



American Academy of Pediatrics  
DEDICATED TO THE HEALTH OF ALL CHILDREN

# Epigenetics and Health Disparities: Linking Biology and Social Science

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Genomics, &  
Bioinformatics

**St. Regis Indian Mission: Where my  
great grandmother was baptized**



# Indigenous Peoples in NY State



New York and Michigan have the largest indigenous populations east of the Mississippi River. Niagara Falls has a higher percentage of Native American than any city east of the Mississippi. More than 2,000 American Indians live in Buffalo proper.

# Jim Jarvis, MD, FAAP

## Faculty Disclosure Information

In the past 12 months, I have had no financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial service(s) discussed in this CME activity.

I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

“As human beings we belong to an extremely resilient species. Since time immemorial we have rebounded from our relentless wars, countless disasters (both natural and man-made), and the violence and betrayal in our own lives. But traumatic experiences do leave traces, whether on a large scale (on our histories and cultures) or close to home, on our families, with dark secrets being imperceptibly passed down through generations. They also leave traces on our minds and emotions, on our capacity for joy and intimacy, and even on our biology and immune systems.”

*The Body Keeps the Score: Brain, Mind, and Body in the Healing of Trauma, p. 1*

Bessel van der Kolk, 2014

# Our Current Path—

## An all-too-common story: “Mary”

- Pre-conception
  - Mother’s grandparents went to boarding school, parents have had trouble with alcohol; most of them developed diabetes
  - Family income below poverty line, buy food at reservation store
- Pregnancy and Birth
  - Single 15 year old, won’t say who FOB is
  - Intermittent prenatal care
  - WIC foods have to be shared with family
  - Stopped using drugs when found out she was pregnant, cut down but continued smoking and got drunk “just a few times”
  - Mostly kept going to high school thru pregnancy
  - Mary born slightly SGA at 35 weeks gestation, spent 2 wks in hosp.

# “Mary”

## ■ Early Life

- Grandmother already overwhelmed caring for other grandchildren, but agreed to watch Mary while mother tried to stay in school
    - Mary often sitting in front of TV most of day
  - Then put into tribal child care
    - High staff turnover, minimal teacher-student ratio
  - Family got by on commodities and WIC foods
  - Mary gained weight rapidly in 1<sup>st</sup> yr, then stayed >95<sup>th</sup> % ile
  - Mother’s boyfriend moved in
    - Intermittently employed, binged on alcohol and drugs, sometimes hit mother in front of Mary
  - Mary held back to repeat 2<sup>nd</sup> grade as reading difficulties
  - Mary left school after 10<sup>th</sup> grade
- ## ■ Now Mary becomes pregnant...

# Adverse Childhood Experiences (ACE)

- Physical, emotional, sexual abuse; mentally ill, substance abusing, incarcerated family member; seeing mother beaten; parents divorced/separated

--Overall Exposure: 86% (among 7 tribes)

	<u>Non-Native</u>	<u>Native</u>
Physical Abuse-M	30%	40%
Physical Abuse-F	27	42
Sexual Abuse-M	16	24
Sexual Abuse-F	25	31
Emotional Abuse	11	30
Household alcohol	27	65
Four or More ACEs	6	33



# ACEs and Adult Health

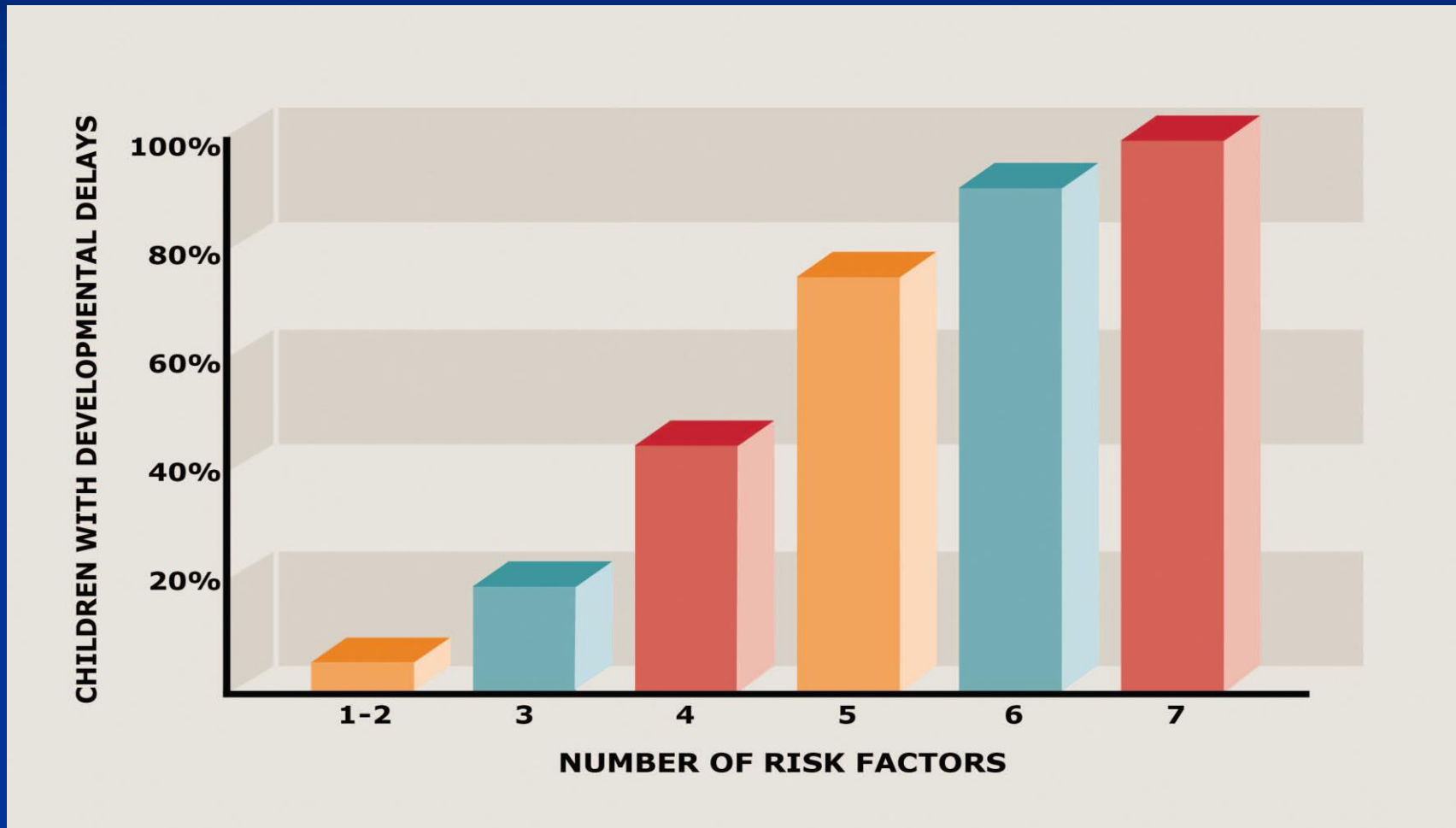
- ACE Score  $\geq 4$ 
  - 4-12 x risk for alcoholism, drug abuse, depression and suicide attempt
  - 2-4 x risk for smoking, teen pregnancy, STDs, multiple sexual partners
  - 1.4-1.6 x risk for severe obesity
  - Strong graded relationship at all levels of ACEs for almost all outcomes, including heart disease

*Am J Prev Med* 1998;14:245-258 and *Circulation* 2004;110:1761-6

- Across 10 countries, adults who experienced  $\geq 3$  childhood adversities
  - Hazard ratios 1.59 for diabetes, 2.19 for heart disease
  - Risk similar to the association between cholesterol and heart disease
    - Both in magnitude as well as population prevalence

*Arch Gen Psychiatry* 2011;68:838-844

# 90-100% chance of developmental delays when children experience 6-7 risk factors



Center on the Developing Child at Harvard website

Source: Barth, et al. (2008)

## Domains of Impairment in Children Exposed to Complex Trauma

### I. Attachment

Problems with boundaries  
 Distrust and suspiciousness  
 Social isolation  
 Interpersonal difficulties  
 Difficulty attuning to other people's emotional states  
 Difficulty with perspective taking

### II. Biology

Sensorimotor developmental problems  
 Analgesia  
 Problems with coordination, balance, body tone  
 Somatization  
 Increased medical problems across a wide span (eg, pelvic pain, asthma, skin problems, autoimmune disorders, pseudoseizures)

### III. Affect regulation

Difficulty with emotional self-regulation  
 Difficulty labeling and expressing feelings  
 Problems knowing and describing internal states  
 Difficulty communicating wishes and needs

### IV. Dissociation

Distinct alterations in states of consciousness  
 Amnesia  
 Depersonalization and derealization  
 Two or more distinct states of consciousness  
 Impaired memory for state-based events

### V. Behavioral control

Poor modulation of impulses  
 Self-destructive behavior  
 Aggression toward others  
 Pathological self-soothing behaviors  
 Sleep disturbances  
 Eating disorders  
 Substance abuse  
 Excessive compliance  
 Oppositional behavior  
 Difficulty understanding and complying with rules  
 Reenactment of trauma in behavior or play (eg, sexual, aggressive)

### VI. Cognition

Difficulties in attention regulation and executive functioning  
 Lack of sustained curiosity  
 Problems with processing novel information  
 Problems focusing on and completing tasks  
 Problems with object constancy  
 Difficulty planning and anticipating  
 Problems understanding responsibility  
 Learning difficulties  
 Problems with language development  
 Problems with orientation in time and space

### VII. Self-concept

Lack of a continuous, predictable sense of self  
 Poor sense of separateness  
 Disturbances of body image  
 Low self-esteem  
 Shame and guilt

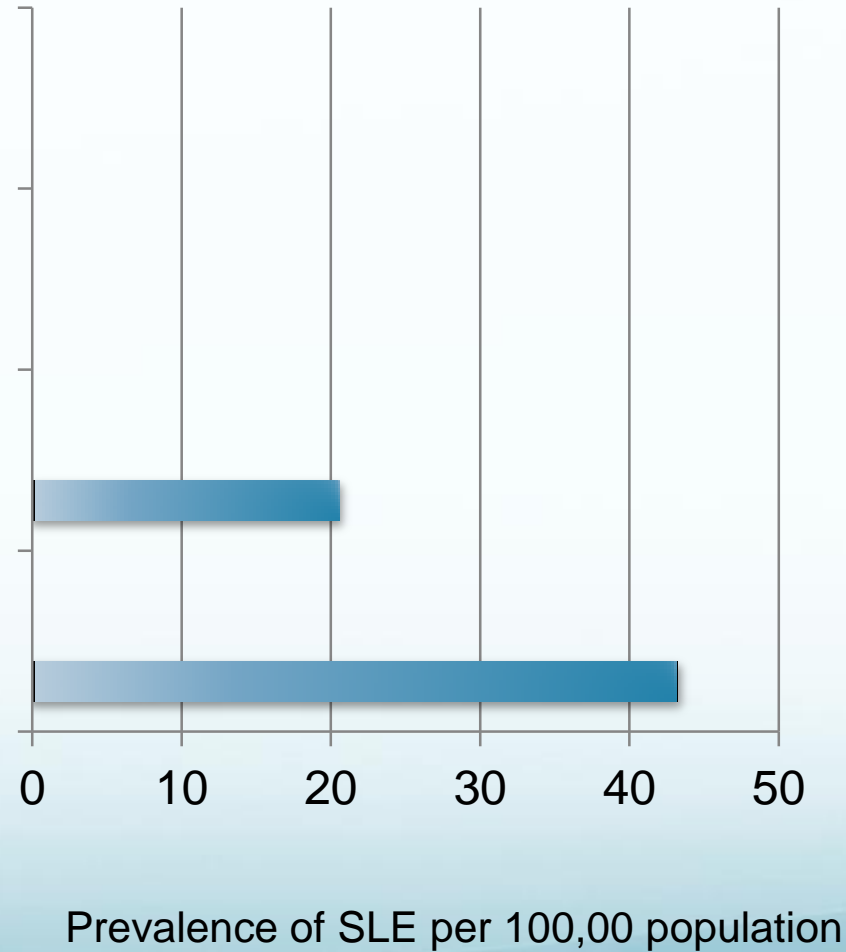
# Most Diseases That Show Health Inequities Are Complex Traits



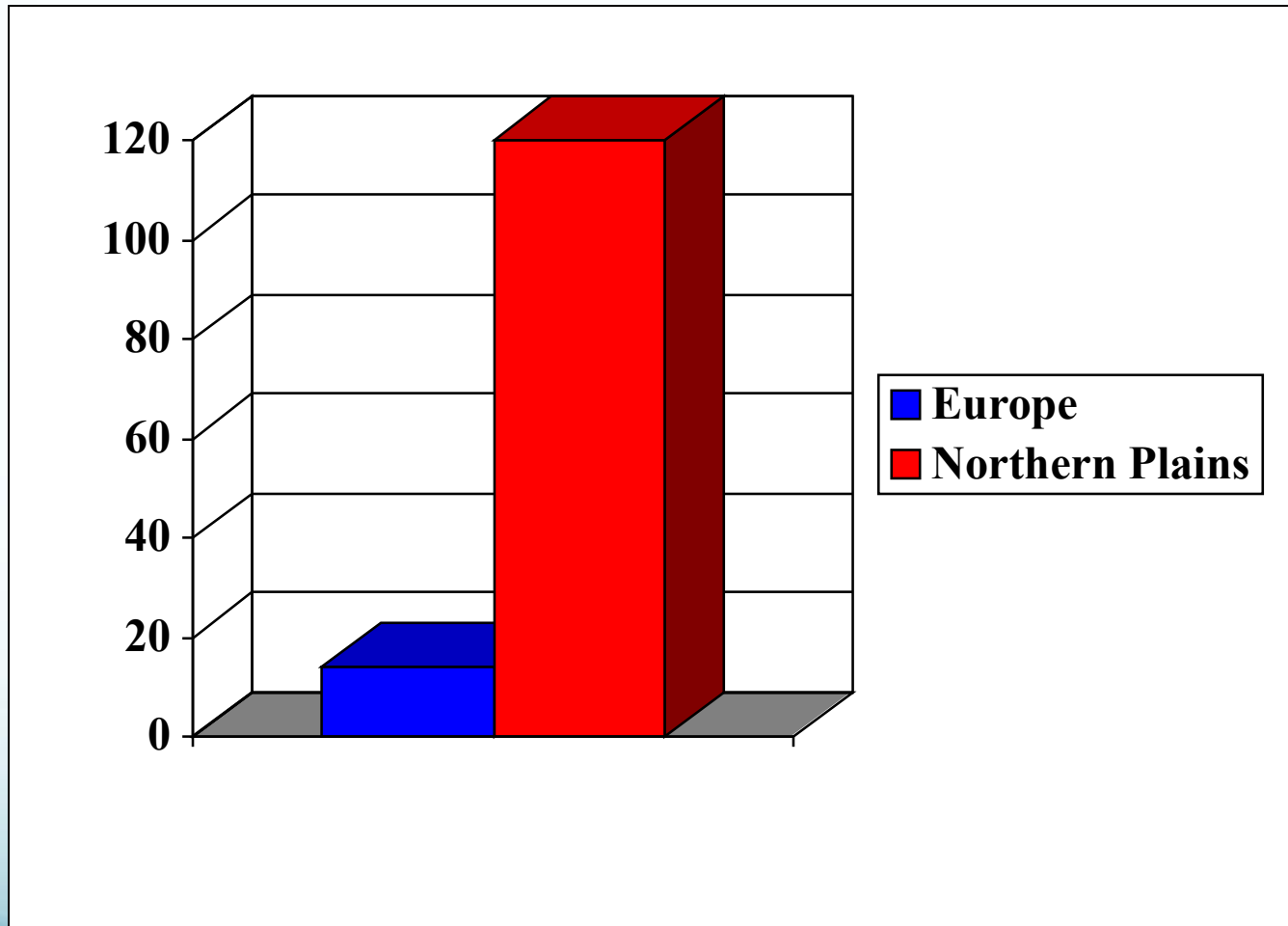
General population



Native American



# Juvenile Idiopathic Arthritis: Northern Plains vs. Europe



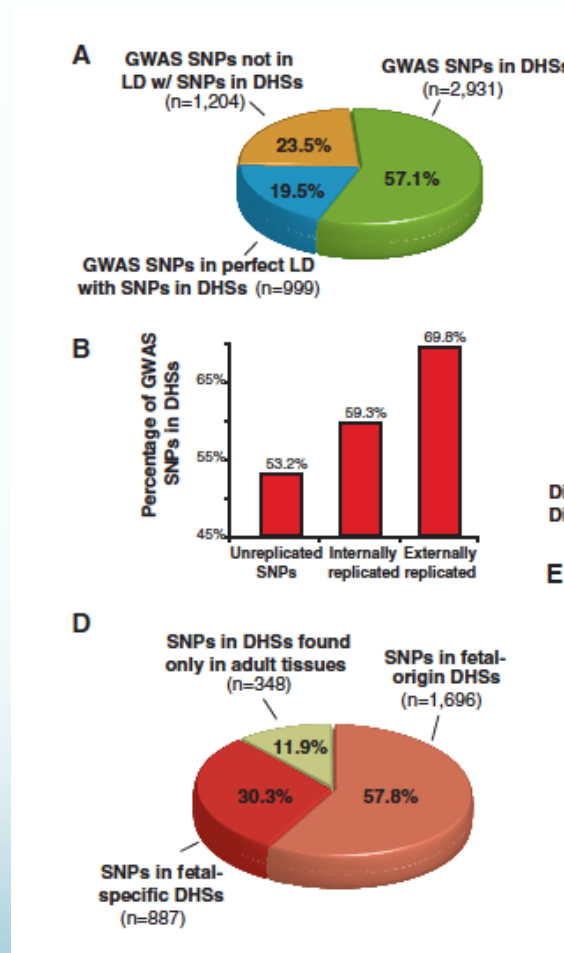
# Most Risk for Complex Traits in NOT in Our Genes

## Systematic Localization of Common Disease-Associated Variation in Regulatory DNA

Matthew T. Maurano,<sup>1\*</sup> Richard Humbert,<sup>1\*</sup> Eric Rynes,<sup>1\*</sup> Robert E. Thurman,<sup>1</sup> Eric Haugen,<sup>1</sup> Hao Wang,<sup>1</sup> Alex P. Reynolds,<sup>1</sup> Richard Sandstrom,<sup>1</sup> Hongzhu Qu,<sup>1,2</sup> Jennifer Brody,<sup>3</sup> Anthony Shafer,<sup>1</sup> Fidencio Neri,<sup>1</sup> Kristen Lee,<sup>1</sup> Tanya Kutyaev,<sup>1</sup> Sandra Stehling-Sun,<sup>1</sup> Audra K. Johnson,<sup>1</sup> Theresa K. Canfield,<sup>1</sup> Erika Giste,<sup>1</sup> Morgan Diegel,<sup>1</sup> Daniel Bates,<sup>1</sup> R. Scott Hansen,<sup>4</sup> Shane Neph,<sup>1</sup> Peter J. Sabo,<sup>1</sup> Shelly Heimfeld,<sup>5</sup> Antony Raubitschek,<sup>6</sup> Steven Ziegler,<sup>6</sup> Chris Cotsapas,<sup>7,8</sup> Nona Sotoodehnia,<sup>3,9</sup> Ian Glass,<sup>10</sup> Shamil R. Sunyaev,<sup>11</sup> Rajinder Kaul,<sup>4</sup> John A. Stamatoyannopoulos<sup>1,12†</sup>

Maurano et al (Science, 2012) showed that most disease-associated SNPs are in non-coding regions that are identified as DNase1 hypersensitivity sites (DHS). Such sites typically represent non-coding but functional parts of the genome.

*Note importance of SNPs in regions active during fetal development.*



# Genetics of JIA

## LETTERS

nature  
genetics

### Dense genotyping of immune-related disease regions identifies 14 new susceptibility loci for juvenile idiopathic arthritis

Anne Hinks<sup>1,2,22</sup>, Joanna Cobb<sup>1,2,22</sup>, Miranda C Marion<sup>3,4,22</sup>, Sampath Prahalad<sup>5,6</sup>, Marc Sudman<sup>7</sup>, John Bowes<sup>1,2</sup>, Paul Martin<sup>1,2</sup>, Mary E Comeau<sup>3,4</sup>, Satria Sajuthi<sup>3,4</sup>, Robert Andrews<sup>8</sup>, Milton Brown<sup>5</sup>, Wei-Min Chen<sup>9</sup>, Patrick Concannon<sup>9</sup>, Panos Deloukas<sup>8</sup>, Sarah Edkins<sup>8</sup>, Stephen Eyre<sup>1,2</sup>, Patrick M Gaffney<sup>10</sup>, Stephen L Guthery<sup>11,12</sup>, Joel M Guthridge<sup>10</sup>, Sarah E Hunt<sup>8</sup>, Judith A James<sup>10</sup>, Mehdi Keddache<sup>13</sup>, Kathy L Moser<sup>10</sup>, Peter A Nigrovic<sup>14,15</sup>, Suna Onengut-Gumuscu<sup>9</sup>, Mitchell L Onslow<sup>7</sup>, Carlos D Rosé<sup>14,15</sup>, Stephen S Rich<sup>9</sup>, Kathryn J A Steel<sup>1,2</sup>, Edward K Wakeland<sup>16</sup>, Carol A Wallace<sup>17</sup>, Lucy R Wedderburn<sup>18</sup>, Patricia Woo<sup>19</sup>, Boston Children's JIA Registry<sup>20</sup>, British Society of Paediatric and Adolescent Rheumatology (BSPAR) Study Group<sup>20</sup>, Childhood Arthritis Prospective Study (CAPS)<sup>20</sup>, Childhood Arthritis Response to Medication Study (CHARMS)<sup>20</sup>, German Society for Pediatric Rheumatology (GKJR)<sup>20</sup>, JIA Gene Expression Study<sup>20</sup>, NIAMS JIA Genetic Registry<sup>20</sup>, TREAT Study<sup>20</sup>, United Kingdom Juvenile Idiopathic Arthritis Genetics Consortium (UKJIAGC)<sup>20</sup>, John F Bohnsack<sup>11,12</sup>, Johannes Peter Haas<sup>21</sup>, David N Glass<sup>7</sup>, Carl D Langefeld<sup>3,4</sup>, Wendy Thomson<sup>1,2,23</sup> & Susan D Thompson<sup>7,23</sup>

Limitations:

1. Chip-based genotyping, thus, limited resolution and can query only known SNPs.
2. Was not a genome-wide study: biased toward immune-related genes.

# Genetics (cont'd)

**Table 1** Regions showing genome-wide significant association with oligoarticular and RF-negative polyarticular JIA

Gene region	Chr.	Position <sup>a</sup>	Most significant SNP	Minor allele	MAF <sub>controls</sub> (n = 13,056)	MAF <sub>cases</sub> (n = 2,816)	Best P value	Model	OR (95% CI)	SNP position
<i>HLA-DQB1 –HLA-DQA2</i>	6	32657916	rs7775055	G	0.02	0.12	$3.14 \times 10^{-174}$	Dominant	6.01 (5.30–6.81)	Intergenic
<i>PTPN22</i>	1	114303808	rs6679677	A	0.10	0.14	$3.19 \times 10^{-25}$	Additive	1.59 (1.45–1.73)	Intergenic
<i>STAT4</i>	2	191973034	rs10174238	G	0.23	0.28	$1.28 \times 10^{-13}$	Additive	1.29 (1.20–1.37)	Intron
<i>PTPN2</i>	18	12782448	rs2847293	A	0.17	0.20	$1.44 \times 10^{-12}$	Additive	1.31 (1.22–1.41)	Intergenic
<i>ANKRD55</i>	5	55440730	rs71624119	A	0.25	0.20	$4.40 \times 10^{-11}$	Additive	0.78 (0.73–0.84)	Intron
		55442249	rs10213692 <sup>b</sup>	C	0.25	0.20	$2.73 \times 10^{-11}$	Additive	0.79 (0.74–0.80)	Intron
<i>IL2-IL21</i>	4	123387600	rs1479924	G	0.29	0.24	$6.24 \times 10^{-11}$	Additive	0.79 (0.74–0.85)	Intergenic
<i>TYK2</i>	19	10463118	rs34536443	G	0.05	0.03	$1 \times 10^{-10}$	Additive	0.56 (0.47–0.67)	Coding (NS)
<i>IL2RA</i>	10	6089841	rs7909519	C	0.11	0.08	$8 \times 10^{-10}$	Additive	0.72 (0.64–0.80)	Intron
<i>SH2B3-ATXN2</i>	12	111884608	rs3184504	A	0.49	0.54	$2.60 \times 10^{-9}$	Additive	1.20 (1.13–1.27)	Coding (NS)
		111932800	rs7137828 <sup>b</sup>	C	0.49	0.54	$1.61 \times 10^{-9}$	Additive	1.20 (1.13–1.28)	Intron
<i>ERAP2-LNPEP</i>	5	96350088	rs27290	G	0.44	0.47	$7.50 \times 10^{-9}$	Dominant	1.32 (1.20–1.45)	Intron
		96357178	rs27293 <sup>b</sup>	A	0.44	0.47	$7.37 \times 10^{-9}$	Dominant	1.31 (1.19–1.43)	Intron
<i>UBE2L3</i>	22	21922904	rs2266959	A	0.19	0.22	$6.20 \times 10^{-9}$	Dominant	1.24 (1.15–1.33)	Intron
<i>C5orf56-IRF1</i>	5	131813219	rs4705862	T	0.44	0.39	$1.02 \times 10^{-8}$	Additive	0.84 (0.79–0.89)	Intergenic
		131797547	rs6894249 <sup>b</sup>	G	0.39	0.35	$9.73 \times 10^{-10}$	Dominant	0.76 (0.70–0.83)	Intron
<i>RUNX1</i>	21	36715761	rs9979383	G	0.37	0.33	$1.06 \times 10^{-8}$	Dominant	0.78 (0.72–0.85)	Intergenic
		36712588	rs8129030 <sup>b</sup>	T	0.37	0.33	$5.44 \times 10^{-9}$	Dominant	0.78 (0.71–0.84)	Intergenic
<i>IL2RB</i>	22	37534034	rs2284033	A	0.44	0.39	$1.55 \times 10^{-8}$	Additive	0.84 (0.79–0.89)	Intron
<i>ATP8B2-IL6R</i>	1	154364140	rs11265608	A	0.10	0.12	$2.75 \times 10^{-8}$	Dominant	1.33 (1.20–1.47)	Intergenic
		154379369	rs72698115 <sup>b</sup>	C	0.10	0.12	$1.26 \times 10^{-8}$	Dominant	1.36 (1.22–1.52)	Intron
<i>FAS</i>	10	90762376	rs7069750	C	0.44	0.48	$2.93 \times 10^{-8}$	Additive	1.18 (1.11–1.25)	Intron
<i>ZFP36L1</i>	14	69253364	rs12434551	A	0.47	0.43	$1.59 \times 10^{-8}$	Dominant	0.77 (0.71–0.85)	Intergenic
		69260588	rs3825568 <sup>b</sup>	T	0.46	0.42	$1.24 \times 10^{-8}$	Dominant	0.77 (0.70–0.84)	5' UTR

So, once again, what's *in* these regions?

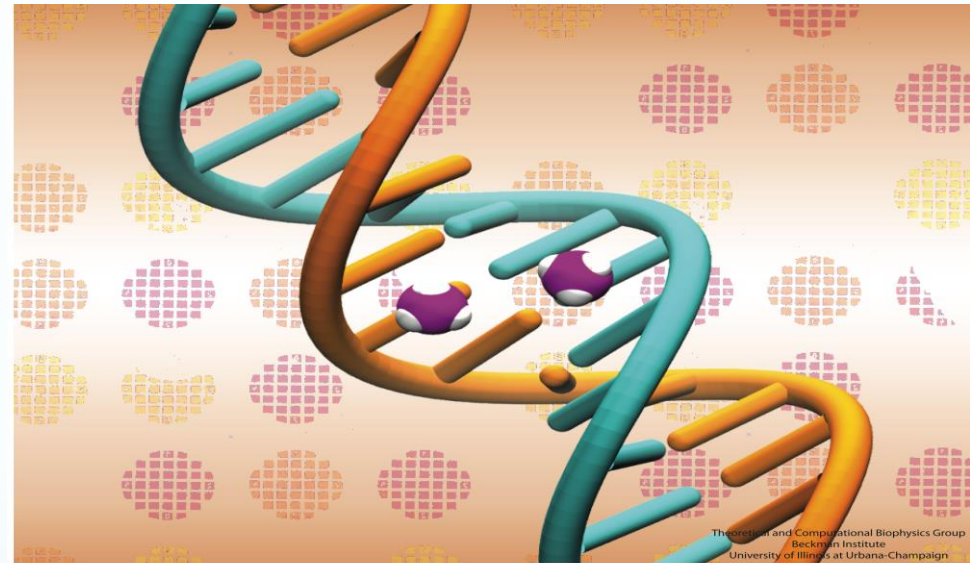


# Epigenetics: Genes and Environment

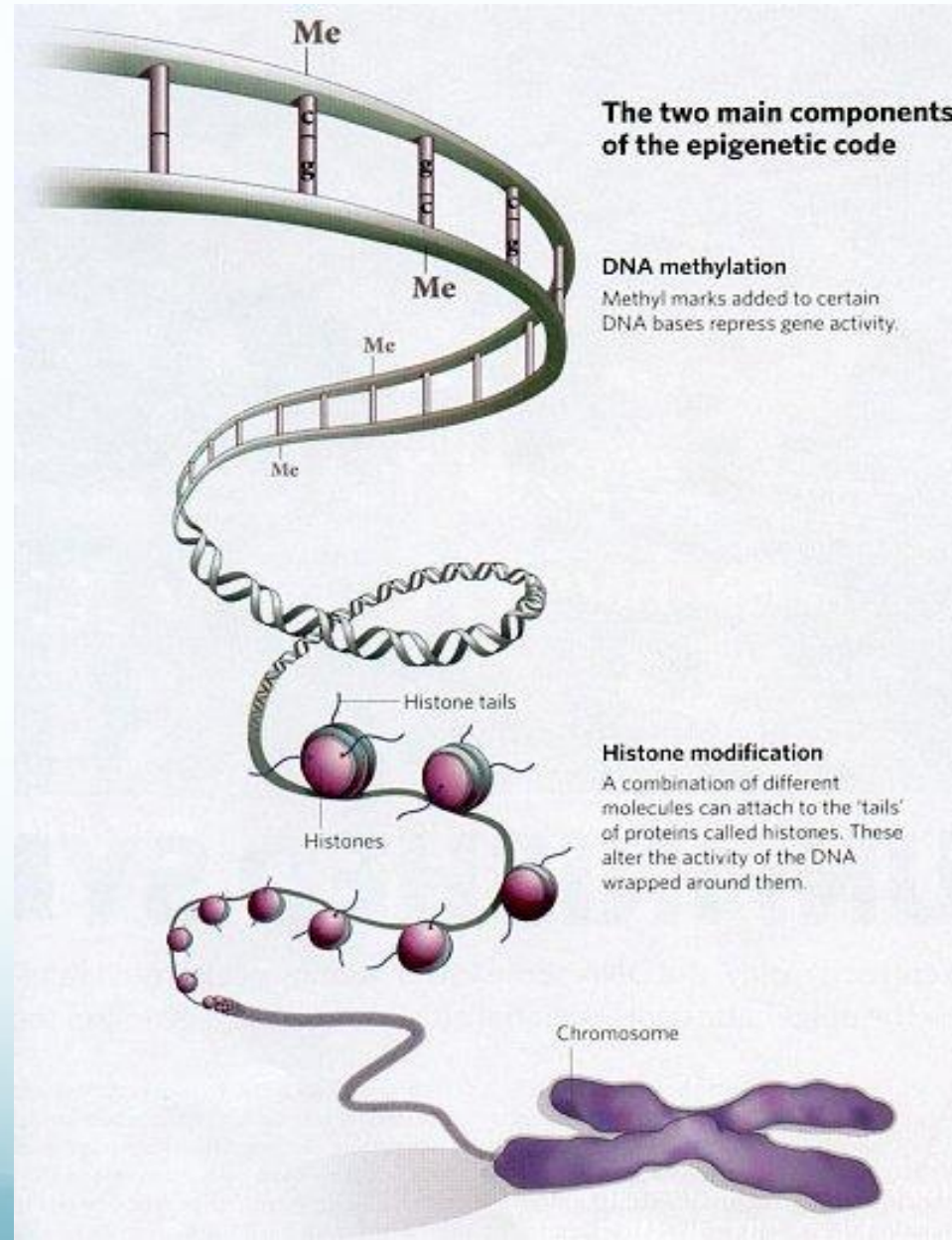


# Epigenetics-Definition

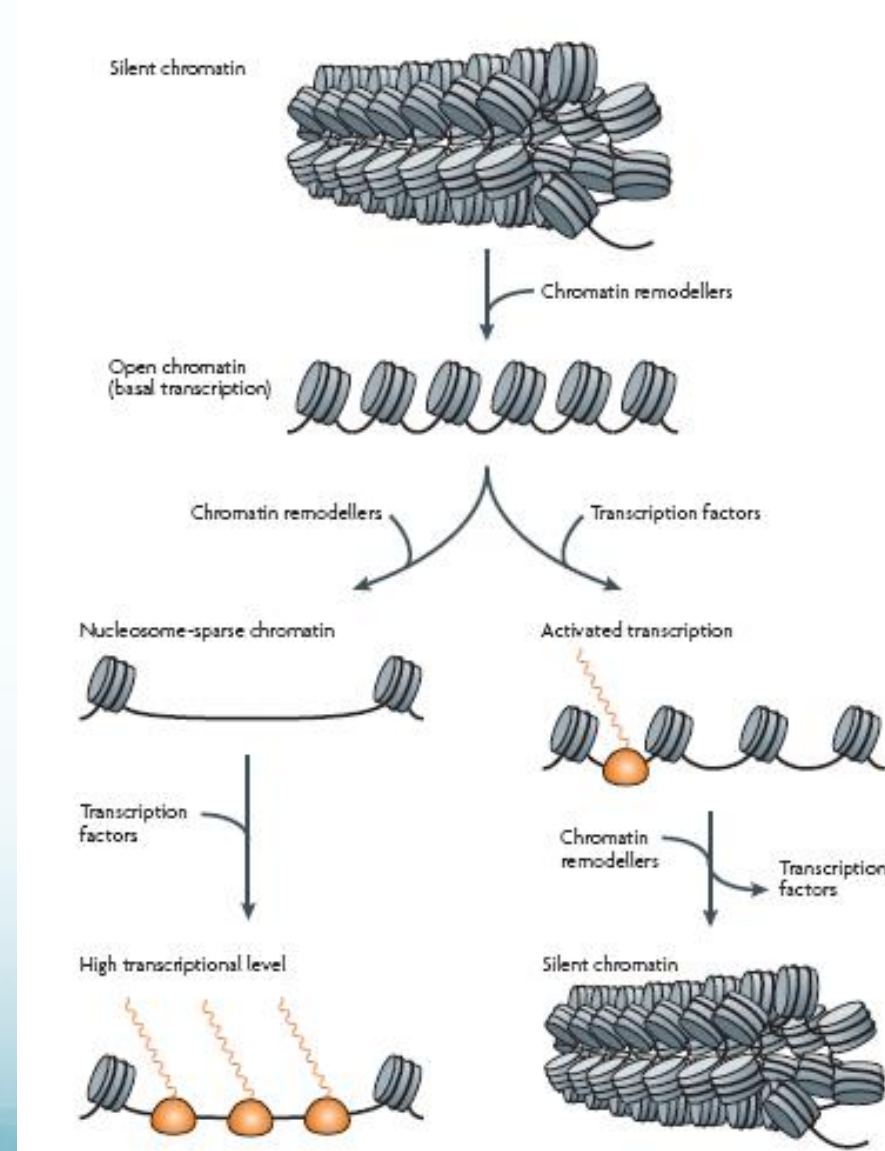
Alterations to DNA or its associated proteins that do not change the actual coding sequence of the DNA but which may have effects on DNA function.



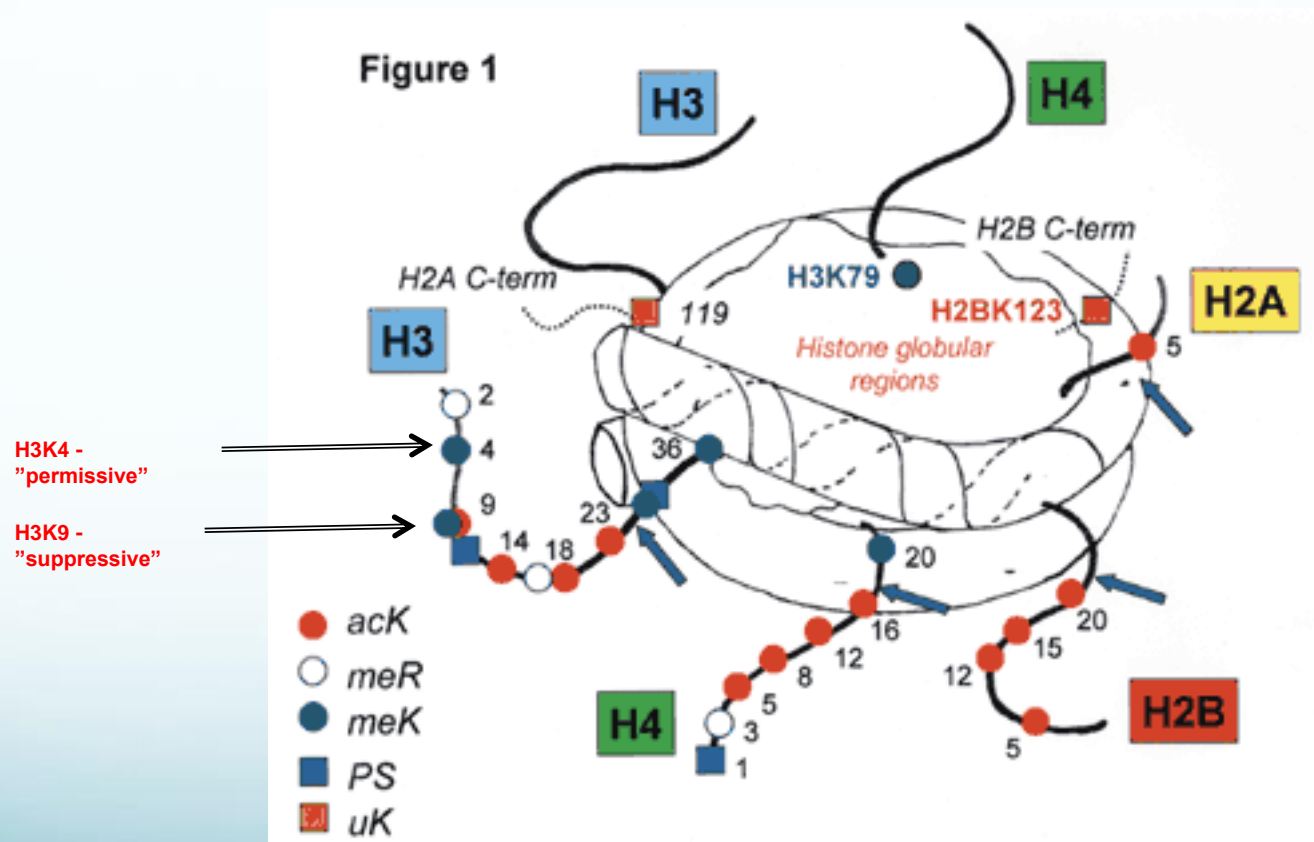
# Epigenetic Alterations



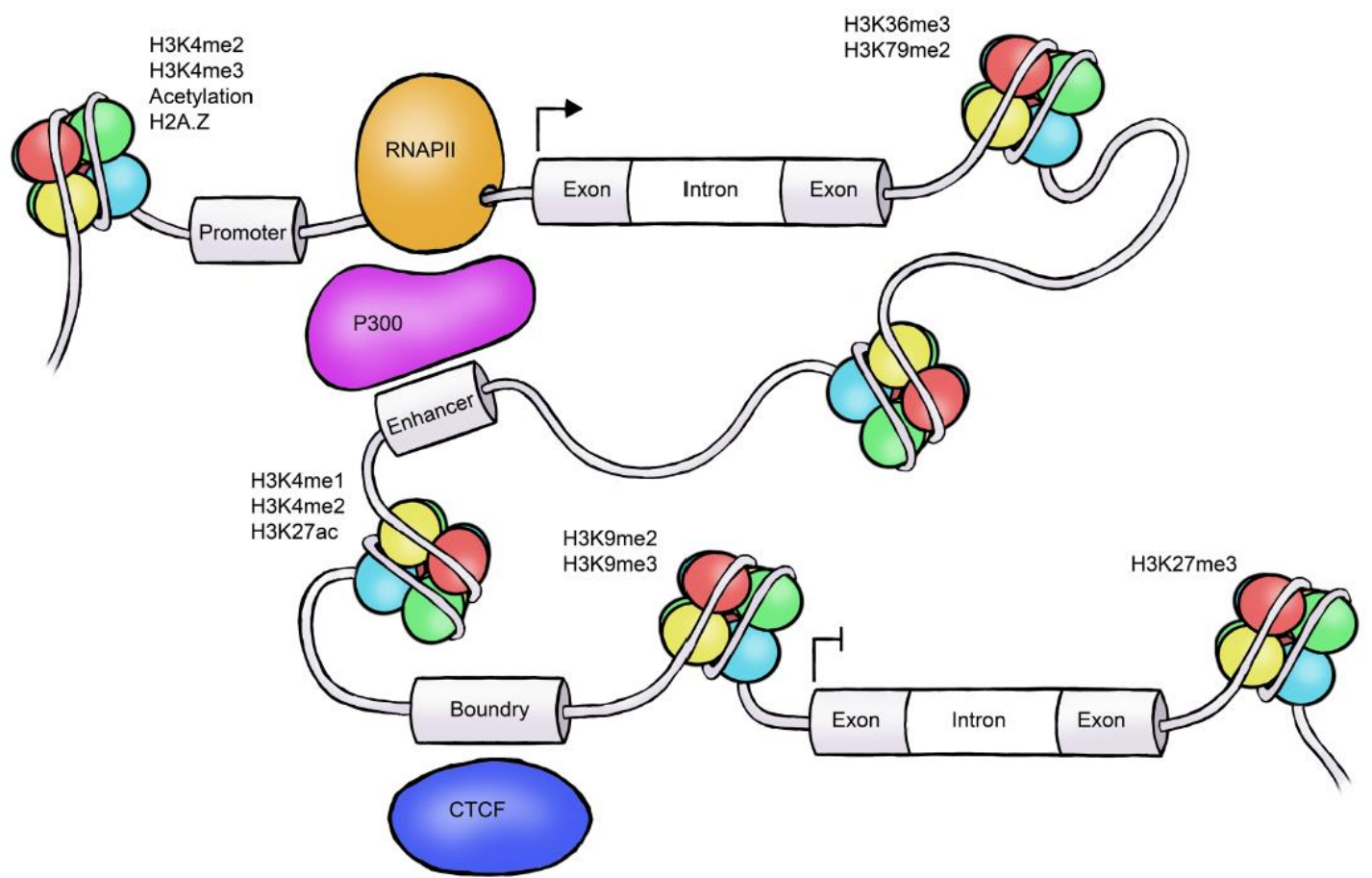
# Regulation of Transcription



# Histone Geometry Suggests A Complex, Combinatorial “Histone Code”



# Functional Elements Defined By Histone Marks



# Functional Elements in JIA GWAS Regions

Disease-Associated Single-Nucleotide Polymorphisms From Noncoding Regions in Juvenile Idiopathic Arthritis Are Located Within or Adjacent to Functional Genomic Elements of Human Neutrophils and CD4+ T Cells

Kaiyu Jiang, Lisha Zhu, Michael J. Buck, Yanmin Chen, Bradley Carrier, Tao Liu, and James N. Jarvis

**Table 1.** Histone marks in the SNP linkage disequilibrium blocks in neutrophils\*

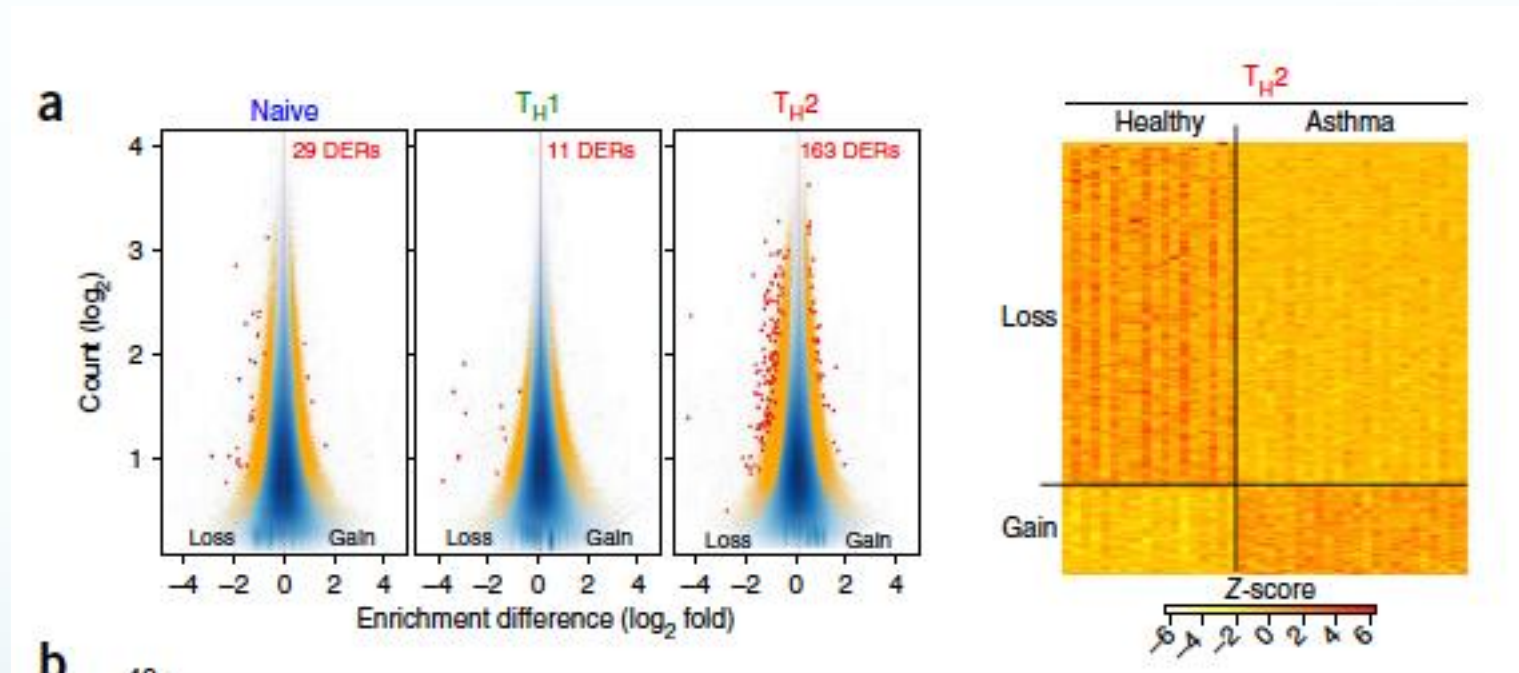
Chr.	Linkage disequilibrium region	GWAS index SNP	No. of H3K4me1+/H3K27ac- enhancers	No. of H3K4me1-/H3K27ac+ enhancers	No. of H3K4me1+/H3K27ac+ enhancers	Enhancer signal
1	114303808–114377568	rs6679677	5	0	4	Yes
1	154291718–154379369	rs11265608, rs72698115†	12	0	8	Yes
10	6078553–6097283	rs7909519	4	0	1	Yes
10	90759613–90764891	rs7069750	2	0	1	Yes
12	111884608–111932800	rs7137828†	0	0	1	Yes
14	69250891–69260588	rs12434551, rs3825568†	0	1	1	Yes
18	12774326–12809340	rs2847293	0	0	0	No
2	191943742–191973034	rs10174238	0	0	0	No
21	36712588–36715761	rs9979383, rs8129030†	0	0	0	No
22	21916166–21983260	rs2266959	3	1	6	Yes
22	37531436–37537058	rs2284033	0	0	0	No
4	123309902–123540758	rs1479924	0	0	0	No
5	55440730–55442249	rs71624119	1	0	0	Yes
5	96220087–96373750	rs27290, rs27293†	10	1	5	Yes
5	131813219–131832514	rs4705862	1	1	3	Yes
6	32592737–32797466	rs7775055‡	0	0	0	No

\* Chr. = chromosome; GWAS = genome-wide association study.

† The linkage disequilibrium blocks associated with these single-nucleotide polymorphisms (SNPs) were obtained from the 1000 Genomes Project pilot 1.

‡ The linkage disequilibrium block associated with this SNP was obtained from HapMap 3.

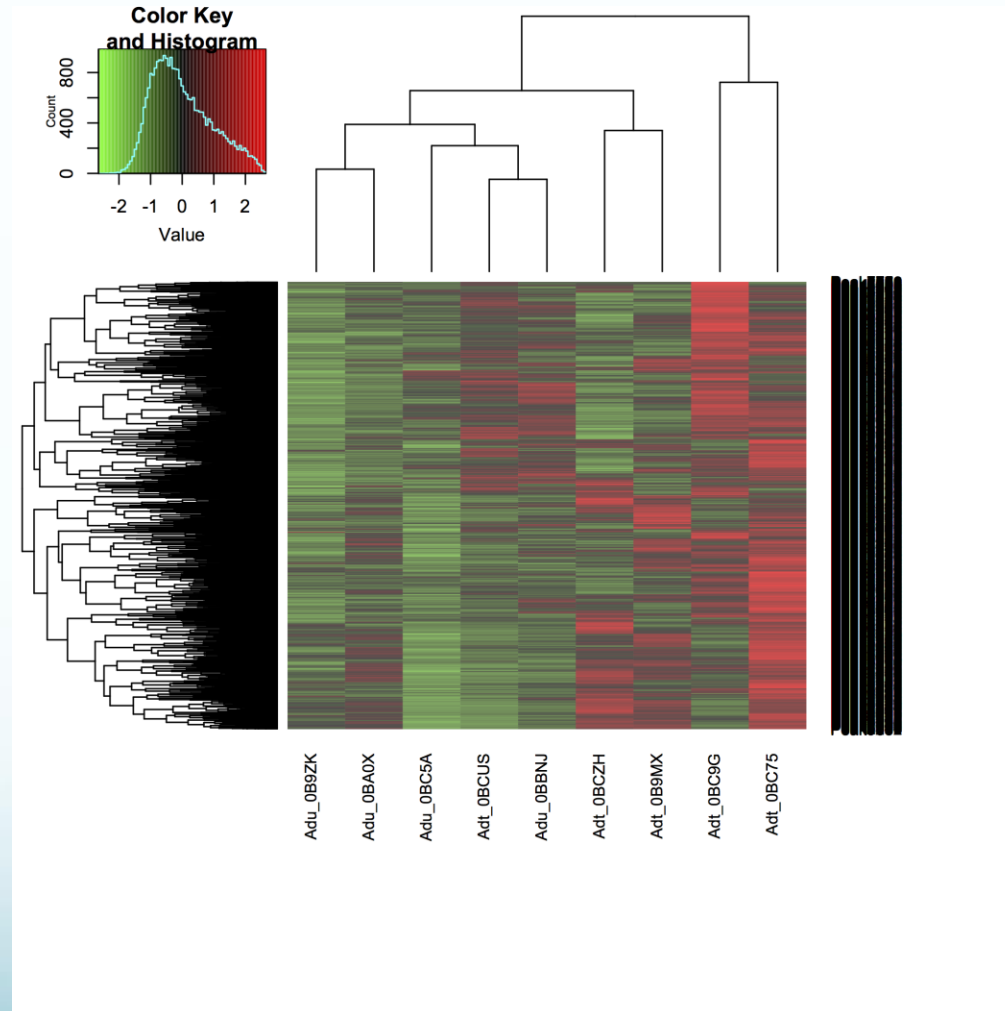
# More Complexity: Disease-Specific Enhancers



Seumois G et al, *Nature Immunol* 2014

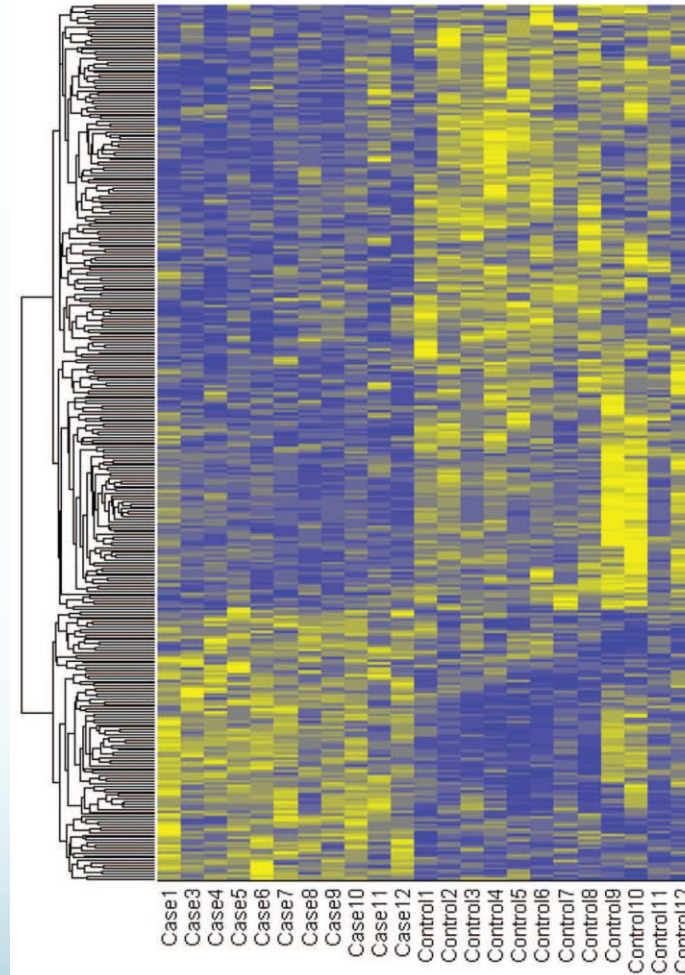


# JIA-Treatment Influences Enhancer Marks



# Methylation and Human Disease: SLE

Methylation  
patterns in  
CD4+ T cells



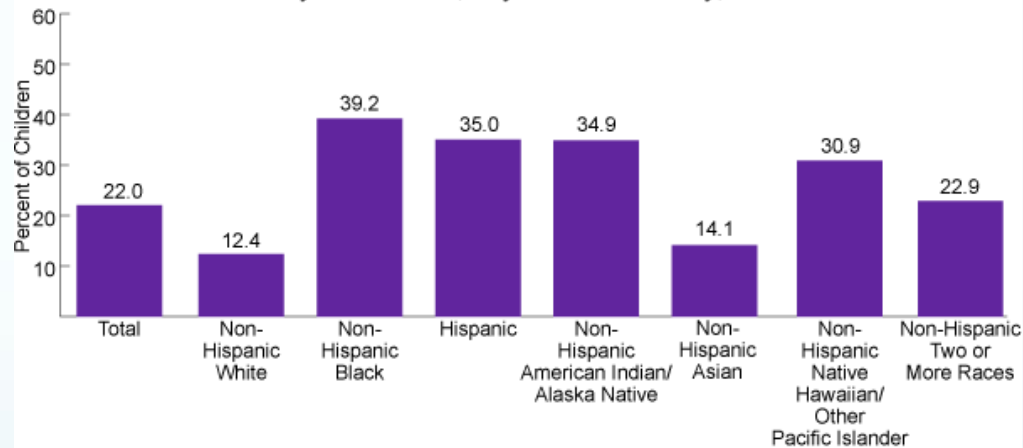
Jeffries MA et al,  
*Epigenetics* 2011.

# So What Does All This Mean?



# Children of Poverty- A National Problem

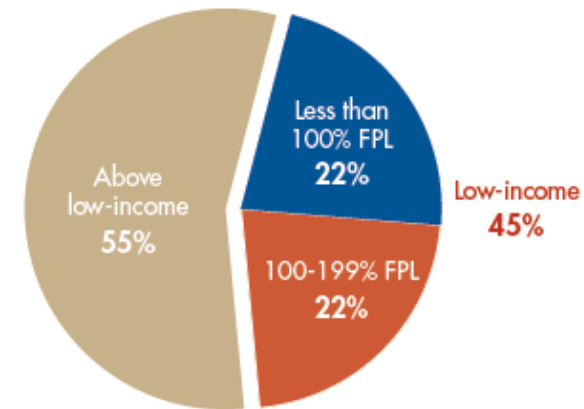
Children Under Age 18 Living in Households with Incomes Below 100 Percent of the Poverty Threshold,\* by Race/Ethnicity, 2010



\*The U.S. Census Bureau uses a set of money income thresholds to determine who is in poverty; the poverty threshold for a family of four was \$22,314 in 2010.

Source: U.S. Census Bureau, Current Population Survey (CPS) Table Creator II for the Annual Social and Economic Supplement. Retrieved from: [http://www.census.gov/hhes/www/cpstc/cps\\_table\\_creator.html](http://www.census.gov/hhes/www/cpstc/cps_table_creator.html). Accessed: March 26, 2012.

Children by family income, 2011



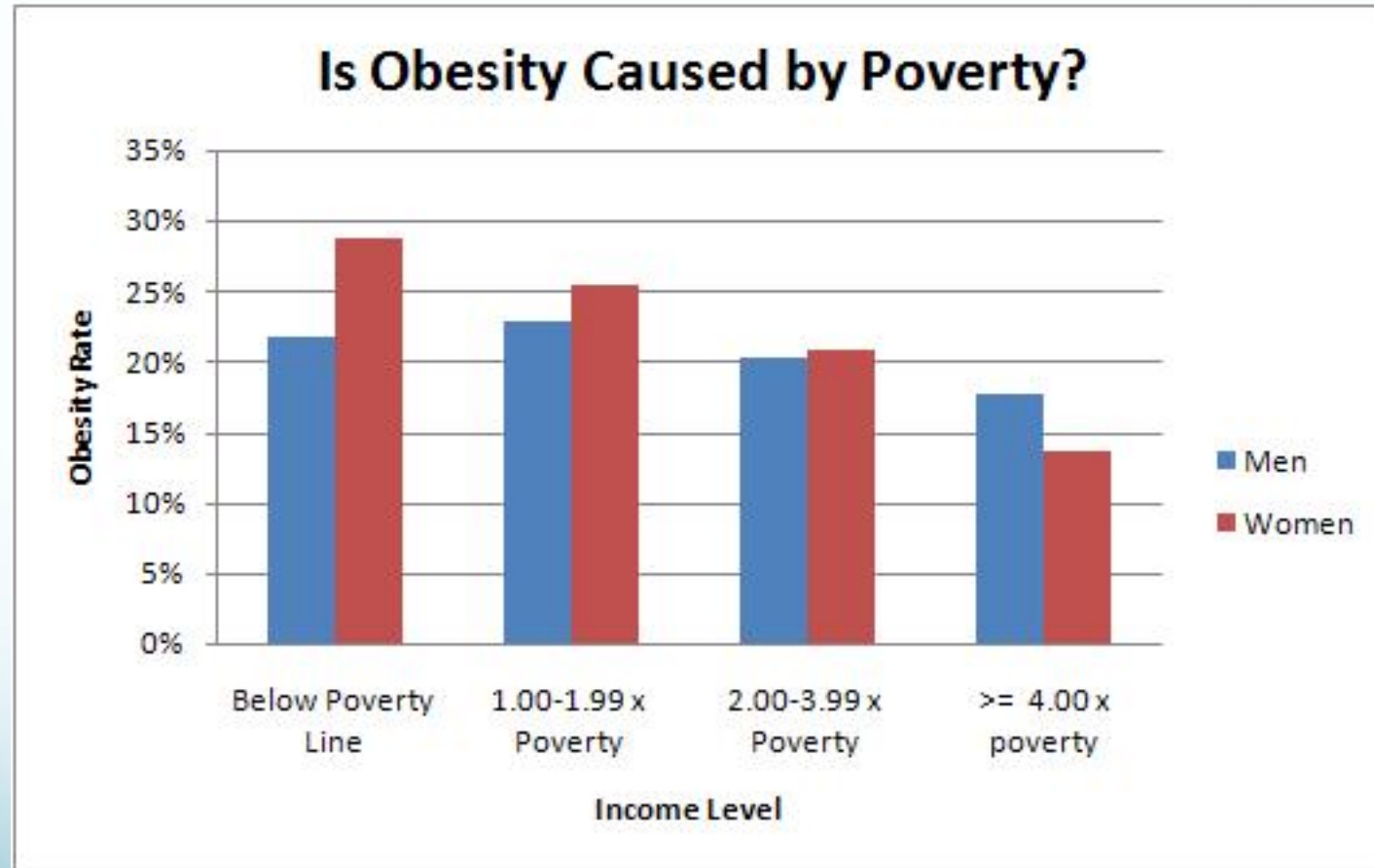
Percentages may not add to 100 due to rounding.

© National Center for Children In Poverty ([www.nccp.org](http://www.nccp.org))  
Basic Facts About Low-Income Children: Children Under 18 Years, 2011

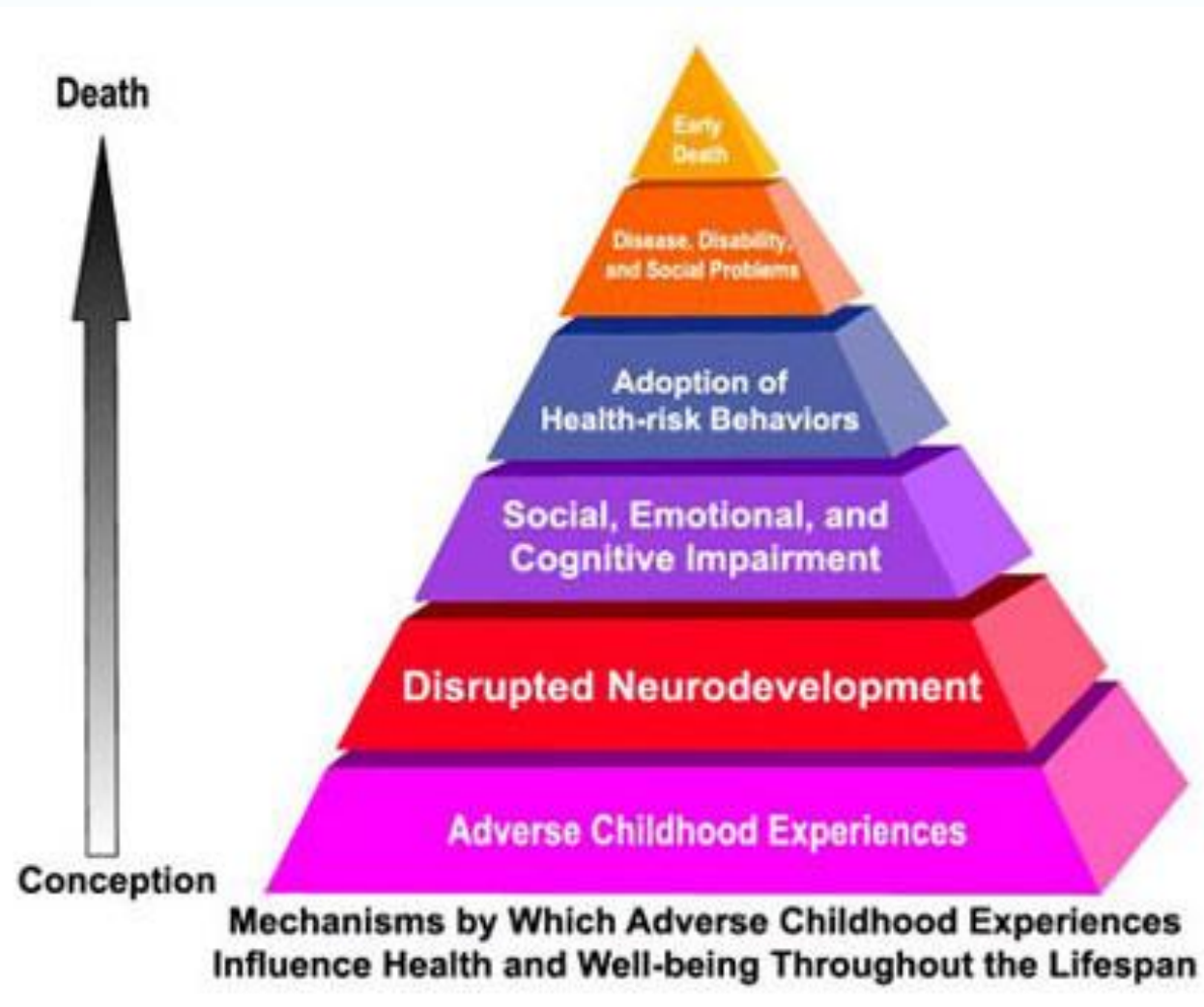
# Where Our Children Grow Up



# Links Between Poverty and Health Measures



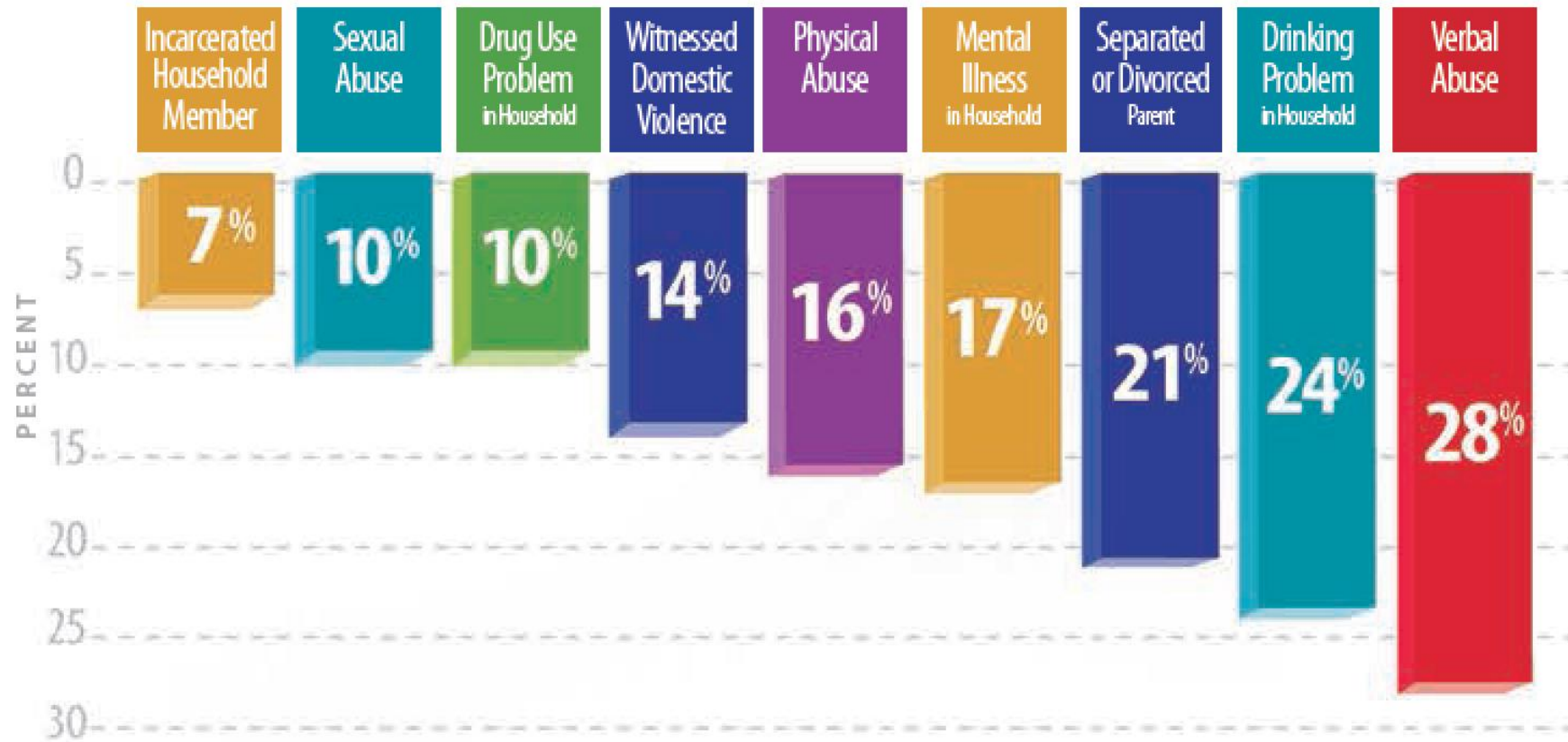
# Adverse Childhood Events: Where Physical Health and Community Health Are Joined



1. Recurrent physical or emotional abuse.
2. Sexual abuse.
3. ETOH or other substance abuser in the home.
4. Incarcerated household member.
5. Someone who is chronically depressed, suicidal, or otherwise mentally ill.
6. Mother being treated violently.
7. One or no parents.
8. Emotional or physical neglect.

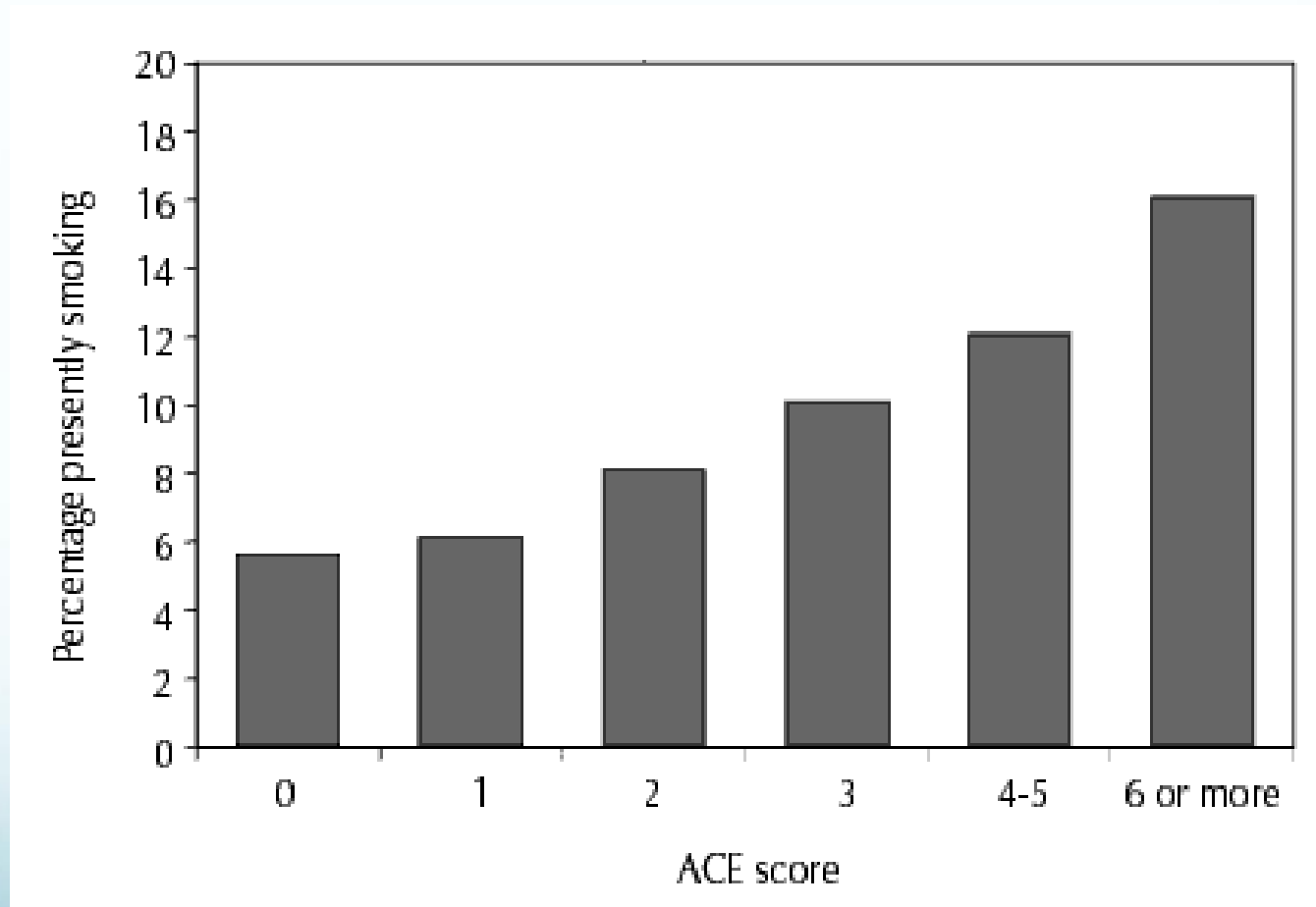
## PREVALENCE OF INDIVIDUAL ACES

MINNESOTA 2011

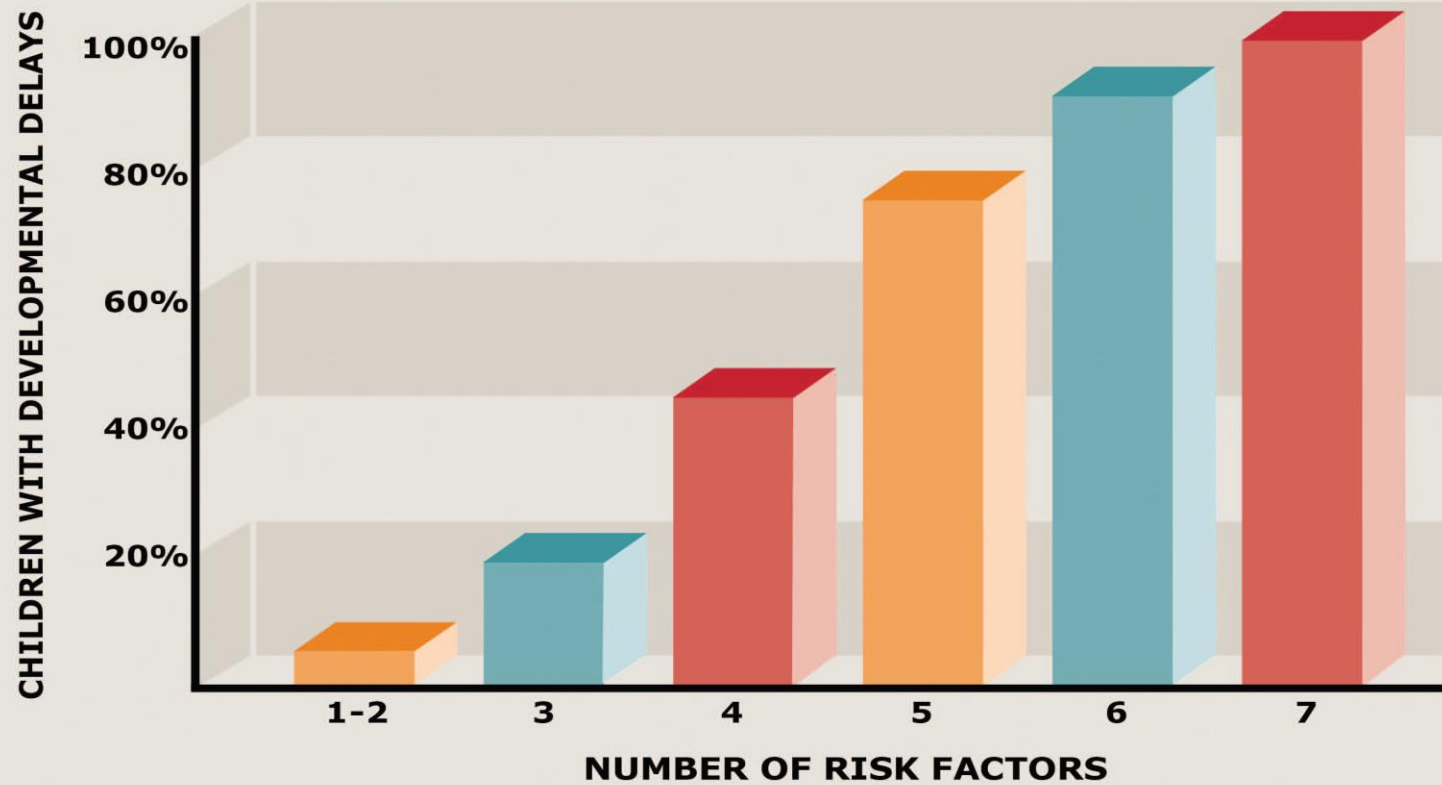




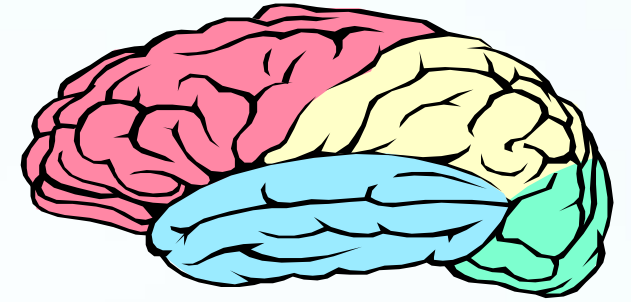
# ACE Score and Smoking Status



# Childhood Development and Parental ACE



# Early Stress



**CHILDHOOD STRESS**

**Hyper-responsive stress response; ↓ calm/coping**

**Chronic “fight or flight;”  
↑ cortisol / norepinephrine**

**Changes in Brain Architecture**

# Defining Adversity or Stress



- How do you define/**measure** adversity?
- **Huge individual variability**
  - **Perception** of adversity or stress (subjective)
  - **Reaction** to adversity or stress (objective)
- **National Scientific Council on the Developing Child (Dr. Jack Shonkoff and colleagues)**
  - **Positive Stress**
  - **Tolerable Stress**
  - **Toxic Stress**

Based on the **REACTION** (objective physiologic responses)

# Defining Adversity or Stress



- **Positive Stress**

- **Brief, infrequent, mild to moderate intensity**
- **Most normative childhood stress**
  - Inability of the 15 month old to express their desires
  - The 2 year old who stumbles while running
  - Beginning school or daycare
  - The big project in middle school
- **Social-emotional buffers** allow a return to **baseline**  
(responding to non-verbal clues, consolation, reassurance, assistance in planning)
- **Builds motivation and resiliency**
- Positive Stress is **NOT** the **ABSENCE** of stress



# Defining Adversity or Stress

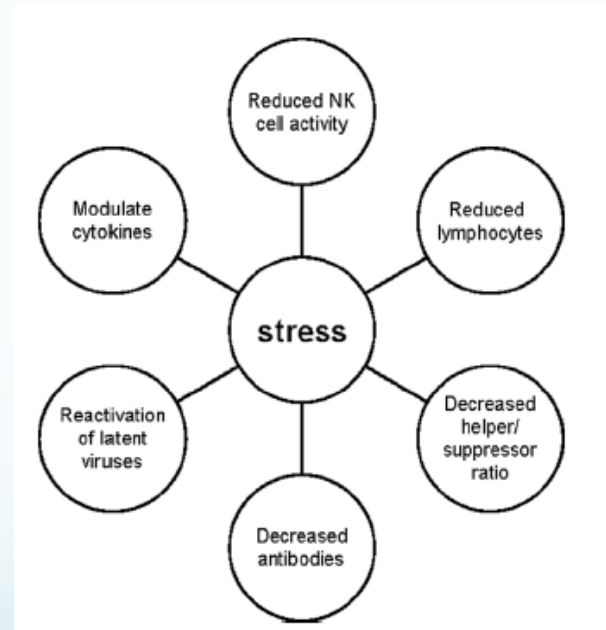
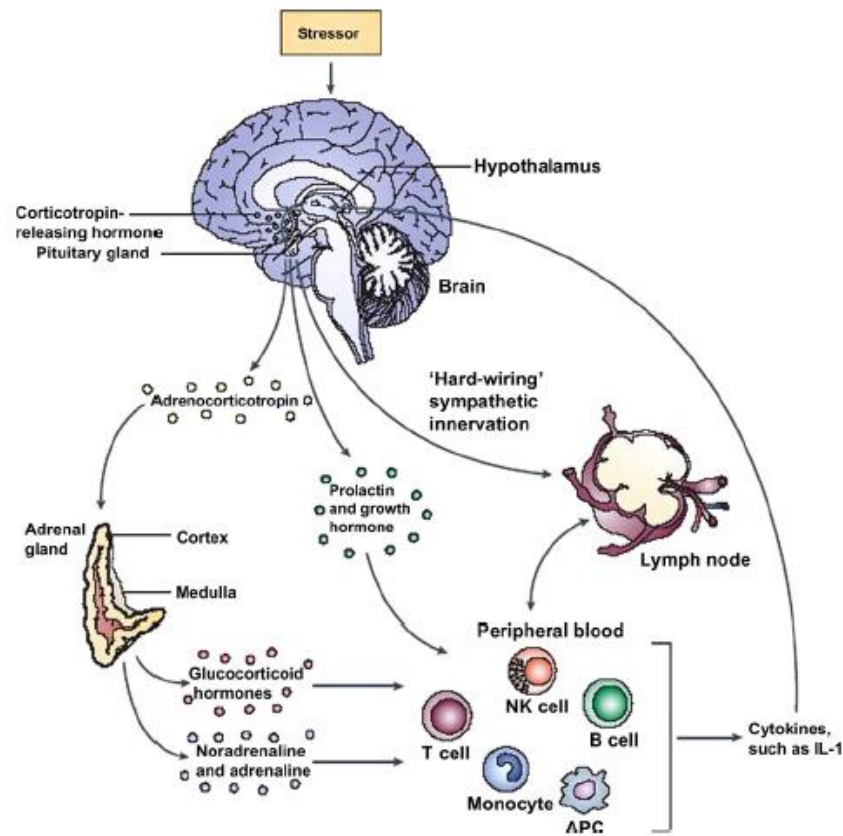


- **Toxic Stress**

- Long lasting, frequent, or strong intensity
- More extreme precipitants of childhood stress (**ACEs**)
  - Physical, sexual, emotional abuse
  - Physical, emotional neglect
  - Household dysfunction
- **Insufficient social-emotional buffering**  
(Deficient levels of emotion coaching, re-processing, reassurance and support)
- Potentially permanent changes and long-term effects
  - **Epigenetics** (there are life long / intergenerational changes in how the genetic program is turned **ON** or **OFF**)
  - **Brain architecture** (the mediators of stress impact upon the mechanisms of brain development / **connectivity**)



# Stress: An Immune Modifier



# Inflammation and Complex Traits in Children



Preterm birth



Obesity



Bronchopulmonary dysplasia



Asthma

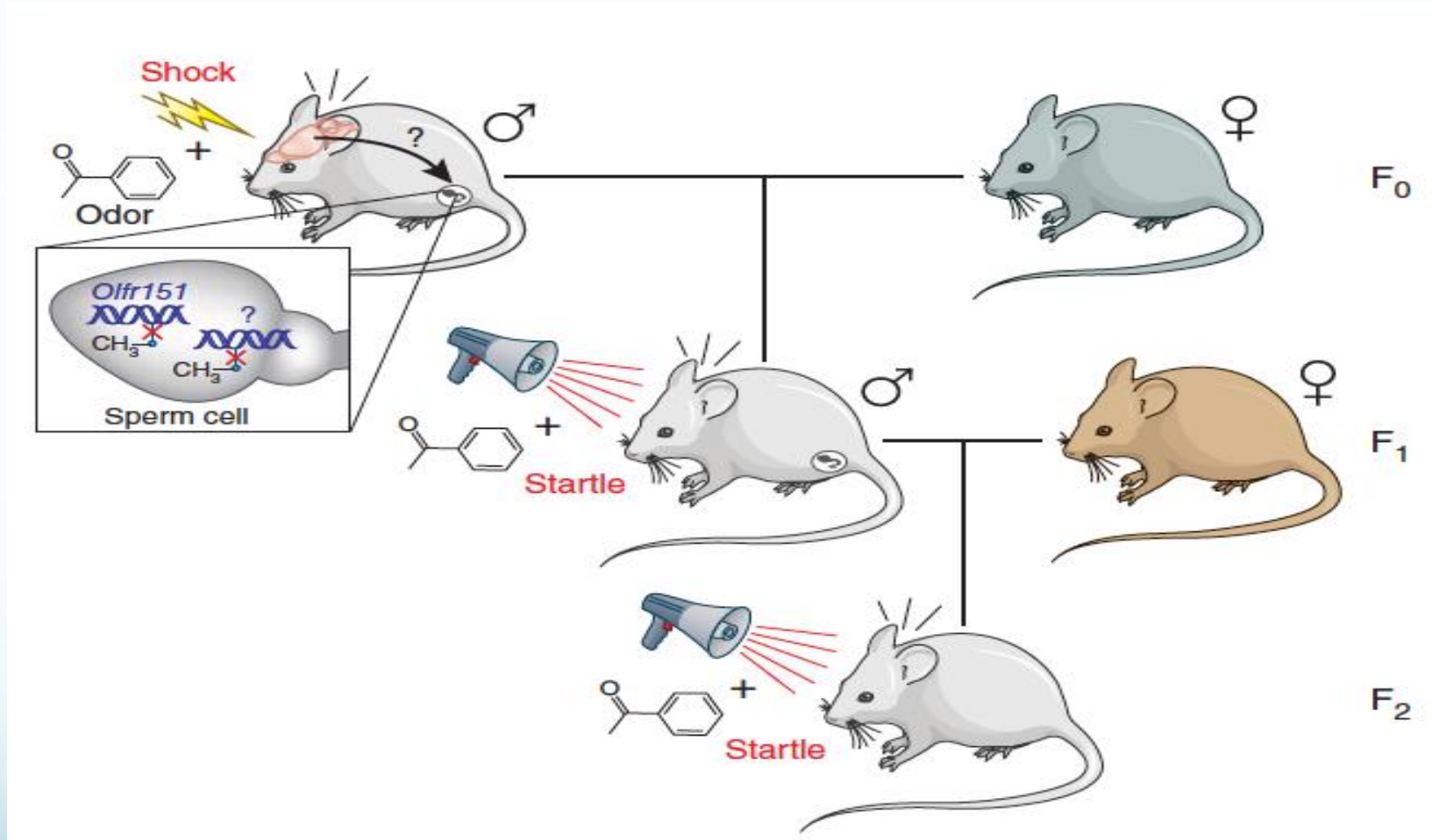
(Asthma rates increase with ACE exposure - Wing et al  
Ann Allergy Asthma Immunol 2015; 114: 379)



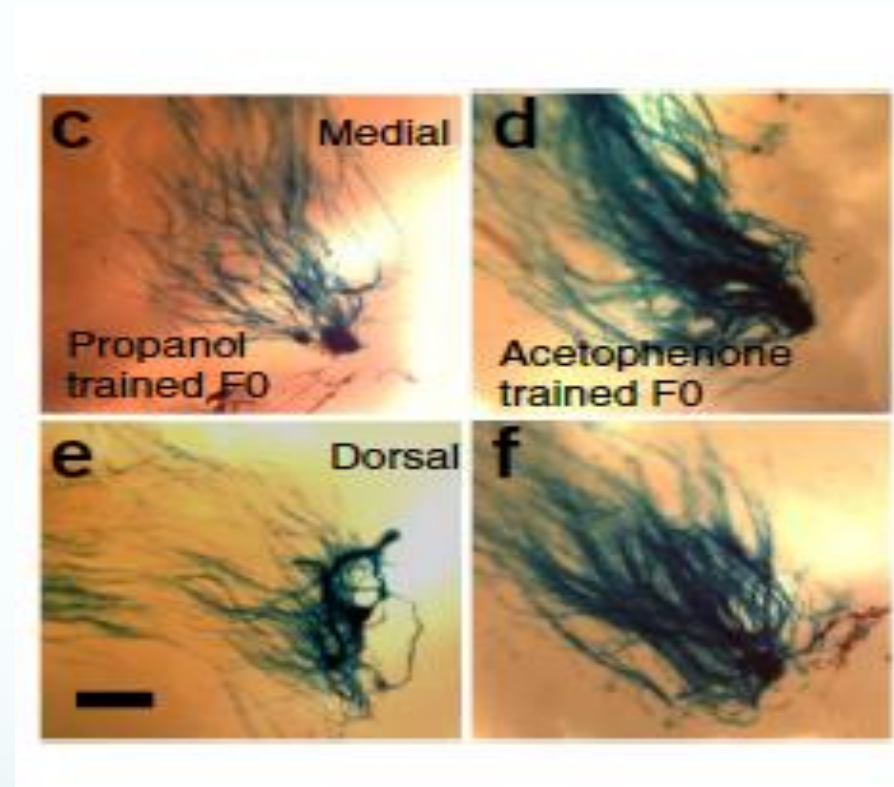
# Maybe Just Saying, “Eat Your Vegetables” Isn’t Enough



# Epigenetics and Behavior

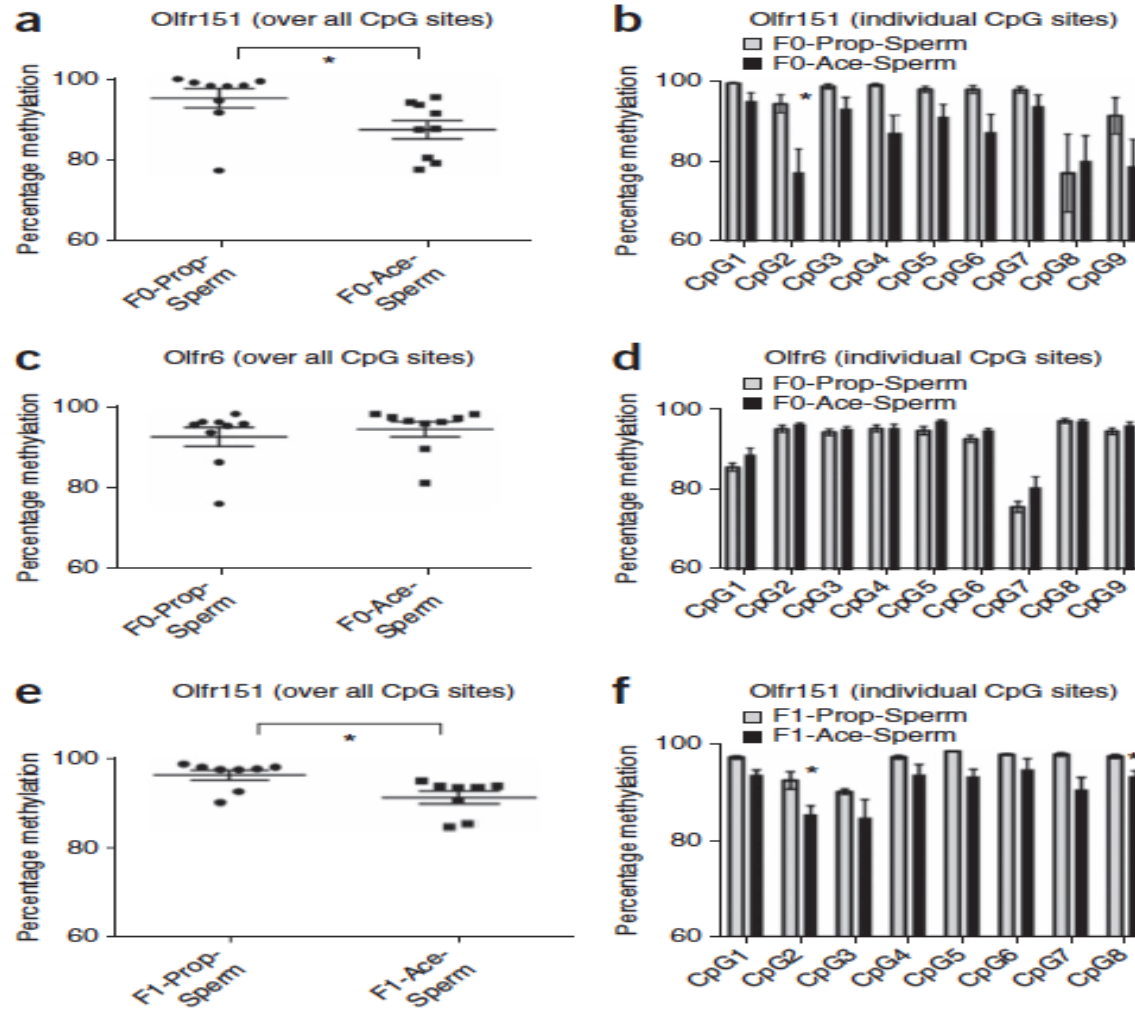


# Epigenetics and Behavior: Brain Rewiring



Beta galactosidase staining of select olfactory regions: F1 offspring

# Epigenetics and Behavior: Methylation of *Olf51*



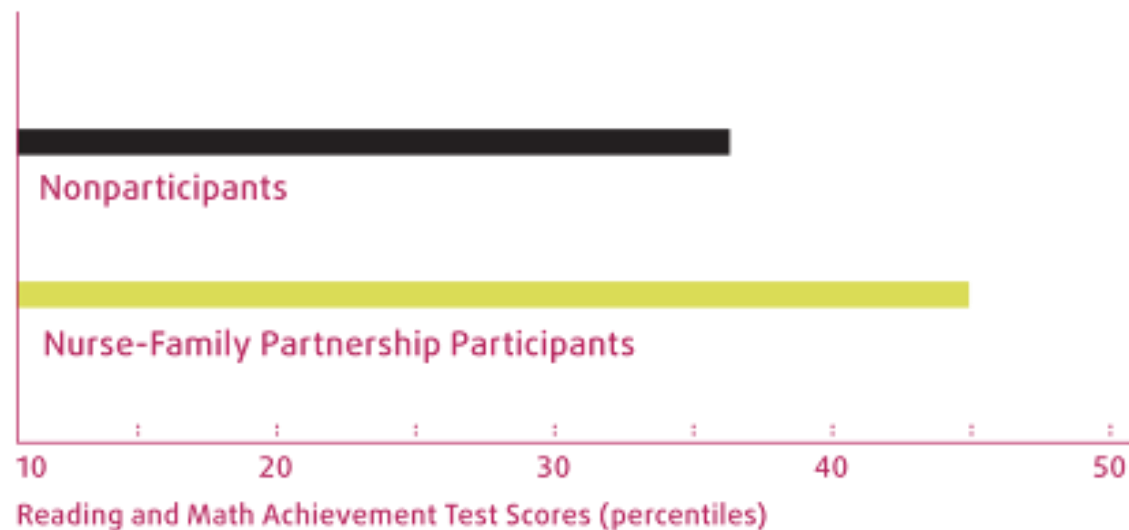
# Stronger Parents Raise Stronger Children

- Infant mental health
- Court referral programs
  - Zero to Three's Infant-Toddler Court Teams
    - Intervention includes referral of young parents to behavioral health for parenting assessment/training
- Prenatal/Early Life Home Visiting
  - Evidence-based interventions proven to improve the life trajectories of low income women and children
  - Positive effects now shown up to *age 19 yrs*



## Academic Achievement

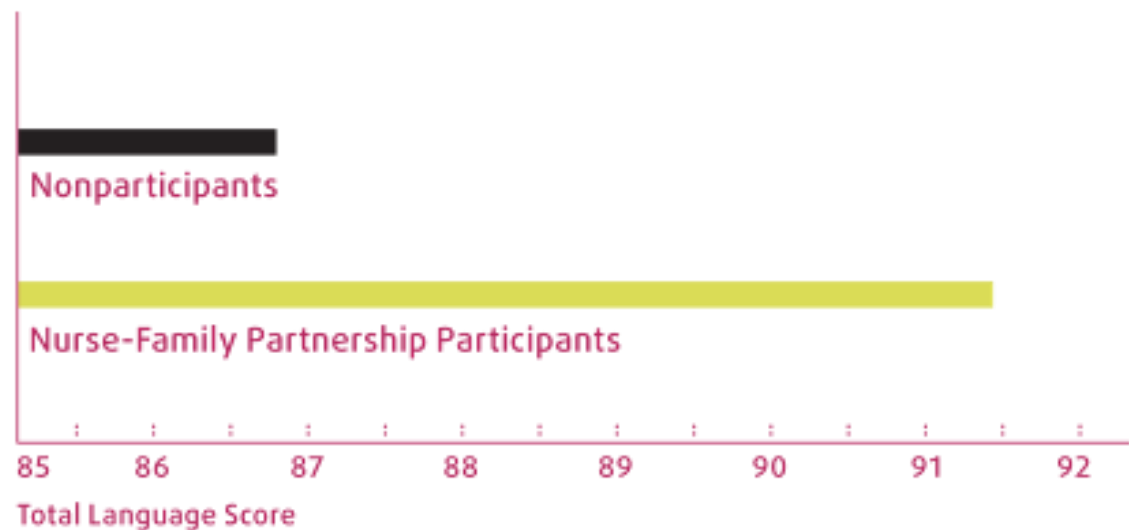
Grades 1-3, Age 9—Memphis  
(Born to low-resource mothers)



Source: Reproduced with permission from *Pediatrics*, Vol. 120, e838, Copyright © 2007 by the AAP.

## Preschool Language Scale

Age 4—Denver  
(Born to low-resource mothers)

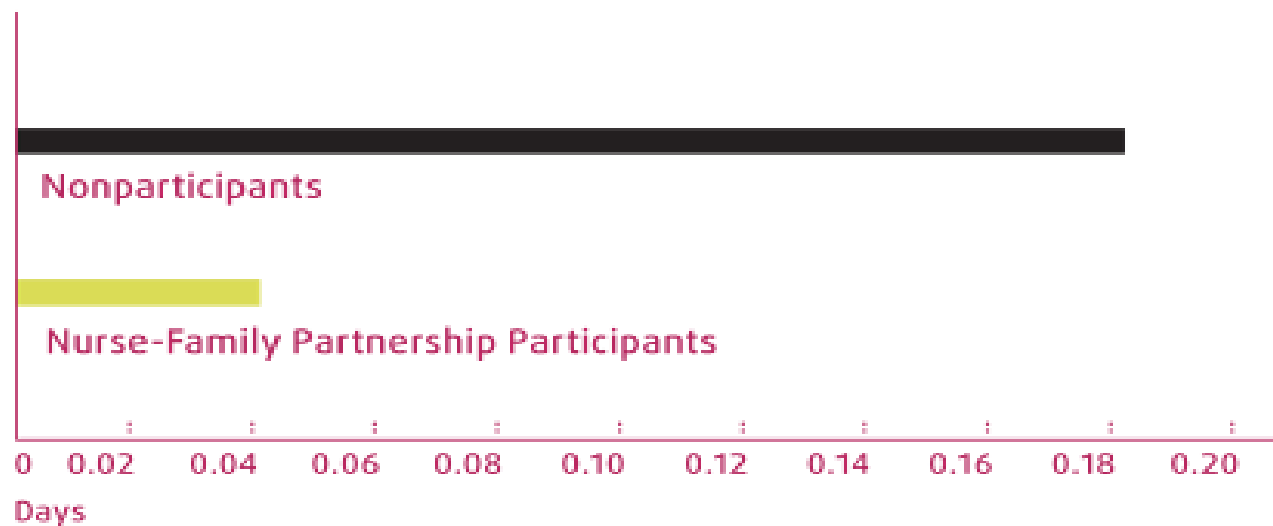


Source: Reproduced with permission from *Pediatrics*, Vol. 114, 1565, Copyright © 2004 by the AAP.



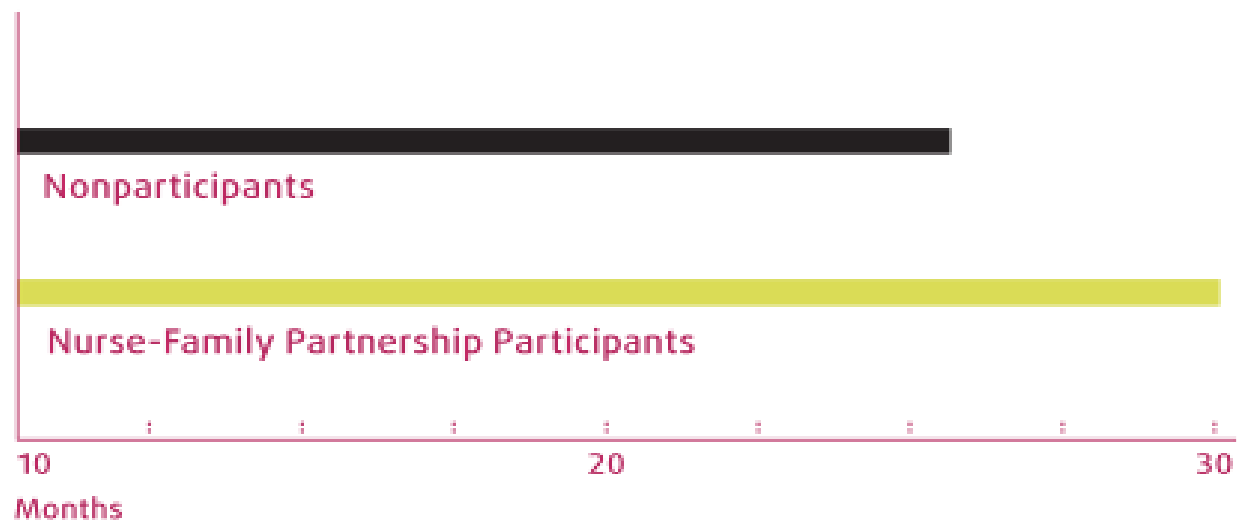
## Days Hospitalized for Injuries

Birth to age 2—Memphis



## Months Between Births

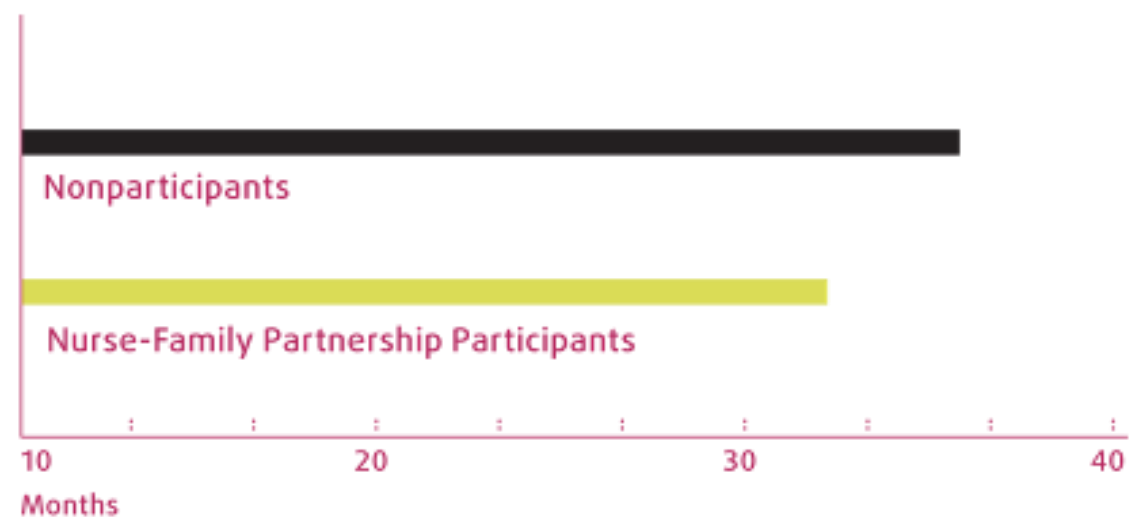
Between first and second child  
(by first child's fifth birthday)—Memphis





## Months Receiving Welfare Assistance (AFDC)

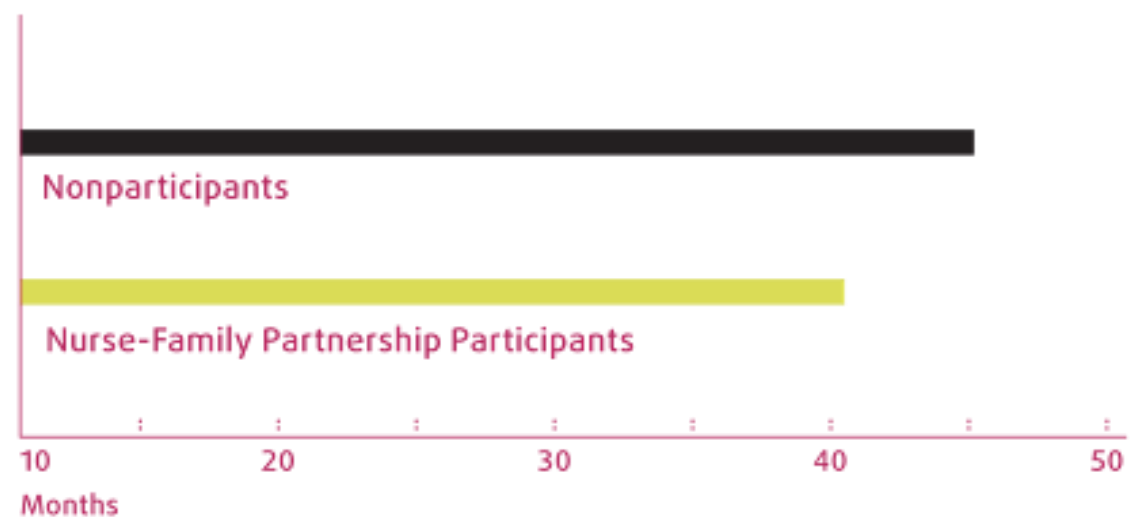
Birth through age 5—Memphis



Source: *JAMA*, 2000, Vol. 283, 1987, Copyright © 2000, American Medical Association. All rights reserved.

## Months Receiving Food Stamps

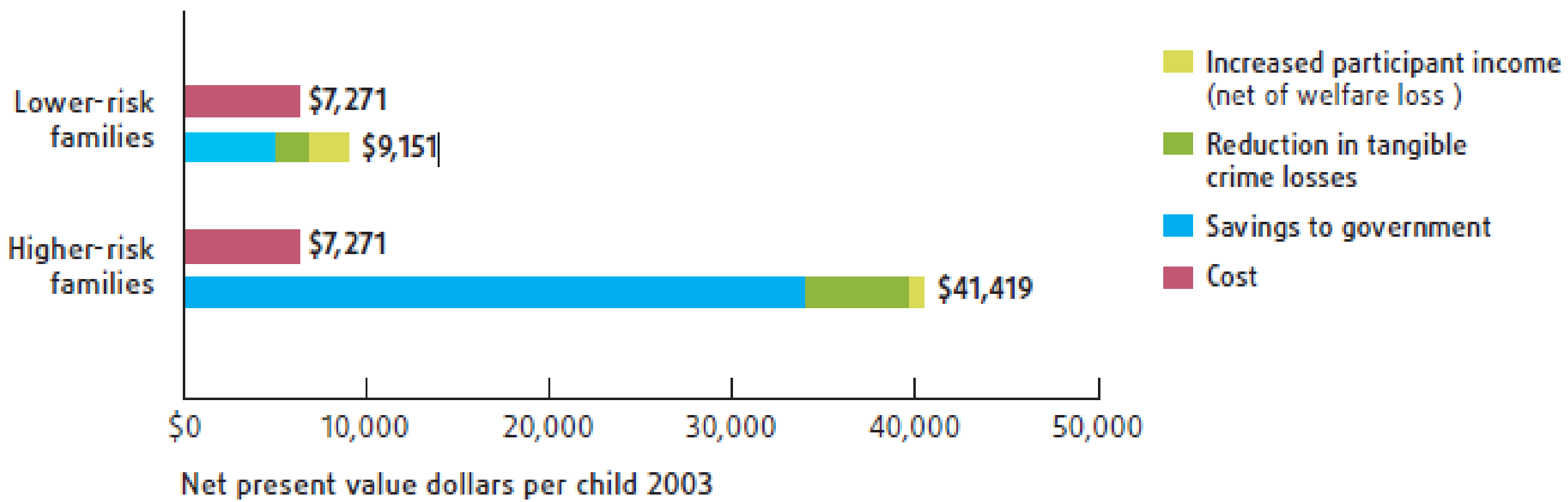
Birth through age 5—Memphis



Source: *JAMA*, 2000, Vol. 283, 1987, Copyright © 2000, American Medical Association. All rights reserved.



# Monetary Benefits



Source: 2005 RAND Corporation Study

# Family Spirit Impact: Pregnancy to Age 3

## Parenting

- Increased maternal knowledge <sup>1,2,3,4</sup>
- Increased parent self-efficacy <sup>3,4</sup>
- Reduced parent stress <sup>2,4</sup>
- Improved home safety attitudes<sup>3</sup>

## Mothers' Outcomes

- Decreased depression. <sup>1,2,4</sup>
- Decreased substance use <sup>4</sup>
- Fewer risky behaviors <sup>3,4</sup>

## Child Outcomes

- Fewer social, emotional and behavior problems through age 3. <sup>2, 3, 4</sup>
- Lower clinical risk of behavior problems over life course <sup>4</sup>



Decreased Externalizing,  
Internalizing and Dysregulation

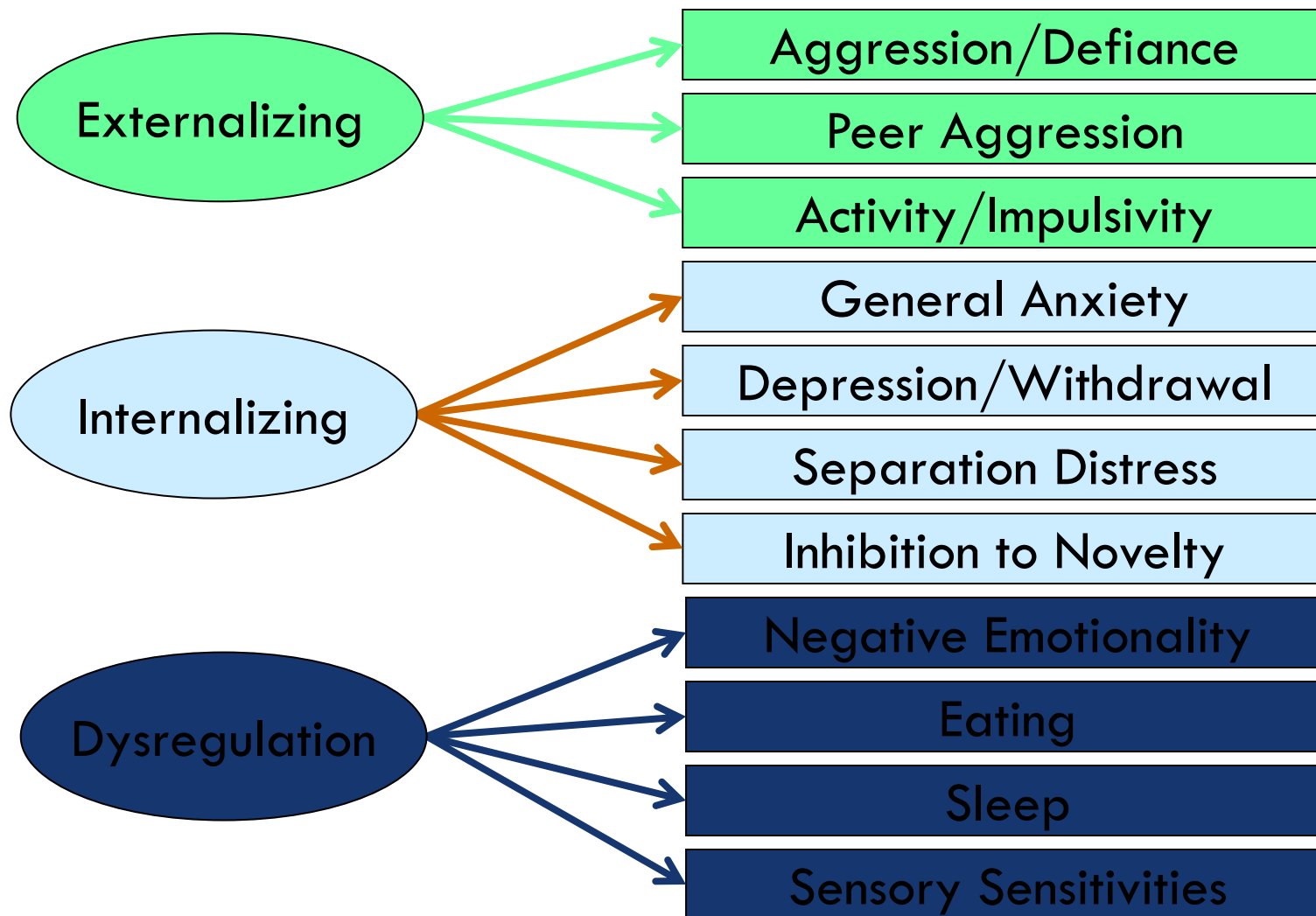
1 Barlow A, Varipatis-Baker E, Speakman K, et al *Arch Pediatr Adolesc Med.* 2006;160:1101-1107

2 Walkup J, Barlow A, Mullany B, et al. *Journal of the American Academy of Child and Adolescent Psychiatry.* June 2009.

3 Barlow A, Mullany B, Neault N, et al. *American Journal of Psychiatry.* January 2013.

4 Barlow A, Mullany B, Neault N, et al. *American Journal of Psychiatry.*, February 2015.

# ITSEA Problem Domains and Subscales within Domains



# Parenting and Early Childhood Behavior Problems Associated with Obesity

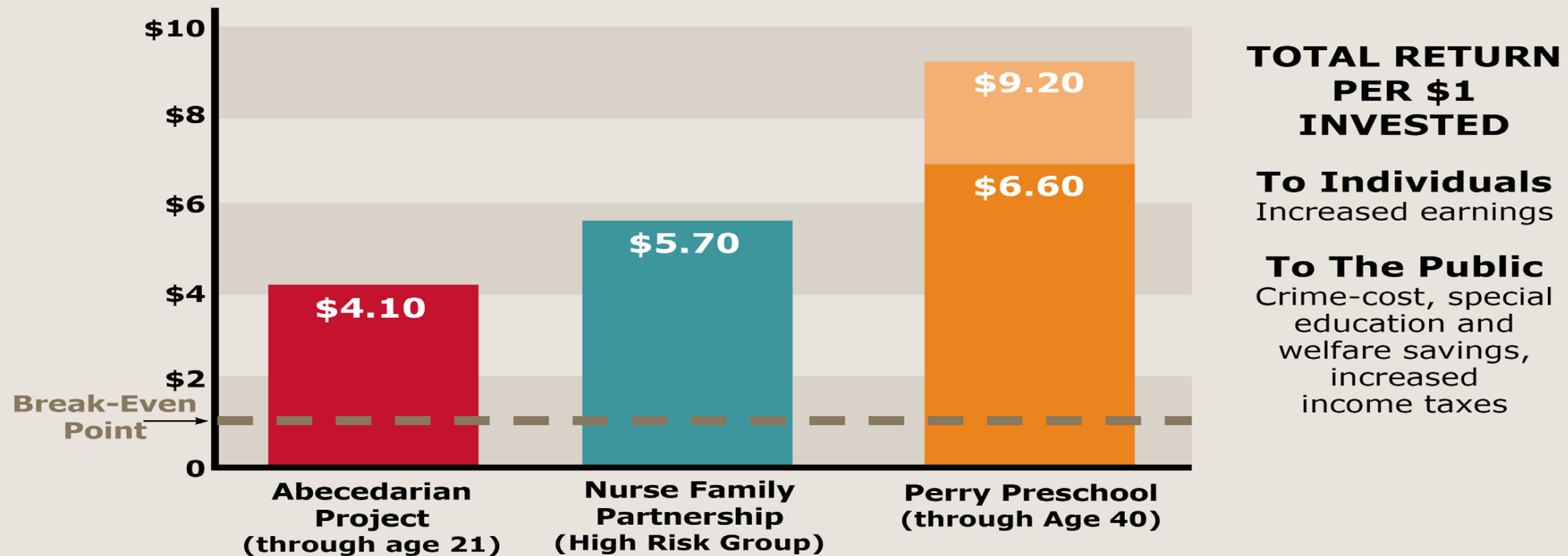
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- Negative parenting (inconsistent discipline; restrictive, coercive parenting) associated with increased obesity risk in children.
  - [Int J Obes \(Lond\)](#). 2006 Dec;30(12):1766-74.
  - [Trends Endocrinol Metab](#). 2013 Apr 19 E-pub
  
- Externalizing behaviors at 24 mos associated with higher BMI at 24 months and thru age 12
  - [BMC Pediatr](#). 2010 Jul 14;10:49
  
- Obese children have higher rates of externalizing and internalizing disorders.
  - [Acad Pediatr](#). 2013 Jan-Feb;13(1):6-13



# \$4-\$9 in returns for every dollar invested in early childhood programs



[Center on the Developing Child at Harvard website](#)

Sources: Masse, L. and Barnett, W.S., A Benefit Cost Analysis of the Abecedarian Early Childhood Intervention (2002); Karoly et al., Early Childhood Interventions: Proven Results, Future Promise (2005); Heckman et al., The Effect of the Perry Preschool Program on the Cognitive and Non-Cognitive Skills of its Participants (2009)

# “Early Life Investments Substantially Boost Adult Health”

- Carolina Abecedarian Project
  - 4 cohorts of disadvantaged children born 1972-77
    - Intervention provided from birth to age 5 years
  - Intervention:
    - Level of language, emotional regulation, cognitive skills
    - Caregiving/supervised play
    - Nutrition: 2 meals and a snack at childcare center
    - Primary pediatric care
- In their mid-30s: lower prevalence of CVD and metabolic disease risk factors including BP, A1C, obesity, HDL

# The Path We *Could* Take

## Rewind: “Mary’s” life

- As soon as mother’s pregnancy diagnosed:
  - Matched with a home visitor/case manager
    - Weekly/biweekly visits focusing on developing a mentoring-type relationship, building on mother’s strengths, helping her to set goals, teaching her new skills
    - All services needed were offered and tailored to her needs
    - WIC foods supplemented so mother had enough good food even though shared with family
    - Mother rewarded for participation in each component
  - Mother went to 90% of her prenatal appointments
    - All but first urine drug screen negative and most cotinine screens
  - Mary born at 39 wks gest, normal weight for gestation

# Rewind: “Mary”

- Visits from home visitor continued until Mary was 2 yrs old
- Mother set/achieved goals: became a CNA through health occupations class and graduated from high school
  - Mary cared for during day by excellent tribal child care program: bonding, learning, good food, social skills, active play, tribal language all emphasized
- Mother attended parenting classes
  - Praised and hugged Mary, appropriately disciplined her
  - Ate dinner together and read to Mary most evenings
  - Left her boyfriend when he wouldn't stop drinking
- Mary's weight stayed around the 90<sup>th</sup> percentile
- Mary graduated from high school, went to tribal college, got a good job, married a guy she met at college
- Now Mary becomes pregnant...





Isn't this among the most important work we can do for our patients and communities?

“The medicine is already within the pain and suffering. You just have to look deeply and quietly. Then you realize it has been there the whole time.” Duran, 2006

## **CONCLUSION:**

**It is easier to build strong children than to repair broken men.**

**Frederick Douglass**



# Generous Funding From:



National Institute  
of Allergy and  
Infectious Diseases

