

Chemical & Psychological Stressors and Health

Rosalind J. Wright, MD, MPH

Horace W. Goldsmith Professor

Vice Chair for Clinical Translational Research

The Jack and Lucy Clark Department of Pediatrics

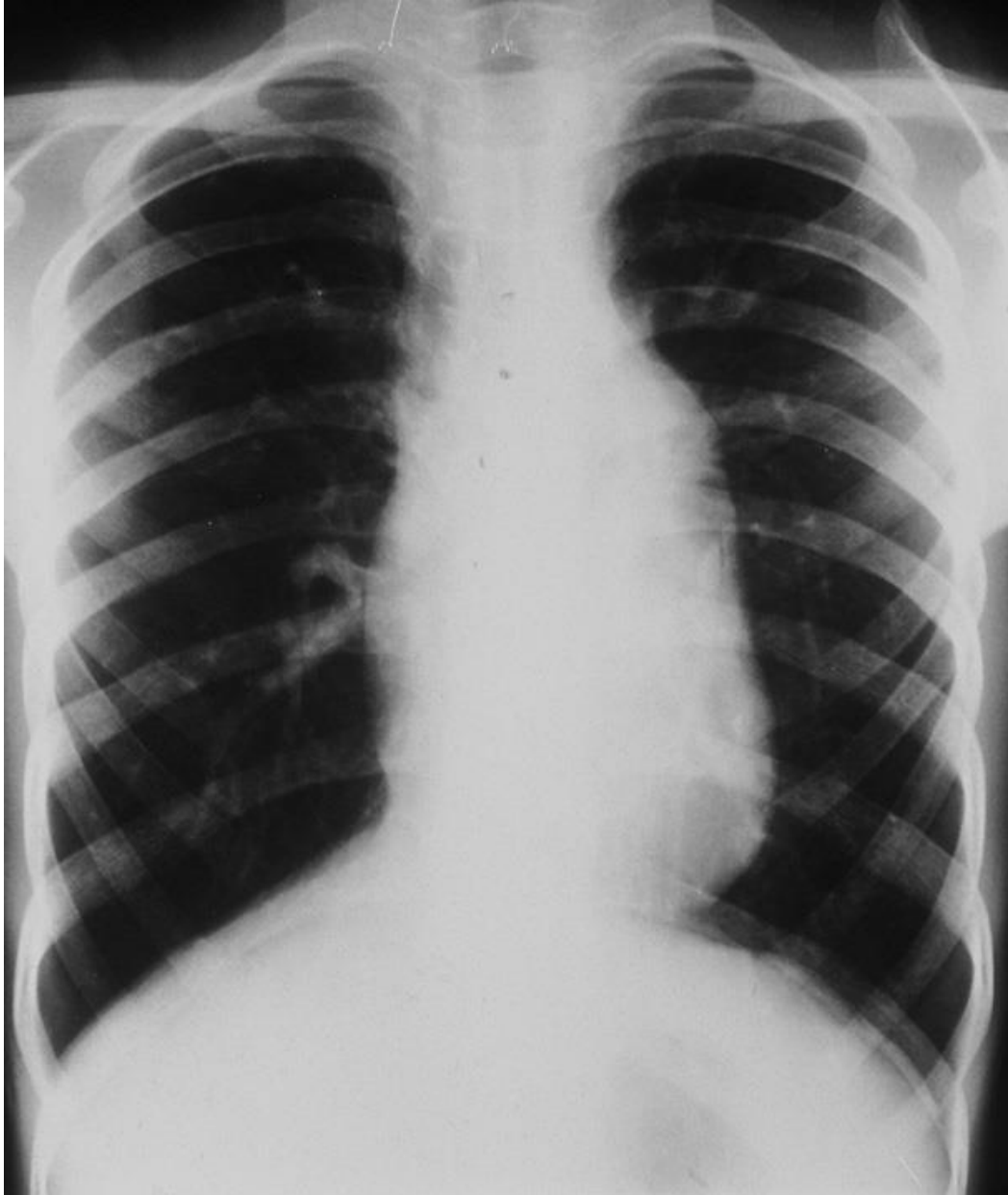
Kravis Children's Hospital

Icahn School of Medicine at Mount Sinai



**Mount
Sinai**

*The Mindich Child Health
and Development Institute*



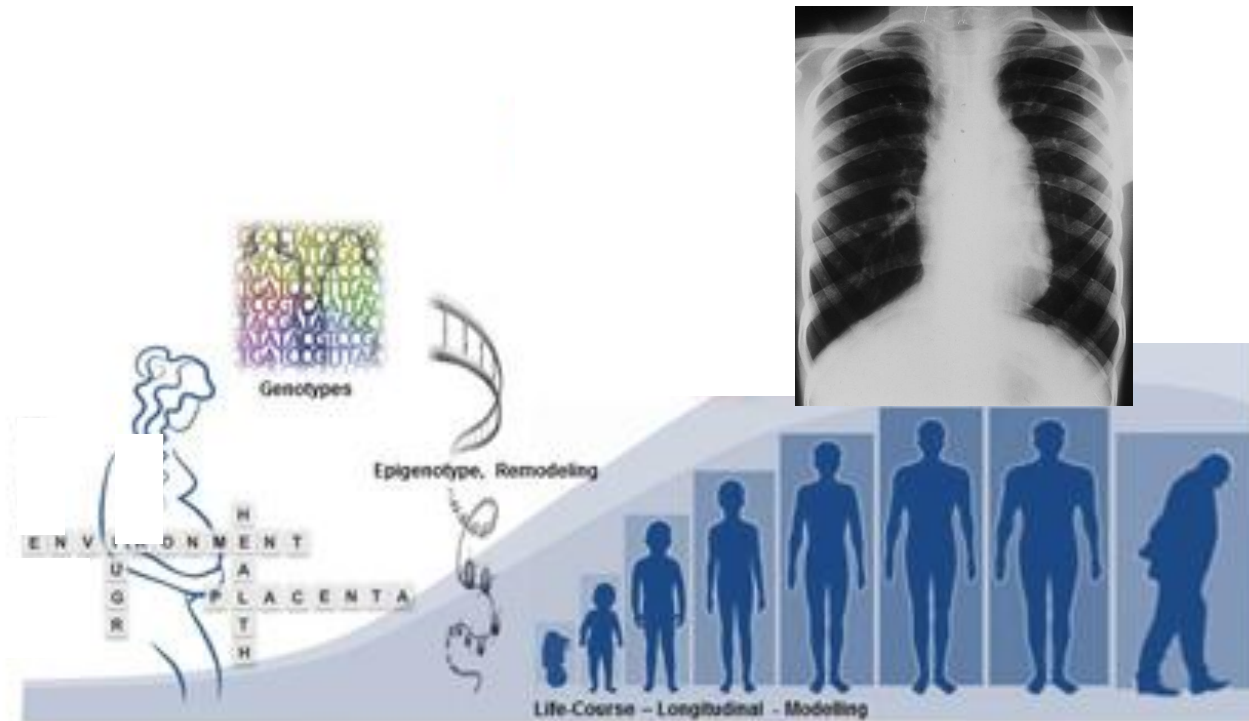
Chronic Disease Challenge

50 yr old man, 40 pack
year smoking history.

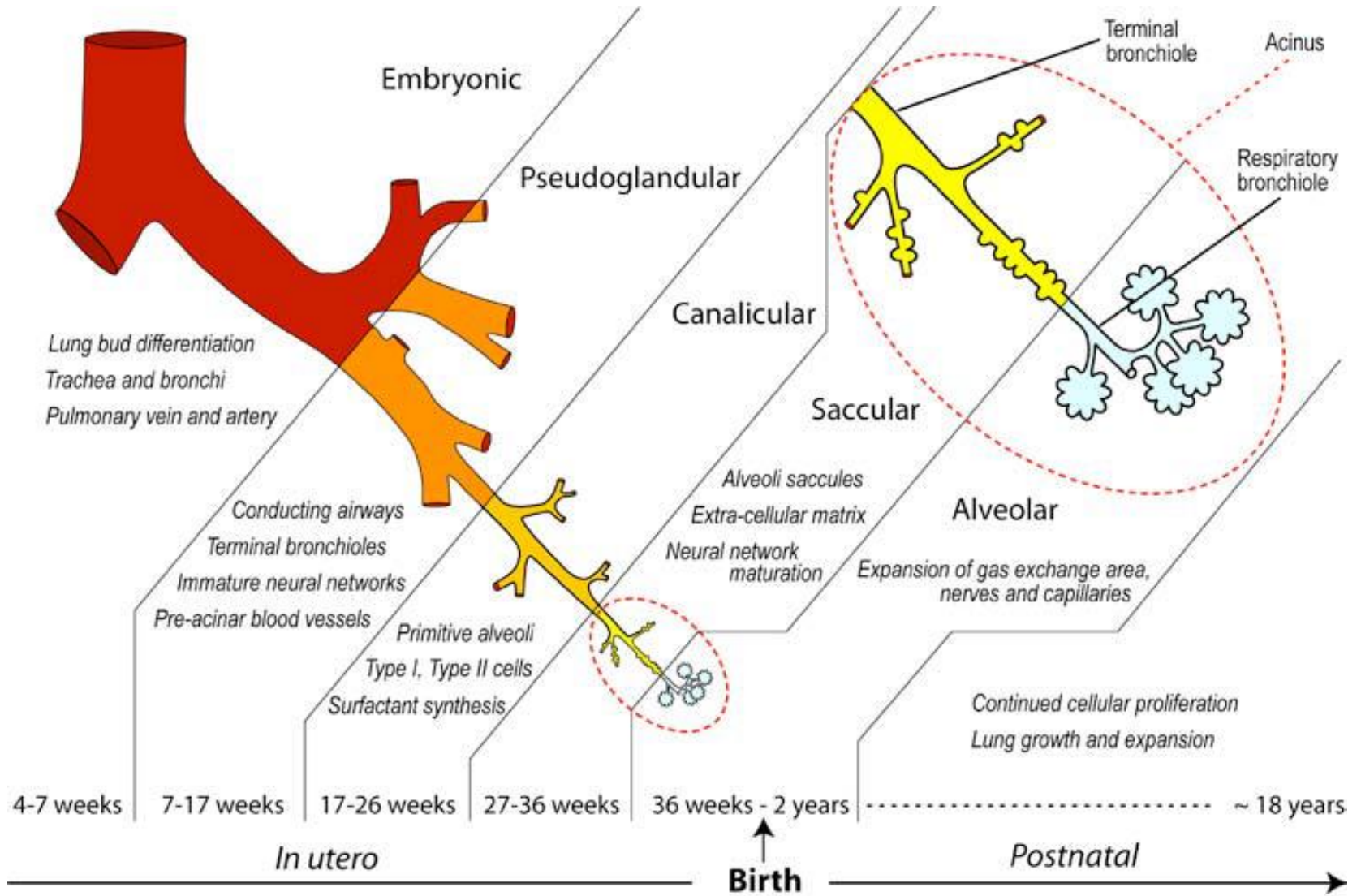
Diagnosis?

Prevention vs. Management

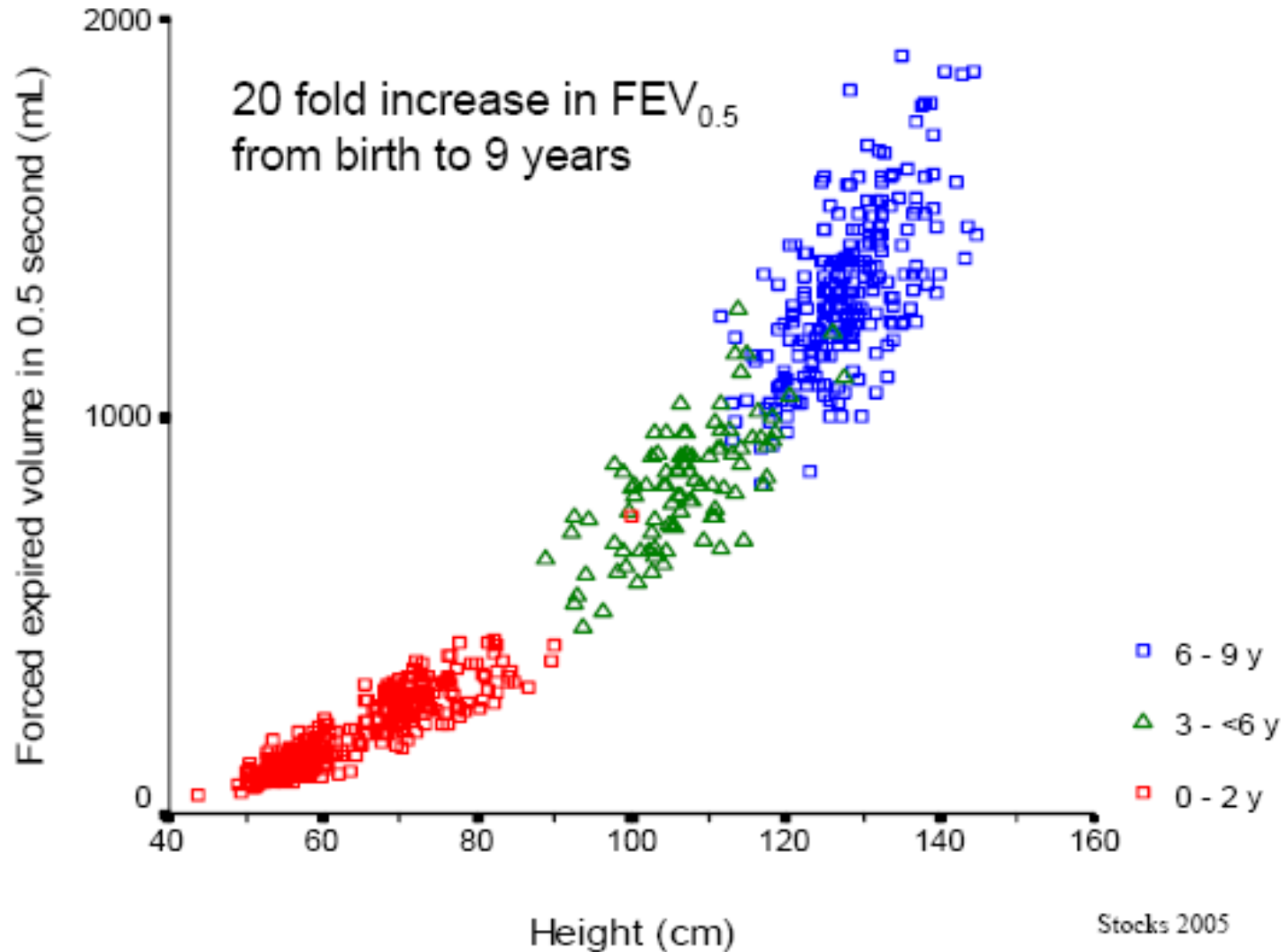
Lifecourse Framework: Importance of Early Life Events



How environmental exposures in early life – chemical, nutritional, and social – influence health and development in childhood and across the human life span.



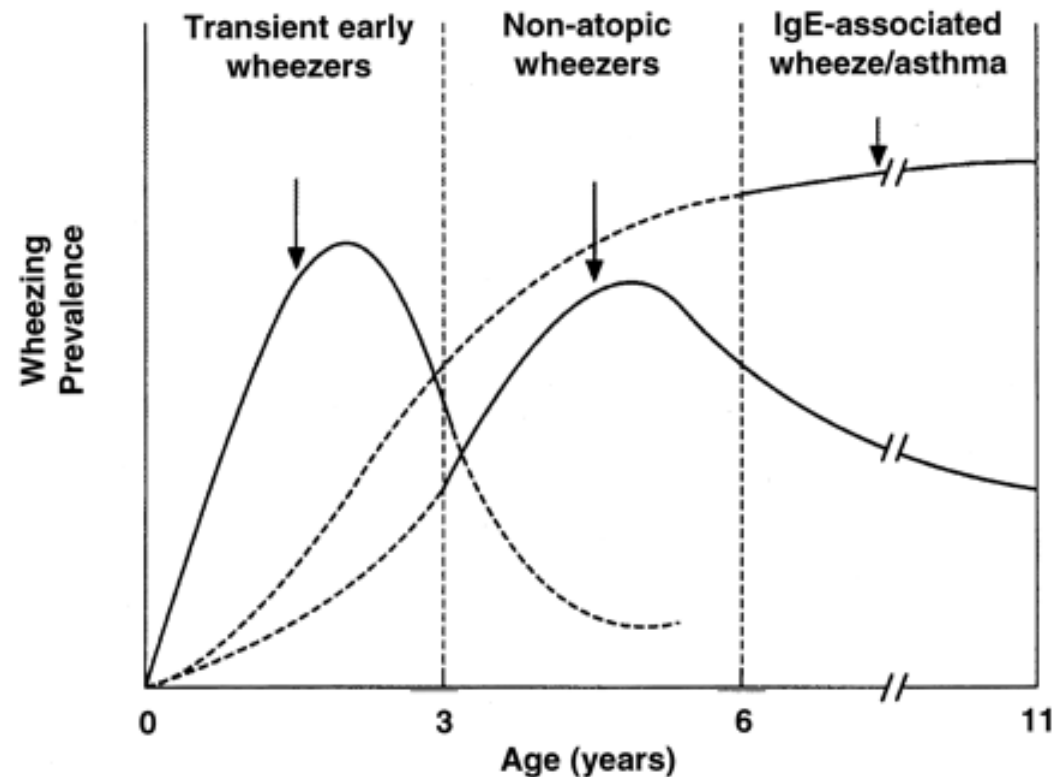
Rapid Growth and Development During Early Childhood

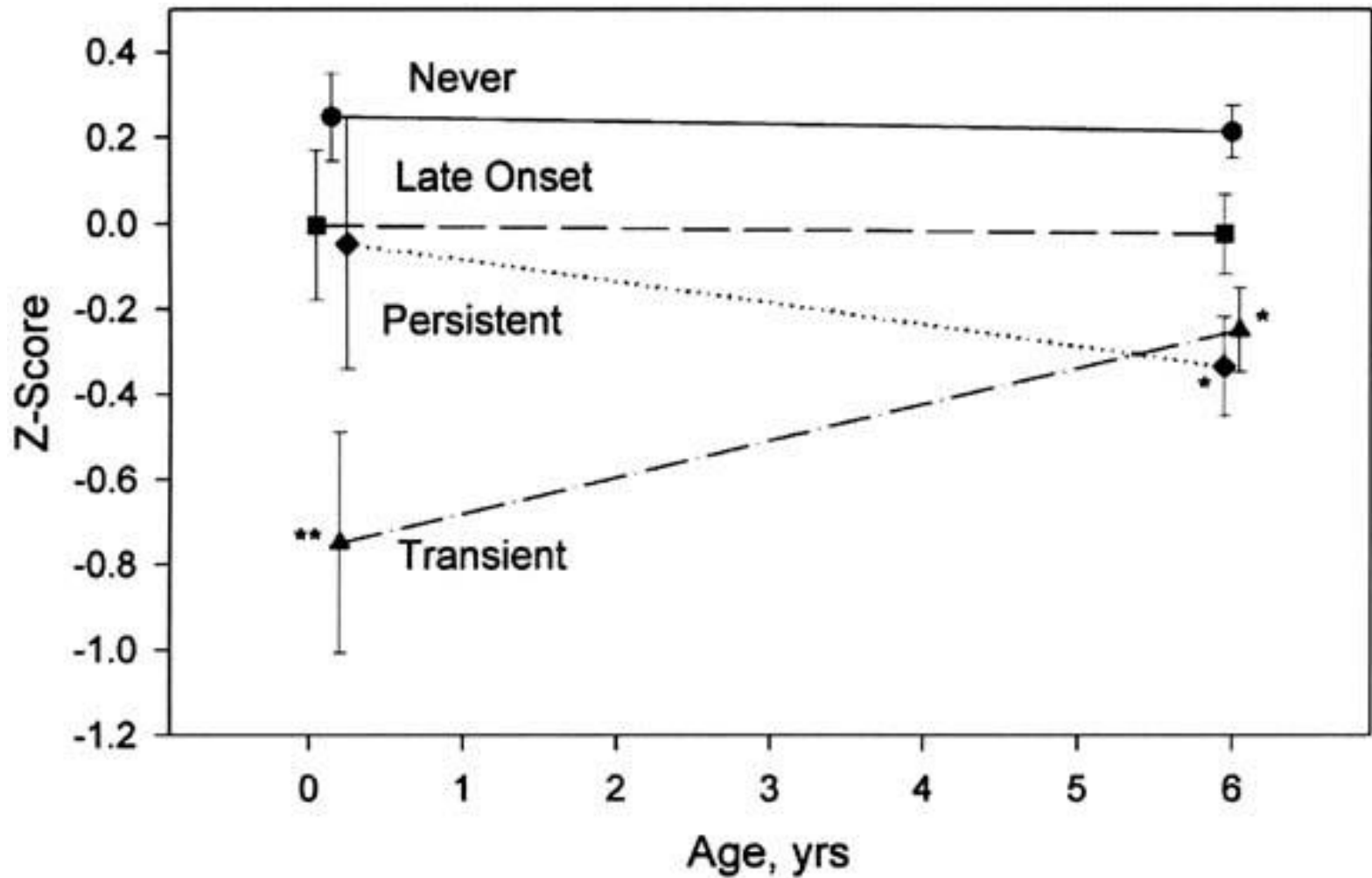


Infant Wheezing Phenotypes

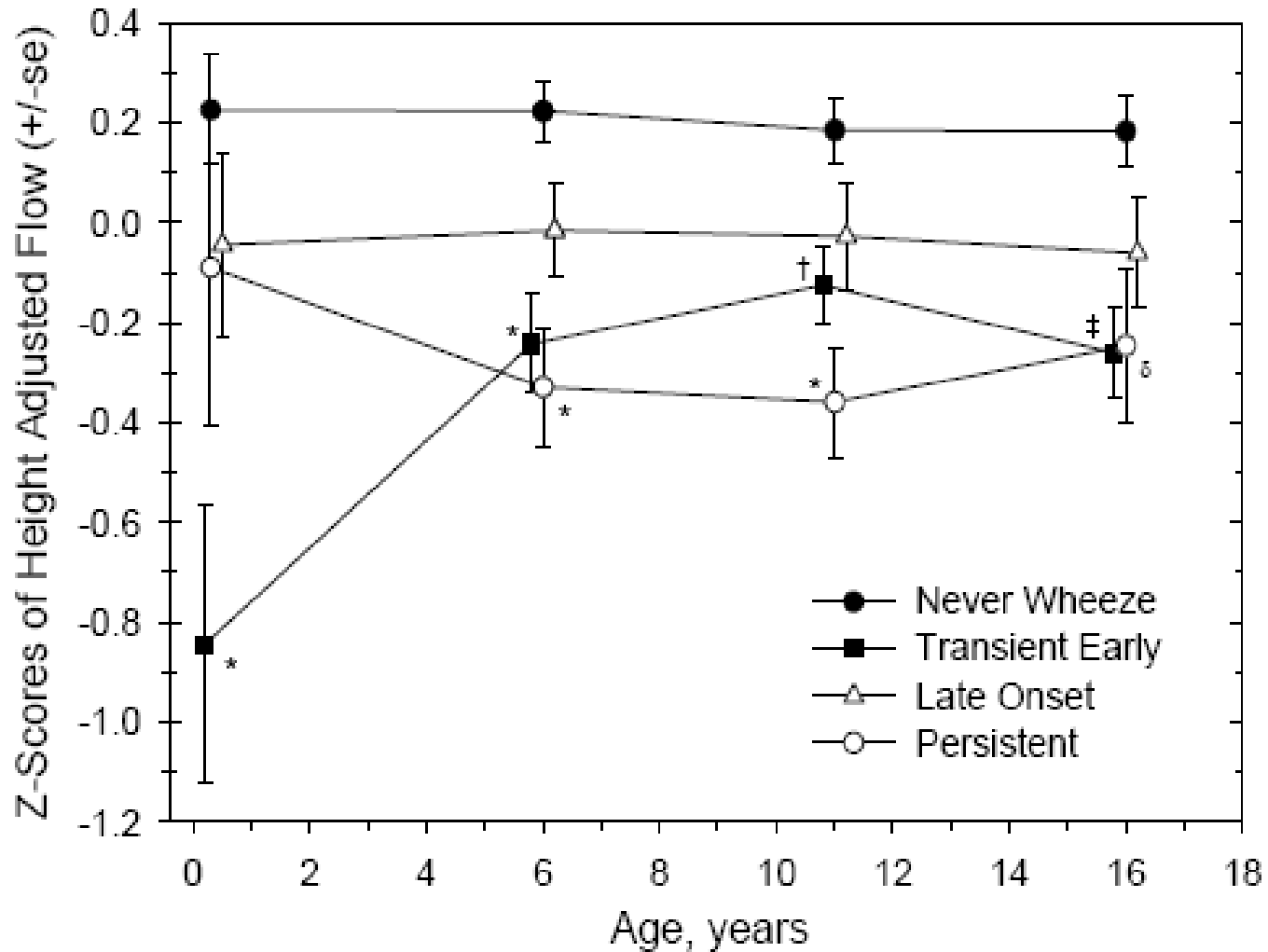
- ▶ Transient wheeze
- ▶ Non-atopic (viral induced) wheeze
- ▶ Atopic wheeze

- ▶ Stein RT et al Thorax 1997;52:946-52
- ▶ Martinez FD Pediatrics 2002;109:362-7



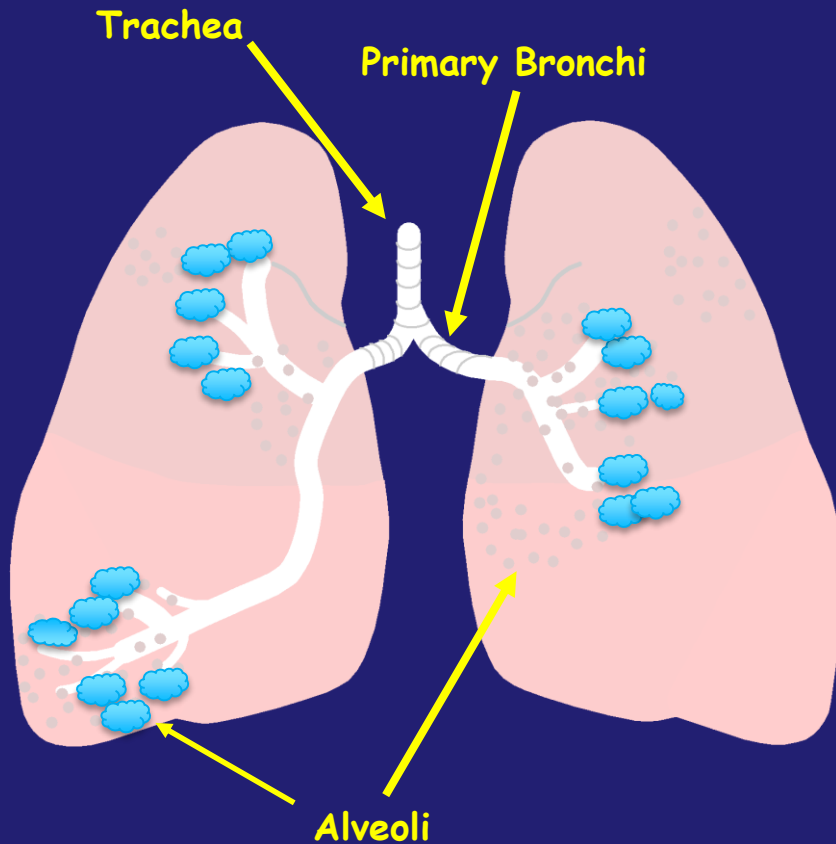


Evolution of lung function in
Infant Wheezing Phenotypes



Further evolution of Lung Function

Central Determinants in Development of the Respiratory System



Aberrant or excessive pro-inflammatory immune responses, both locally and systemically

Regulatory pathways involving collaboration of innate and acquired immune responses important

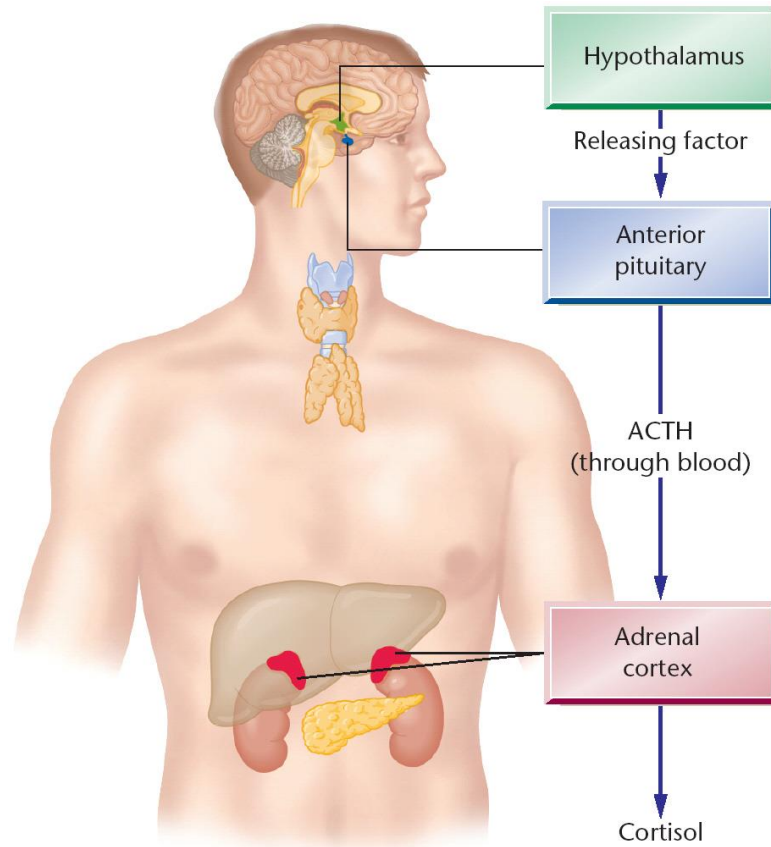
Factors outside immune system - neurohormonal phenotypes - may also influence underlying processes

Is toxic stress taking our breath away?



How does toxic stress get ‘into the body’ to impact respiratory health?

Neuroendocrine - Immune Interactions



Stress Physiology is Organized Around Two Systems:

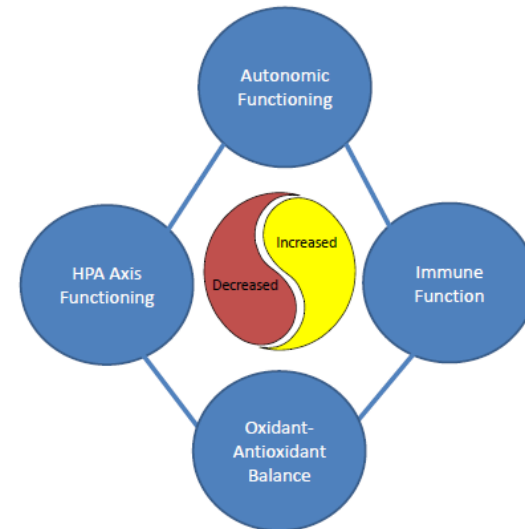
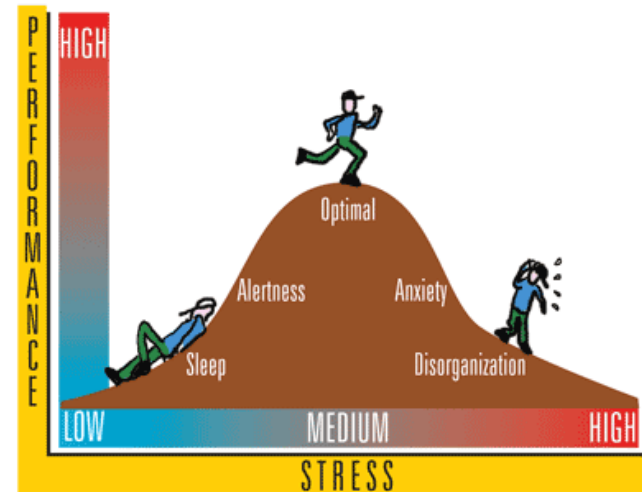
- Sympathetic-Adrenomedullary (SAM) System
- Hypothalamic-Pituitary-Adrenocortical (HPA) System

These systems are regulated in the brain
Interaction with immune system functioning

BIOLOGY OF STRESS

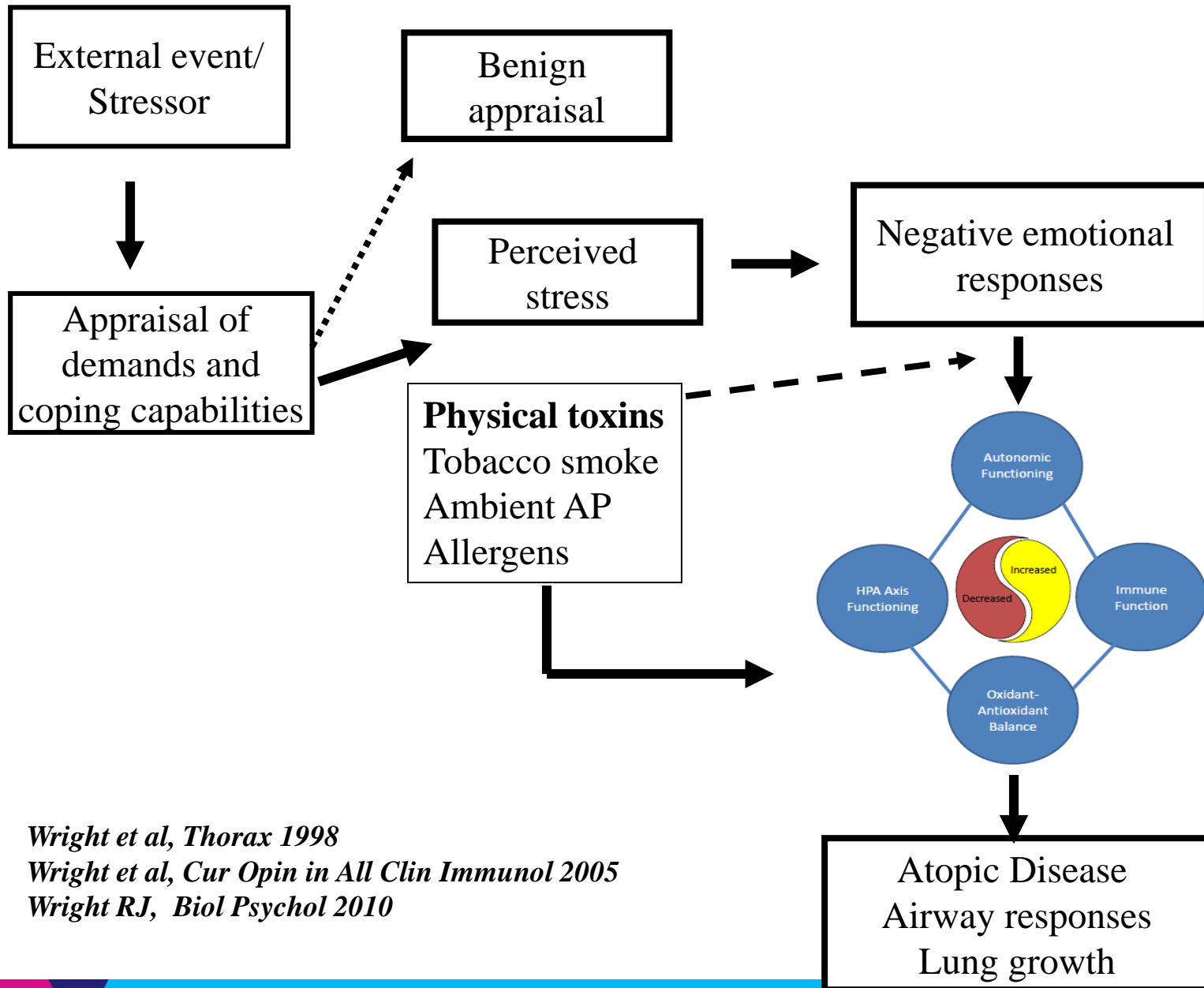
- ▶ The stress reaction is neither good nor bad in itself
- ▶ Depends on circumstances
- ▶ Stress is useful when it protects us in times of danger or helps us to adapt in times of change.

Stress Performance Connection



OPTIMAL BALANCE = HEALTH

Overview Model



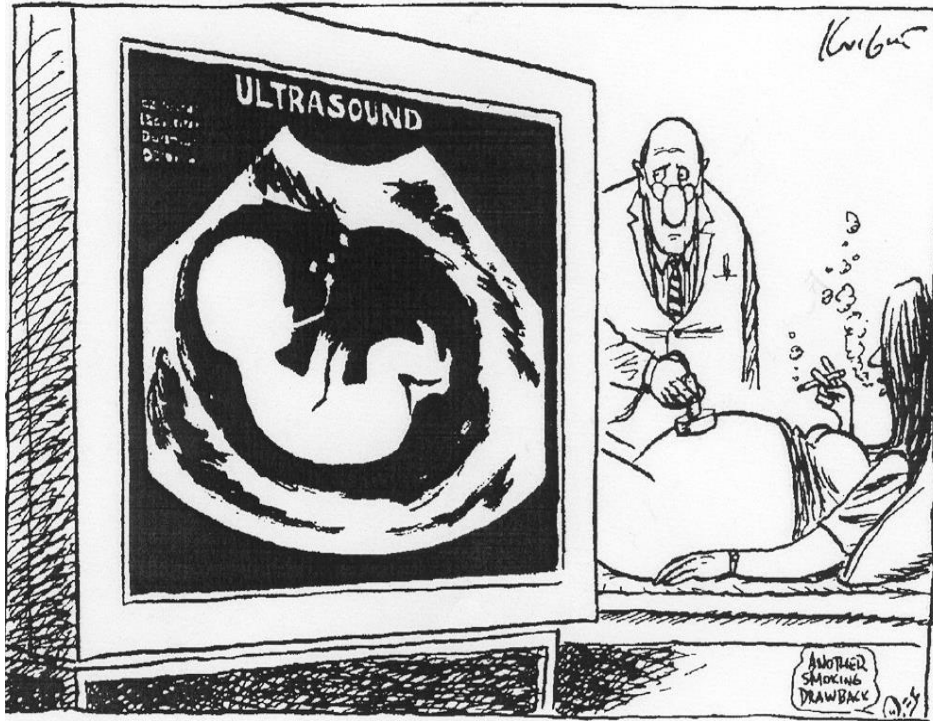
Wright et al, Thorax 1998

Wright et al, Cur Opin in All Clin Immunol 2005

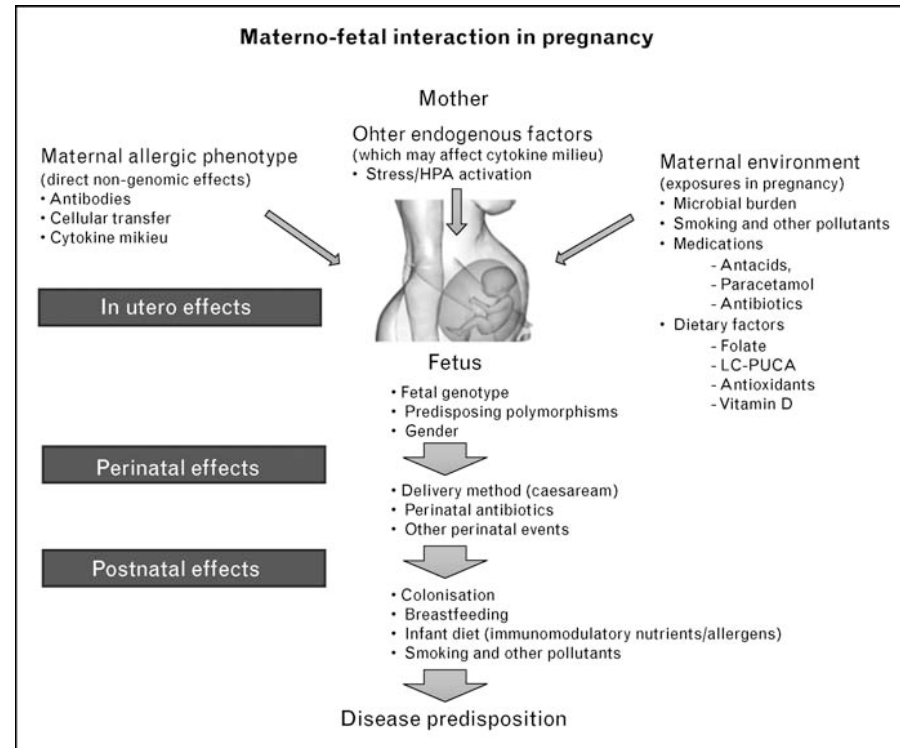
Wright RJ, Biol Psychol 2010

Social & Physical Toxins

Impact Fetal Programming - Similar Magnitude of Effect



By Mark Knight, reprinted with permission of the Herald and Weekly Times, Melbourne, Australia.



Prescott & Clifton, *Cur Opin All Clin Immunol* 2009; 9:417-26

Pregnancy cohort studies

Asthma Coalition on Community, Environment & Social Stress (ACCESS)

**Air
Pollution**

Stress

Allergens

**Tobacco
Smoke**

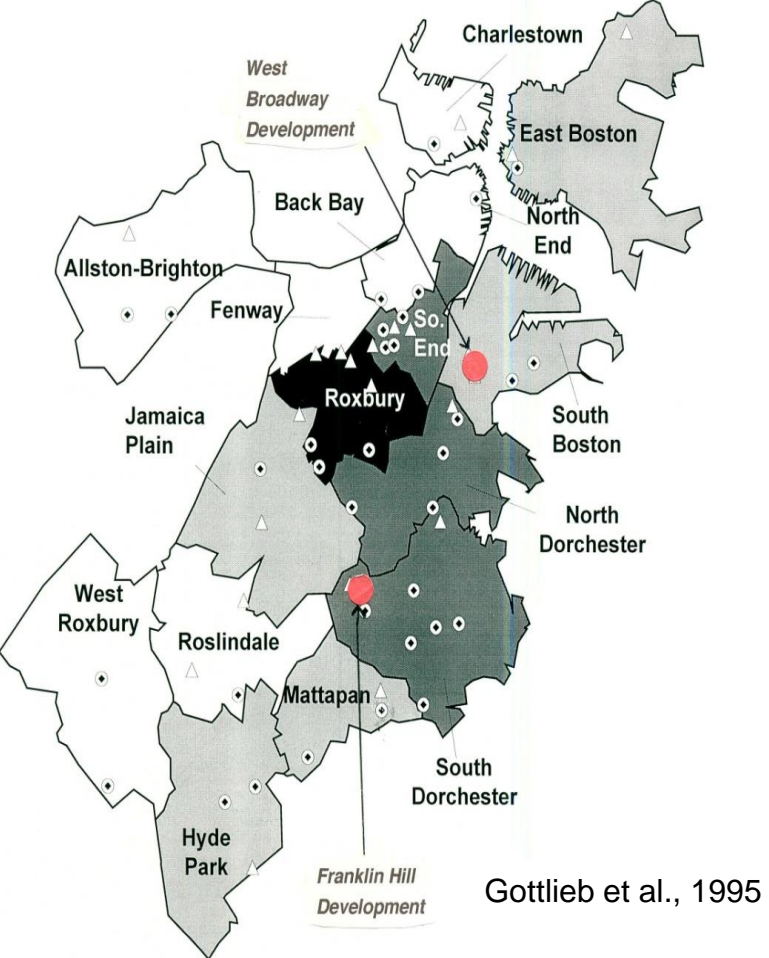


Diet

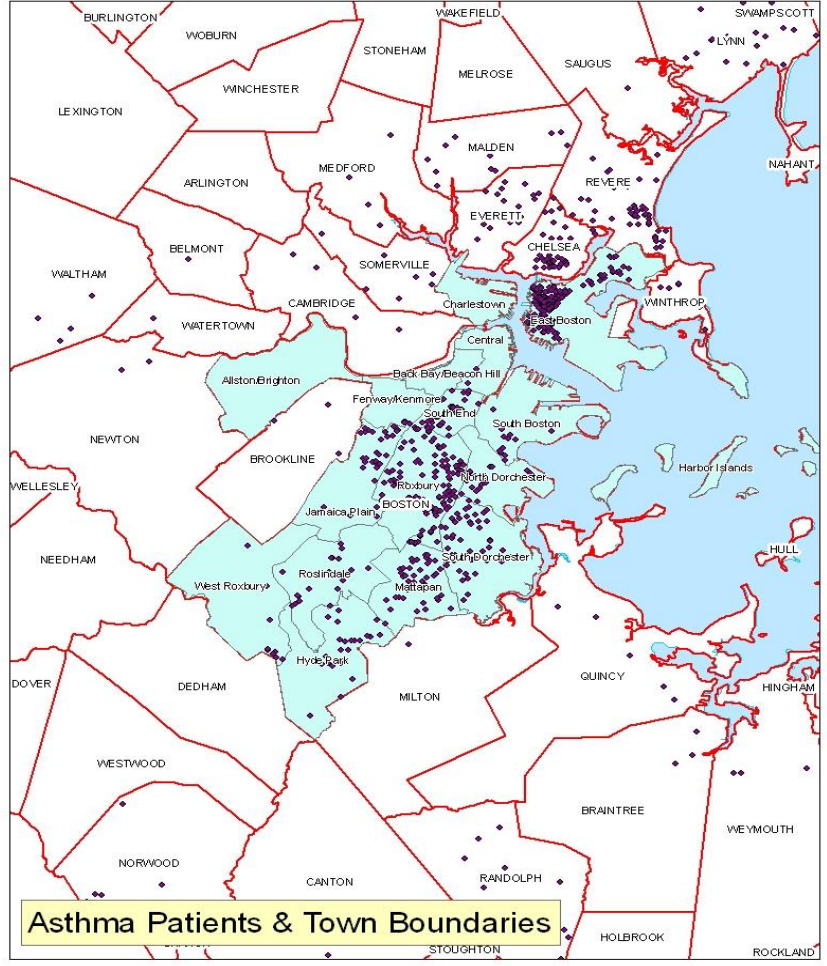


- ▶ 955 pregnant women recruited Aug 2002 – Sept 2009
- ▶ Enrolled through prenatal clinics at BWH & BMC and affiliated CHCs & WIC centers
- ▶ 50% Hispanic, 35% AA, 15% Caucasian
- ▶ Primarily lower-SES

Motivation for ACCESS Cohort Design



Gottlieb et al., 1995



Central Theories

- ▶ **Co-occur**

Exposure 1 present usually Exposure 2 present

- ▶ **Proxies**

Exposure 1 & 2 co-vary → effect of Exposure 2

- ▶ **Interactions**

- Additive

Exposure1 + Exposure2 = effect Exposure 1+2

- Synergistic

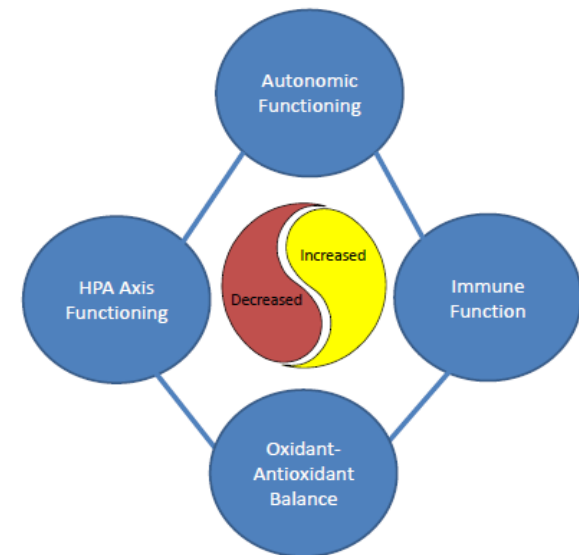
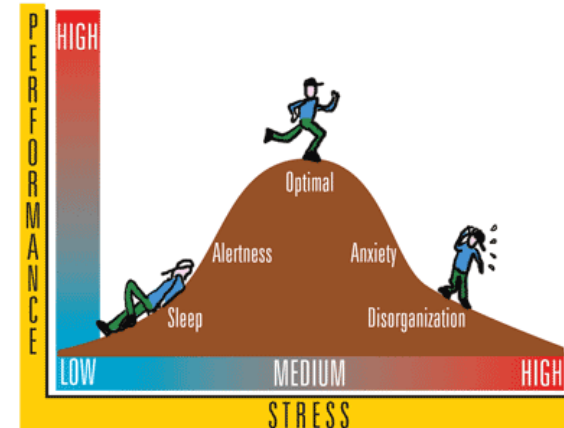
Exposure1 + Exposure 2=effect > Exposure 1+2

**Independent impact of
psychological stressors?**

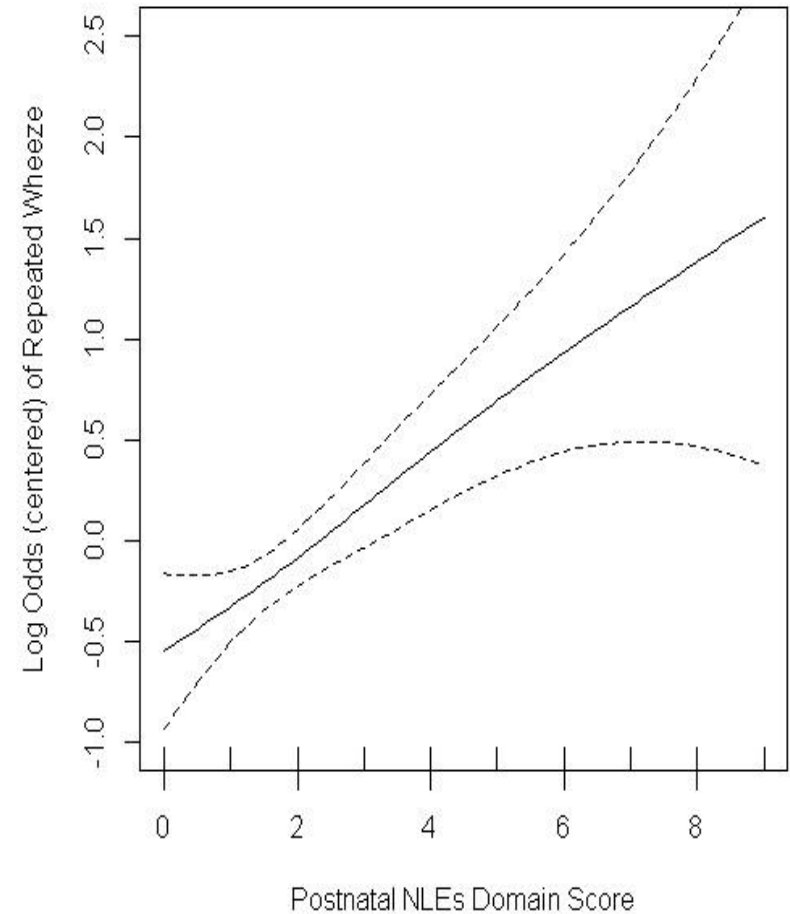
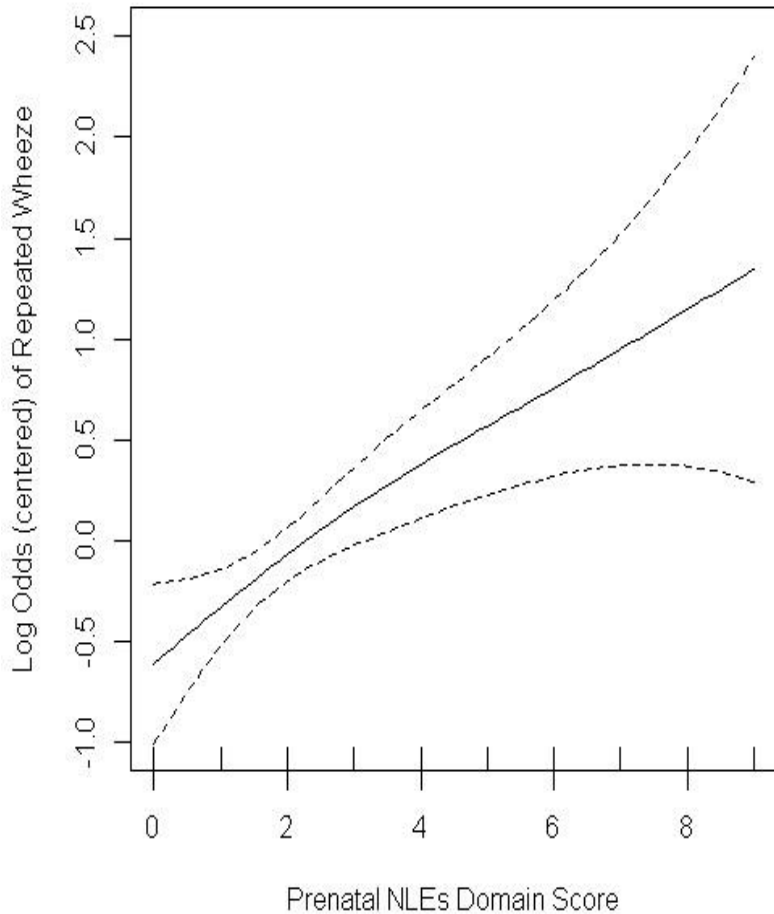
Cumulative Stress Domains

- ▶ Financial strain
- ▶ Racism/discrimination
- ▶ Relationships
- ▶ Community/interpersonal violence
- ▶ Other negative life events (housing, landlords, fear of eviction, etc.)

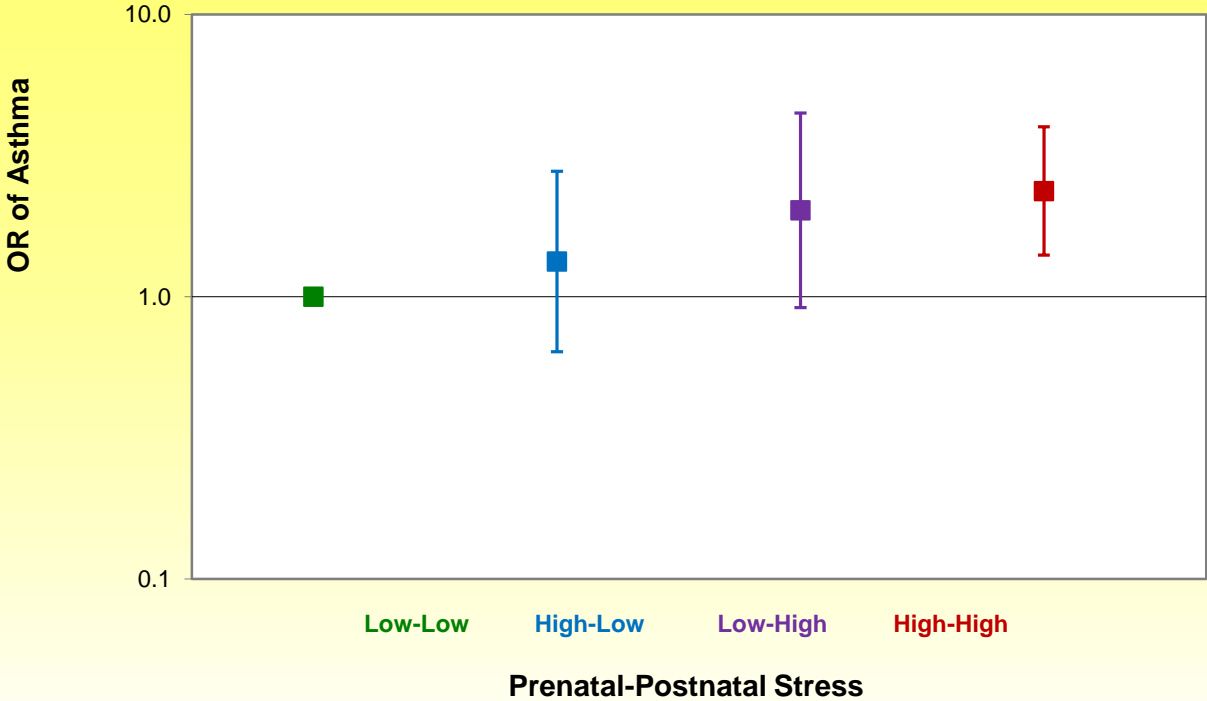
Stress Performance Connection



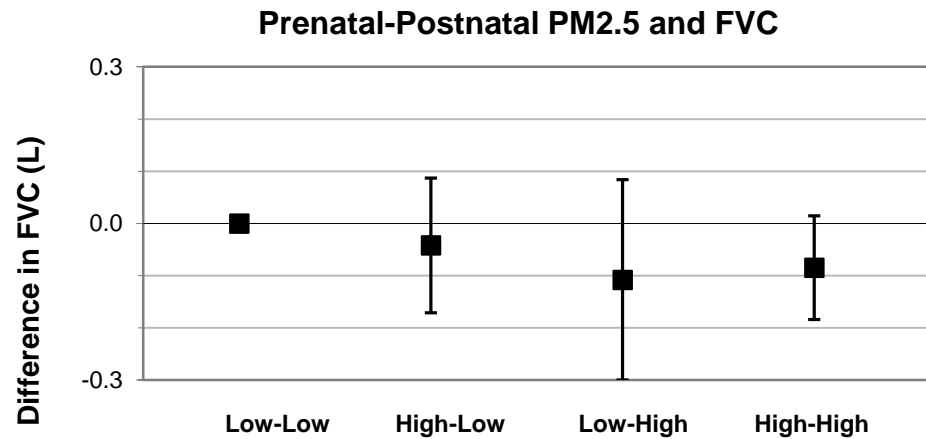
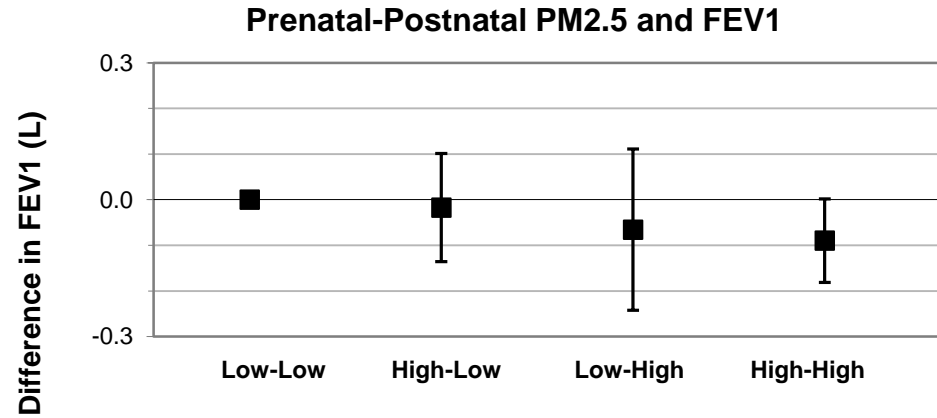
Pre- and Postnatal Maternal Stress and Child Repeated Wheeze: Adjusted GAMs



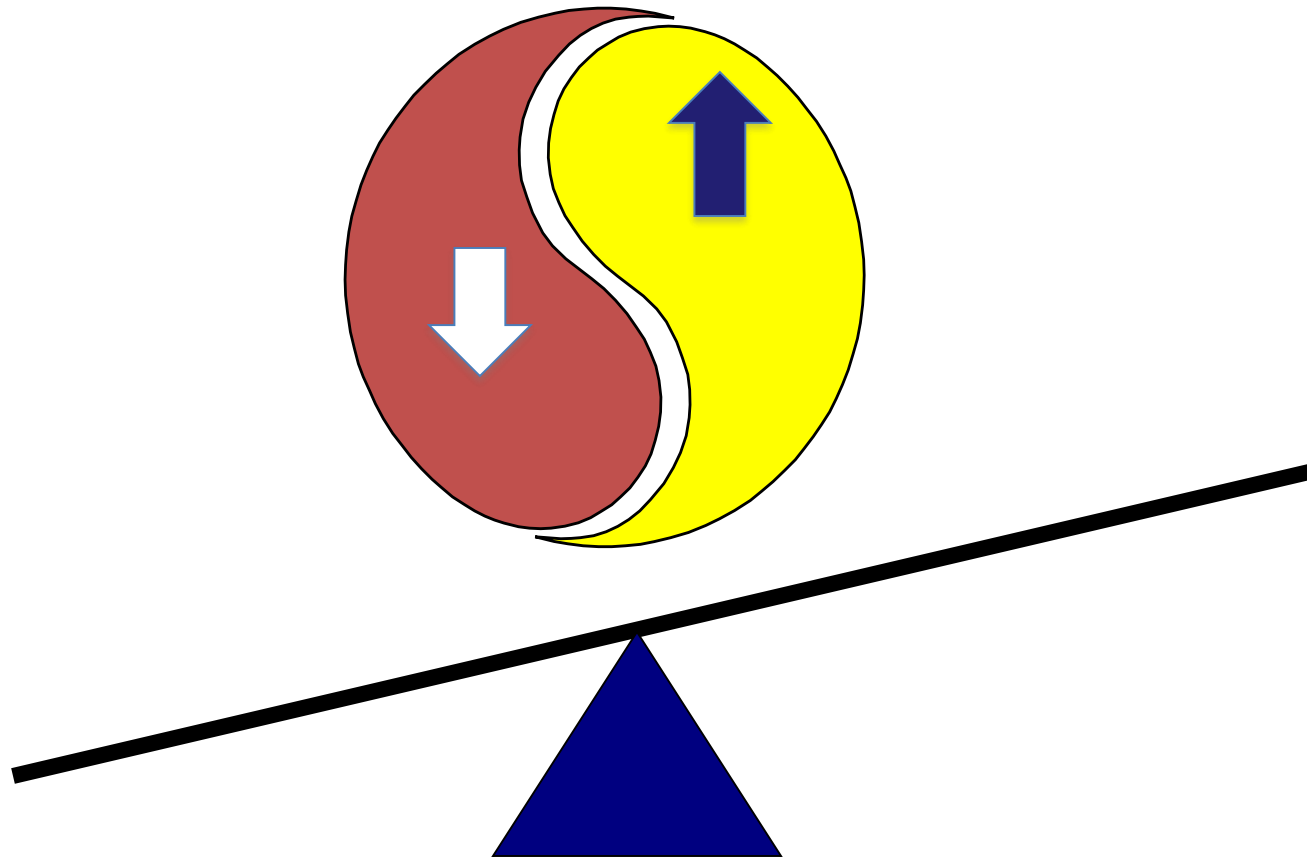
Prenatal-Postnatal Stress and Asthma by age 6 years



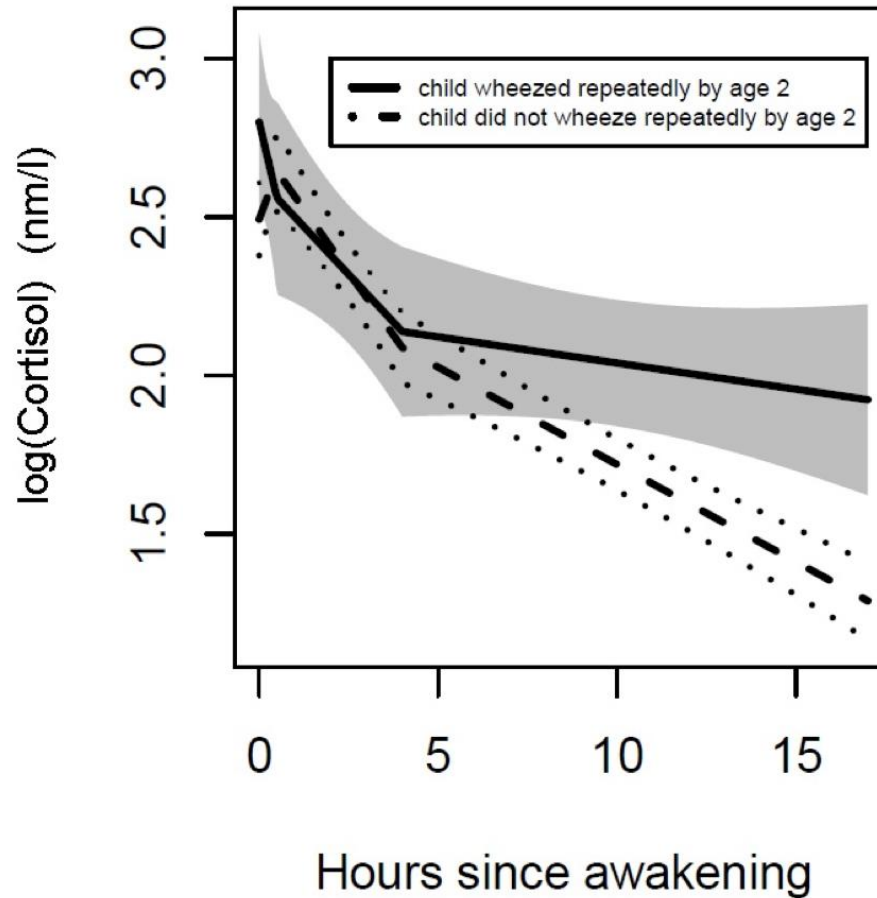
Pre/Postnatal Stress and Lung Function



Stress-elicited Imbalance in Prenatal Key Regulatory Systems

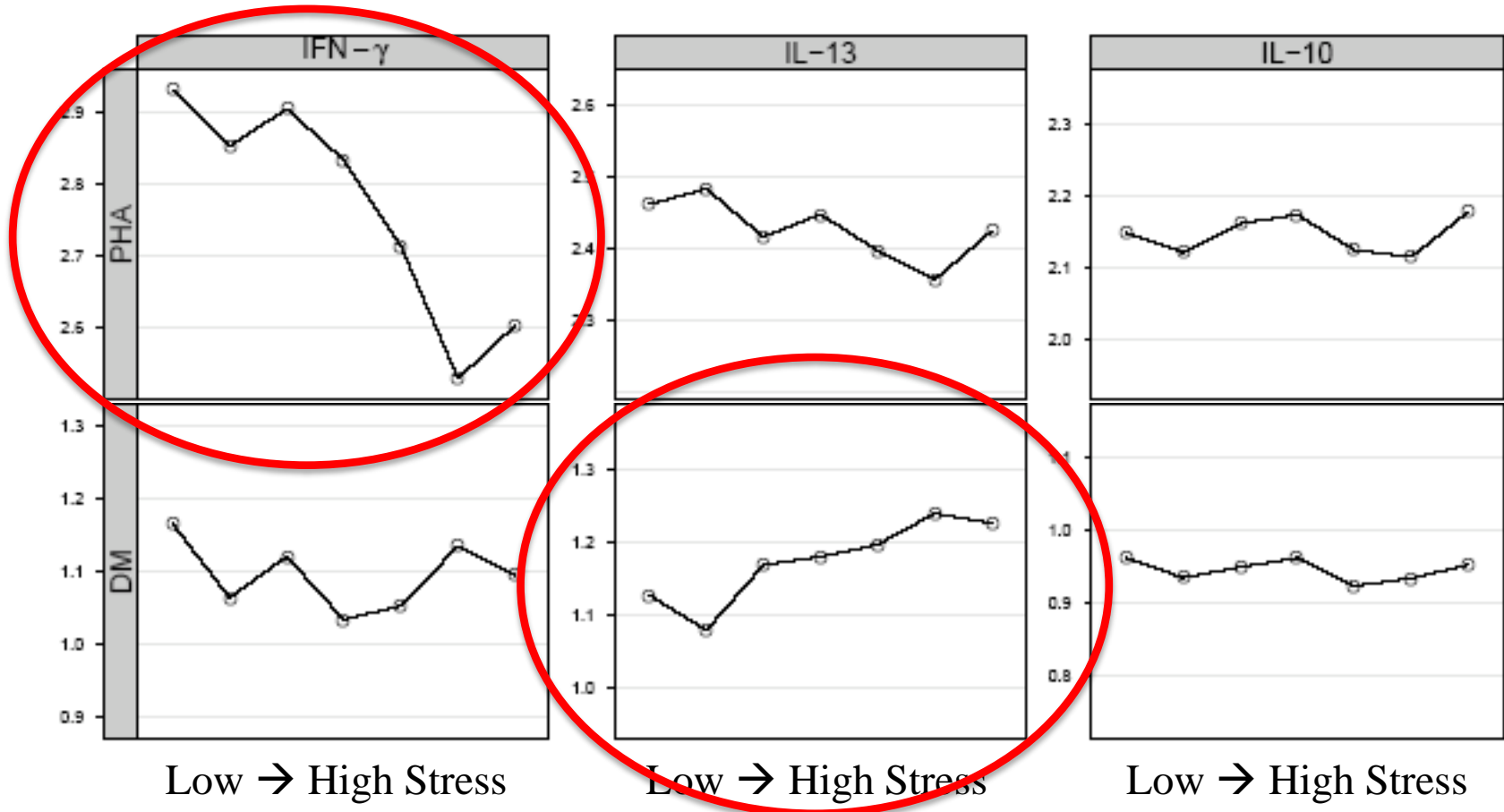


Maternal prenatal cortisol trajectory associated with early asthma risk in children

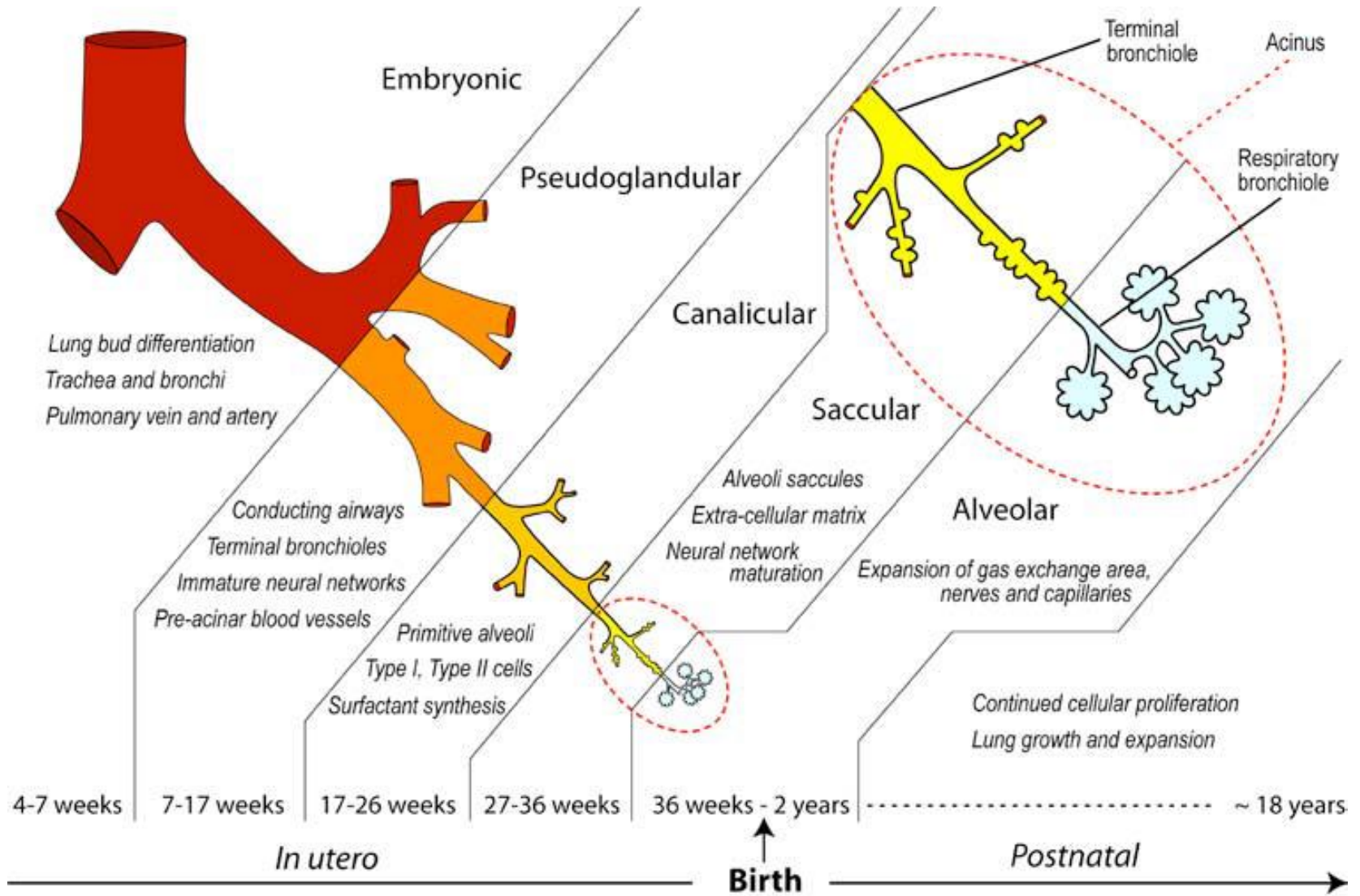


Wright RJ et al. *Am J Res Crit Care Med* (2013)

Higher prenatal maternal stress alters child's immune response at birth



Wright RJ et al., AJRCCM 2010; 182:25-33.



Important

Nature of Stressor?



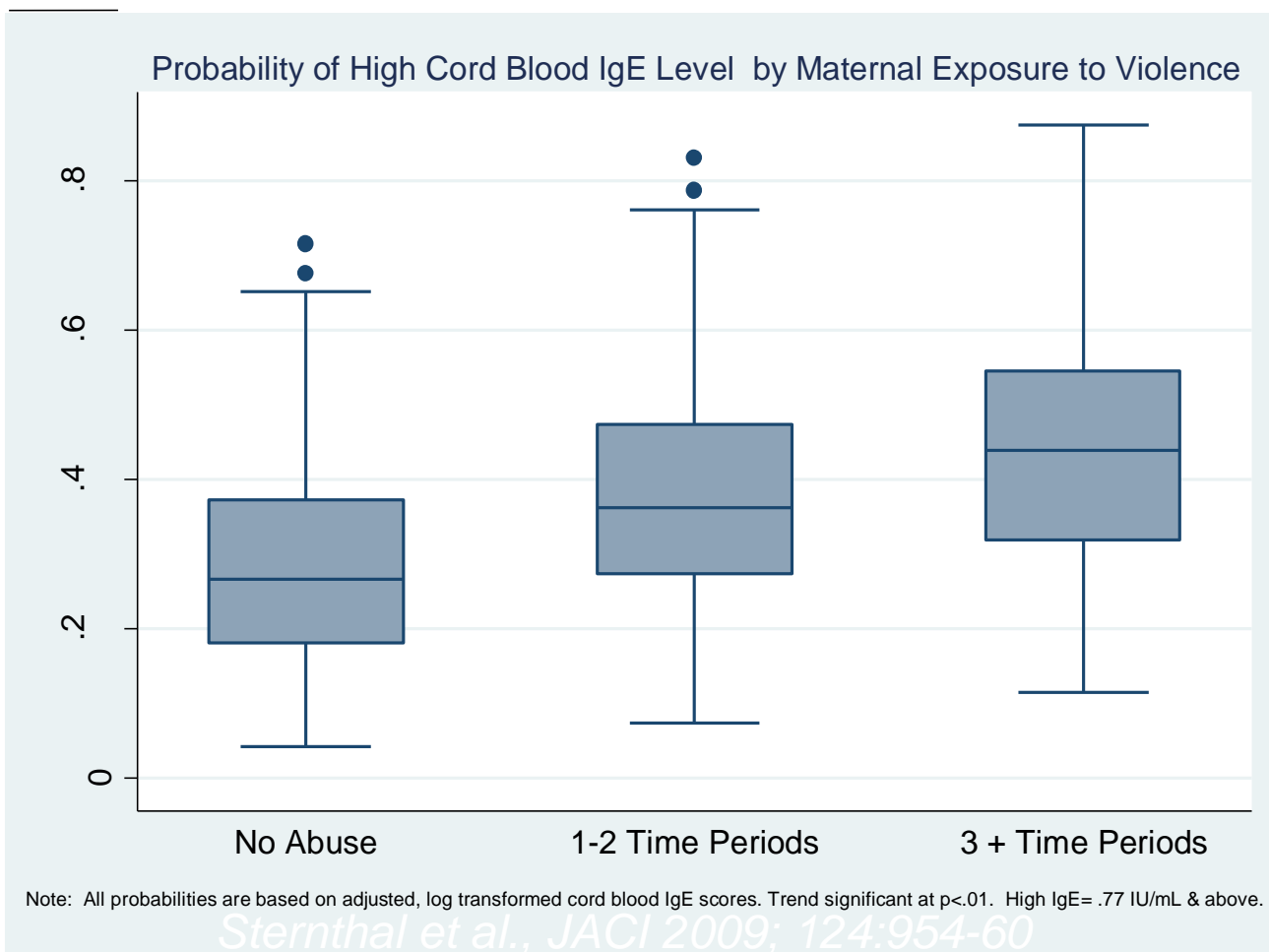
Timing?



Maternal interpersonal trauma and cord blood IgE levels in an inner-city cohort: A life-course perspective

Michelle Judith Sternthal, PhD,^a Michelle Bosquet Enlow, PhD,^b Sheldon Cohen, PhD,^c Marina Jacobson Canner, MA,^d John Staudenmayer, PhD,^e Kathy Tsang, MHA,^d and Rosalind J. Wright, MD, MPH^{a,d} *Boston and Amherst, Mass, and Pittsburgh, Pa*

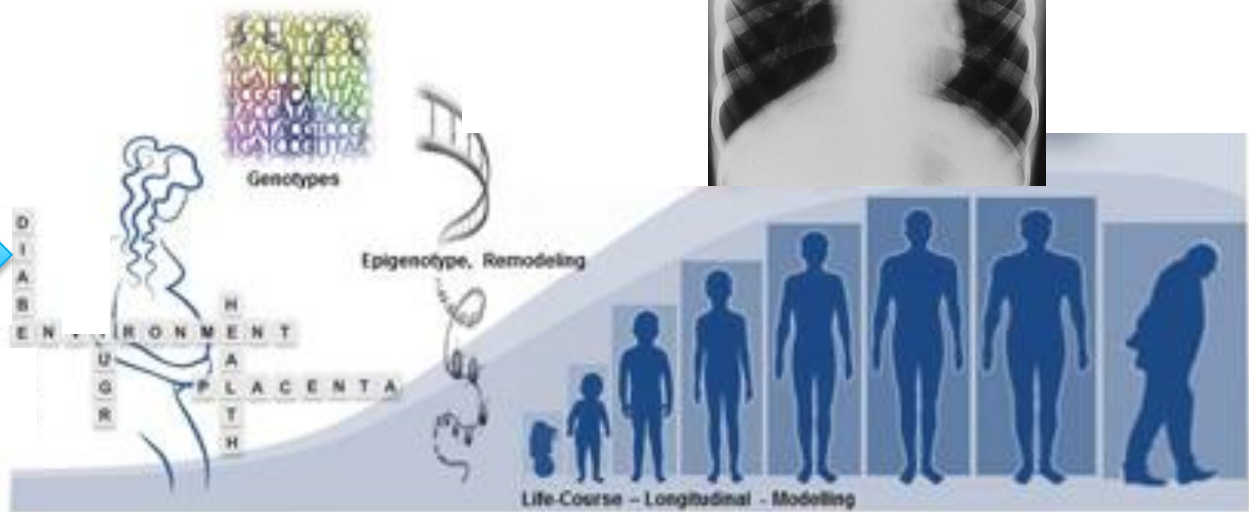
JACI 2009



Lifecourse Framework: Importance of Early Life Events



Preconception
Stress



Air Pollution, Community Violence, and Wheeze

Chiu Y-HM et al., JACI 2013

Table: Prenatal maternal exposure to air pollution and community violence in relation to repeated wheeze in children: Logistic Regression Models

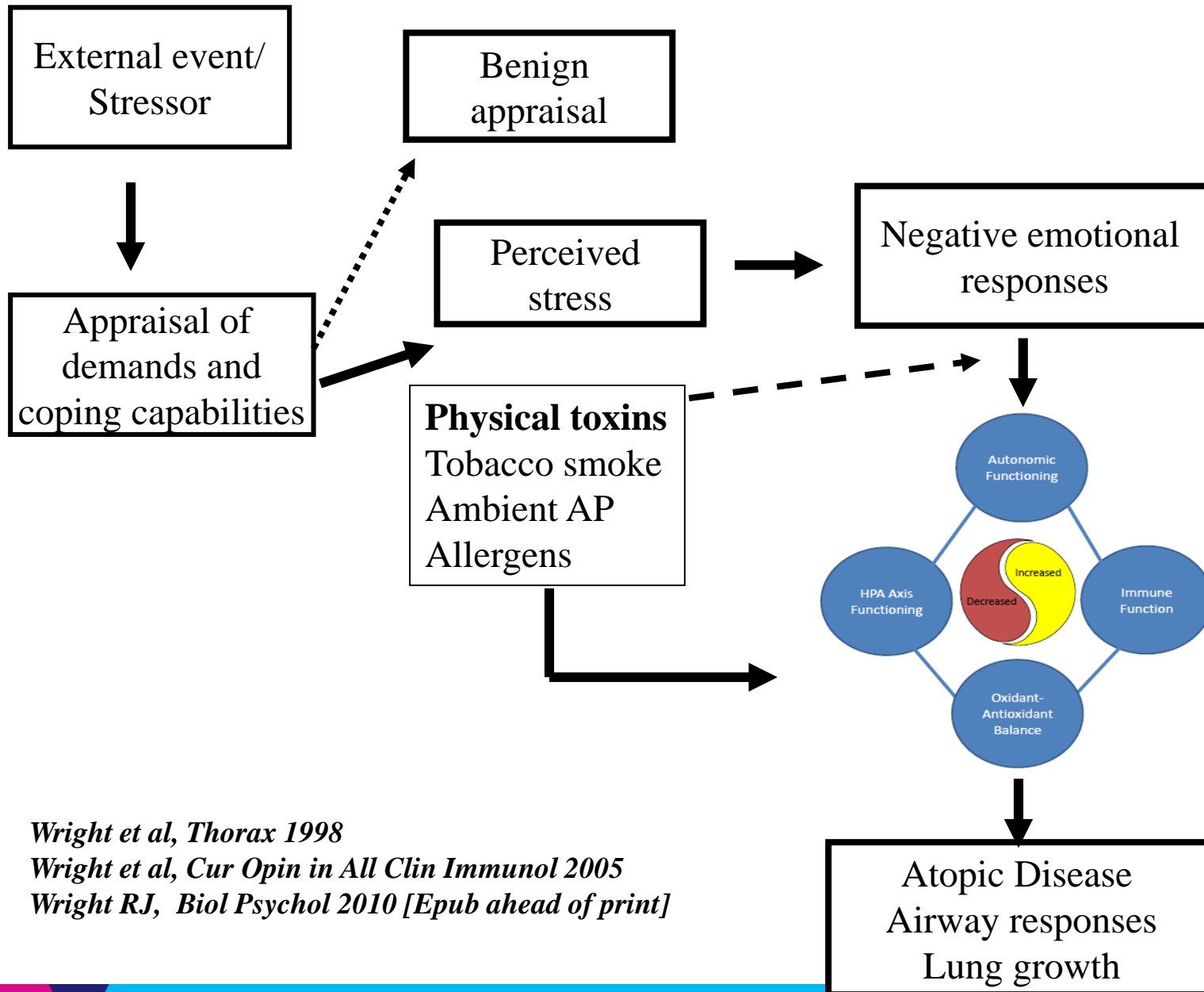
Variables	Unadjusted Model			Multivariable-adjusted Model ^a						
				Model 1			Model 2			
	OR	95%CI		OR	95%CI		OR	95%CI		
<u>BC & ECV Model</u>										
Prenatal BC exposure										
Low (\leq median, 0.38 $\mu\text{g}/\text{m}^3$)	Ref	--	--	Ref	--	--	Ref	--	--	
High (>median)	1.61	0.98	2.66	1.52	0.92	2.51	1.84	1.08	3.12	
Prenatal community violence										
Low	Ref	--	--	Ref	--	--	Ref	--	--	
Medium	1.44	0.79	2.62	1.43	0.78	2.61	1.34	0.71	2.52	
High	2.08	1.25	3.46	1.95	1.16	3.27	1.95	1.13	3.36	
<u>PM_{2.5} & ECV Model</u>										
Prenatal PM_{2.5} exposure										
Low (\leq median, 11.2 $\mu\text{g}/\text{m}^3$)	Ref	--	--	Ref	--	--	Ref	--	--	
High (>median)	1.61	0.98	2.66	1.57	0.98	2.51	2.02	1.20	3.40	
Prenatal community violence										
Low	Ref	--	--	Ref	--	--	Ref	--	--	
Medium	1.44	0.79	2.62	1.50	0.82	2.75	1.41	0.75	2.68	
High	2.08	1.25	3.46	2.16	1.29	3.61	2.15	1.24	3.71	

^a Model 1 included air pollution and community violence. Model 2 additionally adjusted for child's gender, season of birth, maternal race, education level, atopy, and prenatal cockroach allergen exposure.

Interactions?

**Psychological stressors
enhance effects of
chemical/physical toxins**

Overview Model

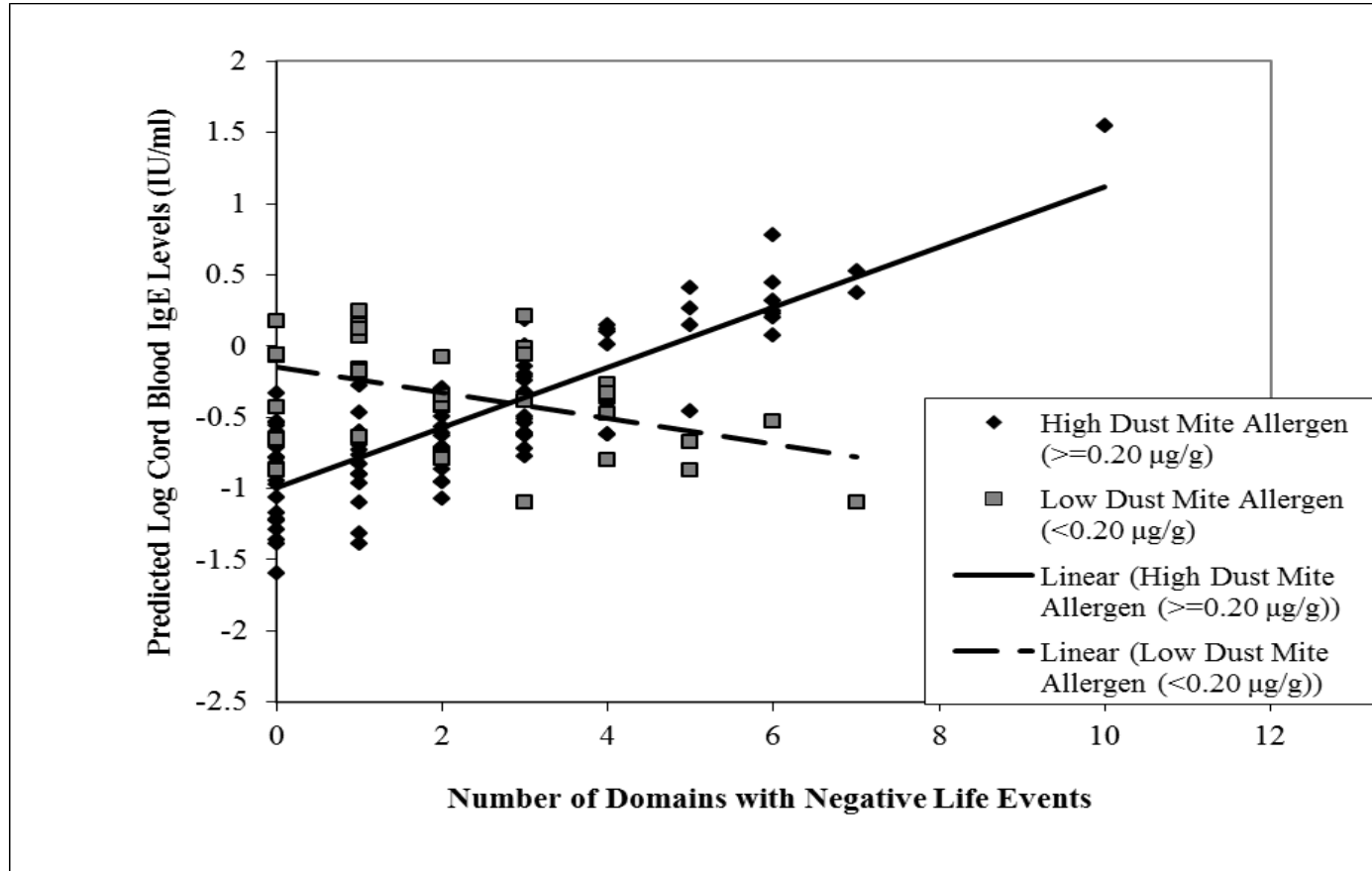


Wright et al, Thorax 1998

Wright et al, Cur Opin in All Clin Immunol 2005

Wright RJ, Biol Psychol 2010 [Epub ahead of print]

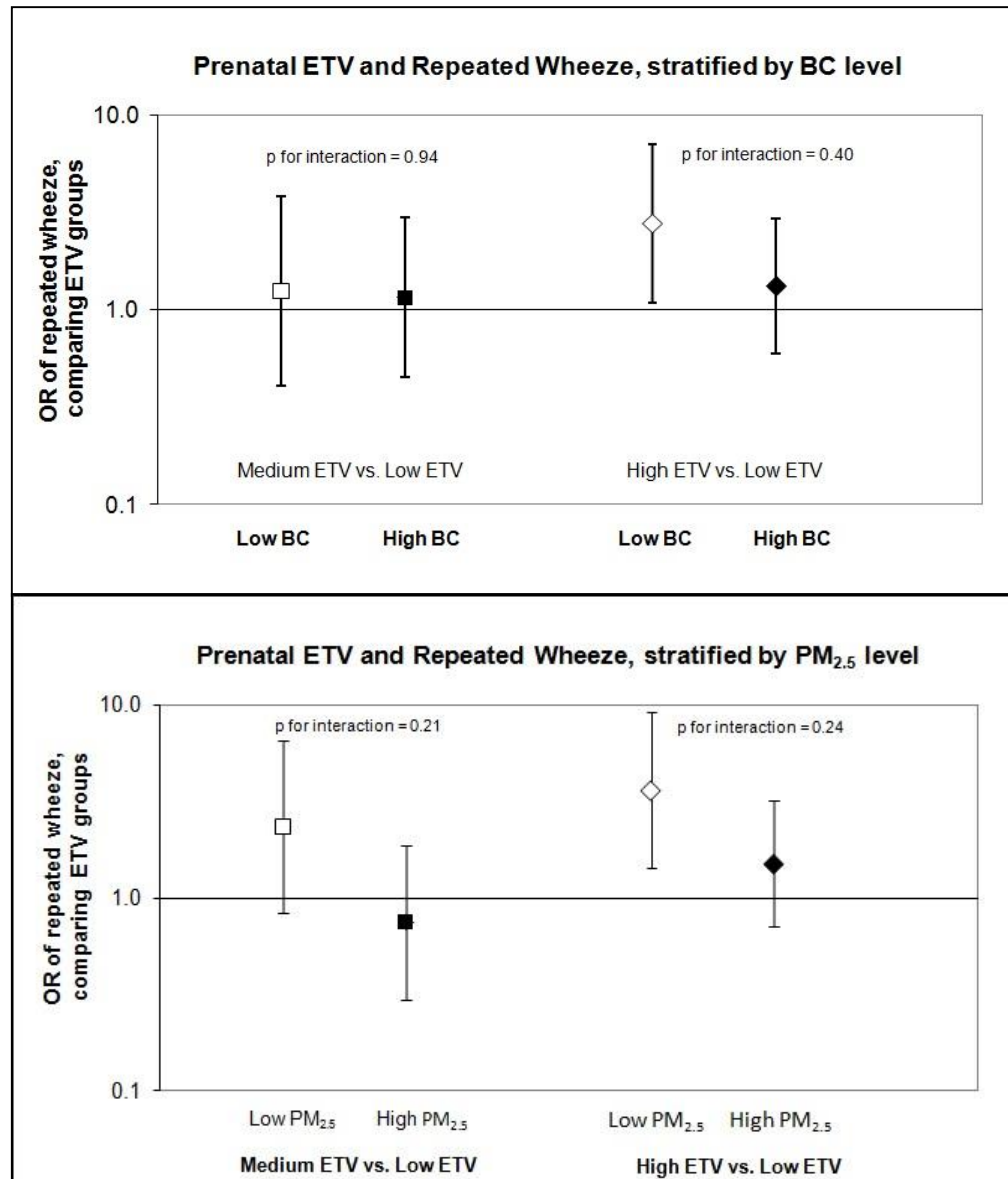
Prenatal stress and dust mite predicts cord blood IgE



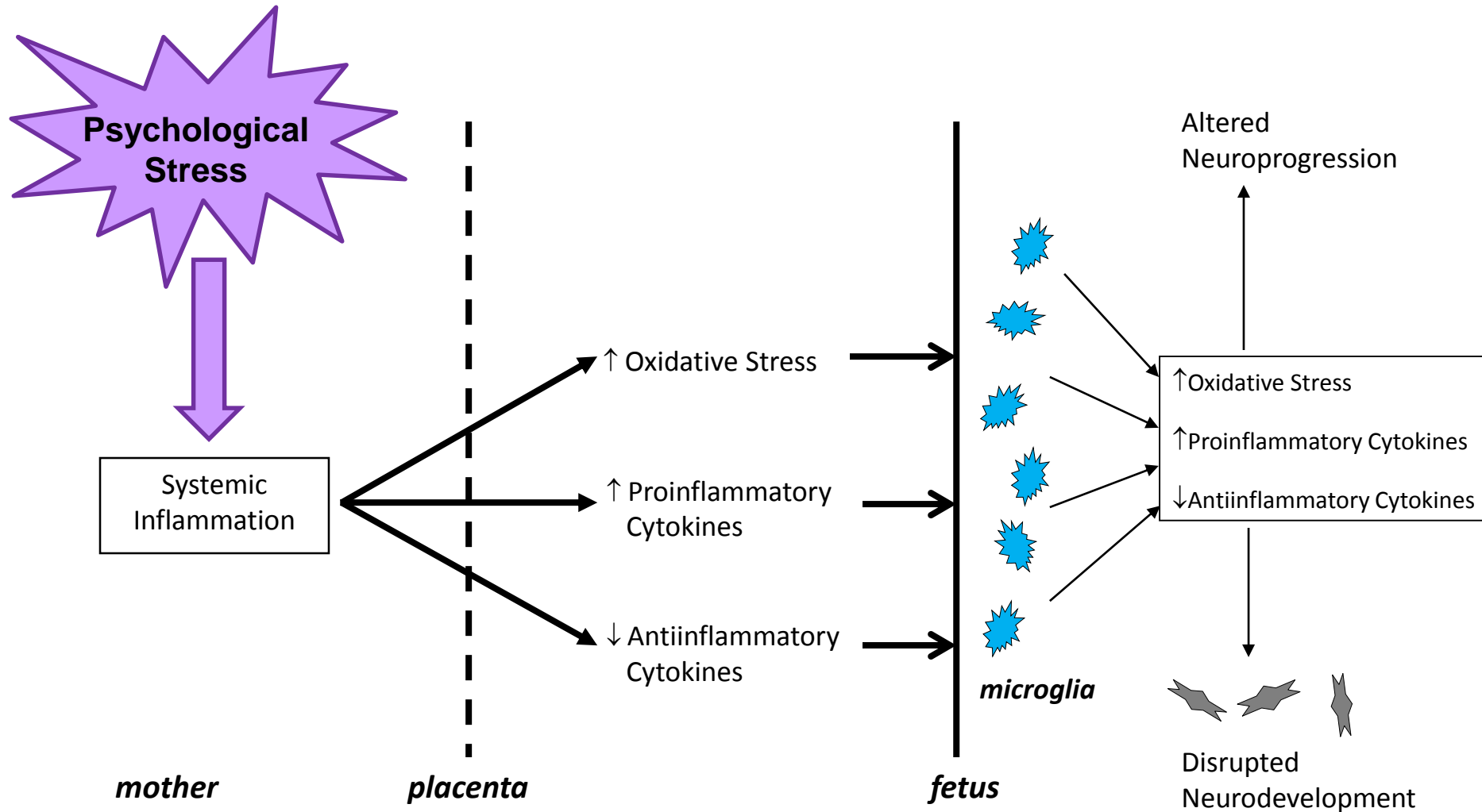
Peters J, et al., Allergy 2012; 67:545-51.

Results for Multiplicative Interaction

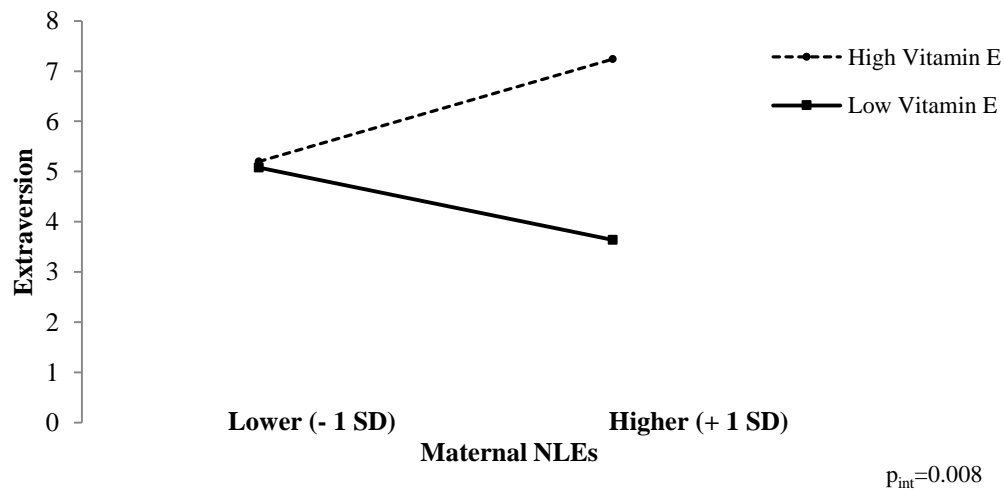
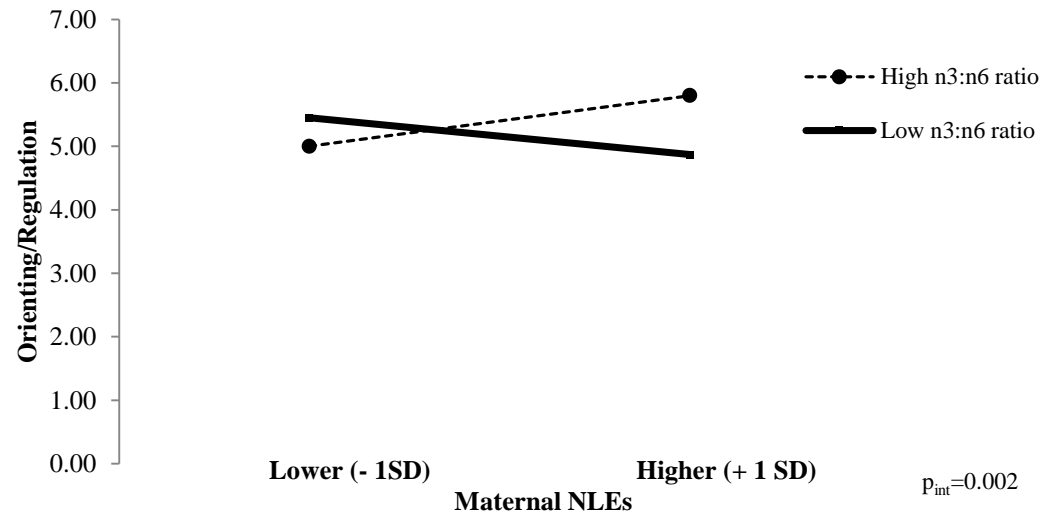
Chiu Y-HM et al., JACI 2013



How mother's prenatal psychological stress impacts fetal brain development?



Prenatal Stress (NLEs) and Early Temperament: African American Mother-Child Pairs



Summary

- ▶ Socially toxic environments are **NOT** simply a marker of a more toxic physical environment
- ▶ Social contexts and consequent stress may be as detrimental to children's health as chemical toxins
 - Social pollutants/toxins
- ▶ Psychological stress disrupts biological systems overlapping with those altered by physical pollutants/toxins
- ▶ Psychosocial stress may impact host resistance such that physical toxins (e.g., indoor allergens, traffic-related air pollution) may have adverse effects, even at relatively lower doses
- ▶ Interventions to reduce stress and/or stress effects (e.g., antioxidant intake) may also reduce toxicity of chemical/physical toxins

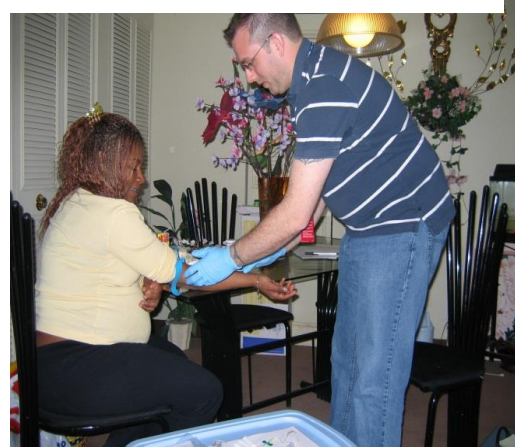


“It is easier to build strong children than to repair broken men.”

Frederick Douglas



Asthma Coalition for Community, Environment and Social Stress



Co-investigators

Joel Schwartz (HSPH)
Brent Coull (HSPH)
Diane Gold (HSPH)
John Staudenmayer (UMass)
Robert Wright (MSSM)
Michelle Bosquet-Enlow (HMS)
Thomas Platts-Mills (UVa)
Thomas Ritz (SMU)

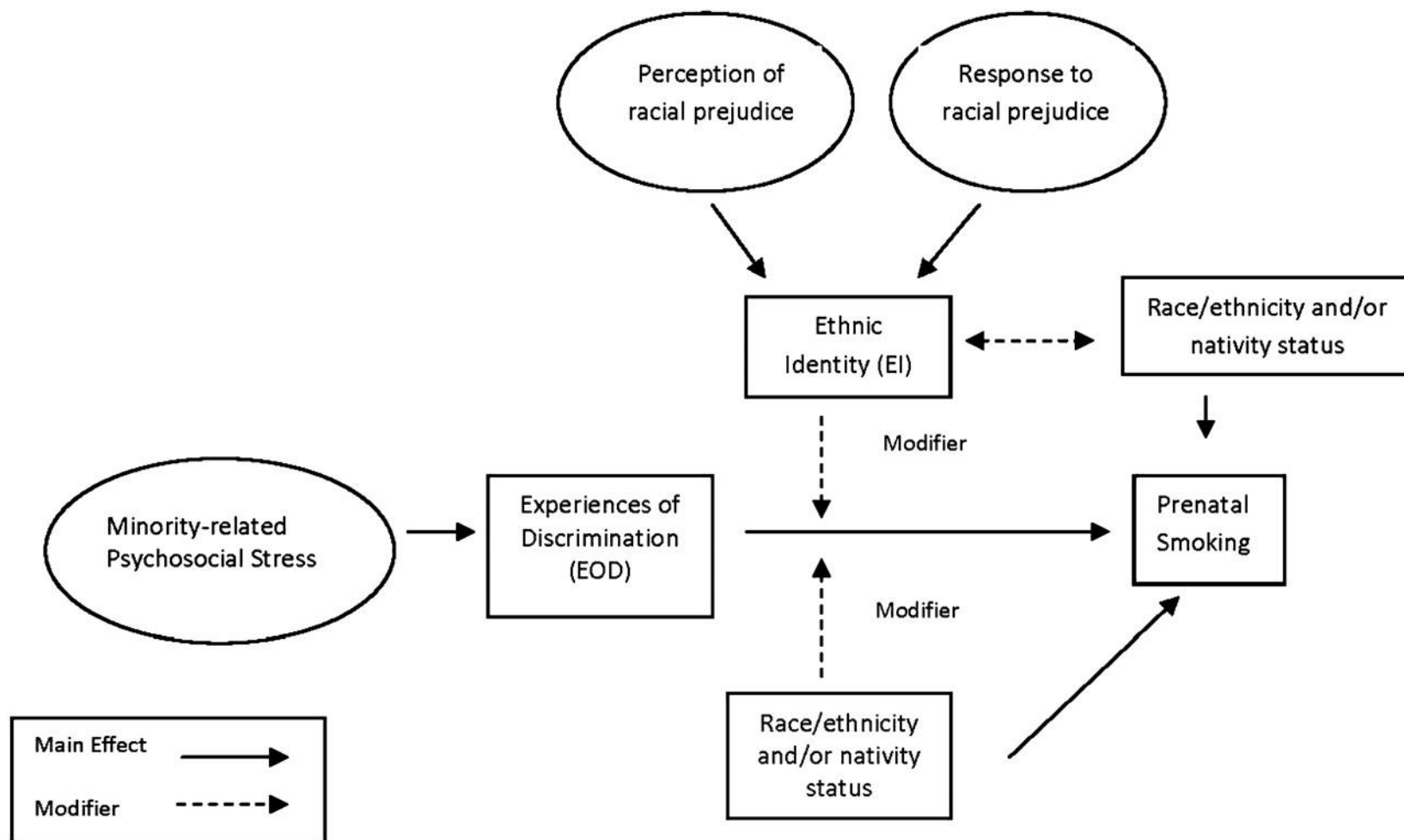
Postdoctoral Students

Shakira Franco Suglia
Junenette Peters
Yueh-Hsiu Mathilda Chiu
Michelle Sternthal
Kelly Brunst
Hannah Schreier

Funding

NIEHS
NHLBI
NIMHD
NIMH
Leaves of Grass Foundation

Linking experiences of discrimination, ethnic identity and prenatal smoking in minority women



Nguyen K H et al. J Epidemiol Community Health 2012;66:315-321

Stress may increase exposure to tobacco smoke in pregnancy

Adjusted odds ratios (95% Confidence Intervals) for experiences of discrimination predicting prenatal smoking, stratified by Race/Ethnicity

	Hispanic (n=412)		Black (n=265)	
Experiences of Discrimination *				
1 or 2 situations	1.00		1.00	
None	2.45	(0.90, 6.70)	1.05	(0.42, 2.62)
3 +	2.08	(0.60, 7.14)	3.36	(1.23, 9.19)

During early childhood the human stress system is under strong social regulation.



Sensitive, responsive, supportive care “buffers” or protects young children from experiencing elevated stress hormone levels

As quality of care decreases, young children become highly stress vulnerable



Stress may increase risk for maternal depression

Adjusted odds ratios (95% Confidence Intervals) for lifetime abuse history and odds of prenatal depression, Project ACCESS

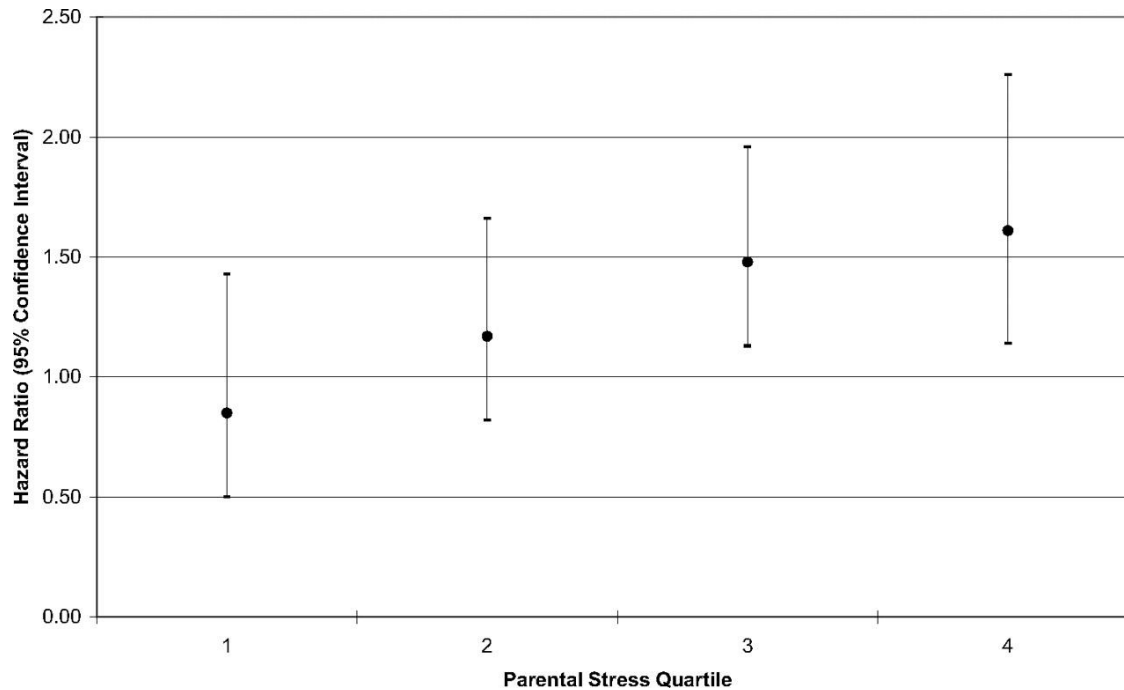
ABUSE EXPERIENCE		
Never (referent group)		
Child/Teem	1.27	(0.94,1.73)
Adult Pre-pregnancy	1.89	(1.35, 2.64)
Pregnancy	1.73	(1.00, 3.02)

Rich-Edwards et al. Int J Epidemiol 2011; 40:375-84

Stress x Environment Interactions

LITERATURE	STUDY TYPE (N)	SUBJECTS	EXPOSURE/ OUTCOME	RESULTS
Shankardass K et al., PNAS 2009	Children's Health Study Prospective school-aged cohort N=2,497	Child (5-9 yrs followed for 3 years)	Prenatal maternal NLEs Dust mite mother's bedroom Maternal Atopy Cord Blood Total IgE	See figure

Effect of TRAP on incident asthma across parental stress quartiles



Adjusted for child age, gender, race/ethnicity and community random effects