Early Infancy as a Critical Period for Development of Obesity and Diabetes

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Thanks to…

Faculty, Trainees, & Staff

Obesity Prevention Program
Department of Population Medicine
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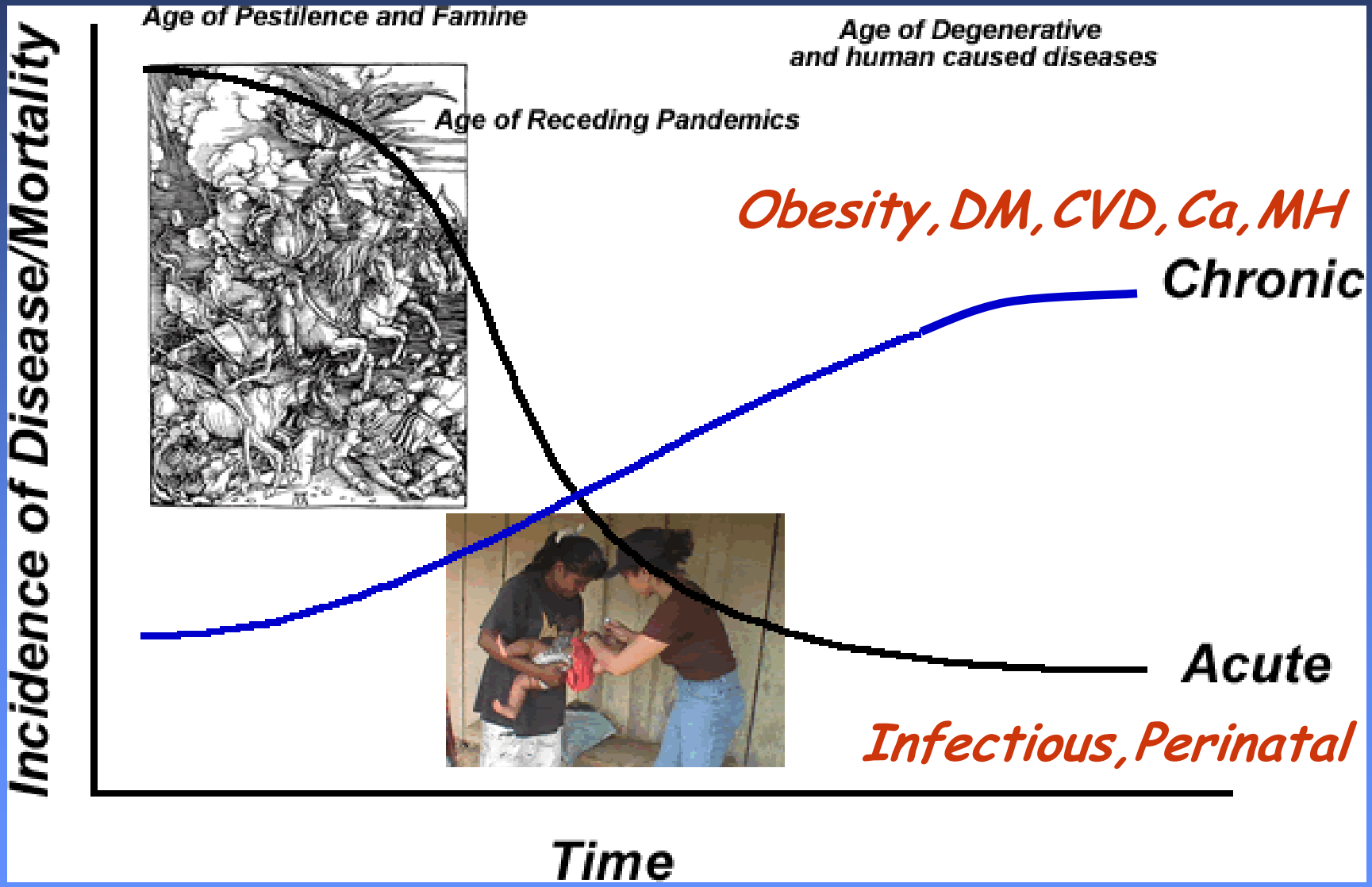
Obesity → Diabetes, CVD

- Leading causes of death/disability in developed world

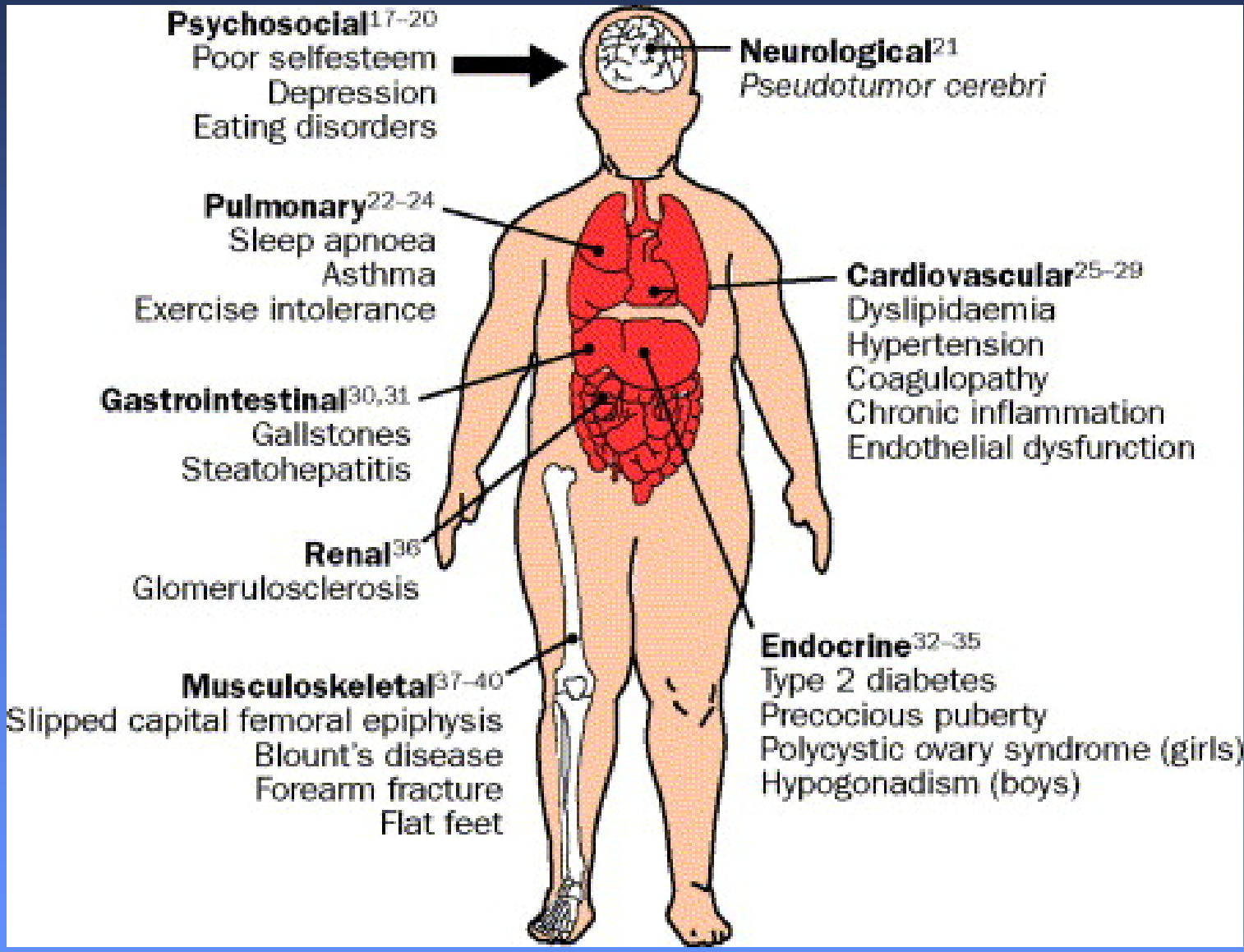
Obesity → Diabetes, CVD

- Leading causes of death/disability in developed world
- Emerging in developing world
  - Nutritional/epidemiologic transition

The Epidemiologic Transition



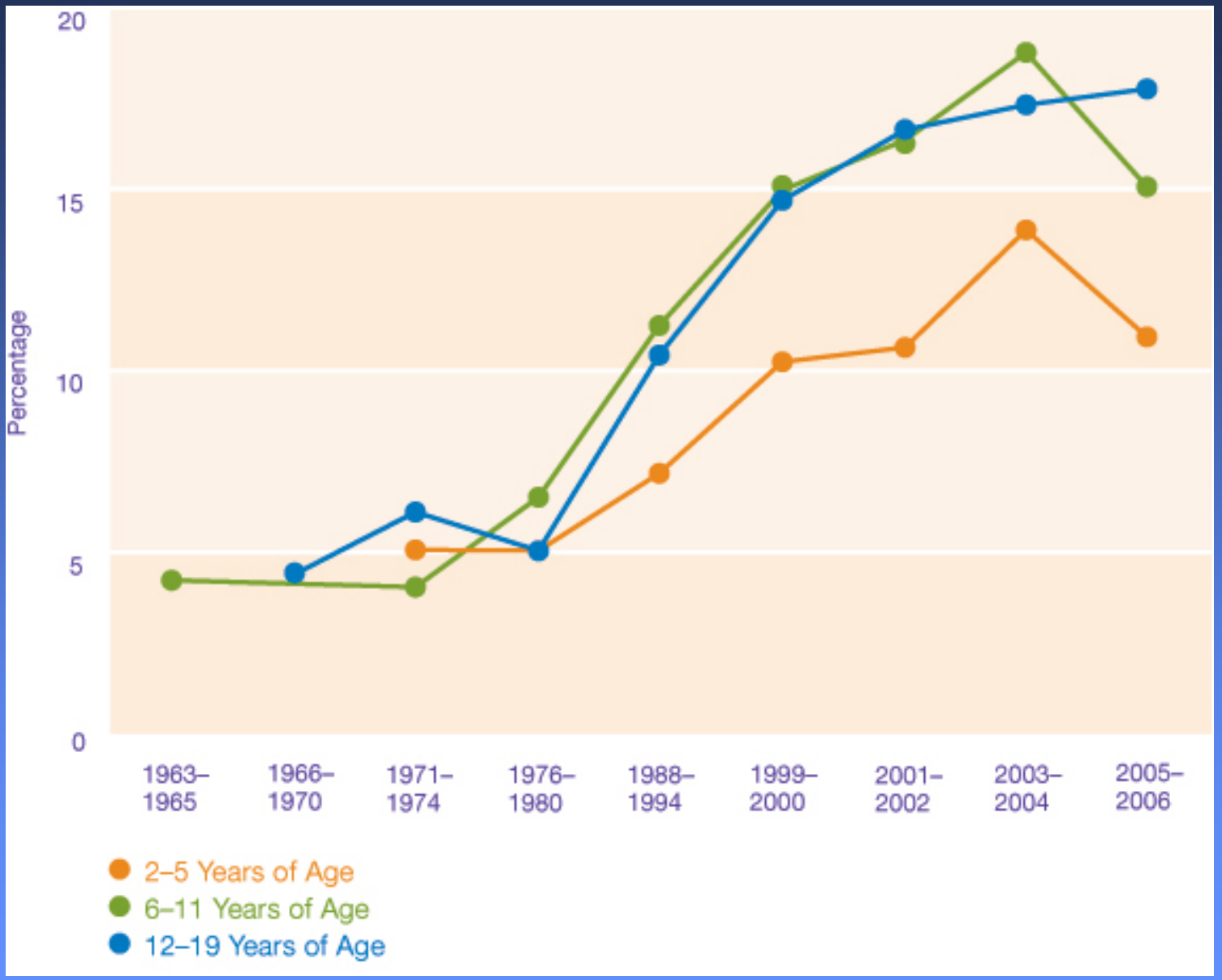
Medical Complications of *Childhood* Obesity



Ebbeling et al., Lancet 2002

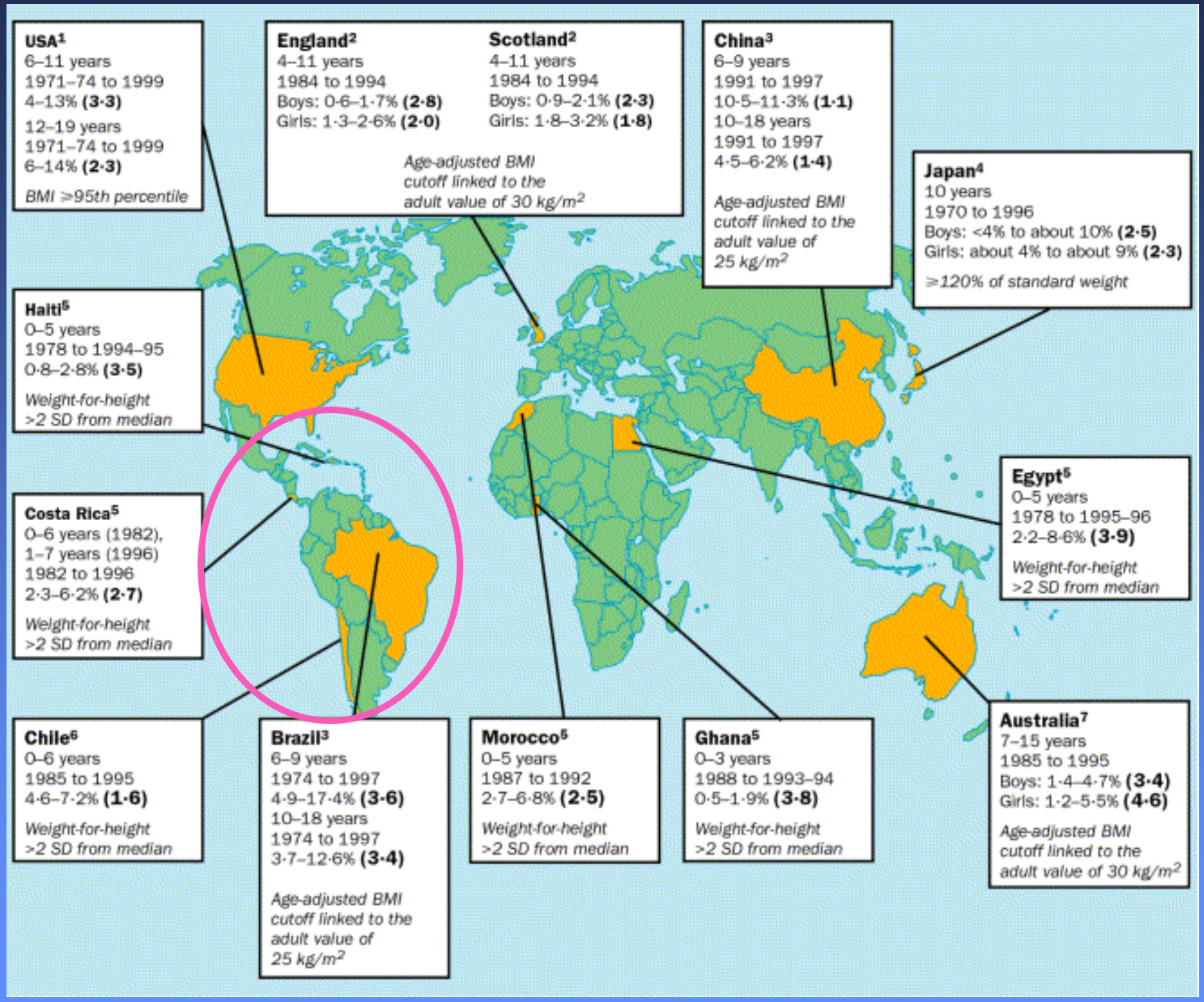
The U.S. Childhood Obesity Epidemic

BMI >95th %'ile



US DHHS, 2001; Hedley et al., 2004; Ogden et al., 2006, 2008

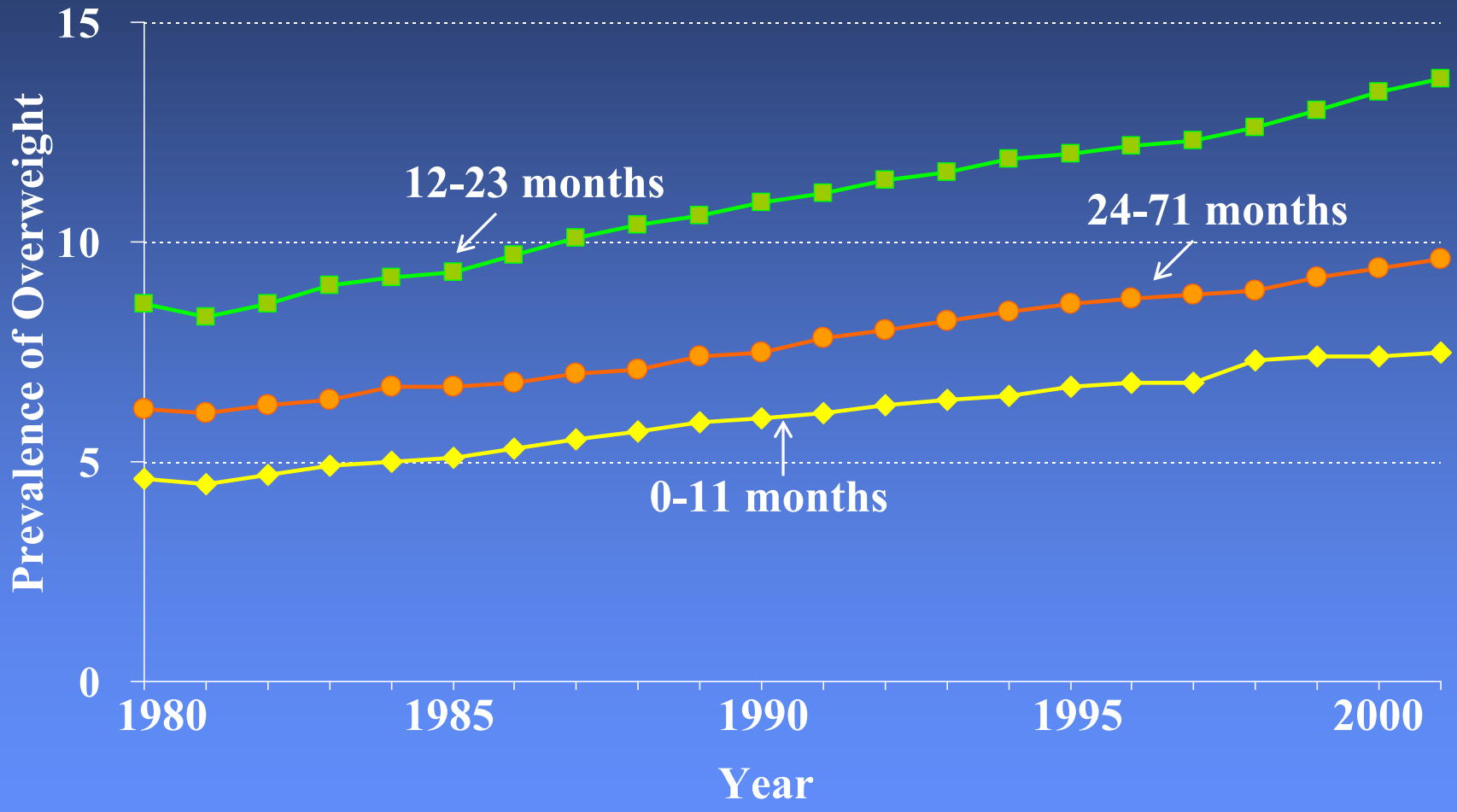
Obesity Increasing in Children Worldwide



Ebbeling et al., Lancet 2002

Obesity Epidemic in Younger Children

Including Infants



Kim et al., Obesity 2006; ~500,000 well child visits in Mass. HMO

Message

- The obesity epidemic includes even our youngest children
  - Prevention must start early

Message

- The obesity epidemic includes even our youngest children
  - Prevention must start early
  - Search for modifiable determinants at early stages of human development

Questions

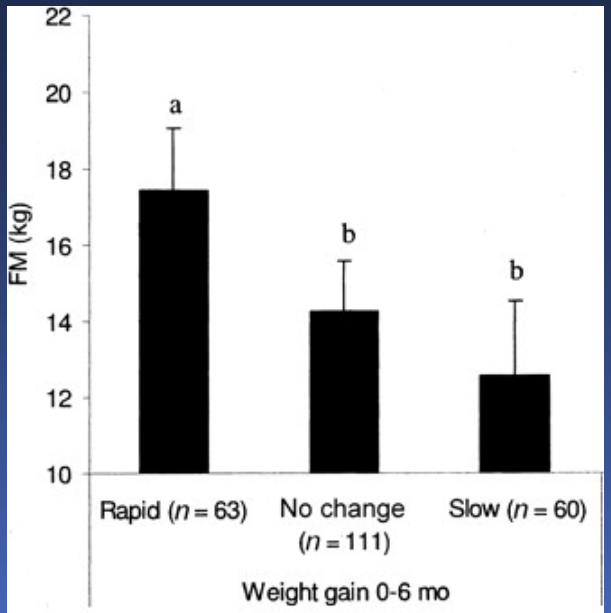
- To what extent is *growth* in early infancy associated with later obesity and its consequences, including diabetes?
- Do these associations apply in low- and middle-income countries as well?
- What are the clinical, public health, and policy implications?

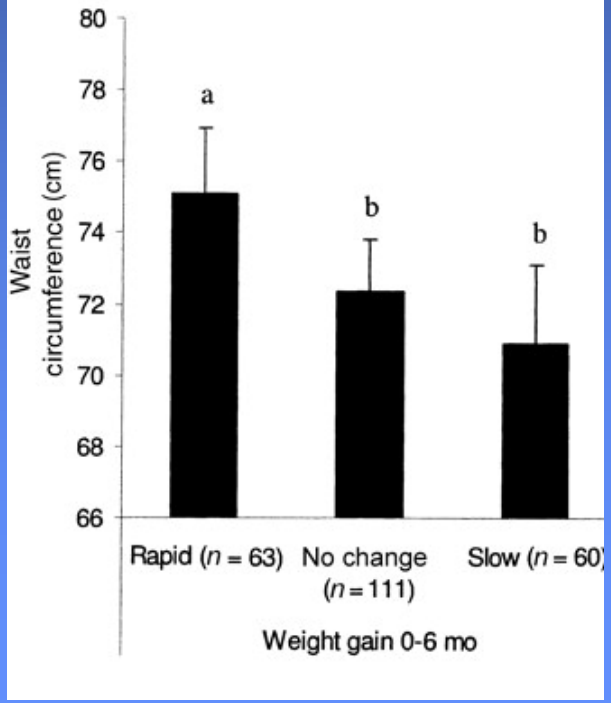
Weight gain in early infancy predicts later obesity

- Systematic Reviews
  - Ong & Loos, Acta Paediatr 2006
  - Monteiro & Victora, Obes Rev 2005
  - Baird et al, BMJ 2005
    - 10 studies, births 1927-1994
    - OR/RR 1.17 - 5.70
    - Consistent for obesity at different ages
    - Most only with body mass index (BMI) as outcome
- Refined outcome in recent studies
  - Body composition: Skinfolds, DXA, MRI, etc
  - Physiology: BP, metabolic factors, etc.

SWEDES study shows weight gain 0-6 mo associated with fat mass and waist circumference at 17 y (also BMI and FFM)

"no change" =
Δ SD -.0.67 to + 0.67

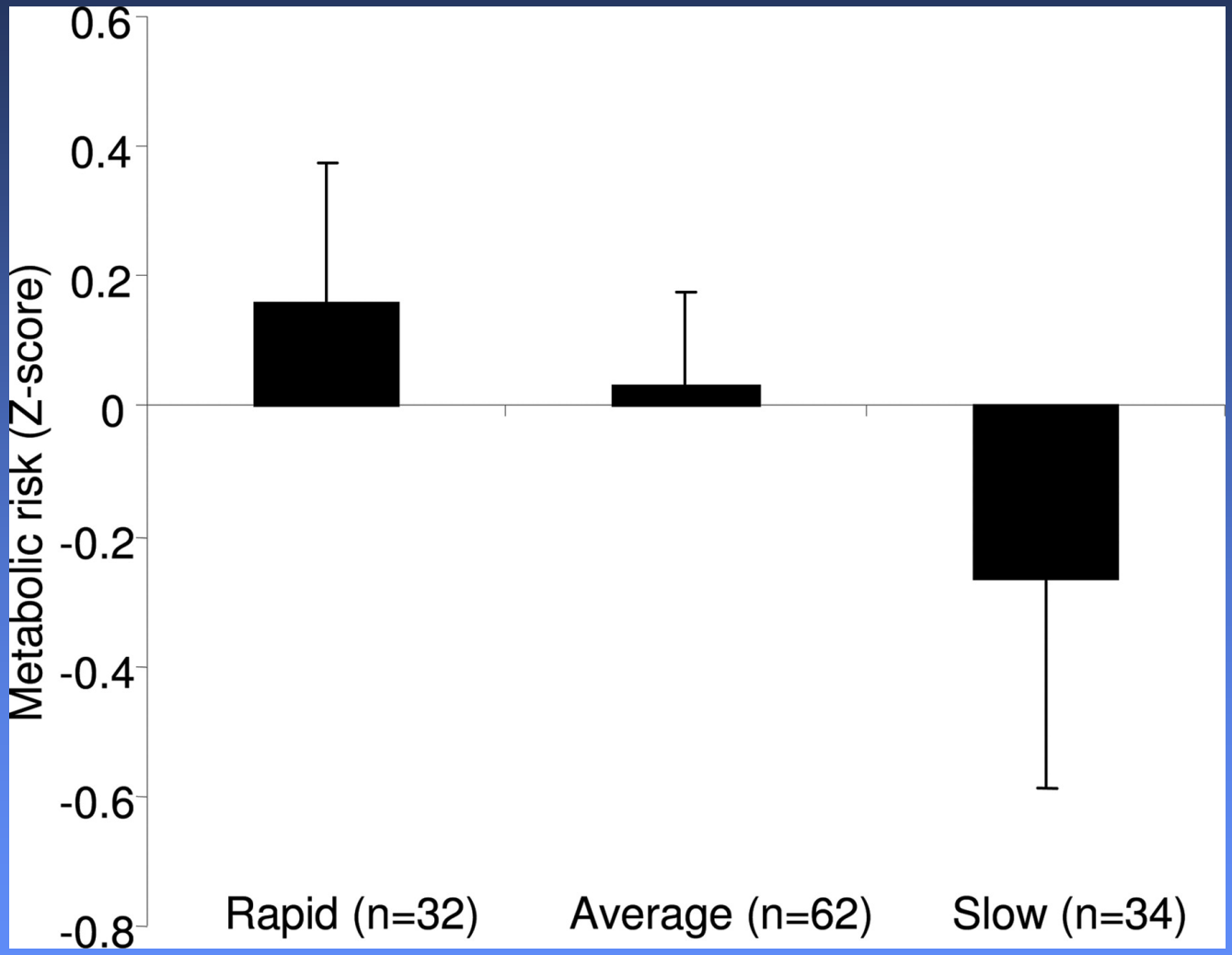




Ekelund et al, Am J Clin Nutr 2006; 83:324

…and with clustered metabolic risk score

WC, BP, TG, HDL-C, Glucose, Insulin



Ekelund et al. J Clin Endocrinol Metab 2007;92:98-103

Project Viva

A Study of Health for the Next Generation

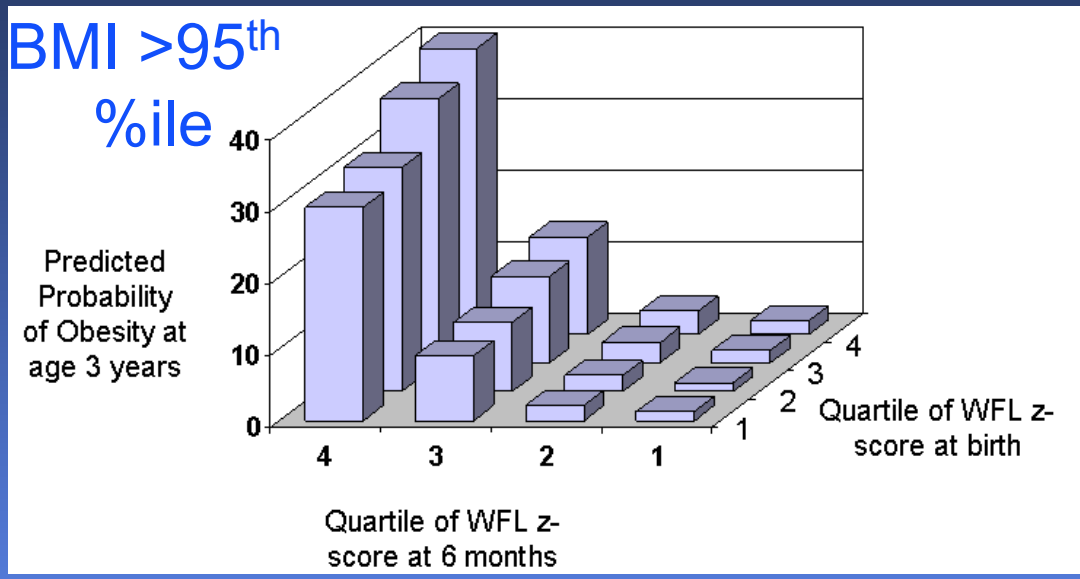
- An NIH-funded prospective cohort study of pregnant women and their offspring
  - To study pre- and peri-natal influences on outcomes of infancy, childhood, adulthood
    - Pregnancy—preterm birth, fetal growth, PE, GDM
    - Childhood—growth/obesity, CVD risk factors, asthma/atopy, cognition/behavior
    - In moms, postpartum weight retention, depression
  - Currently completing 7-year visits

Infant Growth
Project Viva

- Measured weight and length at birth at and 6 months
  - WFL z-score at 6 months adjusted for WFL z-score at birth = Change in WFL-z

Weight-for-length gain in 1st 6 m predicts higher 3-y obesity and BP

Taveras et al, Pediatrics 2009; 123:1177



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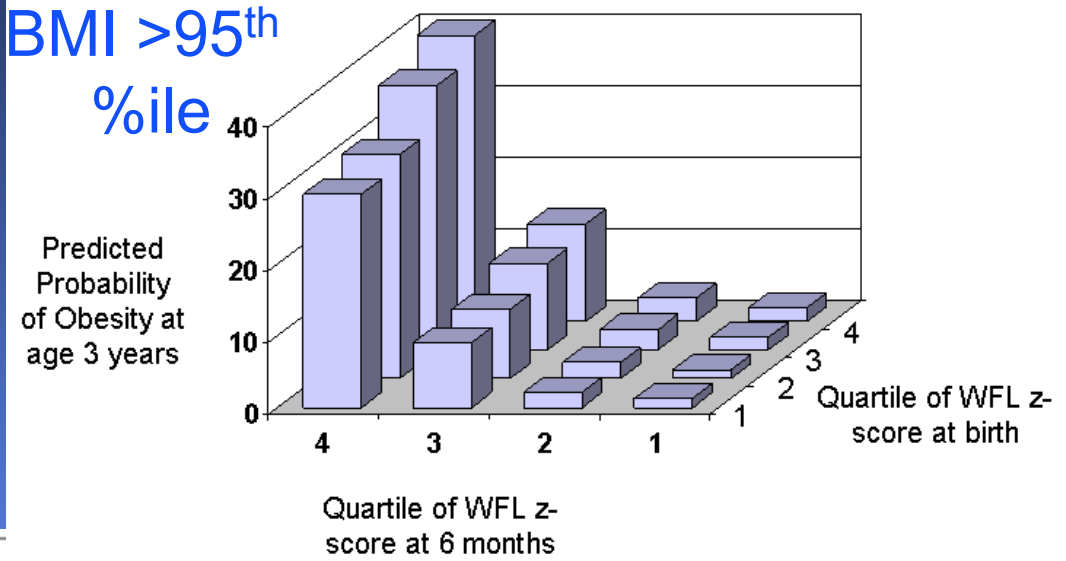
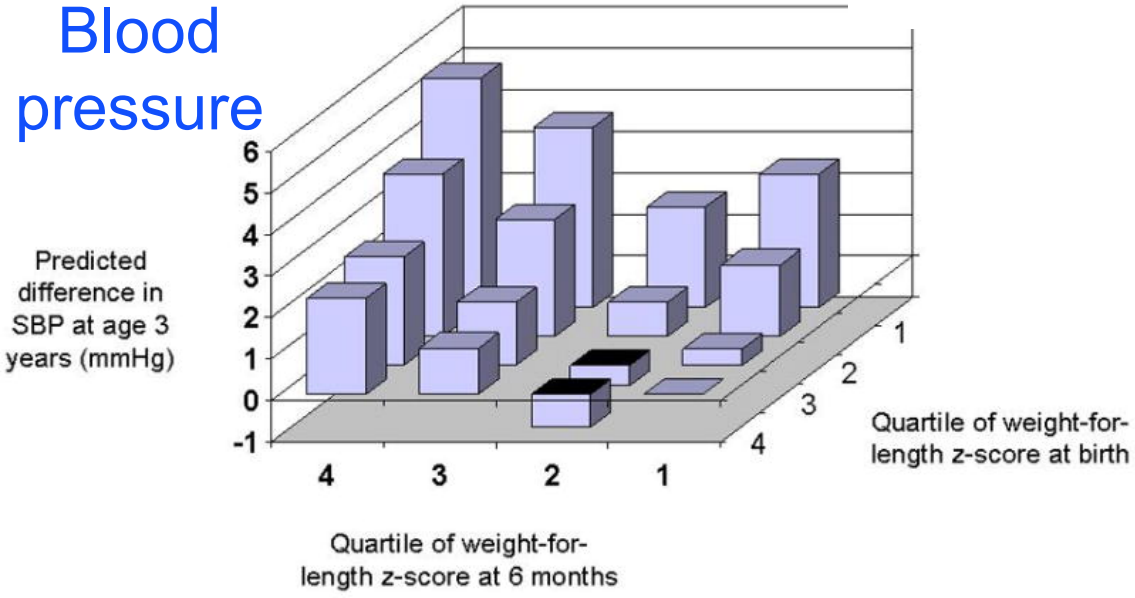
BMI >95th %ile



Blood pressure



Belfort et al., J Pediatr 2007; 151:670

Summary

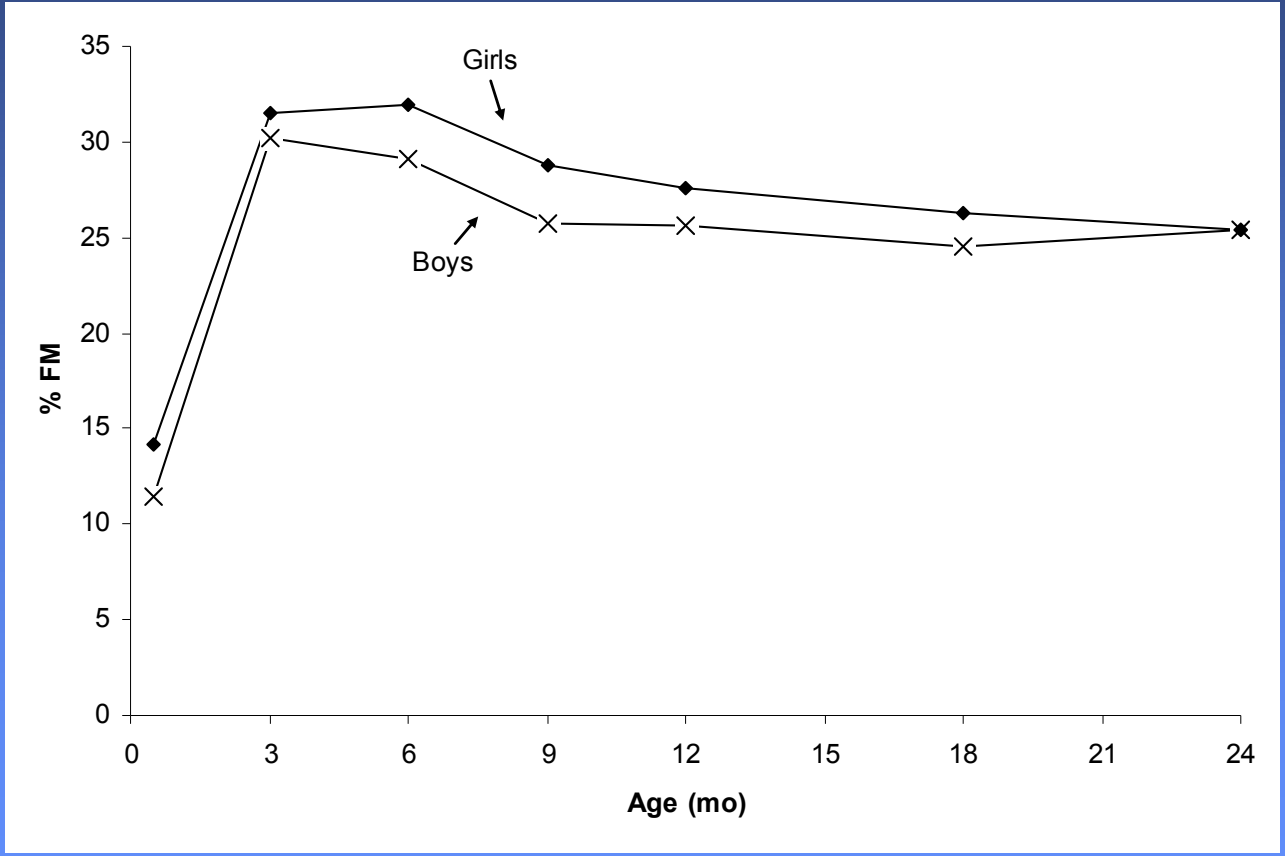
Weight gain in 1st months of life

…in most studies first 3-6 months…

is associated with later BMI, adiposity, and measures of cardiometabolic risk

Biological Plausibility

Weight gain in the first few mo is primarily gain in fat, whereas fat-free mass accumulates preferentially after that age

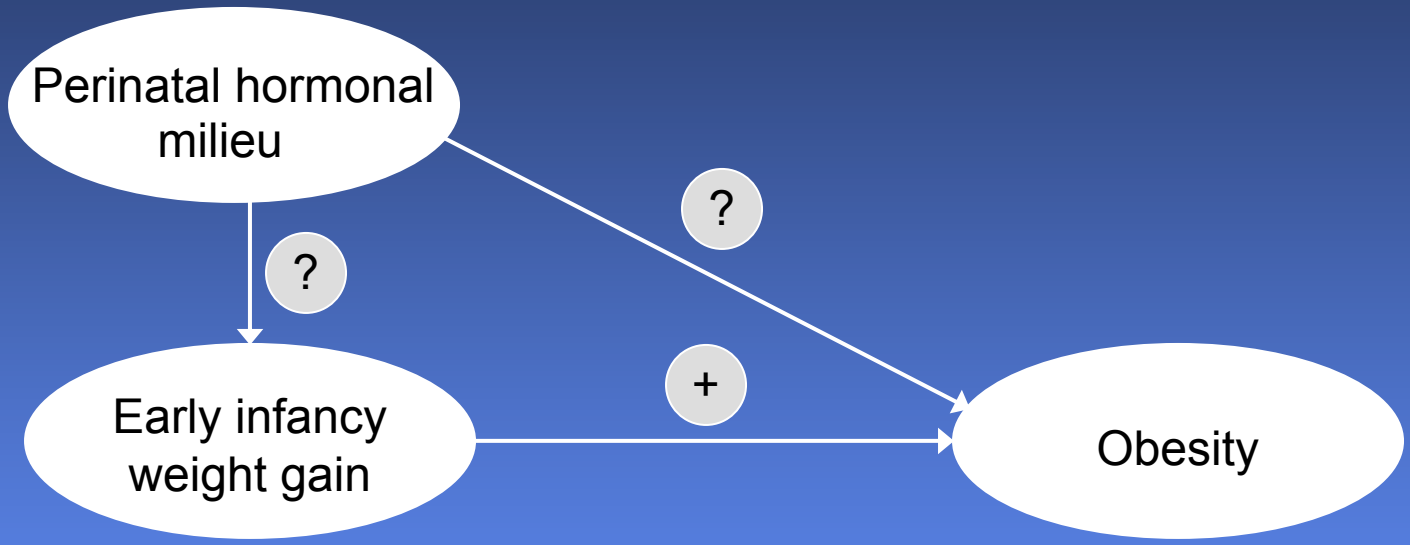


K Ellis et al.

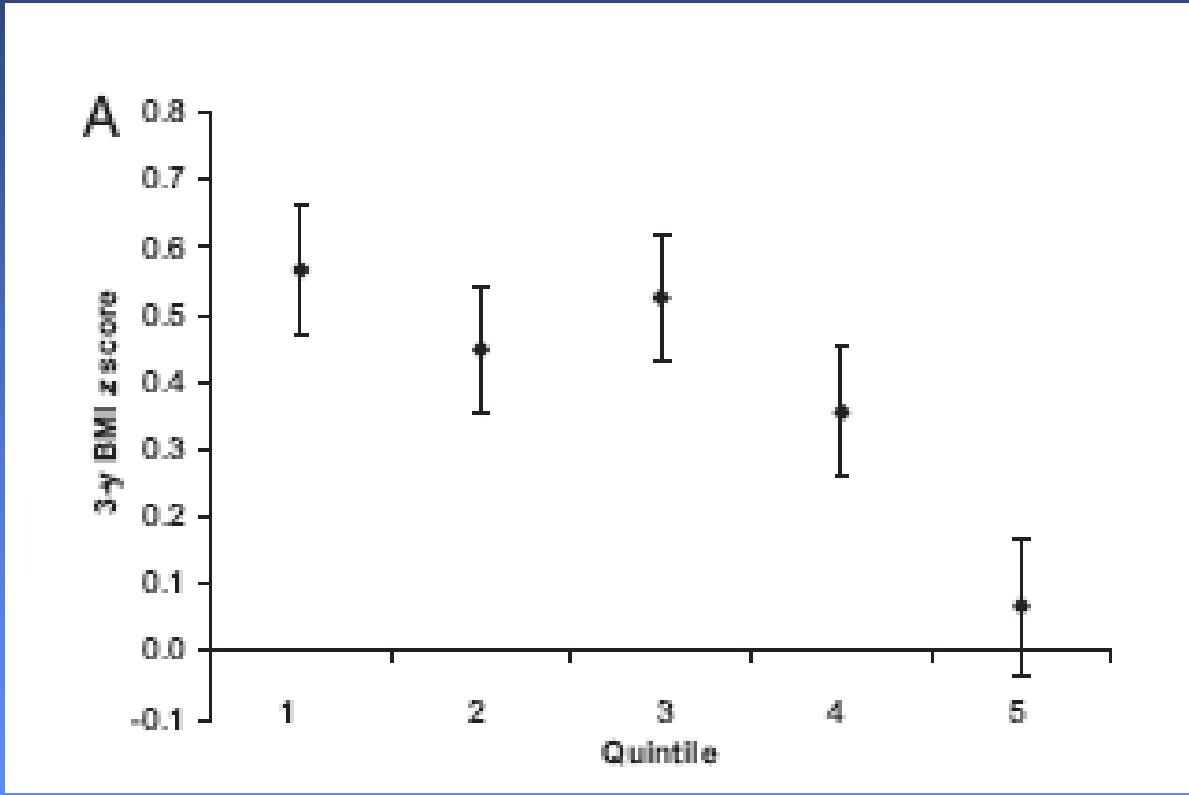
What are the determinants of infant growth?

…that also predict later obesity

"Beyond infant feeding"


Perinatal hormonal milieu
?
?
Early infancy weight gain
+
Obesity

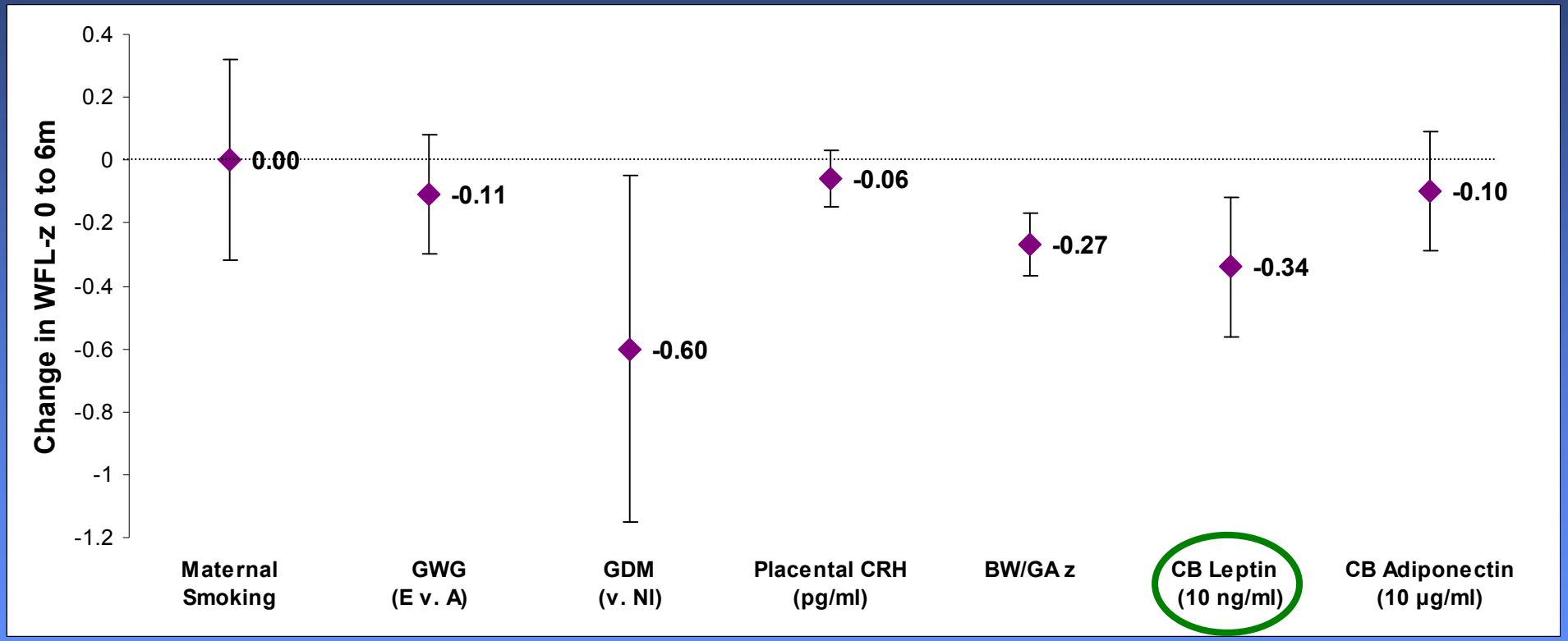
Cord blood leptin predicts lower 3-year BMI z-score



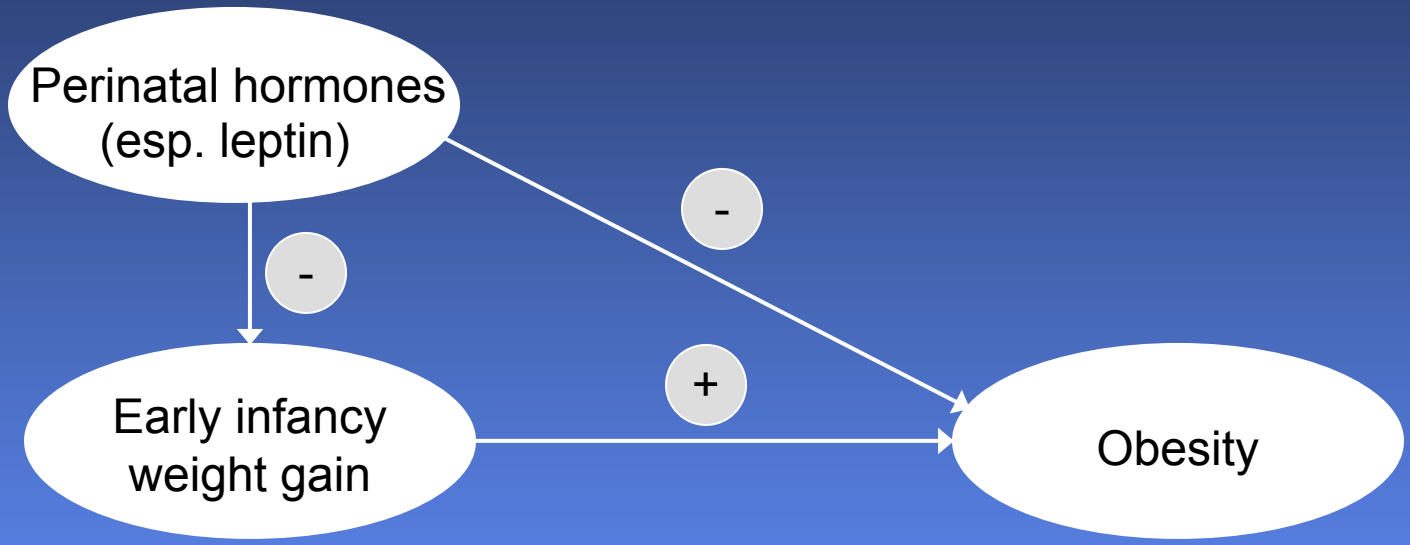
Mantzoros et al. Pediatrics 2009;123:682-689

Modifiable Predictors of Childhood Obesity

Which ones also predict early infancy weight (WFL) gain?



M. Parker et al., J Pediatr in press


Perinatal hormones
(esp. leptin)
-
-
Early infancy
weight gain
+
Obesity

Summary
Developed countries

- Weight gain in early infancy strongly predicts later obesity and cardio-metabolic risk factors
- Infant feeding may not be the main explanation
- Appears to be entrained pre/peri-natally by endocrine factors
  - Esp. leptin?

Does infant weight gain predict obesity in low/middle income countries?

- Consortium on Health Oriented Research in Transitional Societies (COHORTS)
  - 1982 Pelotas (Brazil) Birth Cohort
  - Institute of Nutrition of Central America and Panama Cohort (Guatemala)
  - New Delhi (India) Study
  - Cebu Longitudinal Health and Nutrition Survey (Philippines)
  - Birth to Twenty (South Africa)

Infant weight gain and obesity-metabolic-CV outcomes

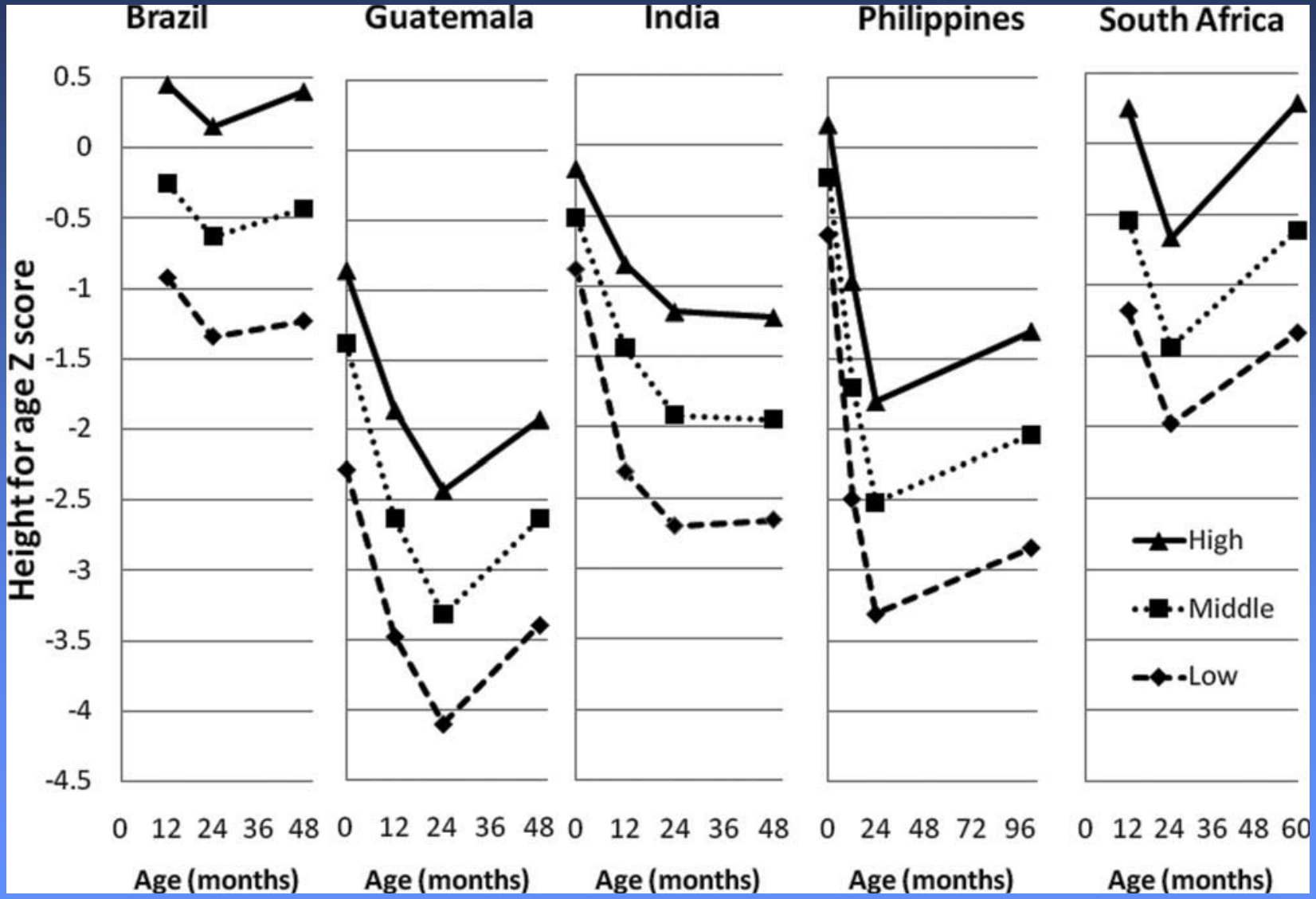
- In COHORTS, weight gain in first 2 y of life predicts
  - Better schooling
  - Higher BP but not more so than weight gain later in childhood
- In Pelotas
  - Weight gain after 2 v. before 2 y predicts
    - Waist circumference and WHR
    - Lipid levels

Timing of growth effects different in lower v. higher income settings?

- Possible, but
  - In COHORTS, gain in *length* in 1st two years predicts adult stature, and
  - Length faltering in 1st two years is common
  - Therefore, beneficial effects of weight gain could be due to linear growth

Length/height-for-age z-score in childhood

Stratified by thirds of attained adult height



Stein et al. Am J Hum Biol 2010; 22:353-359

Stunting & overweight now more common than wasting in N.E. Brazil

Table. Prevalence of extreme anthropometric measurements in children under five years. State of Alagoas, Northeastern Brazil, 2006.

Age (months)	n	Underweight[a] (%)	Wasting[b] (%)	Stunting[c] (%)	Overweight[d] (%)
≤ 6	202	2.0	2.5	7.4	9.9
6.1 to 12	175	5.1	0.0	10.3	12.6
12.1 to 24	330	3.0	1.5	12.1	11.5
24.1 to 36	276	2.2	0.4	14.1	8.3
36.1 to 48	242	2.1	1.2	7.9	9.5
48.1 to 60	161	3.7	1.9	8.1	5.6
Total	1,386	2.9	1.2	10.4	9.7

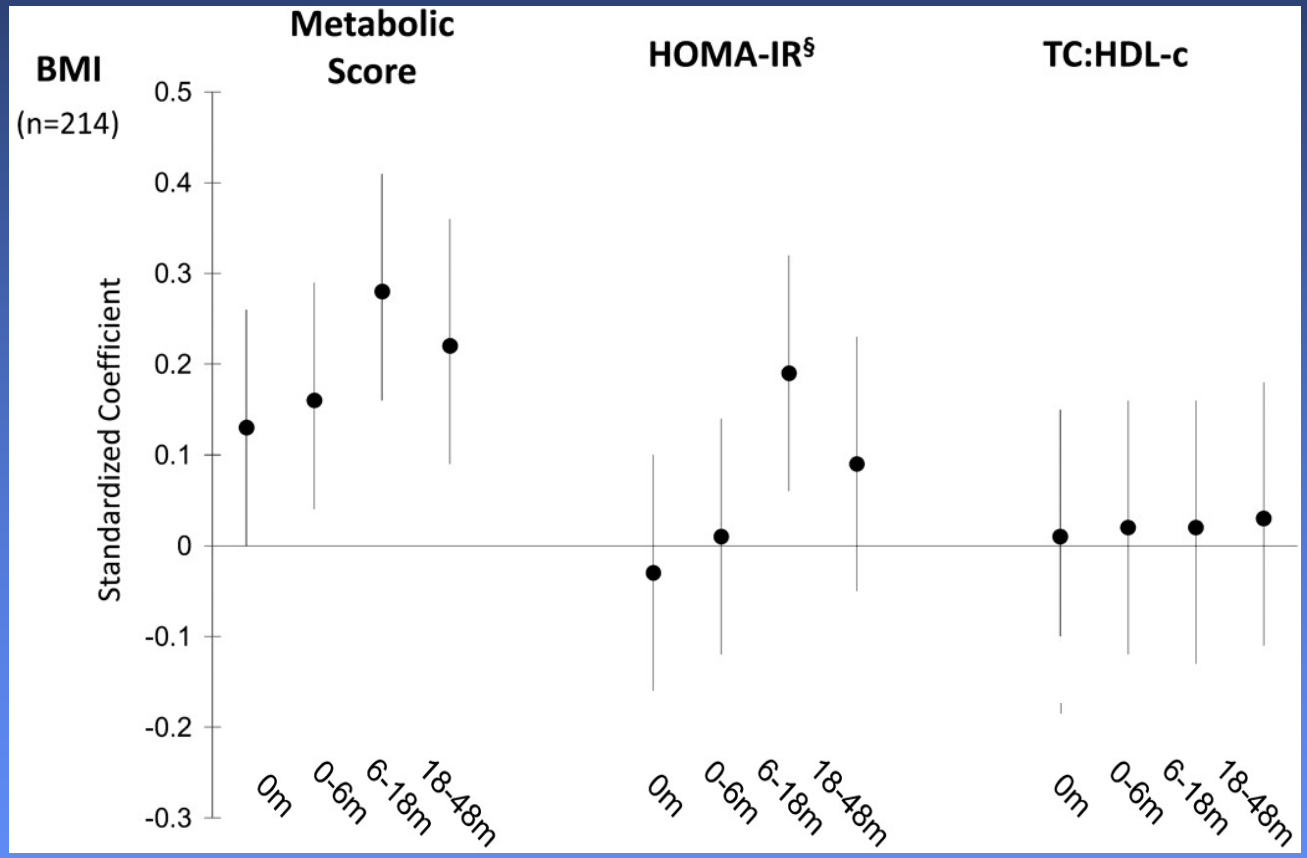
[a] Weight-for-age z-score < – 2
[b] Weight-for-height z-score < – 2
[c] Height-for-age z-score < – 2
[d] Weight-for-height z-score > 2

Ferreira & Luciano, Rev Saúde Pública Epub Feb 26, 2010

Timing of growth effects different in lower v. higher income settings?

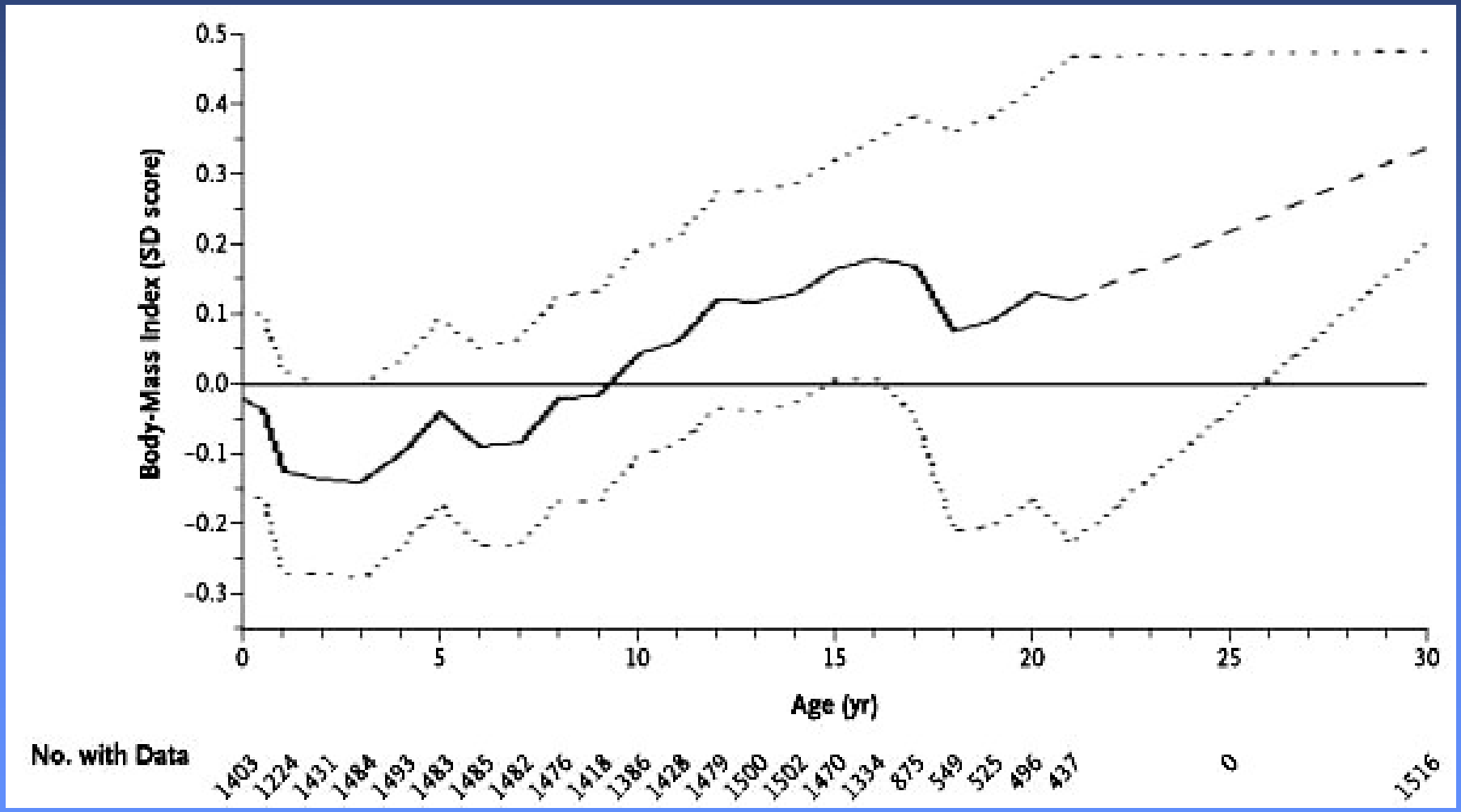
- Possible, but
  - In COHORTS, gain in *length* in 1st two years predicts adult stature, and
  - Length faltering in 1st two years is common
  - Therefore, beneficial effects of weight gain could be due to linear growth
  - Need information on weight-for-length
    - [Even better—body composition]

BMI gain predicts 4-year metabolic score (Waist/height, glucose, insulin, TG, HDL-C), but not HOMA-IR or TC:HDL-C in Chile



Corvalan, C. et al. Am J Clin Nutr 2009;90:547-555
Chilean National Nursery School Council Program

Lower initial BMI & steeper child trajectory predicts IGT or DM in India compared with cohort as a whole (0.0)

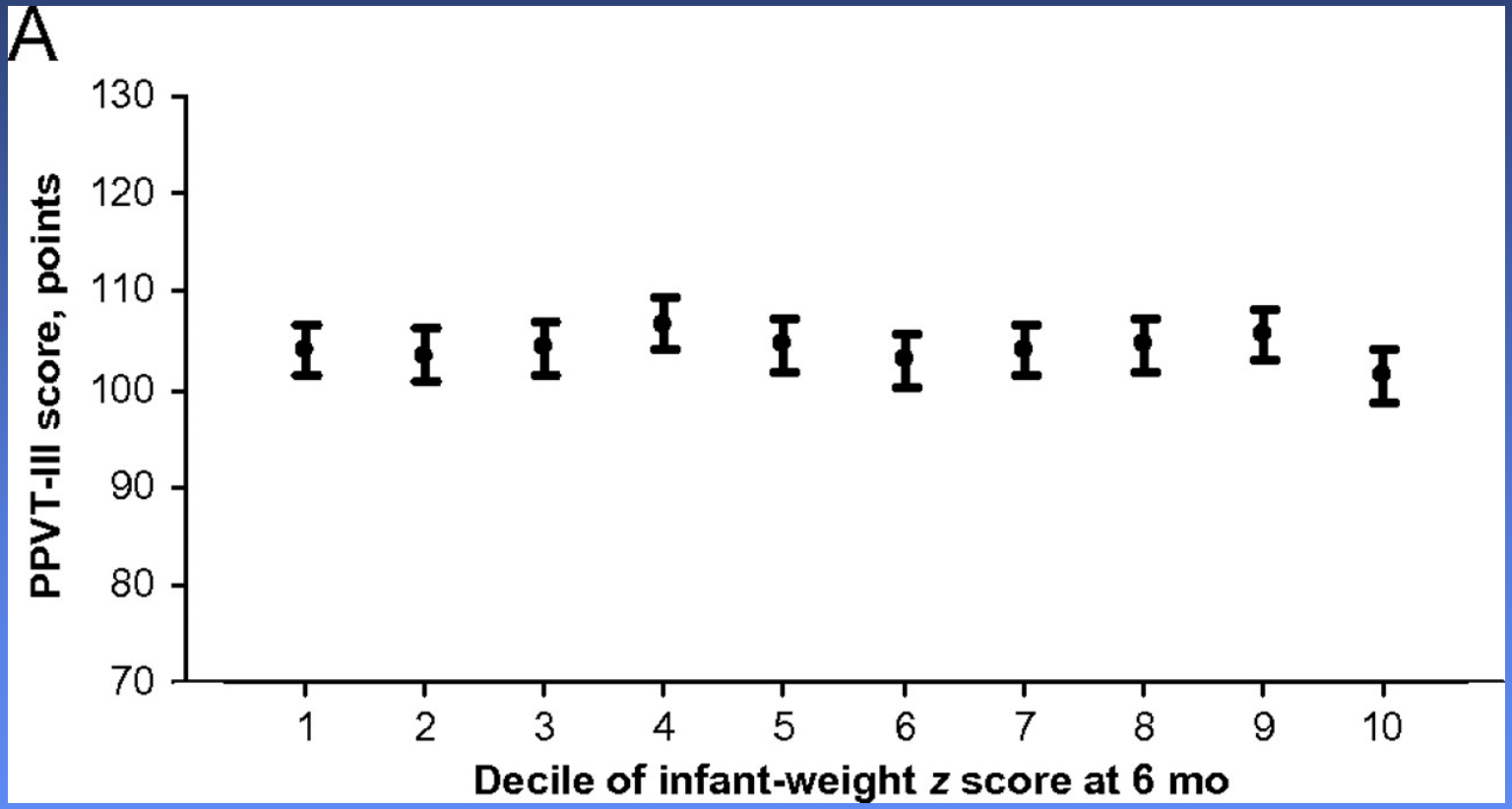


Bhargava, et al., NEJM 2004; India

Reduce Excessive Infant Weight Gain?

- What is optimal weight gain?
- Could be different for different kids
  - Weighing benefits v. risks
  - Obesity/CVD v. neurocognition
  - Full term v. premature
  - Low/middle v. higher income populations

Weight (WFL) gain in early infancy does not predict 3-year cognition



Belfort, M. B. et al. Pediatrics 2008;122:e689-e695

Reduce Infant Weight Gain?

- What is optimal weight gain?
- Could be different for different kids
  - Weighing benefits v. risks
  - Obesity/CVD v. neurocognition
  - Full term v. premature
- How to achieve the optimal??

Research Directions

- Linear growth v. excessive weight gain
- Body composition
  - Techniques appropriate for longitudinal epidemiologic studies in babies
- Countries in transition
  - Stunting in combination with obesity
- Racial/ethnic minorities

Clinical/Public Health/Policy Implications

- Optimal gain in length in first 2 years
  - Nutrition, infection
- Do not overfeed term SGA infants
- Otherwise, could do more harm than good by trying to change infant growth without knowing more about phenomenon, determinants, modifiability