Neurodevelopmental Outcomes of Children with Prenatal Opiate Exposure

Henrietta S. Bada, MD, MPH
Professor and Vice Chair, Academic Affairs
Department of Pediatrics
College of Medicine
University of Kentucky

Dr. Bada has no conflicts of interest
She has documented that she has nothing to disclose.

Outline

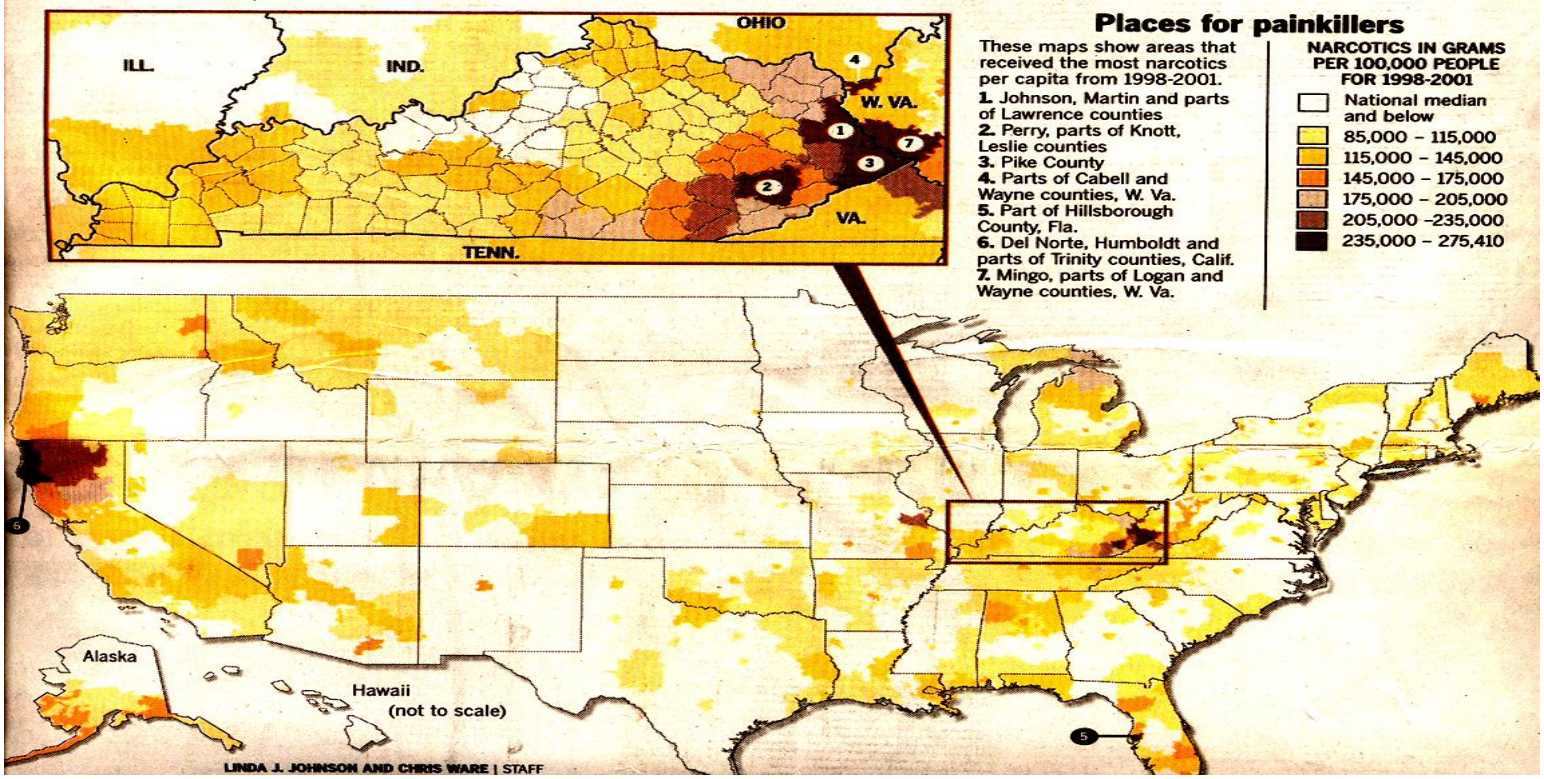
- Epidemiologic significance of NAS
- Potential factors that may affect short term and long term outcomes
- Studies of outcomes post discharge in the first few years of life
- Reported outcomes on opiate exposed children at later ages to early adolescence
- Effects of other drug exposures
- Factors that may change outcome trajectories

JANUARY 19, 2003 | SUNDAY | METRO FINAL EDITION

SPECIAL REPORT | PRESCRIPTION FOR PAIN

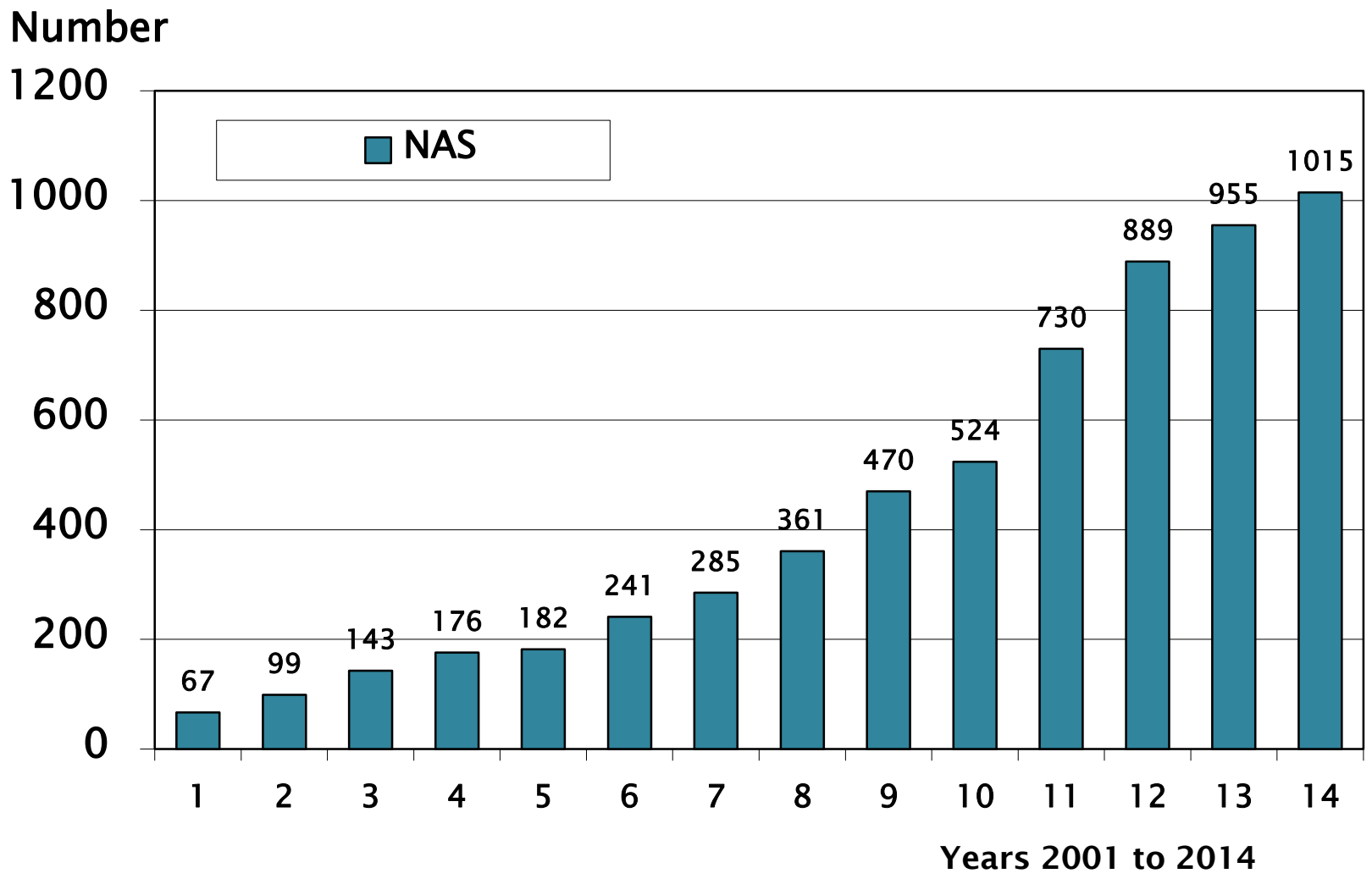
EASTERN KENTUCKY: PAINKILLER CAPITAL

INVESTIGATION REVEALS NARCOTICS FLOOD MOUNTAIN COUNTIES AT HIGHEST RATE IN NATION



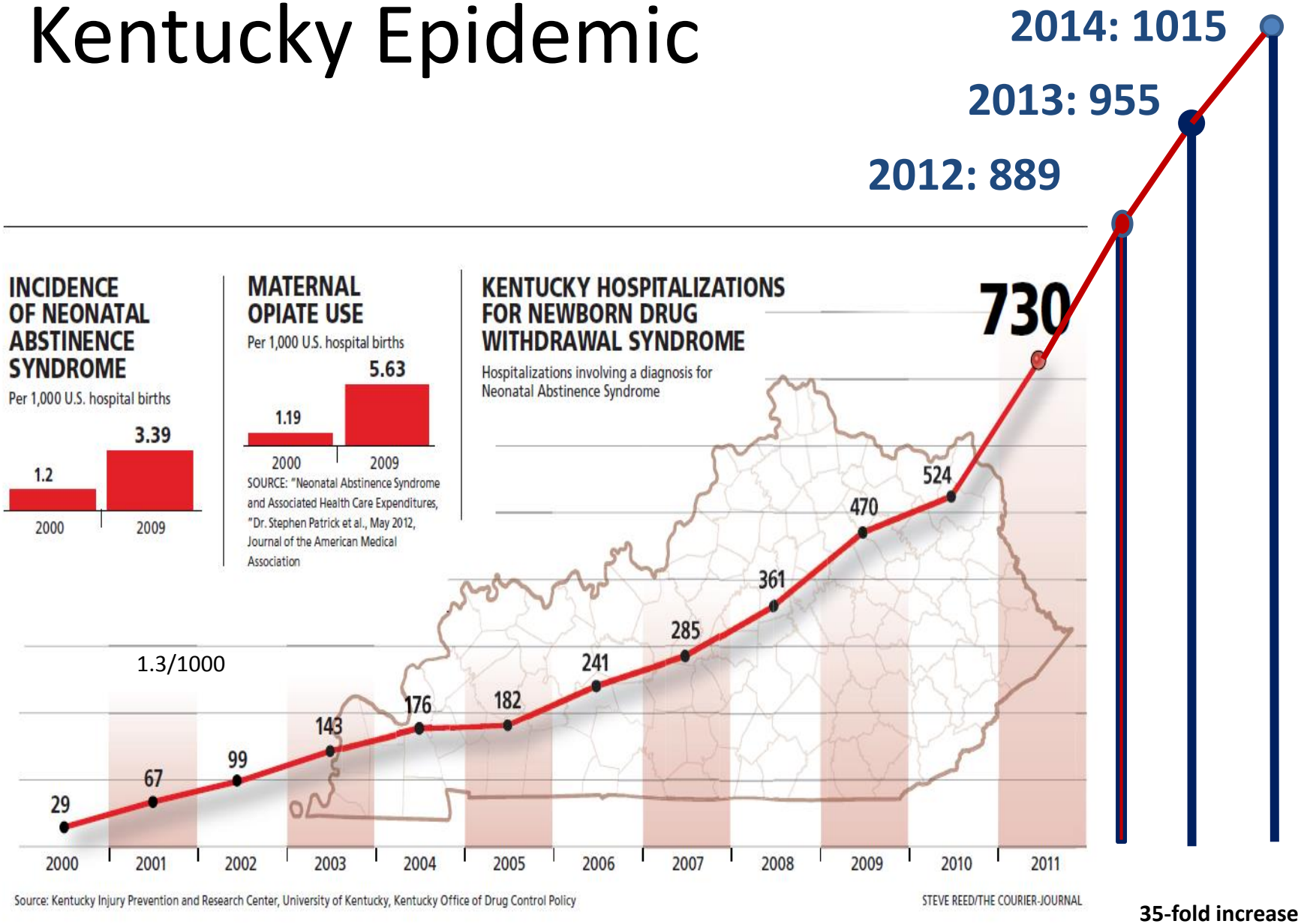
Source: Drug Enforcement Administration

NAS Hospitalizations (Kentucky Newborns)



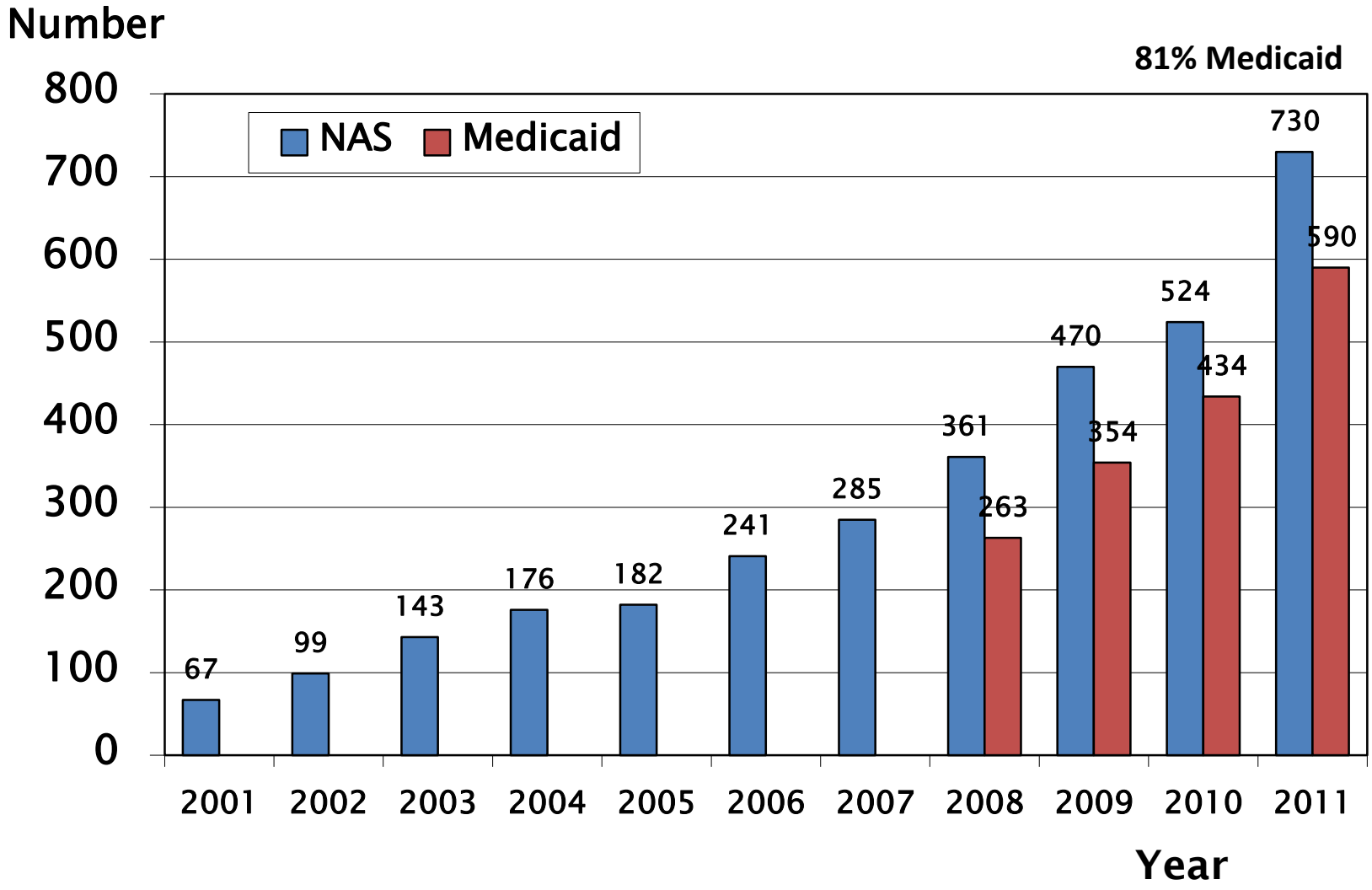
16-fold increase (from 1.3/1000 to 20.3/1000 hospital births)

Kentucky Epidemic



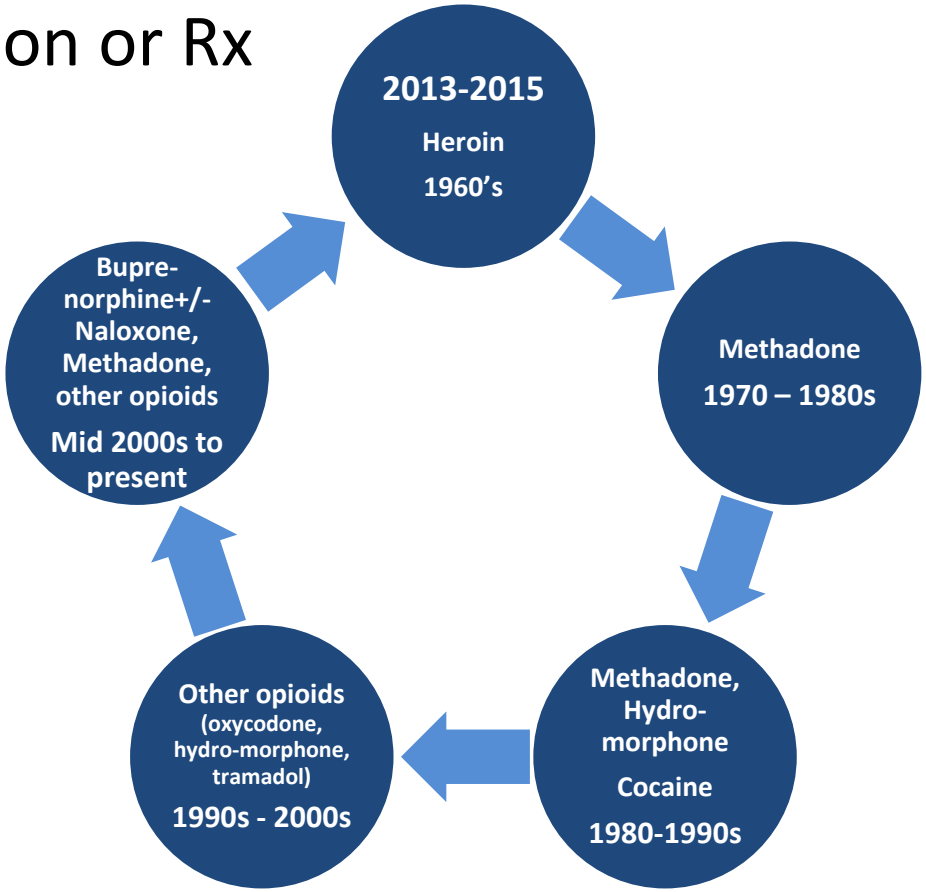
0.58/1000 → **9/1000** → **35-fold increase** **20.3/1000**

NAS Hospitalizations (Kentucky Newborns)



Neonatal Abstinence Syndrome

- NAS will not disappear
- Will only increase and or evolve from different opioid formulation or Rx



Perinatal Factors That May Affect Long-term Outcomes

- Duration of in utero drug exposure
- Dose-effect relationship
- Maternal polydrug use (legal, other Rx, illegal)
- Withdrawal symptoms versus drug effects
- Severity of withdrawal manifestations
- Continuing drug exposure from postnatal treatment
  - Type of drug, duration of postnatal treatment
- Family, environmental factors

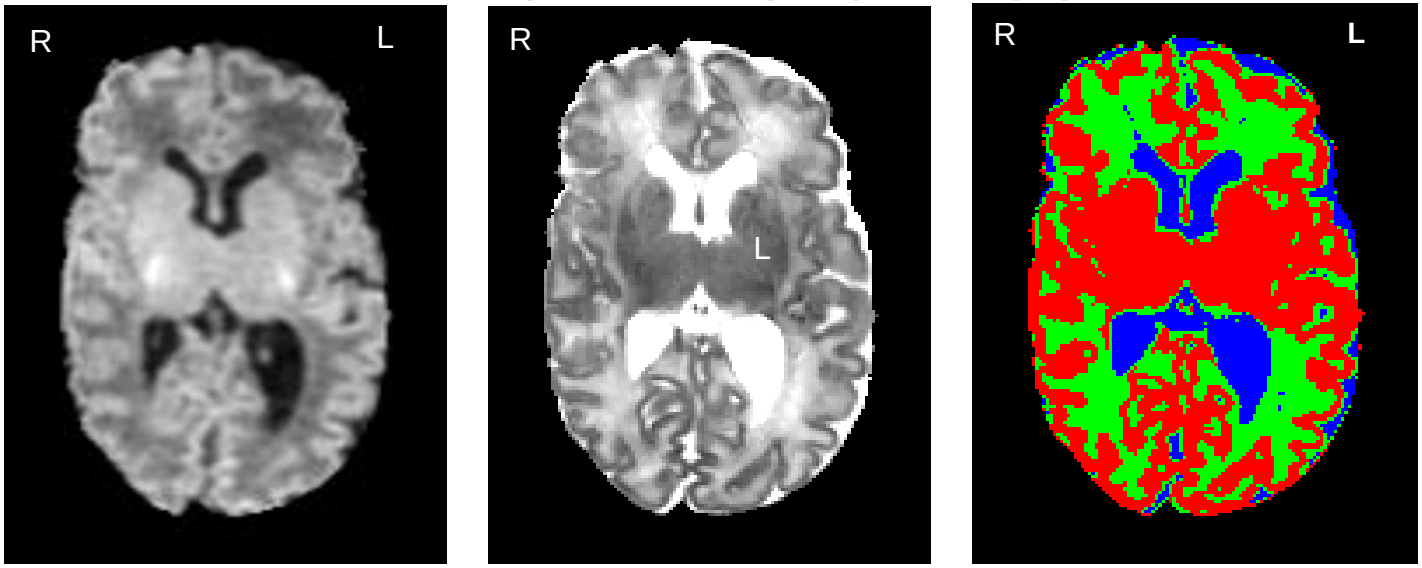
The Newborn With Prenatal drug Exposure Including Opiates

- Low birth weight
- Small head circumference
- Congenital malformations (over reported)
- Signs of drug effects
  - Abnormal tone may persist for months
- Seizures & abnormal EEG pattern; abn. sleep pattern
- Signs of **withdrawal** (drug dependency)

MRI: Brain Volumes

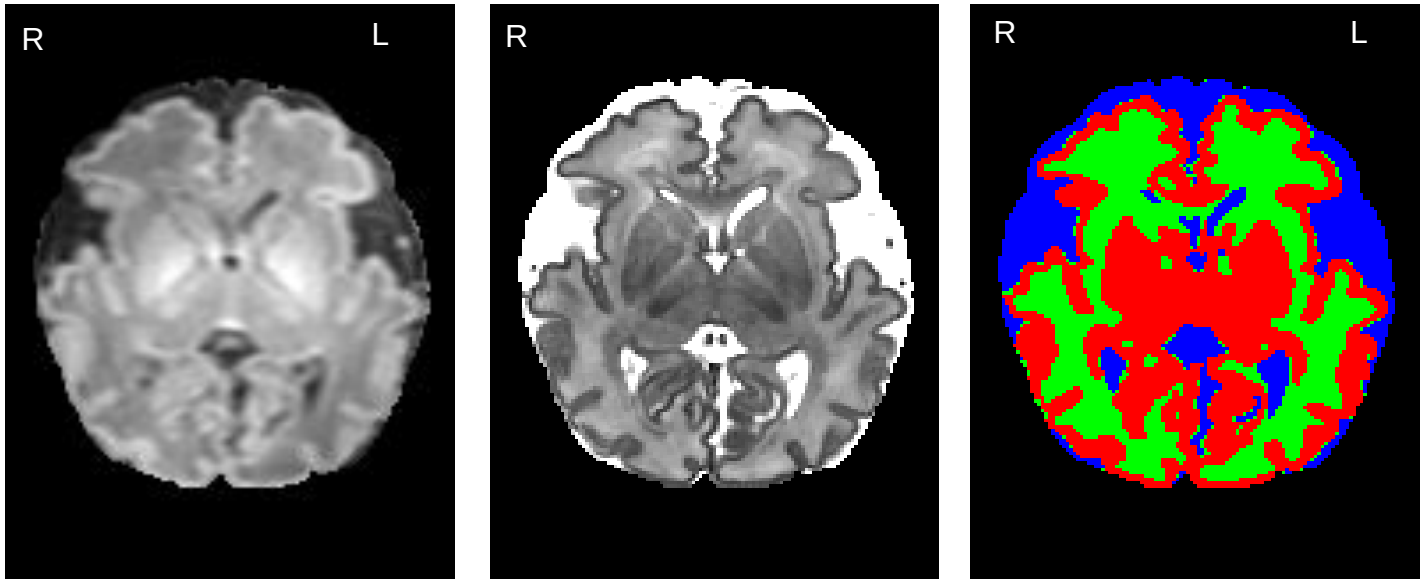
Term

No opiate exposure



Term

Lortab use during pregnancy



The Developing Brain

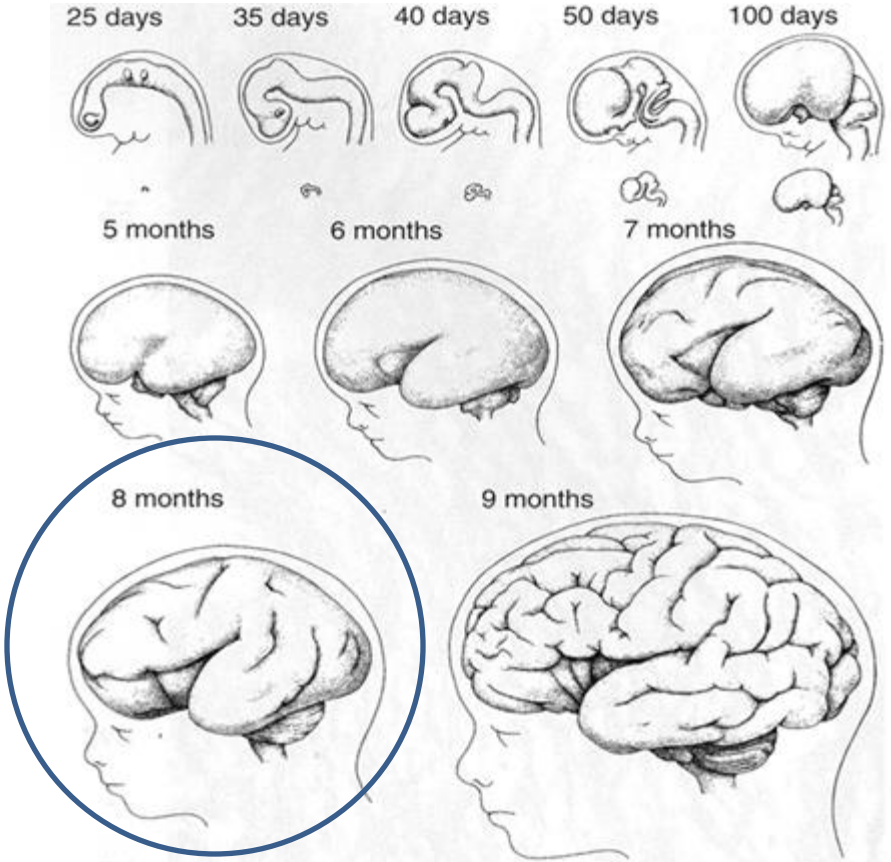
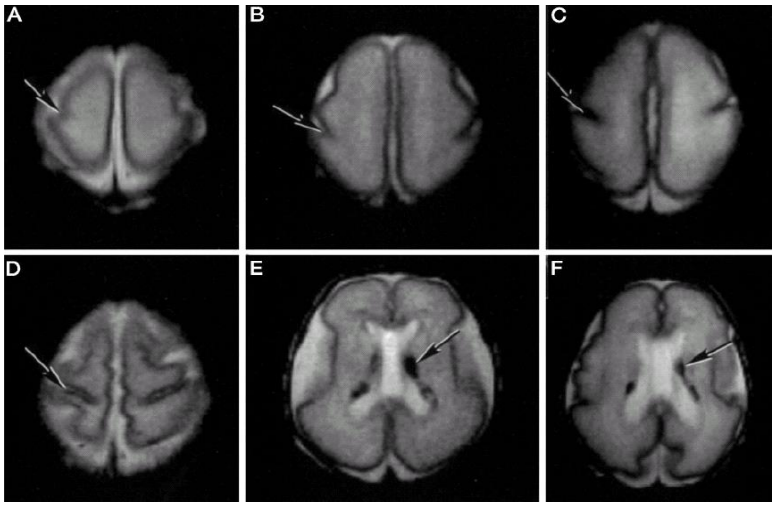


Figure 2-19 Schematic depiction of gyral development in human brain. Note the particularly prominent changes in the last 3 months of gestation. (From Cowan WM: *Sci Am* 241:113, 1979.)



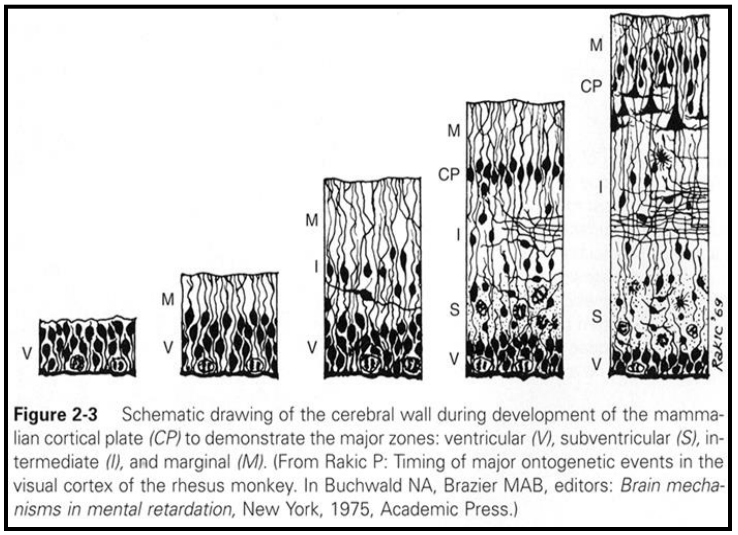
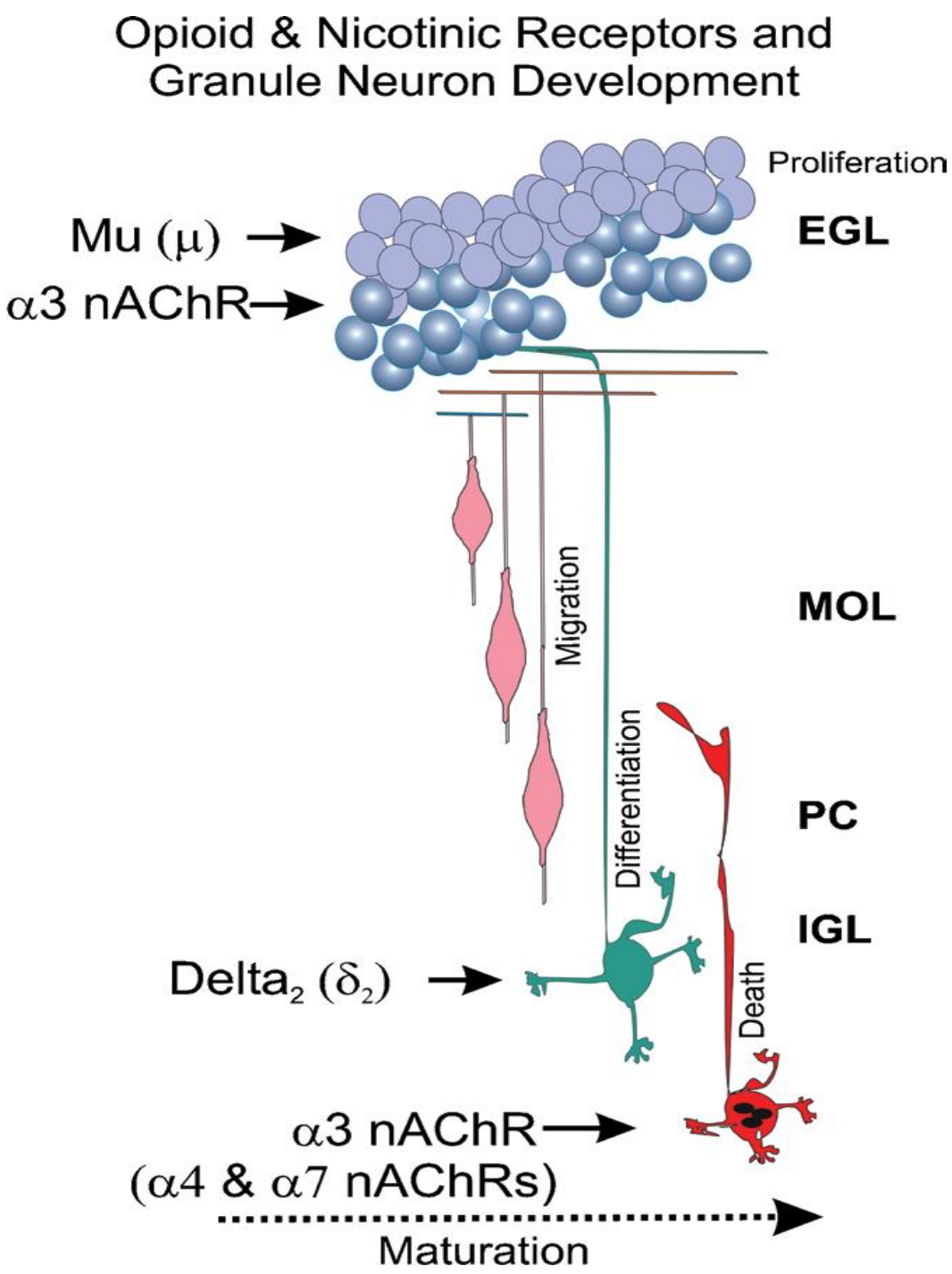


Figure 2-3 Schematic drawing of the cerebral wall during development of the mammalian cortical plate *(CP)* to demonstrate the major zones: ventricular *(V)*, subventricular *(S)*, intermediate *(I)*, and marginal *(M)*. (From Rakic P: Timing of major ontogenetic events in the visual cortex of the rhesus monkey. In Buchwald NA, Brazier MAB, editors: *Brain mechanisms in mental retardation*, New York, 1975, Academic Press.)

Prenatal Exposure & Brain Development

- **All legal and illegal drugs will affect brain development; effects dependent on stage of gestation the fetus had drug exposure**
- **Various stages of brain development**
  - **Dorsal induction (3-4 weeks)**
  - **Ventral induction (5-6 weeks)**
  - **Neuronal proliferation (2–4 months)**
  - **Migration (3-5 months)**
  - **Organization (6 months – years postnatal)**
  - **Myelination (birth to years postnatal)**



Opioid and nicotine actions during granule cell development

EGL – external granular layer

MOL- molecular cell

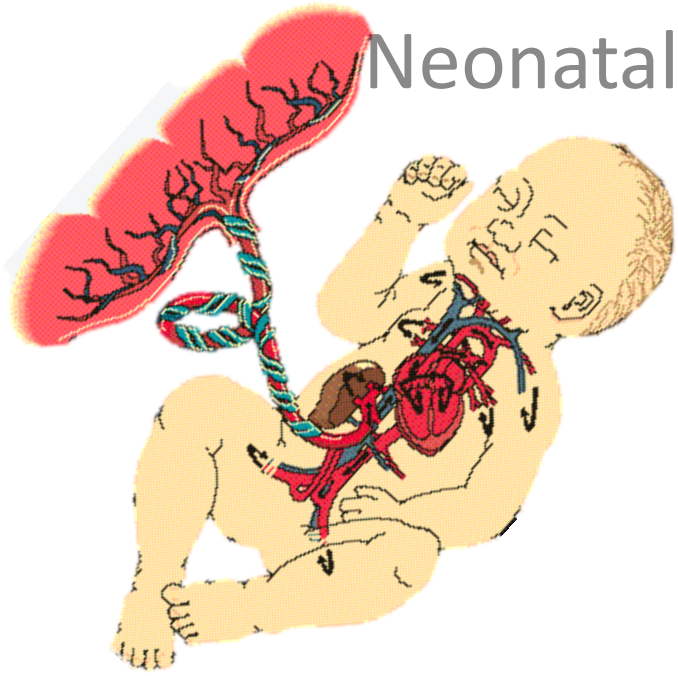
IGL – Internal granule layer

PG - purkinje cell

Hauser et al.
The Cerebellum 2003

Opiate Exposure Effects

Neonatal Abstinence Syndrome



Prenatal Exposure & Brain Development

- Behavior Teratology Framework: **Vulnerability of the CNS to injury extends beyond fetal, neonatal, and infancy stage**
    - Most frequent manifestations of injury to the developing CNS do not result in nervous system malformations but in **functional abnormalities that may not be detected at birth but later in childhood, adolescence, or adulthood.**

- Related to Barker hypothesis: Any perturbation during fetal development may have enduring effects on later behavior.

Maternal and Family Factors

- **Maternal age**
- **Co-morbidities (psychological/psychiatric disorders)**
  - **Depression, anxiety disorders, PTSD, etc.**
- **Pregnancy complications**
- **Sexually transmitted diseases (increasing prevalence of Hepatitis C)**
- **Hospitalizations (due to violence)**
- **Parenting**
- **High-risk lifestyle**
- **CPS reporting and involvement**
- **Discharge placement: biological parent, kinship care, non-kinship care**

Significant Maternal Conditions

Conditions	Exposed % (n=1185)	Non-Exposed % (n=7442)	Adjusted Odds Ratios 95% CI
Hepatitis	2.9	0.6	4.8 (2.6-8.9)
HIV tested	31.4	27.7	1.1 (1.0-1.4)
Positive HIV	12.0	1.9	8.2 (4.3-15.4)
AIDS	0.9	0.1	19.5 (4.1-91.6)
Syphilis	11.3	1.5	6.7 (4.8-9.6)
Gonorrhea	4.5	1.8	1.9 (1.3-3.0)
Chr Hypertension	3.9	2.6	1.3 (0.9-2.1)
Psych/Nervous Dis	2.4	1.0	4.0 (2.2-7.4)

Bauer CR et al. Am J Obstet Gynecol 2002

Significant Pregnancy/labor Characteristics

Characteristics	Exposed % (n=1185)	Non-Exposed % (n=7442)	Adjusted Odds Ratios (95% CI)
Hospitalizations	11.5	10.8	1.08 (0.89-1.3)
Hospitalizations due to violence	0.7	0.0	16.9 (6.4-44.6)
Hospitalizations due to detox	1.2	0.0	29.6 (13.00-66.5)
Medications during pregnancy	59.9	71.0	0.6 (0.5-0.7)

Bauer CR et al. Am J Obstet Gynecol 2002

Living Situation At Discharge

	Cocaine (n=717)	No Cocaine (n=7442)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
CPS report/referral	275 (38.5%)	74 (1.0%)	62.18 (43.37-89.15)	42.98 (28.77-83.20)
Discharge with biological mother	570 (81.2%)	7350 (99%)	0.04 (0.03-0.06)	0.05 (0.03-0.10)
Home with bio father	6	15	0.17(0.05-0.63)	0.09 (0.01-0.88)
Home with other relative	38	14	1.57 (0.63-3.93)	n.s.
Foster or pre-adoptive family	61	36	0.78 (0.36-1.67)	n.s.
Congregate facility	28	2	8.93(1.30-61.41)	9.69 (1.37-68.65)
Mother wishes for child adoption	15	26	6.10 (2.63-14.16)	5.65 (1.72-18.53)

Bauer CR et al. Arch Pediatr Adolesc Med 2005

Table 2 Number of Children by Each Type of Living Arrangement for Each Visit from Discharge

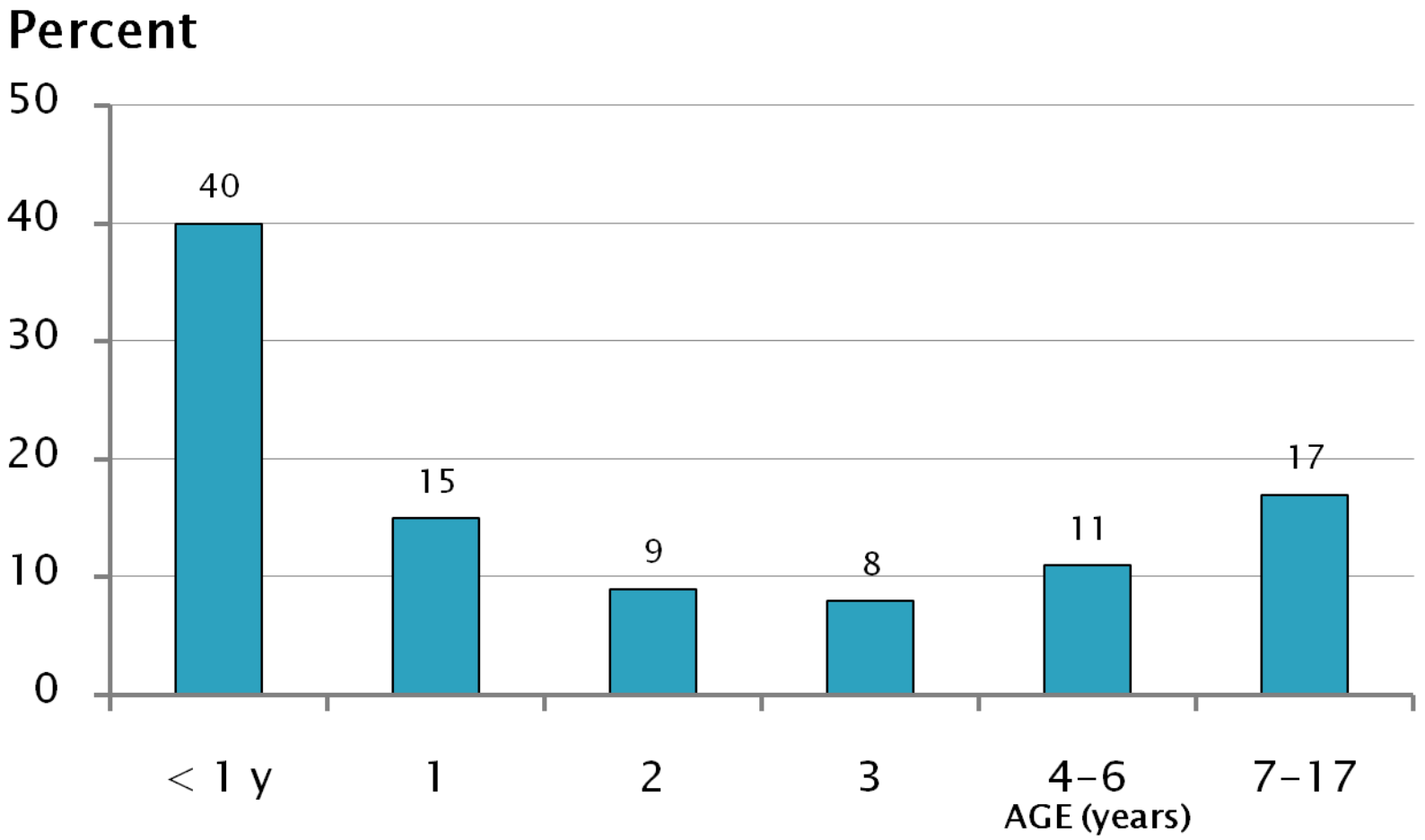
Living Situation	Discharge	12 Months	24 Months	36 Months
Biological mother	1262	1195	1155	1118
Subsequently left this arrangement to others	94	59	55	
Entered from other arrangements		32	22	19
No. who died		5	3	1
Biological father, mother not in the home	5	22	37	38
Subsequently left this arrangement to others	3	5	13	
Entered from other arrangements		20	20	14
Grandparent(s)	35	46	54	72
Subsequently left this arrangement to others	21	9	13	
Entered from other arrangements		32	17	31
Other relatives	1	44	50	56
Subsequently left this arrangement to others	0	12	11	
Entered from other arrangements		43	18	17
Nonrelative foster care	67	71	80	87
Subsequently left this arrangement to others	26	8	7	
Entered from other arrangements		31	17	15
No. who died		1		1
Institution/group home	17	3	2	5
Subsequently left this arrangement to others	17	1	0	
Entered from other arrangements		3	0	3

For each living arrangement, the number of children who left and the number who entered that specific arrangement since previous visit are shown.

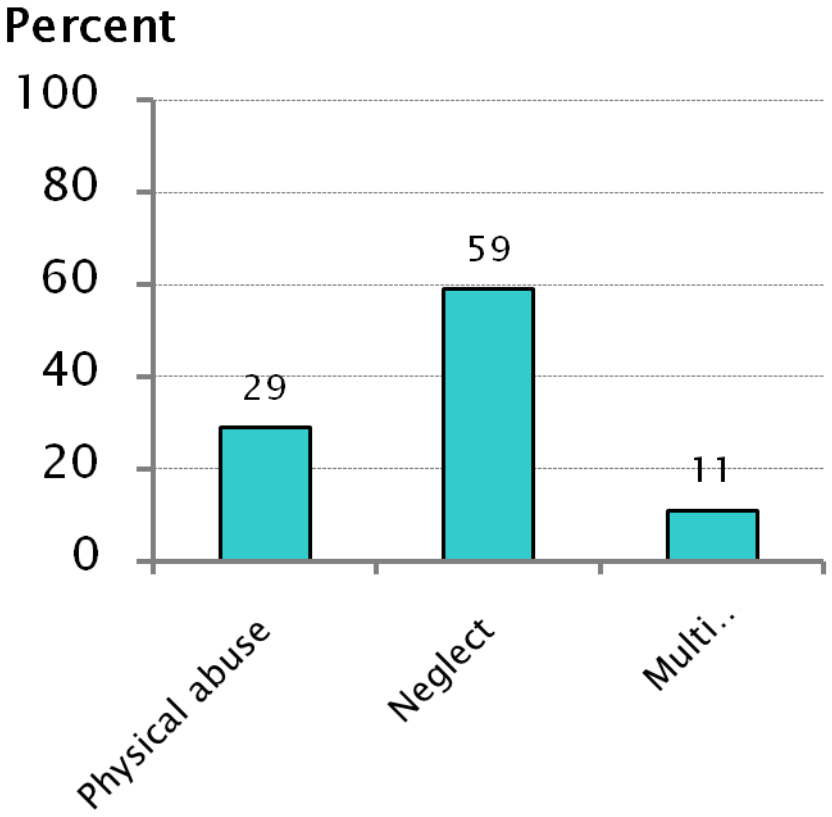
Bada H et al. J Dev Behav Pediatr 2005

POST DISCHARGE OUTCOMES

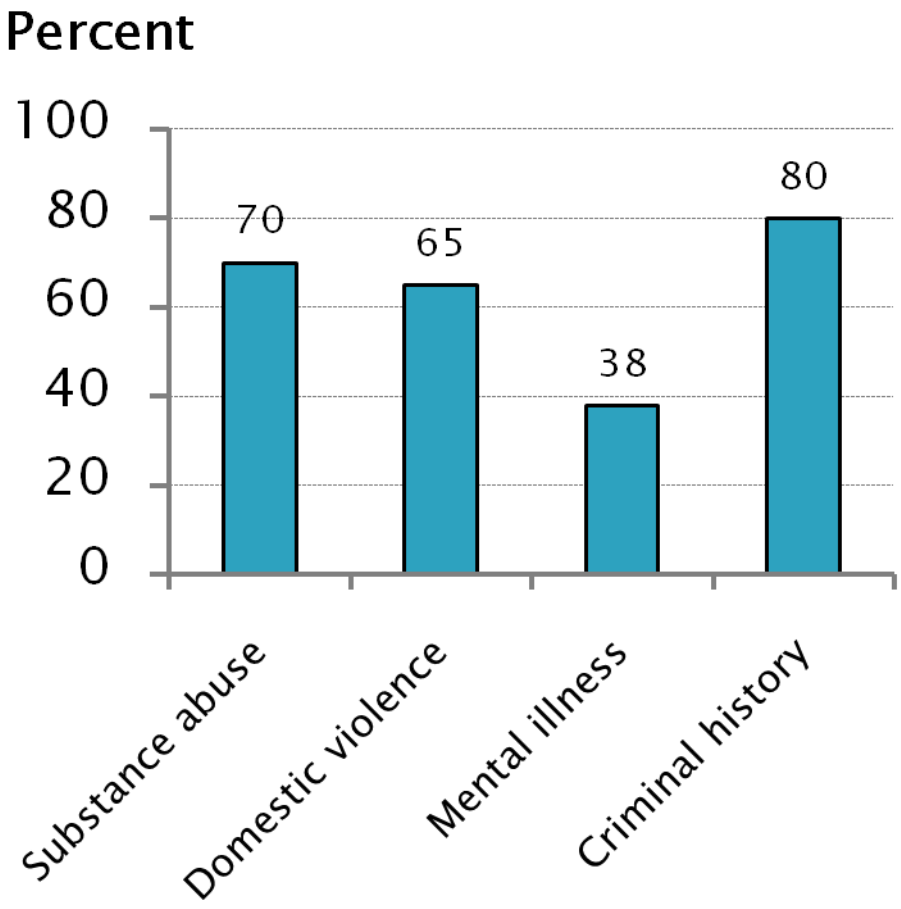
Age of Child (Fatalities/Near Fatalities (KY 2006 -2010)



Child Fatalities/Near Fatalities (KY 2006-2010)

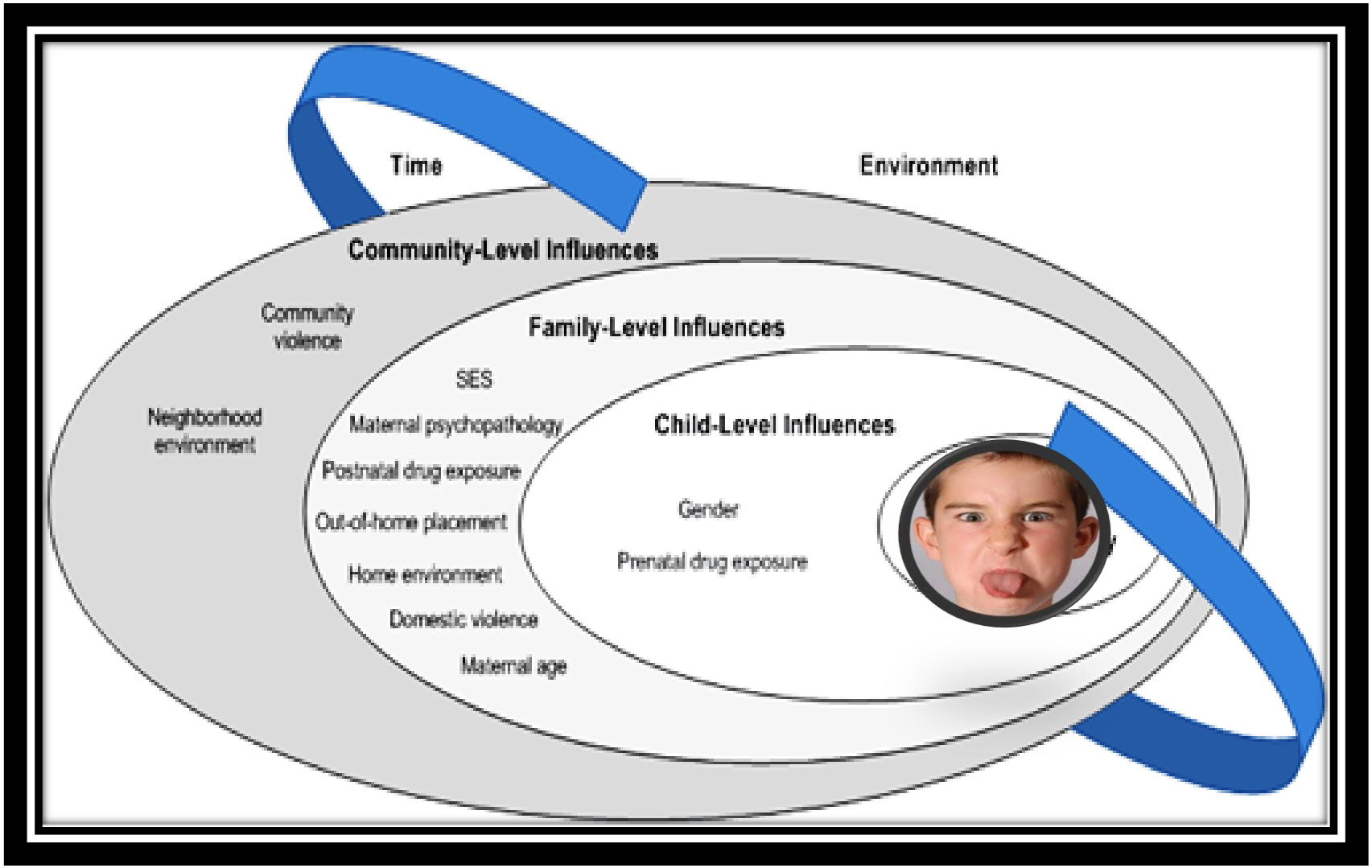


Categories of maltreatment



Risk factors in fatalities/near fatalities

Complexity in Outcomes: Influence of Cumulative Risks



Individual, Maternal, and Family Factors

- **Polydrug or Other Drug Use (rarely single drug use) affecting fetal brain development**
- **Maternal, family/caretaker, and community have influences on child development.**

Early Childhood Outcomes of Opiate-exposed Children

OUTCOME IN THE FIRST YEAR

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

Strauss ME, Ostrea EM, Stryker, JC (n=113; 53/113 “addicted”)

Outcome categories 1 year*	Opiate-exposed n=25	Not opiate-exposed n=26	p value
Mental Developmental Index (MDI)	**113.4 (10.2)**	**114.8 (11.3)**	**n.s.**
Psychomotor Developmental Index (PDI)	**102.8 (11.0)**	**110.4 (9.7)**	**<0.01**
% growth retardation Weight/Height/Head Circ	**14/52/21**	**4/27/22**	**<0.01**

* Attrition issues: unable to track, incarceration, refuse to return, etc.

J Pediatr 1976; 89 (5): 842-846

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

Wilson GS, Desmond MM, Wait RB (n=125; no Rx – 29; methadone Rx-39; controls-57)

Outcome at 1 year	Opiate-exposed; No Rx (n=29)	Methadone Rx (n=35)	Drug free (n=55)
Mental Developmental Index (MDI)	**97.2 (17.6)**	**99.3 (15.5)**	**105.5 (15.6)**
Psychomotor Developmental Index (PDI)	**92.2 (19.2)***	**89.9 (12.6)***	**99.0 (14.5)**
Poor Fine Motor	**75%***	**82%***	**50%**
Short attention span	**29%***	**24%****	**7%**

J Pediatr 1981; 98(5): 716-722

*p<0.05 Compared to controls
**p<0.01 compared to controls

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

Bunikowski R et al. (One year follow-up)

(n=34 Opiate exposed, all smoked; 42 nicotine for exposure)

Measures*	Opiate-exposed n=27	Not opiate-exposed n=42	p value
Griffiths Developmental Quotient: Average	**100.5 (9.3)**	**107.9 (17.2)**	**<0.05**
Locomotor	**100.8 (13.6)**	**111.4 (16.9)**	**<0.05**
Personal/social	**104.1 (10.9)**	**107.3 (9.2)**	**n.s.**
Hearing & speech	**97.0 (8.6)**	**98.8 (9.1)**	**n.s.**
Hand & eye	**100.7 (10.9)**	**105.6 (9.7)**	**n.s.**
Intellectual performance	**100.5 (9.3)**	**107.9 (17.2)**	**<0.05**

* 7 with questionnaire, no visit

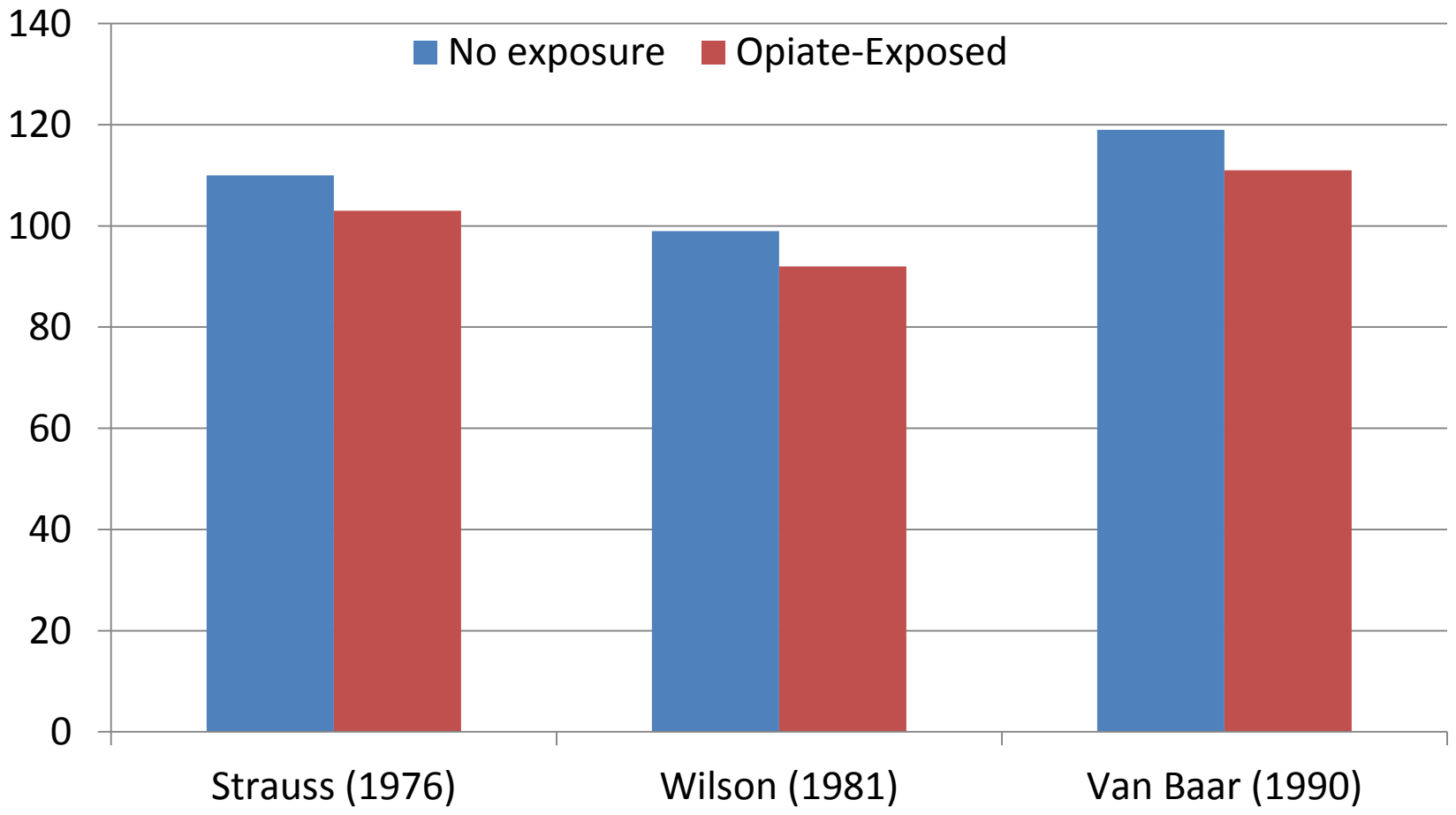
Eur J Pediatr 1998 157:724-730

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

- Van Baar, A (1990)
- 35 Exposed infants (1983-1985); 26/35 term with follow-up
- Methadone, heroin +/-cocaine and other drugs (30% used methadone only in the 3rd trimester)
- 37 comparison infants
- Bayley Scales 6 and 12months
- Control for gestation in the analysis

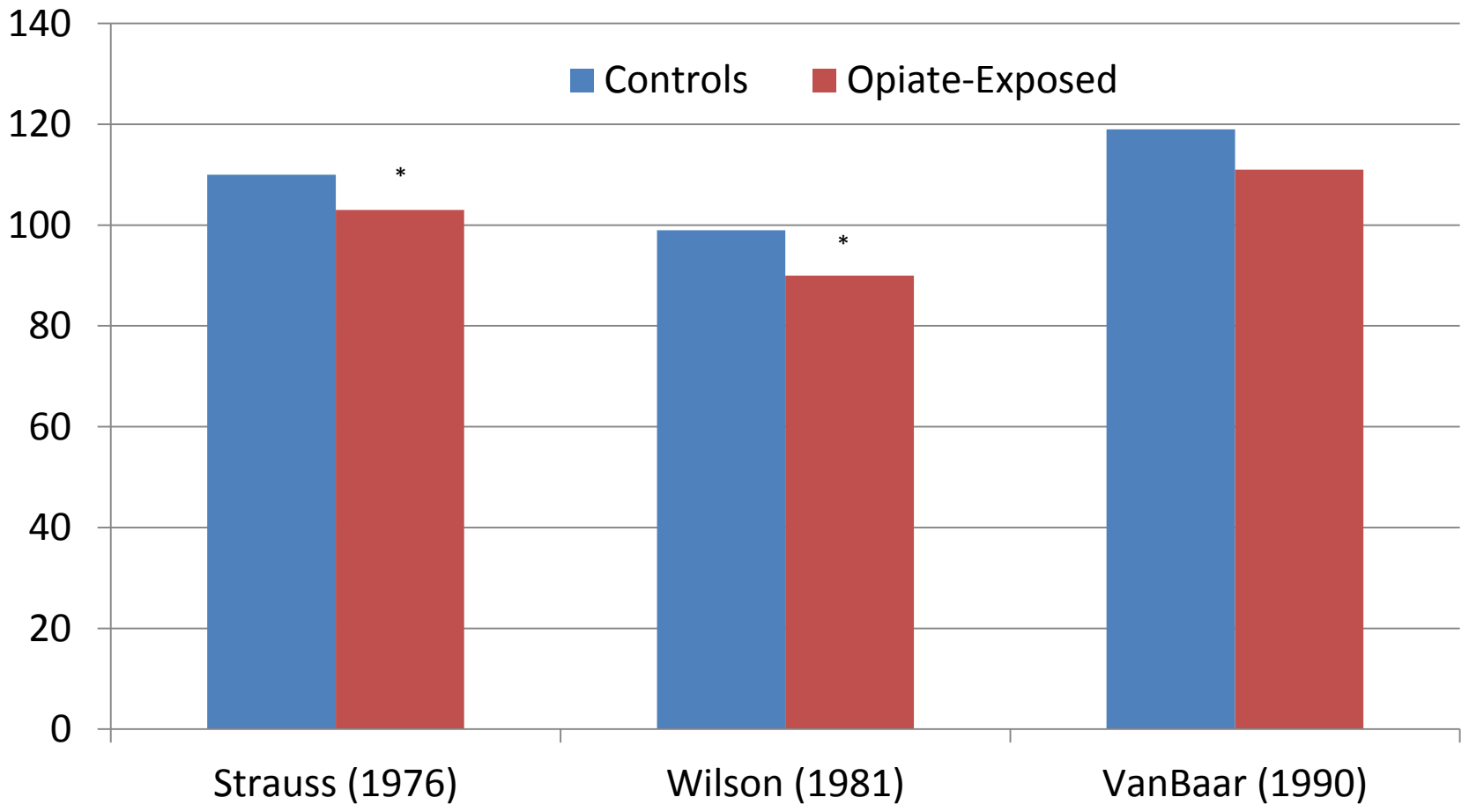
Van Baar A, *J Child Psychol Psychiat* 1990; 31(6): 911-920

Mental Developmental Index at 1 Year



One Year: No significant difference between exposed and non-exposed

Psychomotor Development at 1 Year



*p<0.05

Long Term Follow-up of Opiate Exposed Children

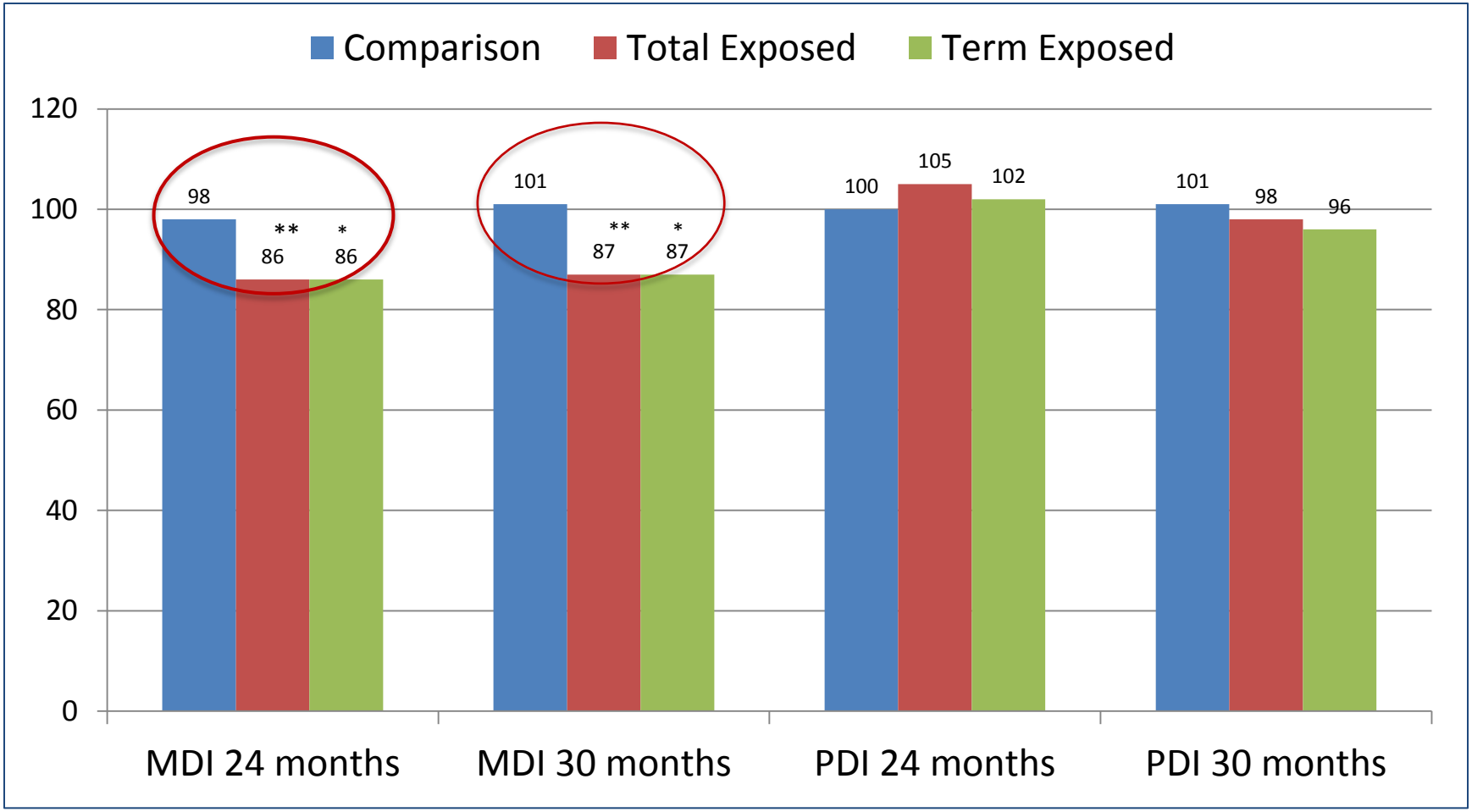
OUTCOMES: AGE 2-3 YEARS

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

- Van Baar, A (1990)
- 35 Exposed infants (1983-1985); 26/35 term with follow-up
- Methadone, heroin +/-cocaine and other drugs (30% used methadone only in the 3rd trimester)
- 37 comparison infants
- Bayley Scales 18, 24, and 30 months
- Control for gestation in the analysis

Van Baar A, *J Child Psychol Psychiat* 1990; 31(6): 911-920

2 – 3 Year Outcomes Of Infants Exposed to Opiate In-utero (MDI and PDI)



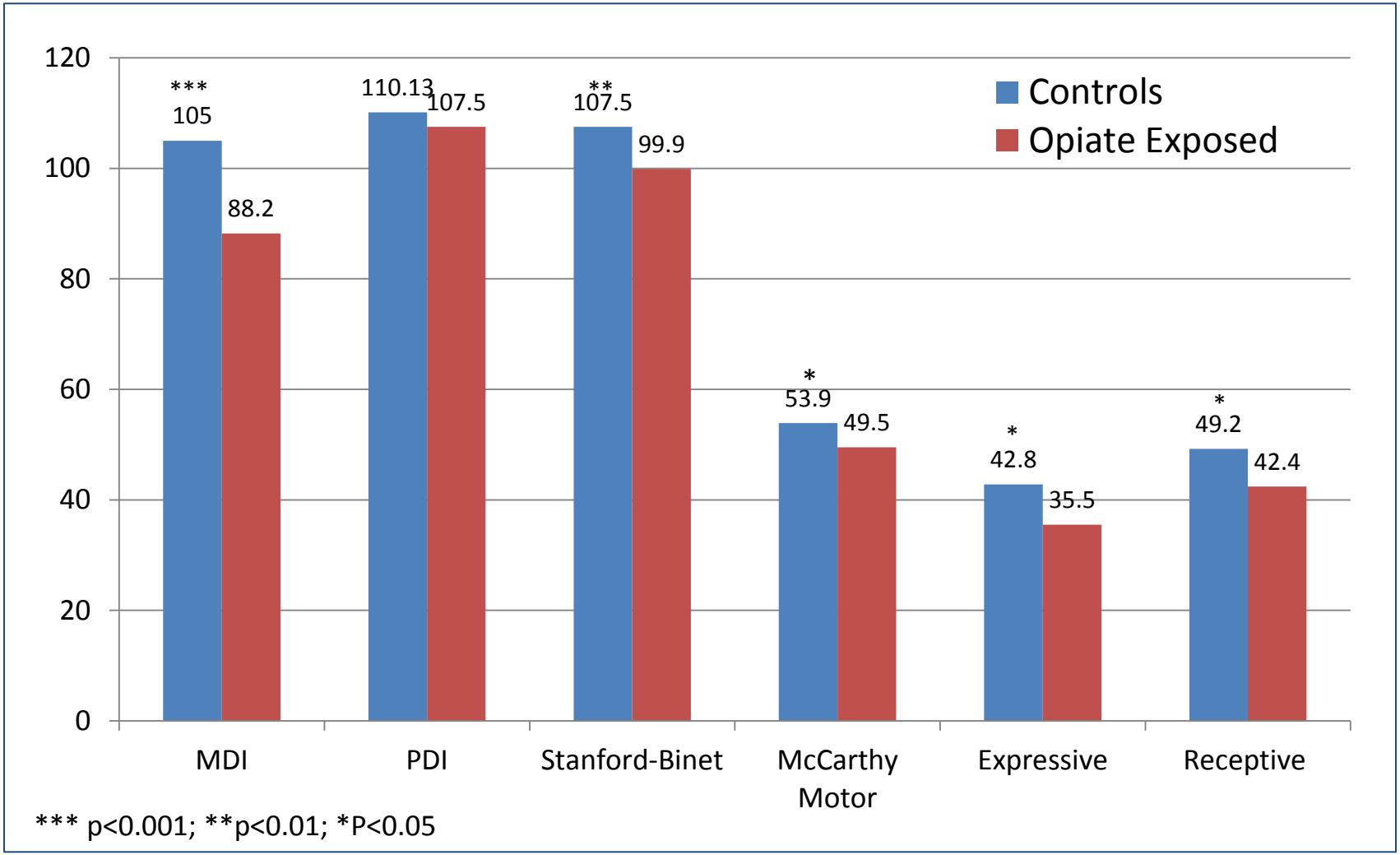
van Baar A, *J Child Psychol Psychiat* 1990; 31(6): 911-920

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

- **Hunt et al, 2008** (**133** cases/**103** controls)
- Cases: mothers compliant with methadone program
- Controls: negative for drug use history and drug screen
- Follow-up at 18 months and 36 months

Early Human Development 2008; 84:29-35

Outcomes of Exposed Versus Controls



Hunt et al. *Early Human Dev* 2008 ; 84:29-35

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

Hunt et al. 2008 (133 cases/103 controls)

Measures at 3 years	Opiate- exposed	Controls
IQ	99.9 (15.1) ↓	107.5 (13.4)
Motor (McCarthy)*	49.5 (8.7) ↓	53.9 (8.3)
Expressive Language*	35.5 (7.9) ↓	42.8 (12.6)
Receptive Language*	42.4 (11.6) ↓	49.2 (11.4)

* Results expressed as T scores

Early Human Development 2008; 84:29-35

Long Term Follow-up of Opiate Exposed Children

SUMMARY OF OUTCOMES: AGE 2-3 YEARS

Significantly Lower Cognitive Abilities

Low MDI or Low IQ

Poor Language Development

Long Term Follow-up of Opiate Exposed Children

OUTCOMES AFTER AGE 3 YEARS

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

Olofsson et al. 1983

- N=89 (methadone, morphine, heroin)
- 72/89 with follow-up 1-10 years
- 25% normal physical, mental, and behavior
- **56%: hyperactive, aggressive, with lack of concentration and social inhibition**
- 10% severe psychomotor impairment
- 11% moderate psychomotor impairment
- 5 depravation syndrome; 2 spastic tetraplegia, 1 rubella syndrome

Acta Paediatr Scand 72:407-410, 1983

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

Olofsson et al. 1983

- N=89
- 72/89 with follow-up 1-10 years
- 43% removed from the home
- Average environment change: 6/child; maximum 30
- Average change in caregiver: 5/child; maximum 11

"These findings indicate that there is an urgent need for politicians, social welfare and health personnel to reexamine their roles in helping these children, who will otherwise develop into a new generation of social losers."

Acta Paediatr Scand 72:407-410, 1983

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

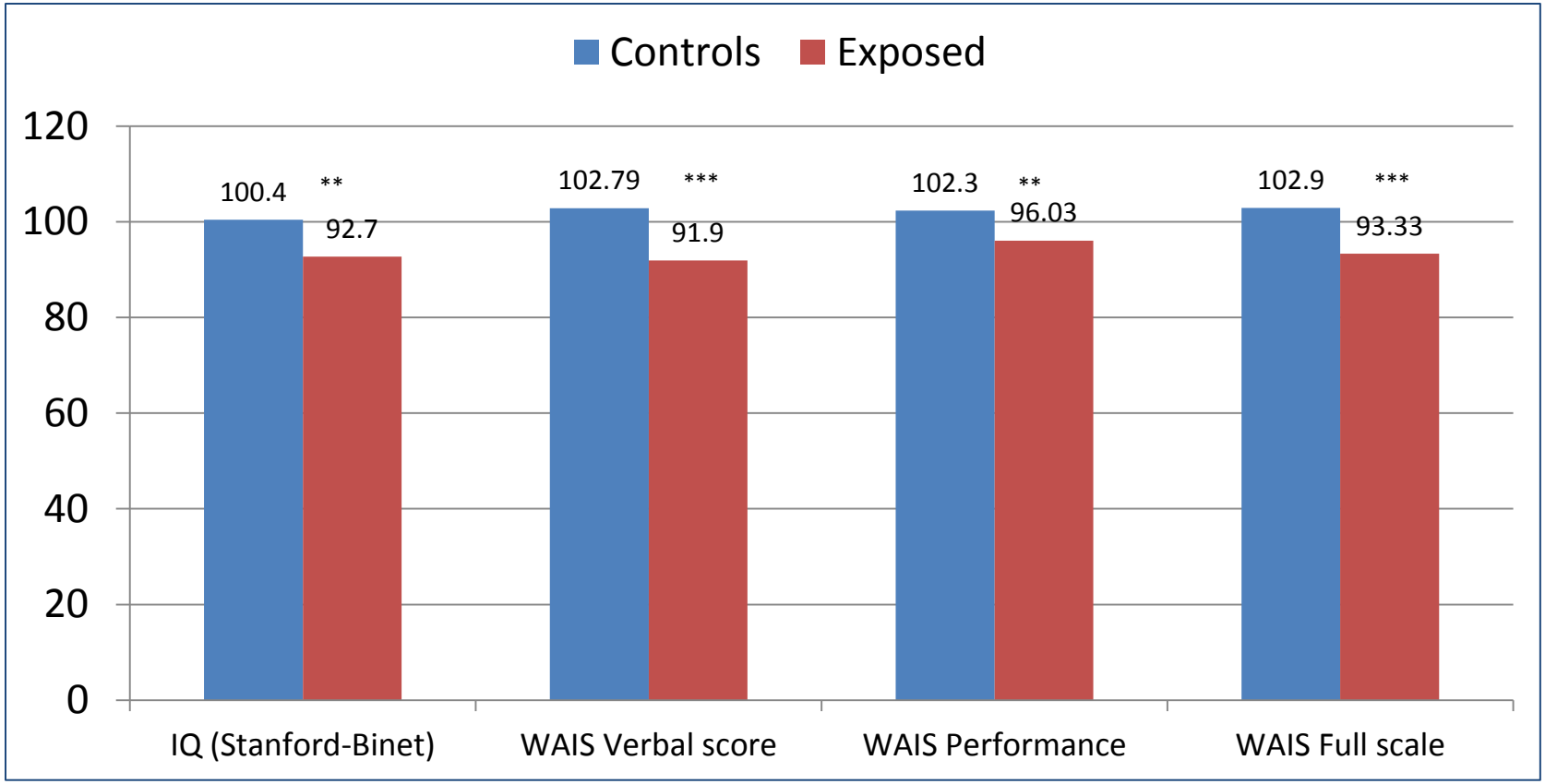
Bauman P & Levine S (1986)

70 exposed (methadone); 70 non-exposed; **3 to 6 years** of age

Measures 3 – 6 years	Non-exposed n=70	Opiate exposed n=70	p value
IQ (Stanford-Binet)	**100.4 (18.36)**	**92.7 (15.4)**	**0.002**
WAIS Verbal score	**102.79 (20.96)**	**91.90 (17.28)**	**<0.001**
WAIS Performance	**102.3 (14.95)**	**96.03 (12.44)**	**0.003**
WAIS Full scale	**102.90 (18.3)**	**93.33 (13.90)**	**<0.001**

The International Journal of the Addictions 1986; 21(8): 849-863

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

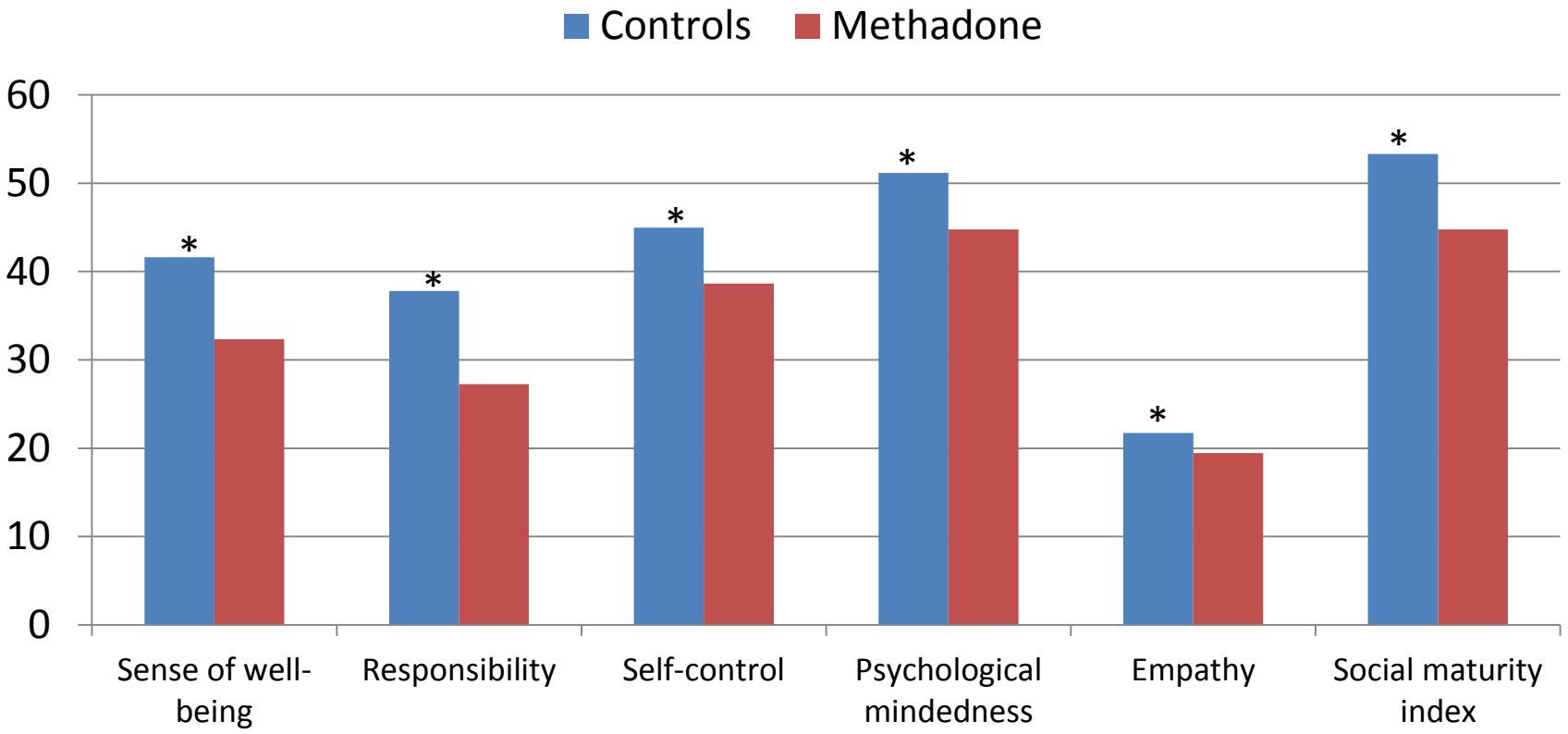


**p<0.01; ***p<0.001

The International Journal of the Addictions 1986; 21(8): 849-863

Personality Structure and Functioning

California Psychological Inventory



*all significant p<0.001

The International Journal of the Addictions 1986; 21(8): 849-863

Behavior and School Outcomes After Exposure to Opiate In-utero

Soepatmi 1994 (67/157 with follow-up)

Measures 3.5-7 years	Opiate- exposed With mothers n=31	Opiate-Exposed Foster care n=34
IQ less than 7 years	104.2 (15.8)	90.9 (13.2) ↓
IQ 7-12 years	91.4 (14.3)	90.6 (14.0)
High total behavior problems score and IQ <85	5.3%	21.9% ↑
School problems =6 years	52%	82% ↑

Soepatmi, *Acta Paediatr Suppl* 1984, 404:36-39

Outcomes After Prenatal Opiate Exposure (4 – 5 years)

Van Baar and de Graaff, 1994 (n=70)

Measures 4 - 5 ½ years	Non-exposed n=35 Mean (SD)	Opiate exposed n=35 Mean (SD)	p value
IQ (RAKIT))	102 (17) 13% below 1SD	90 (22) 41% below 1SD	<0.05
Language Comprehension	52 (6)	46 (6)	<0.01
Expression	50 (6)	46 (6)	<0.05

Dev Med Child Neurol 1994 36:1063-1075

Visual integration and NAS
(Melinder A, Addiction, 2013, 108:2175)

Characteristics/ procedures at 4 years	Comparison (n=23)	Exposed (n=26)	P value
Age (months)	51.6 (1)	52.4 (1.5)	0.05
NAS (methadone/bupre)		61% / 87%	n.s
Smoking		100%	0.000
Birth weight, g	3563 (346)	3104 (658)	0.004
Birth length, cm	50.6 (1.4)	47.7 (3.3)	0.000
Gestational age	39.87 (0.7)	38.95 (2.95)	0.15
Attention problems	50.68 (1.92)	53.9 (5.27)	0.01
Bender Gestalt	17.43 (7.28)	9.96 (4.60)	<0.001
Smooth pursuit (Fast)	59.65 (15.07)	69.77 (13.6)	0.02

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

Ornoy et al. 2001 (160 total)

Follow-up at 5-12 years

33 with DD-fathers

31 with home DD-mothers

34 DD-mothers adopted

32 with low SES

30 controls average SES

Ornoy et al. *Dev Med Child Neurol* 2001 43:668-675

Adverse Neurodevelopmental Outcomes Of Infants Exposed to Opiate In-utero

Ornoy et al. 2001 (160 total)

Measures 5-12 years	Opiate-exposed With mothers n=31	Opiate-Exposed Not-with mothers n=34	Drug Dependent Fathers n=33	Non-exposed Low SES n=32	Non-exposed controls Average SES n=30
WISC-R Verbal IQ	102 (8.8)*#	108 (17.6)	105.7 (18.7)*	100.5 (18.5)*#	110.4 (22.1)
WISC-R Performance	101 (24)*#	106.2 (24.9)*	106.4 (25.7)*	102.8 (16.7)*#	115.3 (22.4)
Externalizing Problems	20.07(13.5)*#	13.5 (9.13)*	16.4 (9.05)*	12.77 (9.48)*	3.6 (4.01)
Internalizing Problems	9.16 (4.94)*#	5.88 (4.99)*	7.87 (5.67)	9.13 (8.46)	3.7 (5.17)

*$p<0.05$, lower/worse than controls; #$p<0.05$, lower/worse than adopted children

Ornoy et al. *Dev Med Child Neurol* 2001 43:668-675

Opioid Exposure and Executive Function

(Konijnenberg C, 2014; Child Neuropsychology)

- 66 children (48-57 months of age)
- 35 opiate exposed (methadone – 24; buprenorphine – 11); 63% treated for NAS;
- 31 comparison children
- Methadone dose at delivery: 85.96 (0-260mg)
- Buprenorphine dose: 12.73 (3-24 mg)
- Neuropsychological testing:
  - WPPSI-R
  - NEPSY (A Developmental NEuroPSYchological Assessment)
  - Day and Night (Stroop Test)
  - BRIEF-P (Behavior Rating Inventory of Executive Function)

Opioid Exposure and Executive Function

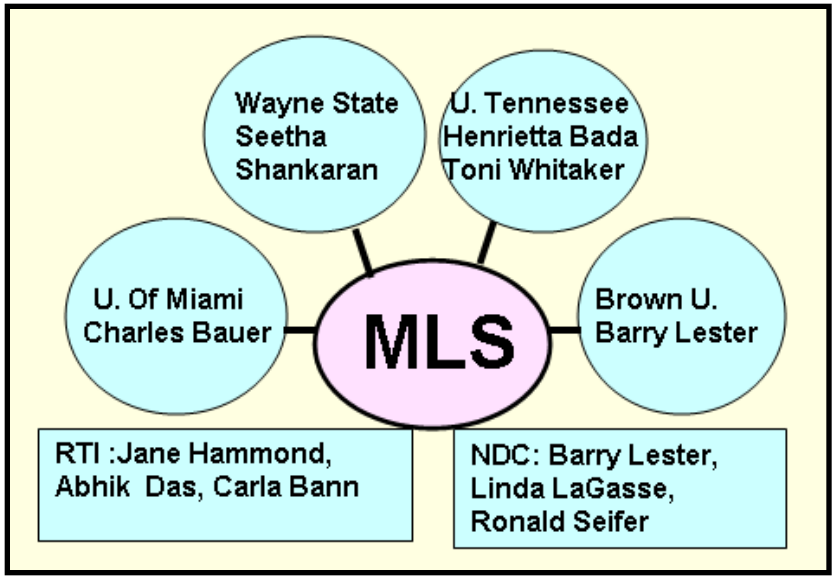
(Konijnenberg C, 2014; Child Neuropsychology)

Tasks	Exposed (n=35)	Comparison (n=31)	p value
WPPSI animal peg	8.31 (3.22)	10.42 (2.78)	0.01
WPPSI – Block design	8.14 (2.14)	9.90 (3.65)	0.02
WPPSI sentences	8.296 (2.80)	11.61 (2.86)	<0.001
NEPSY	16.23 (7.86)	22.48 (7.08)	0.001
BRIEF-P inhibition	55.97 (11.05)	47.42 (7.10)	<0.001
BRIEF-P working memory	57.46 (11.37)	49.13 (9.88)	0.003
BRIEF-P planning	55.29 (11.84)	49.06 (9.39)	0.02
BRIEF-P GEC	55.94 (12.06)	47.94 (9.37)	0.004

Maternal Lifestyle Study (MLS)

MLS is conducted under the auspices of the following Institutes (Program Scientists):

- **NIDA (Nicolette Borek)**
- **NIMH (Julia Zehr)**
- **NICHD NICU Research Network (Rosemary Higgins.**



Phases 1 and 2: The NICHD Neonatal Research Network
NIDA, ACYF, CSAT
Phases 3, 4, 5: NICHD Neonatal Research Network, NIDA, NIMH

Patient Recruitment

- **Enrollment period: May 1993-May 1995**
- **Screening for enrollment**
  - **Birth weight >500 grams**
  - **Gestational Age <43 weeks**
  - **Singletons**
- **Informed consent and maternal interview**
- **Meconium collection**

Results

- **Enrollment**

19,079 - mother/infant dyads screened for recruitment
16,988 - eligible for enrollment
11,811 - consented to study participation
3,184 - no meconium or inadequate for confirmation
7,442 - confirmed non-exposed,
(may have tobacco and or marijuana)
1,185 - exposed (977 – cocaine; 113 opiate only; 92 - opiate and cocaine)
<u>1,388</u> – enrolled in long-term follow-up

Externalizing Behavior Problem: Results From Longitudinal Modeling[1]

Variables	Regn. Coefficient[2]	*p* value
Maternal age	-0.220	<0.001
Prenatal tobacco	0.072	0.044
Prenatal alcohol	0.870	0.015
Prenatal marijuana	-0.014	0.987
Prenatal opiate (year 5)	3.09	0.041
Prenatal cocaine (high use)	3.089	0.003
Caretaker SES	-0.045	0.048
Ongoing tobacco use	1.980	<0.001
Ongoing alcohol use	1.252	0.006

[1] Only effects for prenatal drug exposures and statistically significant ($p < 0.1$) covariates are presented
[2] Adjusted for time trends, site and other covariates listed previously

Bada HS et al. Pediatrics 2007

Opiates and Long Term Behavior Outcomes

Variables	Regn. Coefficient[2]	*p* value
Prenatal opiate (year 5)	3.09	0.041

- **Externalizing behavior problem scores : normed to mean (SD) of 50 (10)**
- **A 3-point upward shift will increase the number of children with scores in the referral or deviant range by 50% (an increase of 16% to 26%).**

Bada HS et al. Pediatrics 2007

Effects of Prenatal Opiate at 13 years From Caretaker and Teacher Report

- **Children with prenatal opiate exposure did not start out with high problem scores at early ages.**
- **From caretaker report: behavior problem scores: worse with time**
  - **Internalizing Behavior Problems**
  - **Total problems**
  - **Attention problems**
- **From teacher report**
  - **Attention Problem Scores worse with time**

Bada HS et al. Neurotoxicology Teratology 2011

Long Term Follow-up of Opiate Exposed Children

SUMMARY OF OUTCOMES **AFTER** AGE 3 YEARS

Lower IQ scores than non-exposed children (8-15 points difference)

Considering that normal IQ is mean (SD) = 100 (15); a 10-point lower mean IQ in exposed children translates to a probability of an increase in the number of children in the below average range from 16% to 36%.

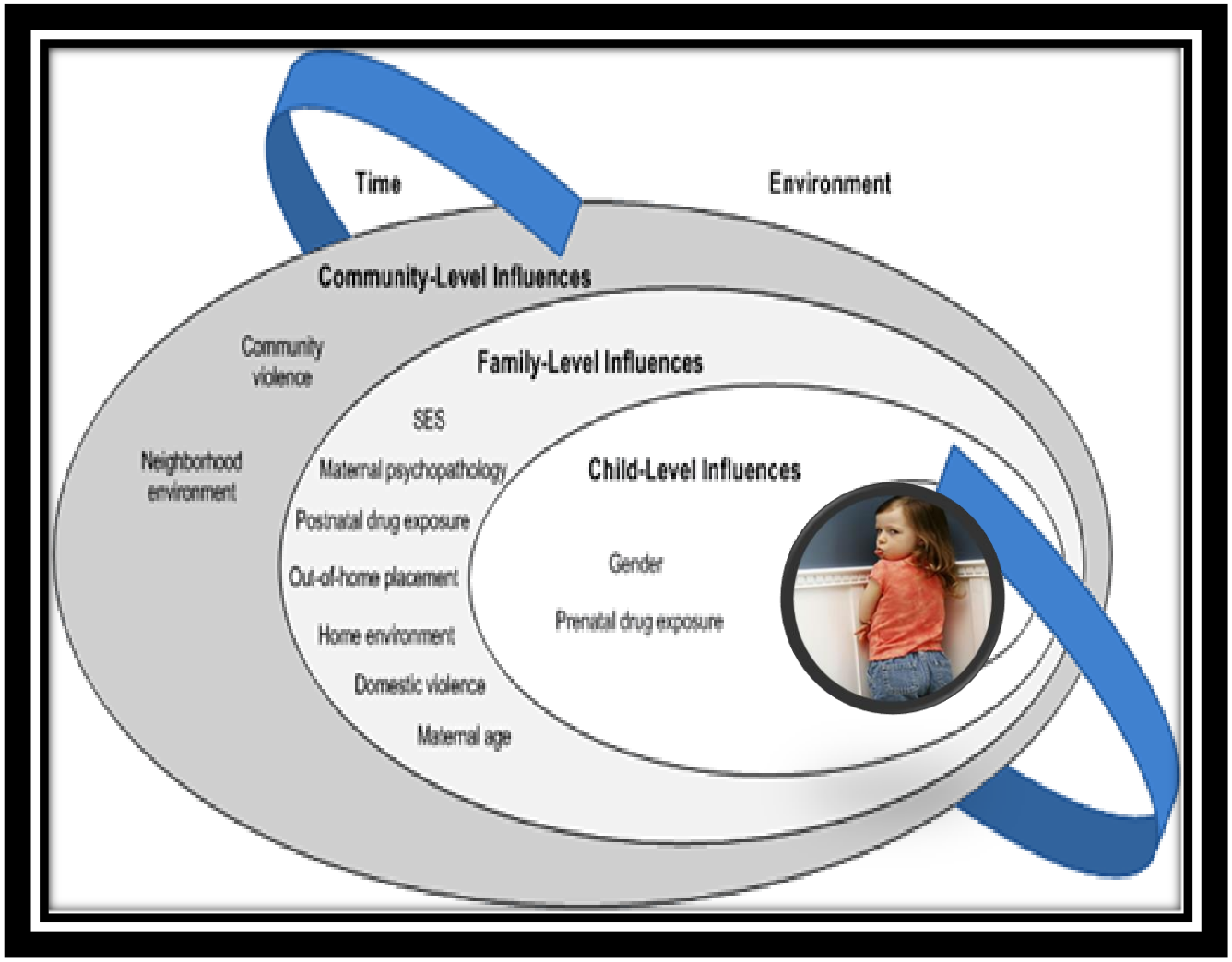
Poor Language development

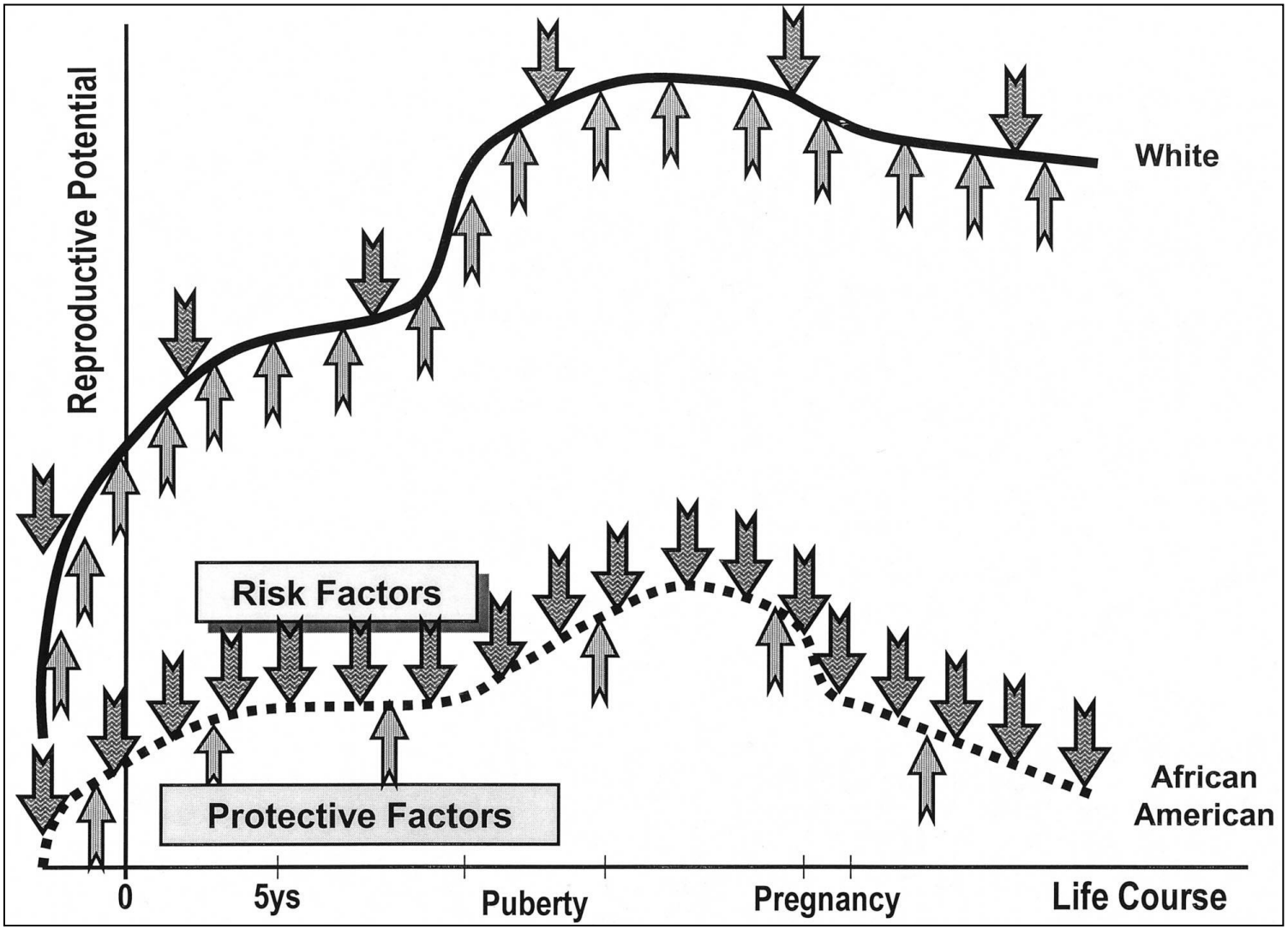
Behavior and school problems: 1 out of 4 children.

Summary: Prenatal Opiate Drug Exposure and Outcomes at Late childhood

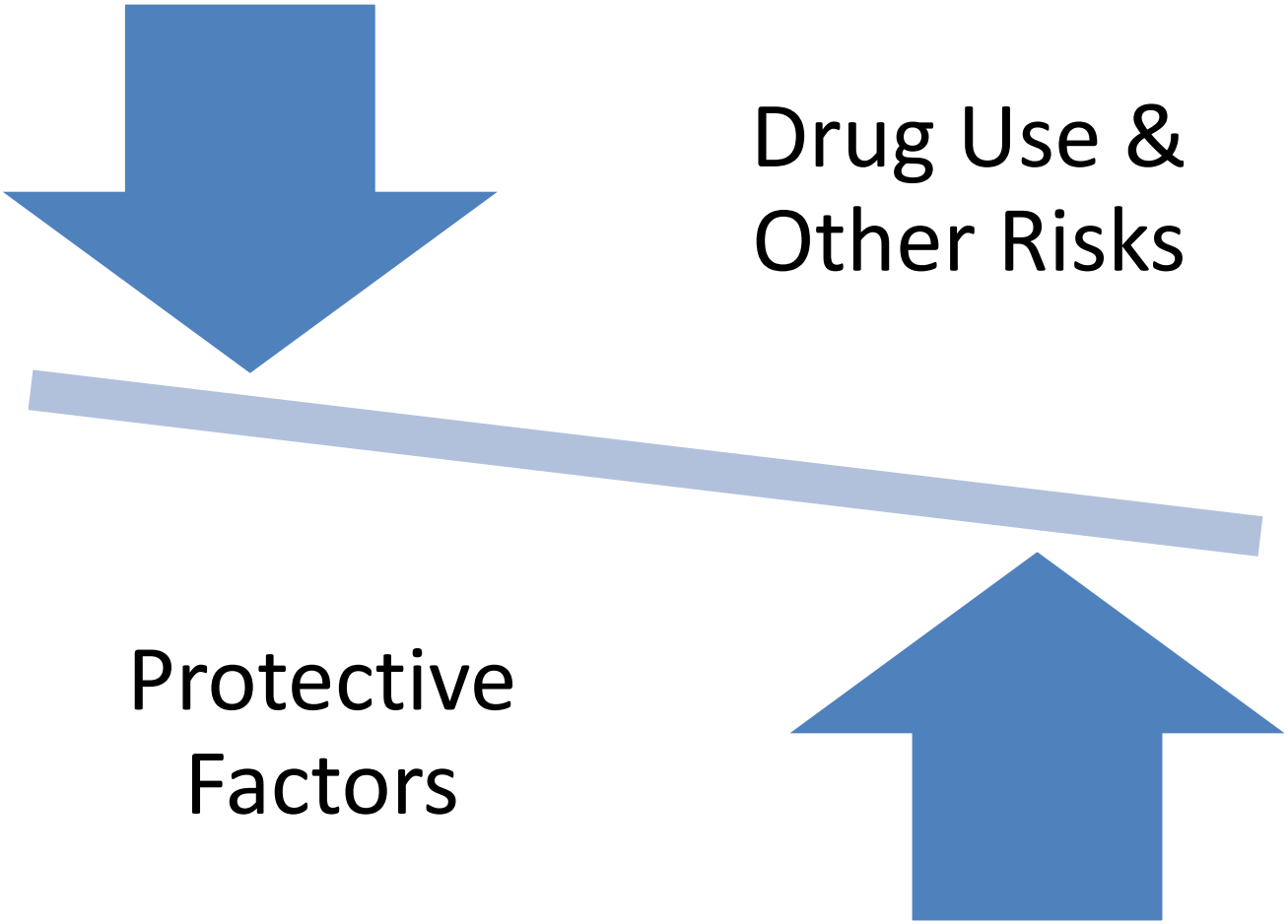
- 8 to 15-point difference (lower) in IQ scores after prenatal opiate exposure compared to non-exposed children
- Lower Language scores in Exposed Children
- Maternal opioid replacement treatment was not associated with improved cognitive development in exposed children
- Higher rates of behavior problems that become worse with time
- Need more research on the appropriate treatment of infants with NAS, Rx that will not continue or aggravate the effects of in utero exposure
- These prenatal and post natal drug exposure effects and other factors could have implications for antisocial behavior, child mental health, and school functioning.
- More research to mitigate behavior problems in exposed children

Complexity in Outcomes: Cumulative Risks Will Influence Outcomes




Reproductive Potential
White
Risk Factors
Protective Factors
African American
0
5ys
Puberty
Pregnancy
Life Course

CAN WE CHANGE CHILD OUTCOMES?



Risks and Protective Factors

	Risk	Protective Factors
Individual	Male	Resilience
	Small head	Temperament
	Low verbal or full IQ	
	Overweight (medical problems)	
Family	Depression, psychological functioning	Secure attachment
	Domestic violence	Home
	Illegal and legal drug Use	Caretaker involvement
		Caretaker supervision
		Family support/resources
Community	Violence	Neighborhood
	Gangs, Crimes	Friends, extracurricular activities

Risk and Protective Factors

- Determine outcomes considering the balance between cumulative risk and protective index
  - **High risk index – low protective index**
  - **High risk index – high protective index**
  - **Low risk index – low protective index**
  - **Low risk index – high protective index**

Bada HS, Pediatrics 2012; 130(6):e1479

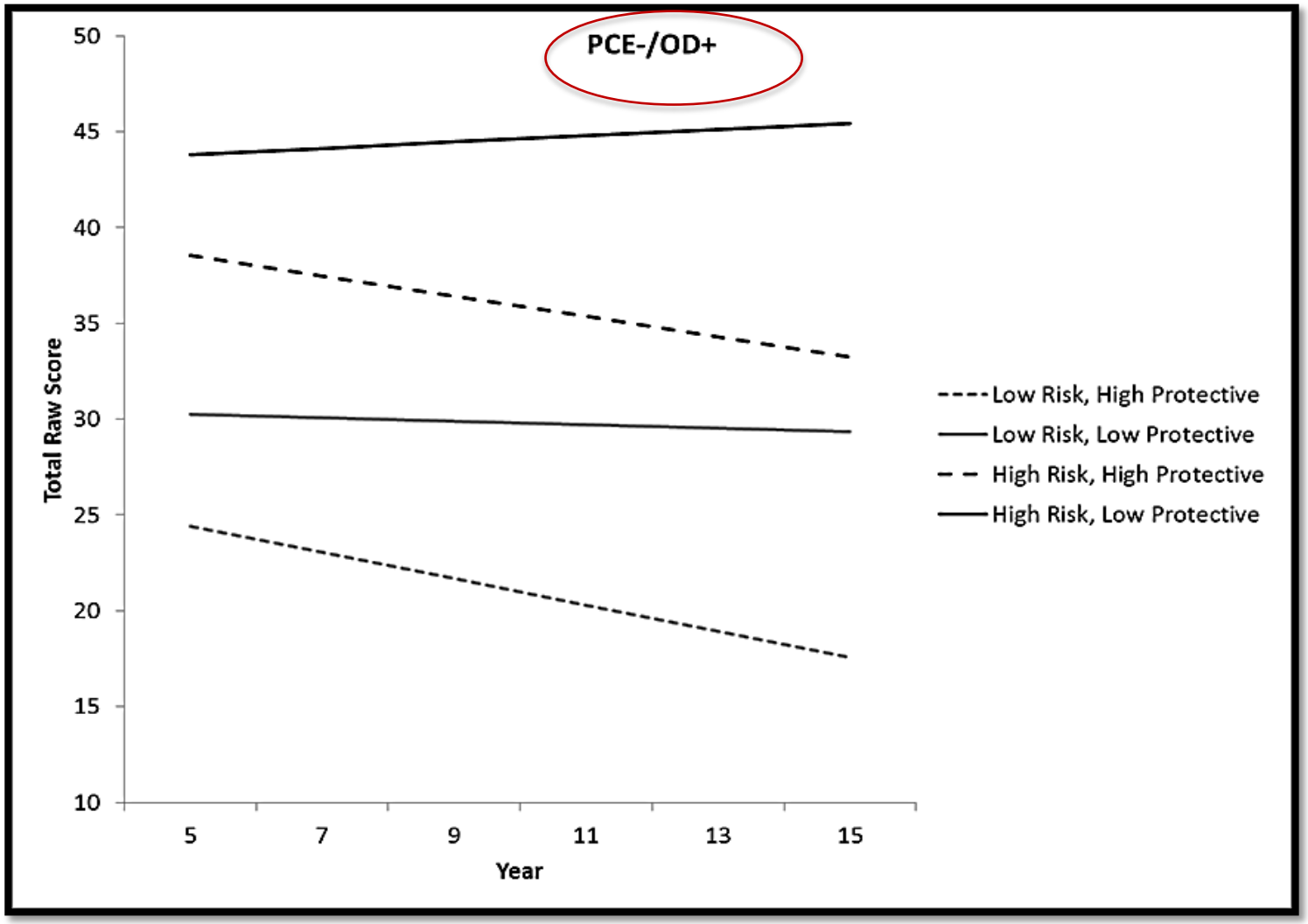
Categories of Prenatal Drug Exposure

- **High Cocaine/Other Drug Exposure (High PCE/OD)**
- **Some Cocaine/Other Drug Exposure (Some PCE/OD)**
- **Other Drugs/No Cocaine (PCE-/OD+)**
- **No Cocaine/No other drugs (PCE-/OD-)**

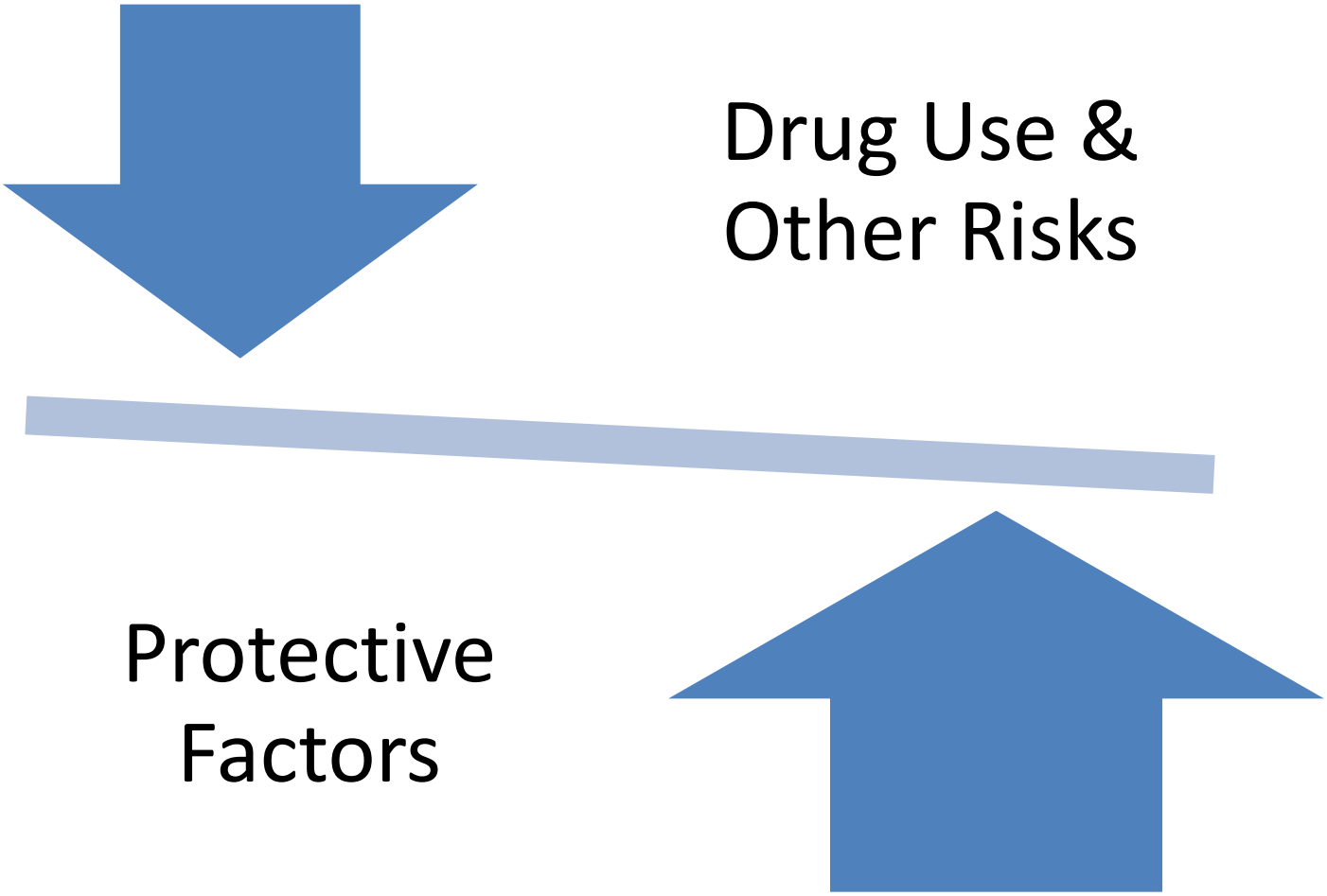
Problem Behaviors

- **Externalizing Behavior Problems**
  - **Delinquent behavior**
  - **Aggressive behavior**
- **Internalizing Behavior Problems**
  - **Withdrawn**
  - **Somatic complaints**
  - **Anxious/depressed**
- **Total Behavior Problems**
  - **Externalizing, internalizing, social problems, thought problems, attention problems, sex problems**

Total Behavior Problems: Balance of Risk and Protective Factors



YES: WE CHANGE CHILD OUTCOMES!



Long Term Outcomes of Prenatal Opiate Exposure

SUMMARY AND CONCLUSION

Clinical and Policy Implications

- **Prenatal opiate exposure often occurs in the context of polydrug exposure**
- **High incidence of withdrawal (NAS) in illegal opiate use or even maternal medical replacement therapy (methadone or buprenorphine)**
- **Increase in likelihood of adverse effects noted at later childhood or adolescence**
- **Lower IQ, lower language scores, higher rate of behavior problems among exposed children**

Clinical and Policy Implications

- **Adverse outcomes are noted even with maternal opioid treatment during pregnancy; therefore focus much needed to treatment of neonatal abstinence syndrome and on child development.**
- **Prenatal exposure effects can be aggravated by environmental risks but can also be mitigated by protective factors (at individual, family, and community levels)**
- **Need to explore interventions to minimize the adverse effects of prenatal drug exposure.**
- **We need to address maternal treatment, child treatment and development**

the entangled web

it takes a village to disentangle the world of the drug-exposed child

Thank you