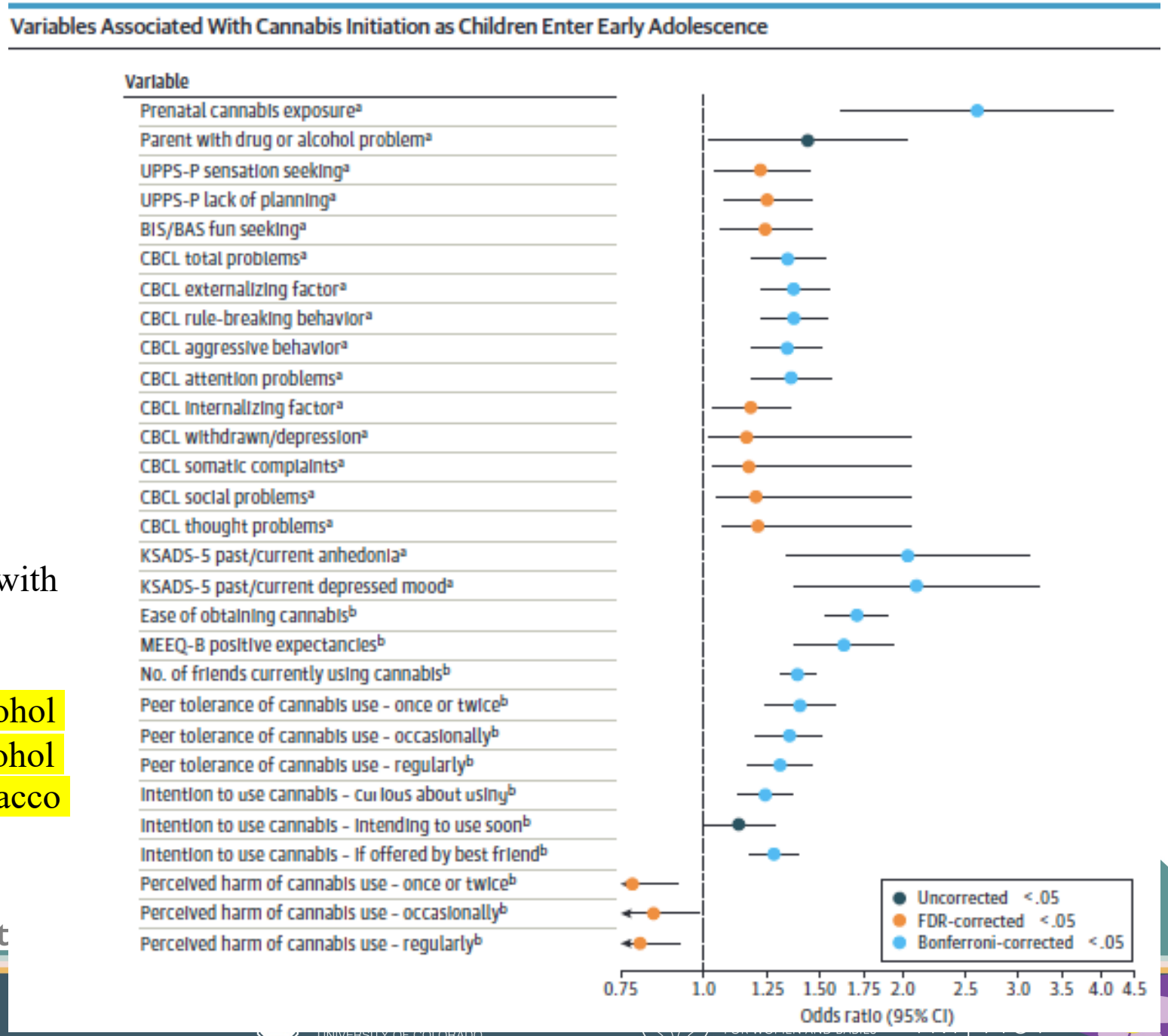
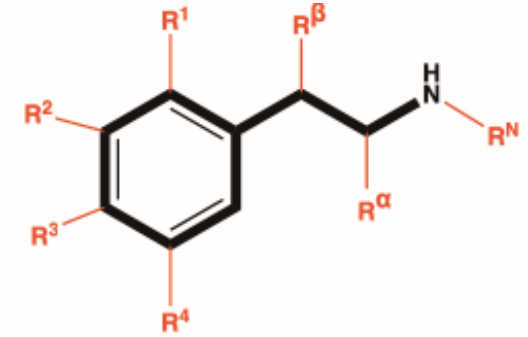
"…prenatal cannabis exposure was associated with the largest risk for cannabis use initiation (OR, 2.60; 95% CI, 1.62-4.17); this association remained when additionally controlling for alcohol and tobacco use initiation, family or parent alcohol or drug problems, and prenatal alcohol and tobacco exposure (OR, 2.16; 95% CI, 1.17-3.97)."

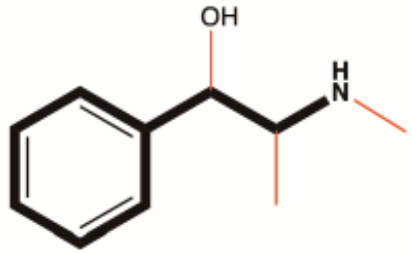


Amphetamines

- Are a large and heterogeneous class ☺



General structure of beta-phenylethylamine derivatives



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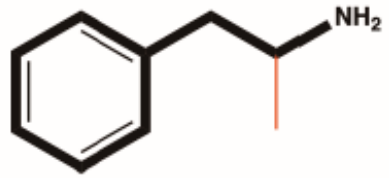
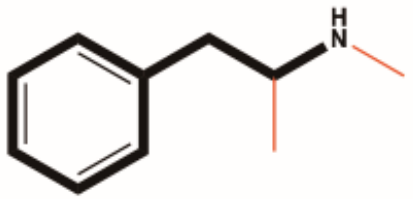
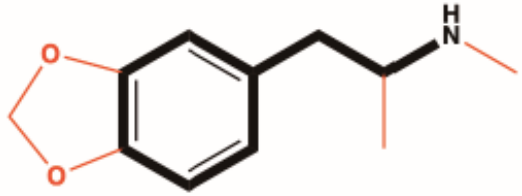


Amphetamine



Methamphetamine



MDMA

Jîtc ̆a, G.; ́Osz, B.E.; Tero-Vescan, A.; Vari, C.E. Psychoactive Drugs—From Chemical Structure to Oxidative Stress Related to Dopaminergic Neurotransmission. A Review. Antioxidants 2021, 10, 381.

Amphetamines

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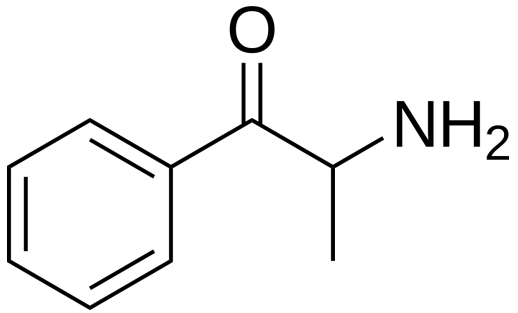
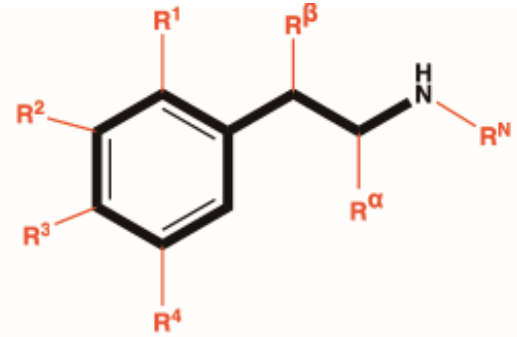
Cathinone structure ("bath salts")





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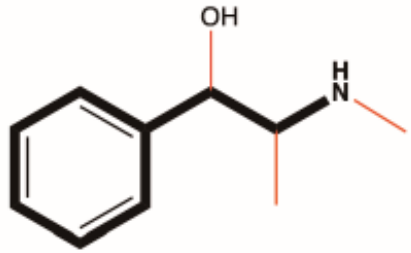

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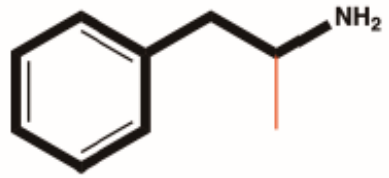

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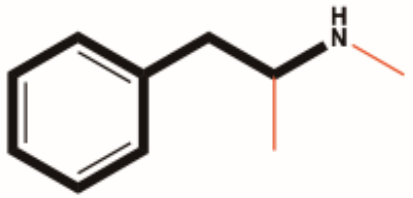

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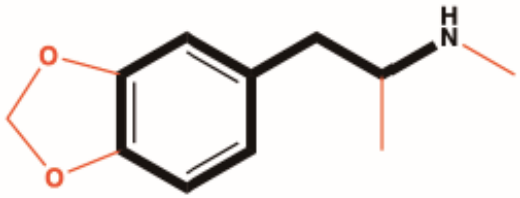

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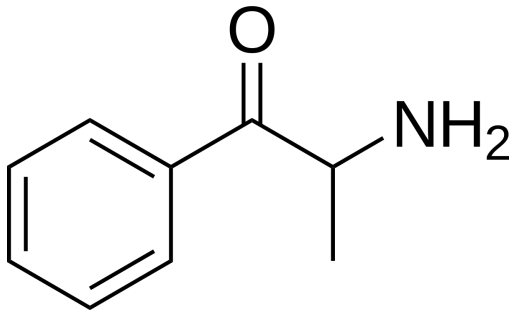
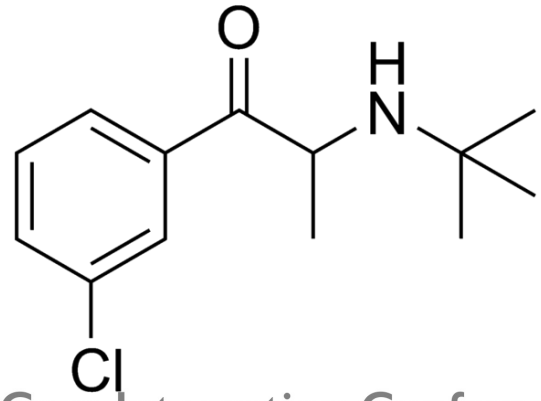
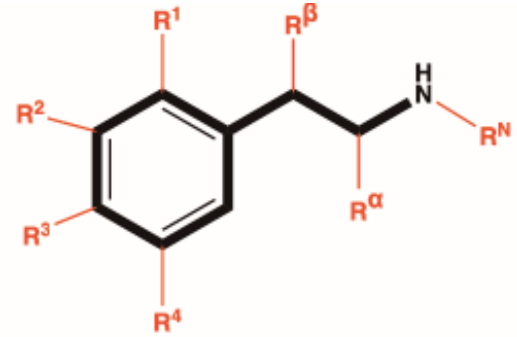


Bupropion structure





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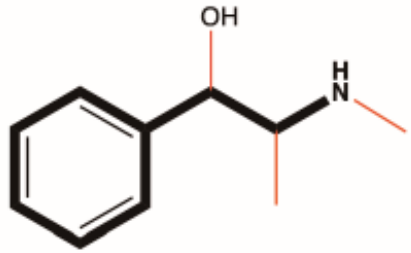

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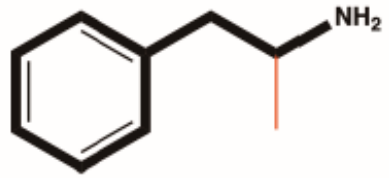

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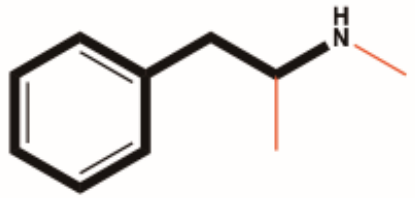

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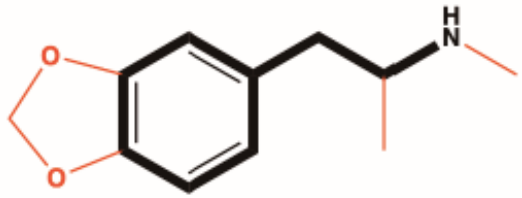

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Methamphetamine

- Heightened emotional reactivity
- Increased risk of anxiety and depression in toddler/early school years

Prenatal Methamphetamine Exposure and Childhood Behavior Problems at 3 and 5 Years of Age

LaGrasse et al

PEDIATRICS Volume 129, Number 4, April 2012

Infant Development, Environment, and Lifestyle study (IDEAL)
Prospective, longitudinal study
Los Angeles, California; Honolulu, Hawaii; Des Moines, Iowa; and Tulsa, Oklahoma
N=330 children (166 exposed and 164 comparison)
Child Behavior Checklist at ages 3 and 5 years

Prenatal Methamphetamine Exposure and Childhood Behavior Problems at 3 and 5 Years of Age

LaGrasse et al

PEDIATRICS Volume 129, Number 4, April 2012

TABLE 4 Behavior Problems Scores According to Prenatal MA Exposure

Outcome	MA Exposure Group				Adjusted [a]					
	Age 3 Years		Age 5 Years		Exposure[b]		Age[b]		Interaction[c]	
	Exposed (n = 141)	Comparison (n = 147)	Exposed (n = 153)	Comparison (n = 151)	β (SE)	P	β (SE)	P	β (SE)	P
Externalizing	53.0 ± 1.9	52.0 ± 2.2	53.1 ± 2.0	49.6 ± 2.3)	2.8 (2.0)	.150	−2.4 (0.8)	.003	2.5 (1.2)	.034
Attention problems	2.6 ± 0.4	2.6 ± 0.4	2.8 ± 0.4	2.7 ± 0.4	0.40 (0.4)	.278	0.01 (0.2)	.995	0.15 (0.2)	.552
Aggressive behavior	12.9 ± 1.3	11.8 ± 1.6	12.6± 1.4	10.0 ± 1.6	2.1 (1.4)	.123	−1.9 (0.6)	.002	1.5 (0.8)	.068
ADHD issues	5.3 ± 0.6	5.2 ± 0.6	5.5 ± 0.6	4.6 ± 0.6	0.62 (0.6)	.259	–0.61 (0.2)	.013	0.78 (0.4)	.029
Internalizing	50.9± 1.8	48.7 ± 2.2	54.2 ± 1.9	50.8 ± 2.2	3.5 (1.9)	.057	2.1 (0.8)	.007	1.1 (1.2)	.350
Emotionally reactive	3.2 ± 0.5	2.3 ± 0.6	3.7 ± 0.5	2.5 ± 0.6	1.4 (0.5)	.006	0.22 (0.2)	.318	0.29 (0.3)	.363
Anxious/depressed	2.8 ± 0.4	2.0 ± 0.5	3.4 ± 0.4	2.3 ± 0.5	1.0 (0.4)	.019	0.35 (0.2)	.010	0.28 (0.3)	.359
Somatic complaints	1.8 ± 0.3	1.8 ± 0.4	2.3 ± 0.4	2.3 ± 0.4	–0.06 (0.3)	.861	0.53 (0.2)	.002	–0.04 (0.2)	.883
Withdrawn	1.5 ± 0.4	1.4 ± 0.5	1.9 ± 0.4	1.7 ± 0.5	0.44 (0.4)	.273	0.37 (0.2)	.033	0.040 (0.2)	.866
Total problems	52.2 ± 1.8	51.1 ± 2.1	52.9 ± 1.8	50.2 ± 2.1	2.9 (1.8)	.119	–0.91 (0.8)	.227	1.63 (1.1)	.134

Data are presented as adjusted mean ± SE unless otherwise noted.

[a] Adjusted analyses tested main effects of MA exposure and child age at assessment (3 vs 5 years) and the interaction of exposure and age, adjusted for prenatal exposure to alcohol, tobacco, and marijuana; birth weight; gender; SES; maternal age; single (no partner); caregiver change; domestic violence; postnatal use of MA; tobacco, alcohol, and marijuana exposure; caregiver psychological symptoms; the quality of the home; child abuse; and study site.

[b] The reference group was the comparison group for analysis of exposure and 3 years for analysis of age.

[c] A least squares mean procedure was applied to follow up a signi cant interaction.

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[c] A least squares mean procedure was applied to follow up a signi cant interaction.

Opioids

- Increased risk of ophthalmologic disorders
- Challenges with executive function
- Increased risk of mental health concerns in adolescence

The Short- and Long-term Effects on the Visual System of Children Following Exposure to Maternal Substance Misuse in Pregnancy

Am J Ophthalmol
2013;156:190–194.

KURT SPITERI CORNISH MONICA HRABOVSKY NEIL W. SCOTT ELIZABETH MYERSCOUGH AND ARAVIND R. REDDY

TABLE 3 Prevalence of Strabismus and Nystagmus in the Study Group (Children Born to Mothers Misusing Substances During Pregnancy) at Presentation and at 5 Years, Compared With Control Group (5-Year-Old Children Referred to the Ophthalmology Department at Preschool Screening)

	Study Group (at Baseline)	Study Group (at 5 Years)	Control Group (at 5 Years)	OR at 5 years (95 CI)
Strabismus, n/N ( )	46/301 (15.3)	42/301 (14.0)	218/7887 (2.8)	5.70 (4.01-8.12)
Nystagmus, n/N ( )	11/301 (3.7)	10/301 (3.3)	3/7887 (0.004)	90.34 (24.73-330.02)

CI confidence interval; n number of cases in current study; N total number of patients in the group; OR odds ratio.

Study group was heterogeneous in terms of substance exposure in utero, though 74% with NOWS
Control group was preschoolers undergoing school vision screening matched for birth year

Spowart KM, Reilly K, Mactier H and Hamilton R 2023) Executive functioning, behavioural, emotional, and cognitive dif culties in school-aged children prenatally exposed to methadone.
Front. Pediatr. 11:1118634.
doi: 10.3389/fped.2023.1118634

Prospective study: 21 children born to methadone-maintained mothers 2008-2010 (12 additional controls) evaluated at age 8-10y Behaviour Rating Inventory of Executive Function, Second Edition (BRIEF®2)

TABLE 4 BRIEF 2 results.

	Mean T-score, exposed children ($n = 19$)	Mean T-score, comparison children ($n = 8$)	95% CI of difference; Mann–Whitney U test p value	Proportion of exposed children classi ed with "potentially" or "clinically signi cant"	Proportion of comparison children classi ed with "potentially" or "clinically signi cant"	95% CI of difference; Fisher exact test p value
BRI	58	49	2 to 16 $p = 0.015$	4/19	0/8	14% to 43% $p = 0.22$
ERI	61	49	5 to 18 $p = 0.002$	5/19	0/8	9% to 49% $p = 0.14$
CRI	58	49	2.5 to 14 $p = 0.007$	5/19	0/8	9% to 49% $p = 0.14$
GEC	61	49	4 to 18 $p = 0.002$	5/19	0/8	9% to 49% $p = 0.14$

CI, con dence interval; BRIEF 2, Behaviour Rating Inventory of Executive Function, 2nd edition; BRI, behaviour regulation index; ERI, emotional regulation index; CRI, cognitive regulation index; GEC, global executive composite.
GEC is the sum of the three regulation indices where a high score indicates more problems.

Mental health in youth prenatally exposed to opioids and poly-drugs and raised in permanent foster/adoptive homes: A prospective longitudinal study

Egil Nygaard[a,b], Kari Slinning[a,b], Vibeke Moe[a,b], Anders Fjell[a], Kristine B. Walhovd[a]

Early Human Development
Volume 140, January 2020, 104910

Prospective cohort, risk group = "opioid and polysubstance" but FASD excluded. Eval at 17-22 yrs of age

Lifetime diagnoses according to MINI interview among the youth in the risk and comparison groups.

	Risk group (n = 45)		Comparison (n = 48)		Bivariate group difference			Controlling for gender, age and caregivers' education[a]		
	n	□	n	□	*OR*	95 CI	p	*OR*	95 CI	p
Major depressive episode	24	53.3	10	20.8	4.34	1.75–10.79	.001	3.43	1.14–10.32	.028
Any manic or bipolar disorder[b,c]	16	35.6	9	18.8	2.39	0.93–6.17	.101	2.26	0.65–7.85	.201
Any anxiety disorder[b,d]	28	62.2	17	35.4	3.00	1.29–6.99	.008	2.48	0.86–7.16	.094
Any drug dependence or abuse disorder	19	42.2	12	25.0	2.19	0.91–5.29	.123	2.12	0.66–6.81	.209
Alcohol dependence	13	28.9	11	22.9	1.37	0.54–3.47	.636	0.95	0.27–3.40	.935
Alcohol abuse	10	22.2	2	4.2	6.57	1.35–31.92	.012	7.50	1.28–44.08	.026
Substance dependence	8	17.8	1	2.1	10.16	1.22–84.92	.013	6.87	0.58–81.30	.126
Substance abuse	6	13.3	1	2.1	7.23	0.84–62.65	.054	3.57	0.27–46.80	.333
Attention deficit, hyperactivity disorder	19	42.2	4	8.3	8.04	2.47–26.22	< .001	5.09	1.24–20.95	.024
Other[b,e]	17	37.8	6	12.5	4.25	1.49–12.10	.007	4.54	1.23–16.81	.023

Note. Pearson's exact 2-tailed chi-square test was used for bivariate analyses. Logistic regression analyses were used to analyze differences between groups, controlling for gender, age and caregivers' education.

[a] Information about caregivers' education is missing for one participant in the risk group; thus, n is one less than for the bivariate analyses.

[b] See Supplementary Table A.3 for details of each specific diagnosis.

[c] Any hypomanic episode, bipolar I disorder, bipolar II disorder, or bipolar disorder NOS.

[d] Any of agoraphobia, social phobia (generalized and nongeneralized), obsessive-compulsive disorder, posttraumatic stress disorder, or general anxiety disorder.

[e] Any of psychotic disorder, eating disorder (anorexia, bulimia or anorexia nervosa), antisocial personality disorder, or moderate or high suicidality.


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Breastfeeding: simply the healthiest
Your milk is your baby's perfect food
Breastmilk can begin a lifetime of good health for your baby
Breastfeeding is healthy for mom
Help Stop the Spread of Colds and Flu!
If you have any of these symptoms:
• Fever
• Cough or Sneezing

Practical strategies

- Optimize the post natal environment
- Maximize positive childhood experiences (the "antidote" to ACEs)

- Many thanks to Bird Gilmartin MD for her help on this section ☺

Practical strategies: in the office

1. Help families identify and strengthen safe, stable, nurturing relationships. Ask caregivers, "What does support look like for you? Who is supporting you? Who is supporting your child besides you?"
2. Help ensure infants are followed in a medical home
3. Routine screening labs for known neurotoxins/neurodevelopmental mediators (e.g., lead and hemoglobin screening)
4. Screen for caregiver mental health and substance use using a validated screening tool (I.e. EPDS, 5Ps, NIDA Quick Screen)
5. Developmental screening for the child with a validated screening tool (e.g. ASQ, MCHAT)
6. For children in out-of-home placement (foster or kinship care), welcome and include biological parents and family members as much as possible.

Practical strategies: referrals

- Early Intervention (for <3 years old) or Child Find (for 2 years 11 months – 5 years)
- Resources to assist with housing, employment, childcare, food, and transportation as needed
- Services that strengthen the parent-child interaction (e.g., dyadic therapy modalities like child parent psychotherapy, parent child interaction therapy)

Practical strategies: harm reduction

- Safe sleep
- Safe and sober caretaking and driving
- Substances/medications up, away, and out of sight
- Lockboxes/lockbags
- Carry naloxone
- Know the Poison Control Number (1-800-222-1222)

Maximizing positive childhood experiences

- Read books every day
- Play – at least 10-15 minutes every day, face to face, no phones
- Name feelings – both yours and your child's; encourage children to name their own feelings as they grow
- Teach a relaxation/regulation skill (belly breathing, guided imagery, emotion scales (red/yellow/green zone), progressive muscle tightening and relaxation etc)
- Help children create a physical "safe space" at home ("cozy corner," box, closet etc)
- Avoid multitasking with your child as much as possible. When your child is talking, stop, put your phone down and listen.
- Catch your child doing a good job and praise them for something specific and concrete
- Set expectations ahead of time, then stick to what you said

Thank you!

- Questions? Comments? Rude remarks? Email me! Laurie.halmo@childrenscolorado.org

- References included throughout, but I can email you a list if you'd like