



Toxic Stress & Asthma

San Francisco Asthma Network Forum

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Acknowledgements



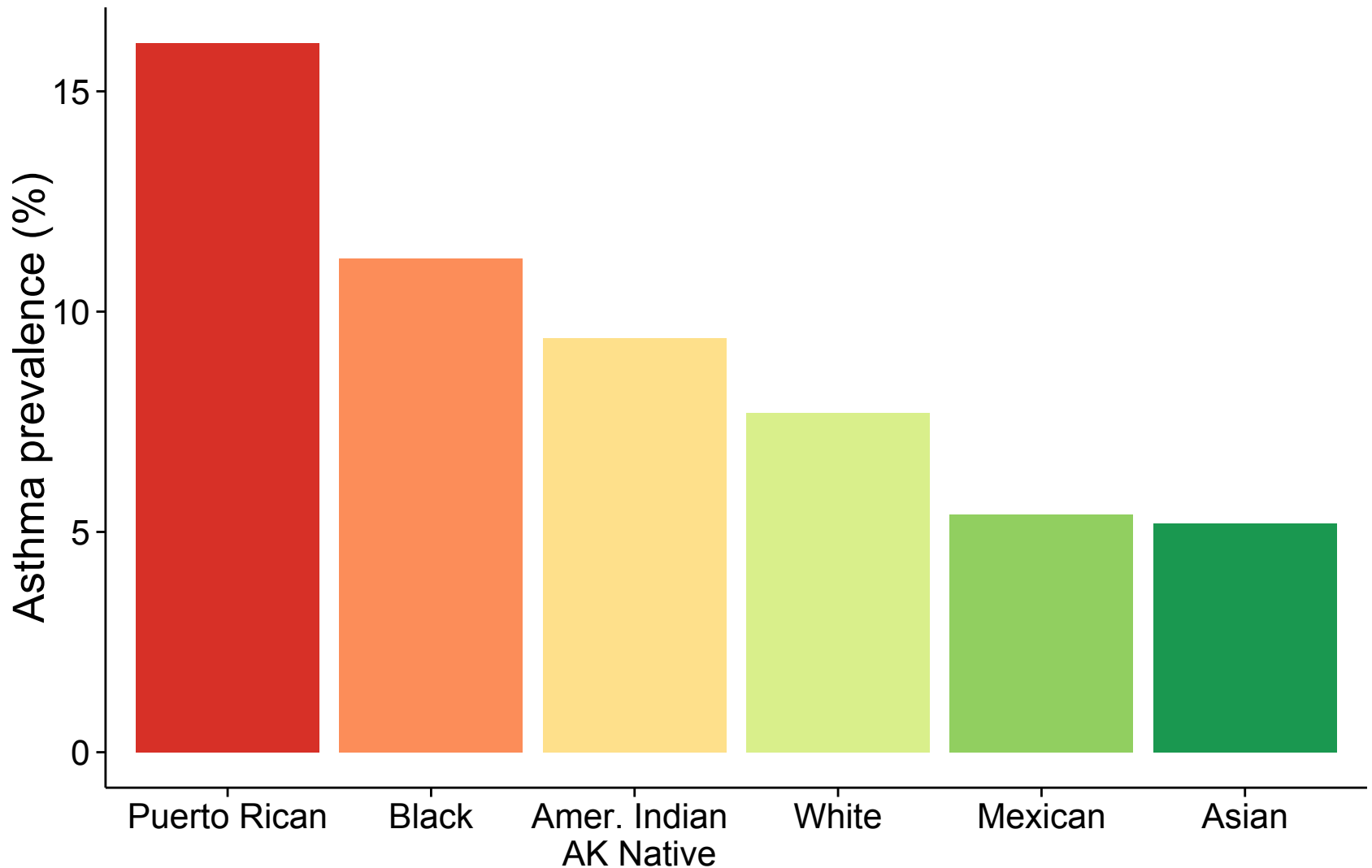
K Nishimura ♦ **Esteban G. Burchard** ♦ **Neeta Thakur** ♦ N Barcelo
J Balayan ♦ C Eng
S Singh ♦ M McGarry ♦ M White ♦ J Galanter ♦ M Pino Yanes ♦ D Hu
S Salazar ♦ M Spear ♦ D Torgerson ♦ S Huntsman ♦ L Caine

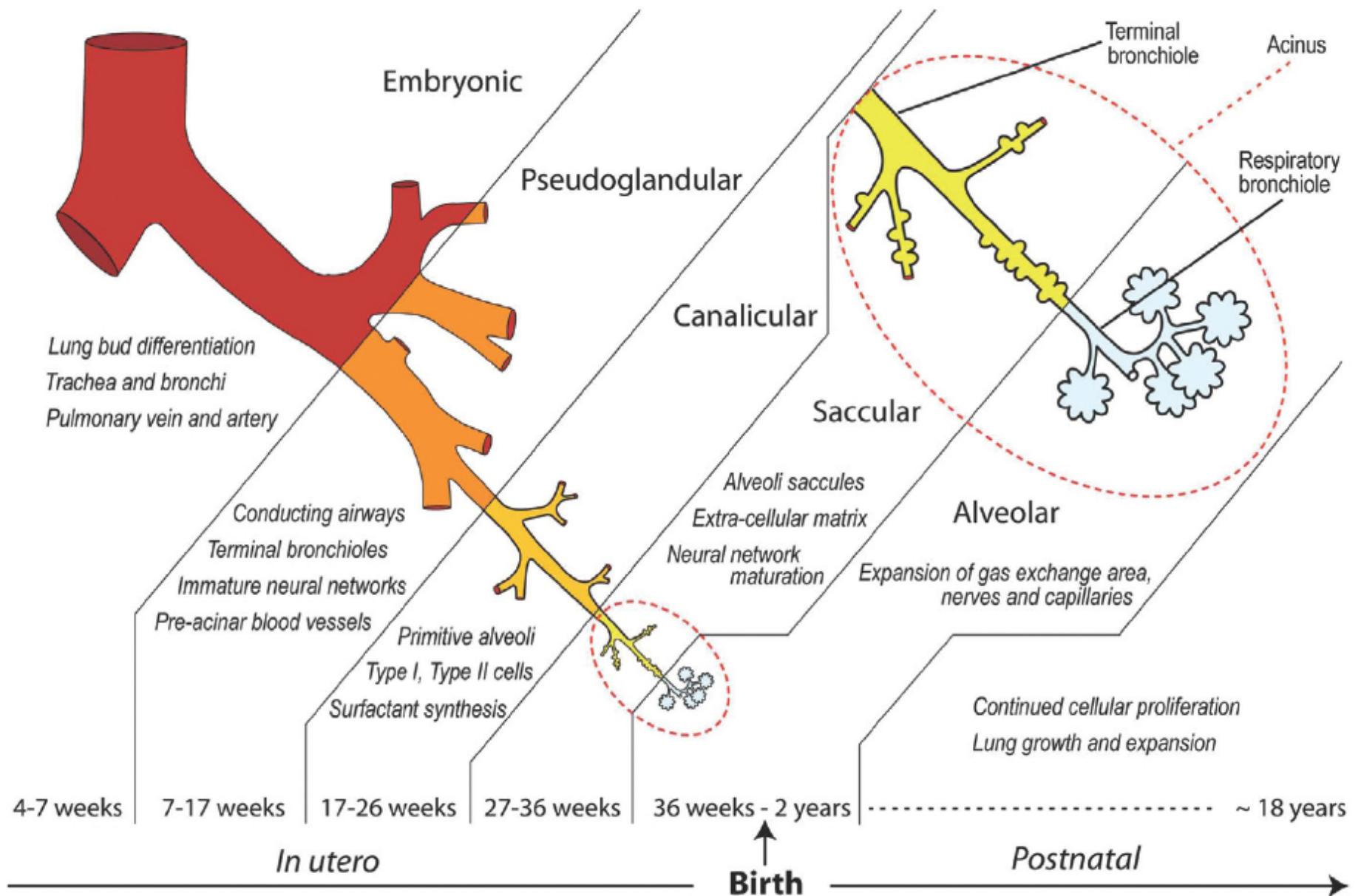
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Learning Objectives

- How does chronic stress affect health?
 - Clinical pathways
 - Epigenetics
- What are biomarkers of stress response?
 - Inflammation
 - Cotinine
- How does toxic stress affect asthma?

Asthma: one size does not fit all





Is Toxic
Stress taking
our Breath
Away?

How?



Positive stress

Brief increases in heart rate
Mild elevations in stress hormones

Tolerable stress

Serious, *temporary* stress responses
Buffered by supportive relationships

Toxic stress

Prolonged stress response activation
Absence of protective relationships

**Nature of
stressor**

**How stressor
is perceived**

**Ability to
cope**

**Physiologic
response**

Stressors

Trauma, Access,
Demographics

Violence, Neighborhood
deprivation, Air pollution

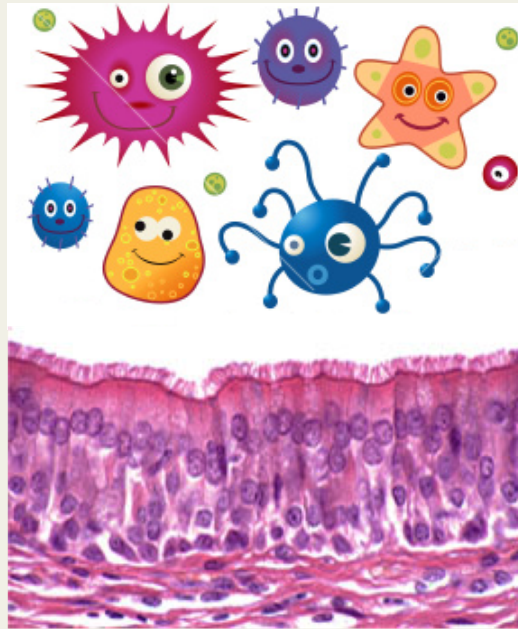
Individual Characteristics

Sex, genes, development,
experience, behavior

Physiologic Response

Glucose, CRP, IL-3, -4, -5, -6,
-13, INF- γ , DHEA-S, lipids, BMI

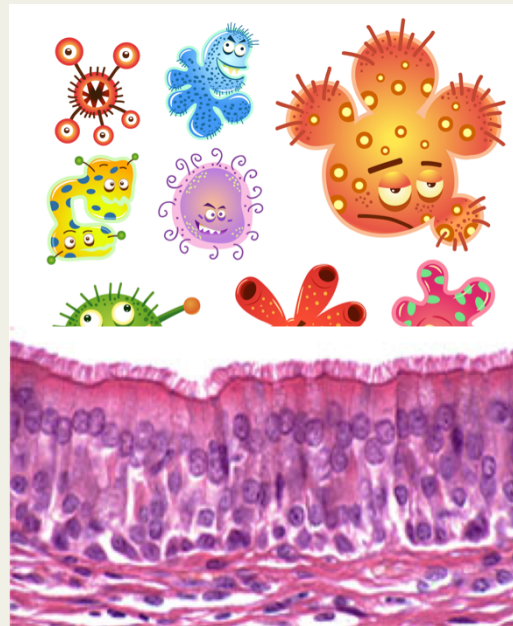
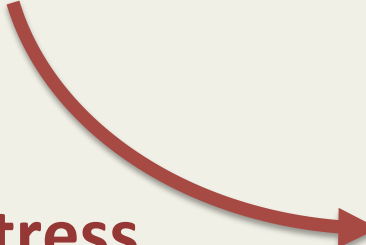
Microbiome



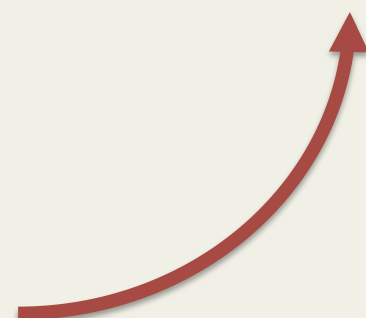
Coping/resilience



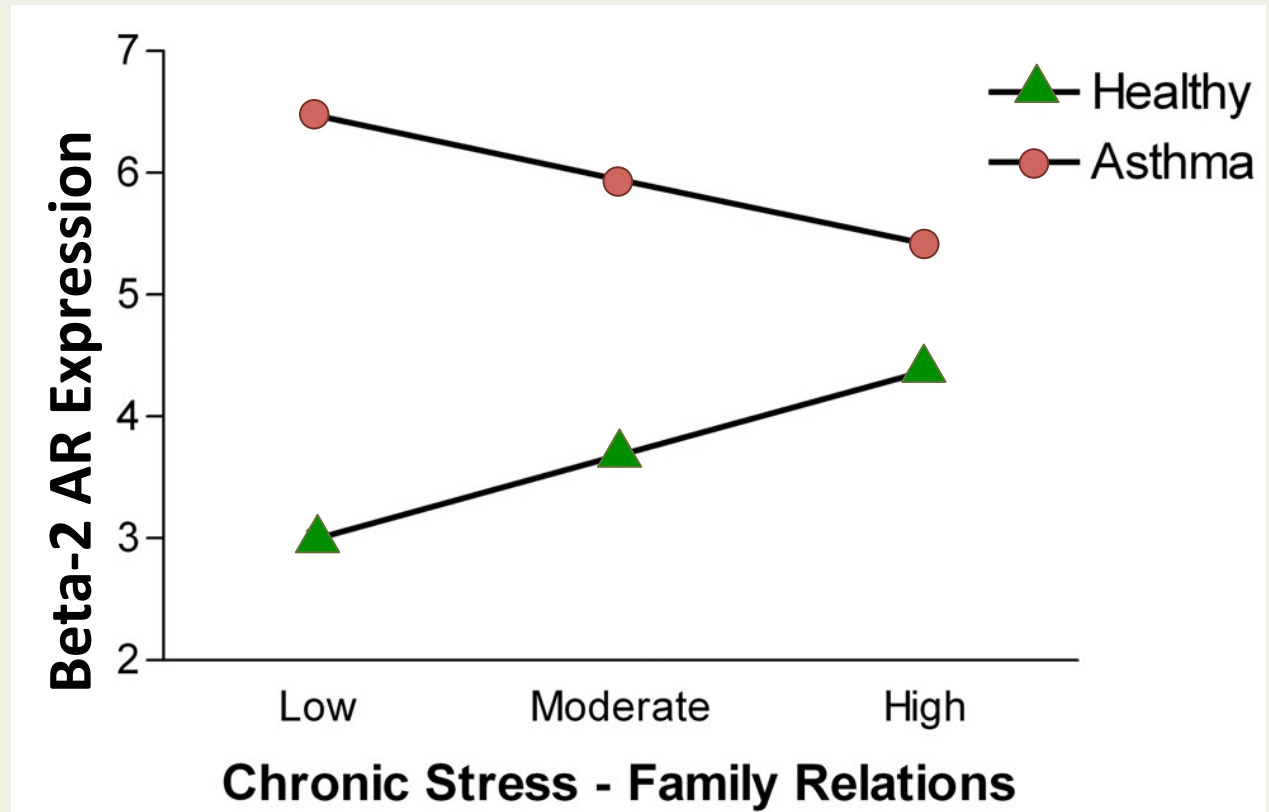
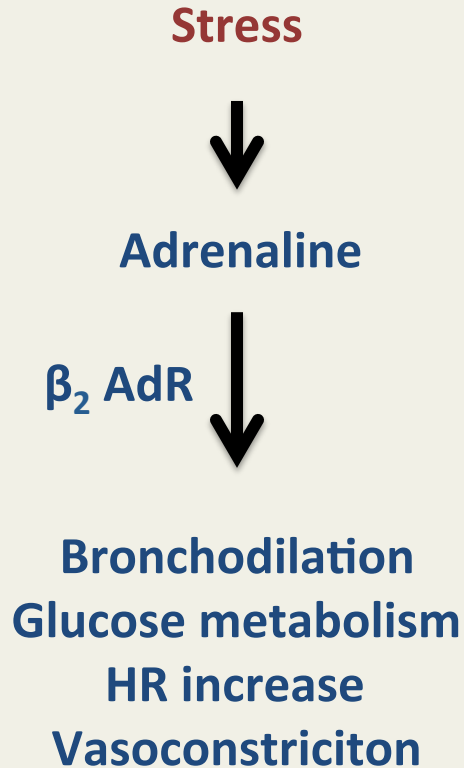
Stress



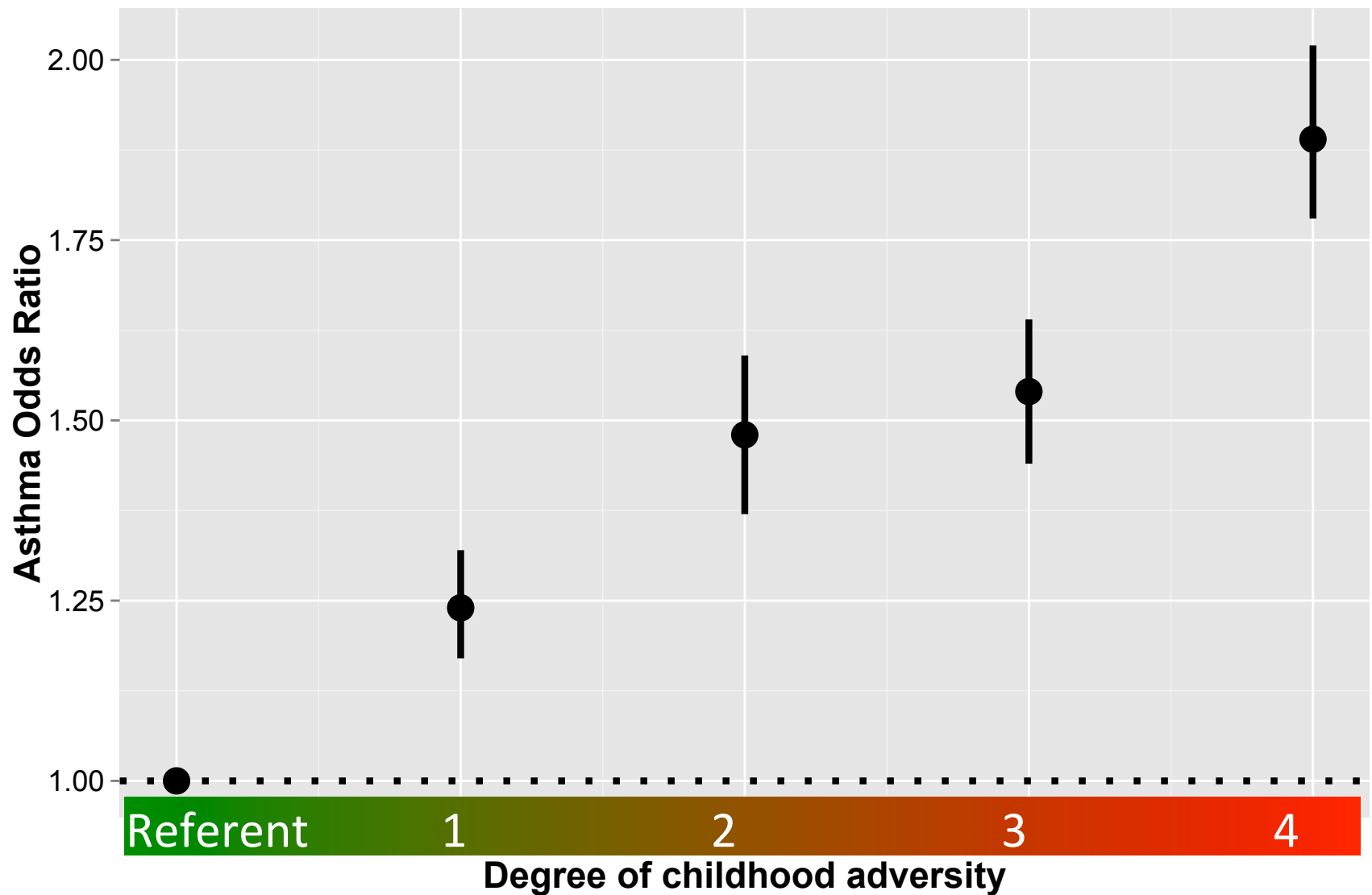
Transition



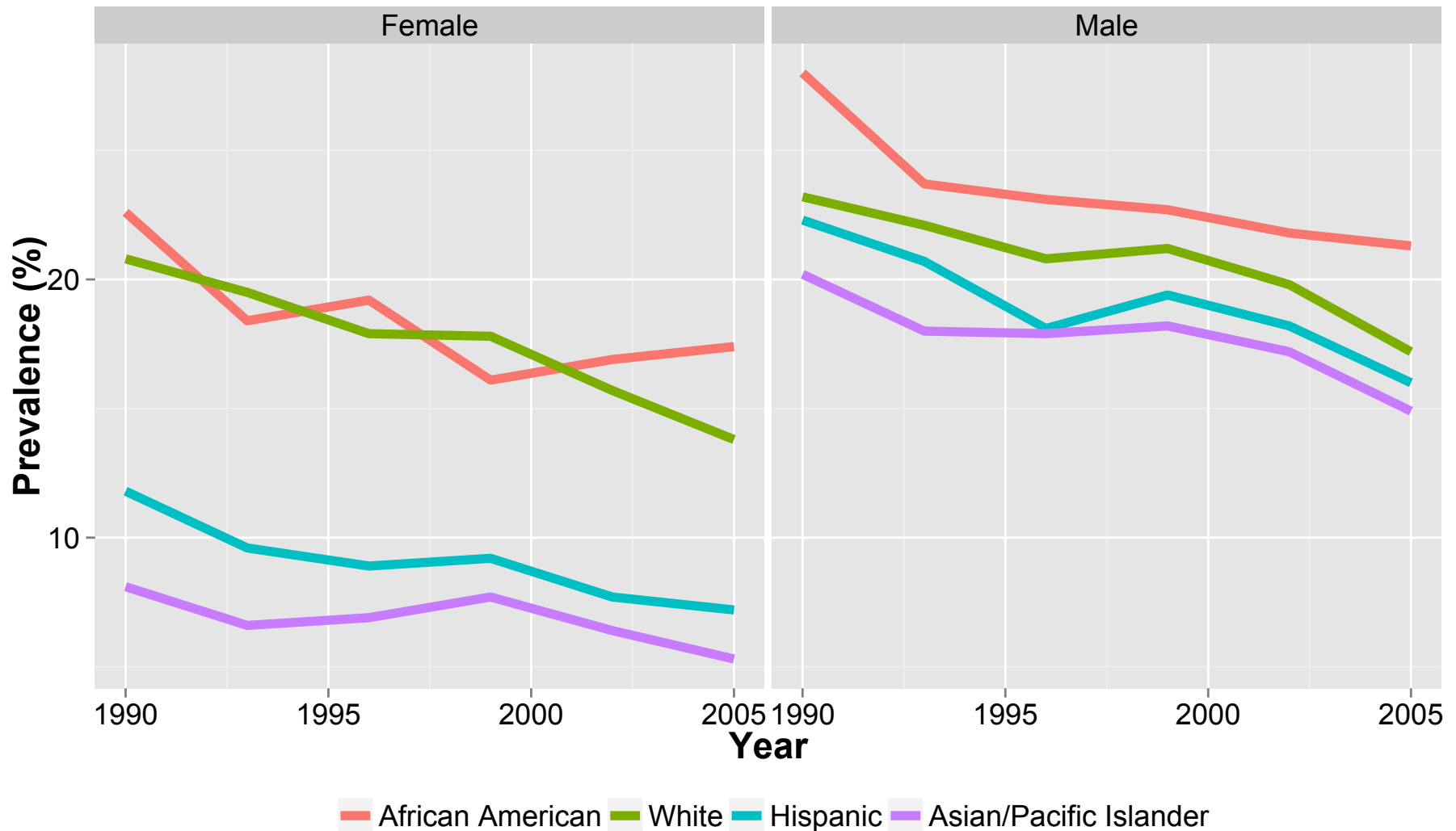
Altered β_2 AR Expression in Asthma



Adverse Childhood Experiences (ACEs)

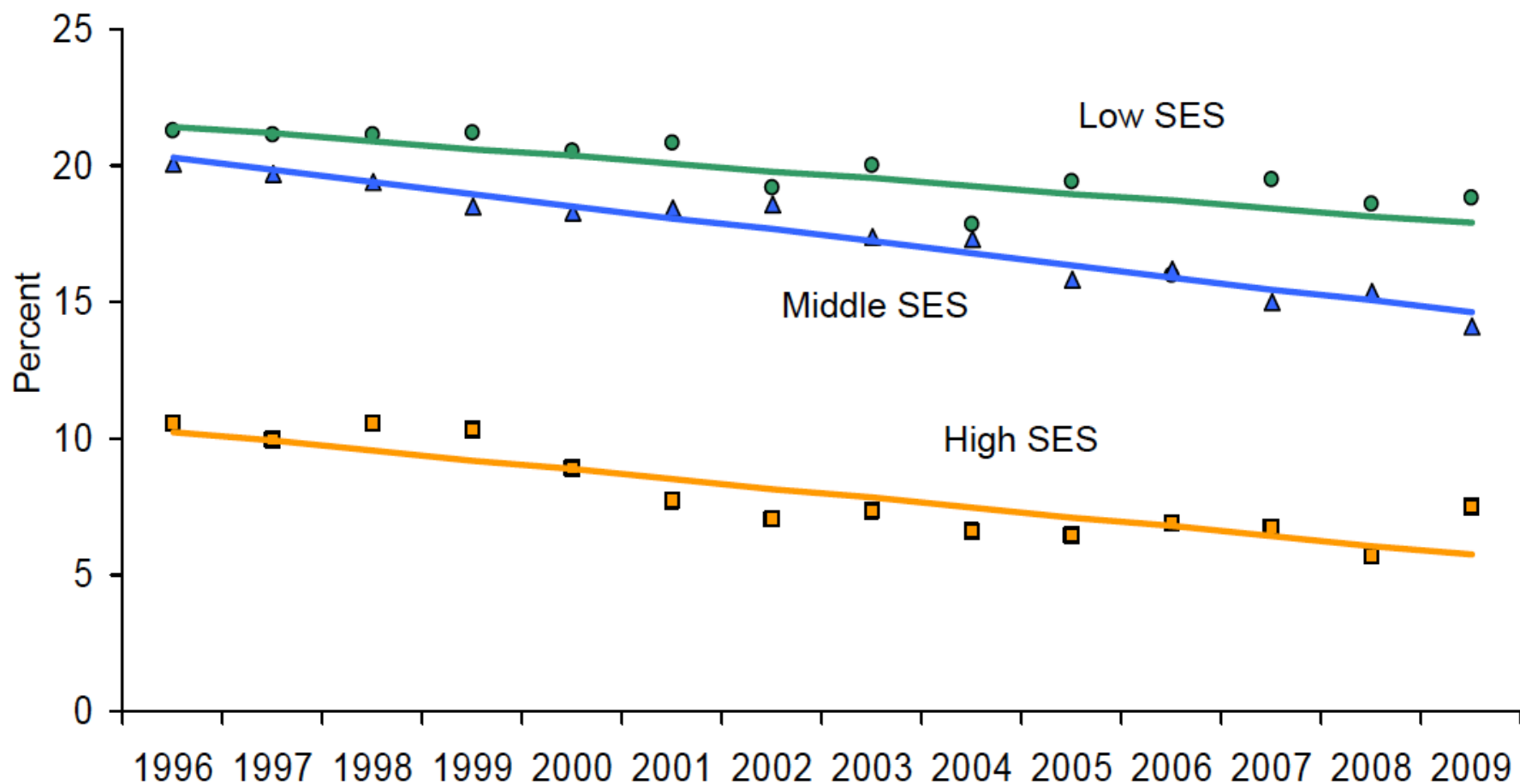


Adult Smoking Prevalence in CA

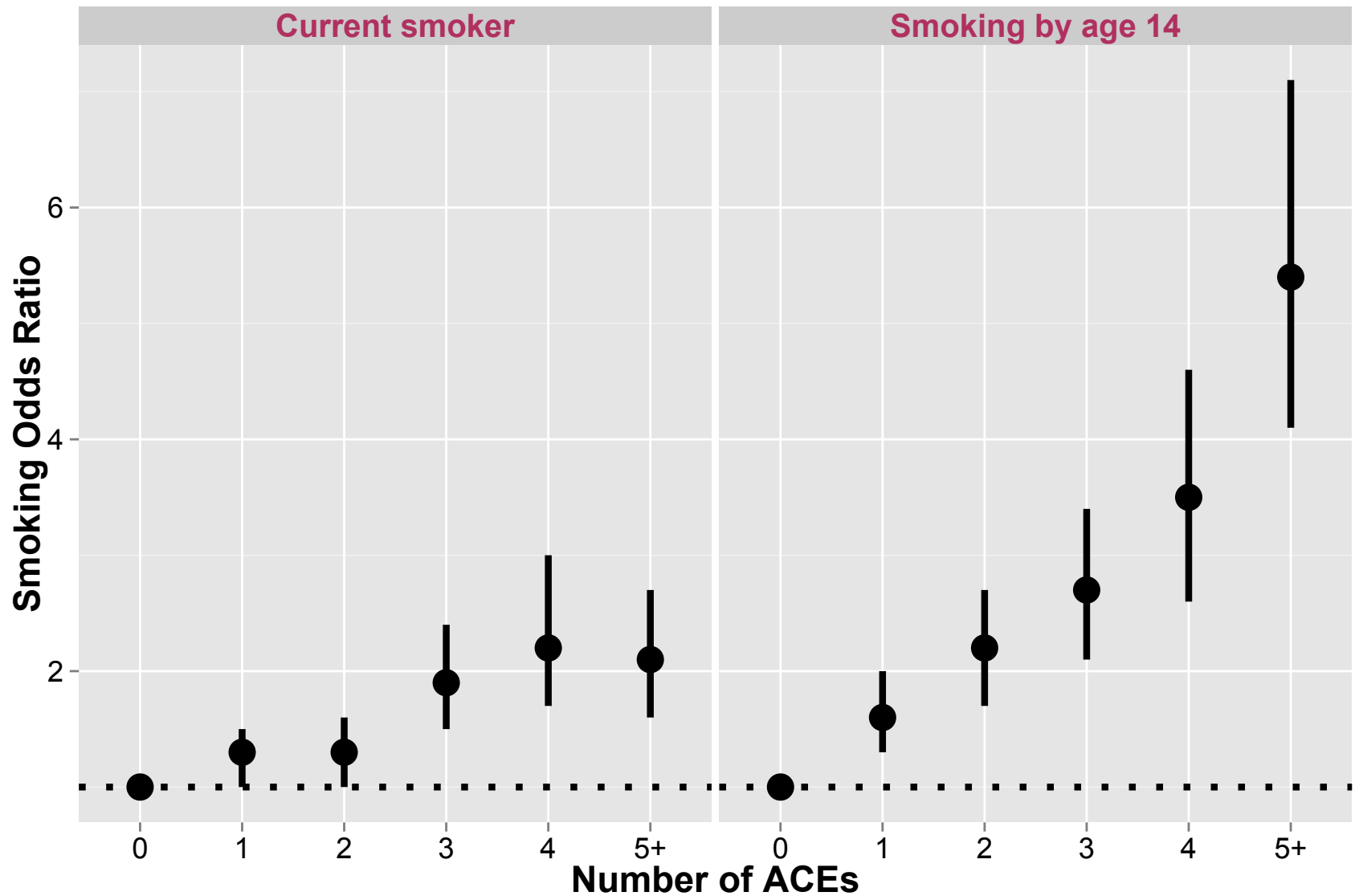




Smoking Prevalence Among California Adults by SES, 1996-2009



ACEs Predict Smoking



Secondhand Tobacco Smoke

- Surgeon General: no risk-free level of exposure
- Increases risk for asthma and asthma exacerbations
- Millions still involuntarily exposed
- Exposure window is important to consider

The Health Consequences of Involuntary Exposure to Tobacco Smoke

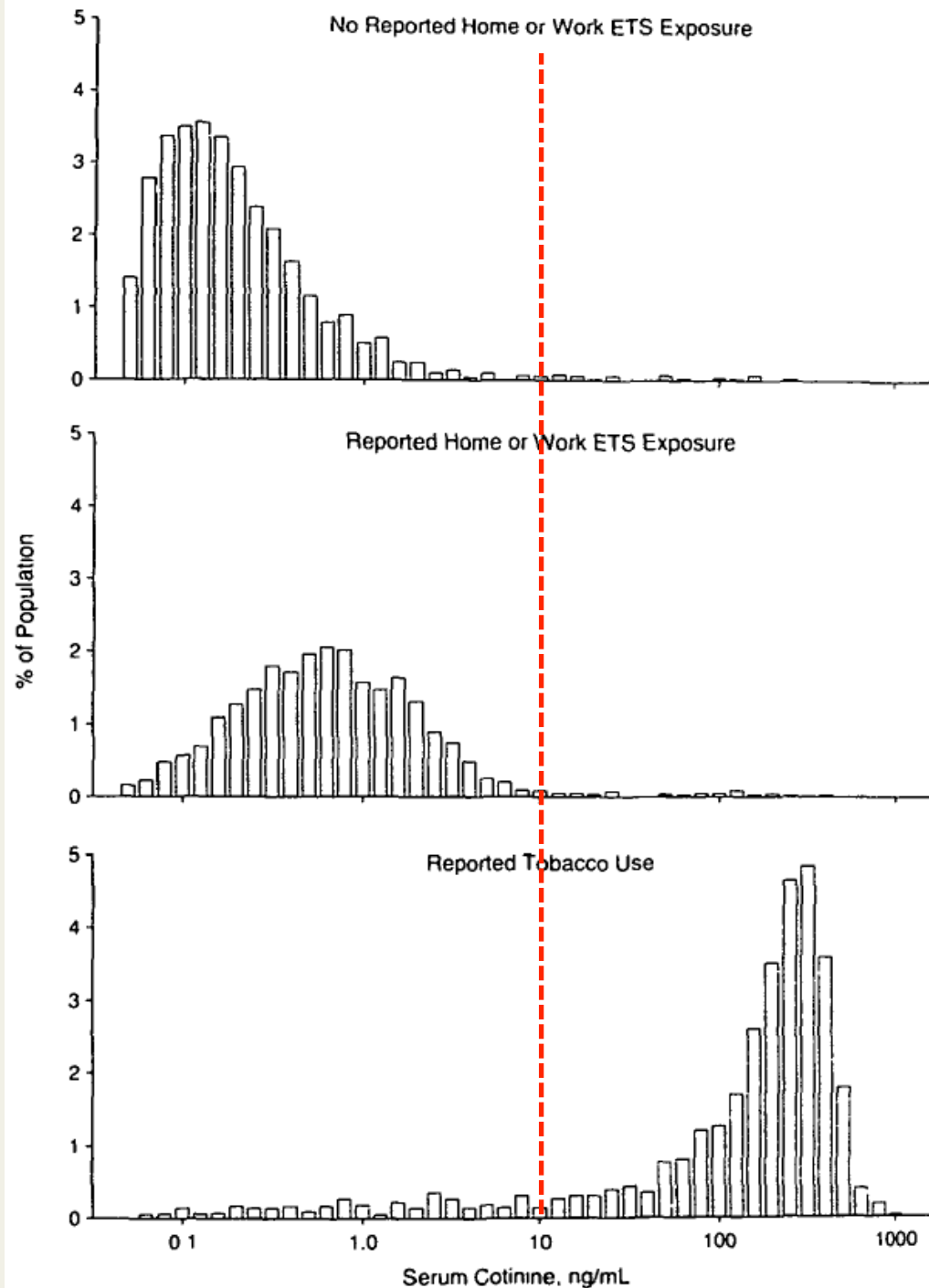
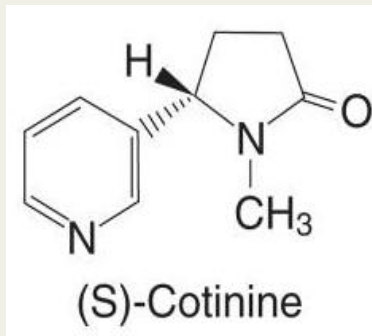
A Report of the Surgeon General



SHS Exposure Among US Adults



Liver $\downarrow$ CYP2A6



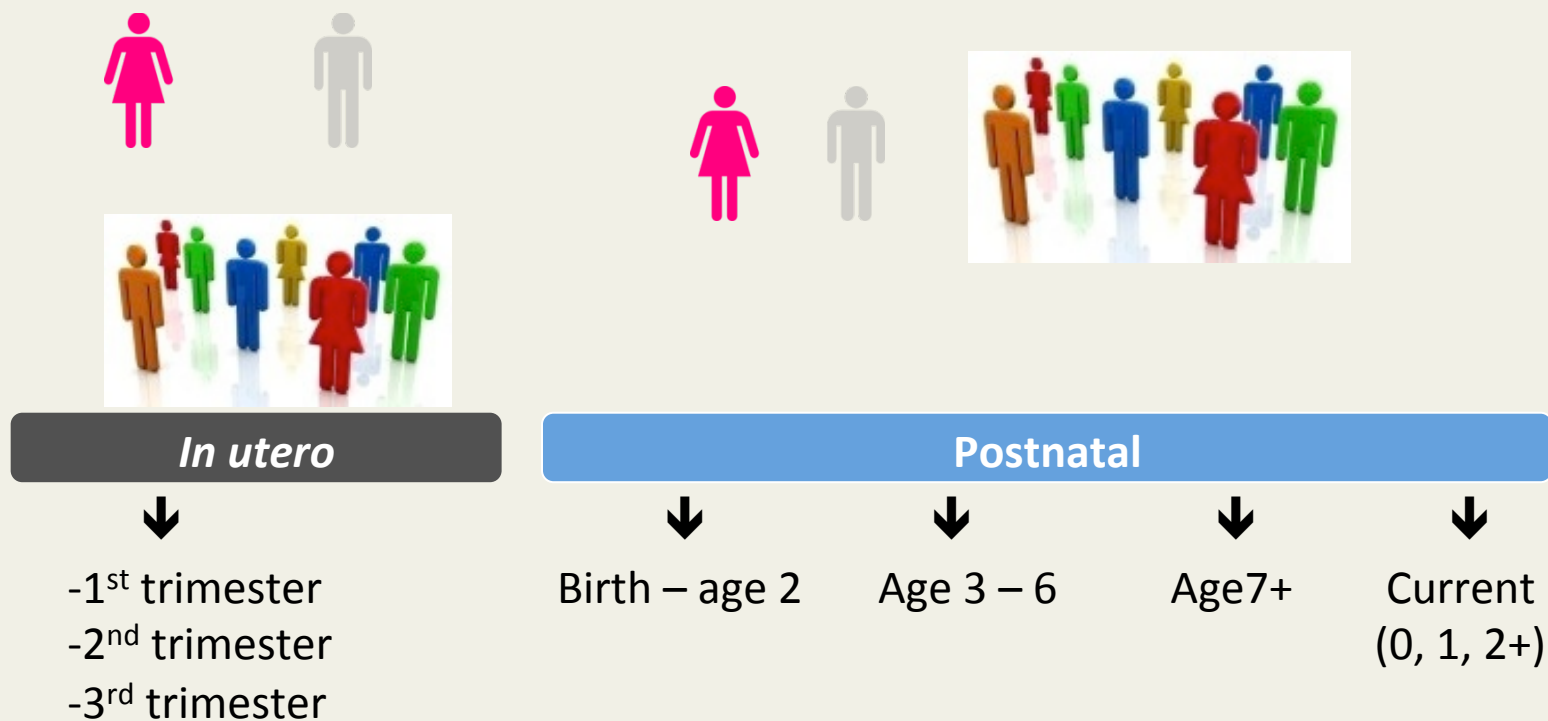
GALA II & SAGE II STUDIES



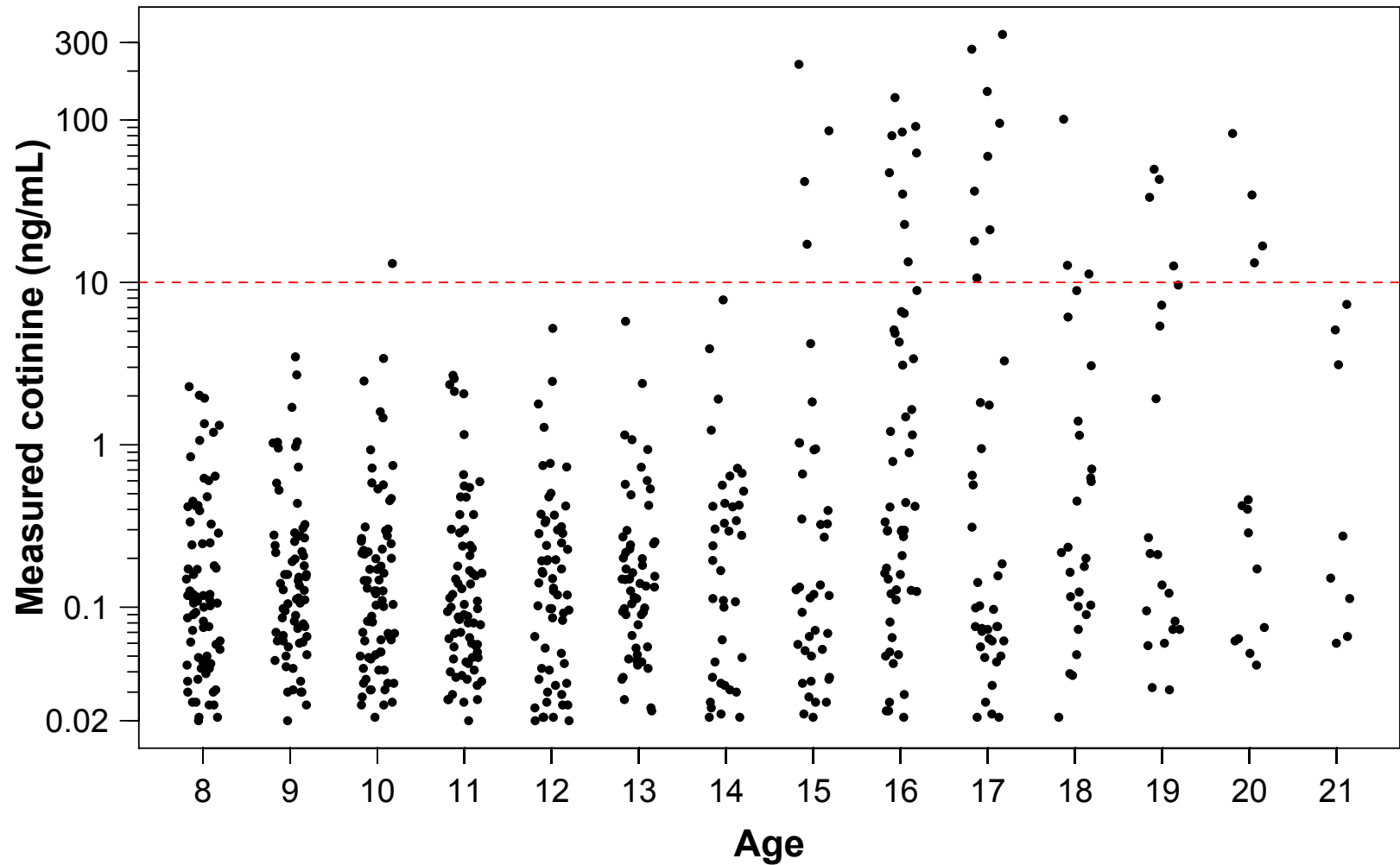
> 6,500 Latino & African American children & young adults (8-21yrs)

Domain	Information Gathered		
Asthma	Spirometry	Drug response	
Medical history & Blood work	Genotyping	Cotinine	IgE
	Methylation	RNA-seq	FeNO
Exposures	Environmental	Nutritional	Social

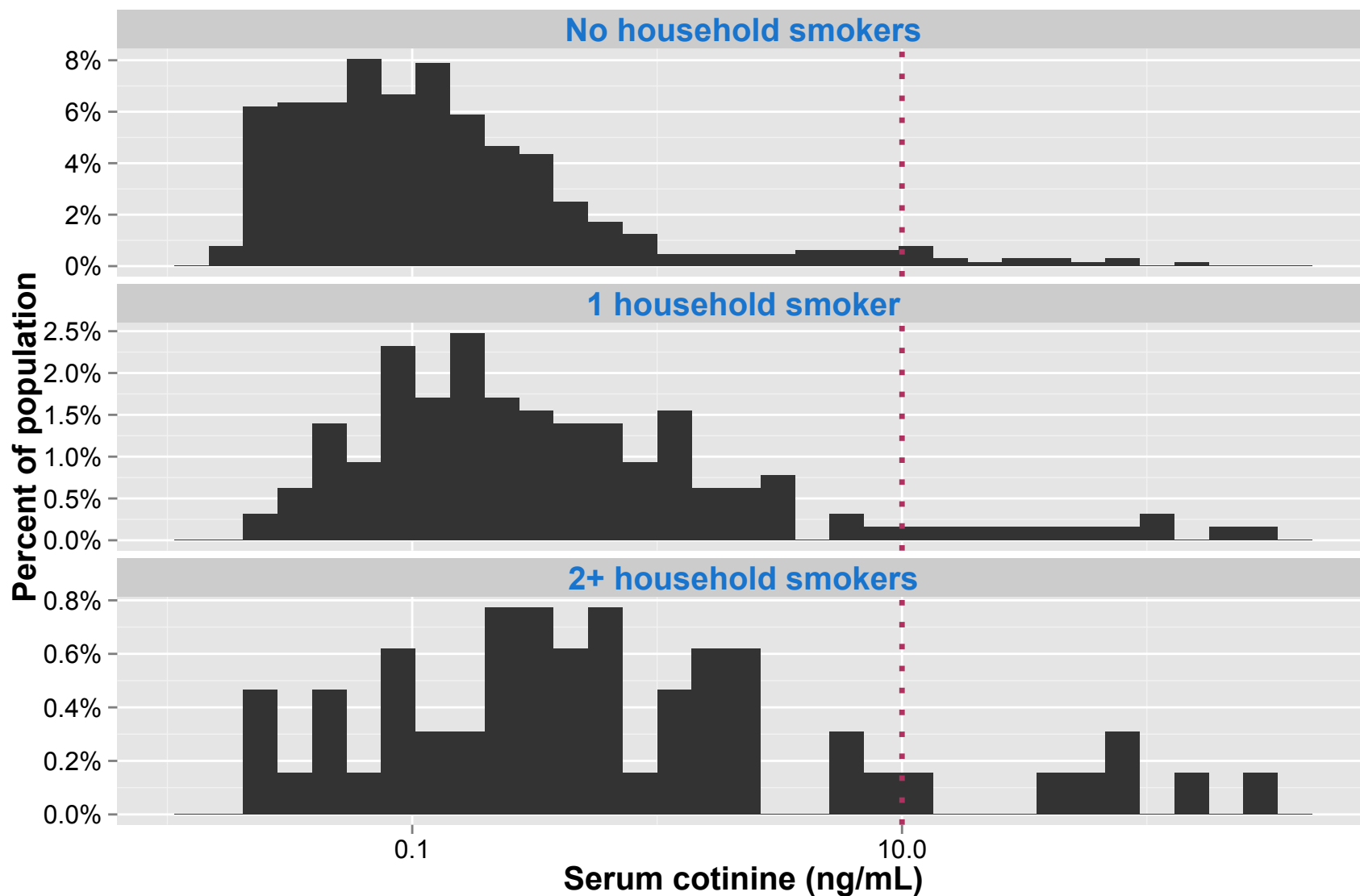
Assessing Tobacco Smoke Exposure



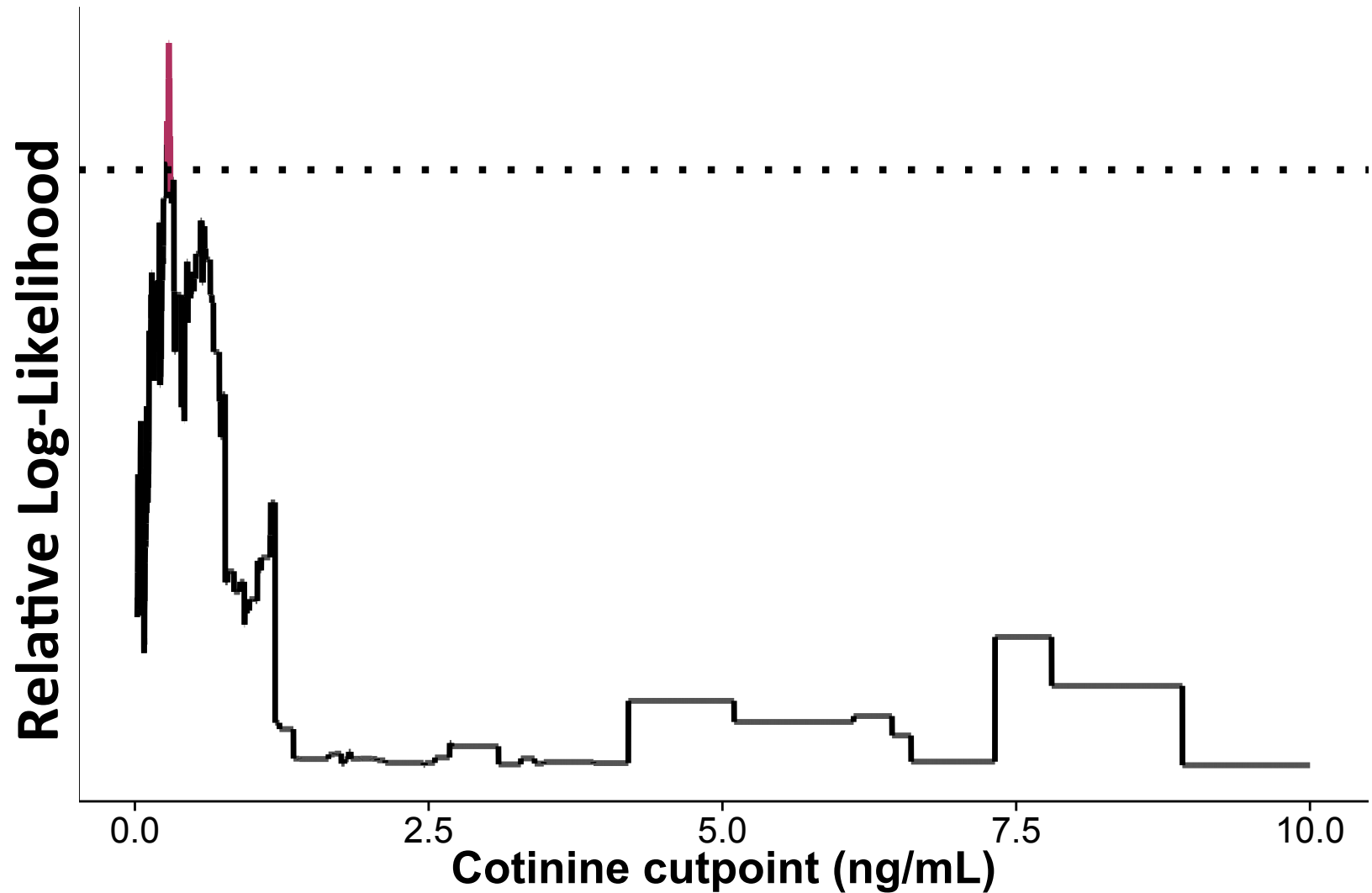
Smoking Begins ~ Age 15



SHS Exposure is Common



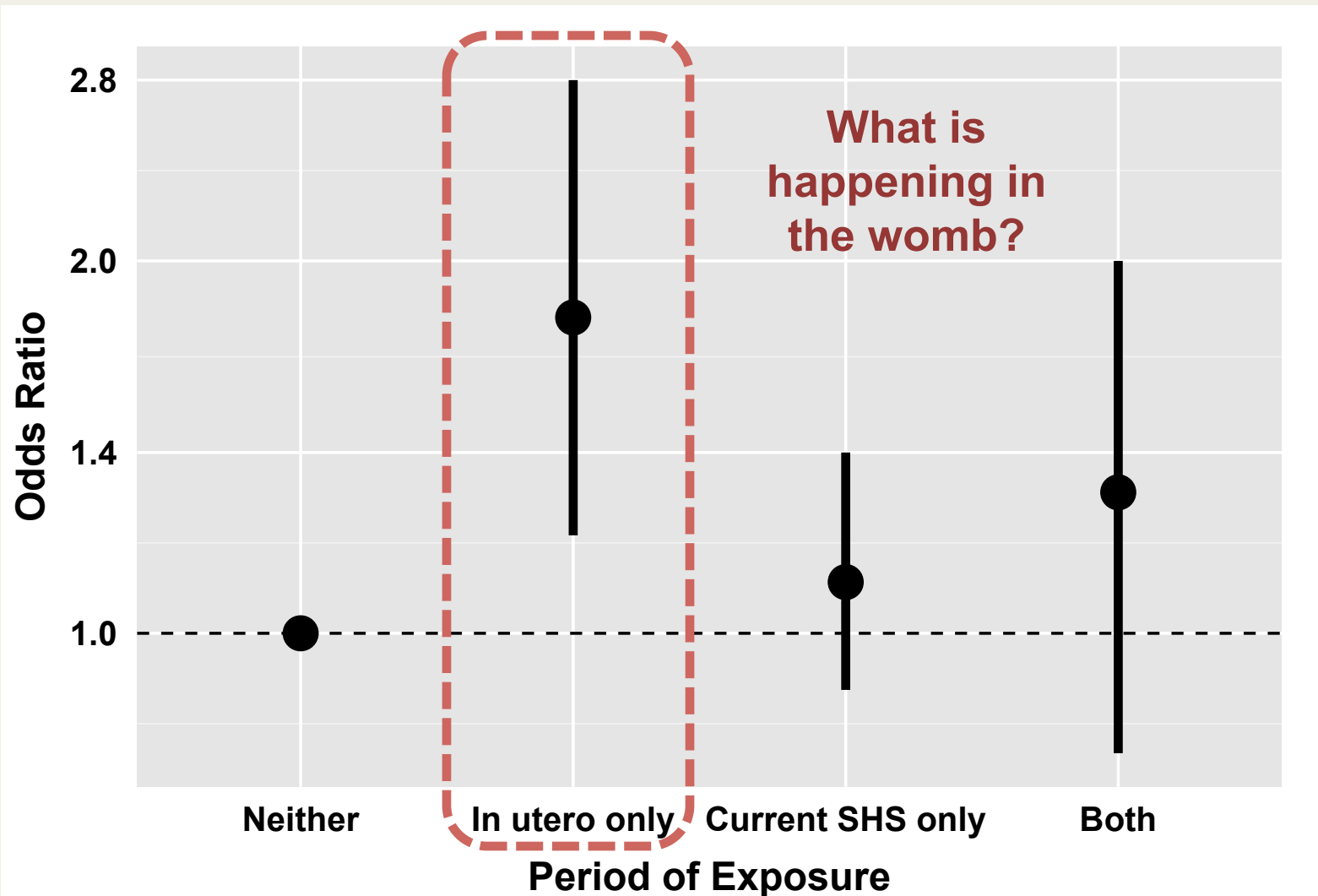
Low SHS Exposure is Still Bad



Smoking During Pregnancy: The Ultimate Involuntary Exposure?

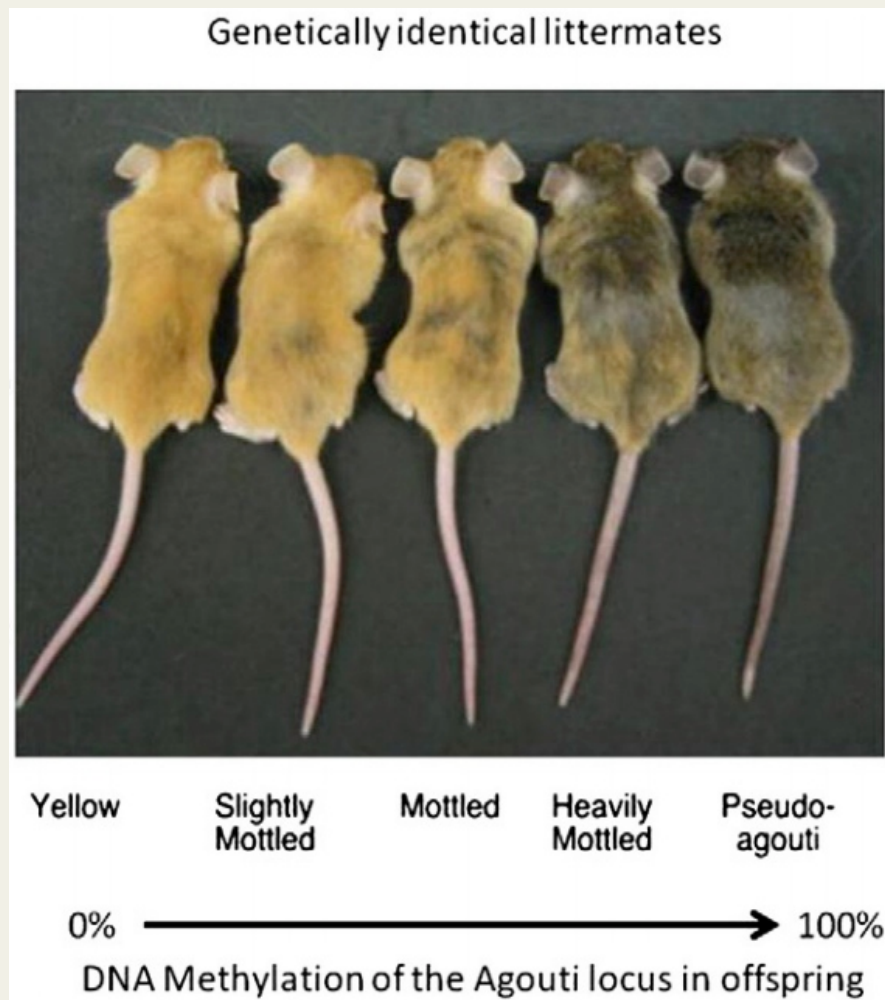


Exposure Period Affects Asthma Control



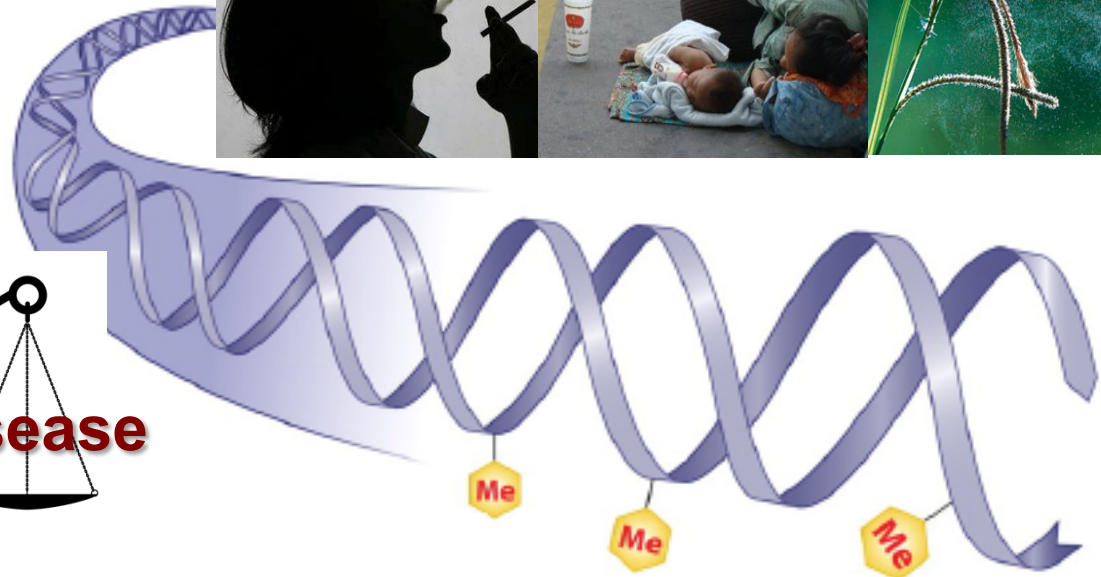
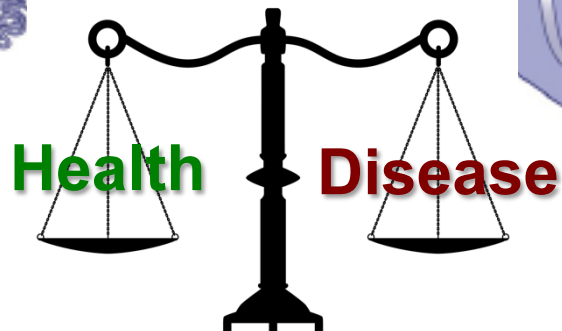
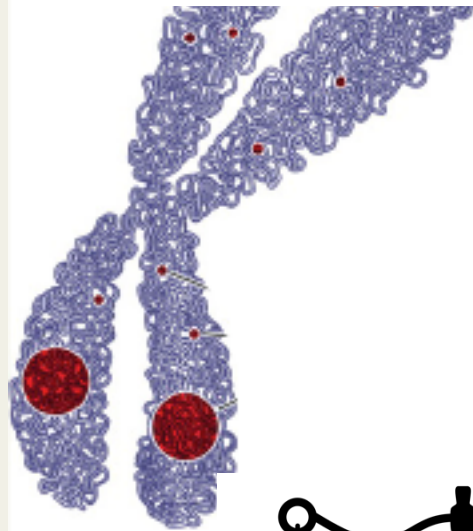
EPIGENETIC MODIFICATION

Identical?



Epigenetic Regulation

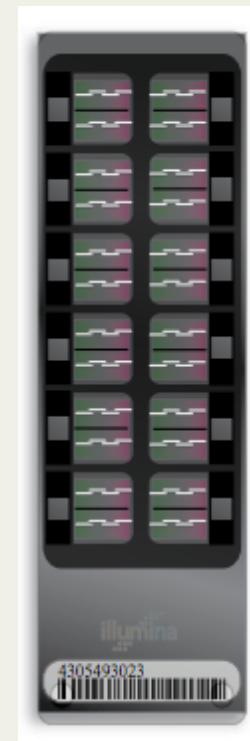
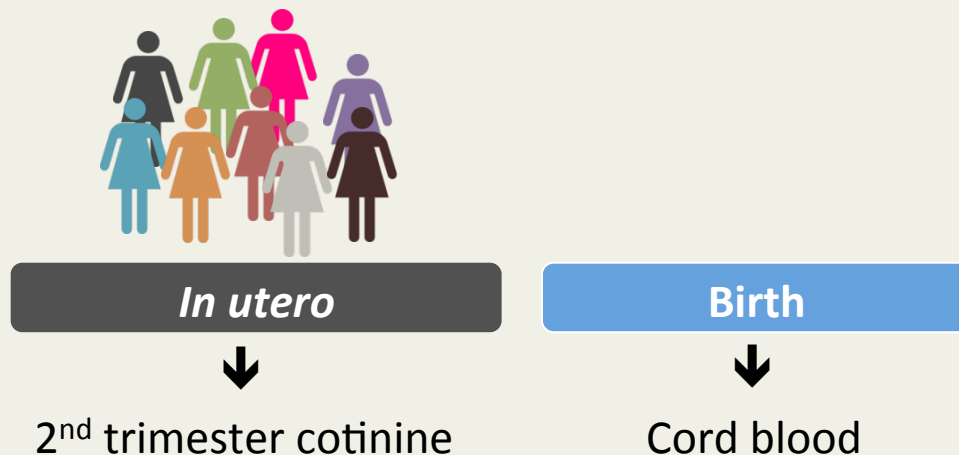
- Regulatory system overlaid on DNA
- Where, when, and how
- DNA methylation most common



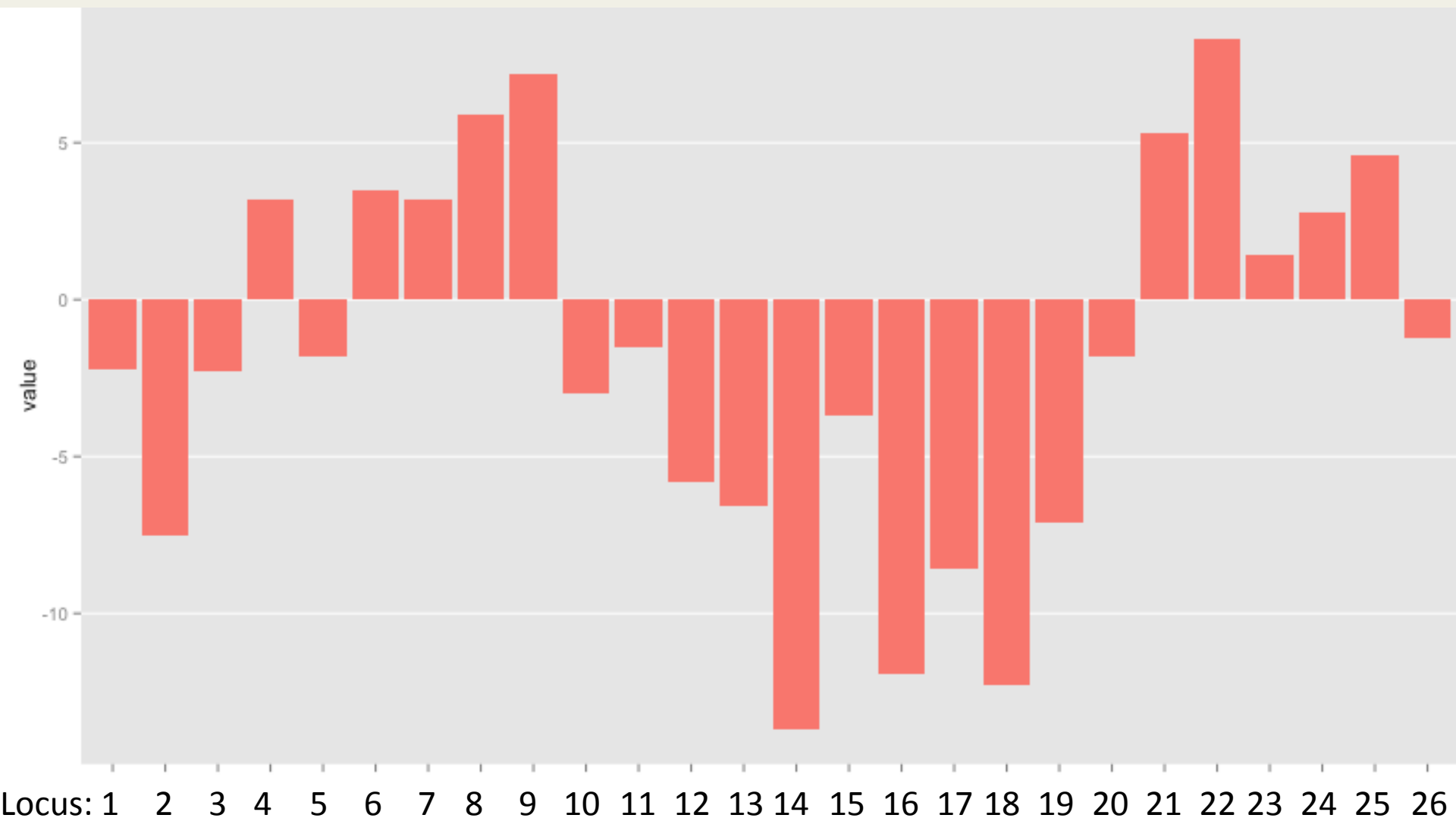
**HOW DOES SMOKING DURING
PREGNANCY AFFECT DNA METHYLATION?**

450K Epigenome-Wide Scan Identifies Differential DNA Methylation in Newborns Related to Maternal Smoking during Pregnancy

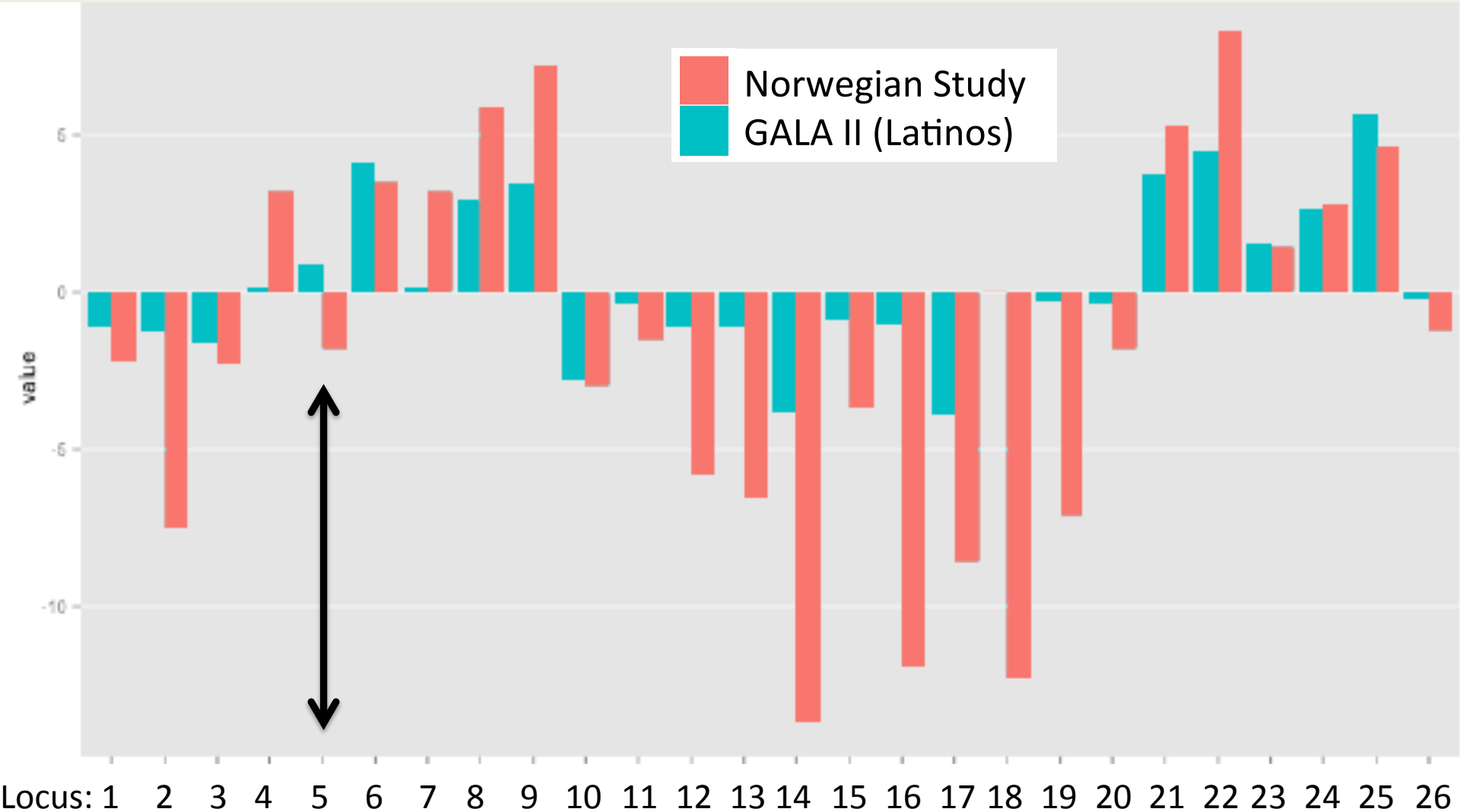
Bonnie R. Joubert,¹ Siri E. Håberg,² Roy M. Nilsen,³ Xuting Wang,¹ Stein E. Vollset,^{2,4} Susan K. Murphy,⁵ Zhiqing Huang,⁵ Cathrine Hoyo,⁵ Øivind Midttun,⁶ Lea A. Cupul-Uicab,¹ Per M. Ueland,⁴ Michael C. Wu,⁷ Wenche Nystad,² Douglas A. Bell,¹ Shyamal D. Peddada,¹ and Stephanie J. London¹



Methylation in Norwegian Newborns

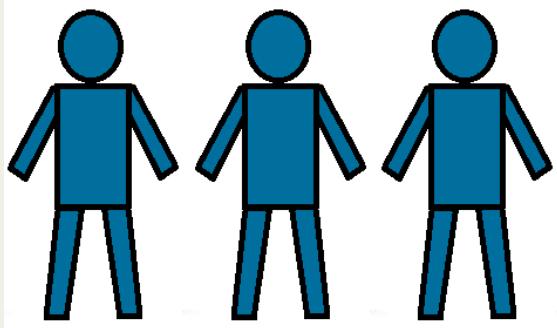


Similar changes in Latino children

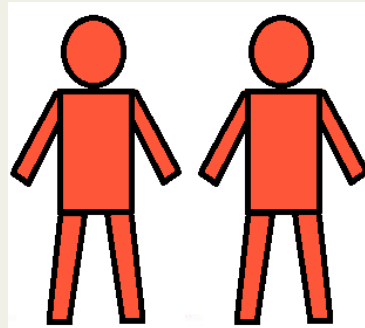


Global Genetic Ancestry In Latinos

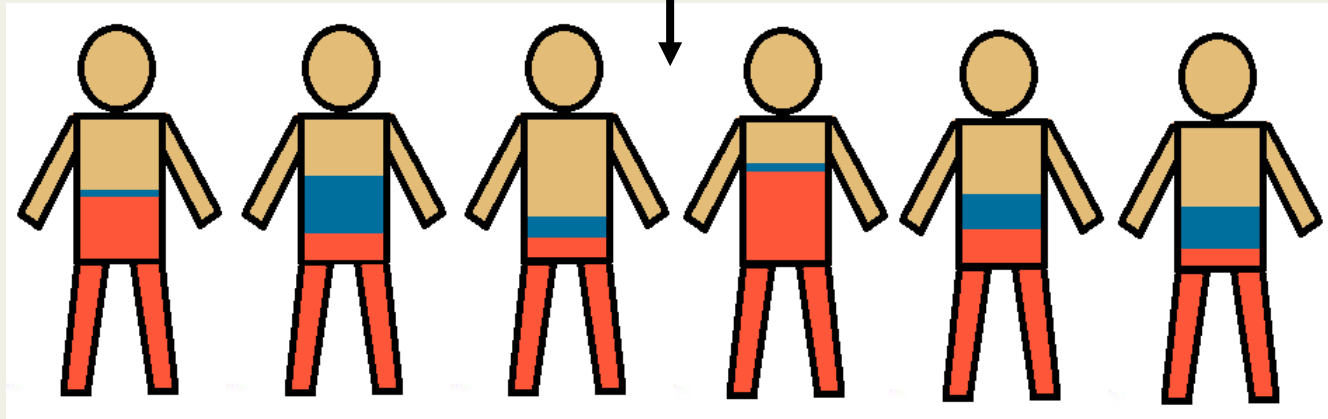
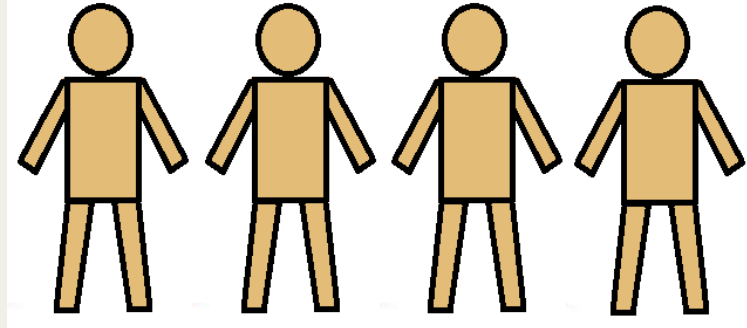
African



Native American

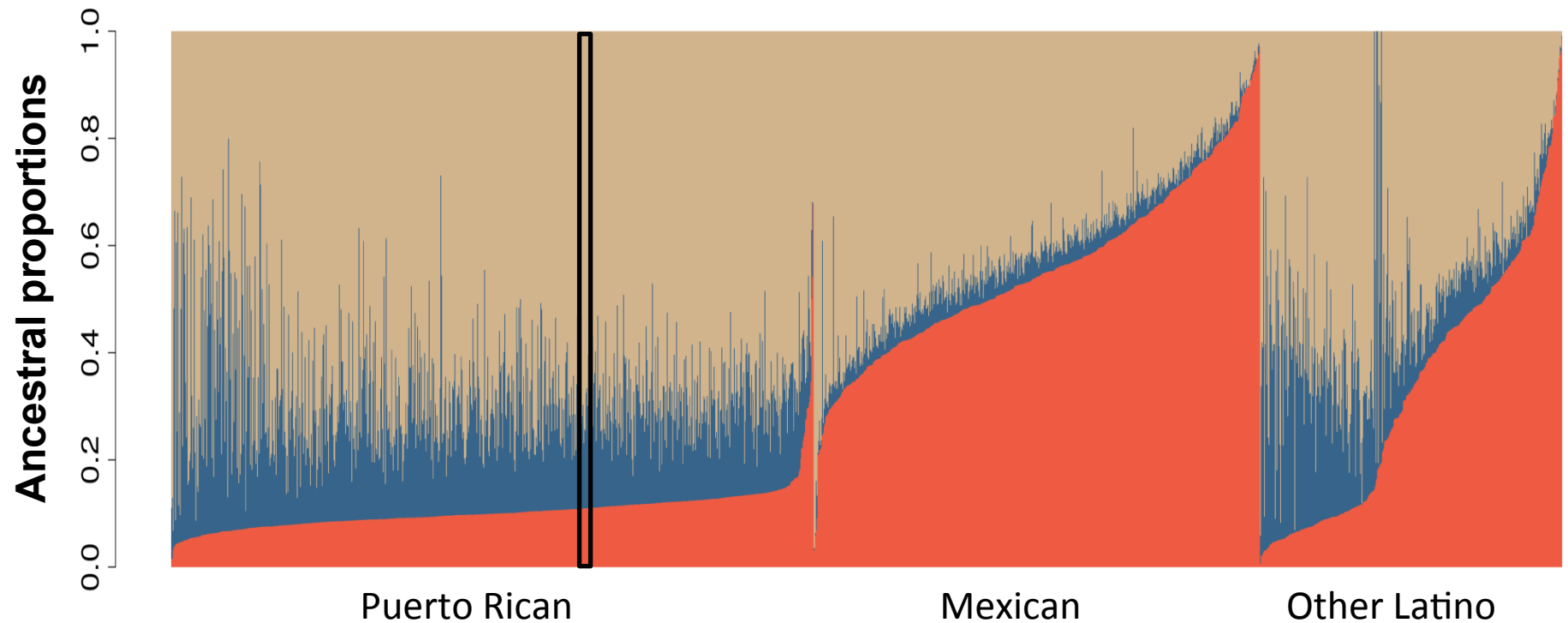


European



Admixed

Global Genetic Ancestry In Latinos



Genetic Ancestry



European

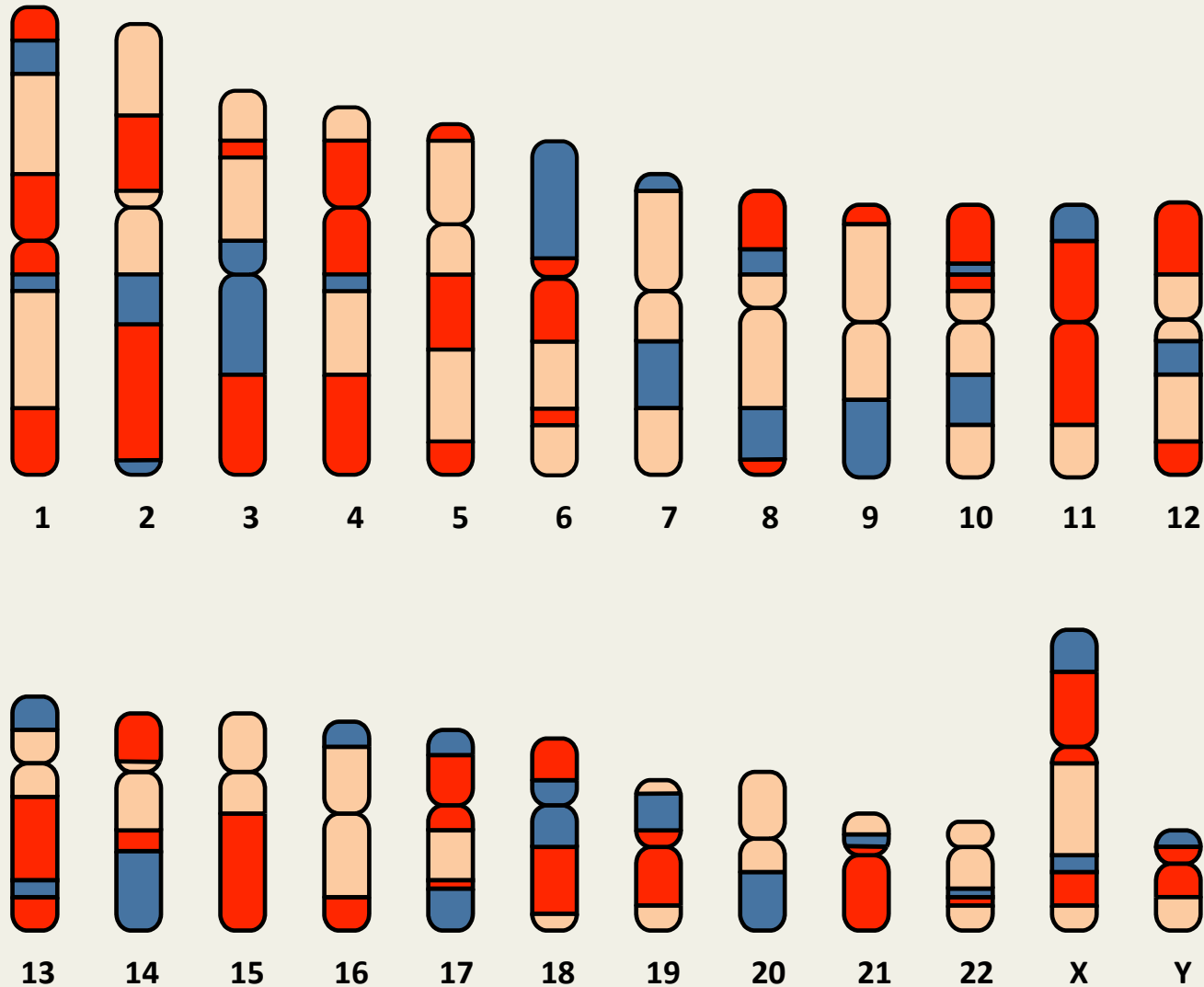


African

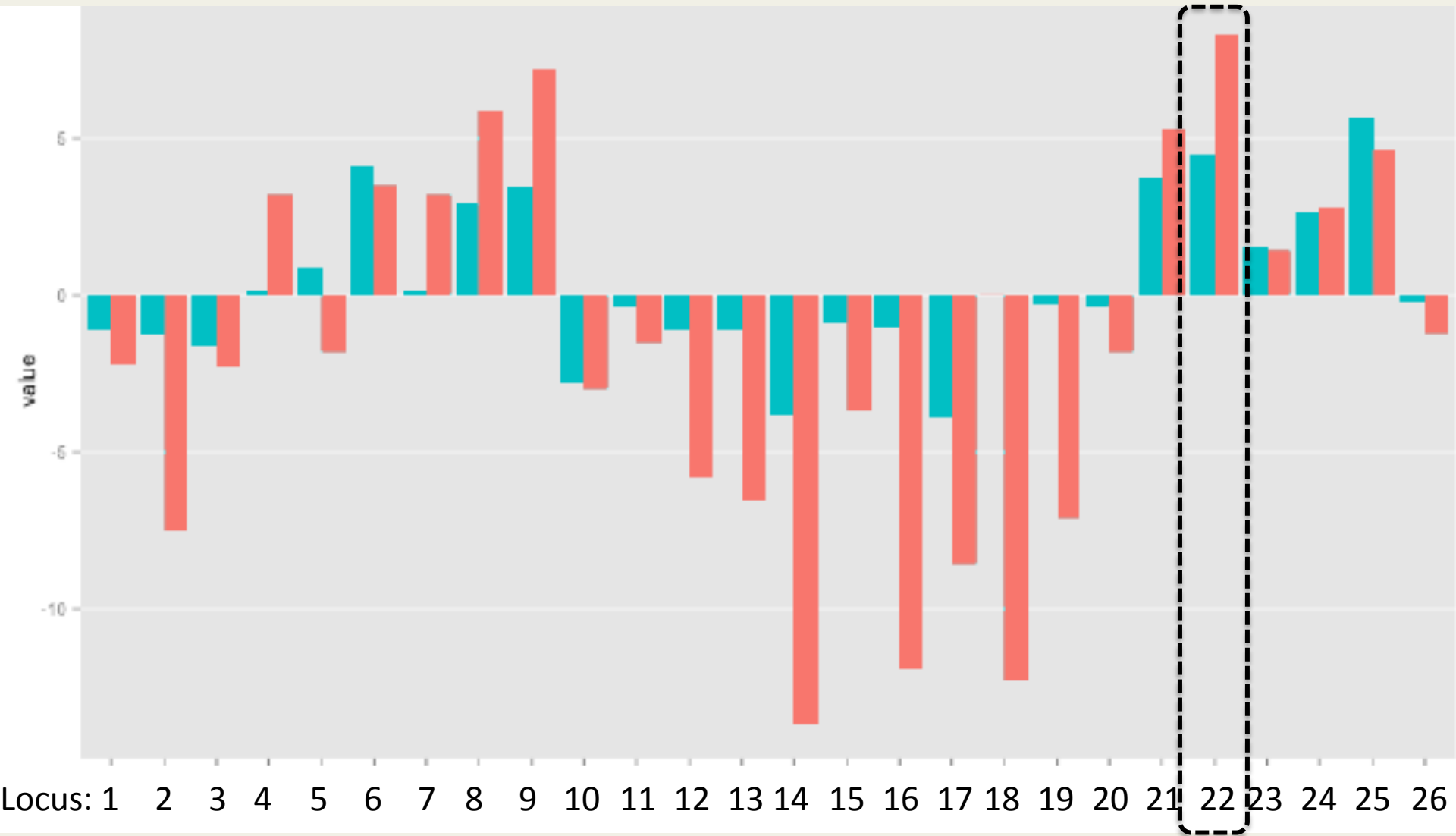


Native American

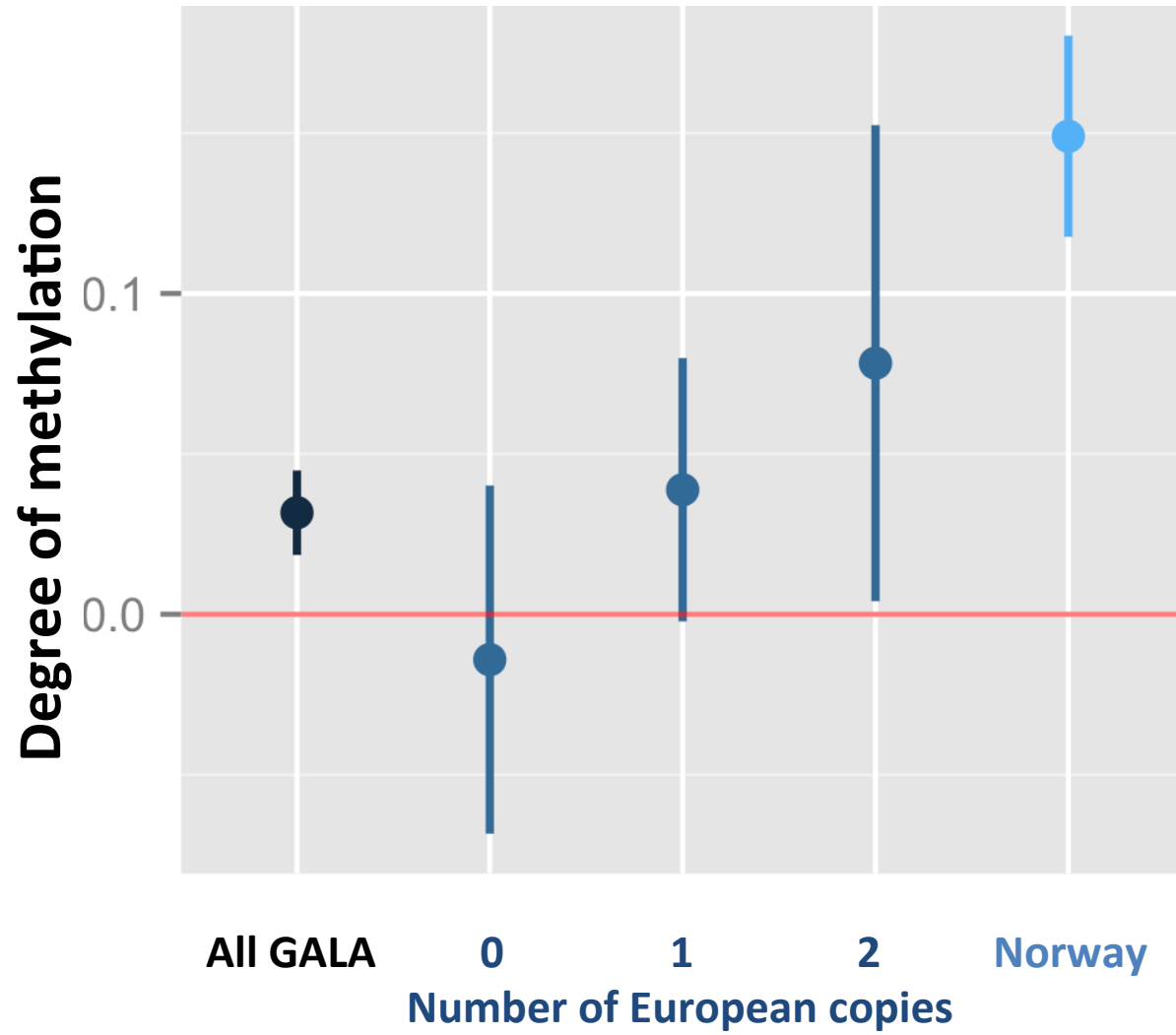
Local Genetic Ancestry In Latinos



Does Local Ancestry Affect Methylation?



MYO1G Gene



Environment



Genetic variation



***PAC1R* gene**

- PTSD Pathway
- Increased methylation with ASTHMA
- Increased methylation with violence



Asthma and toxic stress are complex conditions

**Complex conditions require a multi-pronged and
transdisciplinary approach**

