Impact of Prenatal Substance Use on Child Development: Findings from a 21-year Birth Cohort Study

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SOCIAL SCIENCE RESEARCH INSTITUTE, SOCIAL WELFARE RESEARCH INSTITUTE & BK21 Plus GRADUATE SCHOOL OF SOCIAL WELFARE

Colloquium

Yonsei University Yonhee hall 308
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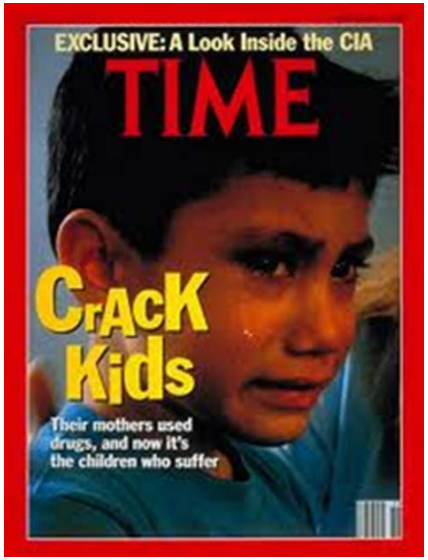
Outline of the Presentation

1. Historical Context of the Research
2. Theoretical Framework
3. Study Design of “Project Newborn”
4. Key Selected Findings
   - Cognition
   - Behavioral outcomes
     - Externalizing behavior
     - Early substance use & Sexual risk behavior
5. Summary & Implication
6. Acknowledgement

Response to the Crack Cocaine Epidemic

- 50,000-100,000 infants per year with prenatal cocaine exposure
- Up to 18% of live births in some urban low SES areas (late 80's early 90's)
- At least 2 million prenatally cocaine exposed infants-young adults



- Steady use of illicit drugs during pregnancy (~ 8%) (The 2017 *National Survey on Drug Use and Health*)
- Worldwide, 0.5-3% of pregnant women are estimated to use cocaine (Lamy & Thibaut, 2010).

Development of Project Newborn

- Center for the Advancement of Mothers and Children (CAMC), Rainbow Babies and Children's Hospital
  - Lynn Singer, Ph.D. and Robert Kliegman, M.D., Co-Directors
  - Initial funding from the RB&C Board of Trustees
  - Offered coordinated neonatal medical, social work and developmental services for mothers and children affected by prenatal cocaine/polydrug exposure
  - Home visiting project developed by Kathy Farkas, Ph.D.
- CAMC now at Metro and is still part of services offered for mothers and children in Cleveland
  - Currently serving opioid/heroin addicted women and infants
  - Involves maternal fetal medicine experts, social work, drug treatment
  - Multiple funding sources through Metro & March of Dimes

Development of Project Newborn

- The National Institutes on Drug Abuse funded several sites
  - CWRU one of the last cohort/study to be funded (1994)
  - Project Newborn one of only 2 to follow children through young adulthood
  - Project Newborn has the highest retention rate among studies
  - One of few national studies that was able to collect biologic samples at birth to verify and quantify prenatal cocaine exposure (infant meconium has drug metabolites dating back to about 4.5 months gestation)
- Lynn Singer, PhD., Principal Investigator (PI), 1994-2007
- Sonia Minnes, PhD., Project Coordinator, Research Associate, and PI, 2007-present
- Meeyoung O. Min, PhD. Co-investigator, 2002-present

Research Questions

- What are the developmental and health outcomes of prenatal cocaine exposure controlling for other prenatal drug (alcohol, marijuana, tobacco) exposures and environmental and biologic factors?
- How do women who use cocaine during pregnancy differ from those who do not?
- How does maternal/caregiver behavior and environment pre and post pregnancy affect child outcome?

Prenatal Drug Exposure: Teratogen

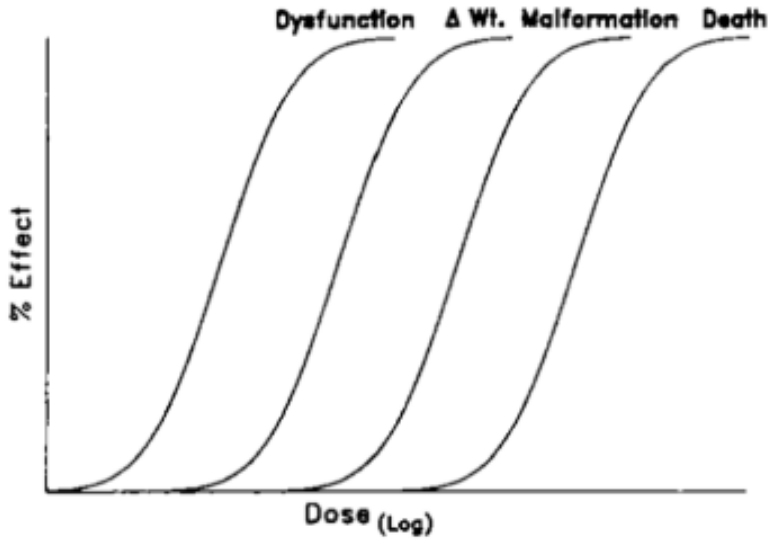
- Any agent that can disturb the development of an embryo or fetus
- Classes of teratogens include:
  - Radiation
  - Maternal infections
  - Chemicals
  - Medications/Drugs

Principles of Teratology

- Four primary teratogenic outcomes:
  - Death
  - Physical malformation
  - Growth retardation
  - Abnormal function
- Effects are a function of:
  - Genetic endowment
  - Fetal environment
  - Postnatal environment
  - Dose level of agent
  - Developmental stage of the embryo or fetus at the time of insult

Neurobehavioral Teratology

- The study of *functional abnormalities not detectable at birth* caused by intrapartum exposure to foreign agents.
- Vulnerability of central nervous system (CNS) injury extends throughout fetal, neonatal and beyond the infancy stage
  - Most injuries to the developing nervous system do not result in CNS malformation, but rather in functional abnormalities, which are often not detectable at birth



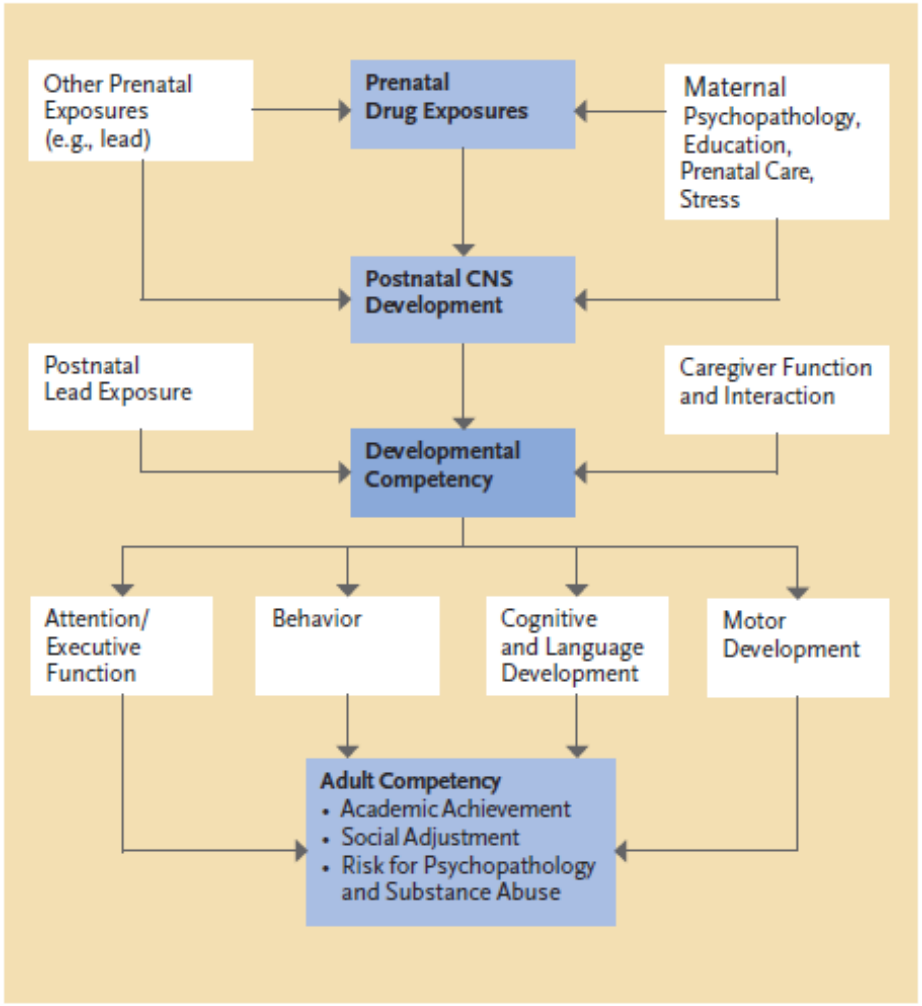
Pathways Impacting Fetal Development

- By altering the monoamine neurotransmitter system involving dopamine, serotonin, and norepinephrine in the prefrontal cortex (Vorhees, 1989; Kosofsky et al., 1994; McCarthy et al., 2014).
  - Disruption in the prefrontal cortex has been implicated in problems of inhibitory control, attention, and executive function, which may be expressed as externalizing behavior problems (Ackerman et al., 2010; Lambert & Bauer, 2012; Buckingham-Howes et al., 2013).
- Maternal cocaine use during pregnancy may also alter brain function indirectly via its vasoconstrictive properties that limit oxygen and nutrition to the developing fetal brain (Thompson et al., 2009).

Indirect Pathways Impacting Child Development

- Prenatal cocaine exposure (PCE) indirectly increases vulnerability to developmental problems through biological and environmental confounders:
  - Prenatal exposure to other drugs (alcohol, tobacco and marijuana)
  - Ongoing parental substance abuse
  - Poor quality of the home environment
  - Suboptimal parenting and maltreatment
  - Caregiver changes and foster care placement

FIGURE 1. Model to Study Effects of Prenatal Drug Exposure on Developmental Outcomes



Adapted from Mayes, 2002.

Model for Prenatal Drug Exposure Research

Minnes, Lang & Singer 2011

Adapted from
Mayes, L. C. (2002). A behavioral teratogenic model of the impact of prenatal cocaine exposure on arousal regulatory systems. *Neurotoxicology and teratology*, *24*(3), 385-395.

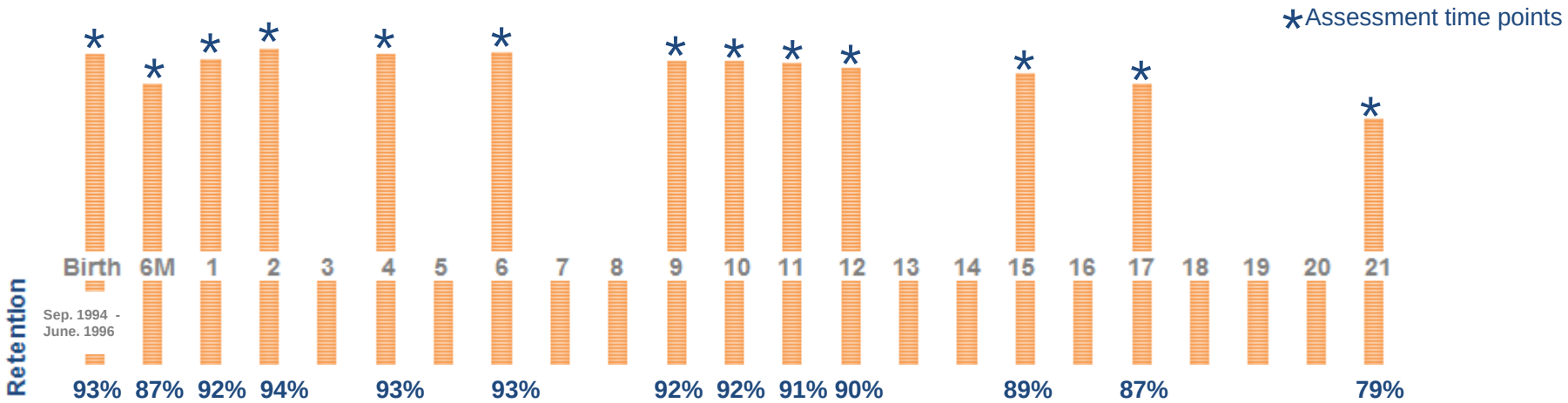
Project Newborn: Study Background

- Height of the crack cocaine epidemic (late 1980-mid 1990s)
- Participants
  - 415 mother-infant dyads
  - Low SES (receiving Medicaid)
  - Maternity ward of Metro Health Medical Center in Cleveland (Infants born from September 1994 to June 1996)
  - Urine toxicology screening completed when women
    - ✓ Appeared intoxicated at delivery
    - ✓ Lack of prenatal care
    - ✓ Previous history of Department of Children Services involvement
    - ✓ Self-admitted substance use during pregnancy to hospital staff

Study Background (cont.)

- Exclusions
  - Women with psychiatric history
  - Non English speaking
  - < 19 years of age
  - Women with chronic illness including HIV
  - Infants diagnosed with Down Syndrome or FAS at birth
- Cocaine-Exposure Status Screening
  - Prenatal Cocaine-Exposure (PCE; *n* = 218)
    - Positive results on any of the fallowing:
      - ✓ Self-report to hospital or research staff
      - ✓ Urine for infant or mother
      - ✓ Meconium Screening
  - Non Prenatal Cocaine-Exposure (NCE; *n* = 197)
    - Negative results on all of the above

Project Newborn Timeline



Phase 1

- Prenatal Exposure to Cocaine/Other Drugs
- Cognitive and Motor Outcomes
- Mental Health
- Behaviors
- Elevated lead levels
- Caregiver Environment

Phase 2

- Cognition/Language (Executive Function, Perceptual Reasoning, Auditory Process)
- Mental Health
- Externalizing Behaviors (aggressive & disruptive behavior)
- Elevated lead levels
- Caregiver Environment

Phase 3

- Substance Use Initiation
- Cognition/Language (Executive Function, Perceptual Reasoning, Auditory Process)
- Externalizing Behaviors
- Substance Use Risk Factors (e.g., violence exposure, parental attachment & monitoring, family conflict)

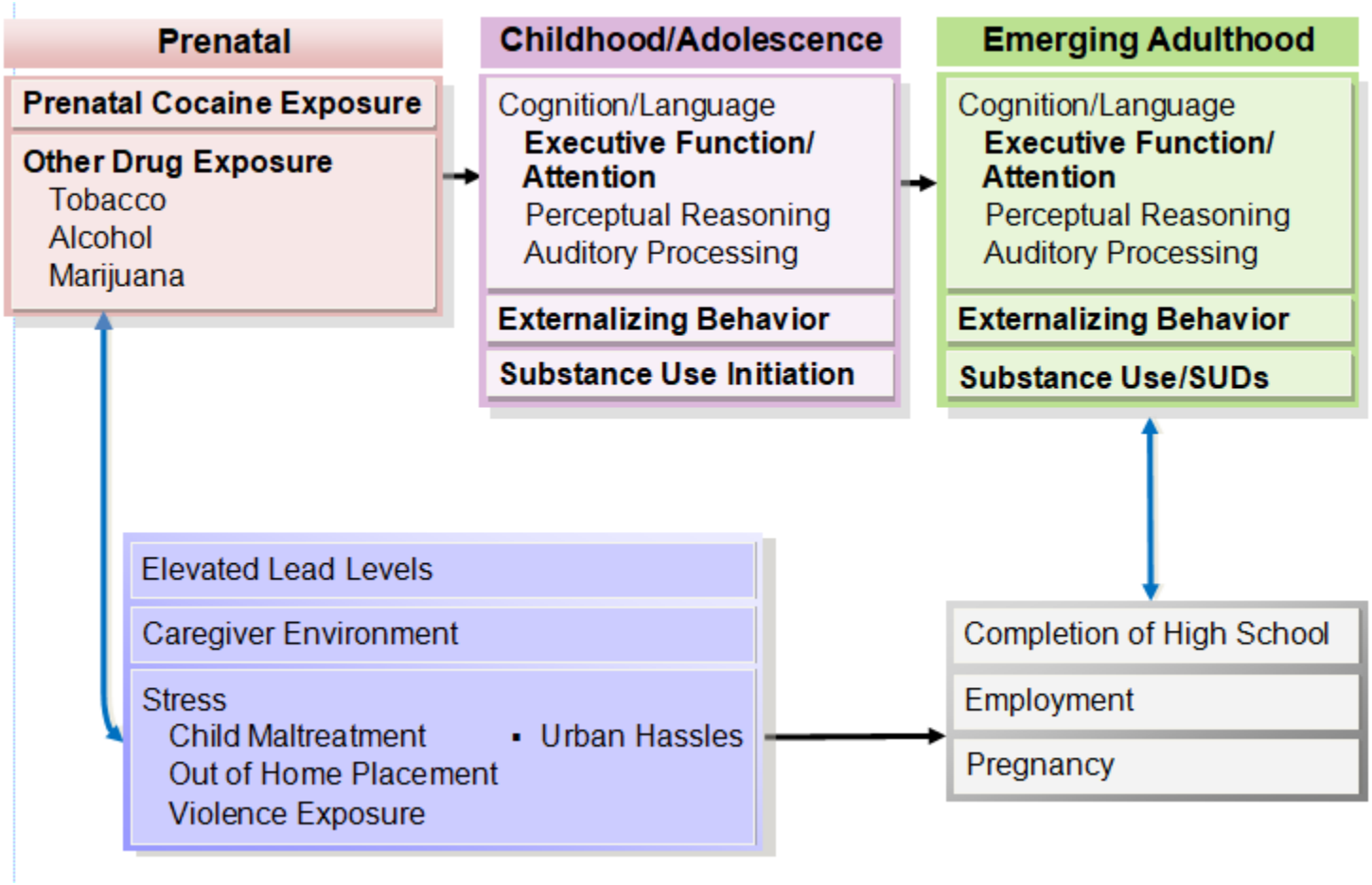
Phase 4

- Substance Use (Marijuana)/SUDs
- Externalizing Behaviors (Sexual Risk Behaviors)
- Cognition/Language (Executive Function, Perceptual Reasoning, Auditory Process)
- Urban Hassles
- Childhood Maltreatment
- Developmental Assets

Phase 5

- SUDs
- Mental Health Disorders
- Externalizing Behaviors (Sexual Risk Behaviors)
- Cognition/Language (Executive Function, Perceptual Reasoning, Attention)

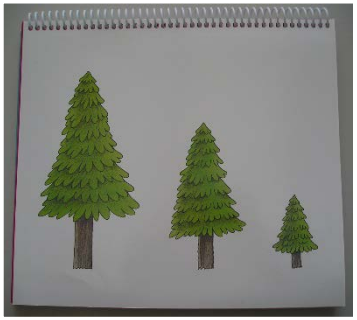
Model of Prenatal Cocaine Exposure

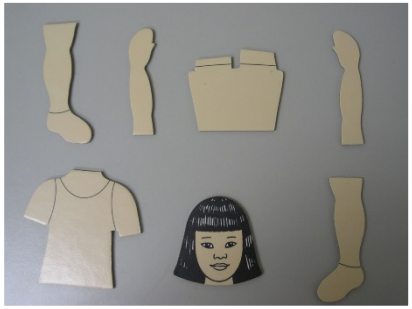
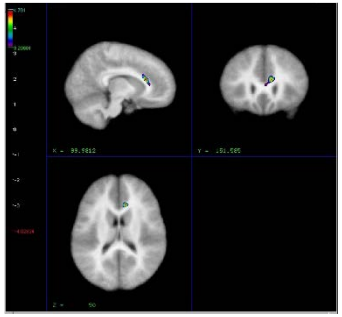


Developmental Assessments





Maternal Characteristics by PCE Status (*N*=415)

	PCE (*n* = 218)		**NCE** (*n* = 197)	
	M	*SD*	*M*	*SD*
Age at birth	**29.6**	**5.0**	**25.7**	**5.0**
African-American, *n* (%)	162	(82.2)	150	(79.4)
Education, years	**11.6**	**1.7**	**12.0**	**1.4**
< high school, *n* (%)	**103**	**(48)**	**61**	**(31)**
Married, *n* (%)	**16**	**(7)**	**34**	**(17)**
PPVT-R standard score	**73.8**	**15.0**	**78.2**	**15.0**
BSI GSI at birth	**0.81**	**0.7**	**0.49**	**0.5**
Low SES, *n* (%)	213	(98)	192	(98)
Prenatal Exposure	*n (%)*	*IQR*	*n (%)*	*IQR*
Alcohol, per week*	**167 (85.2)**	**0.38 - 10.5**	**118 (65.2)**	**0 - 0.8**
Tobacco, per day*	**166 (87.4)**	**3 - 17.5**	**74 (40.9)**	**0 - 5**
Marijuana, per week*	**92 (48.4)**	**0 - 0.6**	**24 (13.3)**	**0 - 0**
Cocaine, units per week	197 (100)	3.38 - 24.5	---	---

PPVT= Peabody Picture Vocabulary Test; BSI=Brief Symptom Inventory; GSI= Global Severity Index; HOME= Home Observation for Measurement of the Environment; IQR=Inter-quartile (25%-75%) range; *significance based on *n* (%); **Bolded if *p* < .05**

Child Characteristics by PCE Status (*N*=415)

	PCE (*n* = 218)		**NCE** (*n* = 197)	
	M	*SD*	*M*	*SD*
Male, *n* (%)	102	(4.7)	96	(49)
Gestational age, weeks	**37.7**	**3.0**	**38.5**	**3.0**
Prematurity (< 37 GA), *n* (%)	**64**	**(29)**	**36**	**(18)**
Hobel Neonatal Risk score	8.3	19.0	6.0	17.0
Birth weight, g[a]	**2709**	**678**	**3086**	**703**
Low birth weight (<2500 g), *n* (%)	**79**	**(36)**	**36**	**(18)**
Small for gestational age, *n* (%)	**26**	**(12)**	**4**	**(2)**
Birth length, cm[a]	**47.2**	**4.0**	**49.9**	**4.0**
Head circumference, cm[a]	**32.3**	**2.0**	**33.4**	**3.0**
Ever in non-kinship foster/adoptive care by age 4, *n* (%)	**66**	**(33.5)**	**11**	**(5.8)**

[a]Adjusted for gestational age; **Bolded if *p* < .05**

PCE on Cognitive Development

Cognitive and Motor Outcomes of Cocaine-Exposed Infants

JAMA. 2002;287:1952-1960

Lynn T. Singer, PhD
Robert Arendt, PhD
Sonia Minnes, PhD
Kathleen Farkas, PhD
Ann Salvator, MS
H. Lester Kirchner, PhD
Robert Kliegman, MD

Context Maternal use of cocaine during pregnancy remains a significant public health problem, particularly in urban areas of the United States and among women of low socioeconomic status. Few longitudinal studies have examined cocaine-exposed infants, however, and findings are contradictory because of methodologic limitations.

Objective To assess the effects of prenatal cocaine exposure on child developmental outcomes.

Design Longitudinal, prospective, masked, comparison birth cohort study with recruitment in 1994-1996.

Setting Obstetric unit of a large US urban teaching hospital.

Cognitive Outcomes of Preschool Children With Prenatal Cocaine Exposure

JAMA. 2004;291:2448-2456

Lynn T. Singer, PhD
Sonia Minnes, PhD
Elizabeth Short, PhD
Robert Arendt, PhD
Kathleen Farkas, PhD
Barbara Lewis, PhD
Nancy Klein, PhD
Sandra Russ, PhD
Meeyoung O. Min, PhD
H. Lester Kirchner, PhD

Context Because of methodological limitations, the results of the few prospective studies assessing long-term cognitive effects of prenatal cocaine exposure are inconsistent.

Objective To assess effects of prenatal cocaine exposure and quality of caregiving environment on 4-year cognitive outcomes.

Design Longitudinal, prospective, masked comparison cohort study from birth (September 1994-June 1996) to 4 years.

Setting Research laboratory of a US urban county teaching hospital.

Participants A total of 415 consecutively enrolled infants identified from a high-risk population screened for drug use through clinical interview, urine, and meconium screens. Ninety-three percent retention for surviving participants at 4 years of age resulted in 376 children (190 cocaine-exposed and 186 nonexposed).

Children with PCE in Foster/Adoptive Care

Table 4. Comparisons of Key Environmental Characteristics That Mediate Child Outcomes, by Caregiver Group*

Characteristic	Cocaine Exposed: Model 1: Biological Maternal/Relative (n = 148)	Cocaine Exposed: Model 2: Foster/Adoptive (n = 42)	Model 3: Nonexposed (n = 186)	Statistic: F	Statistic: *df*	Statistic: χ^2	*P* Value
Prenatal cocaine exposure†	20 (36)	39 (70)		4.8	1, 188		.02
Environmental characteristics							
HOME score	41 (6)	45 (5)	42 (7)	7.9	2, 373		.001‡
Current caregiver PPVT-R score	76 (16)	89 (18)	78 (15)	8.4	2, 349		.001‡
Current caregiver Global Severity Index	0.35 (0.4)	0.22 (0.2)	0.38 (0.4)	2.2	2, 343		.12
Child unadjusted outcomes							
Verbal IQ	79 (12)	83 (9)	82 (13)	3.1	2, 373		.05§
Performance IQ	84 (15)	87 (13)	88 (15)	3.0	2, 373		.05‖
Full-scale IQ	79 (13)	83 (10)	83 (14)	3.8	2, 373		.02‖
Full-scale IQ >100, No. (%)	7 (5)	1 (2)	23 (12)			8.5	.01¶
Full-scale IQ <70, No. (%)	37 (25)	4 (10)	30 (16)			6.9	.03#

Abbreviation: PPVT-R, Peabody Picture Vocabulary Test-Revised.
*Data are presented as mean (SD) unless otherwise indicated.
†Mean number of "rocks" per day × mean number of days per week.
‡Model 2 differs from models 1 and 3.
§No difference by group.
‖Model 1 differs from model 3.
¶Model 1 differs from model 3; combined models 1 and 2 differ from model 3.
#Model 1 differs from models 2 and 3; model 2 does not differ from model 3.

Non-kinship F/A care had positive effects on cognitive and language outcomes through lower caregiver psychological distress, better home environments, higher caregiver IQ and lower blood lead levels. However, these positive effects did not occur across all developmental domains and diminished during adolescence.

PCE on Cognitive Development

Prenatal Cocaine Exposure: Drug and Environmental Effects at 9 Years

Lynn T. Singer, PhD, Suchitra Nelson, PhD, Elizabeth Short, PhD, Meeyoung O. Min, PhD, Barbara Lewis, PhD, Sandra Russ, PhD, and Sonia Minnes, PhD

J Pediatr 2008;153:105-11

Drug and Alcohol Dependence 191 (2018) 37–44

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

Prenatal and concurrent cocaine, alcohol, marijuana, and tobacco effects on adolescent cognition and attention

Lynn T. Singer[a,*], Meeyoung O. Min[b], Sonia Minnes[b], Elizabeth Short[c], Barbara Lewis[c], Adelaide Lang[b], Miaoping Wu[b]

Table III. Adjusted effects of prenatal drug and alcohol exposure and postnatal IDA, lead exposure, and HOME score on child outcomes (n = 293)*

	Prenatal			Postnatal		
	Cocaine	Alcohol	Marijuana†	IDA	Lead	HOME
WISC-IV Subscale						
Verbal comprehension IQ				$\beta = -0.11$; $P < .07$	$\beta = -0.14$; $P < .02$	$\beta = 0.17$; $P < .004$
Similarities				$\beta = -0.12$; $P < .05$		$\beta = 0.18$; $P < .003$
Vocabulary		Third trimester, $\beta = -0.12$; $P < .05$			$\beta = -0.18$; $P < .002$	$\beta = 0.13$; $P < .03$
Comprehension						$\beta = 0.15$; $P < .01$
Perceptual reasoning IQ	$\beta = -0.16$; $P < .02$				$\beta = -0.16$; $P < .007$	
Block design	$\beta = -0.17$; $P < .005$				$\beta = -0.12$; $P < .06$	
Picture concept	$\beta = -0.14$; $P < .03$					
Matrix reasoning	$\beta = -0.11$; $P < .07$				$\beta = -0.18$; $P < .003$	
Working memory IQ		Average, $\beta = -0.14$; $P < .04$				$\beta = 0.16$; $P < .01$
Digit span		Third trimester, $\beta = -0.13$; $P < .04$			$\beta = -0.10$; $P < .09$	
Letter-number sequencing		Average, $\beta = -0.18$; $P < .007$		$\beta = -0.11$; $P < .07$		$\beta = 0.17$; $P < .004$
Processing speed IQ						$\beta = 0.15$; $P < .02$
Coding			Third trimester, $\beta = -0.22$; $P < .0005$	$\beta = -0.11$; $P < .07$		
Symbol search						$\beta = 0.11$; $P < .06$
Full-scale IQ		Third trimester, $\beta = -0.11$; $P < .08$			$\beta = -0.14$; $P < .02$	$\beta = 0.16$; $P < .007$
Full-scale IQ >100	OR = 0.51 (95% CI = 0.24 to 1.11); $P < .09$				OR = 0.43 (95% CI = 0.22 to 0.85); $P < .02$	OR = 1.07 (95% CI = 1.00 to 1.14); $P < .05$
Woodcock-Johnson subscale						
Reading summary score		Third trimester, $\beta = -0.17$; $P < .008$		$\beta = -0.10$; $P < .08$	$\beta = -0.15$; $P < .01$	$\beta = 0.14$; $P < .02$
Letter-word identification					$\beta = -0.15$; $P < .01$	$\beta = 0.13$; $P < .03$
Passage comprehension					$\beta = -0.18$; $P < .003$	$\beta = 0.10$; $P < .08$
Reading fluency					$\beta = -0.15$; $P < .02$	$\beta = 0.11$; $P < .07$
Math summary score				$\beta = -0.12$; $P < .04$		
Calculation				$\beta = -0.12$; $P < .04$		
Applied problems				$\beta = -0.10$; $P < .10$	$\beta = -0.12$; $P < .04$	
Math fluency				$\beta = -0.11$; $P < .07$		$\beta = 0.15$; $P < .02$

*Because the impact of combined cocaine exposure and adoptive/foster care effect was mediated completely by lead exposure, the β values were estimated based on the model without the combined cocaine exposure and adoptive/foster care variable.

†There were several positive correlations of first-trimester marijuana exposure on outcomes ($\beta = 0.13$; $P < .05$) for similarities, vocabulary, and picture concepts); however, because only 1 child was exposed only to marijuana during the first trimester, these were deleted.

Alcohol on Cognitive Development

ORIGINAL ARTICLES

www.jpeds.com • THE JOURNAL OF PEDIATRICS

Association of Fatty Acid Ethyl Esters in Meconium and Cognitive Development during Childhood and Adolescence

Meeyoung O. Min, PhD[1], Lynn T. Singer, PhD[2], Sonia Minnes, PhD[1], Miaoping Wu, MS[1], and Cynthia F. Bearer, MD, PhD[3]

Objective To examine associations between amounts of fatty acid ethyl esters (FAEEs) in meconium and cognitive development in school-aged children exposed to alcohol and drugs in utero.

Table IV. Adjusted association of FAEEs

	Verbal Comprehension*		Working Memory†		Full-Scale IQ‡	
	b ± SE	*P* value	b ± SE	*P* value	b ± SE	*P* value
Ethyl myristate	−3.26 ± 1.67	.053	−4.17 ± 1.96	.035	−3.60 ± 1.79	.046
Ethyl oleate	−2.05 ± 0.91	.025	−2.31 ± 1.06	.032	−2.07 ± 0.97	.035
Ethyl linoleate	−1.81 ± 0.83	.031	−1.90 ± 0.98	.054	−1.77 ± 0.88	.047
Ethyl linolenate	−2.31 ± 1.02	.024	−2.63 ± 1.19	.029	−2.62 ± 1.09	.017

Note. b = regression coefficient.
Significant ($P < .05$) covariates are listed in italics.
*Adjusted for age/visit, birth length, birth mother's education and psychological distress at birth, current caregiver's PPVT-R scores, HOME score, and child race.
†Adjusted for age/visit, birth length, birth mother's education and psychological distress at birth, current caregiver's Block Design scores, and child sex.
‡Adjusted for age/visit, birth length, birth mother's education and psychological distress at birth, current caregiver's Block Design scores, HOME score, and child race.

Common Liability to Addiction

- The co-occurrences of behavioral problems, substance use, and sexual risk behaviors are due to a common vulnerability to behavioral disinhibition (an inability to constrain impulses to behave in socially undesirable ways; Iacono et al., 2008).
- PCE has been shown to be associated with behavioral disinhibition (Ackerman et al., 2010; Lambert & Bauer, 2012), and the common liability accounts for how PCE effects could be expressed differently in different developmental stages (e.g., hyperactivity and aggression in childhood and SU and SRBs in adolescence).
- Utilizing the common liability model, phenotypes associated with behavioral disinhibition (e.g., externalizing behavior) are hypothesized to interact with environmental factors to amplify or mitigate the liability, affecting the likelihood of SU or SRB outcomes.

PCE on Externalizing Behavior

Neurotoxicology and Teratology 32 (2010) 443–451

Contents lists available at ScienceDirect

Neurotoxicology and Teratology

journal homepage: www.elsevier.com/locate/neutera

The effects of prenatal cocaine exposure on problem behavior in children 4–10 years

Sonia Minnes [a,*], Lynn T. Singer [b], H. Lester Kirchner [d], Elizabeth Short [c], Barbara Lewis [c], Sudtida Satayathum [a], Dyianweh Queh [a]

Journal of Adolescent Health 55 (2014) 167–174

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JOURNAL OF ADOLESCENT HEALTH

www.jahonline.org

Original article

Self-Reported Adolescent Behavioral Adjustment: Effects of Prenatal Cocaine Exposure

Meeyoung O. Min, Ph.D. [a,*], Sonia Minnes, Ph.D. [a], Susan Yoon, M.S.W. [a], Elizabeth J. Short, Ph.D. [b], and Lynn T. Singer, Ph.D. [c,d,e]

Adolescent Substance Use

Journal of Adolescence 37 (2014) 269–279

Contents lists available at ScienceDirect

Journal of Adolescence

journal homepage: www.elsevier.com/locate/jado

Externalizing behavior and substance use related problems at 15 years in prenatally cocaine exposed adolescents

Meeyoung O. Min[a,*], Sonia Minnes[a], Adelaide Lang[a], Paul Weishampel[a], Elizabeth J. Short[b], Susan Yoon[a], Lynn T. Singer[c,d,e]

Drug and Alcohol Dependence 134 (2014) 201–210

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Effects of prenatal cocaine/polydrug exposure on substance use by age 15

Sonia Minnes[a,*], Lynn Singer[b], Meeyoung O. Min[a], Miaoping Wu[a], Adelaide Lang[a], Susan Yoon[a]

Adolescent Substance Use

Drug and Alcohol Dependence 176 (2017) 33–43

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

The association of prenatal cocaine exposure, externalizing behavior and adolescent substance use

Sonia Minnes[a,*], Meeyoung O. Min[a], June-Yung Kim[b], Meredith W. Francis[b], Adelaide Lang[a], Miaoping Wu[a], Lynn T. Singer[c]

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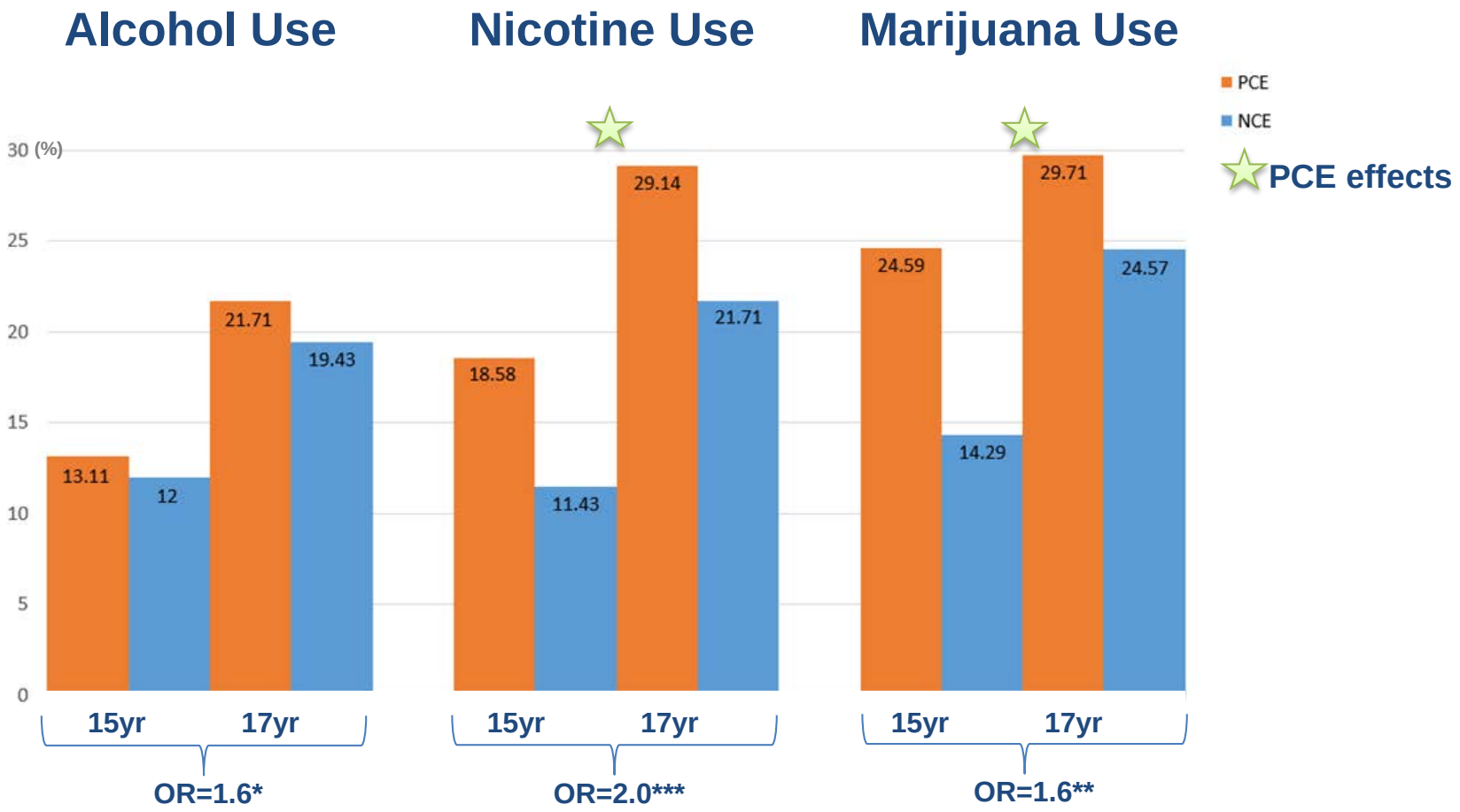
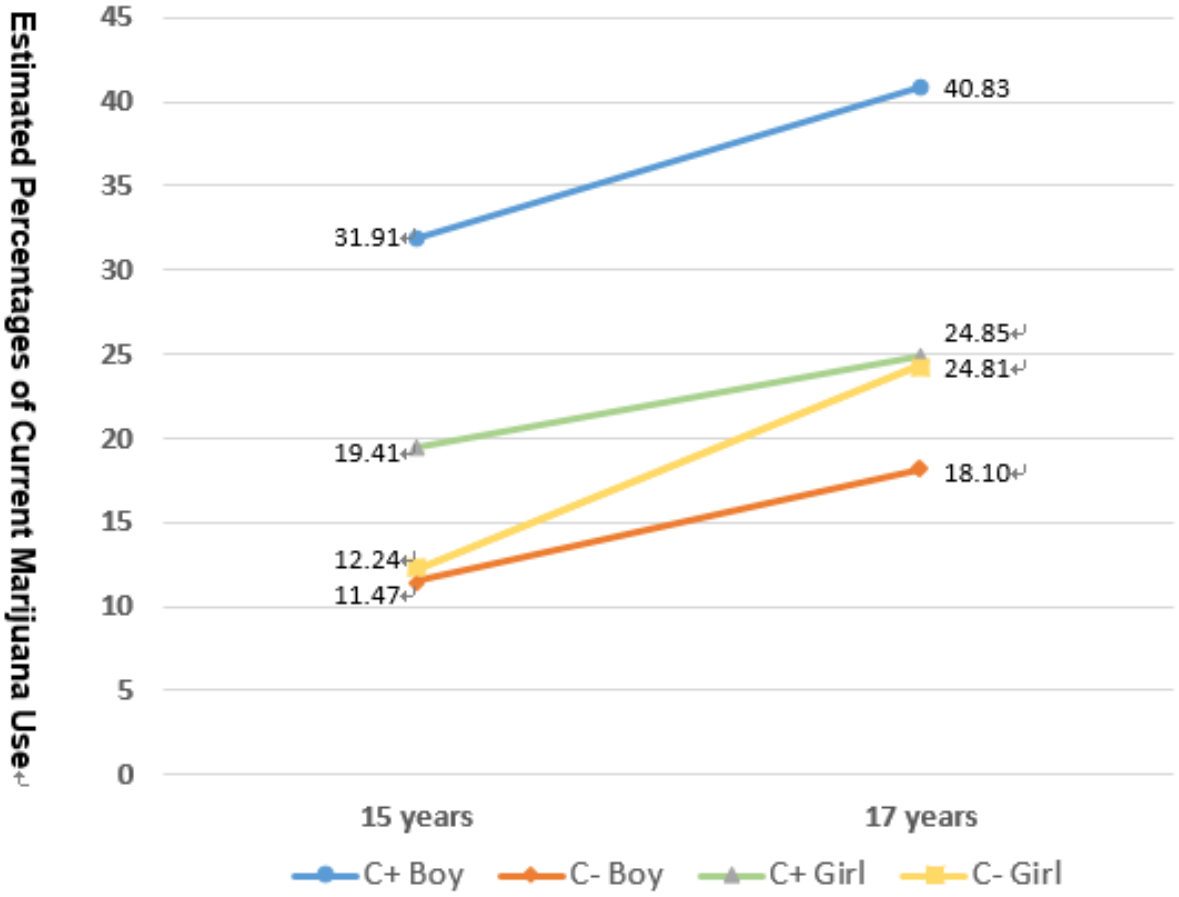
Substance Use by PCE and Age



Marijuana Use at Age 15 and 17 by PCE and Sex



- The negative effects of PCE on marijuana use were more pronounced for boys compared to girls

Adolescent Substance Use Disorder

Table 5
Adjusted association of any substance abuse/dependence at 17 years with PCE status.

	Any Substance Abuse/Dependence[a]			
	Model 1		Model 2	
	OR	95% CI	OR	95% CI
PCE	2.51*	1.00–6.28	1.83	0.71–4.70
Prenatal nicotine exposure [b]	1.52*	1.06–2.17	1.67**	1.14–2.46
Mother's age at birth	0.89**	0.82–0.96	0.89**	0.82–0.97
Marital status	4.46**	1.64–12.10	3.24*	1.14–9.24
Maternal BSI GSI at birth	1.35	0.46–3.93	0.68	0.21–2.23
HOME environment[c]	1.00	0.94–1.05	1.02	0.96–1.08
Violence exposure[d]	1.66**	1.18–2.33	1.49*	1.04–2.13
Externalizing behavior[d]			1.10***	1.05–1.16

BSI = Brief Symptom Inventory; GSI = Global Severity Index; NCE = non cocaine exposed; PCE = prenatal cocaine exposure; CI = confidence interval; OR = odds ratio.
Model 1 = base model without assessing mediating effects of 12 year externalizing behavior.
Model 2 = evaluates 12 year externalizing behavior as a mediator of PCE.

[a] Measured via self-report CDISC. Any substance includes alcohol, tobacco, marijuana, or any other illicit drug.
[b] Average number of cigarettes smoked per day.
[c] Assessed at 15 years.
[d] Assessed at 12 years.
* $p \leq .05$.
** $p \leq .01$.
*** $p \leq .001$.

- A greater number of adolescents with PCE (*n*= 31, 19%) reported abuse or dependence of any substance, including alcohol, nicotine, marijuana, and other illicit drugs, than NCE adolescents (*n*=19, 11%), although the difference was marginally significant (p = .06).
- Externalizing behavior at age 12 fully mediated the effects of prenatal cocaine exposure on any substance use disorder at age 17, supporting the Common liability model.

Sexual Risk Behaviors

Drug and Alcohol Dependence 153 (2015) 59–65

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Effects of prenatal cocaine exposure on early sexual behavior: Gender difference in externalizing behavior as a mediator

Meeyoung O. Min[a,*], Sonia Minnes[a], Adelaide Lang[a], Susan Yoon[a], Lynn T. Singer[b]

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

Pathways to adolescent sexual risk behaviors: Effects of prenatal cocaine exposure

Meeyoung O. Min[a,*], Sonia Minnes[a], Adelaide Lang[a], Jeffrey M. Albert[b], June-Yung Kim[a], Lynn T. Singer[c]

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Effects of PCE on Early Sexual Activity

	OR	95% CI	*p*
Prenatal cocaine exposure	2.24	1.22–4.09	.009
Sex, male	3.06	1.79–5.24	<.001
Prenatal alcohol exposure[a]	0.83	0.64–1.07	.14
Total HOME score	0.96	0.93–1.00	.06
Parental monitoring	0.56	0.37–0.87	.01
Violence exposure	1.52	1.18–1.95	.001

[a] Average.

- Effects of PCE on early sexual activity (sexual intercourse prior to15th birthday) was fully mediated by self-reported externalizing behavior (at age 12) in girls but not in boys, suggesting that the underlying mechanism may be gender-dependent.

Impact of PCE on Adolescent Sexual Risk Behaviors

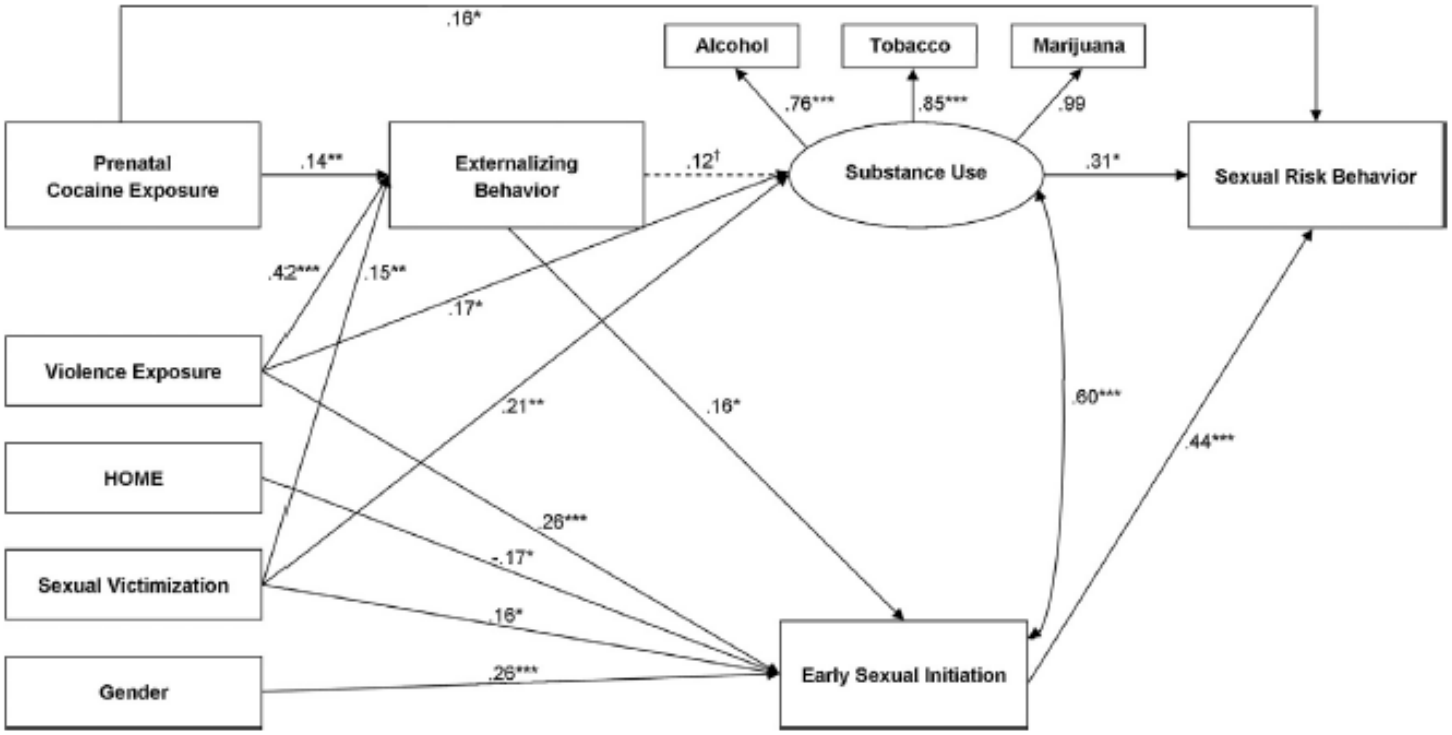

Fig. 1. The impact of prenatal cocaine exposure on adolescent sexual risk behaviors. Rectangles indicate observed variables, and oval represents latent constructs. All path coefficients are standardized. χ^2 (27) = 31.97, p = .23, CFI = .99, TLI = .99, RMSEA = .021 (90% CI = .000–.052), WRMR = .695. $^{\dagger}p \leq .10$, $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$.

Diathesis-Stress Model

- All human behaviors are phenotypes involving a complex transaction of both nature and nurture
- Biological factors often unfold in ways that are influenced by the environment
- Those with a biological vulnerability are likely to be affected adversely by effects of environmental stressors (e.g., childhood maltreatment, maternal depression)

PCE by Environment Interaction

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Full length article

Association of prenatal cocaine exposure, childhood maltreatment, and responses to stress in adolescence

Meeyoung O. Min[a,*], Sonia Minnes[a], June-Yung Kim[a], Miyoung Yoon[a], Lynn T. Singer[b]

Drug and Alcohol Dependence

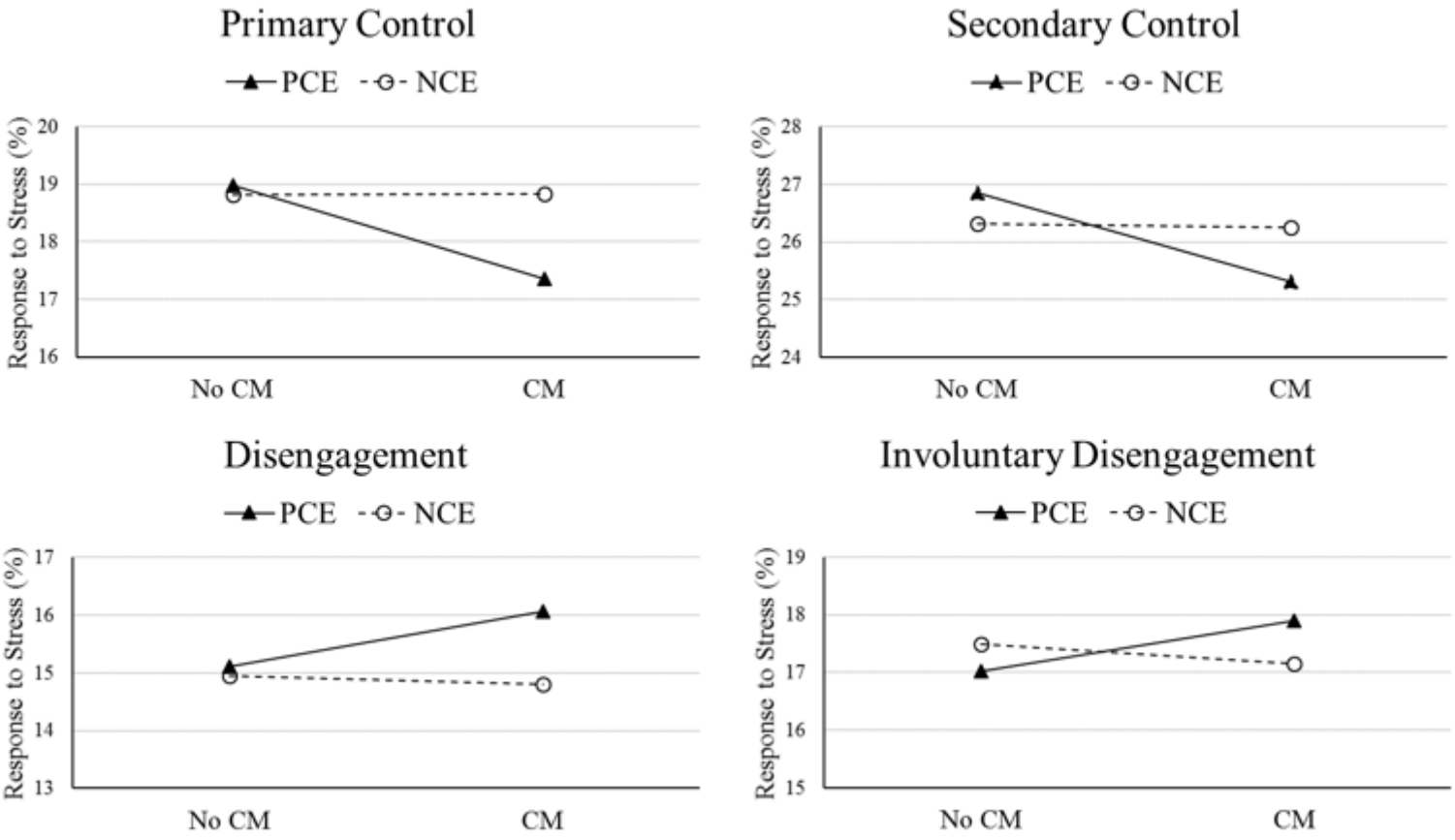
Available online 21 September 2018

In Press, Accepted Manuscript

Developmental trajectories of externalizing behavior from ages 4 to 12: Prenatal cocaine exposure and adolescent correlates

Meeyoung O. Min [a], Sonia Minnes [a], Hyungyong Park [b], Ty Ridenour [c], June-Yung Kim [a], Miyoung Yoon [a], Lynn T. Singer [d]

PCE by Maltreatment Interaction on Stress Response/Coping



Trajectories of Externalizing Behavior: Age 4-12

Elevated-Chronic (*n* = 84)

Accelerated Risk (*n* = 51)

Moderate-Decreasing (*n* = 125)

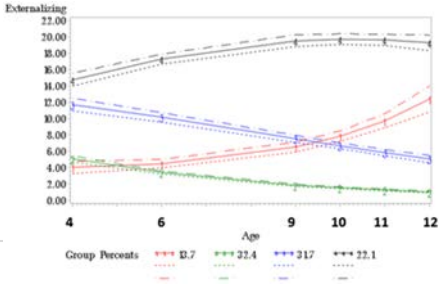
Low-Decreasing (*n* = 126)

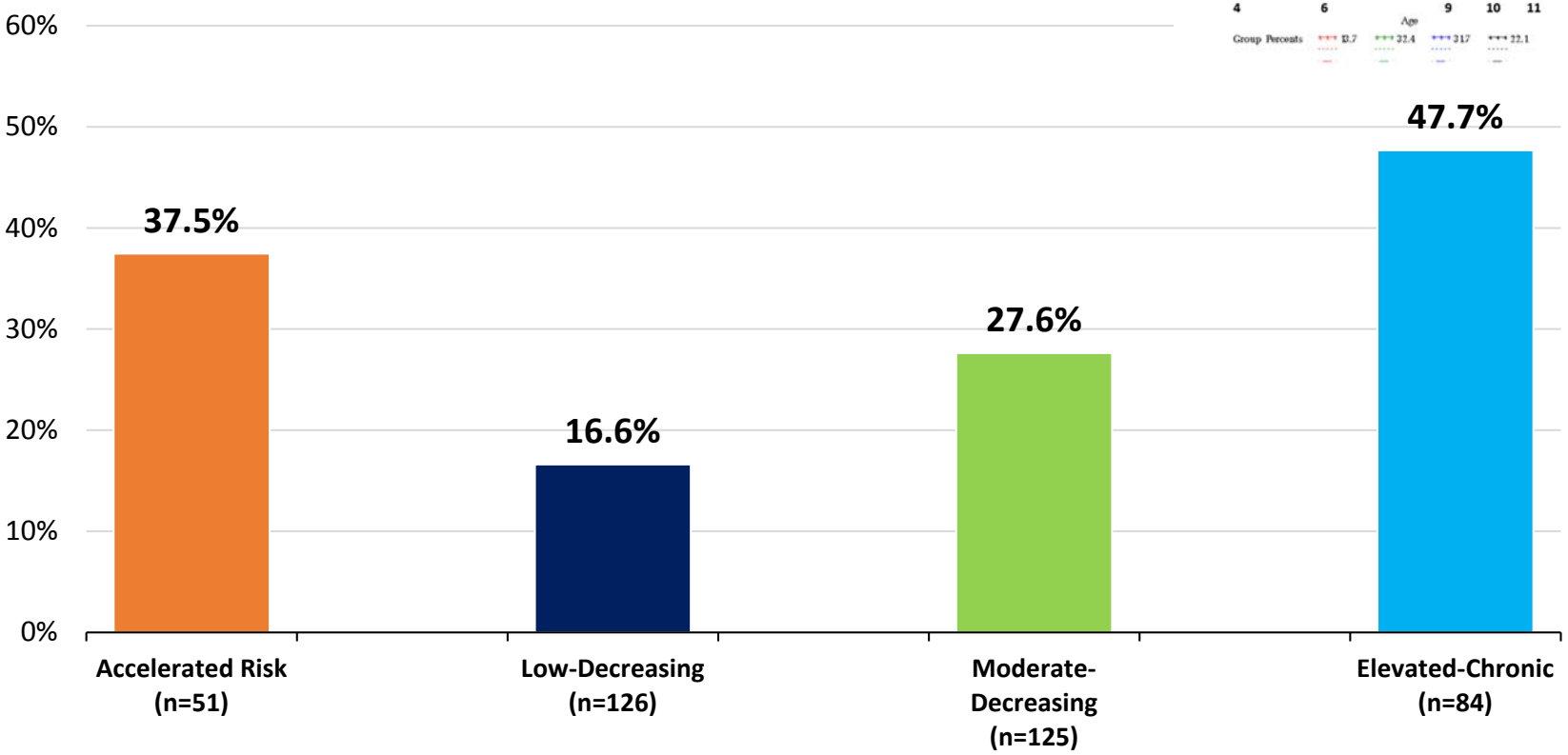
Childhood Correlates by Trajectory Membership

	G1: Accelerated Risk (*n* = 51)	G2: Low-Decreasing (*n* = 126)	G3: Moderate-Decreasing (*n* = 125)	G4: Elevated-Chronic (*n* = 84)
Parental attachment, *M (SD)*	2.14 (0.65)[ab]	**2.35 (0.56)[a]**	**2.13 (0.70)[b]**	**2.05 (0.67)[b]**
Parental monitoring, *M (SD)*	2.31 (0.71)	2.51 (0.60)	2.49 (0.59)	2.40 (0.60)
Family conflict, *M (SD)*	3.19 (2.34)[ab]	**2.21 (2.14)[a]**	**3.09 (2.63)[b]**	**3.45 (2.58)[b]**
Violence exposure, *M (SD)*	**0.97 (1.04)[b]**	**0.45 (0.71)[a]**	**0.45 (0.55)[a]**	**0.79 (0.78)[b]**
Non-kinship care, ages 4 - 12	**6 (12)[a]**	**12 (10)[a]**	**19 (15)[a]**	**30 (36)[b]**
Maltreatment, *n* (%)	**17 (38)[b]**	**19 (17)[a]**	**21 (19)[a]**	**27 (36)[b]**
Sexual victimization, *n* (%)	12 (27)[ab]	**15 (14)[a]**	**19 (17)[a]**	**24 (32)[b]**

Overall gender difference in Parental monitoring (F↑), family conflict (F↑), and violence exposure (M↑); gender difference in maltreatment in G4 (F↑; 49% vs. 25%) and sexual victimization at G2 (M↑; 9% vs. 22%); Different superscript indicates significant difference at $p < .05$

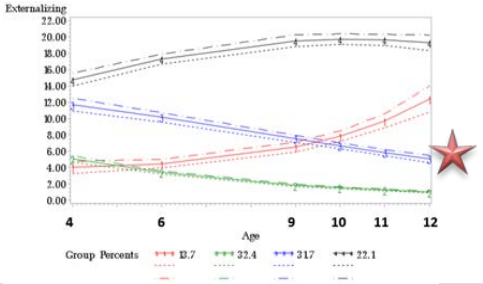
Tobacco Use at Age 15

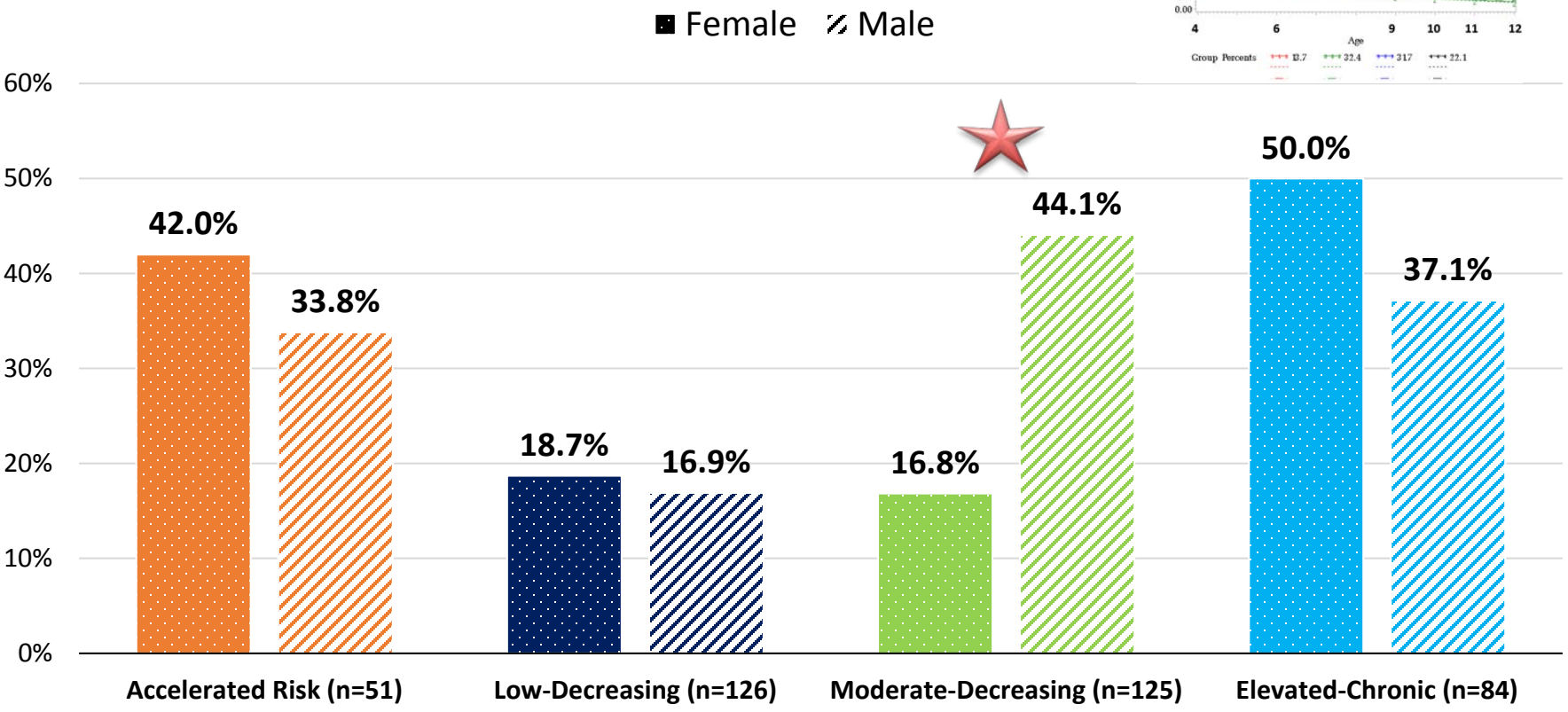




Adjusted for gender, race, family conflict, and *sexual victimization.*
G2 ≠ G1, G4; G3 ≠ G4

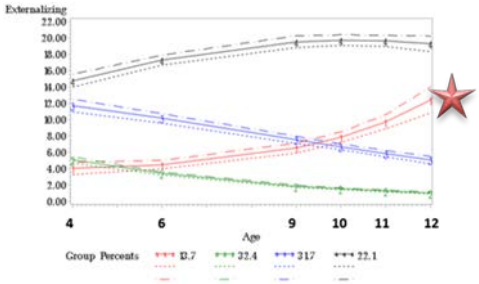
Marijuana Use at Age 15

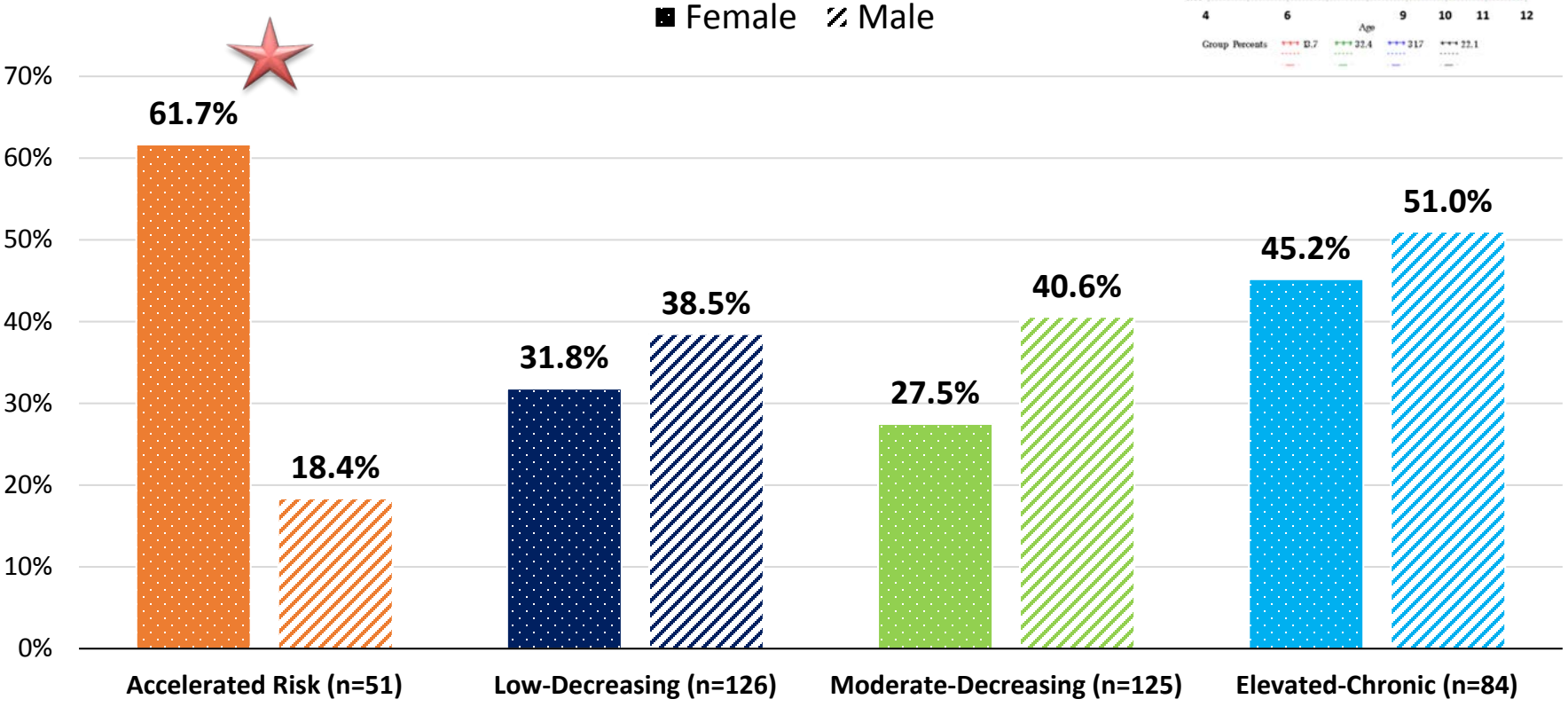




Adjusted for family conflict, *violence exposure,* and sexual victimization.
In boys, G2≠G3; In girls, G2, G3 ≠ G1, G4; Gender difference in G3

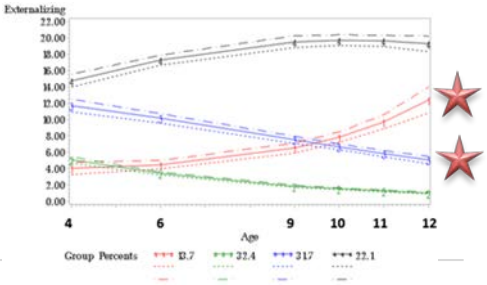
Alcohol Use at Age 15

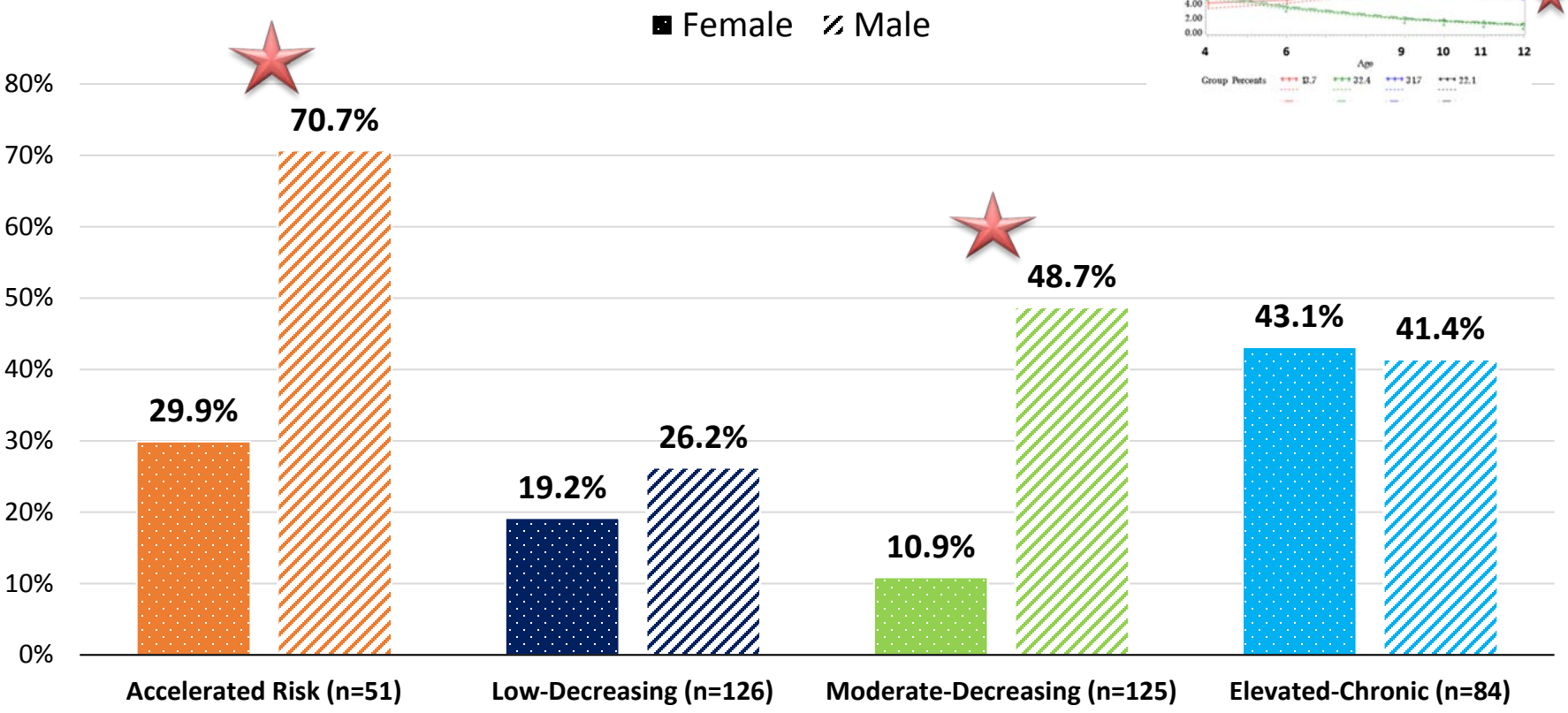




Adjusted for *race, parental monitoring,* and childhood maltreatment.
In boys, G1 ≠ G4; In girls, G1 ≠ G2, G3; Gender difference in G1

Early Sexual Behavior





Adjusted for *parental monitoring*, *violence exposure,* and sexual victimization.
In boys, G2≠G1, G3; In girls, G4≠G3; Gender difference in G1 & G3

Summary & Conclusions

- Other outcomes not highlighted in this presentation
  - Ongoing language deficits not accounted for by environment
  - Attention/Executive functioning problems
  - Lower high school graduation (76% in PCE vs. 86% in NCE, *p*=.027)
- Specific, rather than general, cognitive effects of prenatal cocaine exposure
  - Pattern of problems related to visual spatial processing, nonverbal reasoning
- Delinquency and conduct problems
- Substance use and problems related to substance use
- Gender variation

Clinical Implications

- High quality childcare for prenatally drug exposed children, especially those who remain in biologic or relative care
- Early speech assessment and intervention
- Early screening for problems of executive functioning
- Enrollment in pre-k with focus on a language rich classroom and attention to the development of EF skills

Clinical Implications

- Ongoing evaluation of family functioning, family violence, substance use, depression
- Treatment for women with psychological distress and substance use disorders
- Pre-adoption counseling
- Consider prenatally drug exposed adolescents at risk for substance use and subtle learning problems

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Questions?

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