

# **Preconception Health & Health Care: A Life-Course Perspective**

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**Secretary's Advisory Committee on Infant Mortality  
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# What is Preconception Care?

- A set of interventions that aim to identify and modify biomedical, behavioral, and social risks to a woman's health or pregnancy outcome through prevention and management.

# What Is Preconception Care?

- **Risk Assessment**
  - Reproductive life plan
  - Past pregnancy history
  - Past medical & surgical history
  - Medications & allergies
  - Family & genetic history
  - Social history
  - Behavioral & nutritional assessment
  - Mental health
  - Laboratory testing
  
- **Health Promotion**
  - Family planning
  - Stress resilience
  - Nutritional preparedness
  - Immune allostasis
  - Healthy environment
  
- **Medical & Psychosocial Interventions**
  - Individualized for identified risks
  - Preventive services and primary care

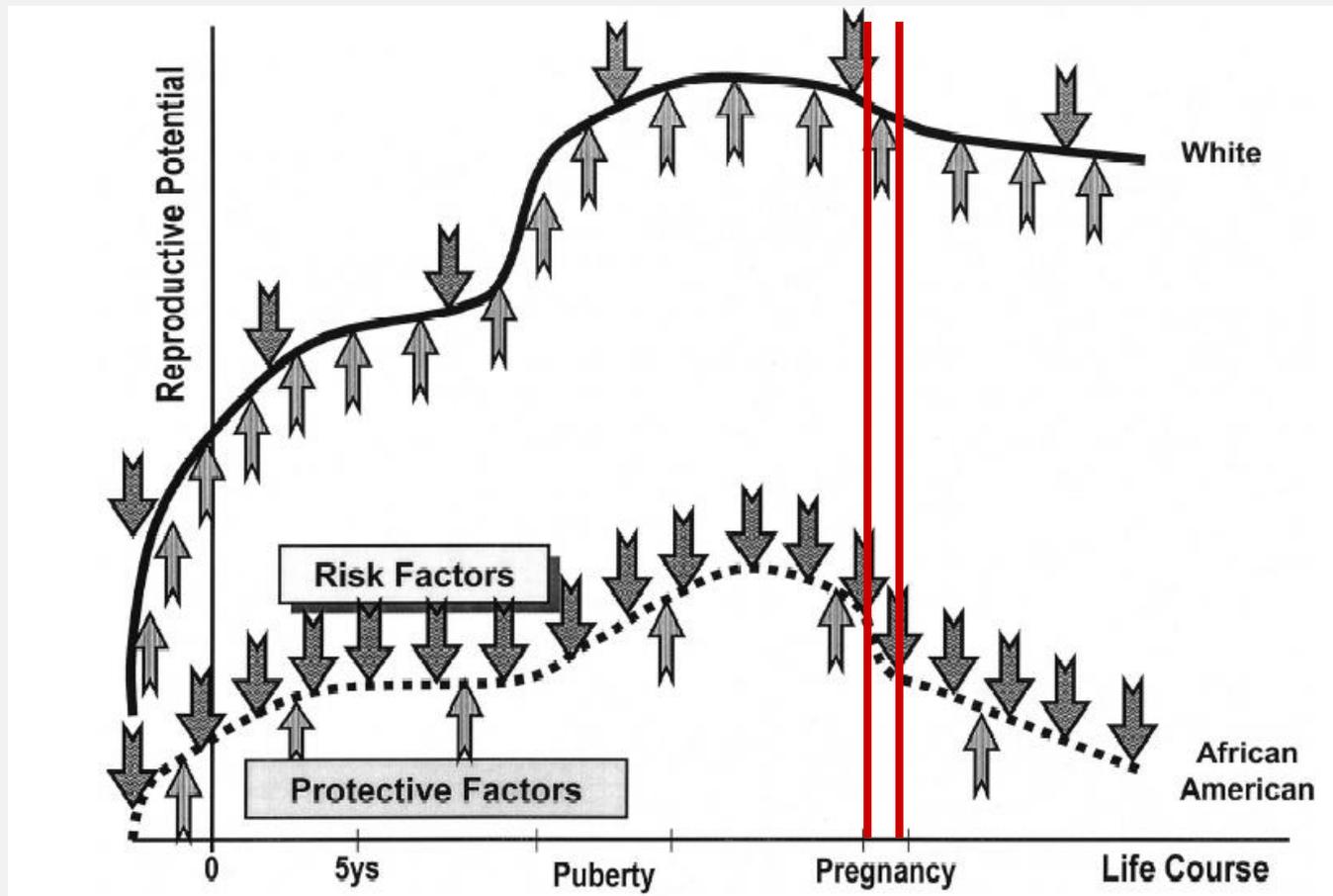
## Summary of the CDC/ATSDR Select Panel's Recommendations to Improve Preconception Health and Health Care in the United States

- ❑ **Recommendation 1. Individual responsibility across the life span.** Each woman, man and couple should be encouraged to have a reproductive life plan.
- ❑ **Recommendation 2. Consumer awareness.** Increase public awareness of the importance of preconception health behaviors and preconception care services by using information and tools appropriate across various ages; literacy, including health literacy; and cultural/linguistic contexts.
- ❑ **Recommendation 3. Preventive visits.** As a part of primary care visits, provide risk assessment and educational and health promotion counseling to all women of childbearing age to reduce reproductive risks and improve pregnancy outcomes.
- ❑ **Recommendation 4. Interventions for identified risks.** Increase the proportion of women who receive interventions as follow-up to preconception risk screening, focusing on high priority interventions (i.e. those with evidence of effectiveness and greatest potential impact).
- ❑ **Recommendation 5. Interconception care.** Use the interconception period to provide additional intensive interventions to women who have had a previous pregnancy that ended in an adverse outcome (i.e., infant death, fetal loss, birth defects, low birthweight, or preterm birth).
- ❑ **Recommendation 6. Prepregnancy checkup.** Offer, as a component of maternity care, one prepregnancy visit for couples and persons planning pregnancy.
- ❑ **Recommendation 7. Health insurance coverage for women with low incomes.** Increase public and private health insurance coverage for women with low incomes to improve access to preventive women's health and preconception and interconception care.
- ❑ **Recommendation 8. Public health programs and strategies.** Integrate components of preconception health into existing local public health and related programs, including emphasis on interconception interventions for women with previous adverse outcomes.
- ❑ **Recommendation 9. Research.** Increase the evidence base and promote the use of the evidence to improve preconception health.
- ❑ **Recommendation 10. Monitoring improvements.** Maximize public health surveillance and related research mechanisms to monitor preconception health.

# Life-Course Perspective

- A way of looking at life not as disconnected stages, but as an integrated continuum

# Life Course Perspective



Lu MC, Halfon N. Racial and ethnic disparities in birth outcomes: a life-course perspective. *Matern Child Health J.* 2003;7:13-30.

# Life Course Perspective

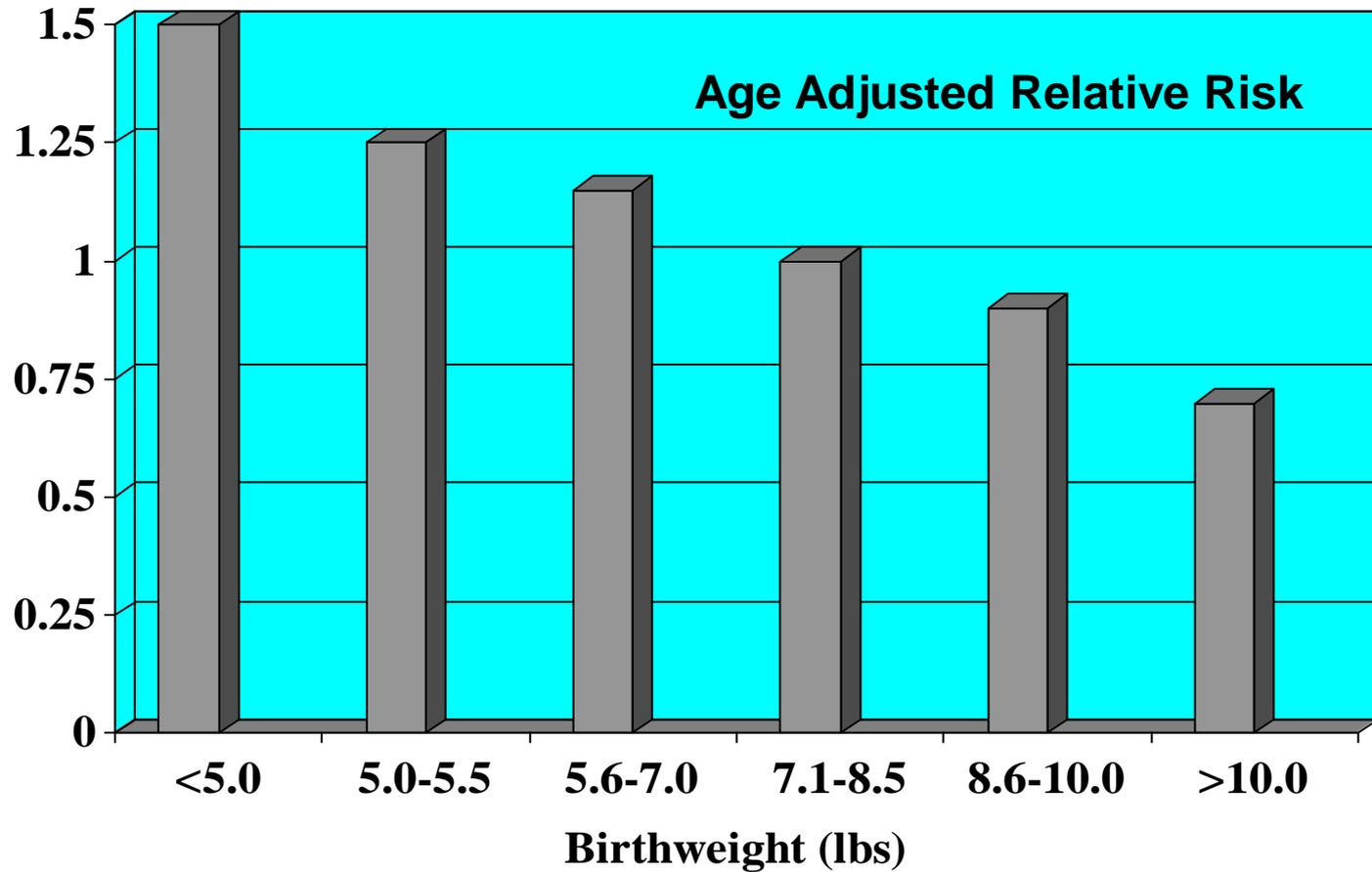
- Early programming
- Cumulative pathways
- Preconception health & healthcare

# Early Programming



# Barker Hypothesis

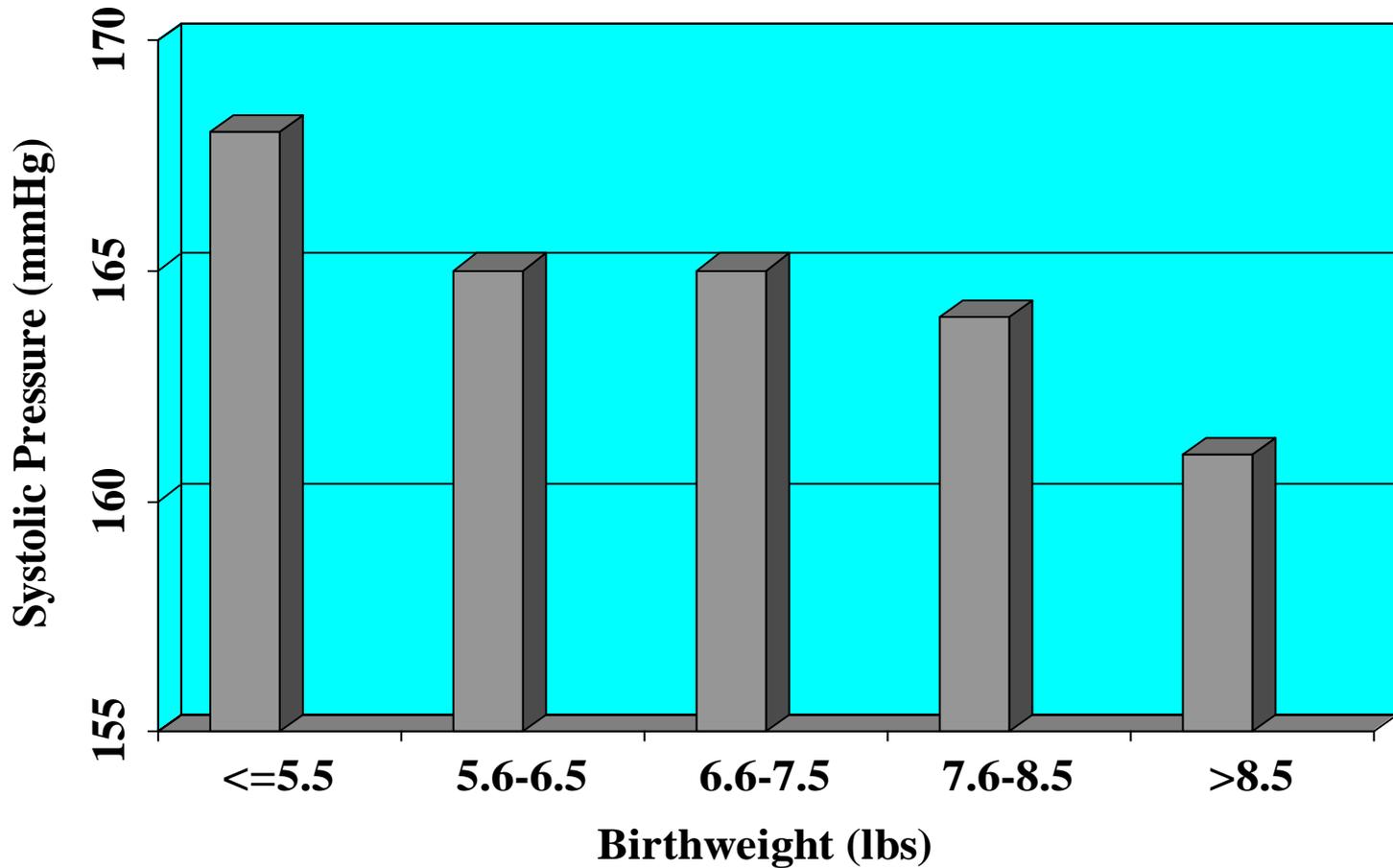
## Birth Weight and Coronary Heart Disease



Rich-Edwards JW, Stampfer MJ, Manson JE, Rosner B, Hankinson SE, Colditz GA et al. Birth weight and risk of cardiovascular disease in a cohort of women followed up since 1976. *Br Med J* 1997;315:396-400.

# Barker Hypothesis

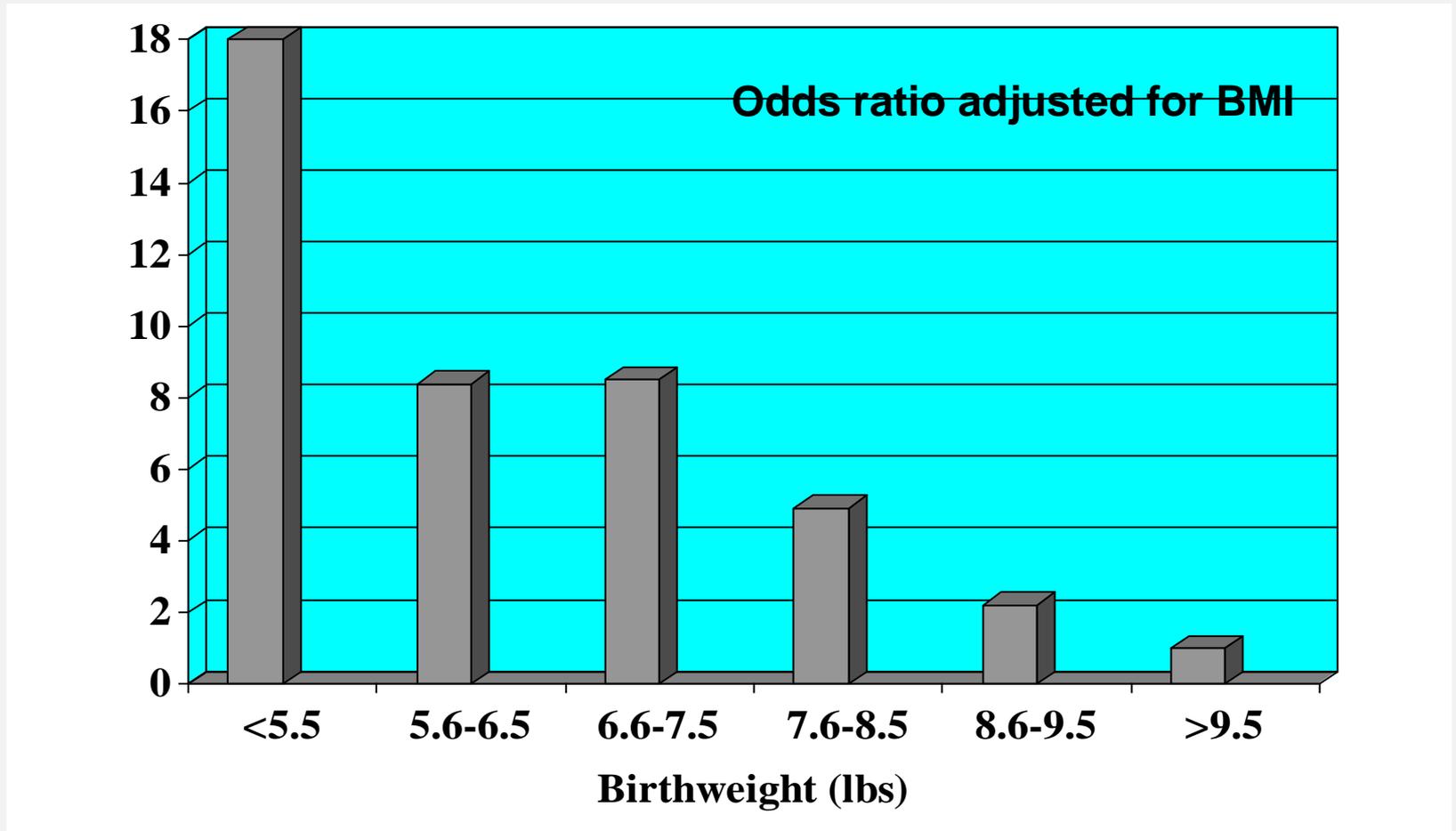
## Birth Weight and Hypertension



Law CM, de Swiet M, Osmond C, Fayers PM, Barker DJP, Cruddas AM, et al. Initiation of hypertension in utero and its amplification throughout life. Br Med J 1993;306:24-27.

# Barker Hypothesis

## Birth Weight and Insulin Resistance Syndrome



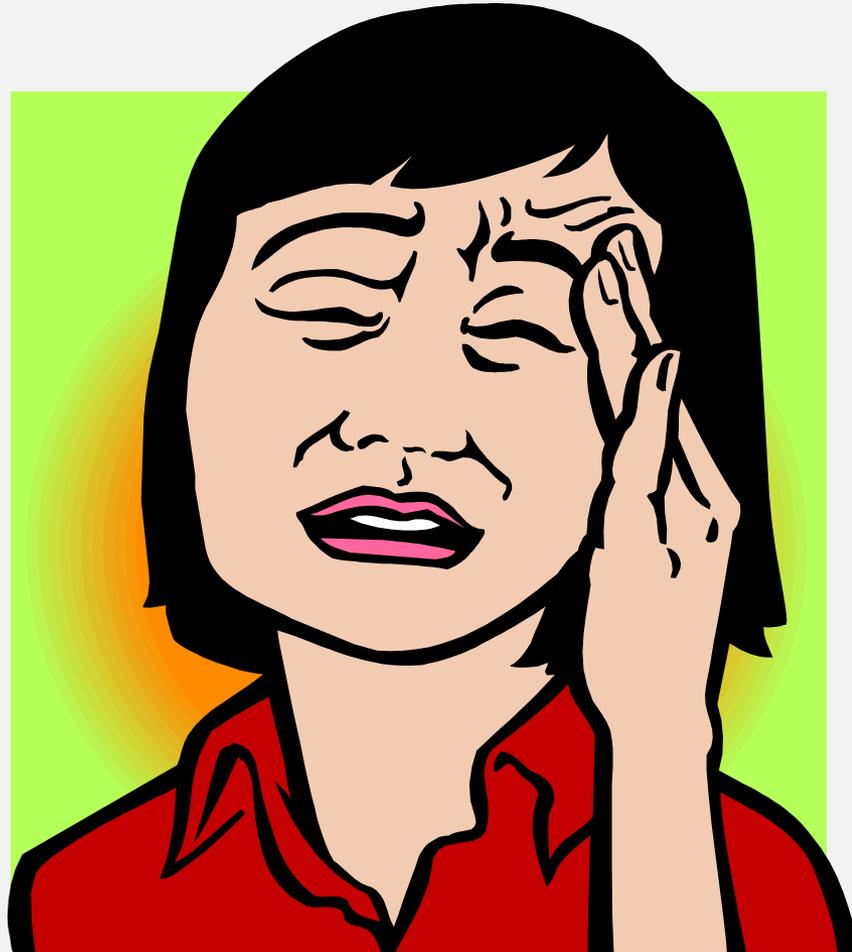
Barker DJP, Hales CN, Fall CHD, Osmond C, Phipps K, Clark PMS. Type 2 (non-insulin-dependent) diabetes mellitus, hypertension and hyperlipidaemia (Syndrome X): Relation to reduced fetal growth. *Diabetologia* 1993;36:62-67.

# Barker Hypothesis

## Birth Weight and Insulin Resistance Syndrome

Birth weight	<5.5	5.6-6.5	6.6-7.5	7.6-8.5	8.6-9.5	>9.5
Odds Ratio	18	8.4	8.5	4.9	2.2	1

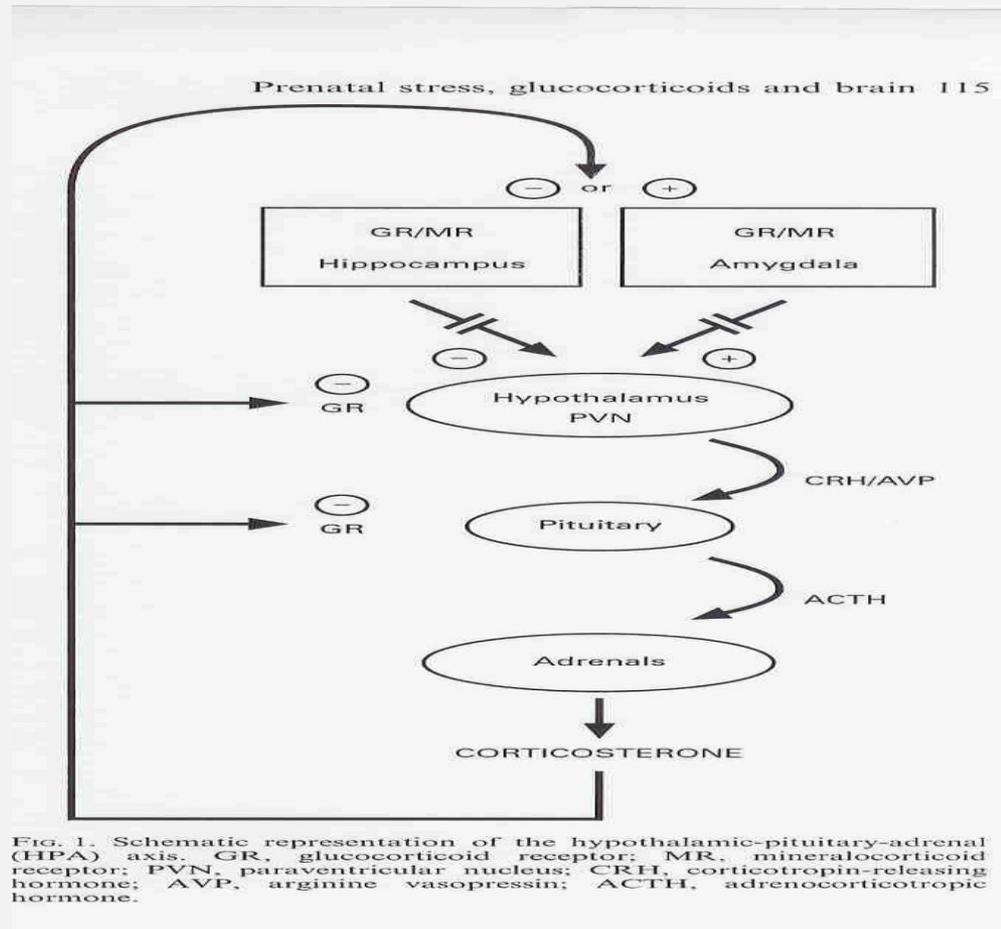
# Maternal Stress & Fetal Programming



# Prenatal Stress & Programming of the Brain

- **Prenatal stress (animal model)**
  - **Hippocampus**
    - Site of learning & memory formation
    - Stress down-regulates glucocorticoid receptors
    - Loss of negative feedback; overactive HPA axis
  
  - **Amygdala**
    - Site of anxiety and fear
    - Stress up-regulates glucocorticoid receptors
    - Accentuated positive feedback; overactive HPA axis

# Prenatal Programming of the Hypothalamic-Pituitary-Adrenal Axis



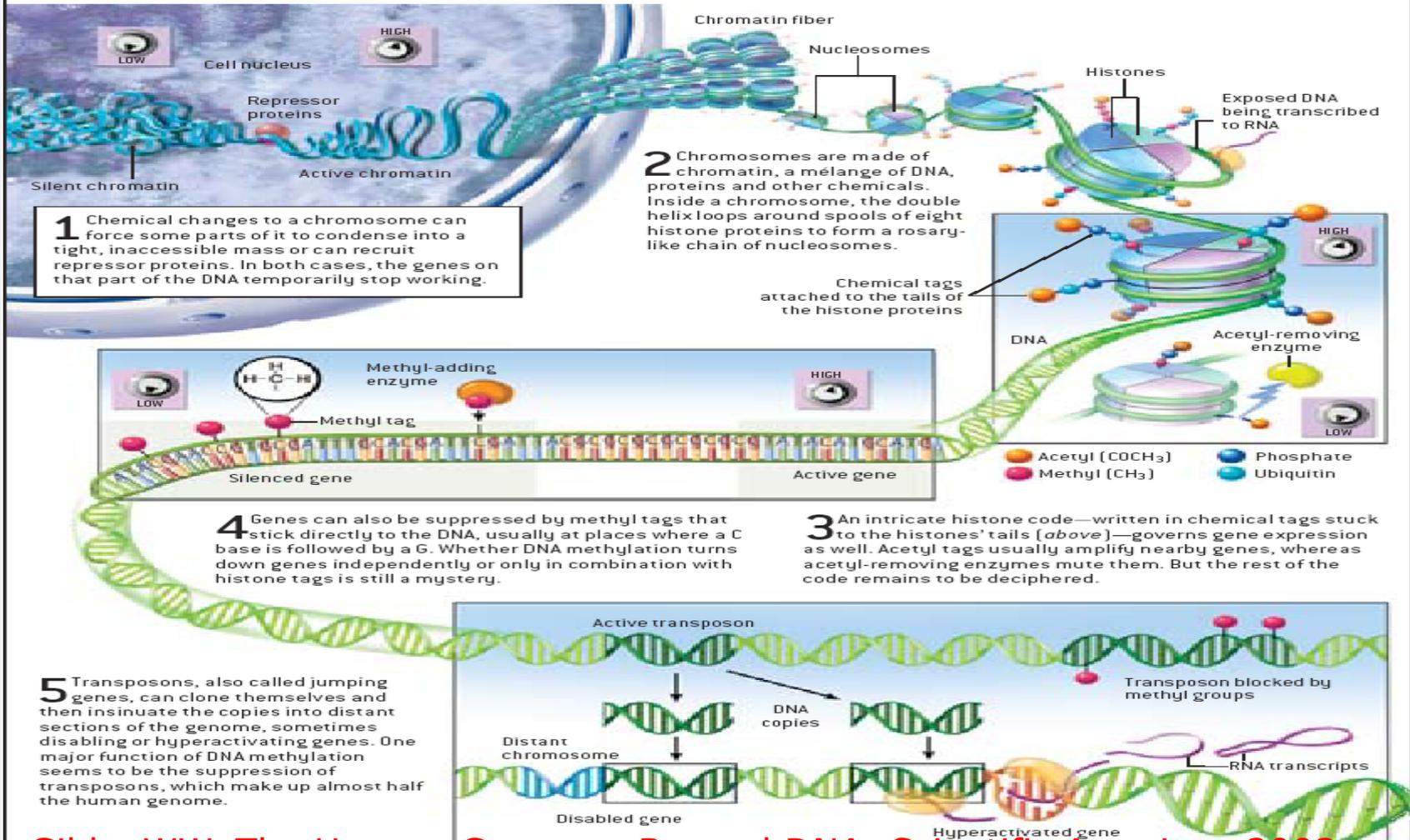
Welberg LAM, Seckl JR. Prenatal stress, glucocorticoids and the programming of the brain. J Neuroendocrinol 2001;13:113-28.

# Epigenetics

## VOLUME CONTROLS FOR GENES

THE DNA SEQUENCE is not the only code stored in the chromosomes. So-called epigenetic phenomena of several kinds can act like volume knobs to amplify or mute the effect of genes. Epigenetic information is encoded as chemical attachments to

the DNA or to the histone proteins that control its shape within the chromosomes. Among their many functions, the epigenetic volume controls muffle parasitic genetic elements, called transposons, that riddle the genome.



# Epigenetics

*Same Genome, Different Epigenome*



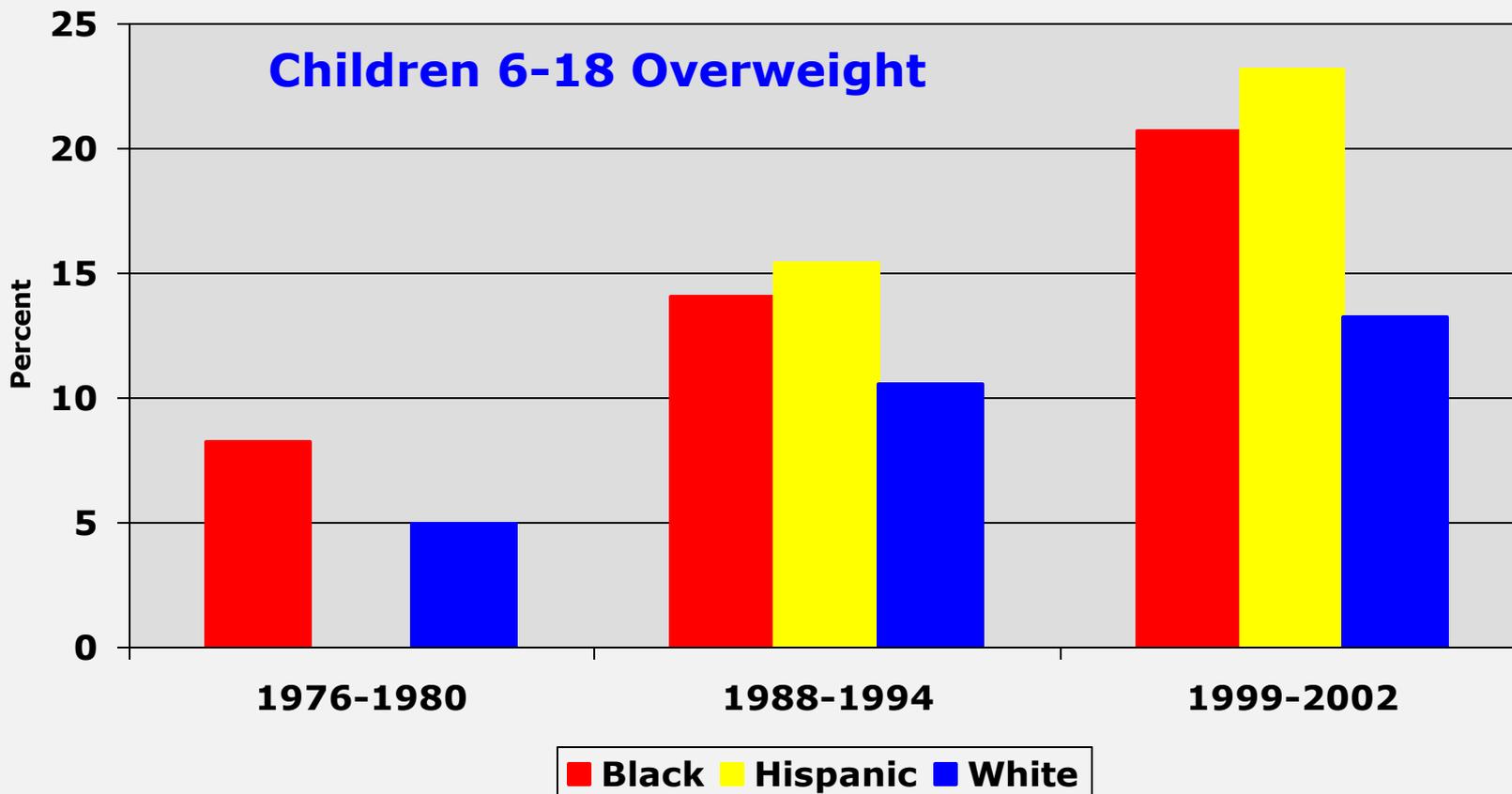
R.A. Waterland, R.A. Jirtle, "Transposable elements: targets for early nutritional effects on epigenetic gene regulation," *Mol Cell Biol*, 23:5293-300, 2003. Reprinted in [the New Scientist 2004](#)

# Prenatal Programming of Childhood Obesity

**OBESITY:** A Weighty Issue  
for Children



# Epidemic of Childhood Overweight & Obesity



Source: National Center for Health Statistics, National Health and Nutrition Examination Survey

Note: Estimate not available for 1976-1980 for Hispanic; overweight defined as BMI at or above the 95<sup>th</sup> percentile of the CDC BMI-for-age growth charts

# Prenatal Programming of Childhood Overweight & Obesity

Matern Child Health J  
DOI 10.1007/s10995-006-0141-8

ORIGINAL PAPER

## Prenatal Programming of Childhood Overweight and Obesity

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**Abstract** *Objective:* To review the scientific evidence for prenatal programming of childhood overweight and obesity, and discuss its implications for MCH research, practice, and policy.

*Methods:* A systematic review of observational studies examining the relationship between prenatal exposures and childhood overweight and obesity was conducted using MOOSE guidelines. The review included literature posted on PubMed and MDCConsult and published between January 1975 and December 2005. Prenatal exposures to maternal diabetes, malnutrition, and cigarette smoking were examined, and primary study outcome was childhood overweight or obesity as measured by body mass index (BMI) for children ages 5 to 21.

*Results:* Four of six included studies of prenatal exposure to maternal diabetes found higher prevalence of childhood overweight or obesity among offspring of diabetic mothers, with the highest quality study reporting an odds ratio of adolescent overweight of 1.4 (95% CI 1.0–1.9). The Dutch famine study found that exposure to maternal malnutrition in early, but not late, gestation was associated with increased

odds of childhood obesity (OR 1.9, 95% CI 1.5–2.4). All eight included studies of prenatal exposure to maternal smoking showed significantly increased odds of childhood overweight and obesity, with most odds ratios clustering around 1.5 to 2.0. The biological mechanisms mediating these relationships are unknown but may be partially related to programming of insulin, leptin, and glucocorticoid resistance *in utero*.

*Conclusion:* Our review supports prenatal programming of childhood overweight and obesity. MCH research, practice, and policy need to consider the prenatal period a window of opportunity for obesity prevention.

**Keywords** Prenatal programming · Childhood obesity · Overweight · Developmental programming · Fetal programming · Gestational diabetes · Maternal malnutrition · Cigarette smoking

Childhood overweight and obesity is a growing problem in the United States and worldwide. The prevalence of childhood overweight in the U.S. tripled between 1980 and 2000 [1]. Today approximately 1 in 6 (16%) U.S. children are overweight with significant racial-ethnic disparities. For example, nearly 1 in 4 (23%) non-Hispanic black girls ages 6 to 19 are overweight, a prevalence almost twice that of non-Hispanic white girls [1].

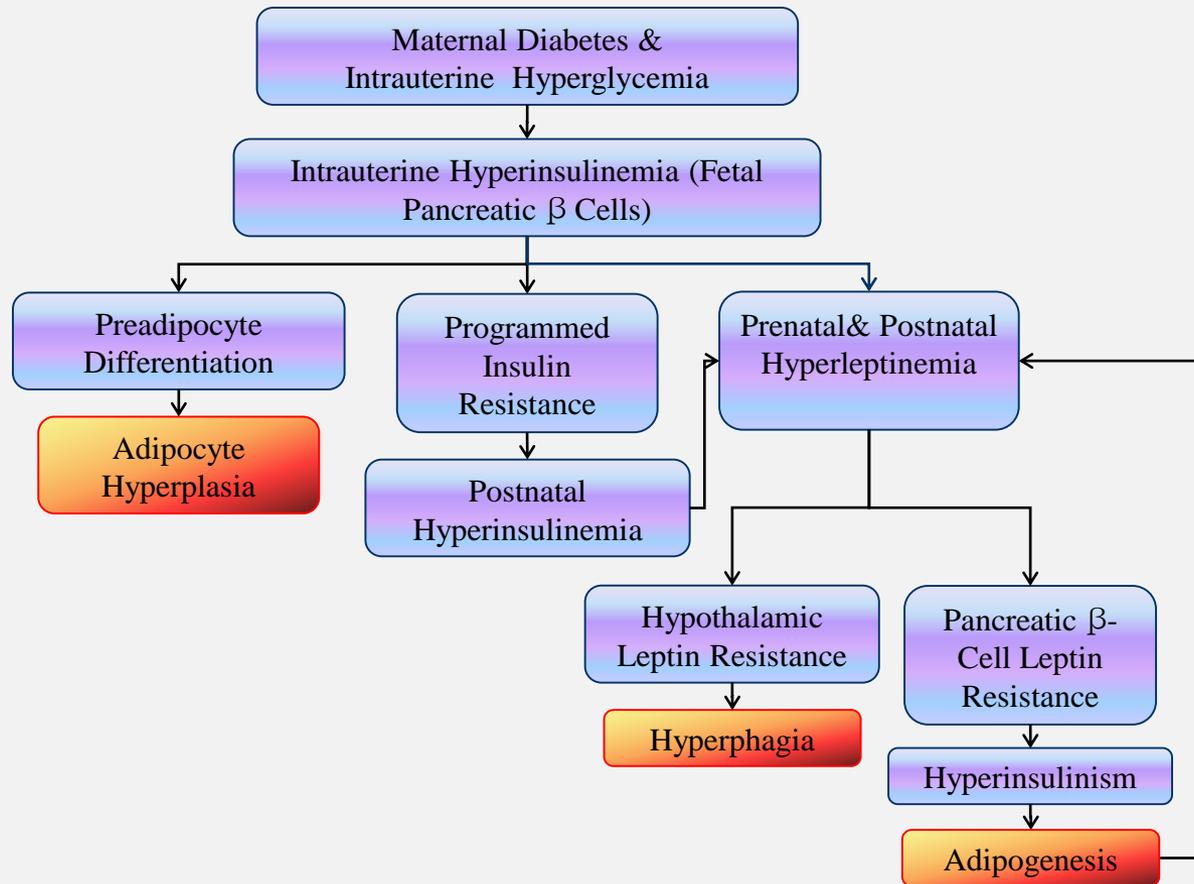
Overweight and obesity has significant lifelong consequences on the health and well-being of children [2, 3]. Childhood obesity is associated with early-onset Type II diabetes mellitus, hypertension, metabolic syndrome, and sleep apnea. It is also associated with cognitive or intellectual impairment and social exclusion and stigmatization as parts of a vicious cycle including school avoidance [3]. Childhood obesity tracks strongly into adulthood [4, 5]; obesity beyond

**Disclaimer:** The opinions expressed in this paper are the authors' and do not necessarily reflect the views or policies of the institutions with which the authors are affiliated.

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# Prenatal Programming of Childhood Obesity

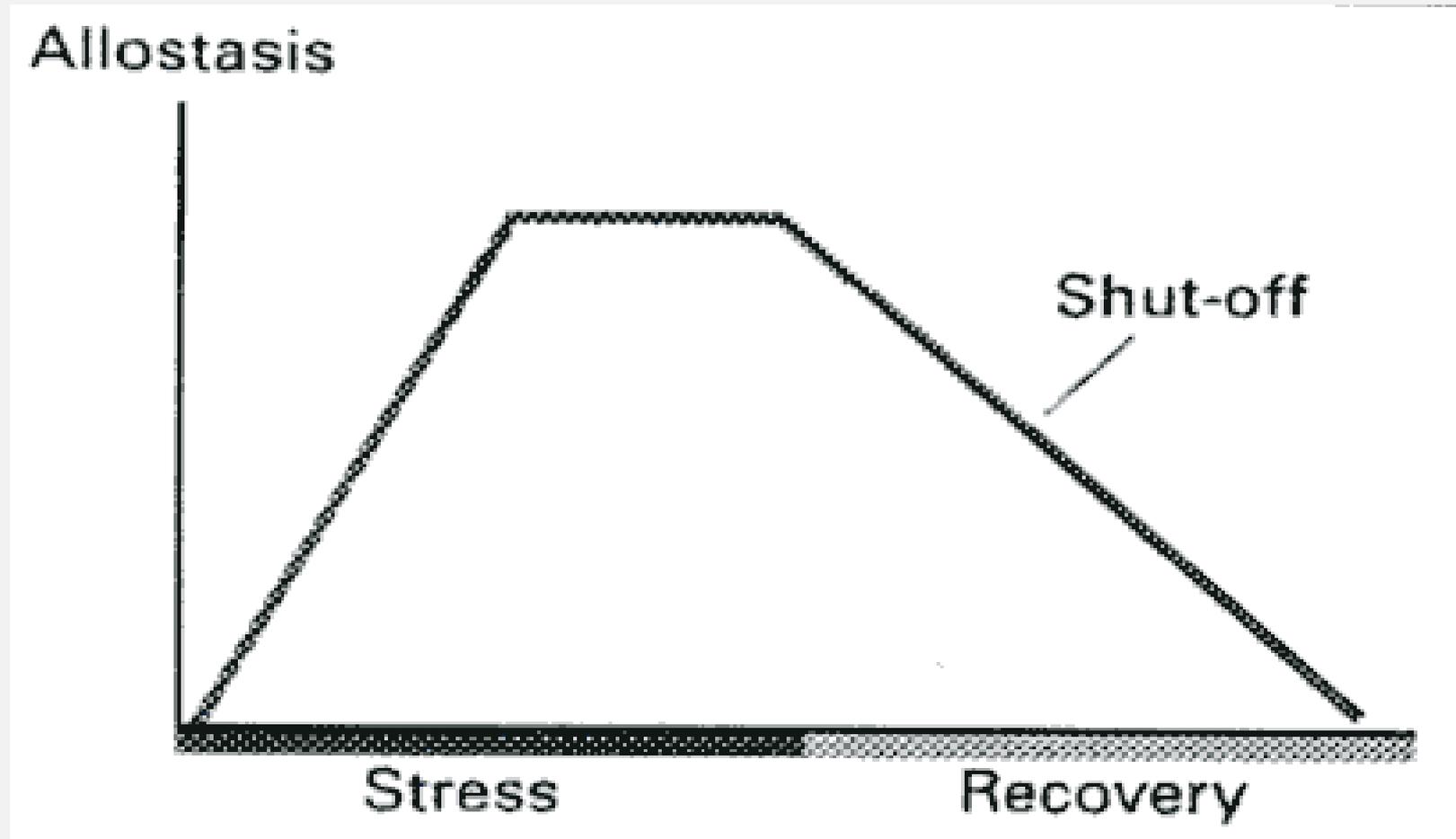


# Cumulative Pathways

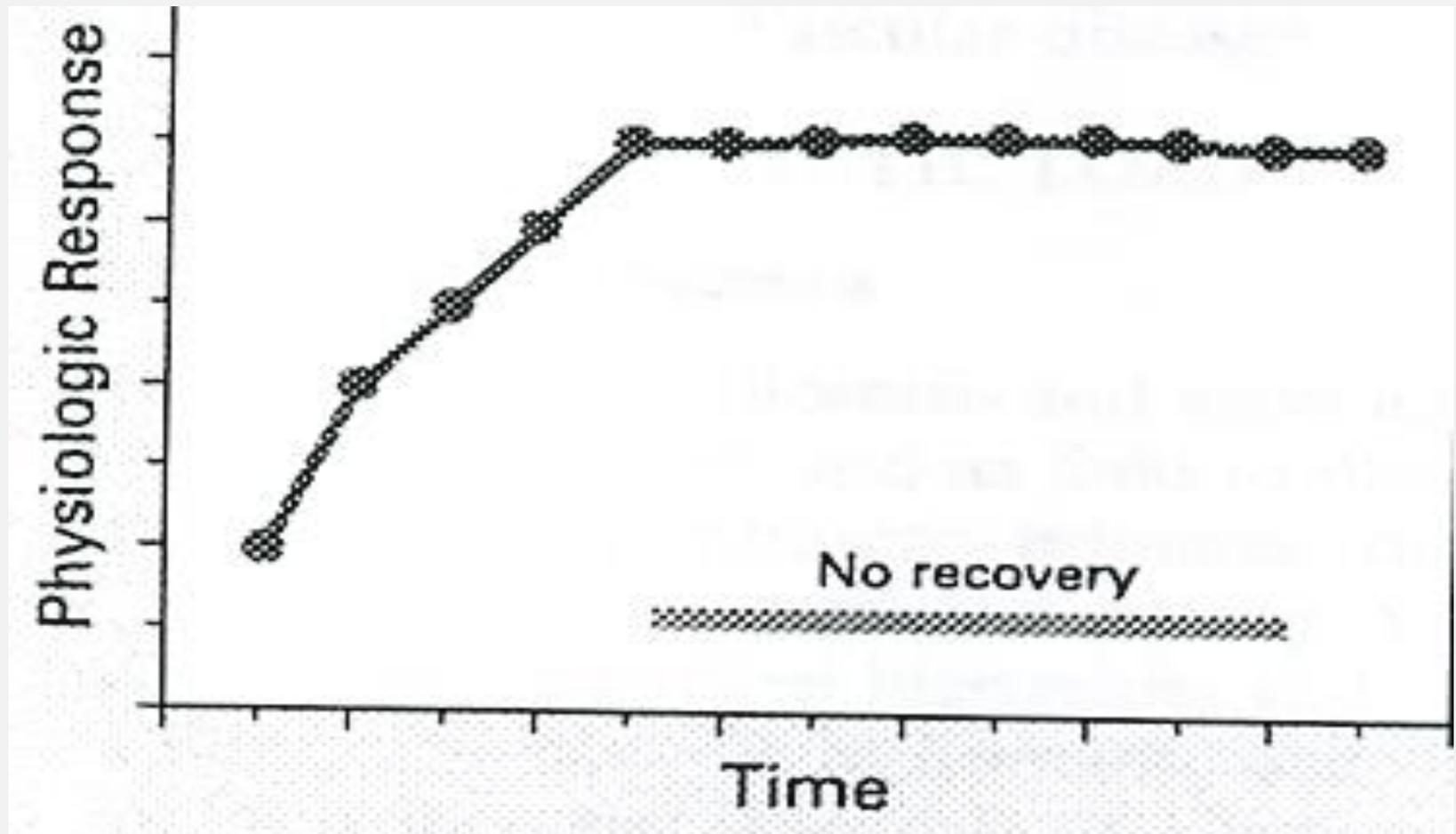


# Allostasis:

## Maintain Stability through Change

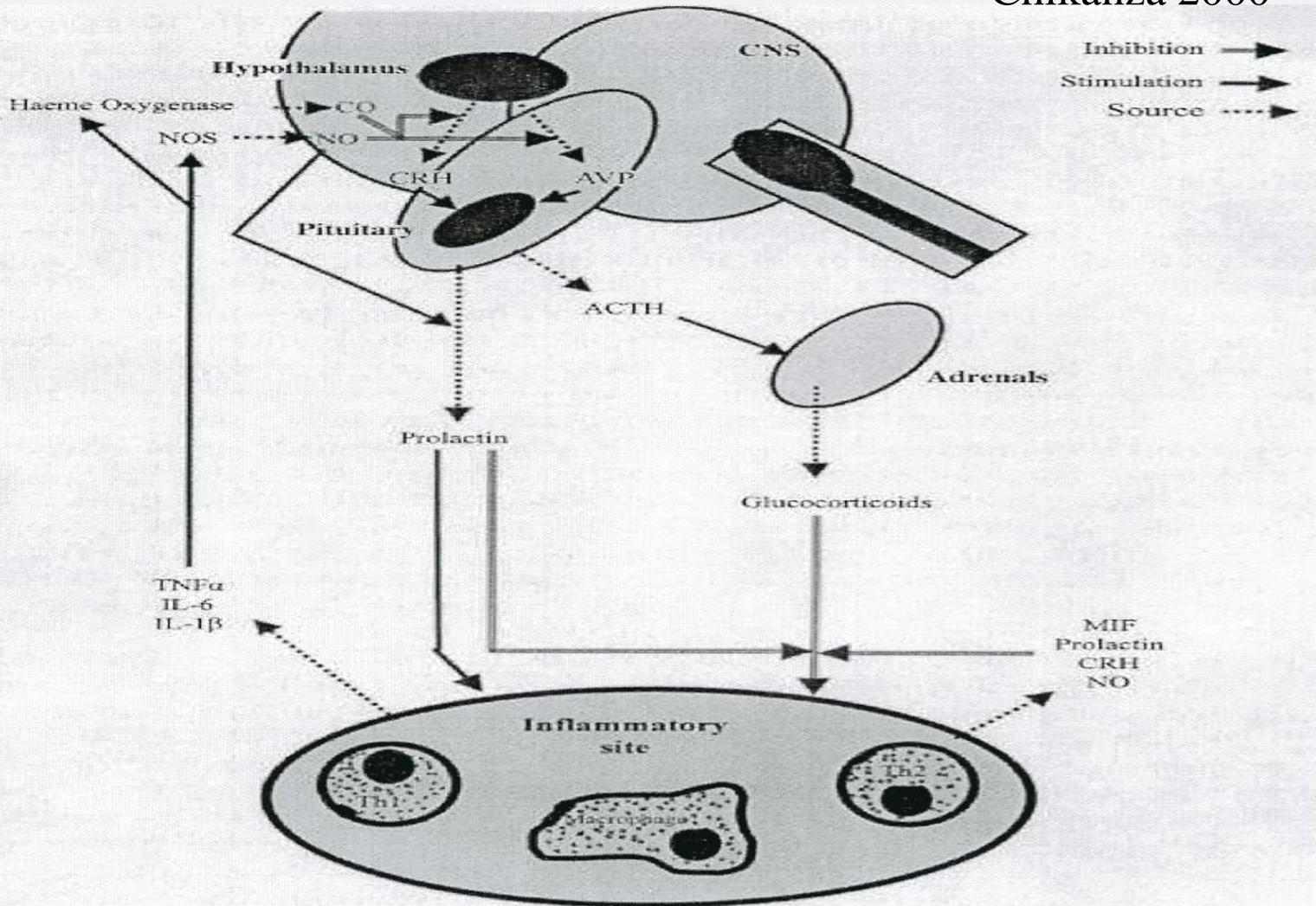


# Allostatic Load: Wear and Tear from Chronic Stress



# HPA Axis & Immune System

Chikanza 2000



# Stressed vs. Stressed Out

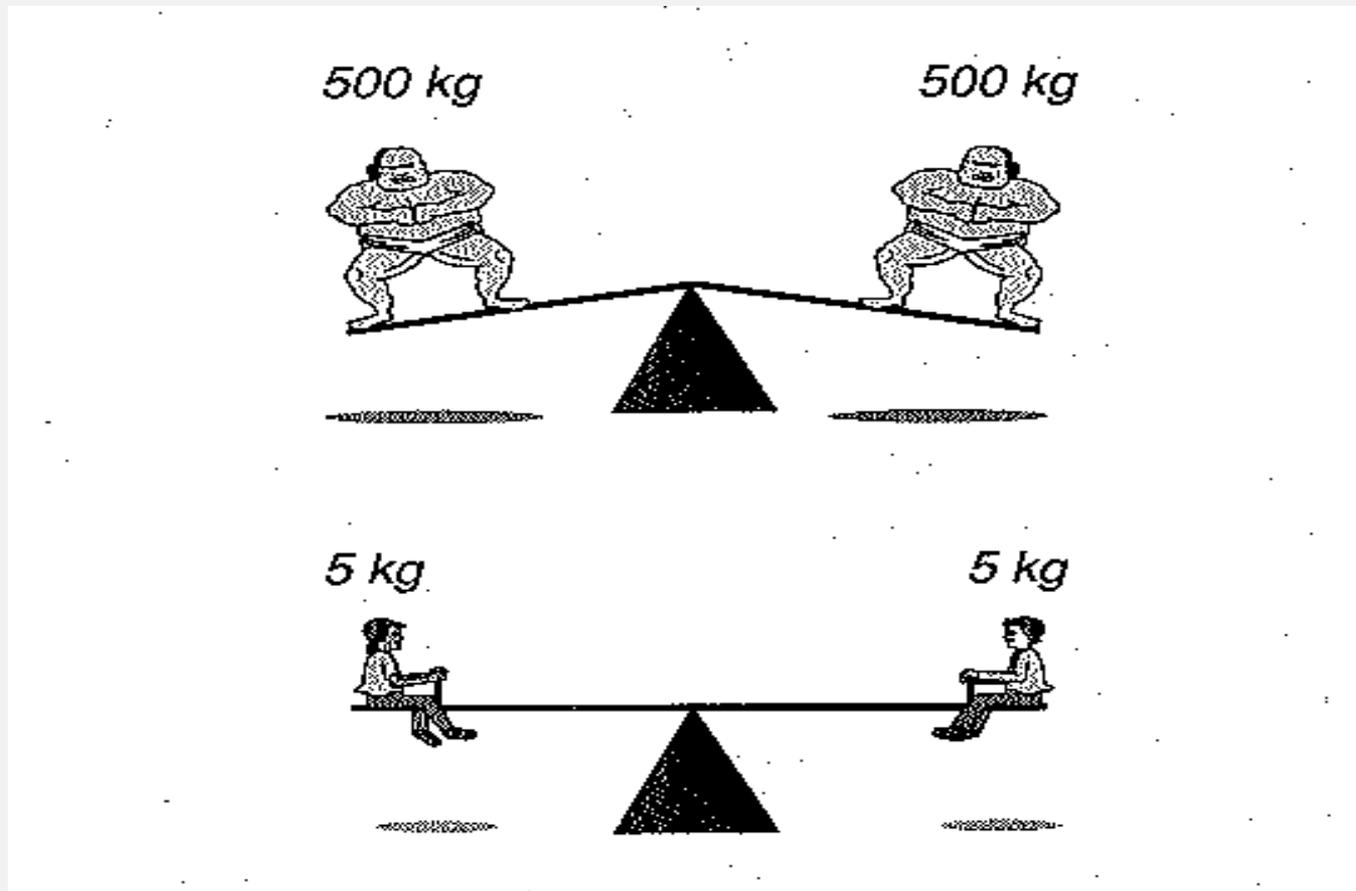
## □ Stressed

- Increased cardiac output
- Increased available glucose
- Enhanced immune functions
- Growth of neurons in hippocampus & prefrontal cortex

## □ Stressed Out

- Hypertension & cardiovascular diseases
- Glucose intolerance & insulin resistance
- Infection & inflammation
- Atrophy & death of neurons in hippocampus & prefrontal cortex

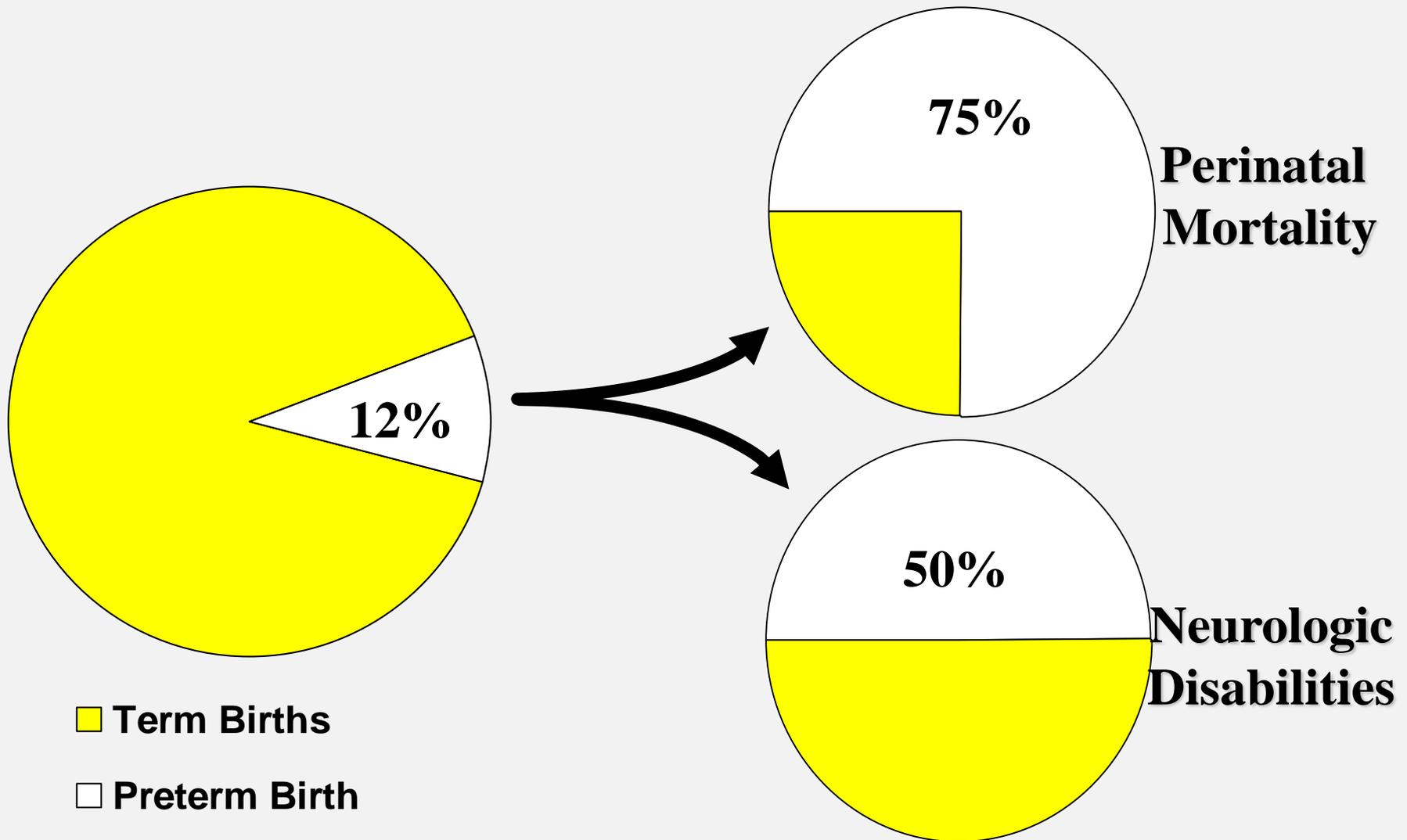
# Allostasis & Allostatic Load



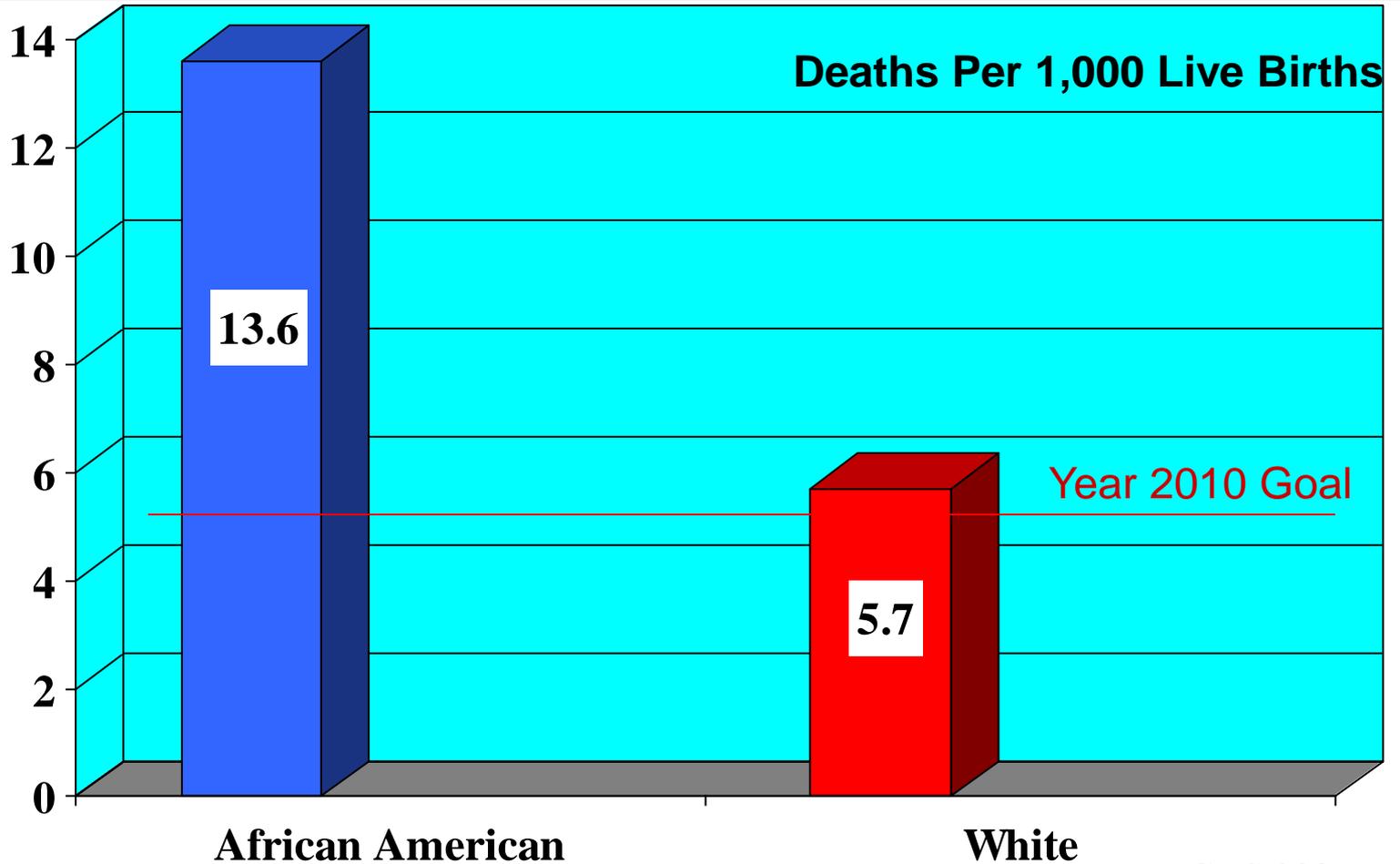
# Rethinking Preterm Birth



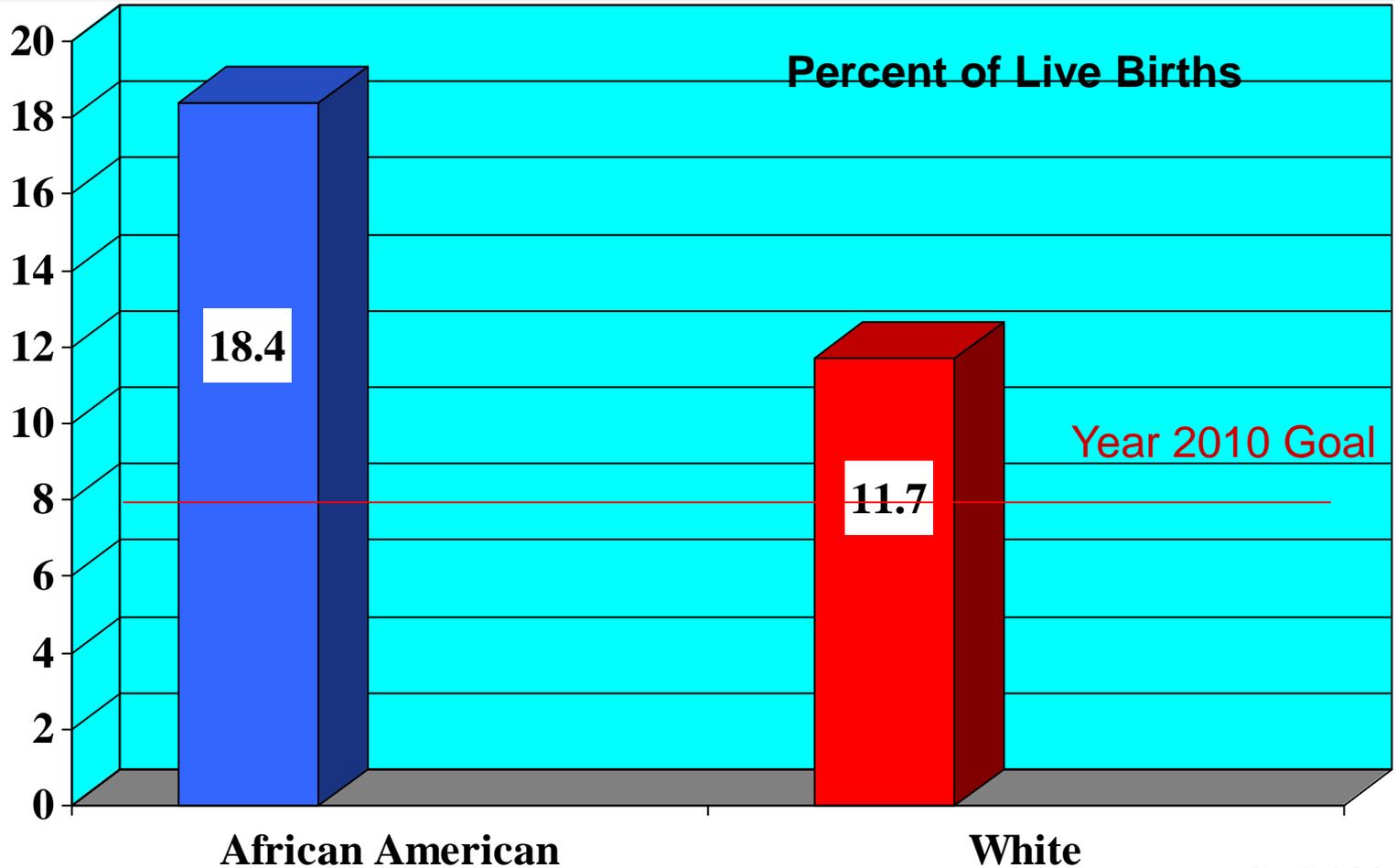
# Sequelae of Preterm Birth



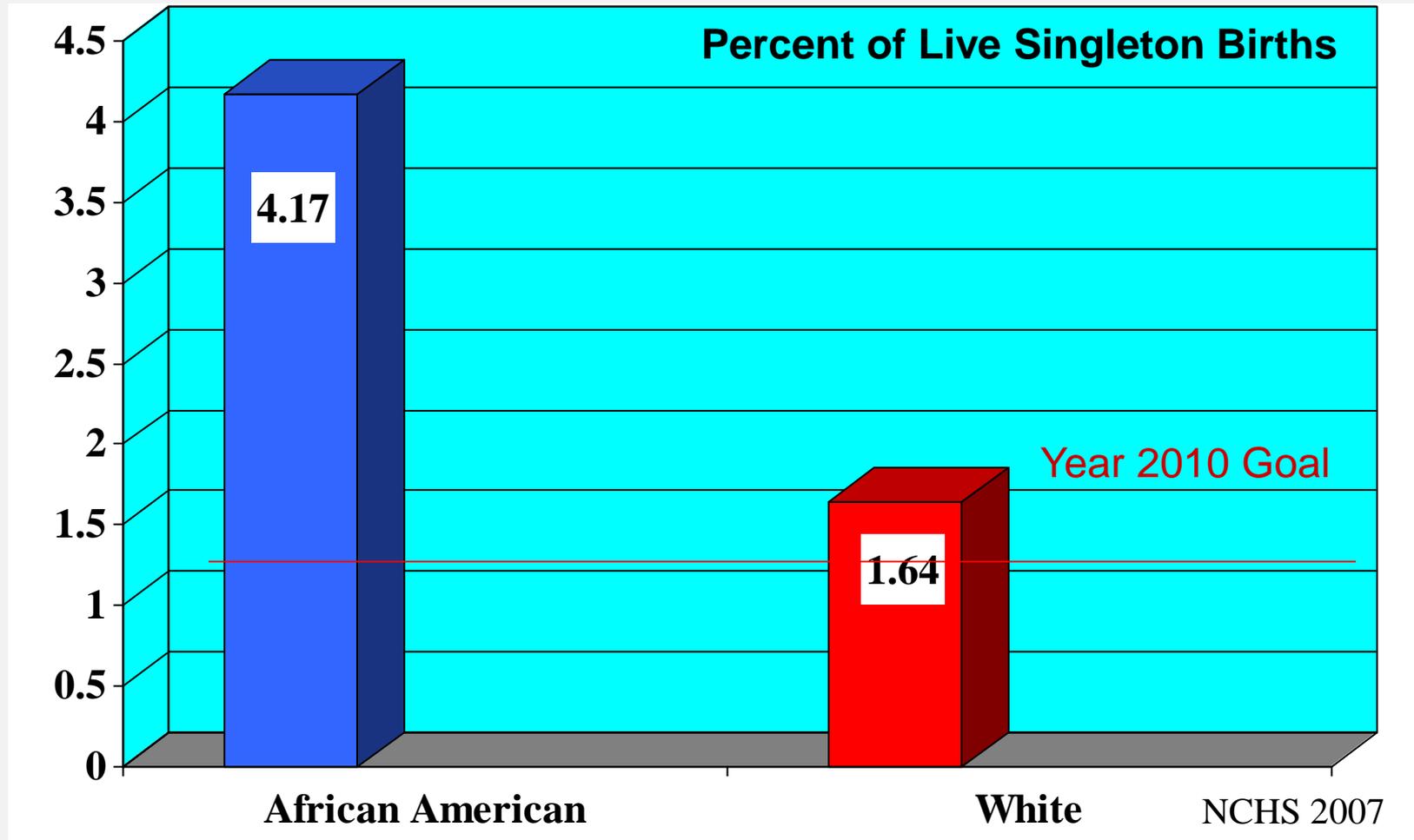
# Racial & Ethnic Disparities Infant Mortality



# Racial & Ethnic Disparities Preterm Births < 37 Weeks



# Racial & Ethnic Disparities Very Preterm Births < 32 Weeks

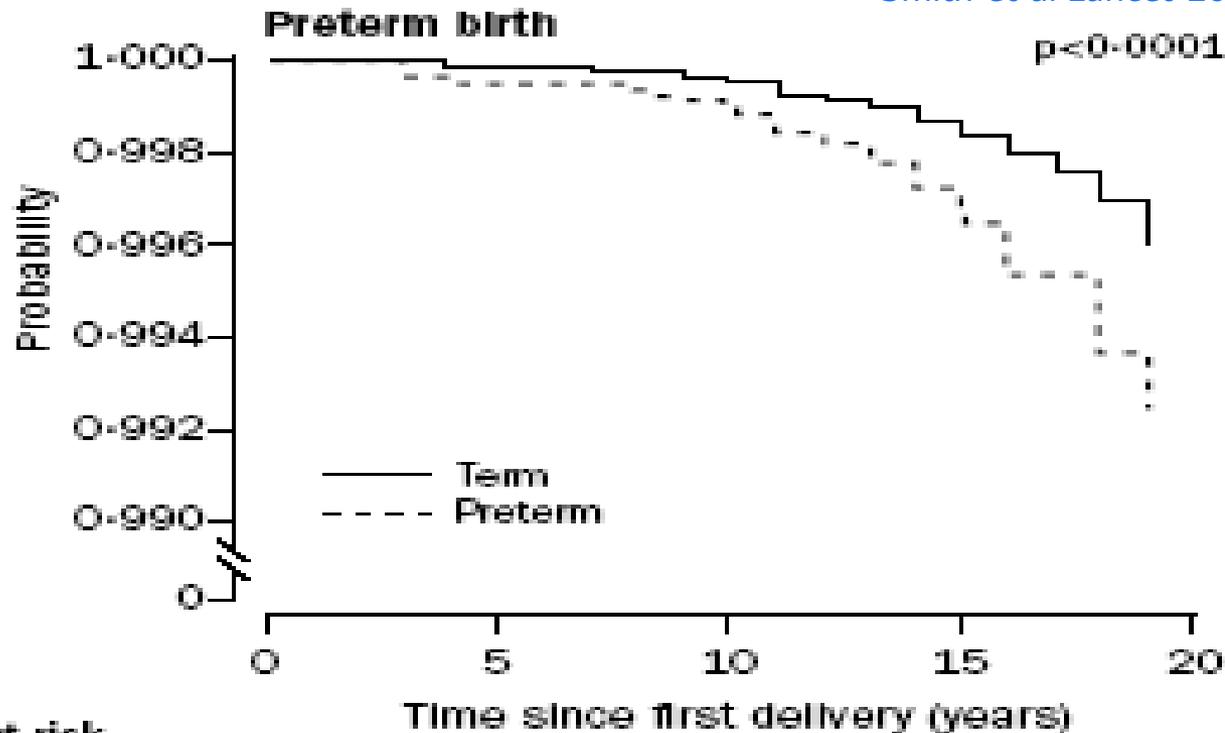


# Rethinking Preterm Birth

**Vulnerability to preterm delivery may be traced to not only exposure to stress & infection during pregnancy, but host response to stress & infection (e.g. stress reactivity & inflammatory dysregulation) patterned over the life course (early programming & cumulative allostatic load)**

# Preterm Birth & Maternal Ischemic Heart Disease

Smith et al *Lancet* 2001;357:2002-06



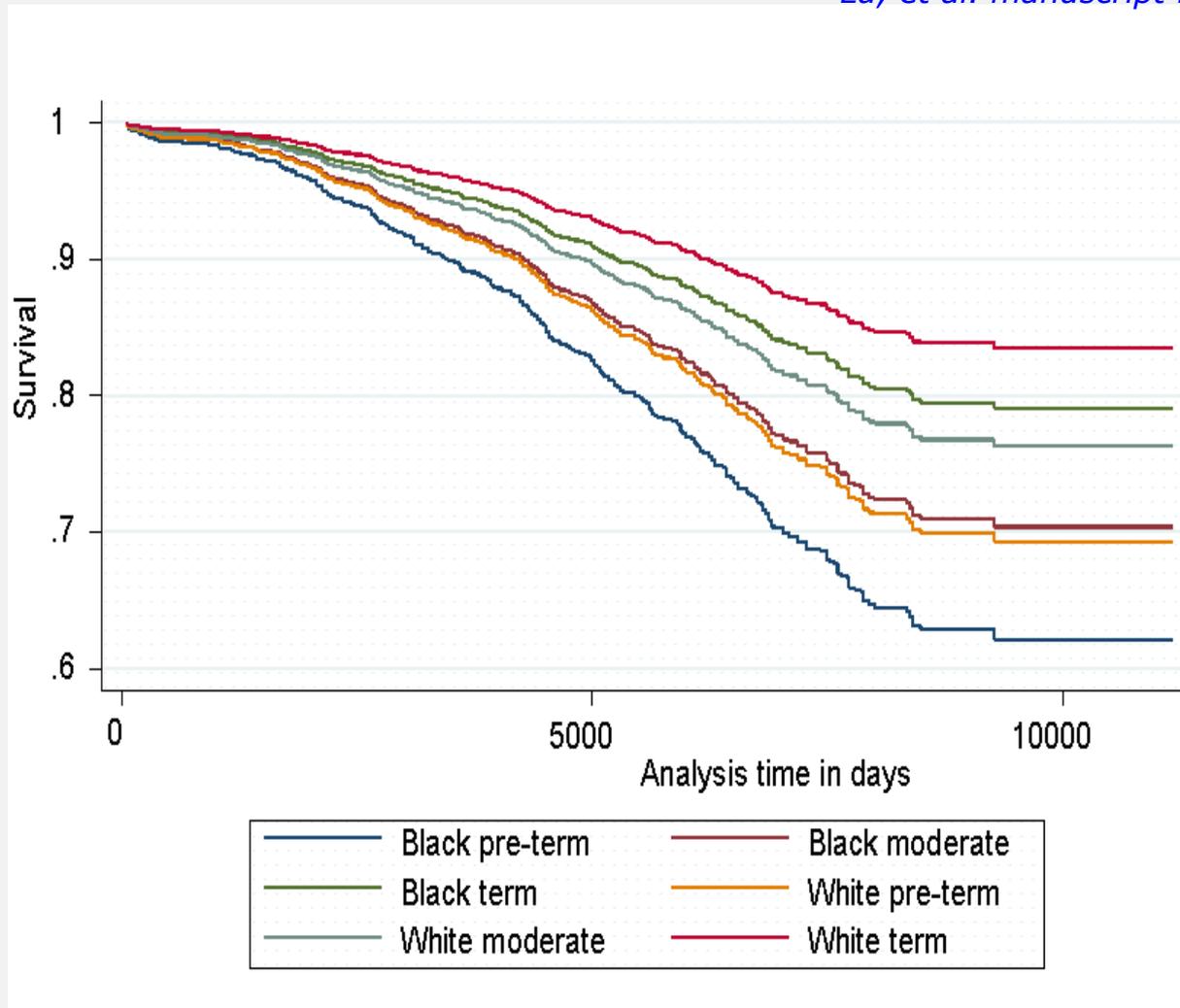
Number at risk

Term	121975	121813	121518	97169
Preterm	7315	7295	7262	5727

Kaplan-Meier plots of cumulative probability of survival **without** admission or death from ischemic heart disease after first pregnancy in relation to preterm birth

# Preterm Birth & Maternal Hypertension

*Lu, et al. manuscript in preparation*



# **Preconception Health and Health Care: A Life-Course Perspective**

**Preconception is a critical period for children's health.**

# Early Prenatal Care Is Too Late

- ❑ **To prevent some birth defects**
- ❑ **To prevent implantation errors**
- ❑ **To restore allostasis**

# Preconception is a critical period for children's health

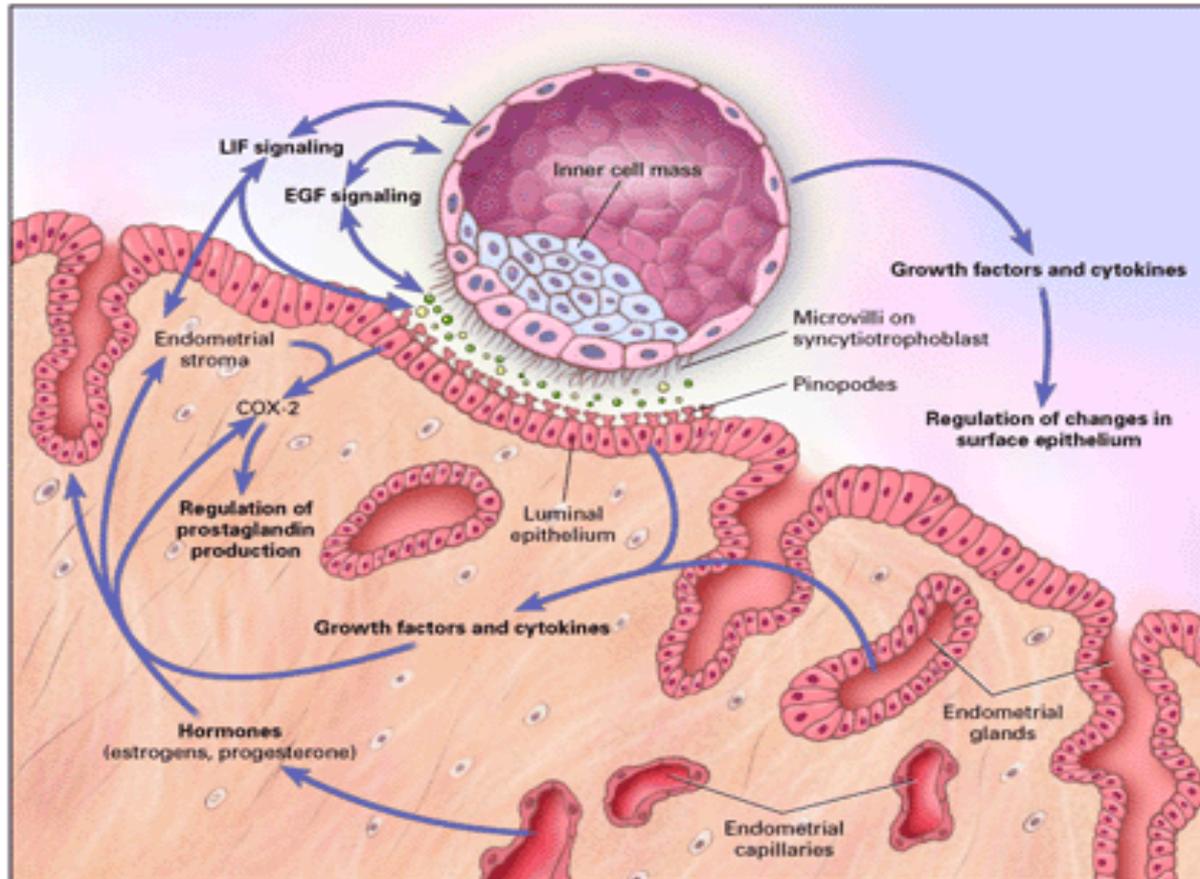
- Folic acid
- Rubella seronegativity
- Diabetes (preconception)
- Hypothyroidism
- HIV/AIDS
- Maternal phenylketonurea (PKU)
- Oral anticoagulant
- Antiepileptic drugs
- Isotretinoins (Accutane)
- Smoking
- Alcohol misuse
- Obesity
- STD
- Hepatitis B

# Preconception Care for Men

- tobacco
- alcohol
- drugs (e.g. anabolic steroids)
- caffeine
- poor diet
- radiation and chemotherapy
- testicular hyperthermia
- diabetes mellitus
- varicoceles
- epididymitis
- 1,2-dibromo-3-chloropropane
- nonylphenol
- polycyclic aromatic hydrocarbons (PAHs)
- polychlorinated biphenyls (PCBs)
- dioxins
- phthalates

# Early Prenatal Care Is Too Late

## Implantation Errors



Norwitz ER, Schust DJ, Fisher SJ. Implantation and the survival of early pregnancy. N Engl J Med. 2001 Nov 8;345(19):1400-8.

# The Role of the Placenta in Fetal Programming

**Table 1.** Associations between placental weight and the placental weight/birthweight ratio (placental ratio) and long term cardiovascular and metabolic outcomes

	Association with later outcome	Reference
<i>Blood pressure</i>		
Small placental weight	↑ adult blood pressure	Campbell et al., 1996
Small placental weight	↑ adult hypertension with diabetes	Eriksson et al., 2000
Small placental volume*	↑ childhood blood pressure	Thame et al., 2000
Large placental weight	↑ adult blood pressure	Barker et al., 1990
Large placental weight	↑ childhood blood pressure	Law et al., 1991
Large placental weight	↑ childhood blood pressure	Moore et al., 1996
Large placental weight	↑ childhood blood pressure (boys only)	Taylor et al., 1997
High placental ratio	↑ adult blood pressure	Barker et al., 1992
High placental ratio	↑ adult blood pressure	Moore et al., 1999
High placental ratio	↑ adult hypertension without diabetes	Eriksson et al., 2000
Placental weight/ratio	- childhood blood pressure	Whincup et al., 1995
Placental weight/ratio	- adult blood pressure	Martyn et al., 1995b
<i>Coronary heart disease</i>		
Small placental weight	↑ coronary heart disease (men)	Forsen et al., 1997
Placental weight	- coronary heart disease (men)	Martyn, Barker & Osmond, 1996
Placental weight	- coronary heart disease (men & women)	Leon et al., 1998
Placental weight	- coronary heart disease (women)	Forsen et al., 1999
Placental weight	- coronary heart disease (men)	Eriksson et al., 2001
Low placental ratio	↑ coronary heart disease (men)	Martyn, Barker & Osmond, 1996
High placental ratio	↑ coronary heart disease (men)	Martyn, Barker & Osmond, 1996
High placental ratio	↑ coronary heart disease (women)	Forsen et al., 1999
<i>Stroke</i>		
Small placental weight	↑ stroke death rates	Martyn, Barker & Osmond, 1996
<i>Glucose tolerance</i>		
Small placental weight	↑ type-2 diabetes	Forsen et al., 2000
High placental ratio	↑ prevalence of impaired glucose tolerance	Phipps et al., 1993
<i>Plasma fibrinogen</i>		
Small placental weight	↑ plasma fibrinogen	Martyn et al., 1995a
High placental ratio	↑ plasma fibrinogen	Barker, Osmond & Meade, 1992

↑ = association found in the direction shown; - = no significant association found.

\*Measured in *mid-trimester*.

**Preconception care is no quick fix for women's health.**

# Where is the A in MCH?

[www.cincinnatichildrens.org](http://www.cincinnatichildrens.org)



# **It take more than preconception care to promote preconception health**

- Sustainable development
- Human development
- Economic development
- Community development

**Preconception care is no silver bullet for disparities in birth outcomes.**

# Closing the Black-White Gap in Birth Outcomes: A 12-Point Plan

1. Provide interconception care to women with prior adverse pregnancy outcomes
2. Increase access to preconception care for African American women
3. Improve the quality of prenatal care
4. Expand healthcare access over the life course
5. Strengthen father involvement in African American families
6. Enhance service coordination and systems integration
7. Create reproductive social capital in African American communities
8. Invest in community building and urban renewal
9. Close the education gap
10. Reduce poverty among Black families
11. Support working mothers and families
12. Undo racism

***All this will not be finished in the first 100 days. Nor will it be finished in the first 1,000 days, nor in the life of this Administration, nor even perhaps in our lifetime on this planet. But let us begin.***

John F Kennedy (1961)





