

# Life Course Factors, Nutrition and Body Composition

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**Stockholm 18-19<sup>th</sup> April 2013**

**Global Health Problems**

**Barker Hypothesis**

**Catch-up growth**

**Conclusions**

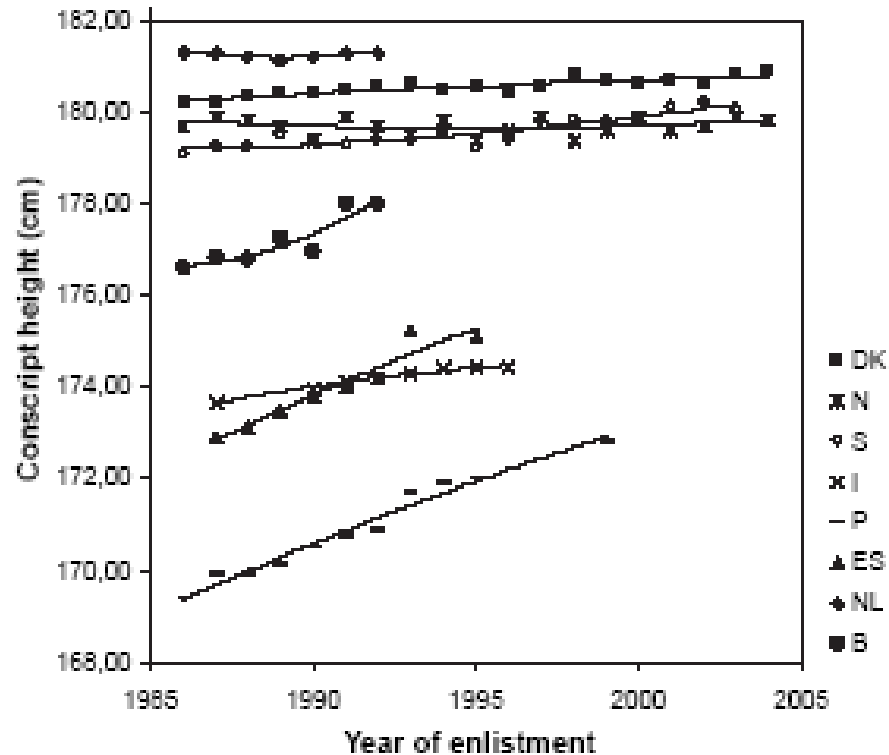
# **Global Health Problems**

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# Europe: Secular Increase in Height



Plateau ~1.8 m:  
Denmark, Sweden,  
Norway, Netherlands  
?genetic potential

Increasing:  
Belgium, Spain,  
Italy, Portugal

Figure 1. Mean conscript height in eight European countries according to year of enlistment. Previously published data from 1987 to 1990 have been included for comparison. B: Belgium; DK: Denmark; ES: Spain; I: Italy; N: Norway; NL: the Netherlands; P: Portugal; S: Sweden.

**Europe: secular increase in height:**

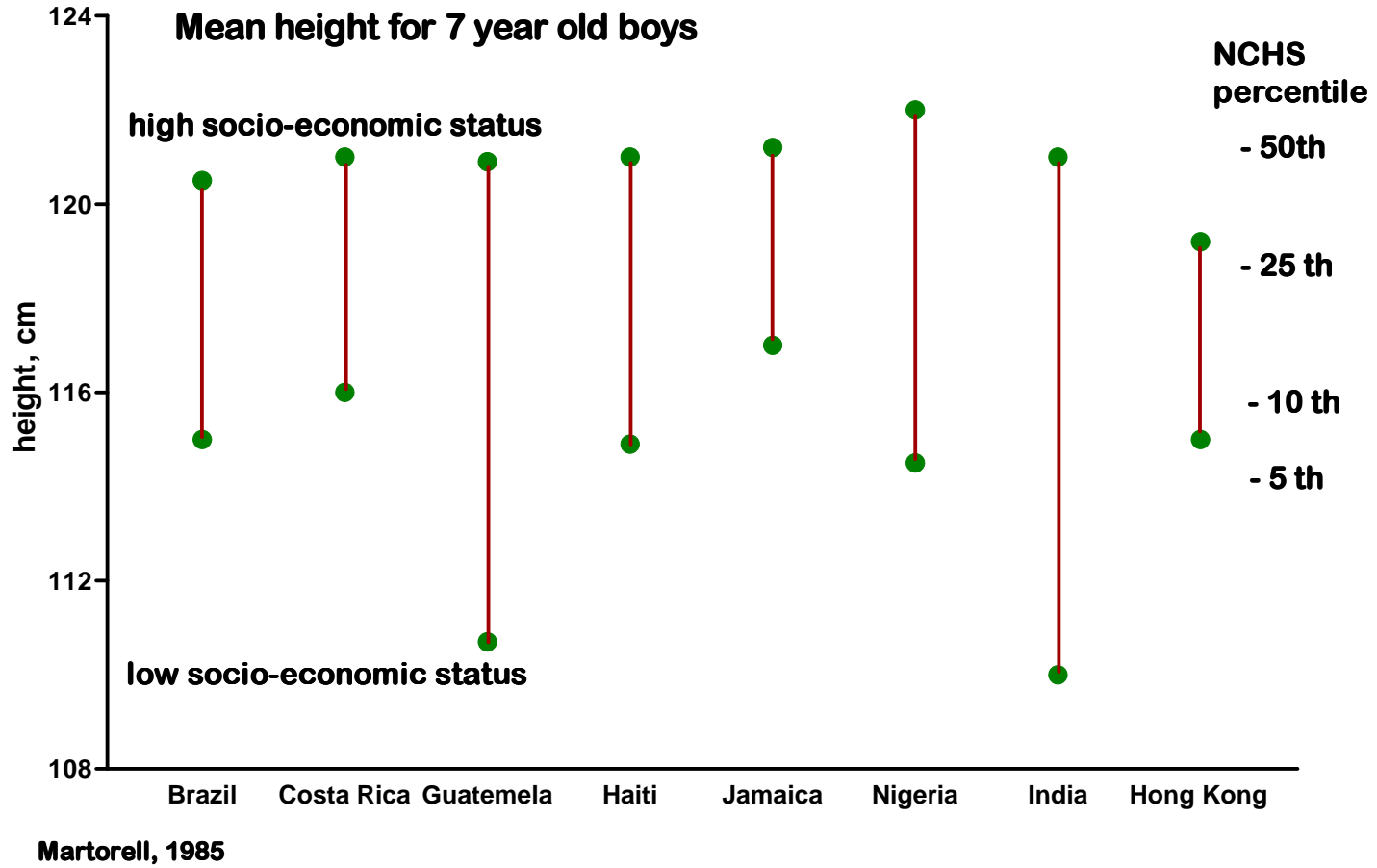
Stopped, 18 years following post-neonatal mortality around 4/1000 deliveries.

**Improving socio-economic conditions**

better nutrition - healthier diet

decrease in infectious diseases

# Social Determinants of Length



## STUNTING: low height for age

More common than wasting  
(thinness, severe acute malnutrition)

Obesity more common than wasting

↑ mortality

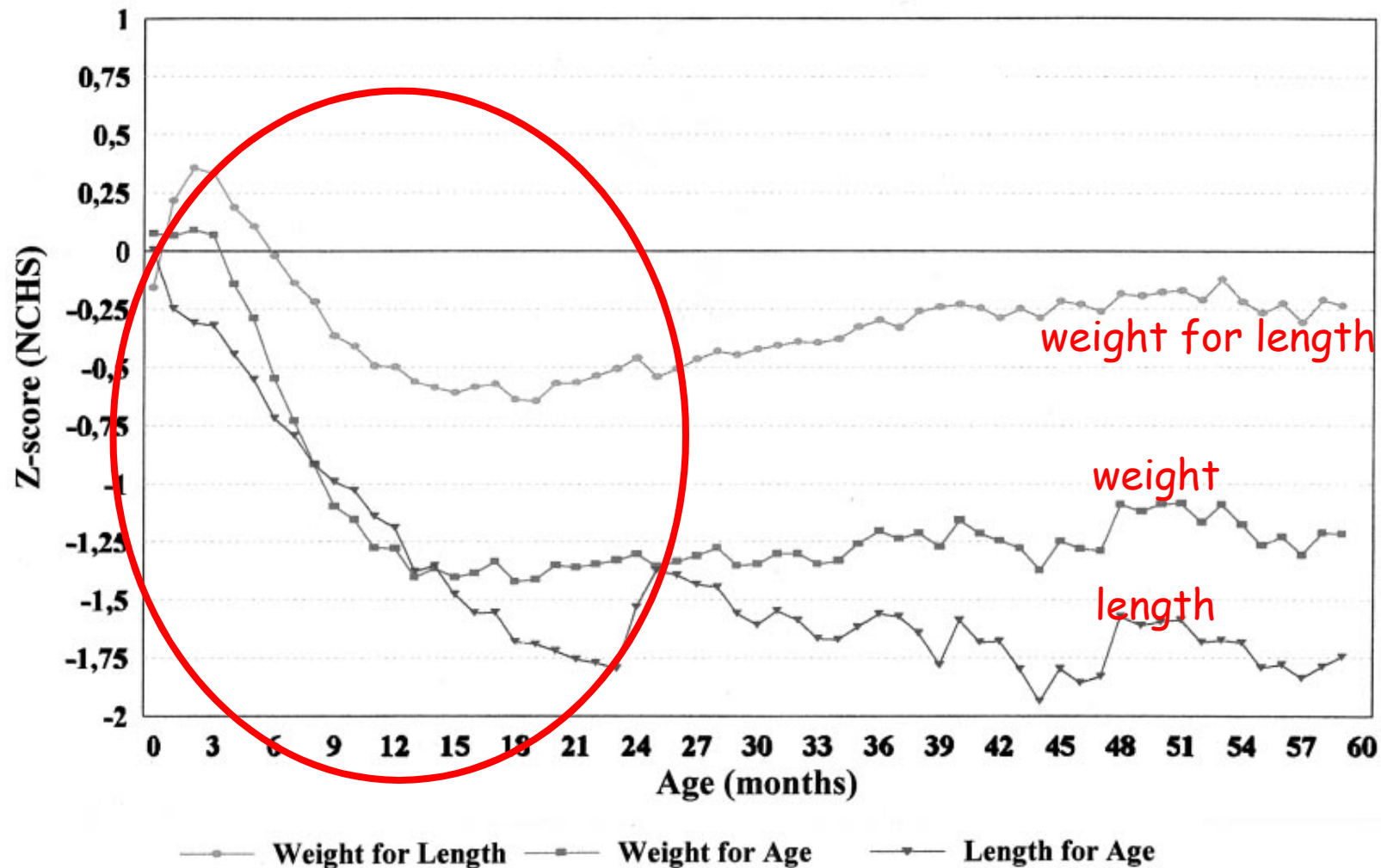
↑ morbidity

↓ physical work performance

↓ intellectual function

↓ Lifelong earning capability

## Global Mean W/A, L/A and W/L



Stunting: by 2 years of age

Deprivation: poor neurocognitive development, obesity



# Global epidemic of obesity

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*“The epidemic of obesity, with its attendant comorbidities --- heart disease, hypertension, stroke, and diabetes --- is not a problem limited to industrialized countries” - WHO TRS 916*

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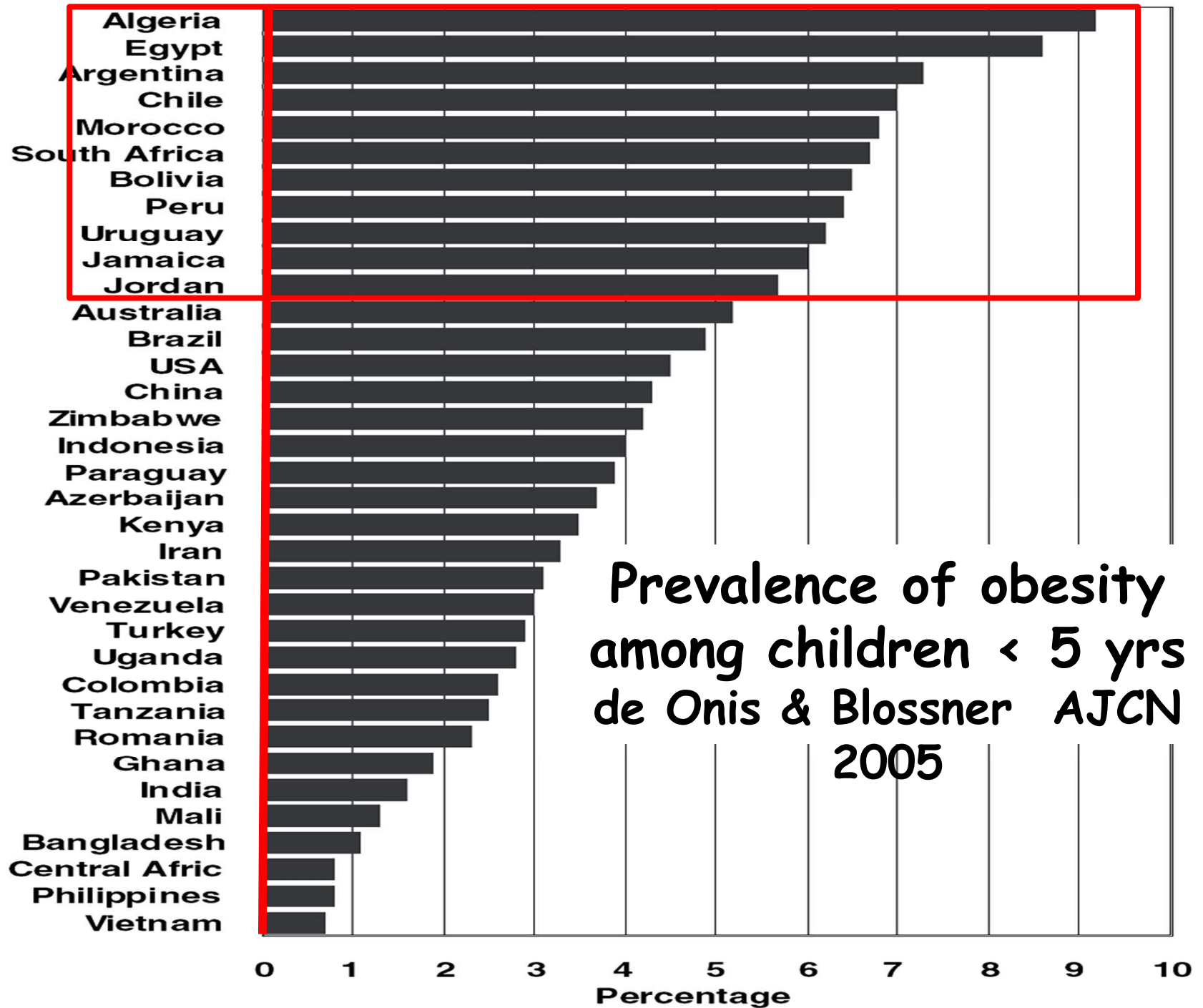
**300 million BMI>30**

**1.5 billion BMI>25**

**1.7 billion BMI>23**

**200 m school-age children overweight**

**35 m under 5yrs overweight**





## Hillary Clinton Launches 1,000 Days Movement September 2010



Double Burden of Malnutrition:

Malnutrition in All its Forms

Underweight, Overweight, Micronutrient Deficiencies

# Global Action Plan for Scaling Up Nutrition (SUN)

Scaling up of evidence-based,  
high priority nutrition interventions

Focusing primarily on the window of opportunity  
conception to 24 months

Multisectoral: underlying socio-economic, intersectoral causes

Integrate: health systems,  
agriculture and food security and social safety nets



## General Assembly

Distr.: Limited  
16 September 2011

Original: English

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Sixty-sixth session

Agenda item 117

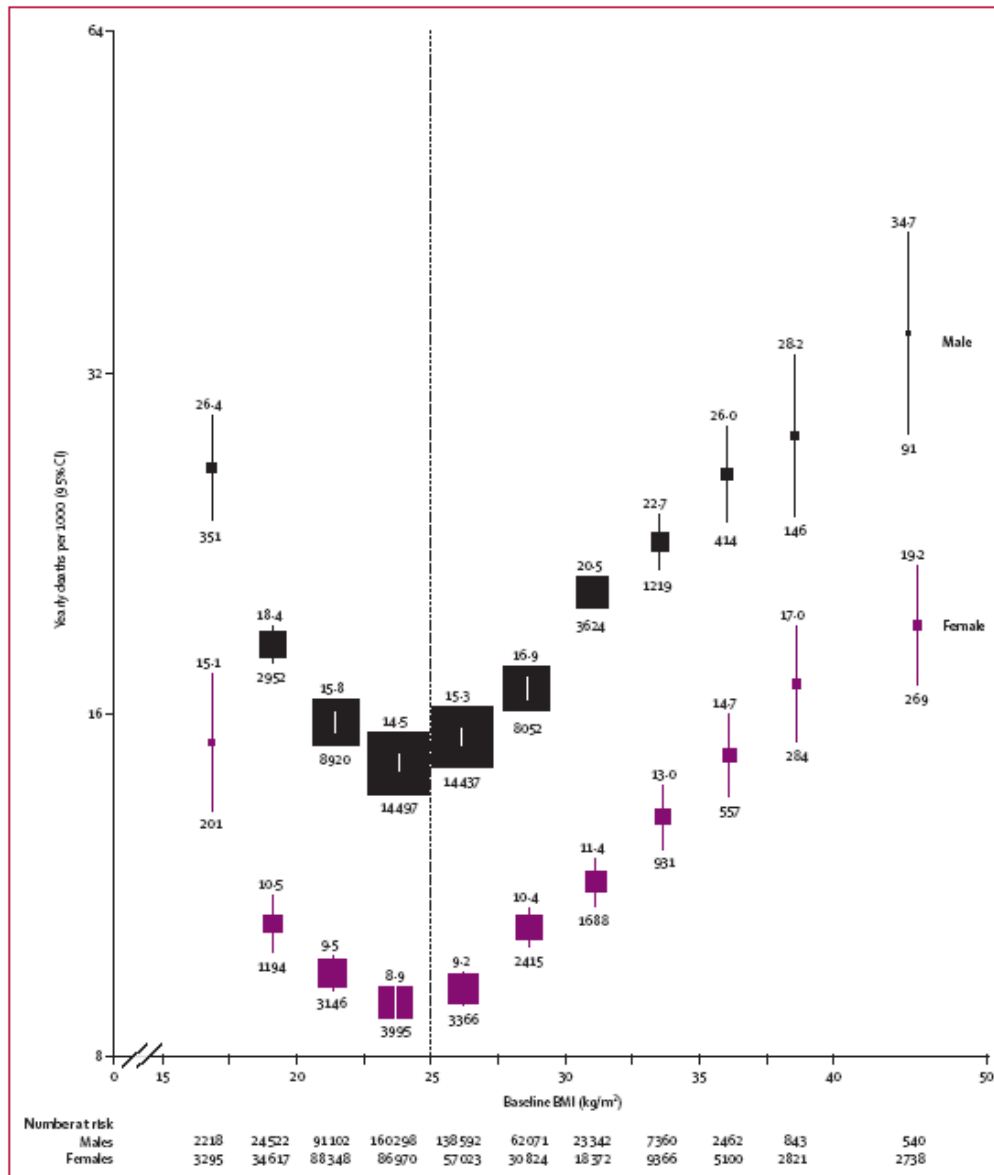
Follow-up to the outcome of the Millennium Summit

Draft resolution submitted by the President of the General Assembly

### **Political declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases**

*The General Assembly,*

*Adopts* the Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases annexed to the present resolution.



## Body Mass Index

U-shaped relationship  
all cause mortality

Preferred range 22-25 kg/m<sup>2</sup>

Figure 2: All-cause mortality versus BMI for each sex in the range 15-50 kg/m<sup>2</sup> (excluding the first 5 years of follow-up). Relative risks at ages 35-89 years, adjusted for age at risk, smoking, and study, were multiplied by a common factor (ie, floated) to make the weighted average match the PSC mortality rate at ages 35-79 years. Floated mortality rates shown above each square and numbers of deaths below. Area of square is inversely proportional to the variance of the log risk. Boundaries of BMI groups are indicated by tick marks. 95% CIs for floated rates reflect uncertainty in the log risk for each single rate. Dotted vertical line indicates 25 kg/m<sup>2</sup> (boundary between upper and lower BMI ranges in this report).

Global Health Problems

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**Barker hypothesis:  
Fetal Origins of Chronic Disease:**



Coronary heart disease,

Stroke,

Type 2 diabetes

Hypertension

Developmental Model for Disorders



# Fetal Origins Hypothesis of Chronic Disease

Disorders originate through **Developmental Plasticity**

Poor nutrient exposure: early life (fetus, infant, early childhood)

Permanent change in structure and function:

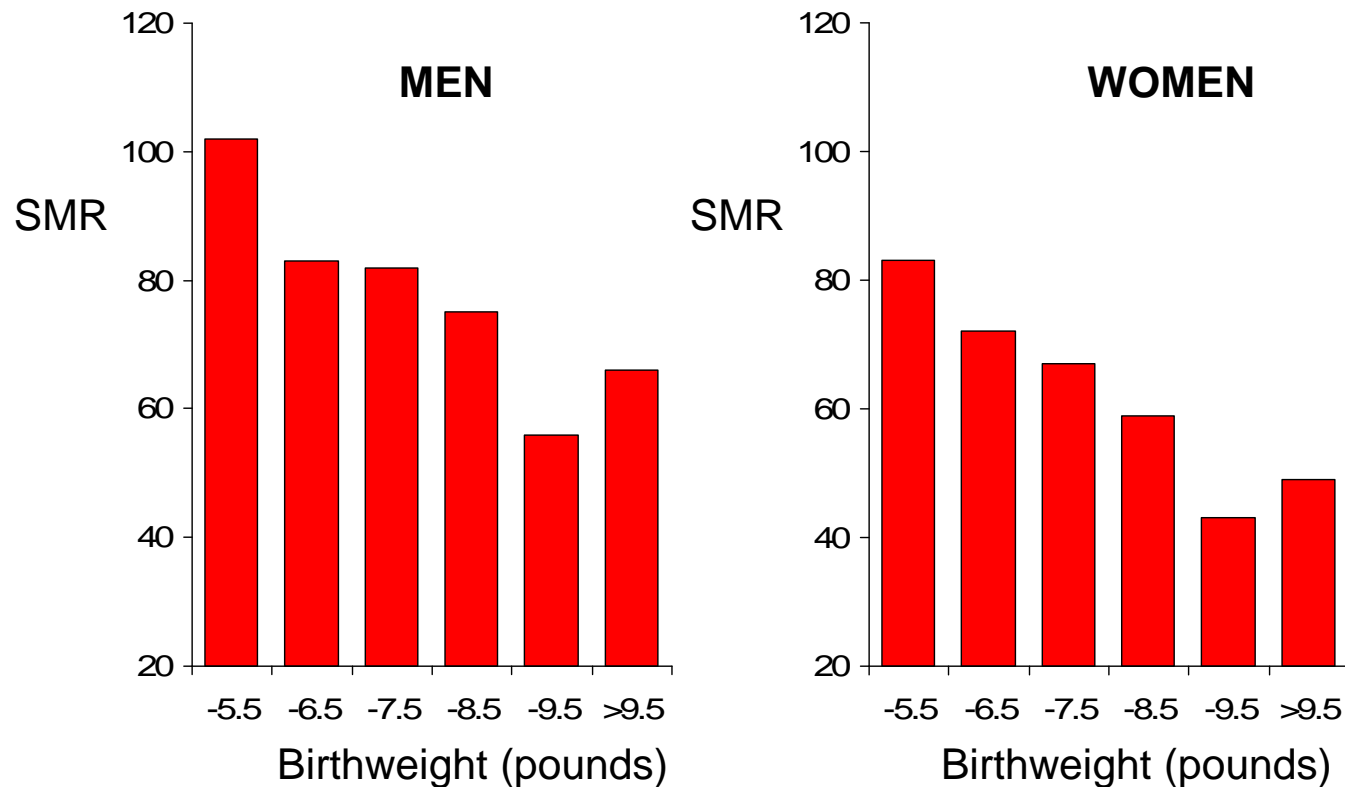
- tissues and organs

Vulnerable period: timing, intensity, duration

# Barker Hypothesis

## Coronary heart disease

Standardised mortality ratios (SMR) in 10141 men & 5585 women

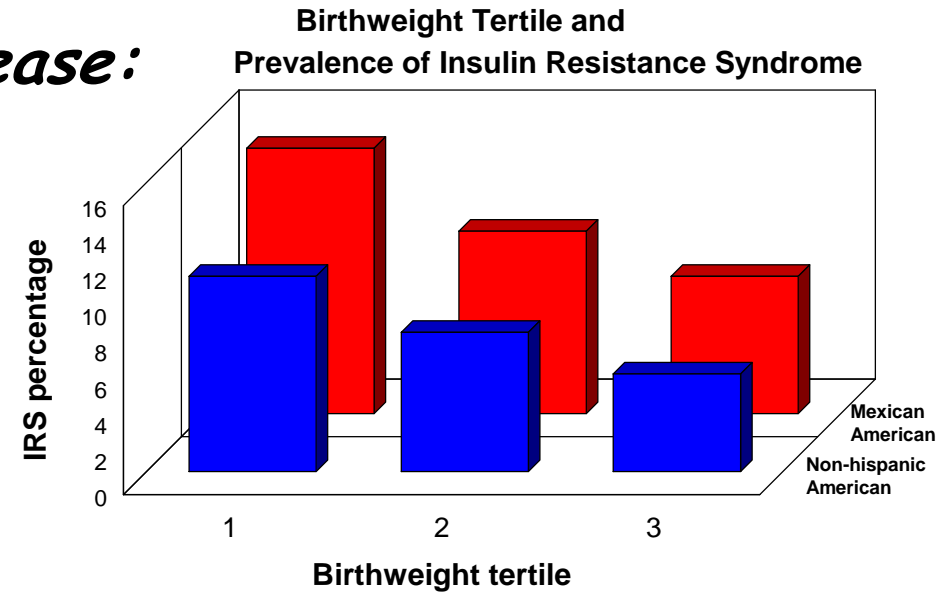


*BMJ 1993;307:1519-24*

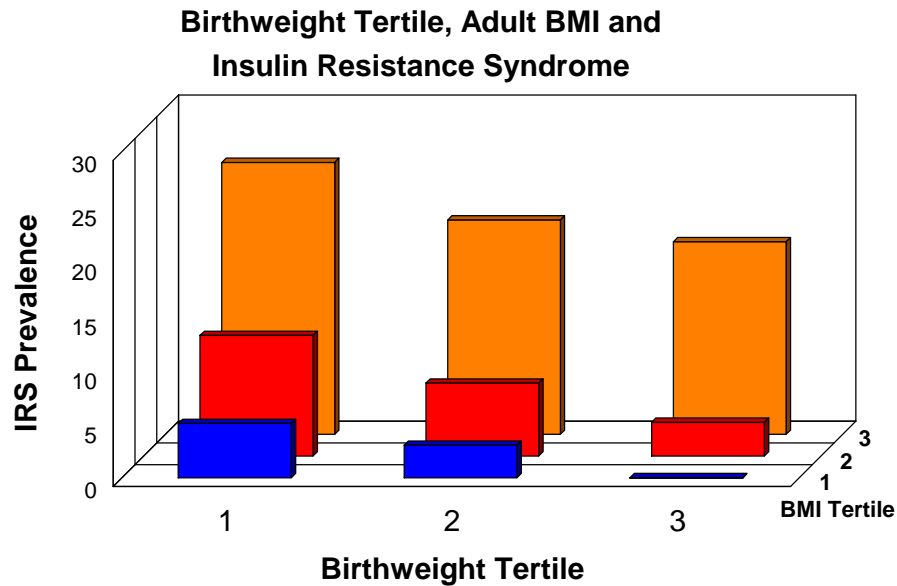
Variable risk across the range of weight at birth & at age one year, which is not a feature of the extremes of the ranges, very low or very high.

# Early Life origins of disease:

Evidence from wide range of international studies



Valdez et al, Diabetologia 1992



Valdez et al, Diabetologia 1994

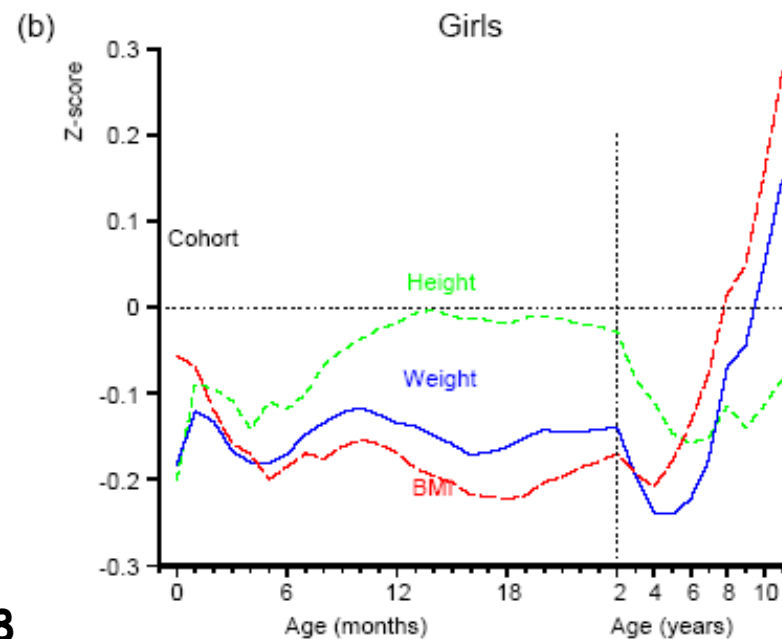
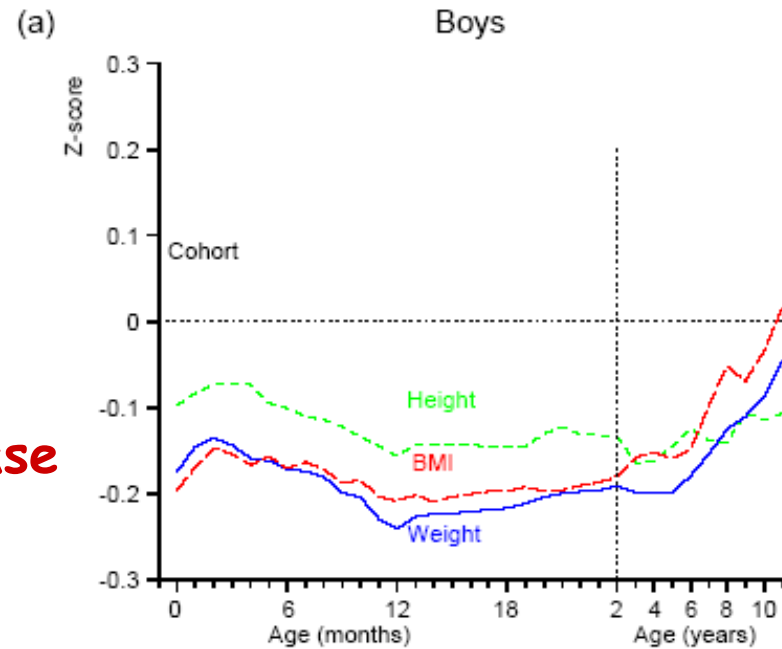
Metabolic changes already evident in childhood by 5 years of age

# Finnish Studies

Adults who had coronary heart disease

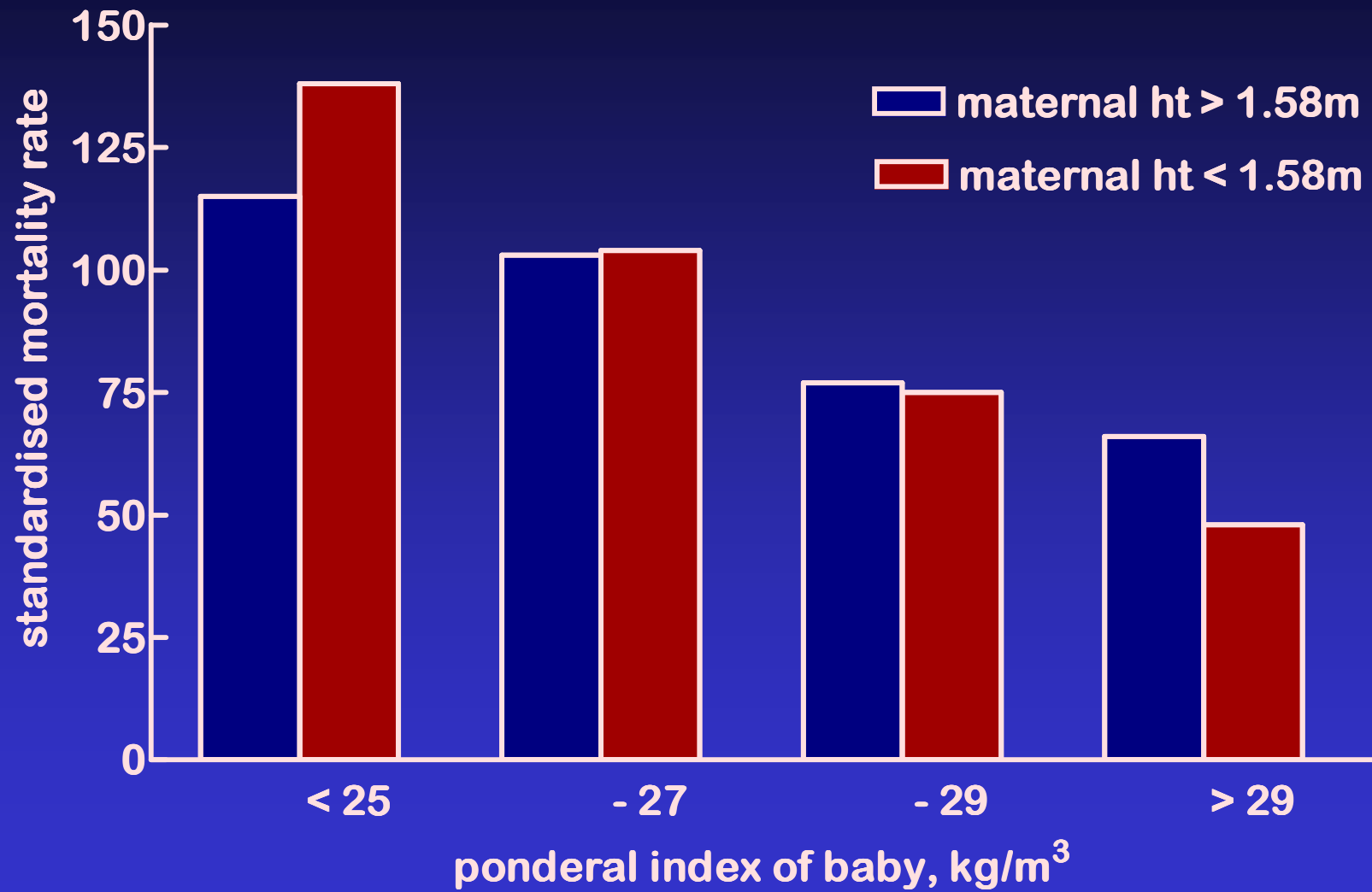
Growth in childhood - to 11 years

Mean z scores for height, weight and body mass index



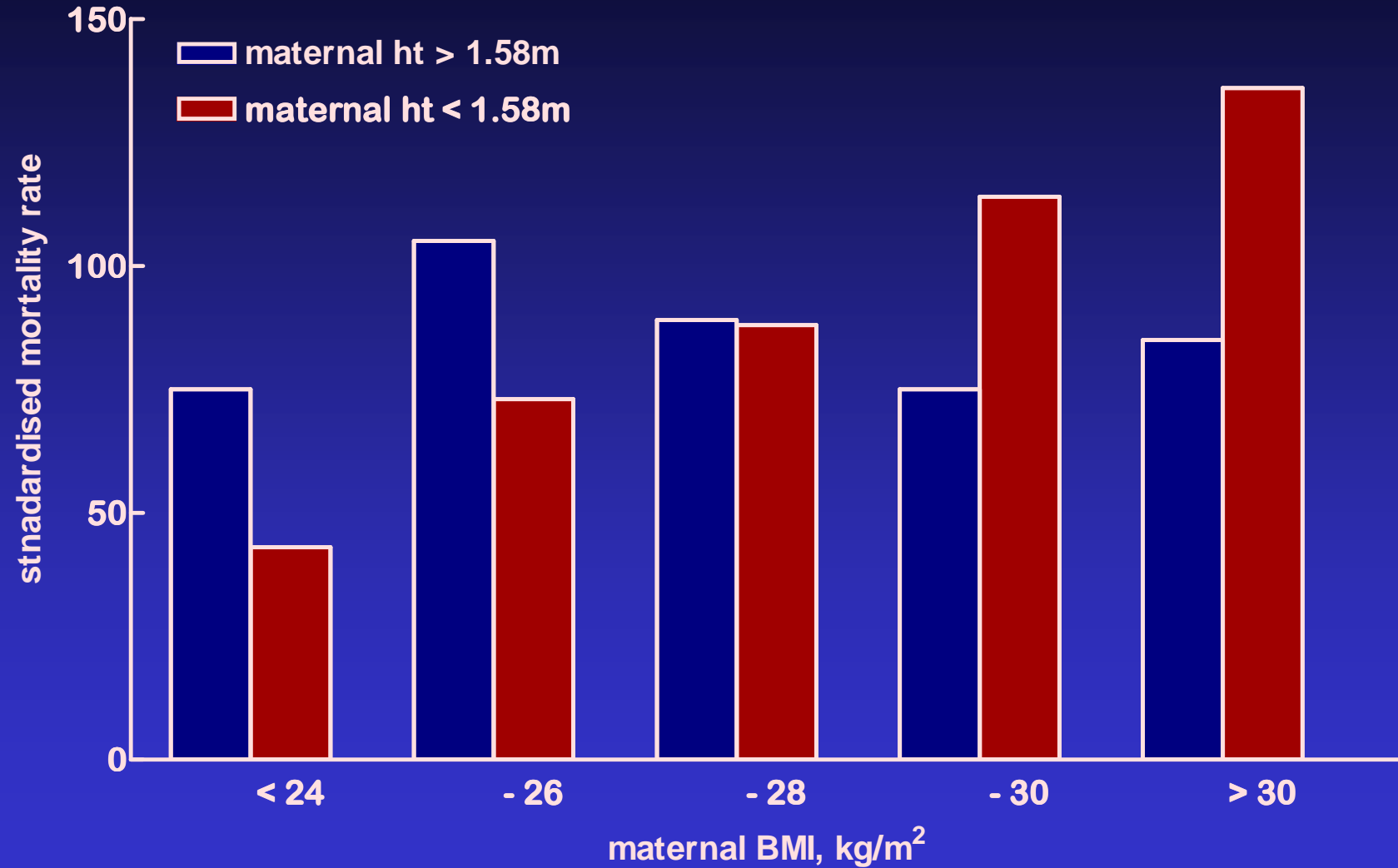
# Coronary Heart Disease: Finnish men

Forsen et al, BMJ 1997, 315, 837-40



# Coronary Heart Disease: Finnish men

Forsen et al BMJ 1997, 315, 837-40



## Coronary heart disease: mother < 1.58 m standardised mortality rate

Ponderal index of baby	BMI of mother					All
	< 24	-26	-28	-30	> 30	
<25	55	106	168	170	224	131
-27	55	70	146	113	134	104
-29	26	54	31	137	149	75
> 29	0	63	26	55	75	48
All	43	73	88	114	136	90

## Stunting and overweight in children Countries in transition

Popkin, Public Health Nutrition 1998, 1, 5-21

High rates of lower birth weights

High rates of stunting in childhood (15-35%)

Increased prevalence of obesity

Changes in dietary habits

Reduced levels of activity associated with urbanization

Increased prevalence of heart disease and type 2 diabetes



Global trend towards increase weight and height:

generally desirable:

**BUT**

increase in weight achieved  
- before increase in height

Increase in childhood overweight and adiposity

Increased risk of shortness/stunting and obesity

# The Thin-Fat Indian Baby

Pune: newborn baby

Weight 2,800g

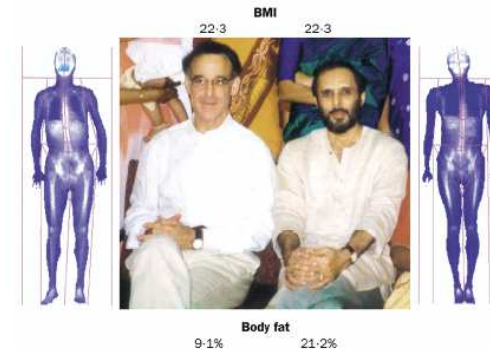
Thin: reduced lean mass.

Relatively adipose: central fat

## Clinical picture

### The Y-Y paradox

Chittaranjan S Yajnik, John S Yudkin



The two authors share a near identical body-mass index (BMI), but as dual X-ray absorptiometry imagery shows that is where the similarity ends. The first author (figure, right) has substantially more body fat than the second author (figure, left). Lifestyle may be relevant: the second author runs marathons whereas the first author's main exercise is running to beat the closing doors of the

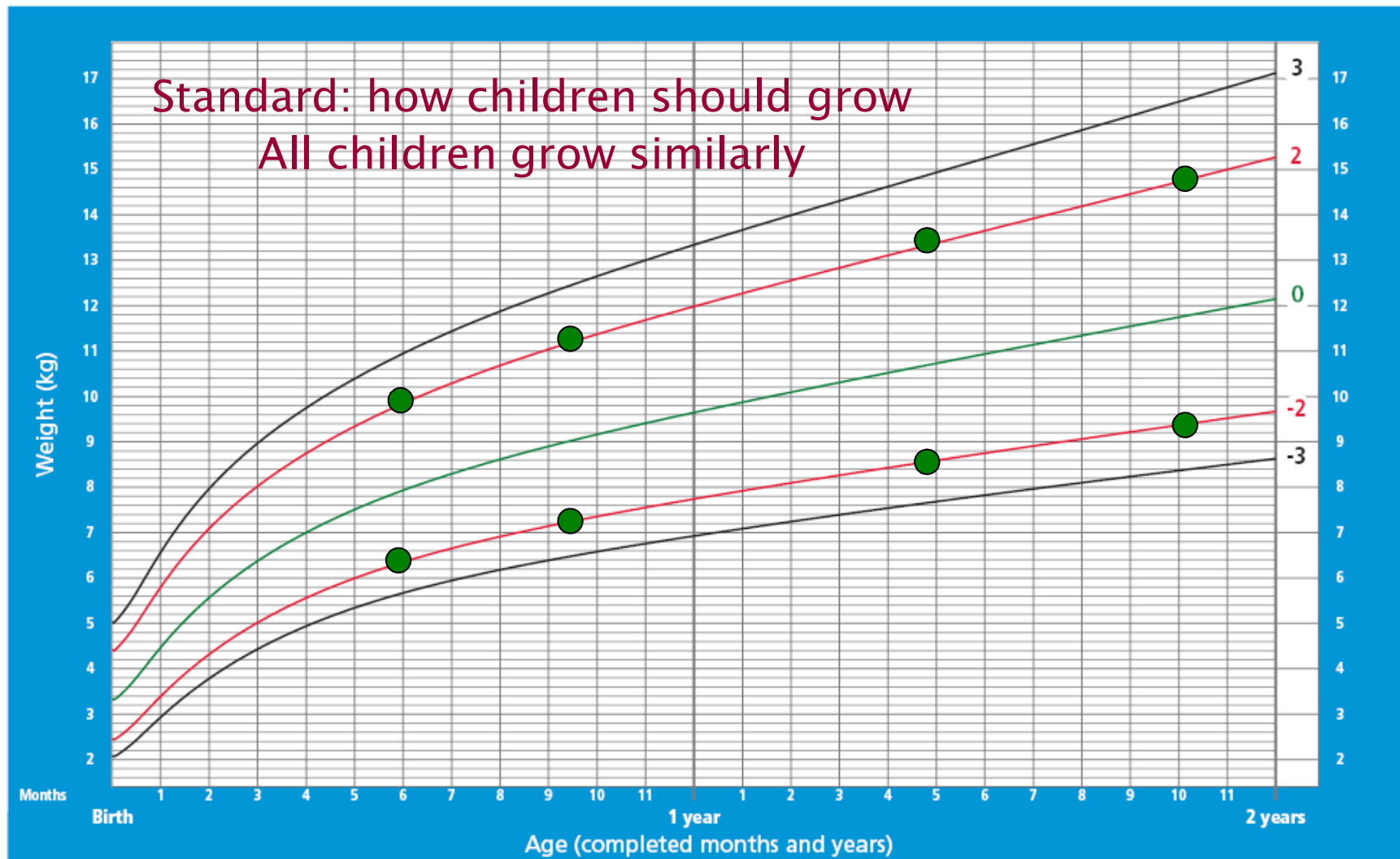
elevator in the hospital every morning. The contribution of genes to such adiposity is yet to be determined, although the possible relevance of intrauterine under-nutrition is supported by the first author's low birthweight. The image is a useful reminder of the limitations of BMI as a measure of adiposity across populations.

Diabetes Unit, KEM Hospital Research Centre, Rasta Peth, Pune 411011, India (C S Yajnik MD); International Health and Medical Education Centre, University College London, UK (J S Yudkin FRCP)

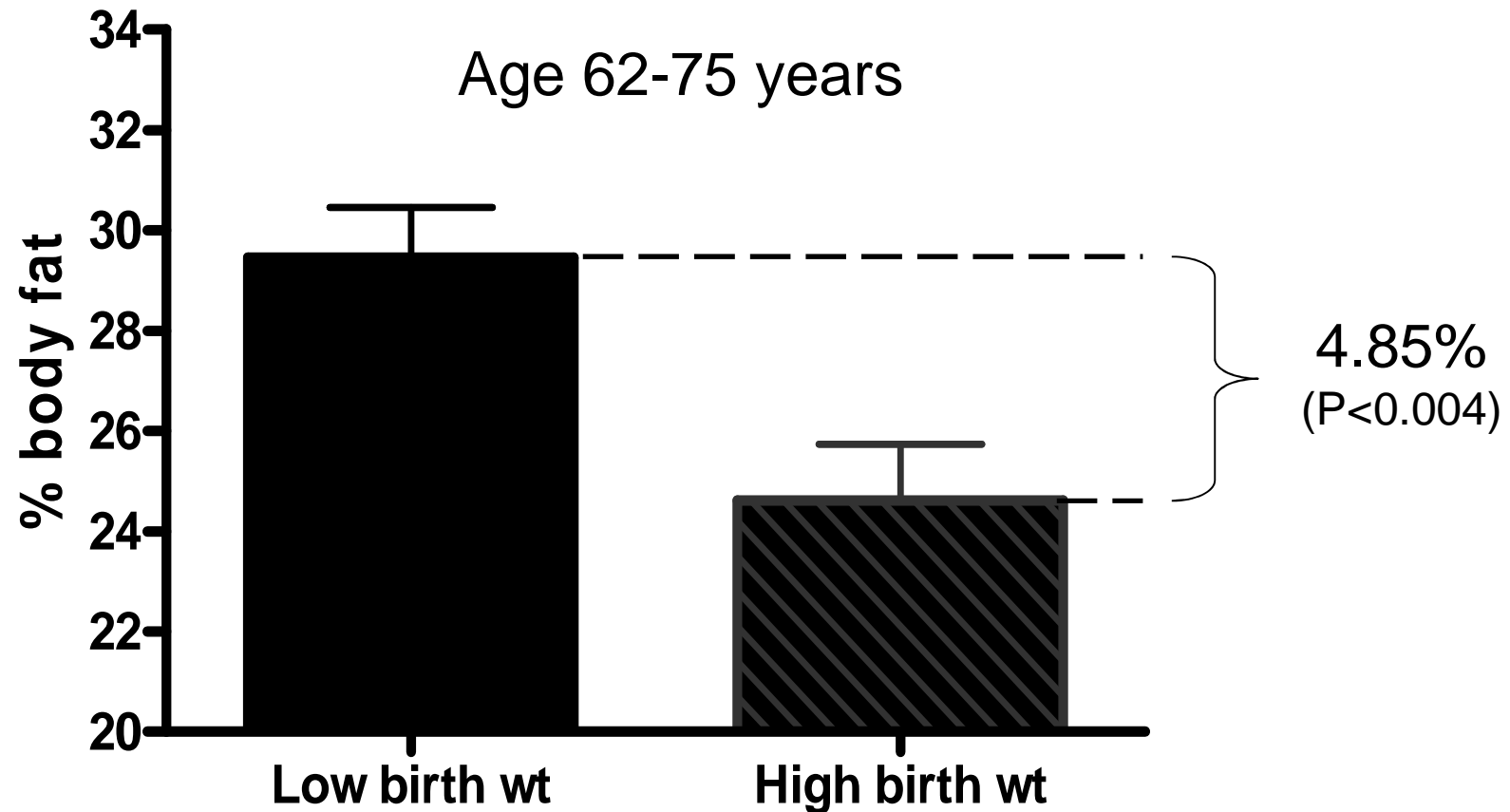
Small Baby: shortness and fatness  
Increased risk type 2 diabetes

# Weight-for-age BOYS

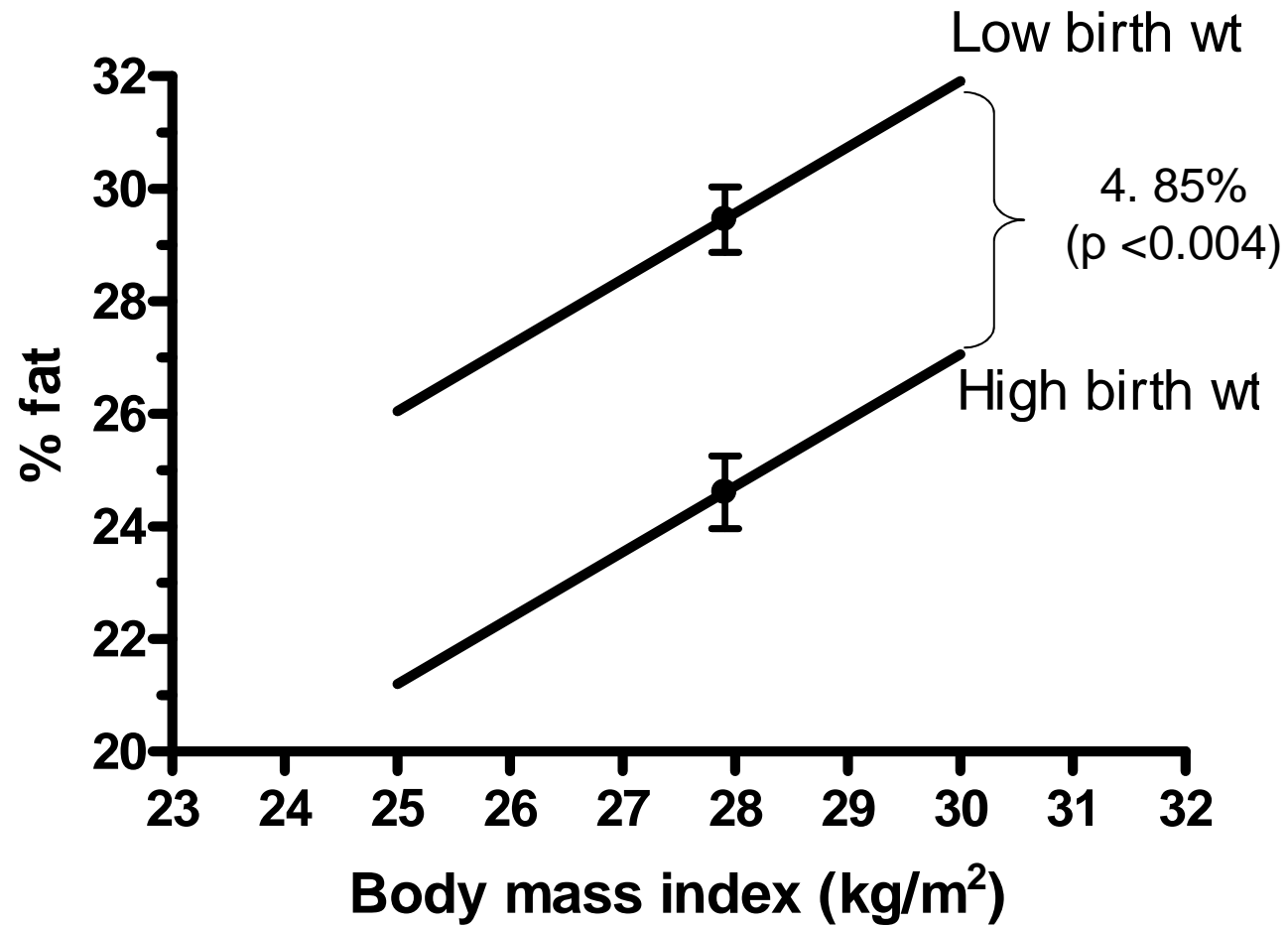
Birth to 2 years (z-scores)



# % fat in low and high birth weight groups (mean $\pm$ sem), adjusted for BMI (27.9 kg/m<sup>2</sup>)



ANCOVA BMI v % fat ( $r = 0.67$ ;  $p < 0.001$ )

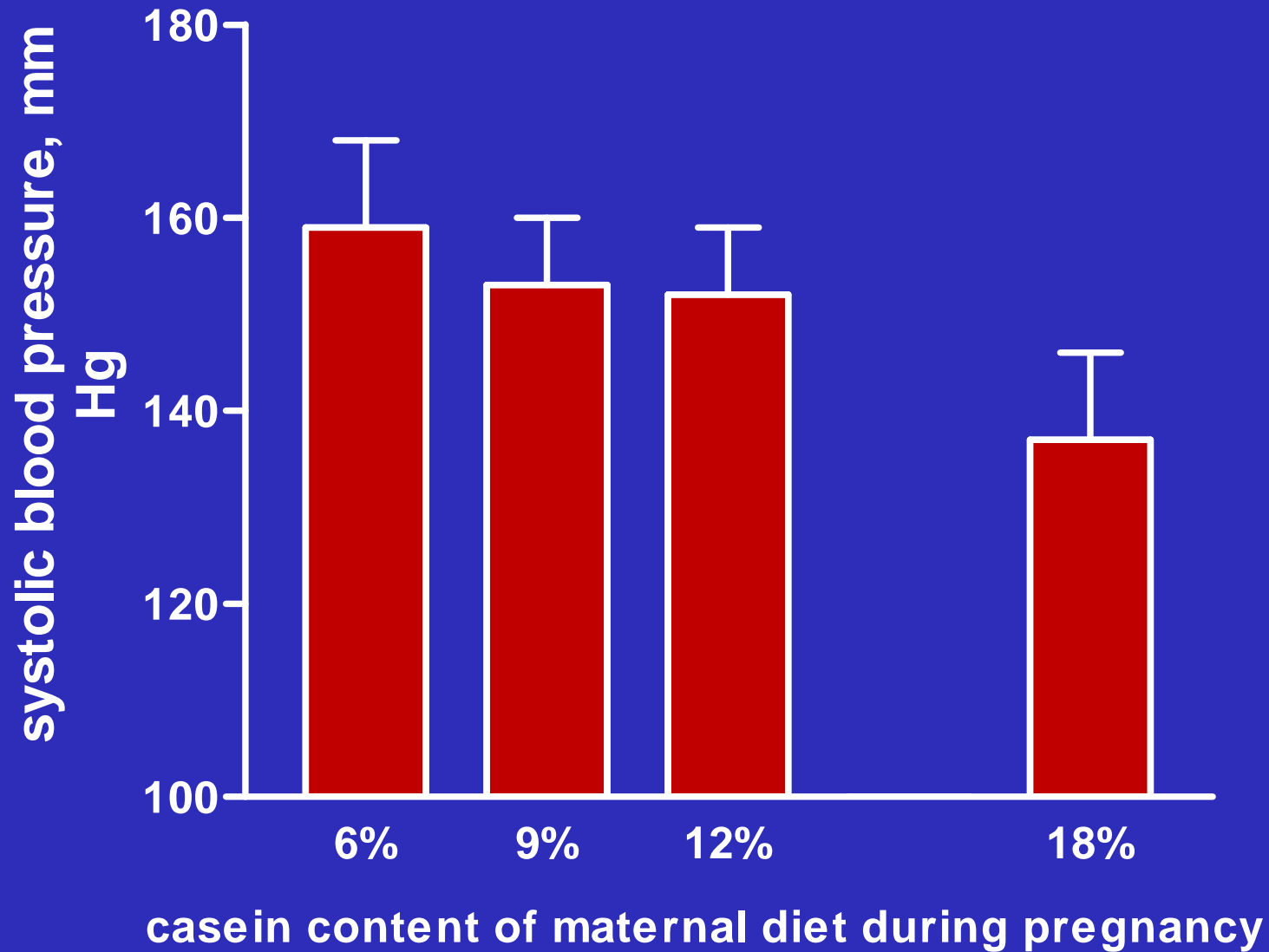


For the same weight or BMI at 70 years of age

Lower birth weight

- less muscle
- more fat
- more central fat
  
- function difference
  
- altered cellular nutrient environment

## Systolic Blood Pressure Maternal Exposure to Protein Diet



## Fetus:

reset of central set-point for key hormonal axes

hypothalamo - pituitary-adrenal

growth hormone - IGF - insulin

thyroid axis

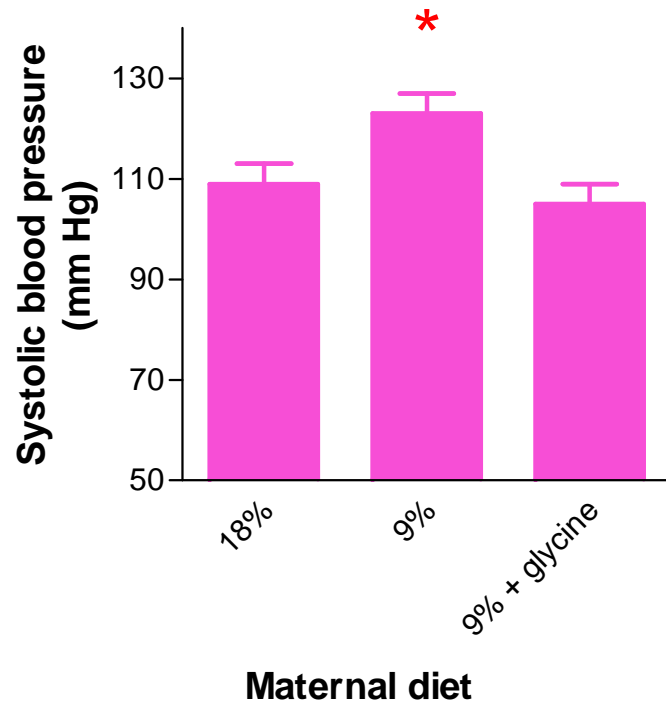
sex steroid axis

- response to diet
- response to stressors

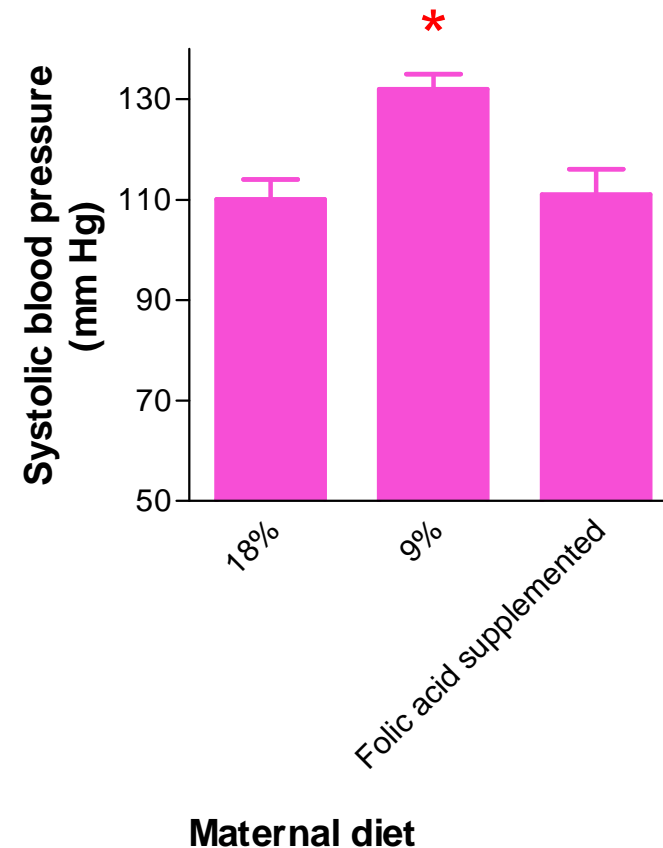


# Glycine and folic acid supplementation prevent hypertension

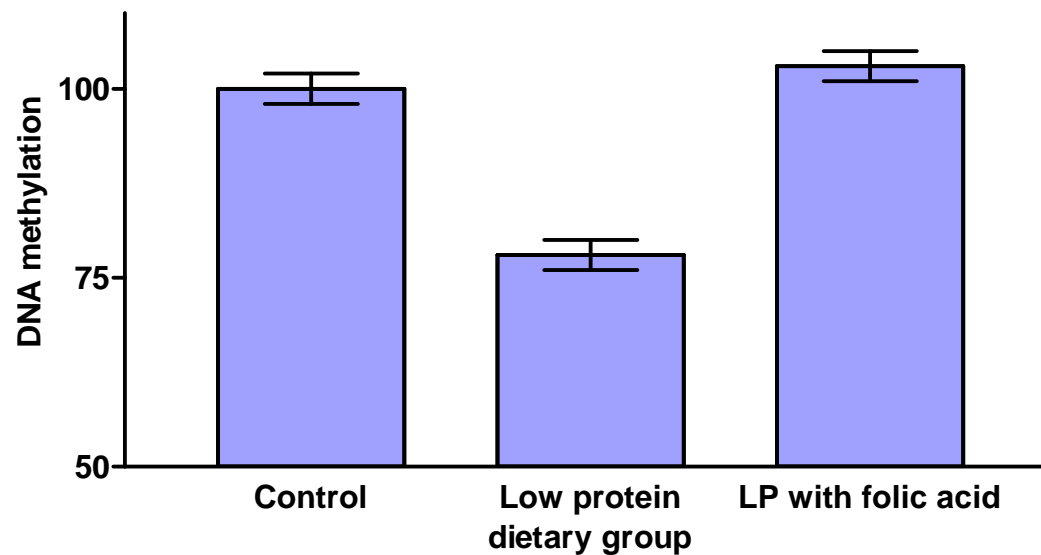
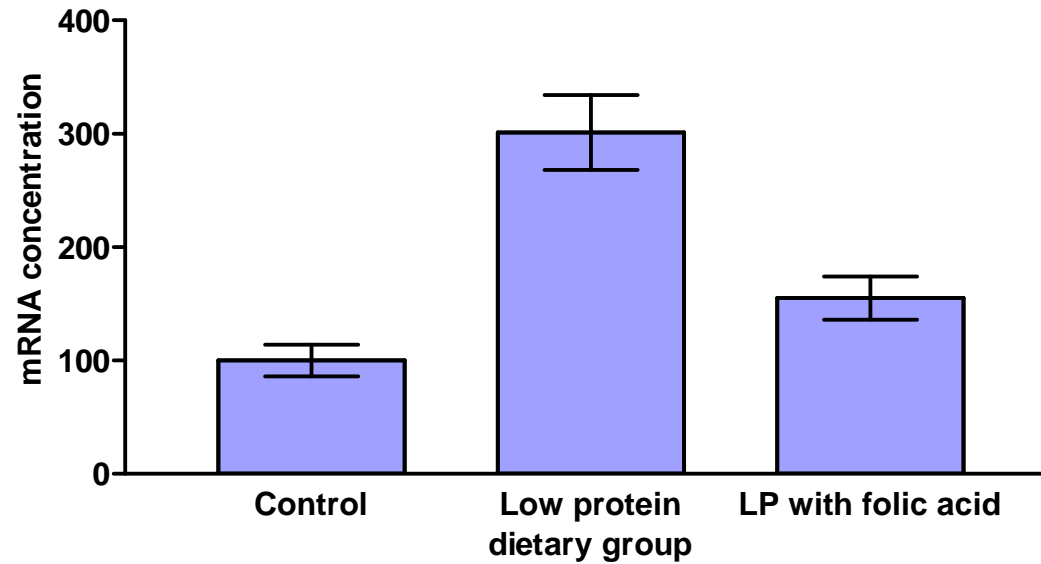
Blood pressure at 4 weeks in females



Blood pressure at 4 weeks in females



# Hepatic Glucocorticoid Receptor: methylation of promoter region of gene and gene expression



# Epigenetics

Stable change in DNA structure

Modifies expression

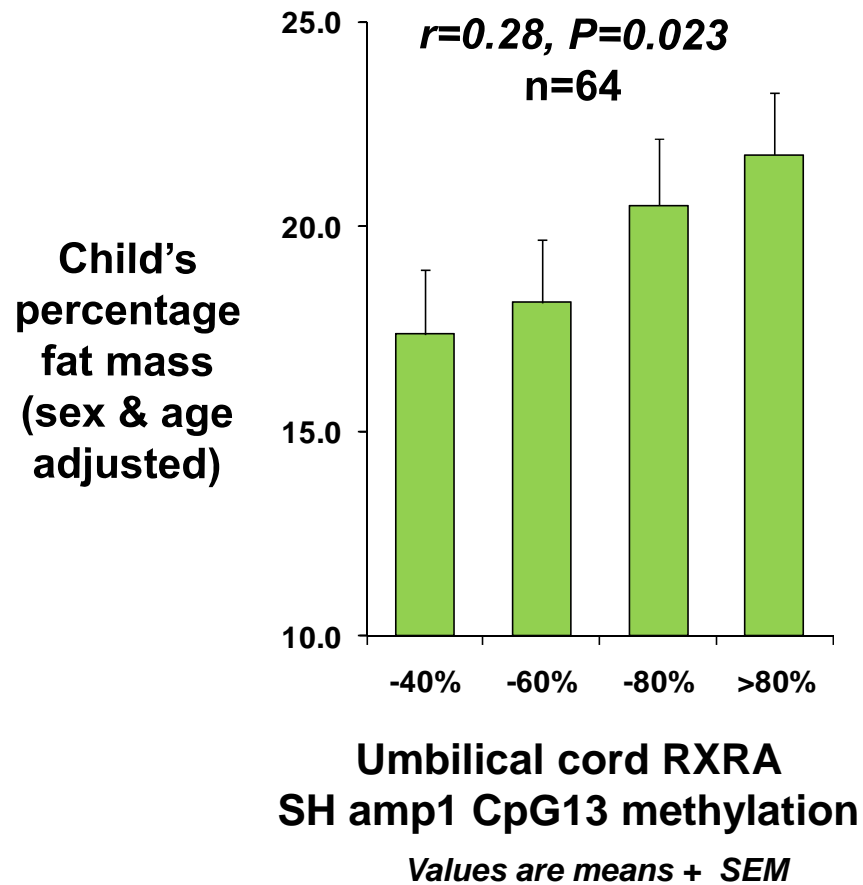
Carried between generations

Variable methylation (protein and folate)

Selective methylation of promoter region

## Methylation promoter RETINOIC ACID RECEPTOR gene umbilical cord

Association adiposity 9 years of age: 'explains' >25% of later adiposity;



Global Health Problems

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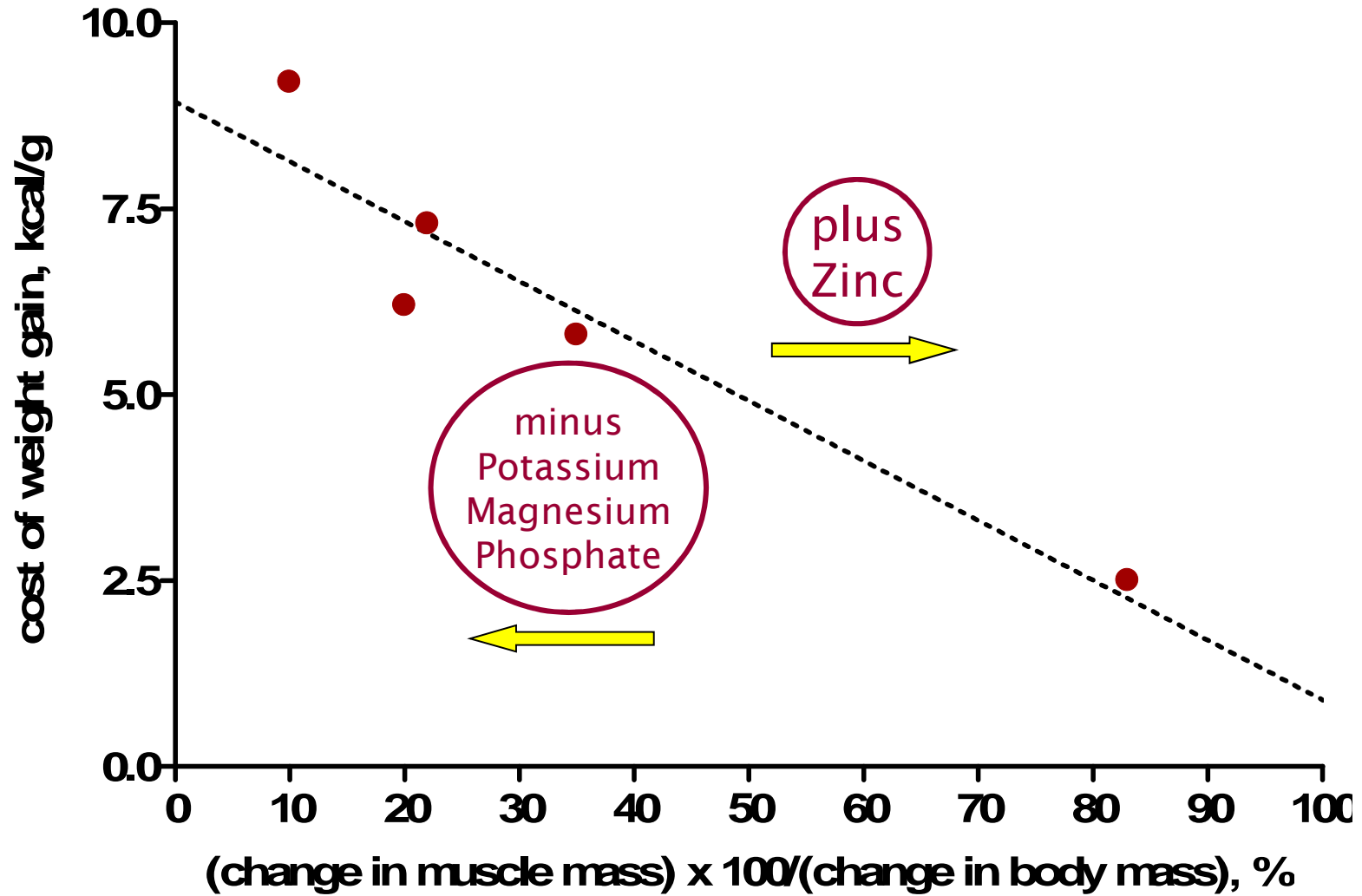
**Catch-up growth**

Conclusions

## Catch-up growth

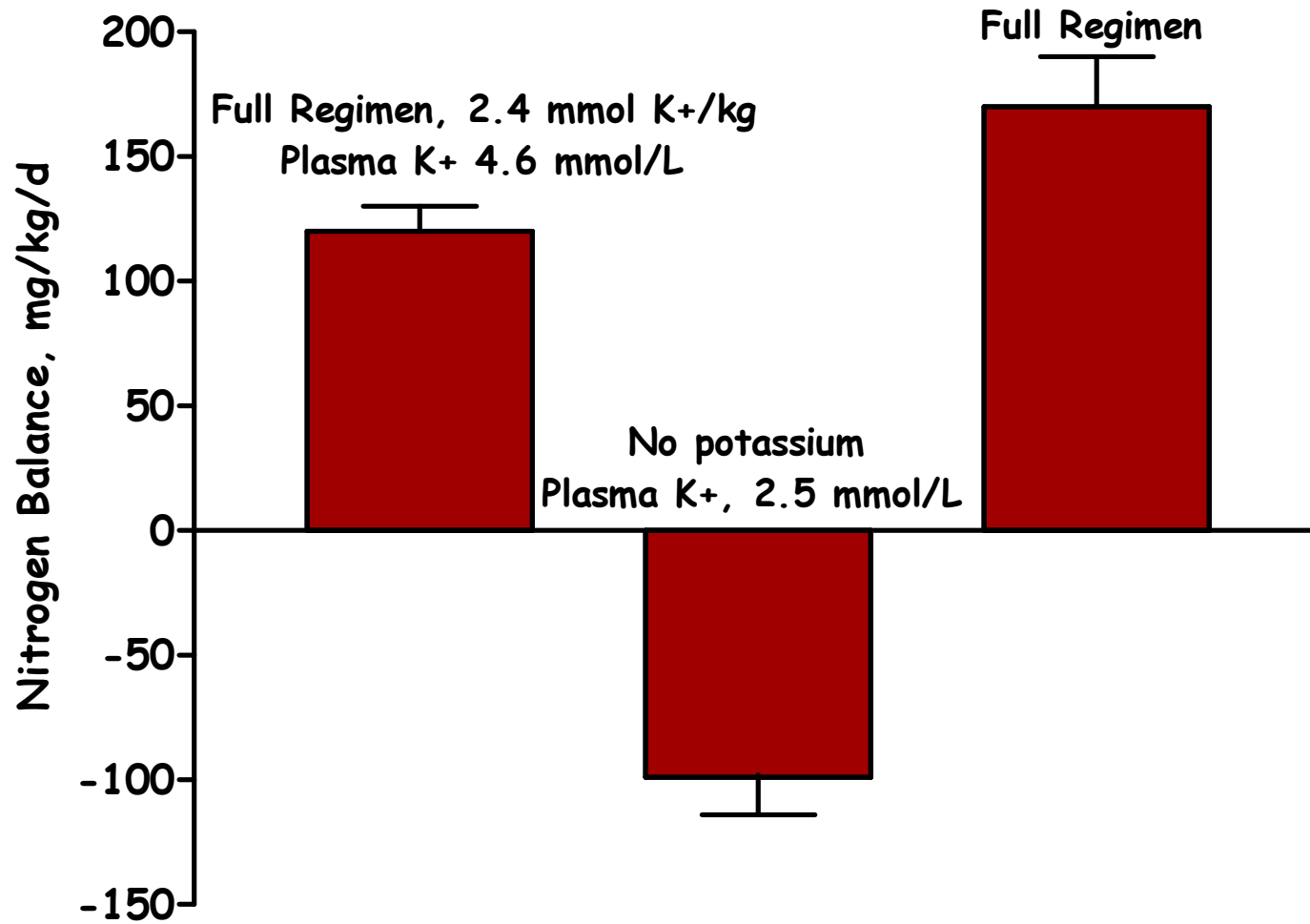
- rapid growth, rate greater than normal
- altered efficiency of growth  
greater tissue gain per unit energy
- Altered pattern of tissue deposition

**Cost of Growth in relation to Change in Body Composition  
during recovery from severe malnutrition  
Jackson, 1977**



# Effect of removing potassium from parenteral nutrition on nitrogen balance

Rudman et al, 1975





Pattern of nutrients retained

Nutrient requirements for net deposition:

- bone
- lean tissue
- adipose (by default)

Nutrient availability - altered pattern tissue deposition:

- energy
- macronutrients
  - dietarily essential, conditionally essential
- micronutrients

Non-essential or conditionally essential Nutrients:  
- do not have to be provided preformed in diet.

Required for metabolism  
- formed from precursors usually readily available in diet.

Amino acids

Longer chain polyunsaturated Fatty acids

High rates of formation

Regulated rates of formation

# FOOD/NUTRIENT INSECURITY

**Diet:**

**Quantity:**

energy

[macronutrients, carbohydrate, lipid (fat), protein]

**Quality:**

Nutrients

[CHO, lipid (essential fatty acids), amino acids, minerals, vitamins, trace elements water, oxygen]

**Activity: Inflammation**

Global Health Problems

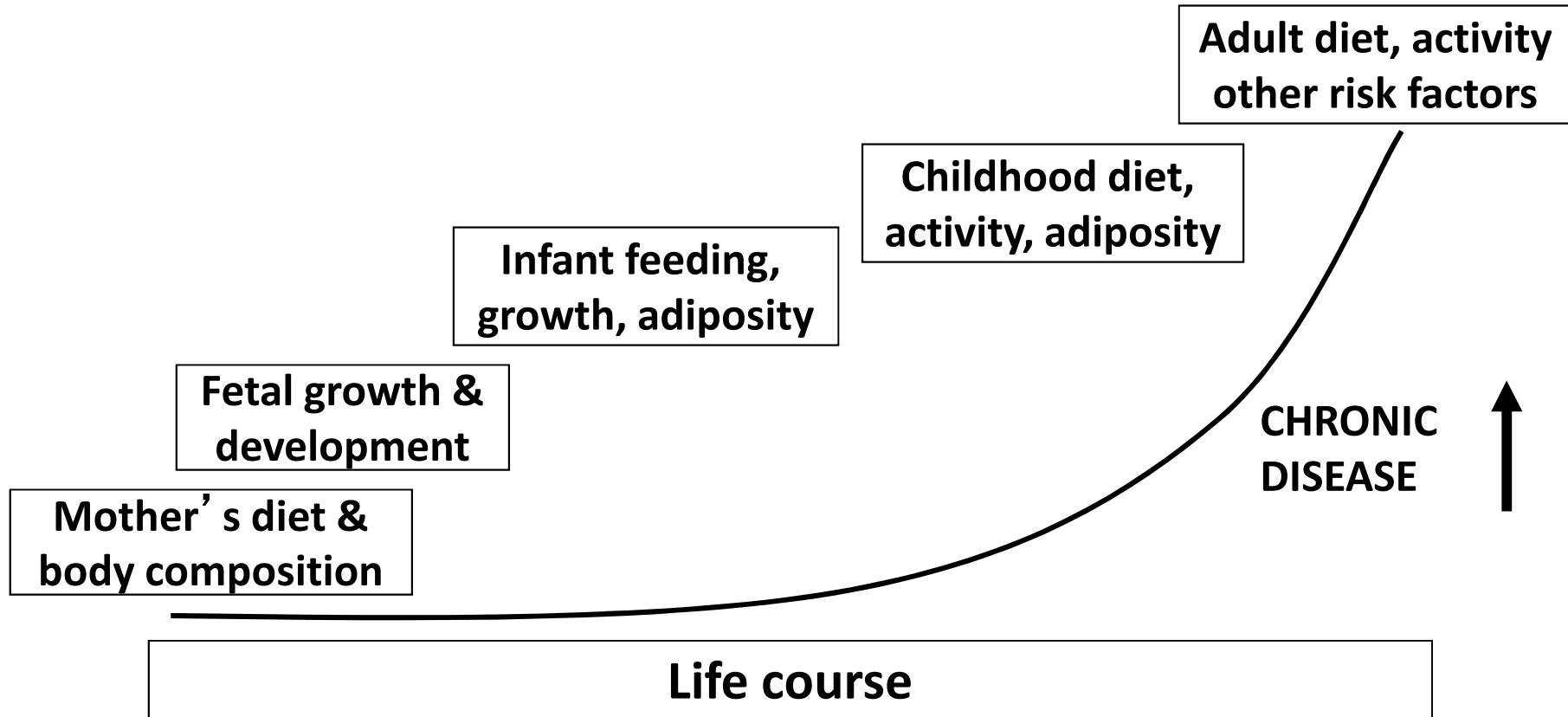
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**Conclusions**

# What happens in the short term matters in the long term

## Life course approach to chronic disease



Standing Committee on Nutrition, United Nations System:  
Chronic disease: impending global burden of ill-health  
Window of vulnerability: preconception to 2 years of age

# Structure and function inextricably linked

## Molecular:

genetic, epigenetic

## Cellular:


membrane structure and function  
receptor function  
signalling, replication, differentiation

## Tissue, organ

Head circumference: brain  
Renal size: nephron number  
Abdominal circumference: hepatic architecture

## Body shape:

height, lean, adipose



Structure  
/function

# Quantity and Quality

Widdowson - "Harmony of Growth"

pace and proportion, partitioning of nutrients

