The History of Baby Food in the United States

NIH Workshop on the Prevention of Obesity in Infancy and Early Childhood
30 October 2013

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Historical Research

- Qualitative

  Multiple sources

  “Proof”: Citation, saturation, triangulation

- Purpose

  Developing a narrative

  Making a larger argument

  Avoiding the “mistakes of the past”

The Industrialization of Baby Food

- An invented product with positives
- Yet also negatives:

  Displacement of breastfeeding

  Primed an “industrial palate”
- Emblematic of the complicated role of “mother-consumer”

Snapshot of Shifting Infant Feeding Advice and Practice

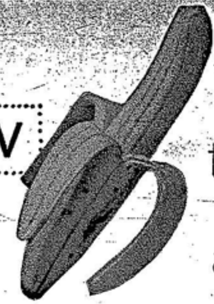
- Late-19th c.: Breast feeding; solids late in first year
- 1920s: More use of milk-based formulas (bottle feeding); solids at 6-8 months
- Post-WWII: Bottle feeding; solids at 4-6 weeks

Baby Food Became a Rite of Passage:

- Discovery and promotion of vitamins
- Medicalization of childbirth and infancy
- Changing philosophies of childrearing
- Industrialization of food supply
- Post-war American society/cultural climate
- Inconclusive medical evidence over early feeding of solids
- Advertising/marketing

"The Tiniest Babies"

Something NEW to coax a COO!

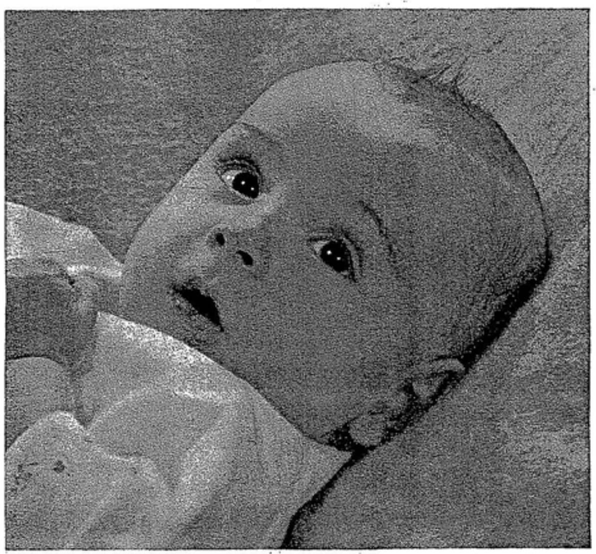


EVEN the tiniest babies have a way of knowing a good thing when they taste it. (And showing their appreciation in a special cooing language all their own.)

Pure pleasure seems to be the natural reaction to Gerber's spanking new Strained Bananas. For they're made of *fully-ripe* fruit—specially processed to preserve the delicate, true-banana flavor and appealing color. What's more, Gerber's Strained Bananas have a velvety smoothness that feels particularly pleasant on baby's tongue.

As you probably know, many doctors recommend bananas as an early supplementary food . . . not only because bananas are very palatable to most babies, but because they provide the energy-giving calories growing babies need. Ripeness of the fruit is stressed . . . because ripeness is the key to easy digestibility. And with Gerber's Strained Bananas you are assured of a just-right degree of ripeness.

P.S. Don't be surprised if you find yourself stealing more than a spoonful or two.



P. P. S. Little smiles are apt to appear after servings of Gerber's other starting solids: Cereals, Strained Meats and Strained Egg Yolks. All famous for delicate, but distinctive flavors and nice-on-the-tongue textures. Each one is designed to fulfill a specific nutritive need in the early infant diet.

Babies are our business... our only business!

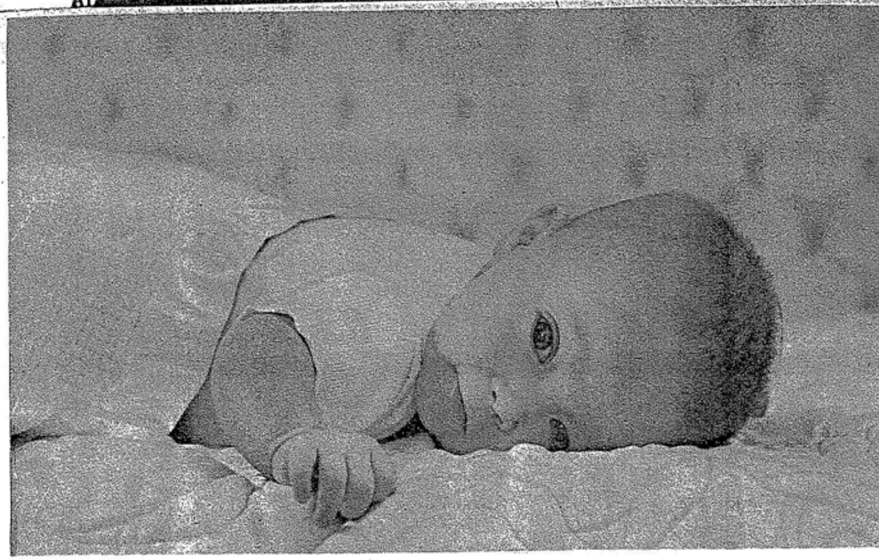
Gerber's® BABY FOODS

Fremont, Michigan

4 Cereals • Over 60 Strained and Junior Foods, Including Meats

(Helpful information for next to nothing. See pages 41 and 42)

“Ready for the Next Step?



All set for the next step, honey?

Ready for something a little more solid in your diet, darling? Sure you are! For as you become increasingly active you need the added nourishment and the feeling of satisfaction that only solid food can give.

Before you know it, your baby, too, will be ready for solid food—usually cereal at the start. When your doctor says baby is all set for this step, you'll find Gerber's Cereals most helpful. First off, Gerber's Cereals are enriched with the supplementary iron most babies need shortly after birth. They are also fortified with bone-building calcium and the important B-vitamins that aid in baby's growth.

Then there's texture! Gerber's Cereals have the creamy-smooth consistency that feels particularly pleasant on a delicate little tongue. They're thoroughly pre-cooked—all you have to do is add milk, formula or water, and serve. (A soupy mixture at first makes the texture more familiar and, therefore, more palatable to baby.) Then too, Gerber's Cereals have the mild, pleasing flavors just right for wakening taste buds. Four in all – Rice, Barley, Oatmeal and Cereal Food (a mixed cereal)—to stimulate mealtime interest.

For your convenience in introducing cereals to baby: Gerber's new Cereal "Quads"... small-sized boxes of all four... compactly wrapped together in sparkling cellophane. Easiest way in the world to let baby sample the cereal variety he wants and needs.

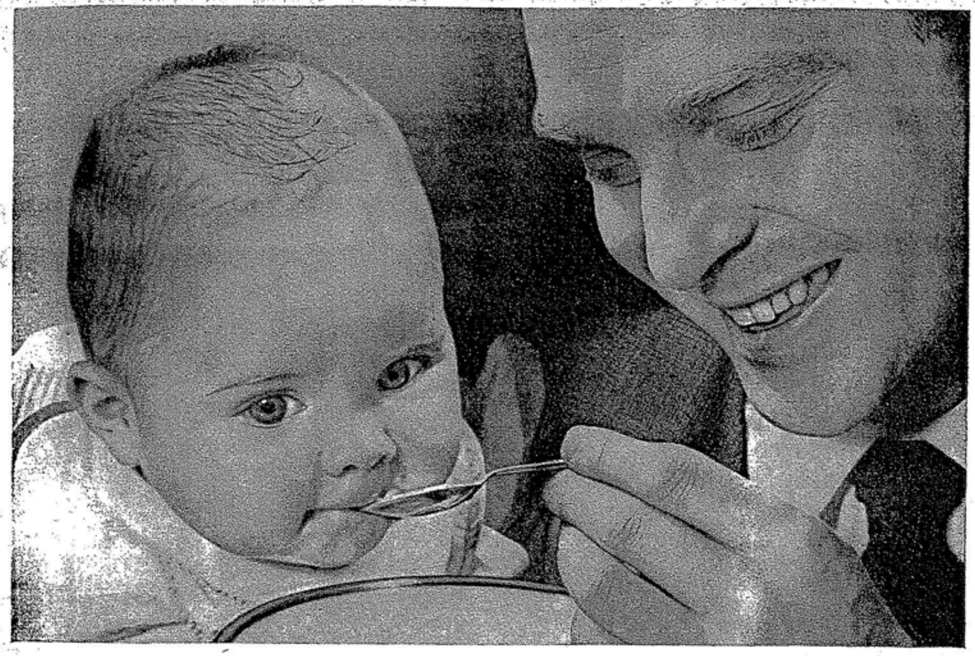
Babies are our business... our only business!

Gerber's®

BABY FOODS

4 CEREALS · 60 STRAINED AND JUNIOR FOODS, INCLUDING MEATS

“Smooth Texture”



WHEN GOOD FELLOWS GET TOGETHER...

It's generally fair weather — when Daddy gives Baby one of Gerber's Cereals! Even tiny infants appreciate the smooth texture right from the start! Gerber's Cereal Food, Strained Oatmeal and Barley Cereal require only a little added milk or formula — and they're ready to serve! Each has added iron, calcium and important B complex vitamins. They'll help keep your baby full of bounce and beams.

Making the food babies like — with the nutritional elements doctors approve—is all we do. *Nothing* else! No wonder we've such a large following of small folks! *Only* Gerber's have everything—from starting Cereals through Strained and Junior Soups, Vegetables, Meats, Fruits and Desserts. Their True-Flavor and Perfected-Texture are famous coast to coast.

Newest claim-to-fame trio, Meats...Gerber's delicious, ready-to-serve meats! Beef, Veal and Liver prepared from Armour selected cuts with important proteins. Strained for tiny babies, Junior (chopped) for older tots. No scraping or cooking necessary. And so money-saving! Gerber's Meats save you as much as 50% over those you'd prepare at home.

... our only business! —— Gerber's

January, 1950

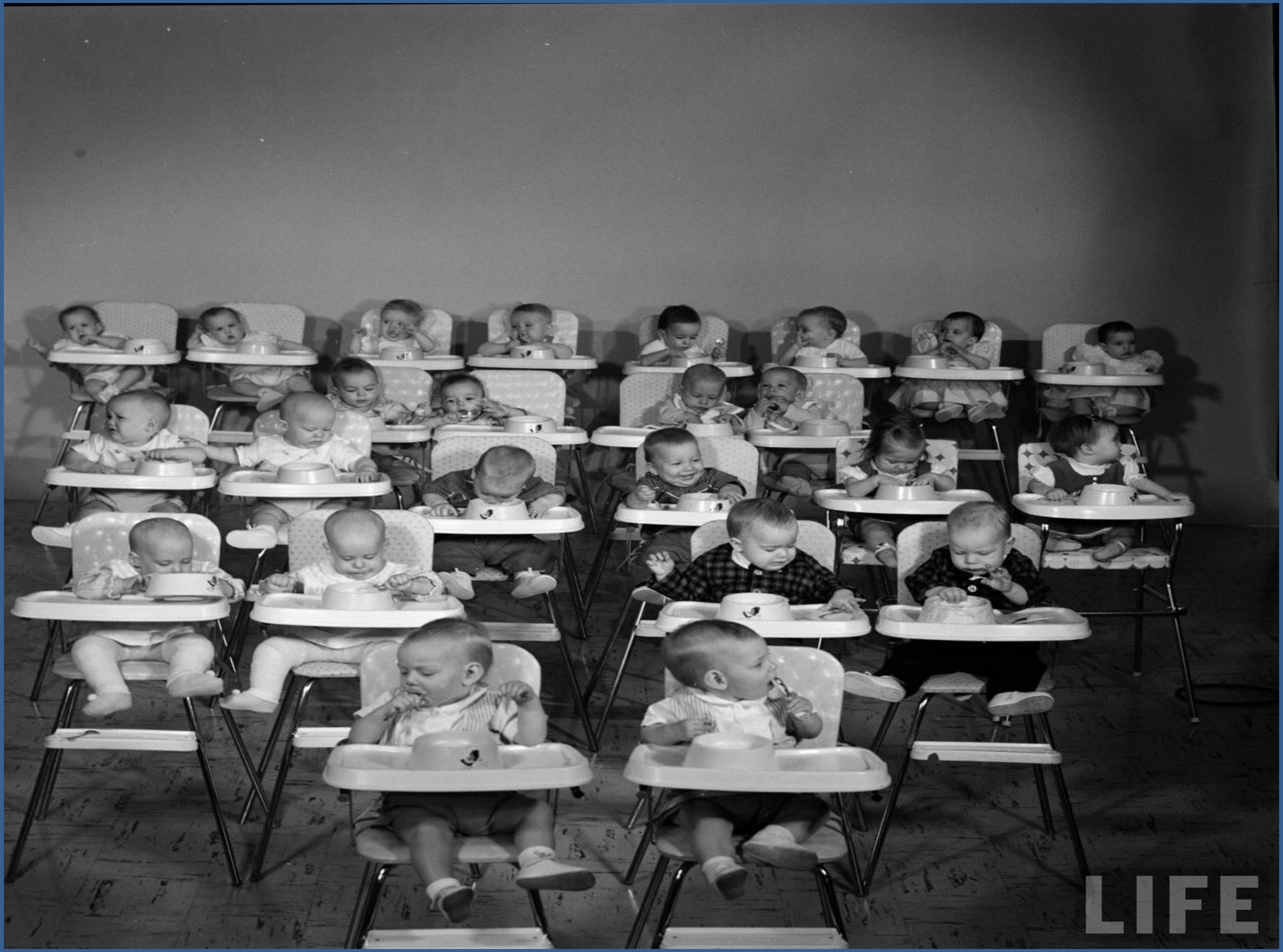
(Helpful information for next to nothing. See pages 49 and 50)

"Babies simply love new Beech-Nut Fruit Dessert!"

The Changing Landscape of Supermarkets

Baby food display in grocery story, 1941.

date 11/4/53 Shaffer's Mkt. Elsmere, Del Box 3 Display



Baby Food Tasting

LIFE Magazine, 1962

Beech-Nut Labels, ca. 1960s

Reevaluation of Commercial Baby Food
Late 1960s-1970s:

- Breastfeeding in decline
- Medical studies re: additives (MSG, modified starch, salt, sugar, nitrites)
- Conclusive studies on early solid feeding
- Critics of international advertising/marketing
- Critics of baby food labeling

Obesity Linked to Early Use of Baby Food

NEW ORLEANS (UPI) —American mothers who start their infants on baby food too soon may be contributing to obesity and degenerative diseases later in life, Johns Hopkins University researchers said Wednesday.

A study by the Johns Hopkins school of hygiene and public health presented to the American Public Health Assn. suggested that "premature introduction of infant foods appears to be a critical factor in excessive nutrient intake" by babies.

The Hopkins scientists said that high nutrient intake in early life was suspected of being a prime cause of obesity and degenerative diseases later in life.

The research paper, presented by Dr. David M. Paige, indicated that at the age of 2 months, "the nutrition needs of the infant are adequately met through formula, breast milk or milk."

97% of the infants in the study were taking dry cereal and 70% were eating strained fruit.

"It is important that mothers do not yield to the strong commercial and peer pressures to introduce baby foods too soon," the researchers said. "Milk foods alone provide adequate nutrition for most babies for the first six months of life."

SLIMLINE
ROSE DOSTI
Los Angeles Times (1923-Current File); Mar 15, 1973;
ProQuest Historical Newspapers Los Angeles Times (1881 - 1987)
pg. K25

SLIMLINE

Reevaluating Feeding of Infants

BY ROSE DOSTI
Times Staff Writer

Infantile obesity is reaching a dangerous peak and steps should be taken to reevaluate infant feeding.

So thinks Dr. Derrick Jelliffe, head of the division of population, family and international health, school of public health, UCLA.

Infantile obesity has been on the increase over the last five years. "My guess is that the change in unbiological patterns of infant feeding is responsible," Dr. Jelliffe said.

"The fat baby has always been desirable in Western and Eastern cultures. We're stuffing more calories down our children's throats more than ever. The age group can be coaxed easily to eat. It doesn't have the controls."

Dr. Jelliffe thinks that change in pattern from breast to bottle feeding has put the controls in mothers' hands instead of the natural supply and demand situation of breast feeding. Earlier introduction to solid foods, such as pureed meats, fruits and vegetables and cereals, also has added calories to the child's diet.

"In 1896 a child was 1 year old before he was introduced to solid foods. Now more solid foods are going down with no really good reason. The reason allegedly given is to provide the child with more iron earlier in life and to introduce him to a wider nutritive diet sooner," he said.

"But there is no concrete proof that a widened diet does the child any better than a naturally limited one," said Dr. Jelliffe.

"Frankly, I think commercial pressure to widen the baby food market is responsible for extending the child's solid food feeding months earlier than necessary," he said.

According to Jelliffe, babies are being given double feedings—his milk and solids—causing an overconcentration of calories and unnecessary stuffing of solids with no controls.

"The problem with overfeeding is that the fat cells determined during the first year of life are the ones we are stuck with. Overfeeding will cause the fat cells to multiply. Those extra cells

Report Questions Solid Food for Baby

There is no nutritional advantage in introducing solid foods to babies too early, according to a report published in an issue of Nutrition and the MD., a newsletter for physicians.

"Solid food introduced before 5 months of age may result in overfeeding and expose the infant to bacteria it is not ready for," the report states.

The infant's neuromuscular system is not adequately developed until 6 months. It's this system that enables him to swallow solids, hold his head up or physically indicate that he is full.

Once the child is old enough for solid food, Nutrition and the MD advises the addition of new, simple foods one at a time at weekly intervals. Iron-fortified infant cereals mixed with human milk or formula is the most appropriate first food, according to the newsletter.

At 9 or 10 months, the report says, most infants are developmentally ready to feed themselves and indicate their own food preferences. By this time, the child should be eating a nutritionally balanced diet from the four food groups of milk, meat, vegetables and fruits and breads and cereals provided by either commerical or homemade baby foods.

The Alternative: Homemade

Renewed interest in making own

- Suitable technology: blenders, freezers, plastic
- Economics
- Health/Safety
- Quasi-feminist activity
- Anti-corporate act of defiance

Responses:

- Industry responds: MSG, salt and sugar removed, organics eventually
- Recommended age to introduce solids creeps back and forth (2-3 months, then 4, then 4-6, then perhaps on the earlier side re: allergies)
- Homemade continues, goes artisanal, commodified
- Commercial baby food sales remain solid
- Baby Food 2.0

The Industrialization of Baby Food

- An invented product with positives
- Yet also negatives:

    Displacement of breastfeeding

    Primed an “industrial palate”

- Emblematic of the complicated role of “mother-consumer”

Thank you!

Bi-directionality in the parent-child feeding relationship

Leann Birch
Center for Childhood Obesity Research
The Pennsylvania State University

How do we determine what interventions to prevent obesity in infancy should look like?

- Review the existing literature on "potentially modifiable" factors that affect infant growth?

- Many of the obvious choices involve modifying aspects of parenting/feeding practices

- However, this assumes that the direction of influence in the parent-child relationship flows primarily from parent to child.

“Responsive” feeding for obesity prevention?

- P caregiving contingent on C behavior & needs, developmentally appropriate, prompt, “caused” by C
- P observes C cues, interprets, acts
- RP associated with positive social, cognitive, health outcomes*;
- Can promoting C self regulation – of emotions, att’n, eating, impact early excessive growth, prevent childhood obesity?
- If RP is our secondary outcome, how do we measure it?
- Avoid controlling “nonresponsive” feeding practices
  - Pressure, restriction -- aren’t these a response to C?

*Eshel, Daelmans, deMello & Martines (2006) Responsive parenting: Interventions and outcomes: Bulletin of the World Health Organization

Bi-directional influence inherent in parent-child relations; “reverse causality” expected, desired*

- Little experimental evidence, most evidence on “potentially modifiable factors” is correlational
- selectiing “potentially modifiable factors” based on associations is risky, costly
- randomized experiments necessary to determine “potentially modifiable”
- testable conceptual models needed to answer Q’s re causality

*Responsive parenting is about promoting “reverse causality”

Do feeding practices (FP) influence child wt status?

- FP are associated with C wt but “reverse causality”?
- C wt status influences use of FP pressure, restriction
- If FP *causally* related to C wt,

  effects should be mediated via influence on C eating
- however few studies have tested for mediation by
  - manipulating feeding practices
  - obtaining measures of all three constructs:

    feeding/parenting, C eating, Cwt

Do feeding practices affect children's eating, wt status?*

Feeding practices

C growth, wt status

C intake, eating behavior, food preferences

* Ventura & Birch, (2008) Does parenting affect children's eating and wt status? IJBNPA, 2008

Changing “potentially modifiable” factors to affect infant intake, sleep, and wt status: SLIMTIME

- Feeding mode: promote breastfeeding
- “responsive” alternatives to “traditional” FP such as
  - pressure, restriction
- guidance on responding to C hunger, fullness cues
- reduce “feeding to soothe” as “default” response to crying
- promote adequate sleep, self-soothing, emotion regulation
- transition to table foods
  - when, what foods, portion size
  - promote acceptance of healthy foods (repeated exposure)

SLIMTIME lessons learned → INSIGHT

- SLeeping and Intake Methods Taught to Infants and Mothers Early in Life (SLIMTIME) Study (R56DK72996)
  - Pilot study conducted 2006-2008

- The Intervention Nurses Start Infants Growing on Healthy Trajectories (INSIGHT) Study (R01DK088244) & SIBSIGHT (R01DK099364)
  - Ongoing trial informed by pilot experience

SLIMTIME Study

- RCT with birth cohort intending to breastfeed
- Two home nurse visits – 2-3 weeks, 4-6 months after birth plus clinical research center visit at 1 year

	Introduction of Solids	Control
Soothe/Sleep	N = 42 2 interventions	N = 39 1 intervention
Control	N = 38 1 intervention	N = 41 0 interventions

Paul IM et al. Obesity, 2011

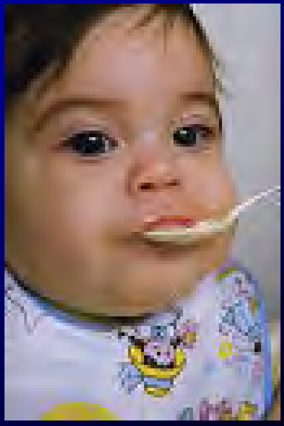
SLIMTIME Inclusion/Exclusion Criteria

- Full or near-term singleton
- No significant morbidities
- Primiparous mother intending to breastfeed
- Pediatric primary care at University-affiliated clinic
- English speaking mother
- Live within a ~30 minute of Hershey

SLIMTIME Interventions

- "<u>Soothe/Sleep</u>" (2-3 weeks)
  – Crying ≠ Hunger; discriminate hunger vs. other distress
  – Soothing strategy: 5 S's (Swaddling, Side/Stomach, Shushing, Swinging, Sucking)
  – Day/night differences

- "<u>Introduction of Solids</u>"
  - delay introduction, hunger/satiety cues (2-3 wks)
  - repeated exposure to vegetables (~4-6 mos)



Results - Demographics

- 110/160 (69%) completed the 1 year follow-up
- Infants completing study
  - 51% female
  - Mean birth weight – 3.33 kg (45th percentile for GA)
- Mothers completing study
  - Mean age – 27.1 years
  - 91% White, 90% married
  - 65% completed college

SLIMTIME Primary Outcome: Weight-for-Length at age 1 year (N=110)

- “Soothe/Sleep” breastfeeding infants slept more, had fewer noctural and total daytime feeds
- “Introduction of Solids” infants – later intro & were more likely to accept novel healthy foods at age 1 year

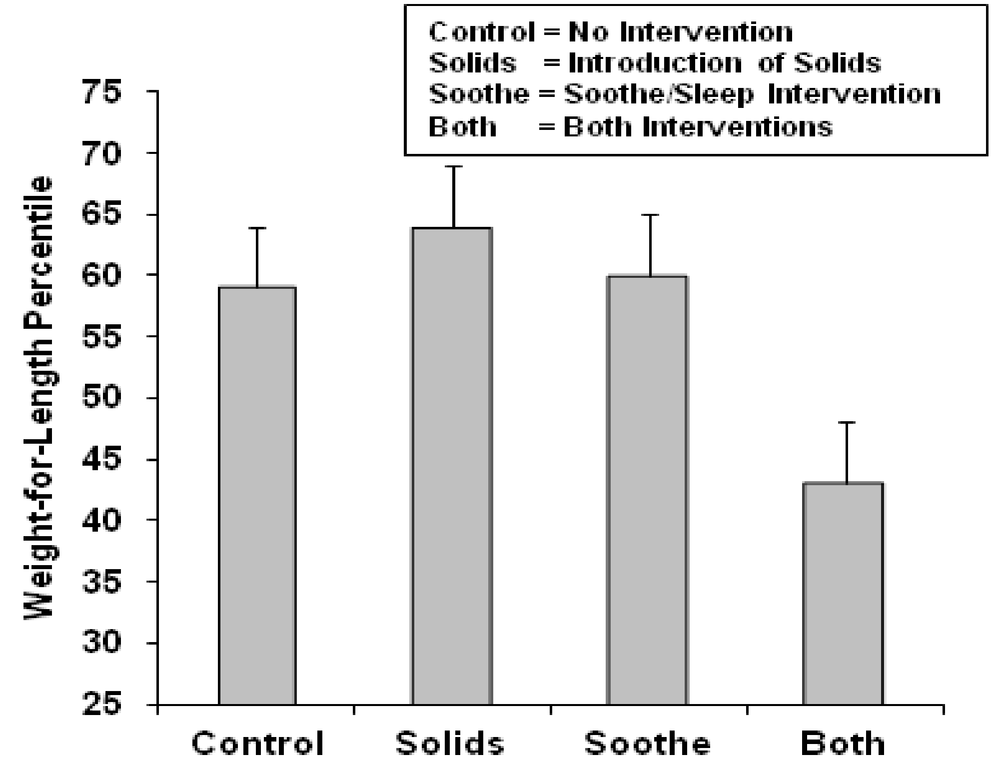
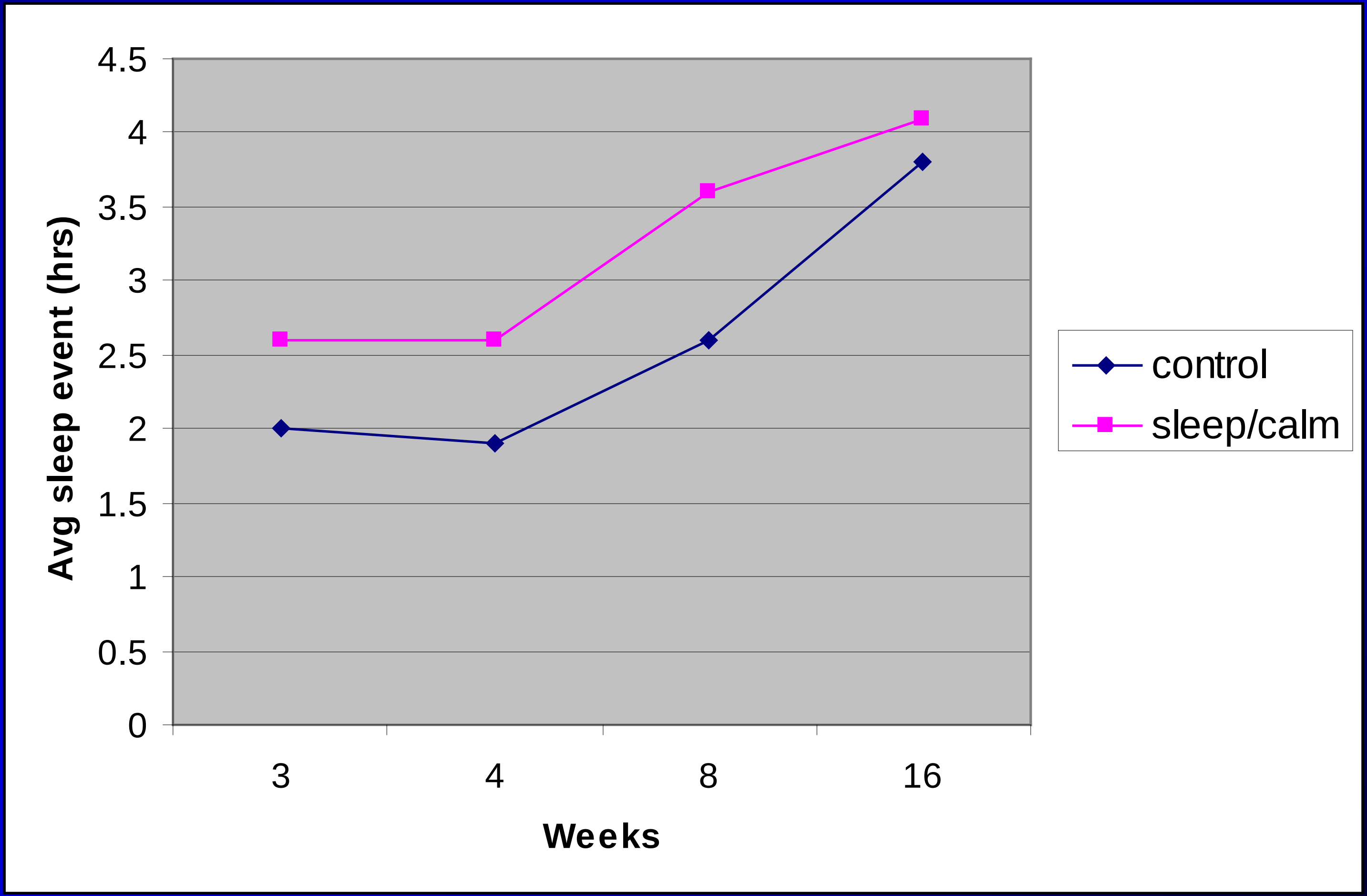
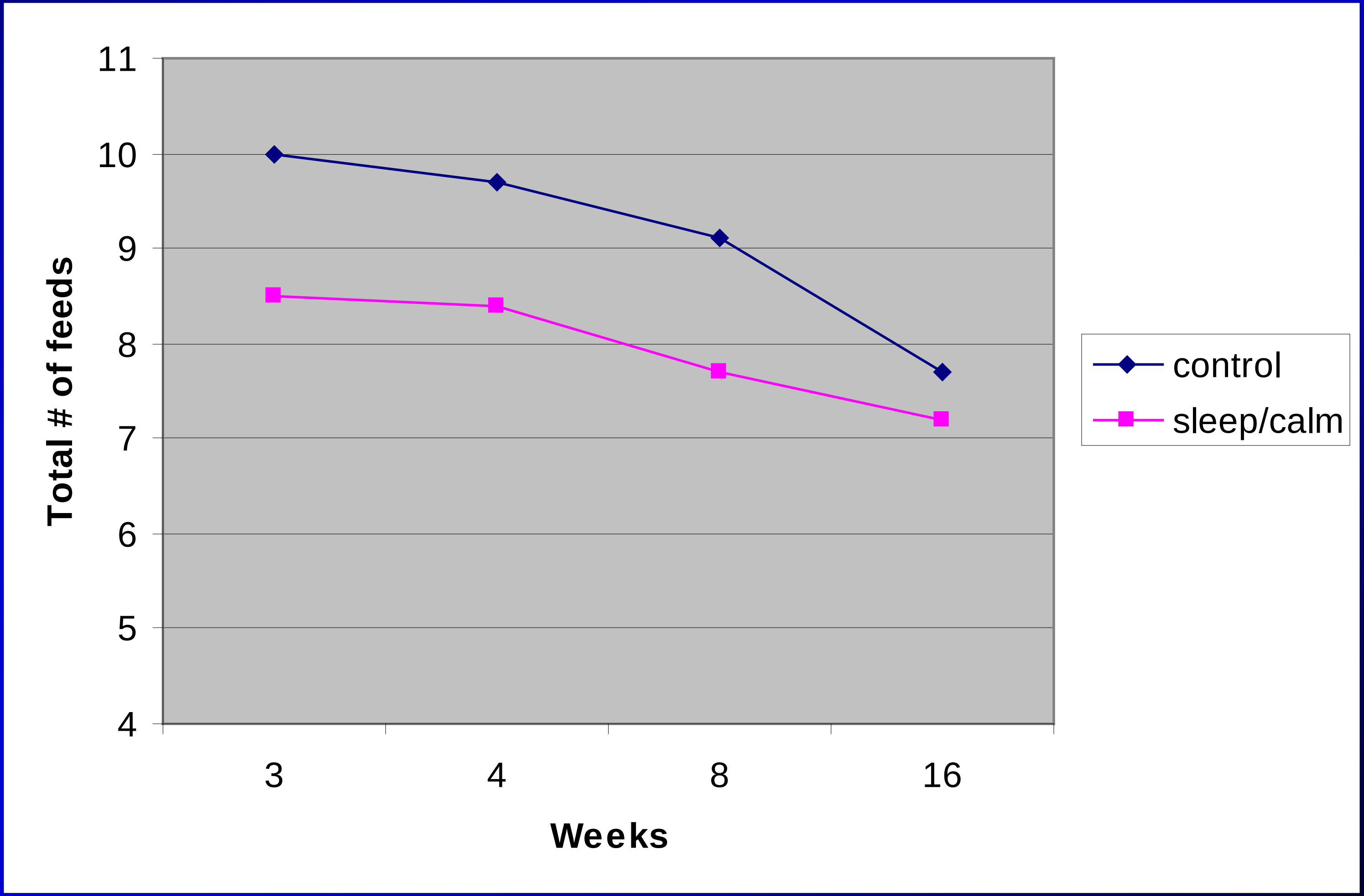


Figure 1 Study group weight-for-length percentiles at 1 year (both interventions group vs. other three groups; $P = 0.009$).

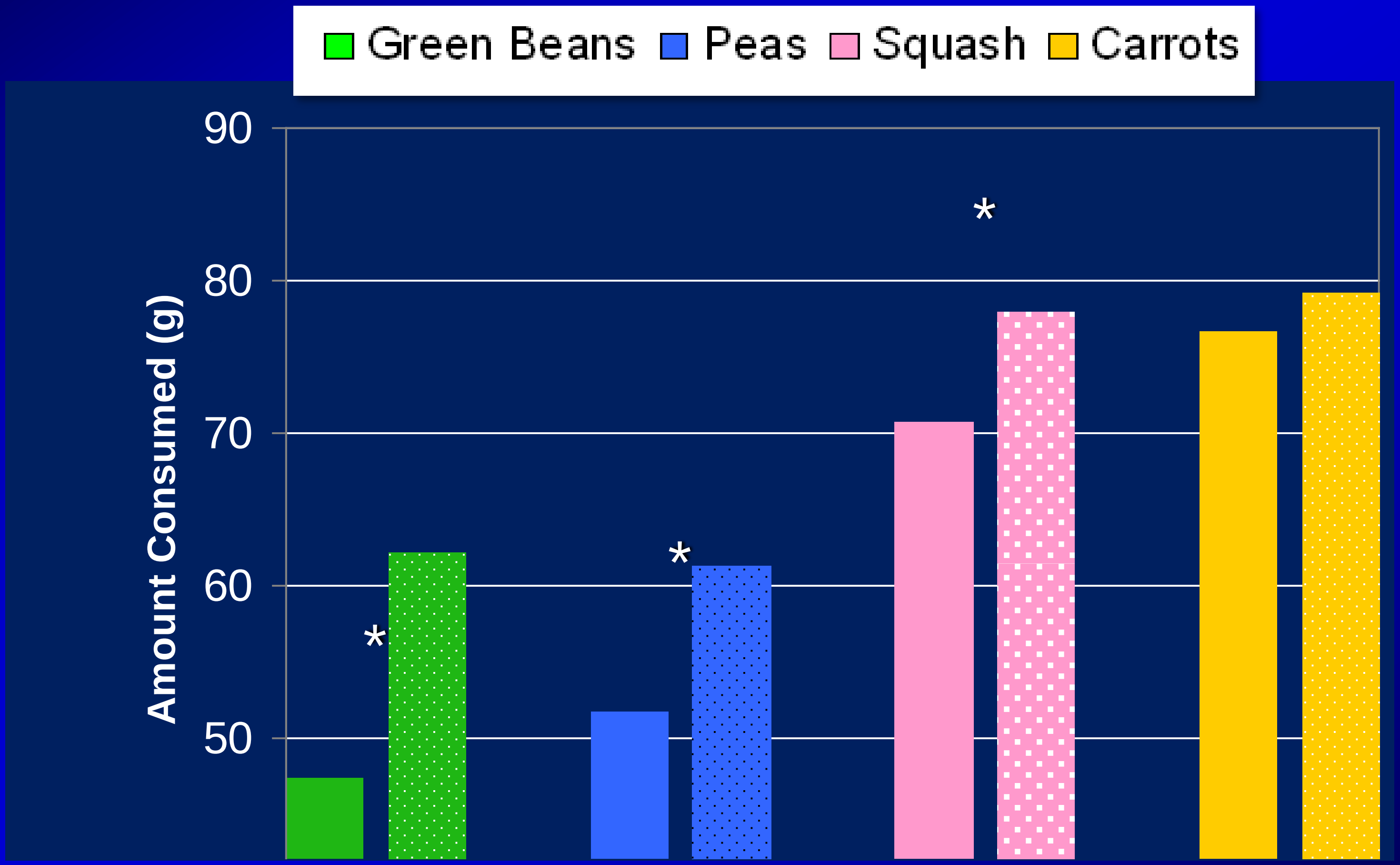
Possible mediators: Soothe/sleep intervention promotes longer night sleep duration



Possible mediators: Soothe/sleep group took fewer feedings than control



Possible mediators:
Effects on transition to solids: repeated exposure increased infants' pureed vegetable intake



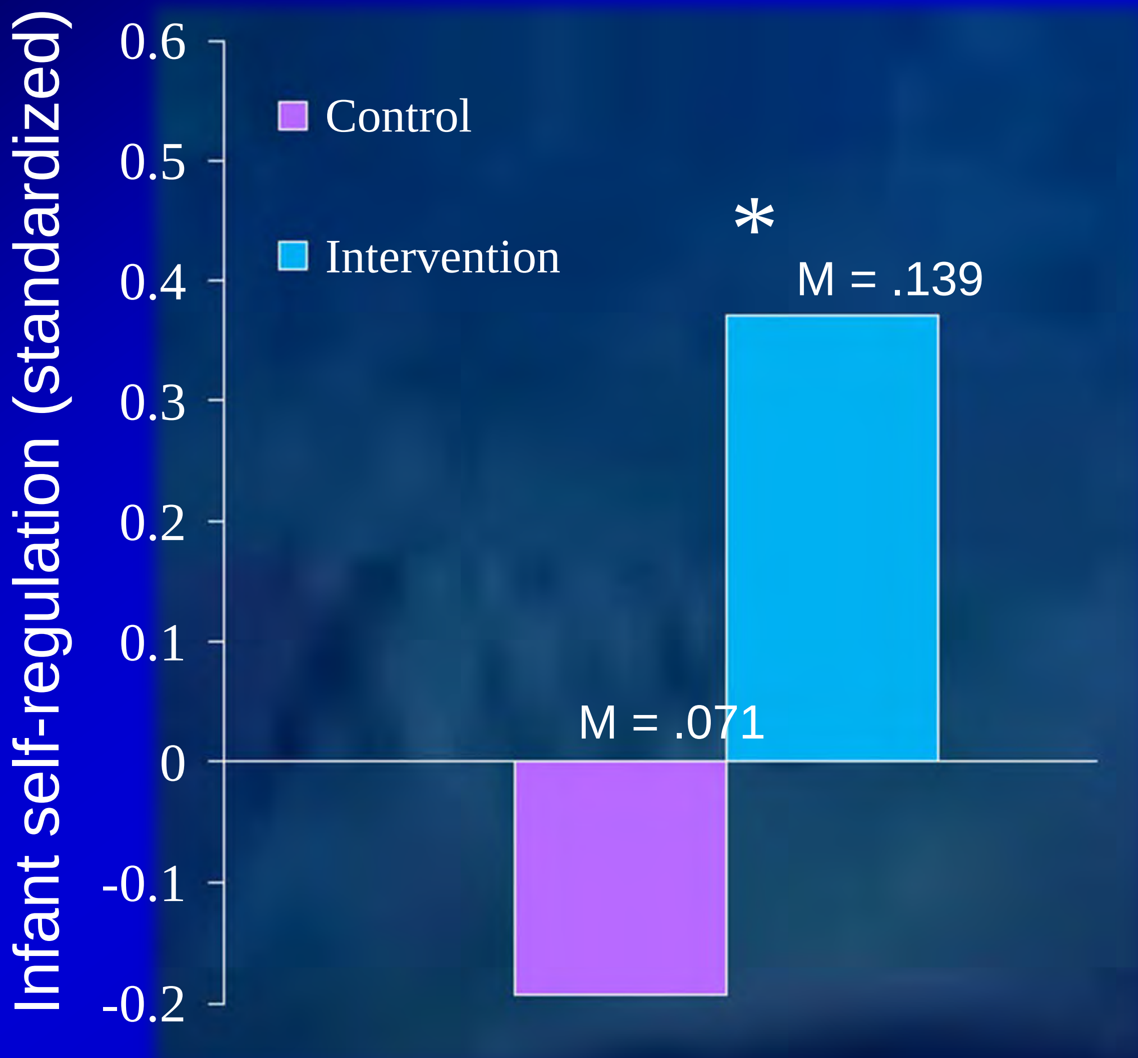
Paul et al. *Obesity* 2011

Possible mediators: At 1 y, 90% of treatment* infants accepted new food, compared to 74% of control

Accept

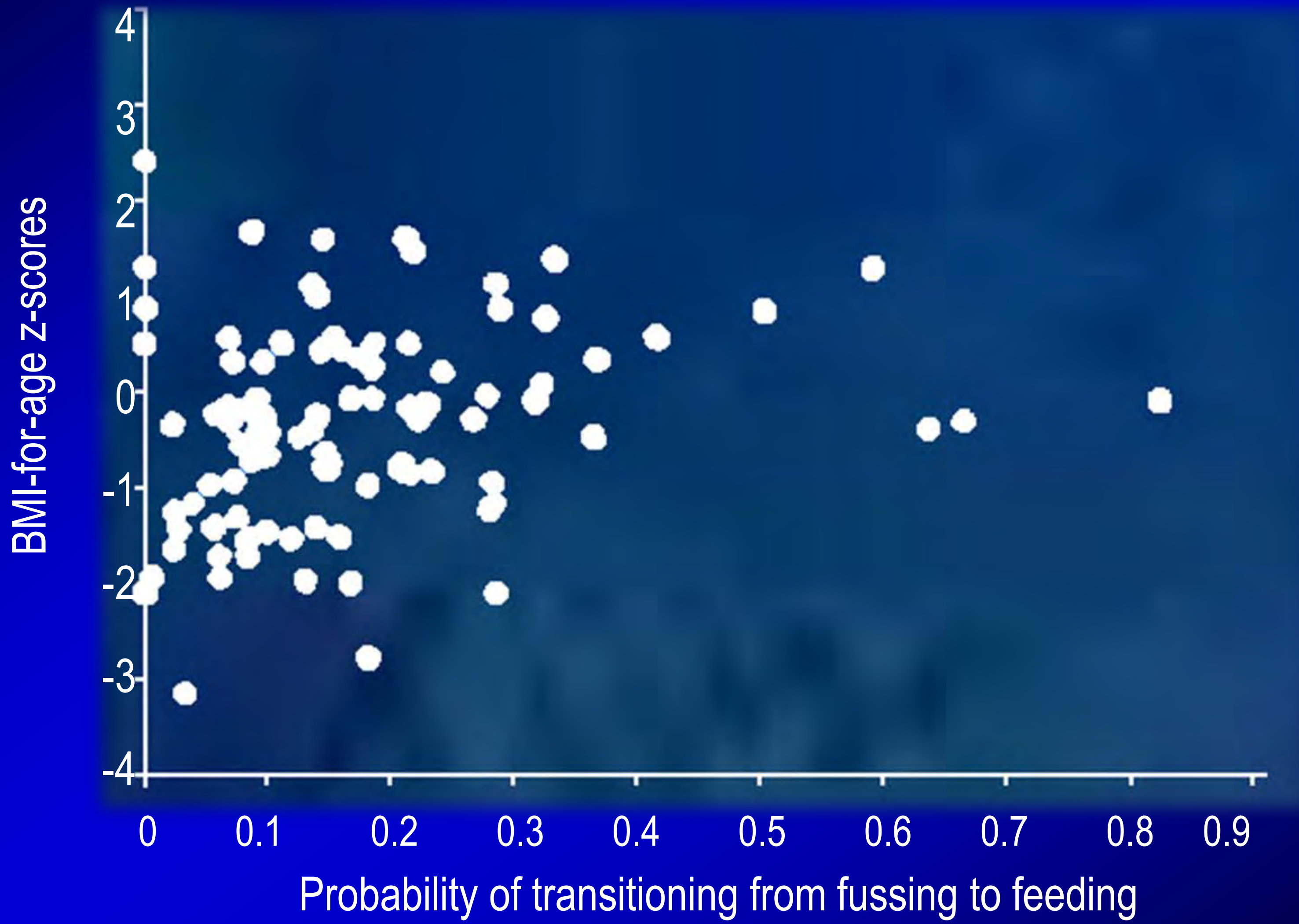
Reject

Infants in soothe/sleep treatment: Effects on self- soothing, regulation of emotions at 1 year, compared to control

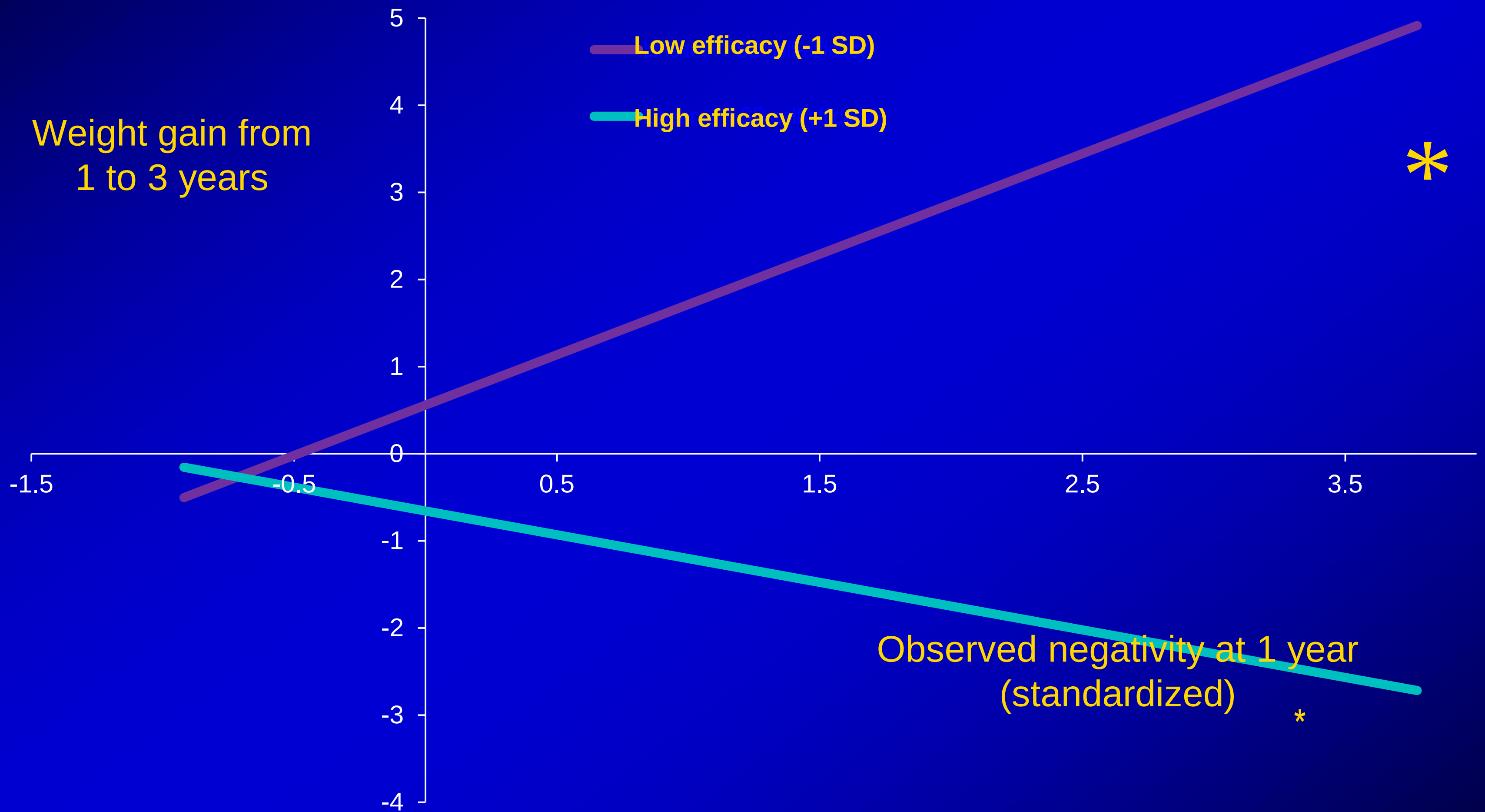


Anzman-Frasca, Stifter, Paul, & Birch, 2011

Infants' probabilities of transitioning from fussing to feeding positively predict their weight status at ~6 mo



Maternal self-efficacy moderated the relationship between observed infant negativity and weight gain



Anzman-Frasca, Stifter, Paul, & Birch, 2013 Infant temperament and parenting self efficacy predict child weight outcome. Infant Behav Dev. 2013

Preventing obesity during infancy: SLIMTIME, A pilot study*

"We are all united in believing that obesity prevention should be our goal; what has held back progress has been the dearth of strategies with clearly demonstrated efficacy…"

"..Paul et al. present pilot data for a bold and innovative approach to the prevention of undue weight gain in infancy"

"Notwithstanding these groundbreaking results, there are some limitations…." – Jack Yanovski

Paul, I. M., Savage, J. S., Anzman, S. L., Beiler, J. S., Marini, M. E., Stokes, J. L., & Birch, L. L. (2011). Preventingobesity during infancy: A pilot study. *Obesity*, *19*, 353-361. doi:10.1038/oby 2010.182

What was the secret to our (limited) success?

- Evidence from prior experimental research on ways that parenting/feeding affect infant intake,feeding:

Matheny, R., Birch, L & Picciano, M. (1990). Control of intake by human milk fed infants: Relationships between feeding size and interval. *Dev. Psychobio.*

Steinberg, L., O'Connell, N., Hatch, T., Picciano, M., & Birch, L. (1992). Tryptophan intake influences infants' sleep latency. *JNutr.*

Pinilla, T.,& Birch, L. (1993). Help me make it through the night: Behavioral entrainment of breast-fed infants' sleep patterns. *Peds.*

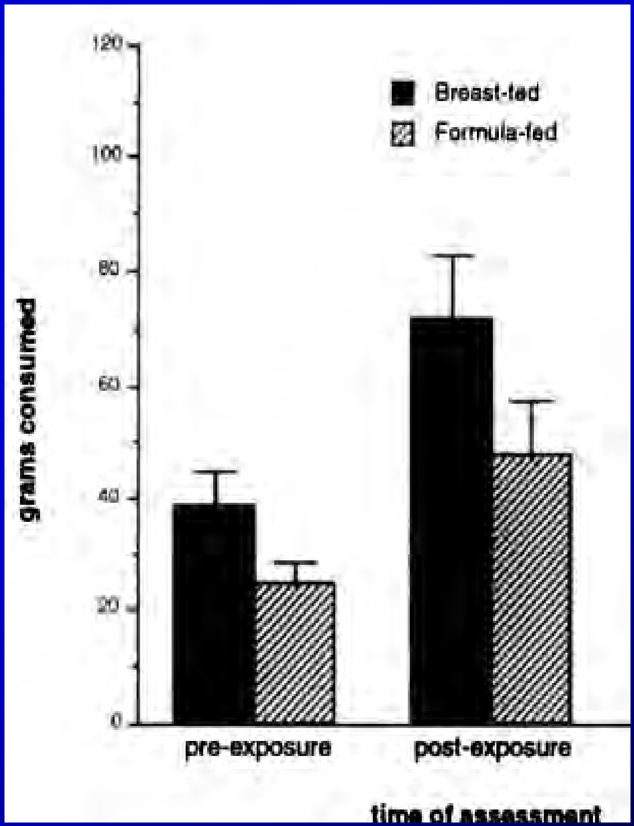
Sullivan, S. & Birch, L. (1994). Infant dietary experience and acceptance of solid foods. *Peds.*

Birch, L., Gunder, L., Grimm-Thomas, K., & Laing, D. G. (1998). Infants' consumption of a new food enhances acceptance of similar foods. *Appetite.*

Repeated Exposure to Vegetables Overcomes Infant Neophobia

1st Exposure

10th Exposure



Sullivan SA and Birch LL, 1994

- To overcome neophobia for low-energy density foods, repeated exposure is often required

What was the secret to our (limited) success?

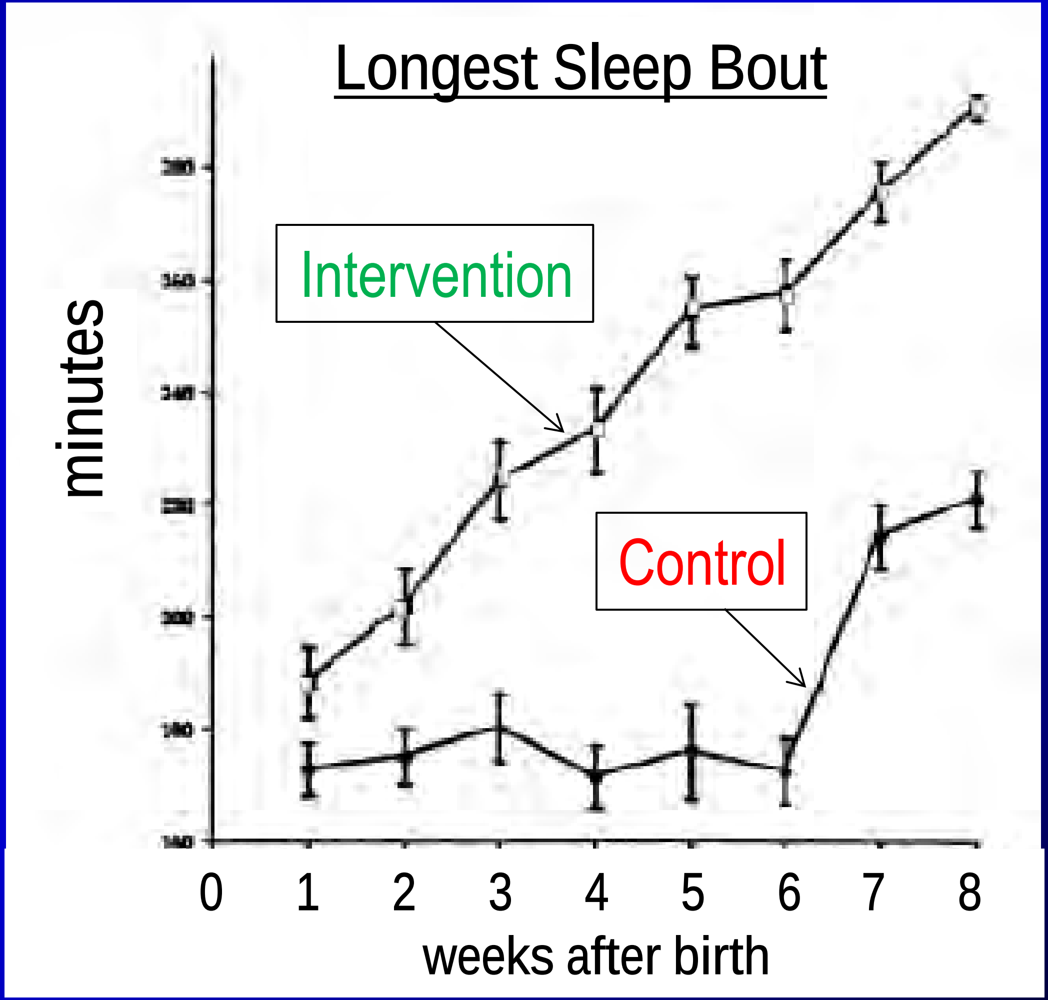
- Evidence from prior experimental, research on ways that parenting/feeding affect infant sleep:

Matheny, R., Birch, L & Picciano, M. (1990). Control of intake by human milk fed infants: Relationships between feeding size and interval. *Dev. Psychobio.*

Steinberg, L., O'Connell, N., Hatch, T., Picciano, M., & Birch, L. (1992). Tryptophan intake influences infants' sleep latency. *JNutr.*

Pinilla, T.,& Birch, L. (1993). Help me make it through the night: Behavioral entrainment of breast-fed infants' sleep patterns. *Peds.*

Teaching mothers soothe/sleep techniques increased infant night sleep duration



Pinilla T and Birch LL. *Pediatrics* 1993; 91: 435-44

Do FP affect child weight status?
Are effects mediated via influence on child eating?
Don't know …

- studies with cross sectional data, report FP and C wt are related but can reflect reverse
- evidence from longitudinal studies C wt status elicits FP.
- FP effects on C wt mediated via effects on C eating
- FP, C characteristics interact to affect wt status.
- What are the implications for building interventions?
- Need more efficient approaches to selecting, testing intervention components prior to conducting RCTs

Provide evidence for causal pathways before building interventions

- experimental designs testing conceptual models,
- use of causal modeling
- which aspects of FP important: portion size, food availability, factors affecting frequency, meal initiation, termination?
- child effects on feeding practices
- parenting style: a moderator of FP?
- moderation--what works for whom? ethnicity, income, education, P,C factors?
- can it be affordable? scalable? sustainable?


Early Insight: Helping parents raise healthy babies in the first 4 months
Fussy
Newborns cry up to 3 ½ hours per day, decreasing around 2 months
Hunger is only one of many reasons why babies cry
A crying baby may not be hungry
Try the 5 S's to calm your baby
Sleeping
1 to 4 month olds sleep 11 to 18 hours per day
Babies sleep for a few minutes to a few hours at a time
White noise may help your baby sleep
Give your baby a chance to go back to sleep on own after waking at night
Active Social Play
Babies can lift their heads, look at and reach for new things
Around 2 months of age, practice tummy time with your baby 2-3 times daily, 10-15 minutes at a time
Your Baby is Unique!
Learn to read your baby's signals
Try different soothing strategies
Use different routines for the day and night
Alert & Calm
Feeding
Your baby only needs breastmilk and/or formula
1 to 2 month olds eat 2-3 oz. every 2-3 hours (8-12 feedings daily)
2 to 4 month olds eat 2-4 oz. every 2-4 hours (6-12 feedings daily)
How much your baby eats may differ, meal to meal and day to day
Learn your baby's hunger and fullness signs
Drowsy
Drowsy babies rub their eyes, yawn, or get a little fussy
Put your baby to bed between 7 and 8 pm
Begin to use a bedtime routine
Put your baby to bed drowsy but still awake
IRB #34493

EarlyInsight for new parents

- Special thanks for generous funding from NIDDK:
  - R56DK72996 → SLIMTIME
  - R01DK088244 → INSIGHT
  - R01DK099364 → SIBSIGHT

"That's all folks…"

Results: Overview

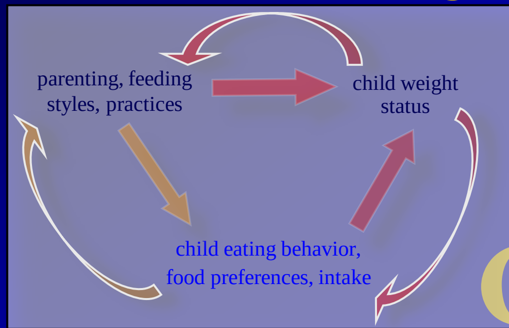
- Did negativity and maternal parenting self-efficacy interact to predict weight outcomes?
  - Yes:
    - *Observed* negativity
    - Weight *gain*
    - β for interaction = -.35, p<.01
  - No:
    - Reported negativity
    - Weight status – cross-sectional
    - No main effects in these analyses either

Correlations between variables of interest

	1.	2.	3.	4.	5.
1. Distress, 16 weeks					
2. Reported negativity, 1 year	.42***				
3. Observed negativity, 1 year	.08	.003			
4. Parenting self-efficacy, 3 weeks	-.16	-.03	-.06		
5. Weight status, 1 year	.11	.007	.09	.03	

*** $p < .001$

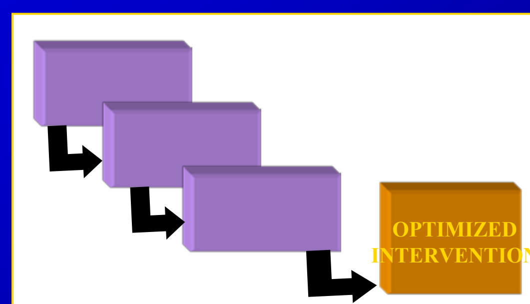
Where do we go from here? Next steps



Conceptual model

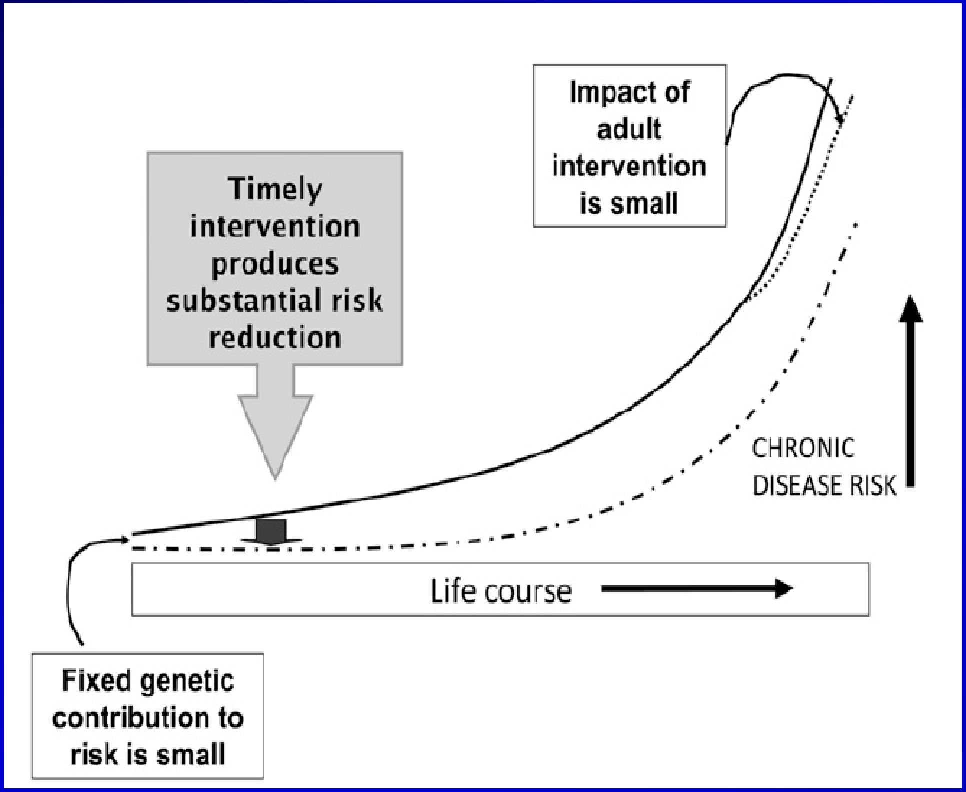
	Outcome Variable (DV)			
	Eating Style		Eating Style	
Total # of Studies	0	Total # of Studies	0	Total # of Studies
Study Designs		Study Designs		Study Designs
Cross-sectional	0	Cross-sectional	0	Cross-sectional
Longitudinal	0	Longitudinal	0	Longitudinal
Experimental	0	Experimental	0	Experimental

Review of the evidence



Next steps

Rationale for Infancy-Based Intervention



Hanson M and Gluckman P, Am J Clin Nutr 2011; 94: 1754S-8S

- Metabolic plasticity
  - programming via epigenetic mechanisms?
- Behavioral plasticity
  - many obesogenic behaviors have origins during infancy

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SCHOOL OF MEDICINE

TODDLER OBESITY PREVENTION

Maureen Black, PhD
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Kristen Hurley, Ph.D.
Yan Wang, MD, DrPH
Laura Latta, MPH
Erin Hager, Ph.D.
Margo Candelaria, Ph.D.
Larry Magder, Ph.D.

RESEARCH OBJECTIVE

- To examine the effects of a randomized controlled trial to preve nd promote healthy diet ehavior among todd

- Funders:
  - USDA NIF
  - NICHD R01
- Collaborato
  - WIC Sa

Missing Methods

- Silhouettes – Perceptions of body size
- Toddler Feeding Behavior
  - Self report
  - Observation
- Physical activity
  - Ankle accelerometry - cutpoints
  - EMA Electronic Momentary Assessment (R03)

Underweight, Overweight, or Within Normal???




Underweight, Overweight, or Within Normal???

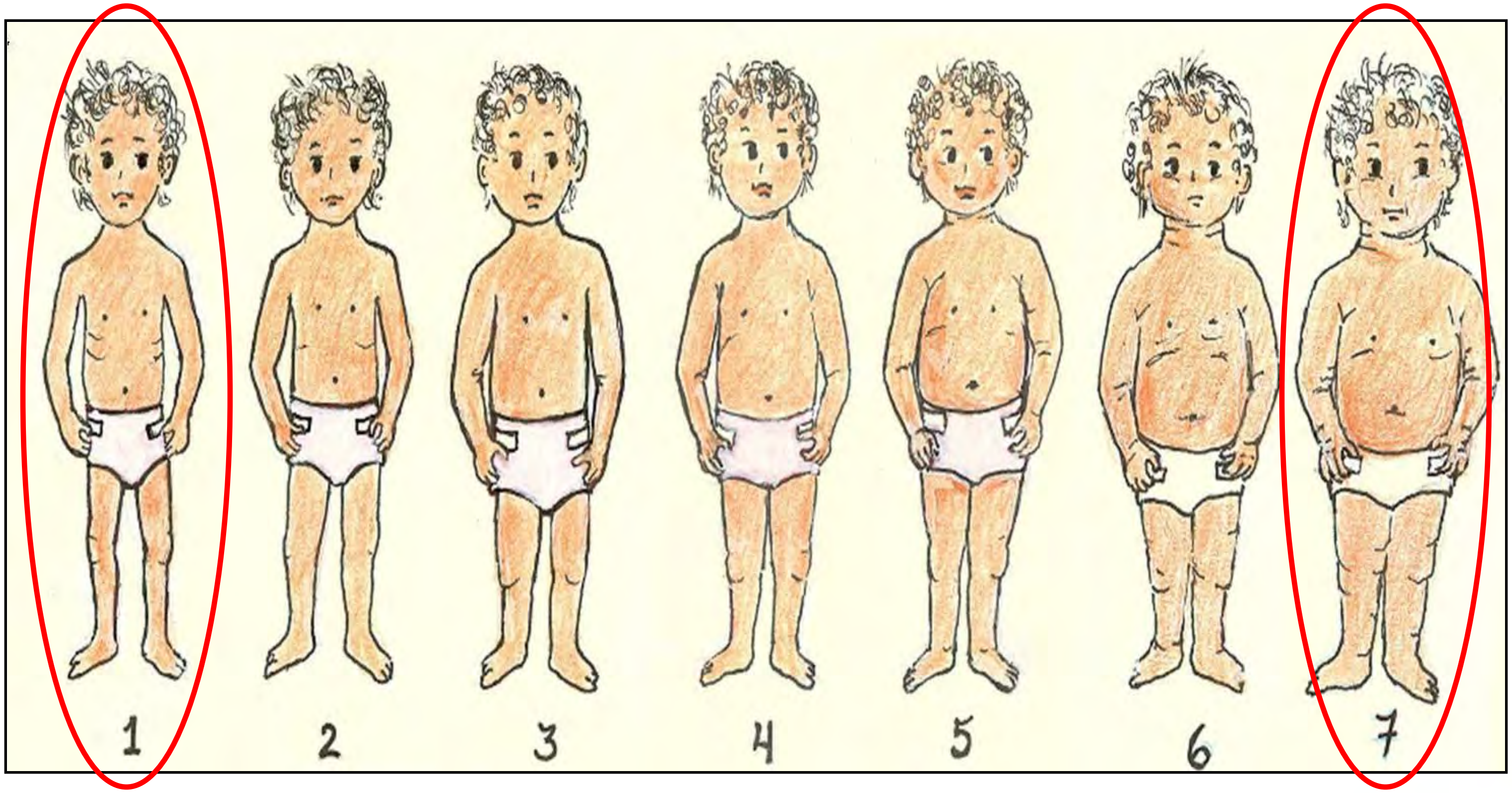
0.4%ile

91%ile

56%ile

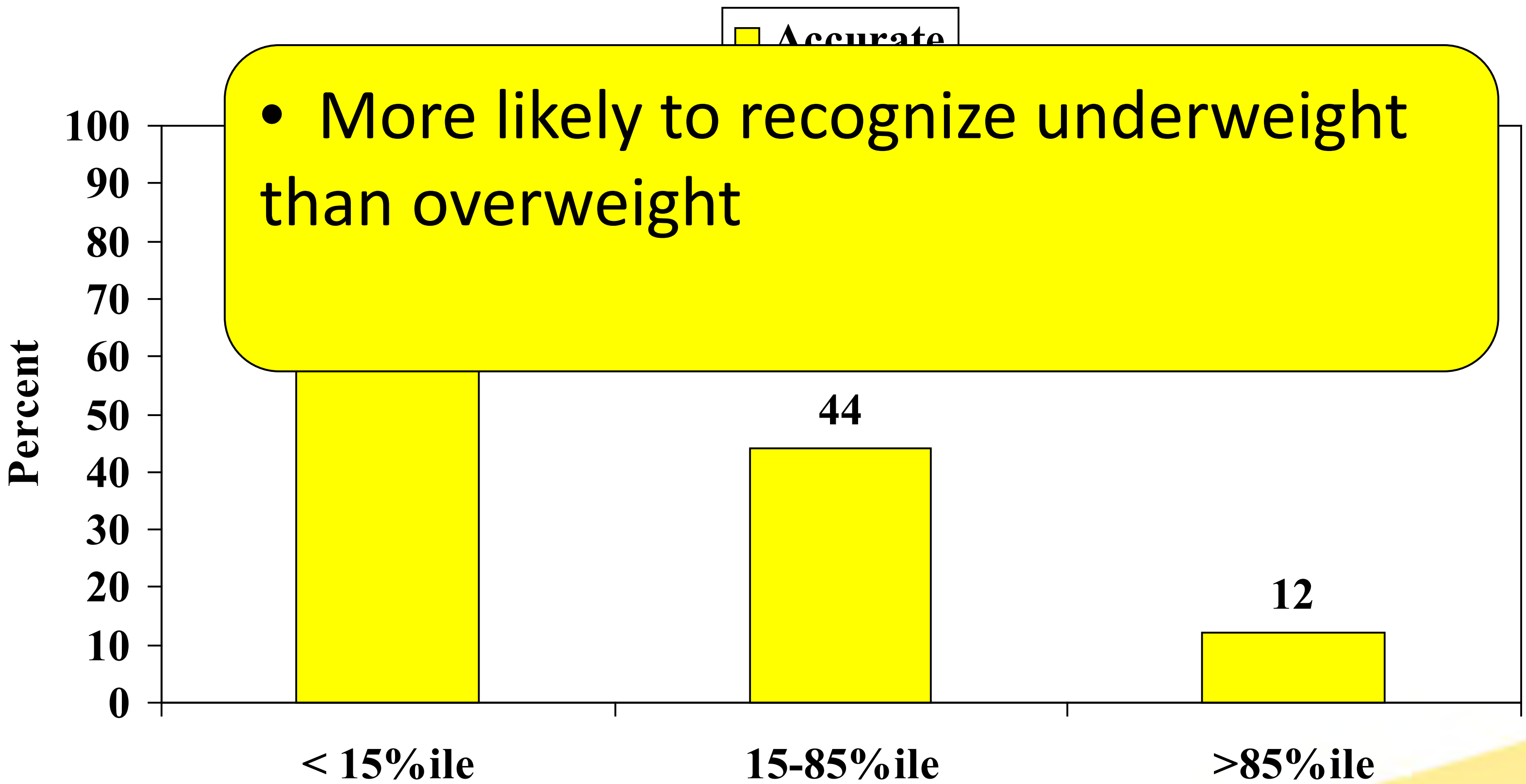
4%ile

Toddler Silhouette Scale



Hager, McGill, Black (2010). *Obesity*

Parent Perceptions of Toddler Body Size

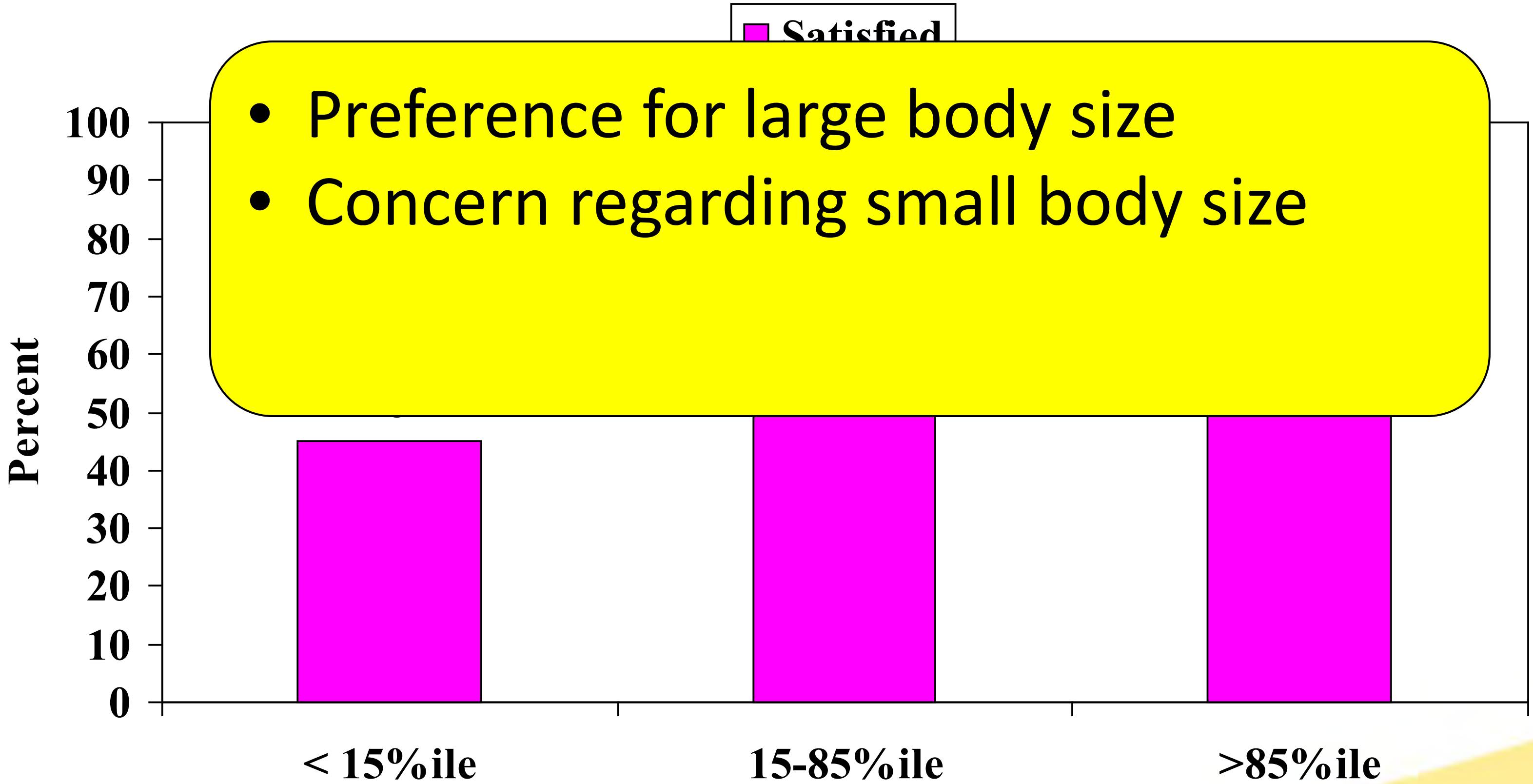


- More likely to recognize underweight than overweight

. . . . .Toddler's Body Size . . . .

Hager, Hurley, Black, 2012, *Archives of Peds*

Parent Satisfaction With Toddler Body Size



- Preference for large body size
- Concern regarding small body size

. . . . .Toddler's Body Size . . . .

Hager, Hurley, Black, 2012, *Archives of Peds*

The Journal of Nutrition
Community and International Nutrition

Systematic Development and Validation of a Theory-Based Questionnaire to Assess Toddler Feeding[1,2]

Kristen M. Hurley,[3,4*] M. Reese Pepper,[3,5] Margo Candelaria,[3] Yan Wang,[3] Laura E. Caulfield,[4] Laura Latta,[3] Erin R. Hager,[3] and Maureen M. Black[3]

[3]Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD; [4]Center for Human Nutrition, Department of International Health, The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; [5]Department of Pediatrics, MedStar Georgetown University Hospital, Washington, DC

- 27 items caregiver report, 5 minutes
- 5 theoretically derived constructs, confirmatory factor analysis:
  - **responsive, forceful, restrictive, indulgent, uninvolved**
- Internally consistent, test-retest, convergent validity
- Low income, racially mixed toddlers

Toddler Feeding Behavior Questionnaire

1. How often do you talk to toddler during meals?
2. How often do you say something positive about toddler's eating?
3. How often do you arrange food to make it more interesting for toddler?
4. How often do you talk to toddler about the food he or she is eating?
5. How often can you tell when toddler is full?
6. How often do you eat with toddler?
7. How often do you praise toddler for eating?
8. How often do you encourage toddler to try a new food?

Responsive

9. How often do you yell or threaten toddler to get him/her to eat enough?
10. If toddler is not hungry, how often do you get him/her to eat anyway?
11. How often do you try hard to get toddler to eat a new food within one meal?
12. How often do you physically struggle with toddler to eat?

Forceful

13. How often are you concerned that toddler is eating too much?
14. How often are you concerned that toddler will become overweight?
15. How often are you concerned that toddler eats too many high fat foods?
16. How often are you concerned that toddler would eat too much if you did not limit?
17. How often are you concerned that toddler will have to diet?

Restrictive

18. How often do you promise a non-food reward if toddler eats?
19. How often do you offer sweets if toddler behaves well?
20. How often do you offer toddler sweets as reward for eating?
21. How often do you let toddler eat while watching TV or playing?
22. How often do you let toddler eat whatever he or she wants?
23. How often do you immediately make something else if toddler doesn't like what is being served?

Indulgent

24. How often are you responsible for the amount of food toddler is served?
25. How often are you responsible for the kinds of foods toddler is served?
26. How often do you know what toddler eats throughout the day?
27. How often do you know when toddler is eating?

Uninvolved

Convergent Validity

	Responsive		Forceful		Restrictive		Indulgent		Uninvolved	
	Value	P	Value	P	Value	P	Value	P	Value	P
Maternal anxiety[2]	−0.17	0.004	0.07	0.24	0.12	0.04	0.12	0.04	0.16	0.007
Maternal depression[3]	−0.25	< 0.001	0.02	0.69	0.15	0.01	0.15	0.009	0.10	0.10
Maternal stress[4]	−0.10	0.09	0.02	0.73	0.10	0.09	0.16	0.006	0.22	< 0.001
Toddler fussiness[5]	−0.13	0.03	0.03	0.54	0.13	0.03	0.22	< 0.001	0.12	0.04
Toddler overweight[6]	0.68 (0.44–1.06)	0.09	0.73 (0.50–1.1)	0.11	1.58 (1.1–2.4)	0.03	0.76 (0.50–1.1)	0.19	0.96 (0.73–1.3)	0.77

Observations

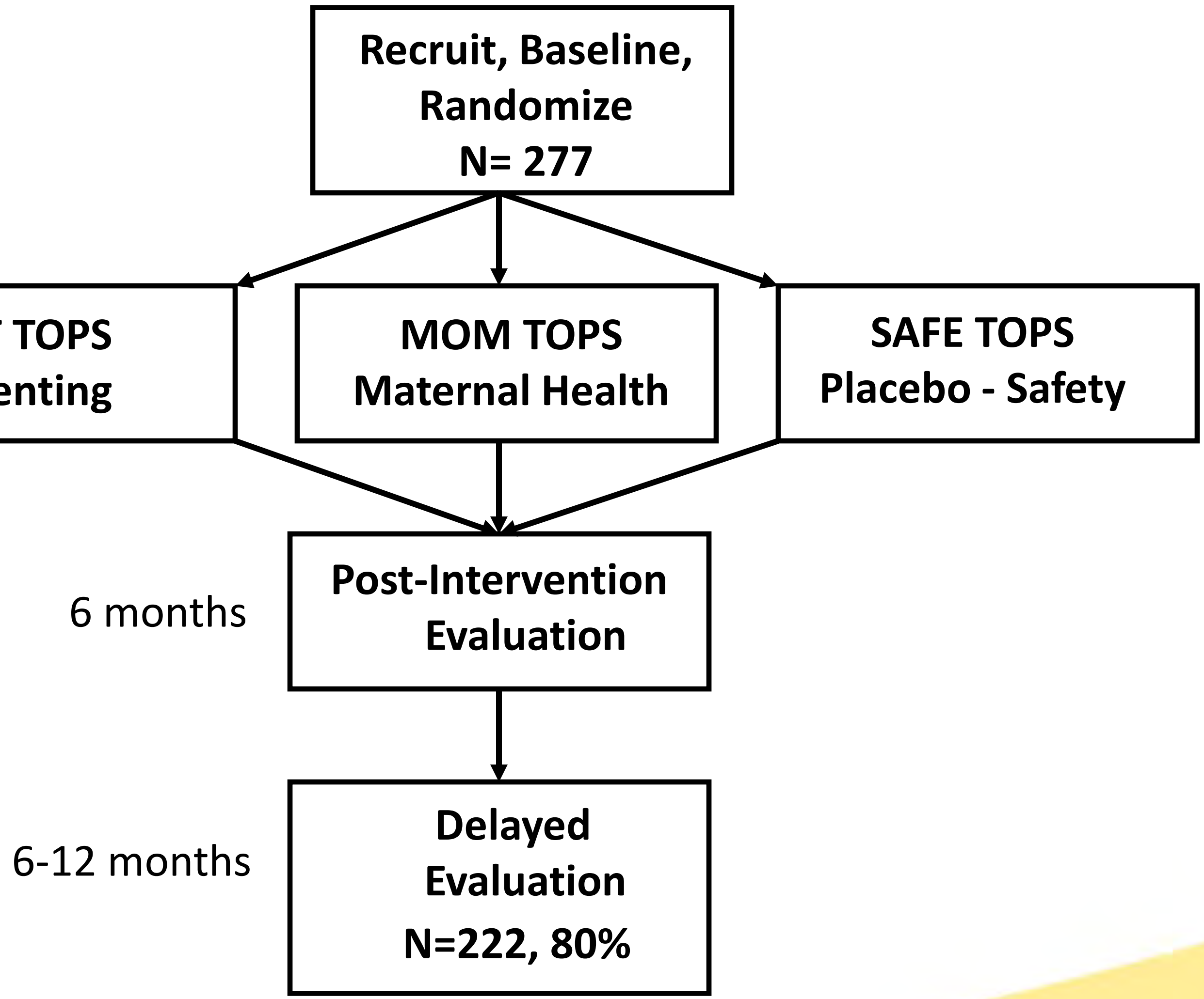
- Emotional Availability Scales
  - Sensitivity and responsivity
  - Global

Forest

- Behavioral observation
  - Noldus
  - Time-stamped mother and child behaviors with affect coding

Trees **Weeds**

DESIGN: RANDOMIZED CONTROLLED TRIAL



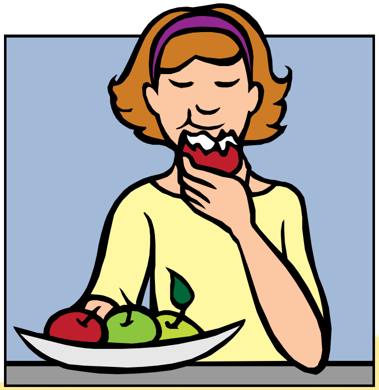
TOPS: RANDOMIZE INTO 3 GROUPS

Parenting

manage behavior, no food

Maternal Lifestyle

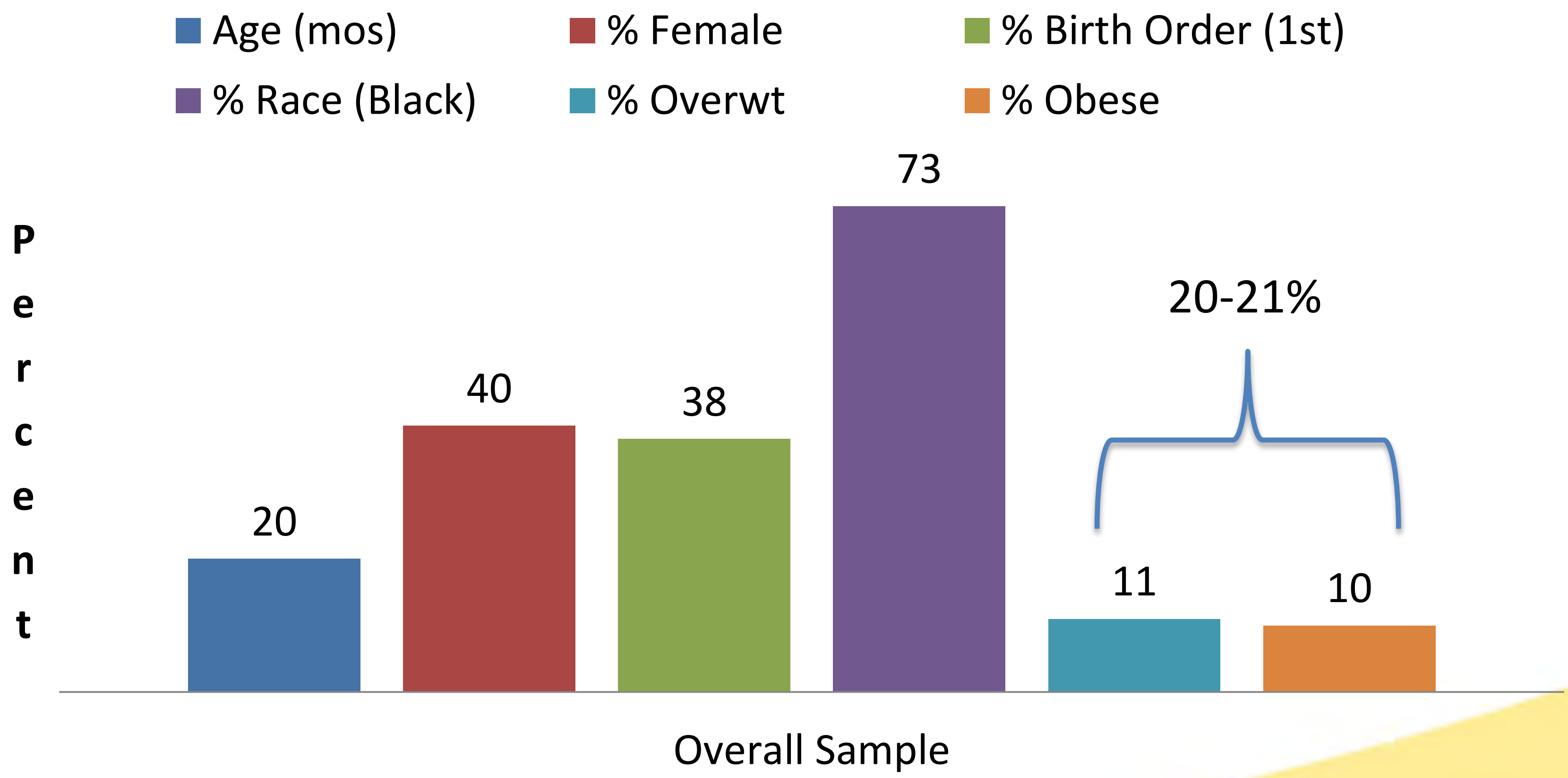
mothers' diet & activity



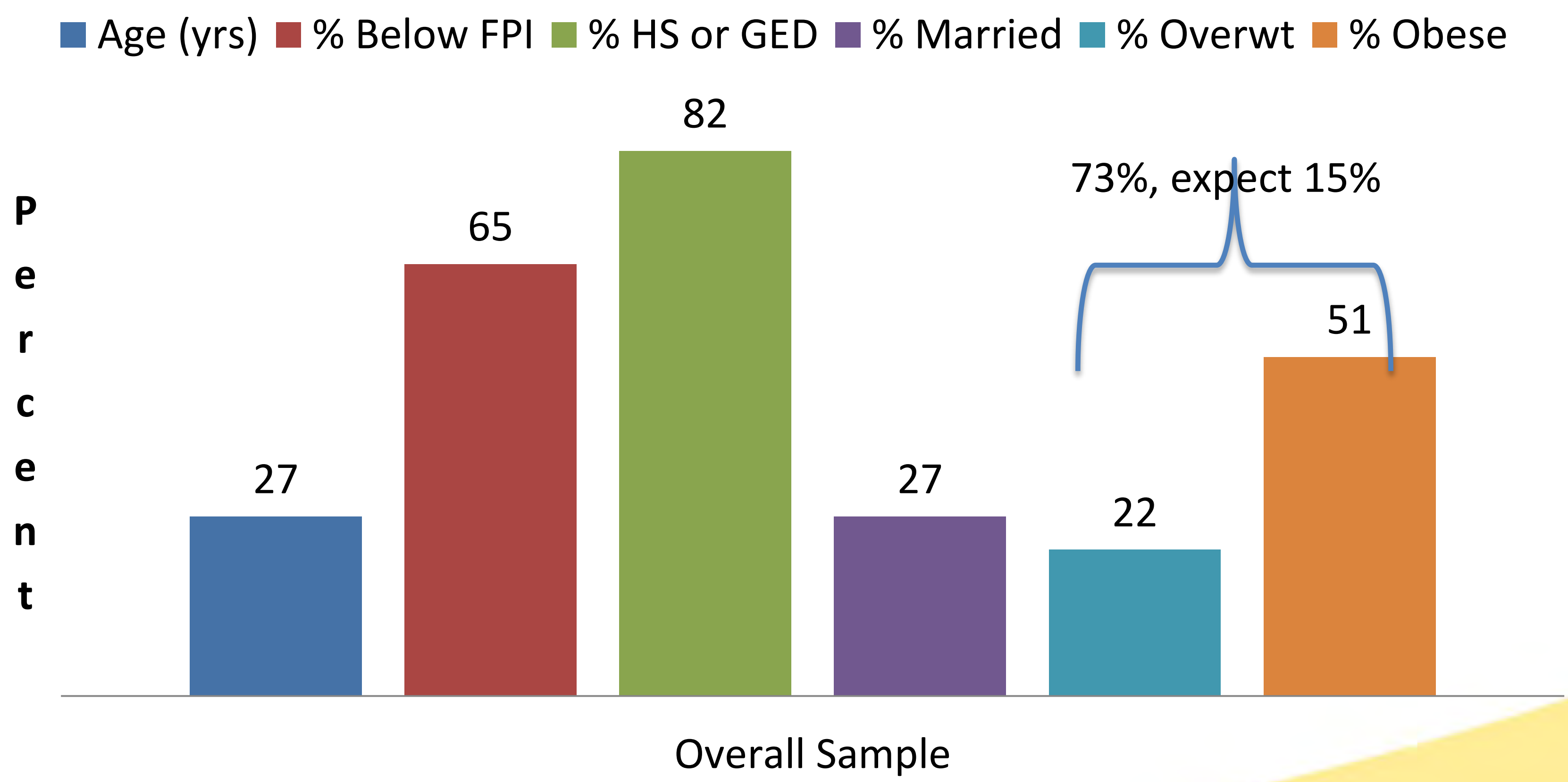
Safety

Placebo

TODDLER DEMOGRAPHICS



CAREGIVER DEMOGRAPHICS



Mothers & toddlers weighed and measured

Wear accelerometers for 7 days - measures minutes in Moderate/Vigorous Physical Activity (MVPA)

24-hour diet recall collected in the homes

Mothers listened to questions presented thru headphones and responded on a computer

Mothers and toddlers videotaped during a meal

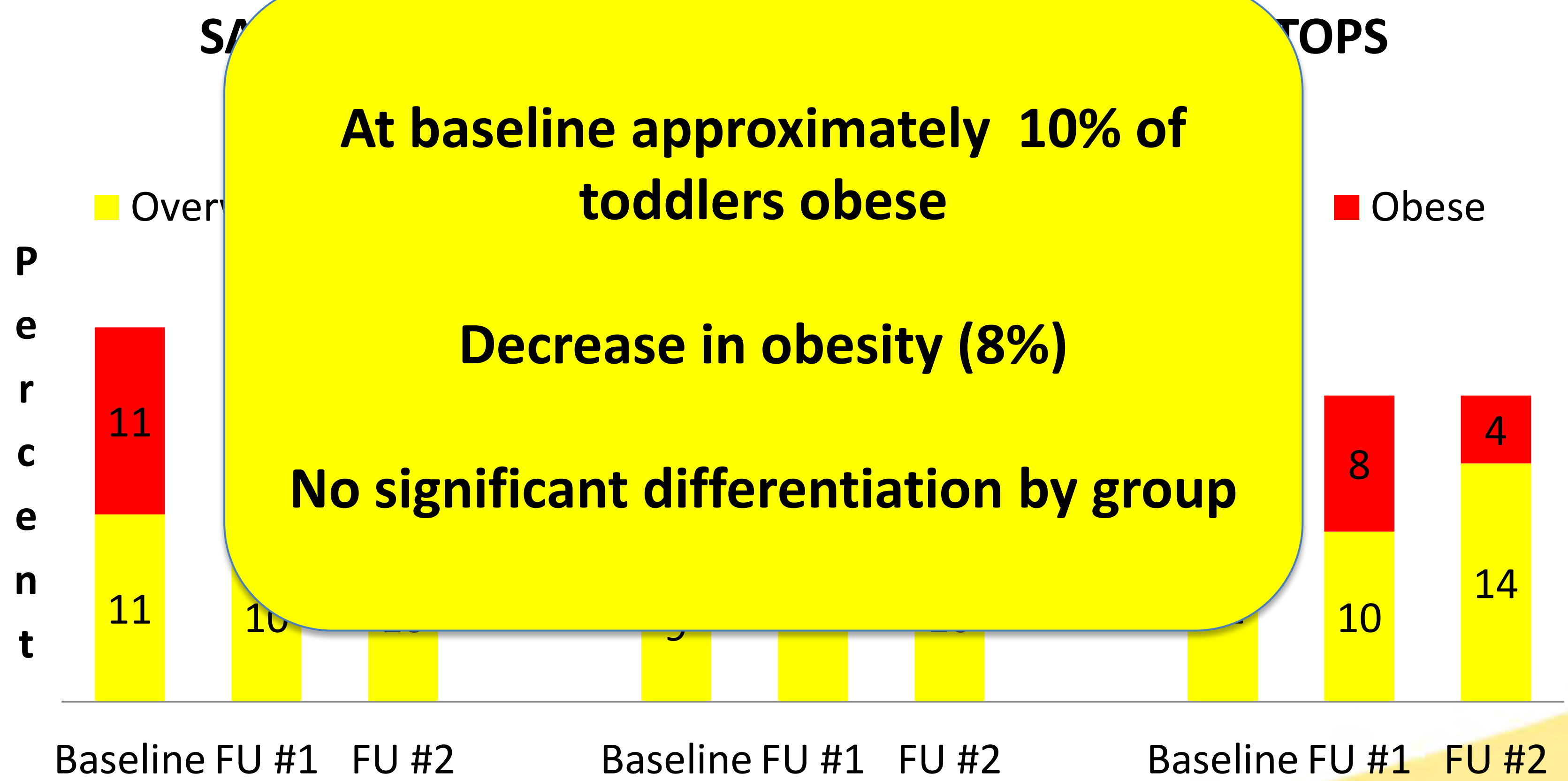
RAs coded using Emotional Availability Scales & Behavioral Scales

INTERVENTION:
SAME PATTERN ACROSS THREE GROUPS

- 8 sessions (manualized by topic area)
  - 4 group
  - 3 individual (telephone)
  - 1 group
- Goal setting (Social Cognitive Theory)
  - Tracking. Evaluate reasons for achieving/not achieving goal
  - Learn to set attainable/sustainable goal
- Healthy snacks and games for mothers and toddlers

CHANGES IN WEIGHT

TODDLER: CHANGE IN % OVERWEIGHT AND OBESE: FOLLOW-UP 1 AND FOLLOW-UP 2

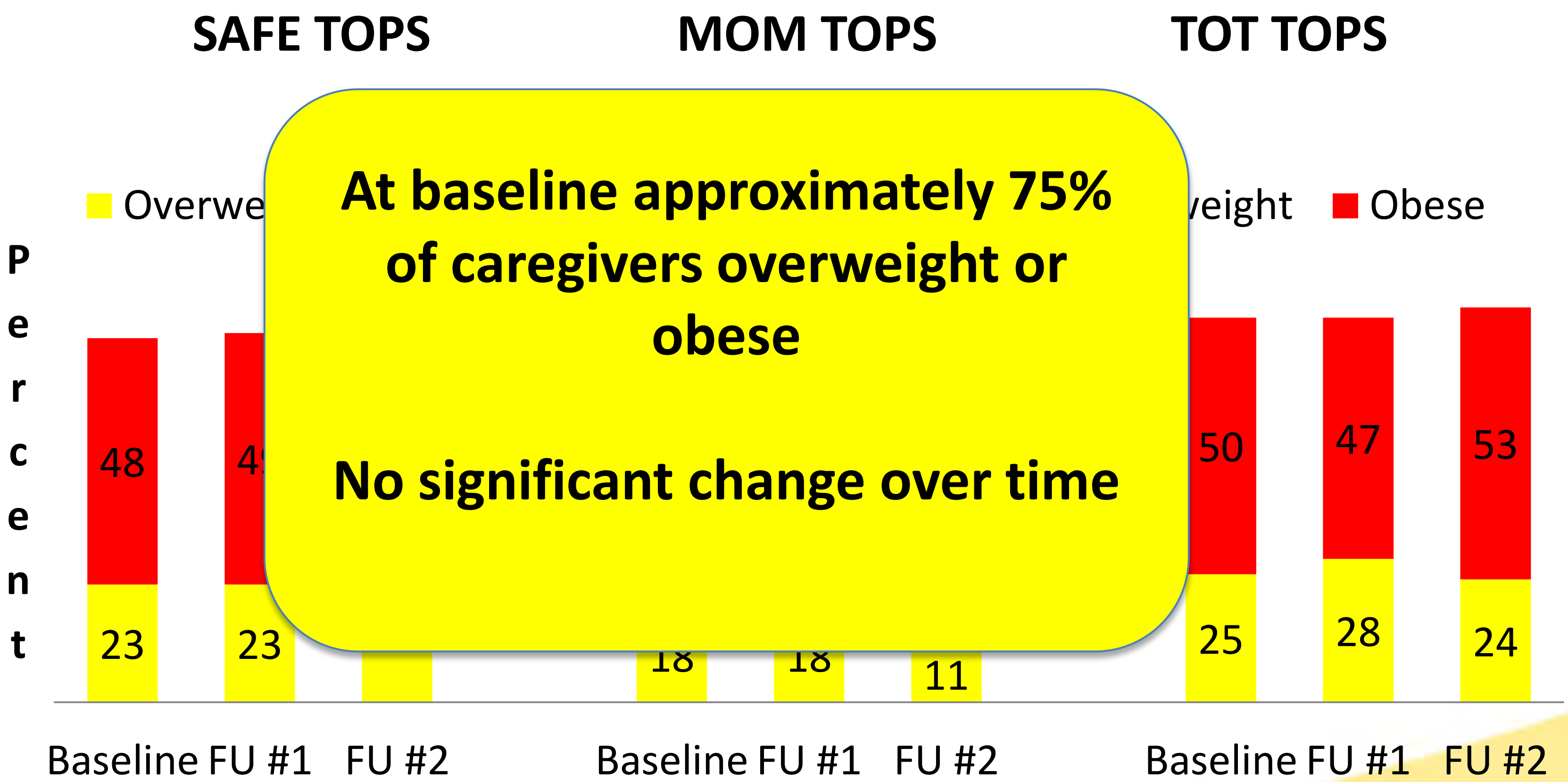


At baseline approximately 10% of toddlers obese

Decrease in obesity (8%)

No significant differentiation by group

CAREGIVER: CHANGE IN % OVERWEIGHT AND OBESE:
FOLLOW-UP 1 AND FOLLOW-UP 2

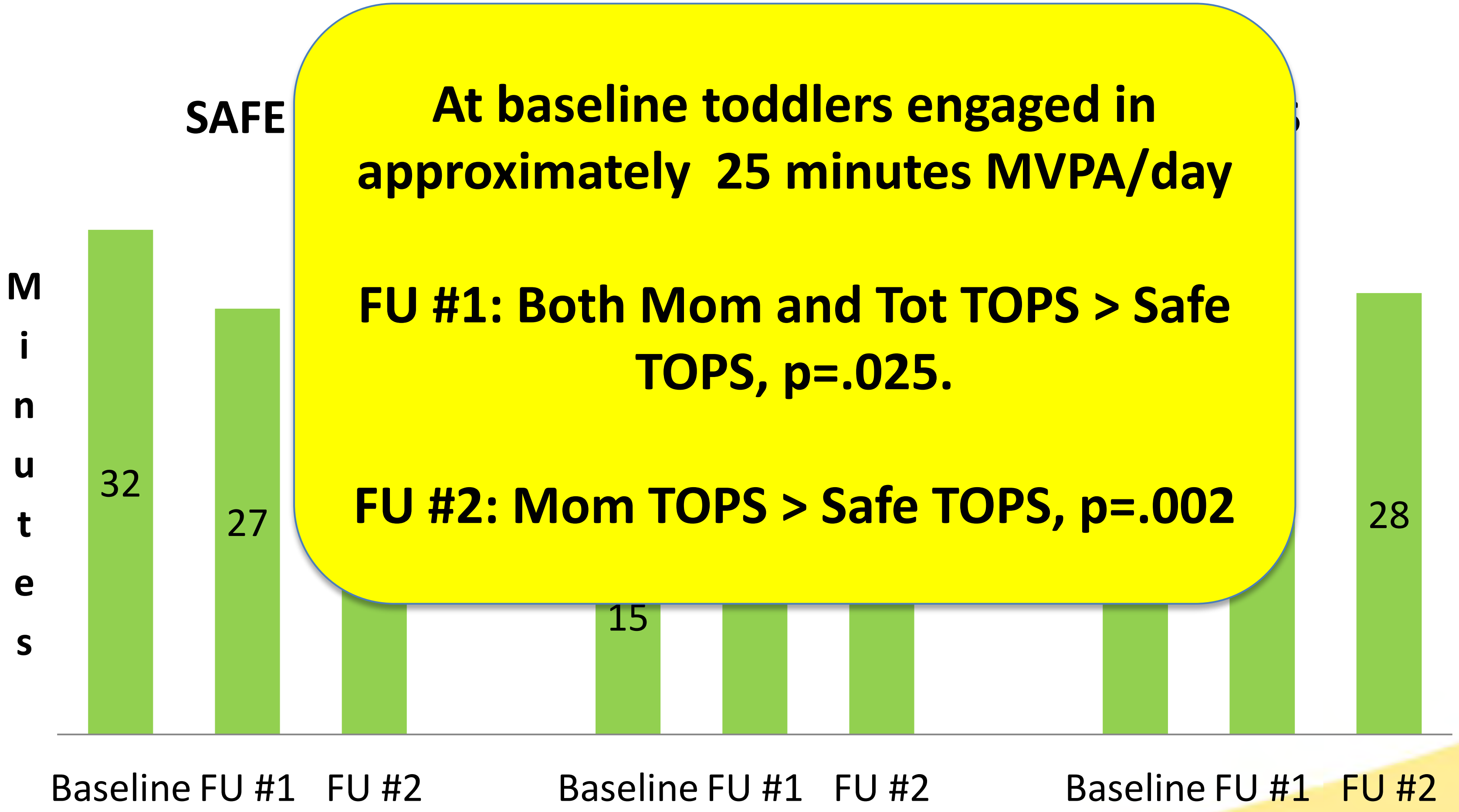


At baseline approximately 75% of caregivers overweight or obese

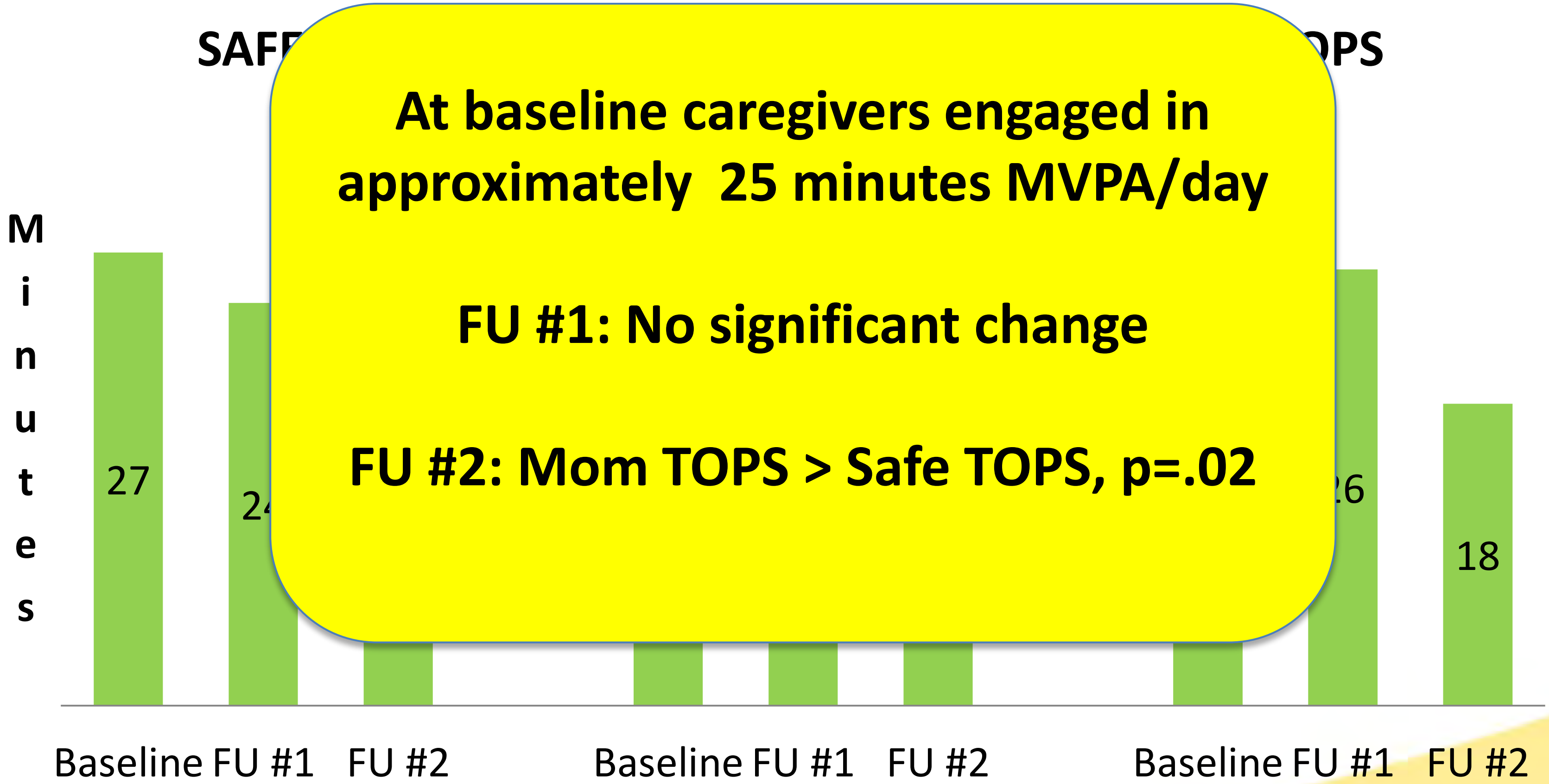
No significant change over time

CHANGES IN PHYSICAL ACTIVITY

TODDLER: CHANGE IN PHYSICAL ACTIVITY: FOLLOW-UP 1 AND FOLLOW-UP 2



CAREGIVER: CHANGE IN PHYSICAL ACTIVITY: FOLLOW-UP 1 AND FOLLOW-UP 2

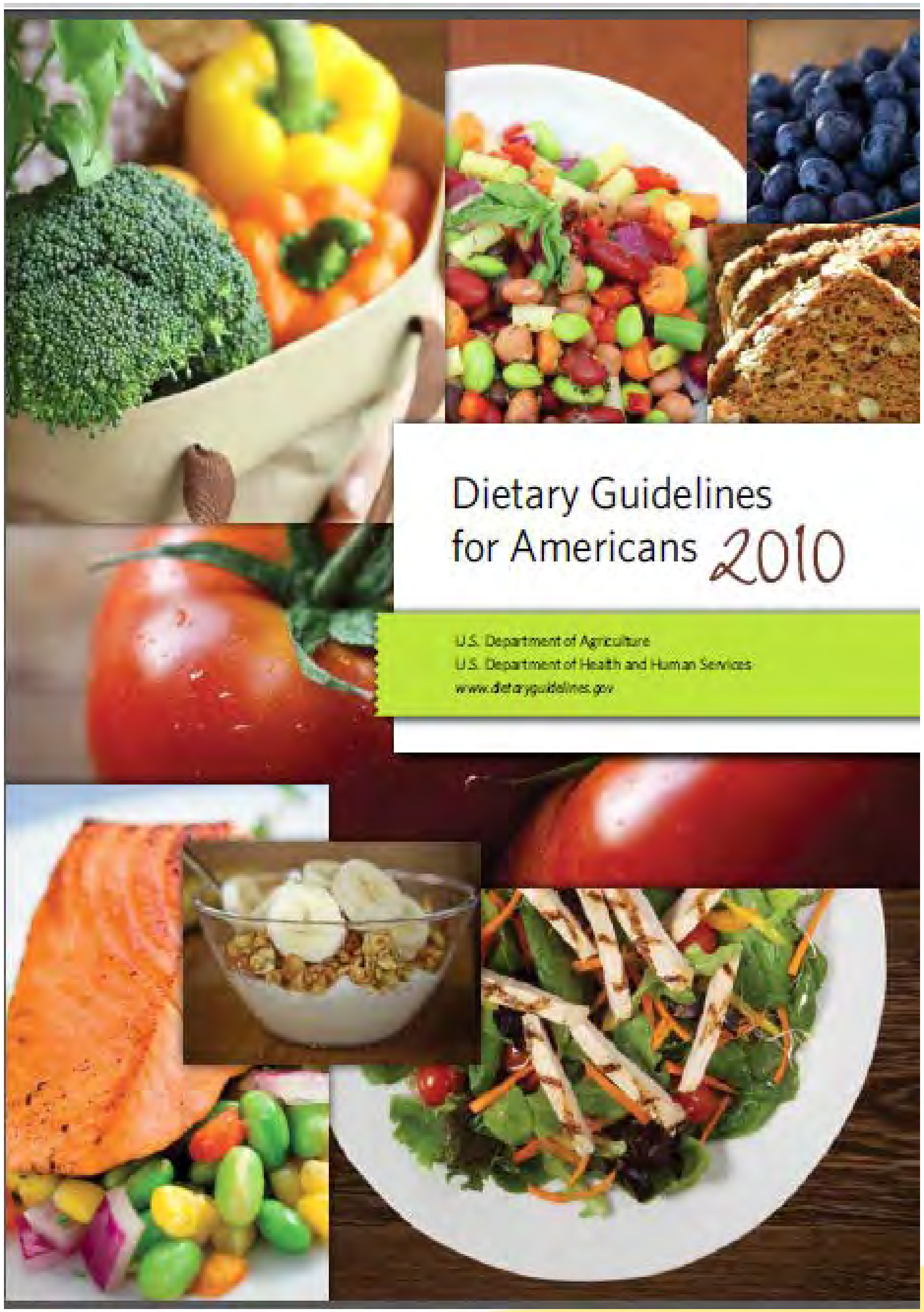


At baseline caregivers engaged in approximately 25 minutes MVPA/day

FU #1: No significant change

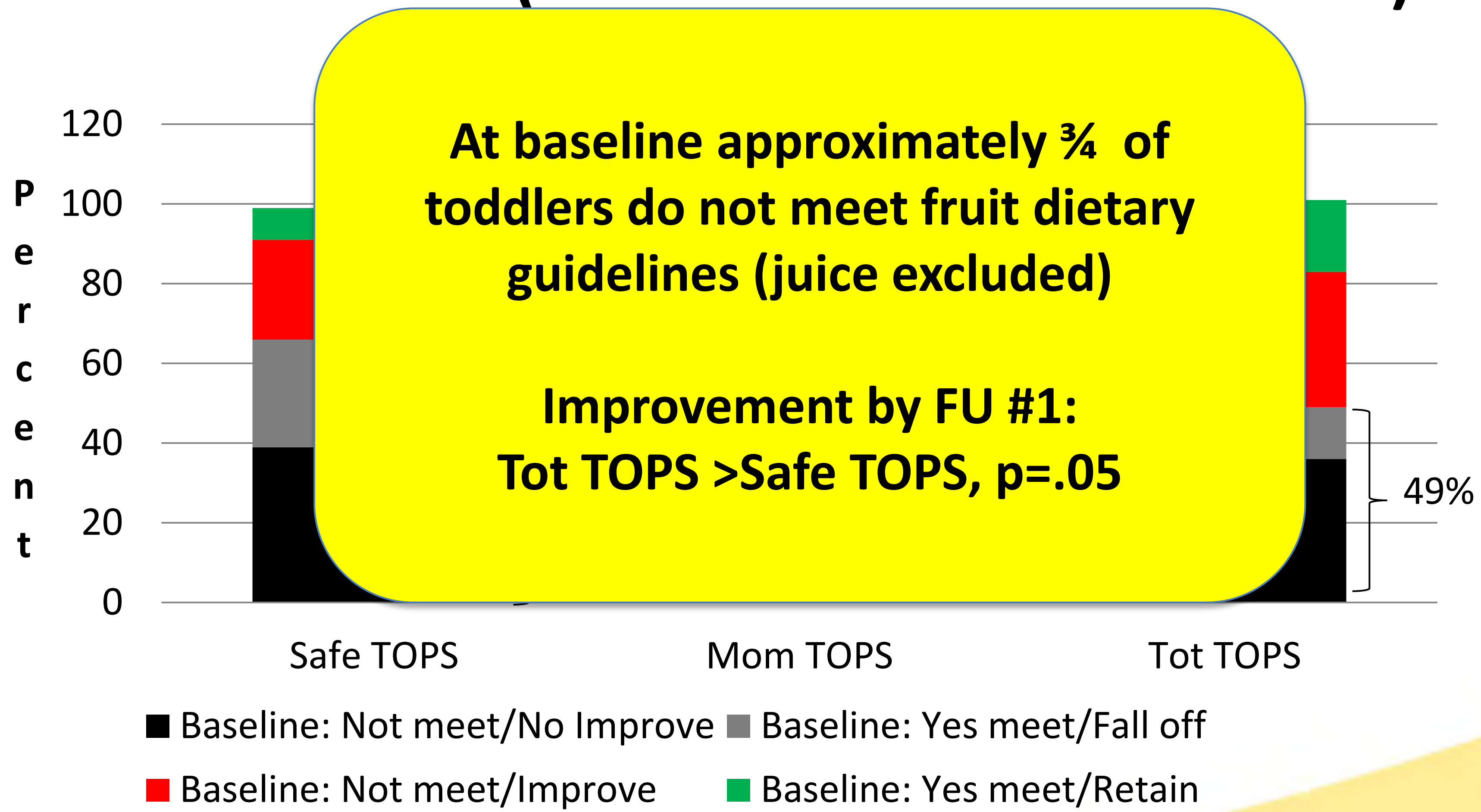
FU #2: Mom TOPS > Safe TOPS, p=.02

CHANGES IN DIET

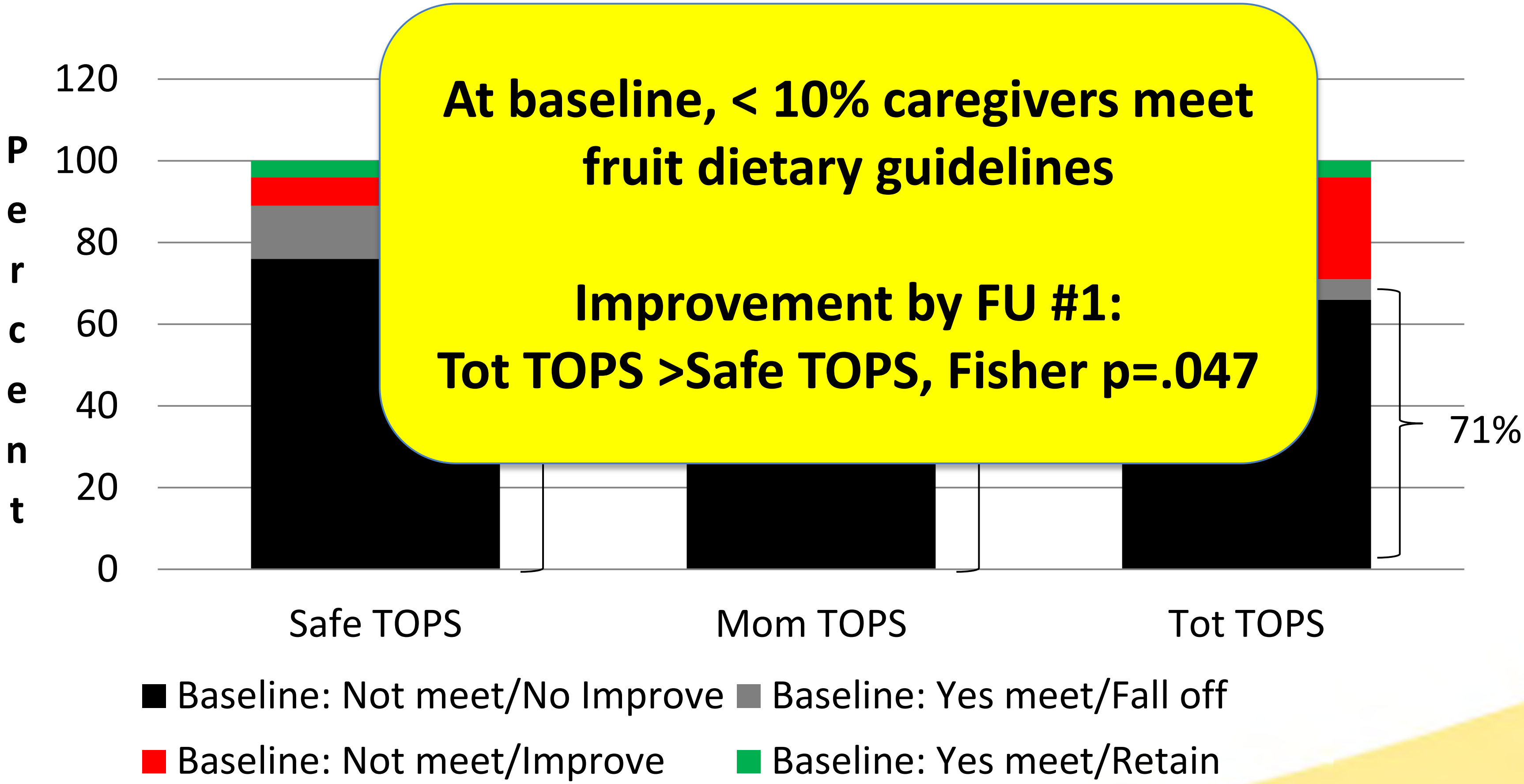


- **Dietary Patterns**
- **Feeding Behavior**

TODDLER: TOTAL FRUIT EXCLUDING JUICE FOLLOW-UP #1 (FOLLOWING INTERVENTION)

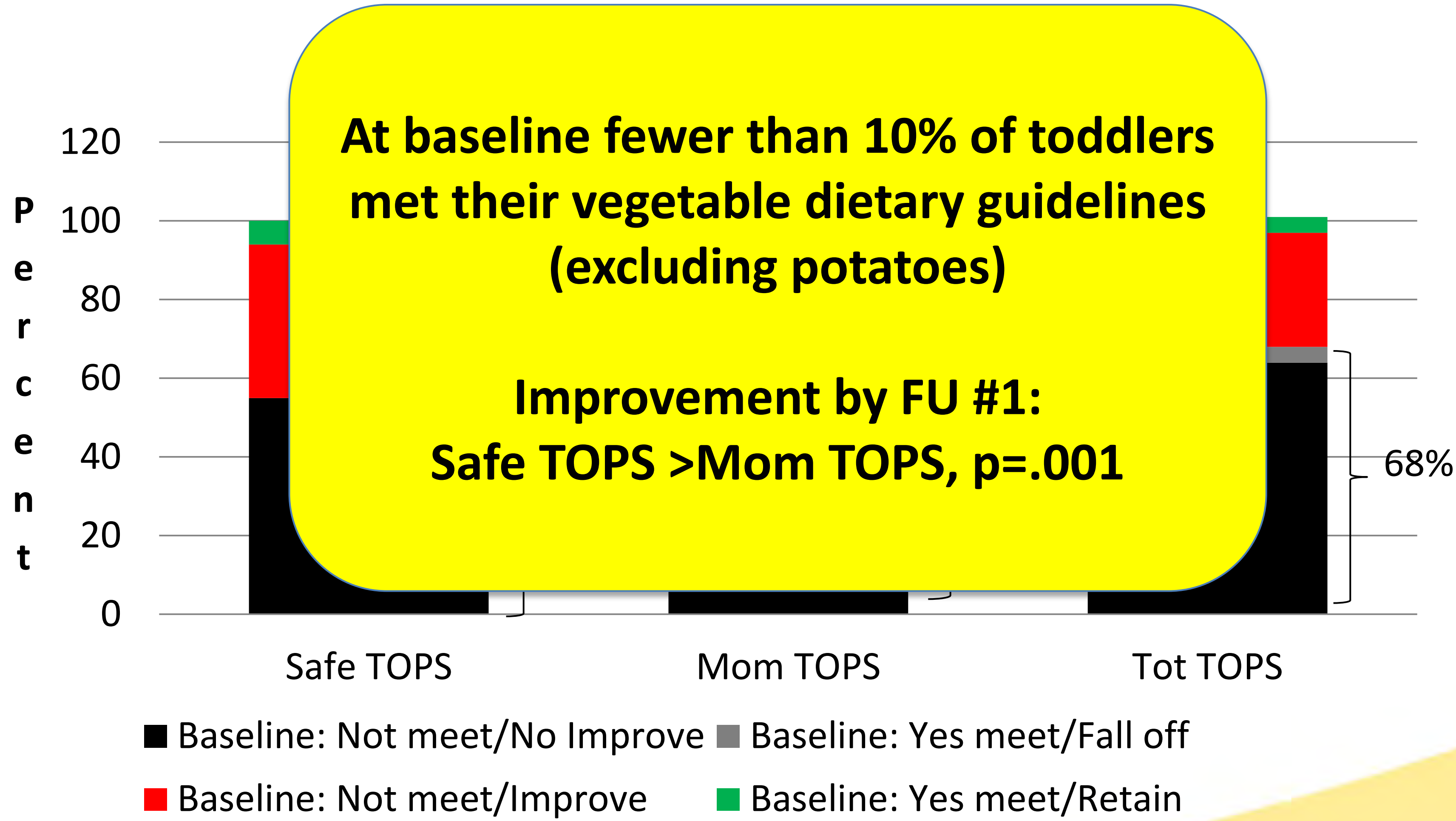


CAREGIVER: TOTAL FRUIT EXCLUDING JUICE FOLLOW-UP 1* (FOLLOWING INTERVENTION)

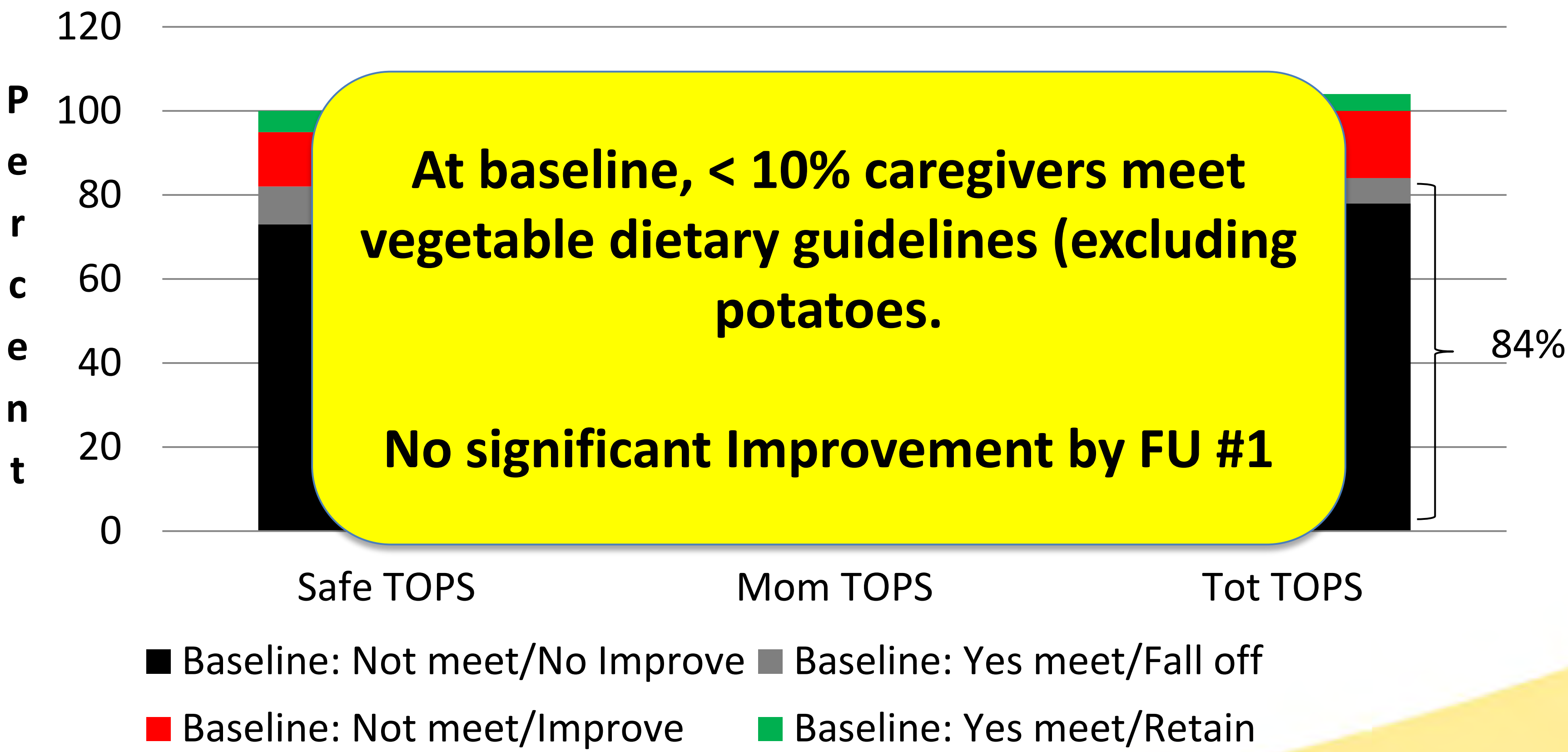


*Removed pregnant women

TODDLER: TOTAL VEGETABLES EXCLUDING POTATOES FOLLOW-UP 1 (FOLLOWING INTERVENTION)



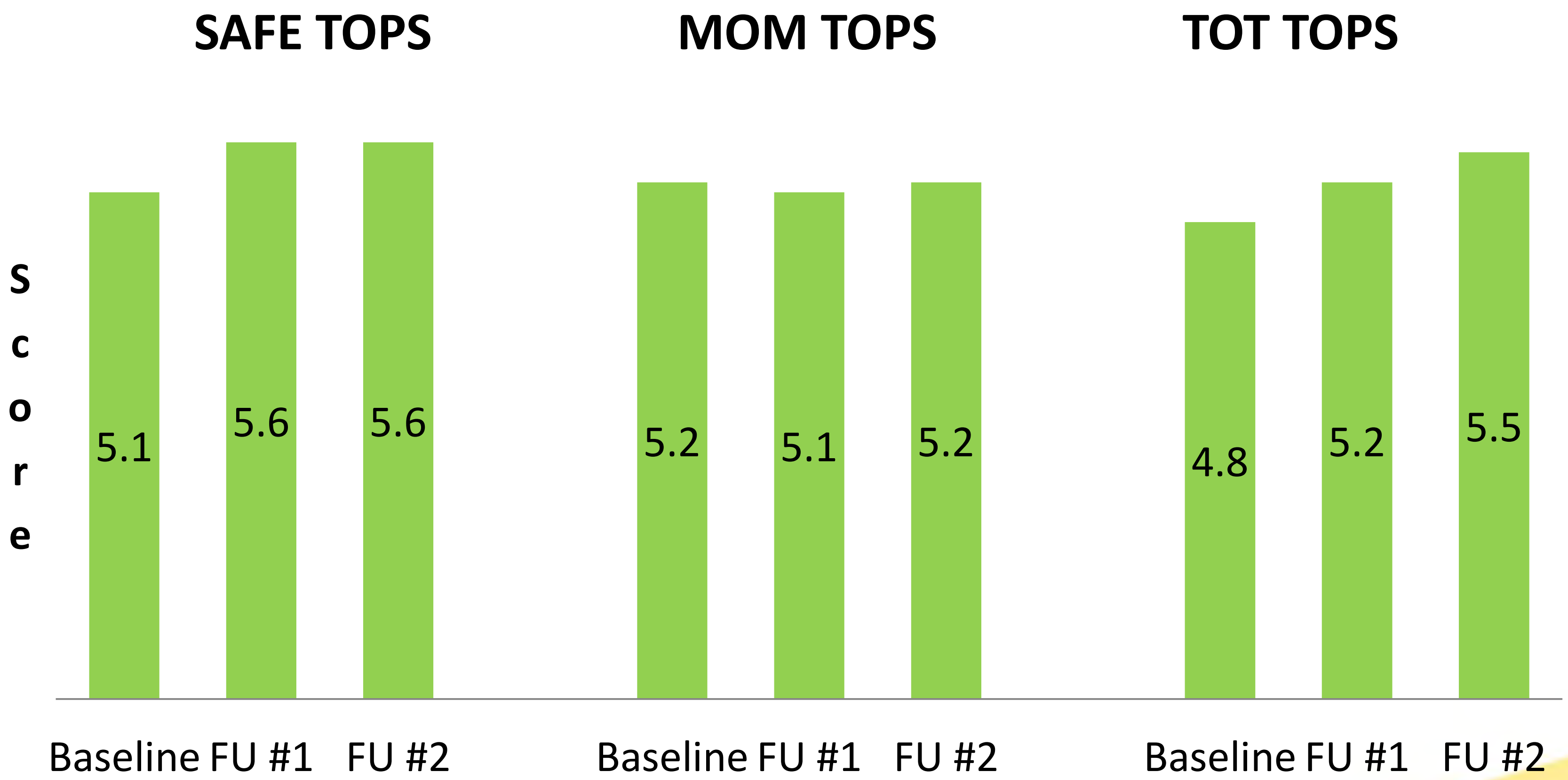
CAREGIVER: TOTAL VEGETABLES EXCLUDING POTATOES FOLLOW-UP 1* (FOLLOWING INTERVENTION)



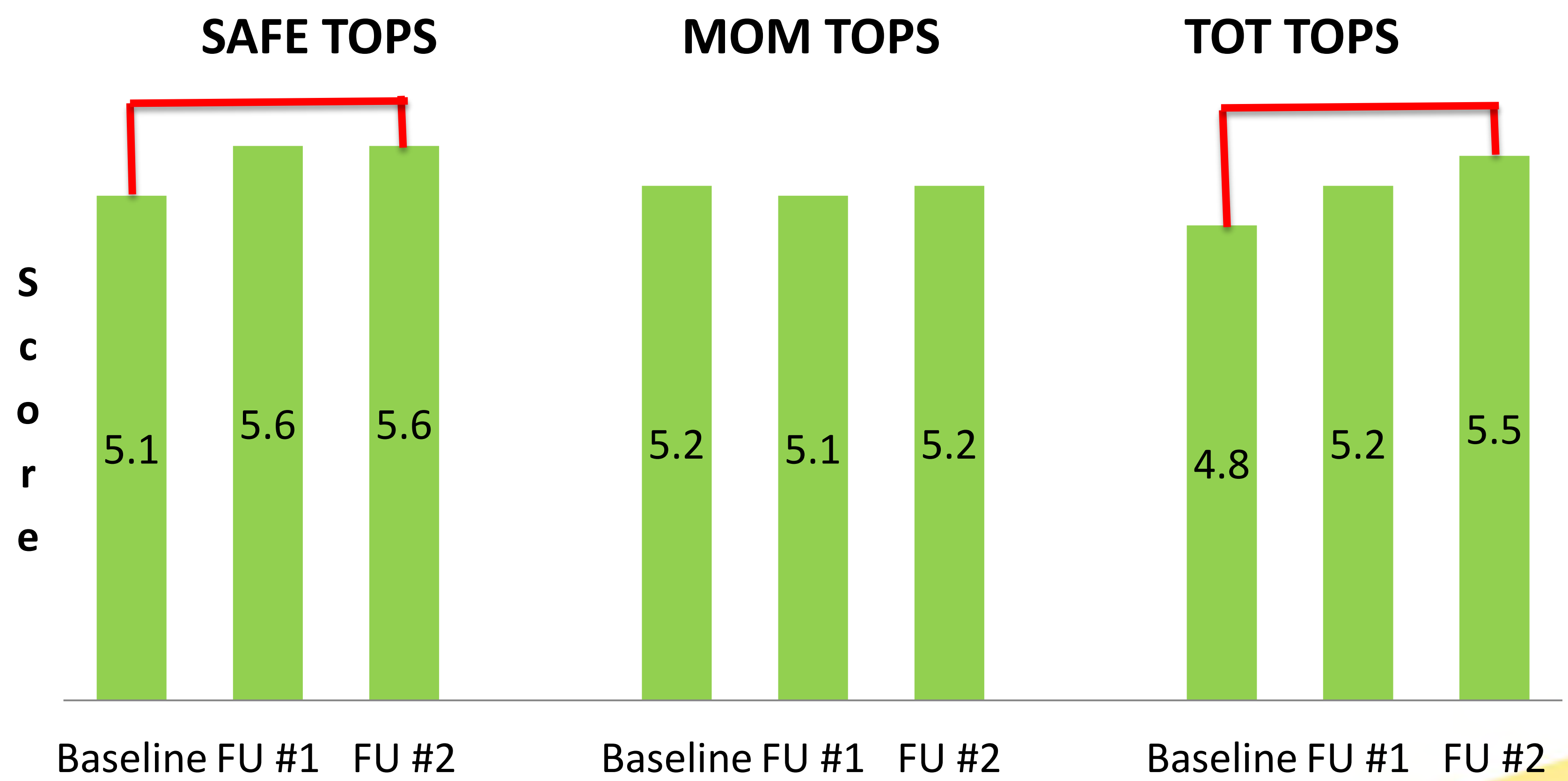
*Removed pregnant women

CHANGES IN FEEDING BEHAVIOR

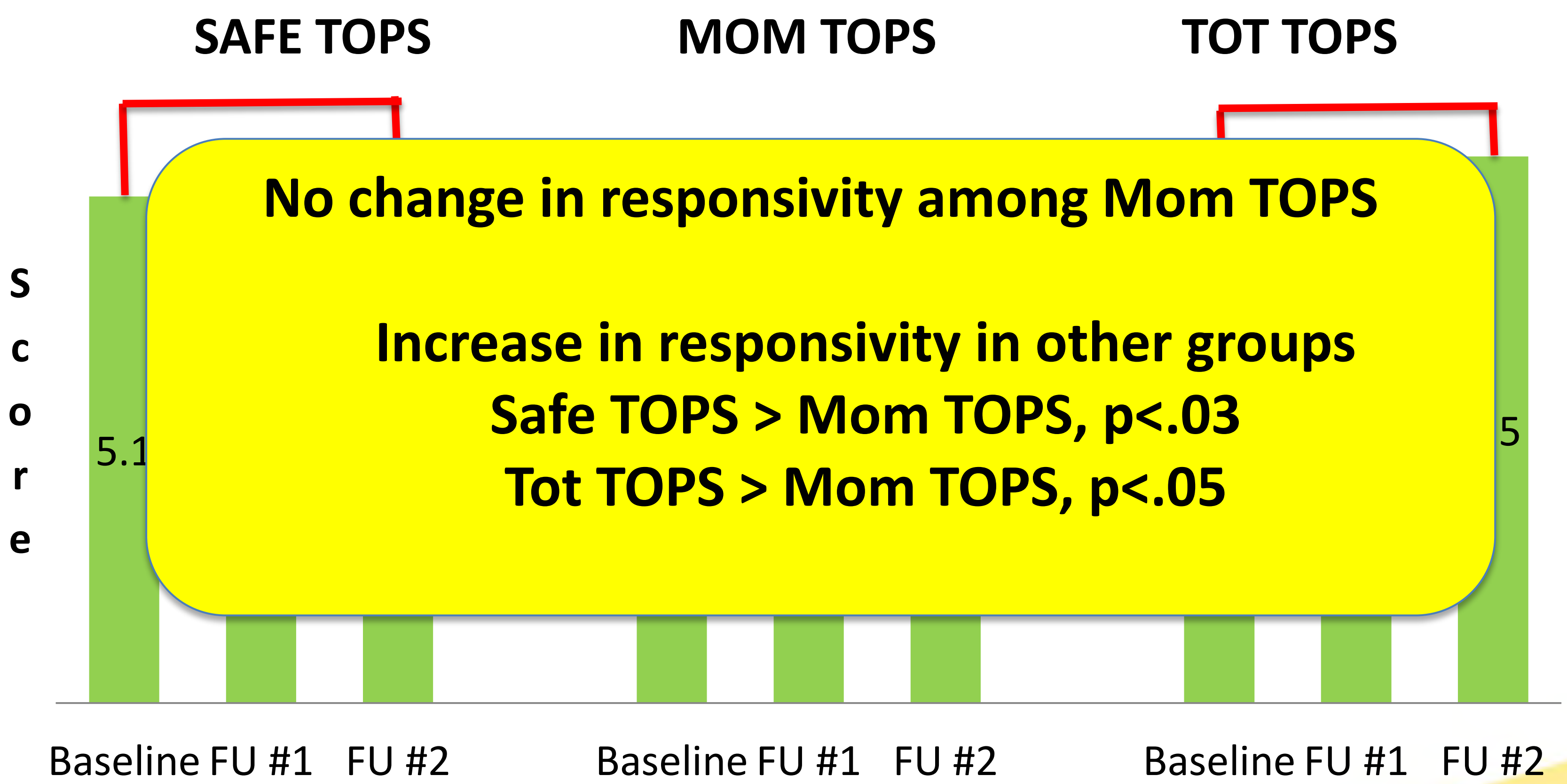
Caregiver/Toddler: Change in Responsive/Non-hostile Interactions: Follow-Up 1 and Follow-Up 2



Caregiver/Toddler: Change in Responsive/Non-hostile Interactions: Follow-Up 1 and Follow-Up 2



Caregiver/Toddler: Change in Responsive/Non-hostile Interactions: Follow-Up 1 and Follow-Up 2



No change in responsivity among Mom TOPS

Increase in responsivity in other groups

Safe TOPS > Mom TOPS, p<.03

Tot TOPS > Mom TOPS, p<.05

CONCLUSIONS (WEIGHT)

1. Excessive weight gain began < 20 months
   - Need for strategies to prevent excessive weight gain during infancy

2. No group differences. Did not see expected increase in weight status from 20-32 months.
   - WIC recipients.

3. 75% caregivers overweight/obese – no change

CONCLUSIONS (PHYSICAL ACTIVITY)

- Toddlers and caregivers increased in MVPA
- Stronger in the maternal lifestyle group (Mom TOPS)
  - Trickle-down from caregiver to toddler?
  - Evidence suggesting joint physical activity (Hager, 2013)

CONCLUSIONS (DIET)

- Few toddlers or caregivers met dietary guidelines for fruits and vegetables
- Modest improvement in toddler & caregiver fruit intake – parenting group (Tot TOPS)
- Placebo group (safety) increased vegetable intake
    - Did goal setting skills, availability of healthy snacks, focus on protecting toddlers (safety), and questions about diet lead to better diet??

CONCLUSIONS (FEEDING BEHAVIOR)

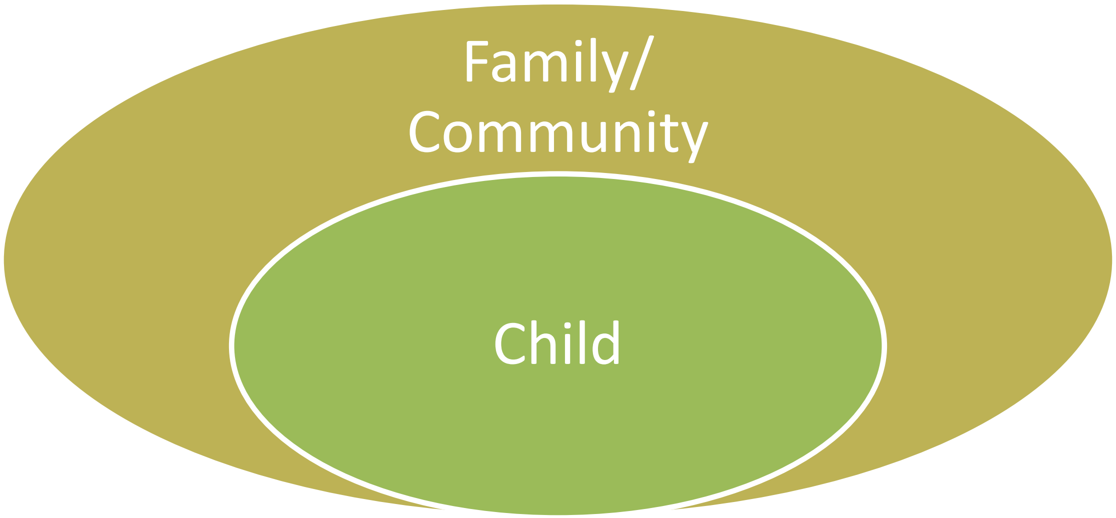
- Helping caregivers focus on their toddlers through **behavior management OR safety** led to increases in responsive/non-hostile interactions

- Focusing on maternal life styles (diet and physical activity) had no impact on feeding behavior

RECOMMENDATIONS

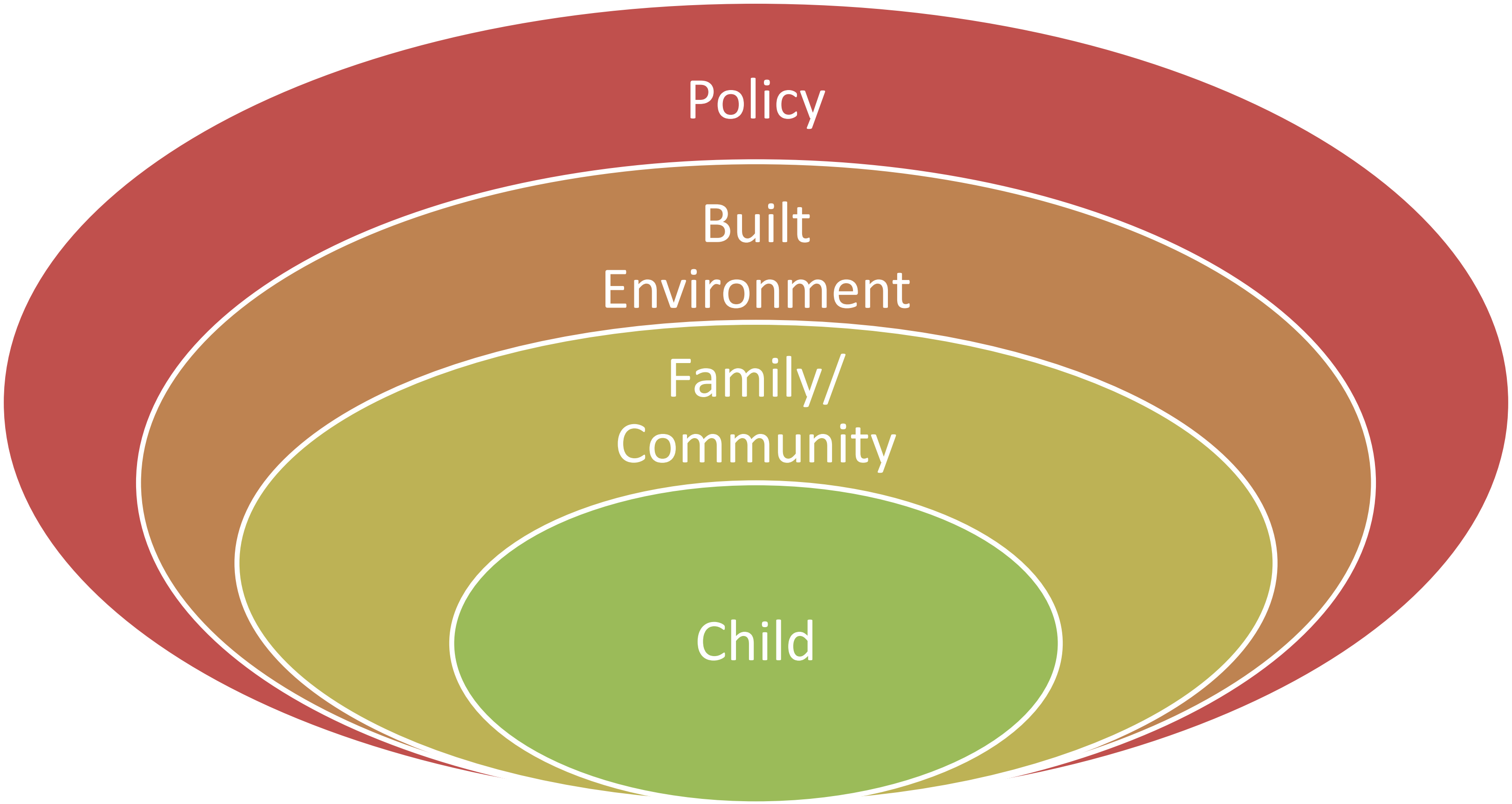
- Behavior change theory
- Early: Before habits established
- Active: Involve caregiver & child
- Context: Relevant to families (overcome barriers)
- Multi-level (social norms)

Rationale: Using Policy to Prevent Obesity in Young Children



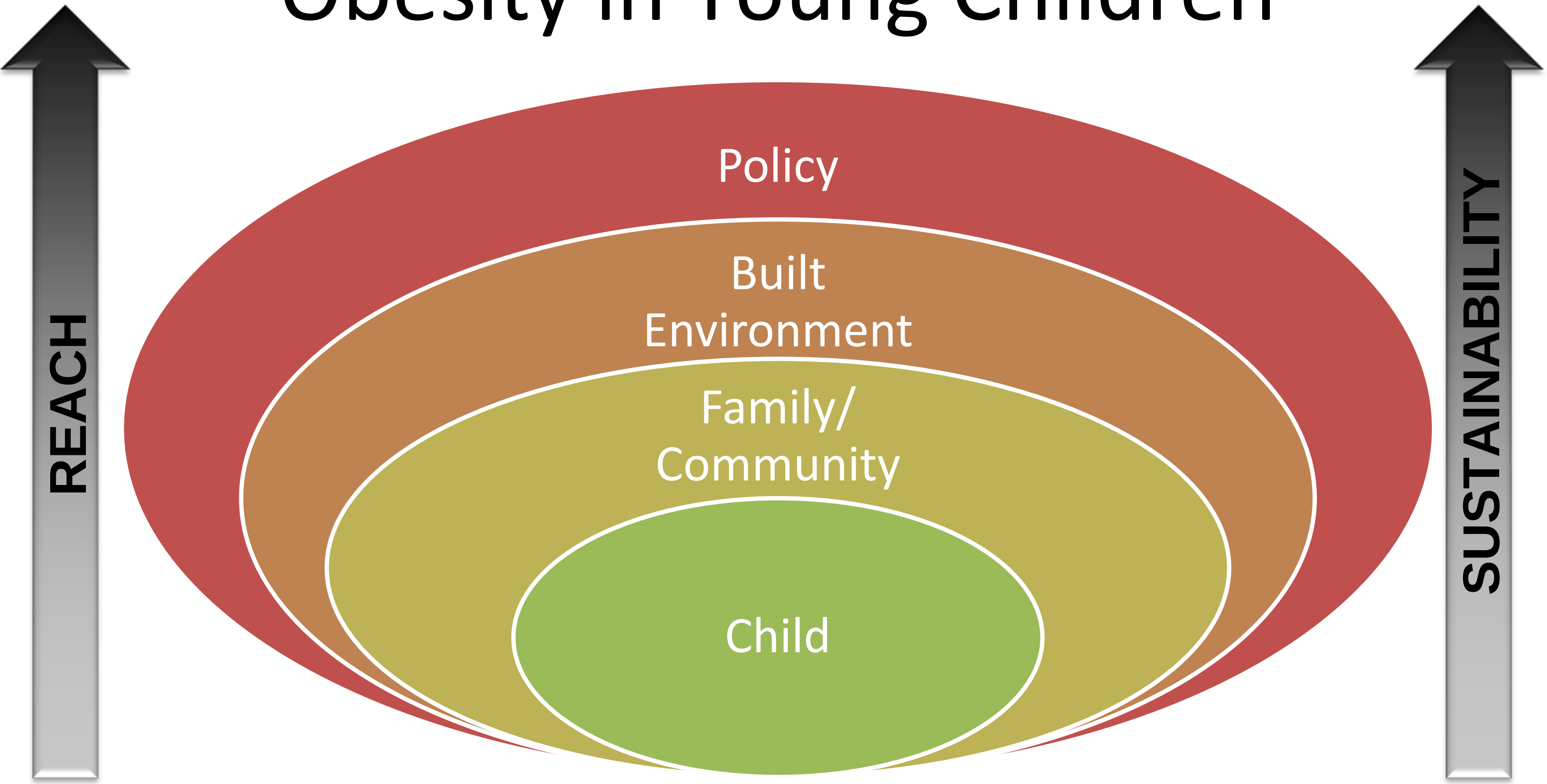
Bronfenbrenner, 1979

Rationale: Using Policy to Prevent Obesity in Young Children



Bronfenbrenner, 1979

Rationale: Using Policy to Prevent Obesity in Young Children

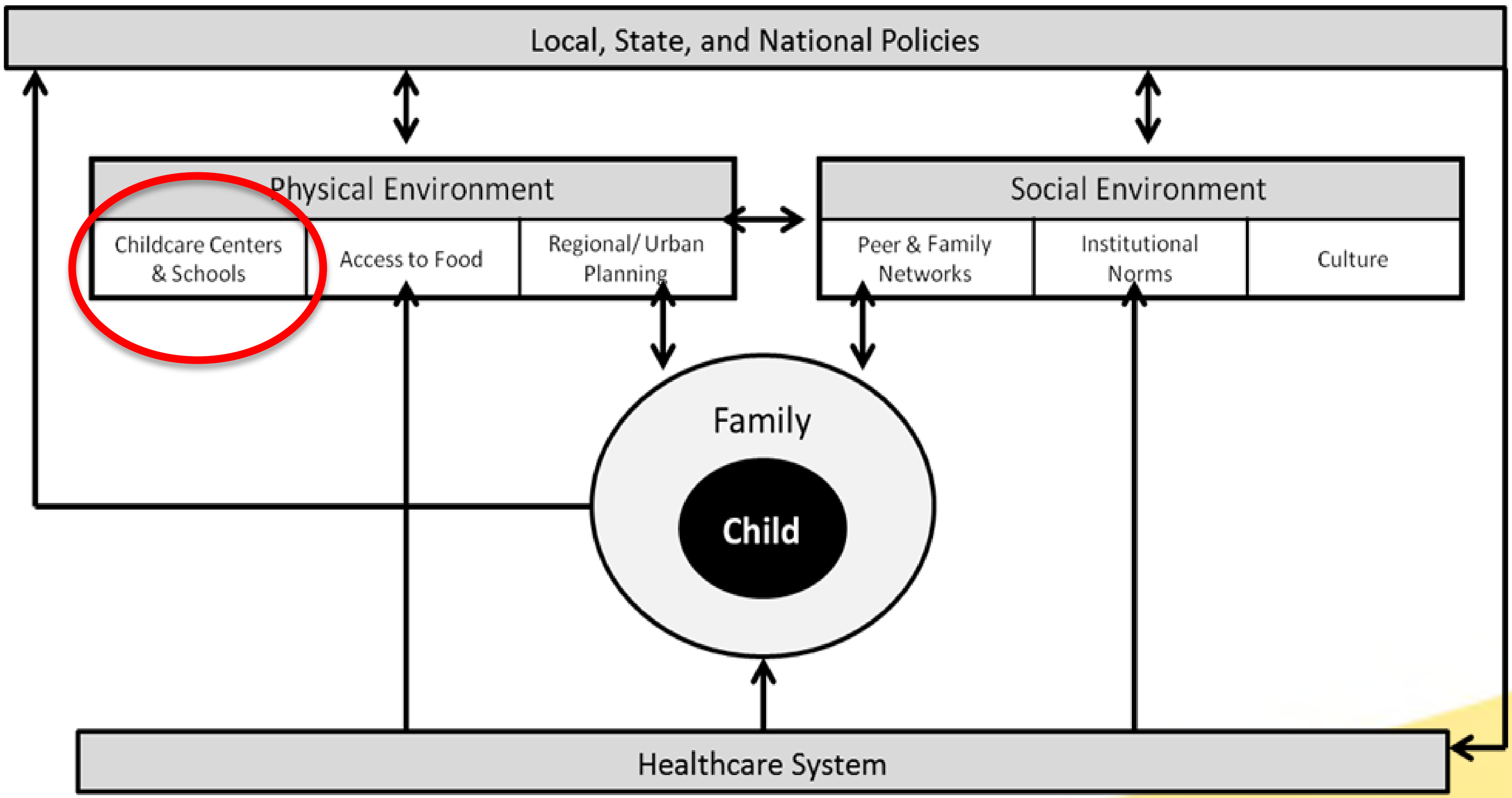


Bronfenbrenner, 1979

Journal of Pediatric Psychology Advance Access published September 6, 2013

Commentary: Pediatric Obesity: Systems Science Strategies for Prevention

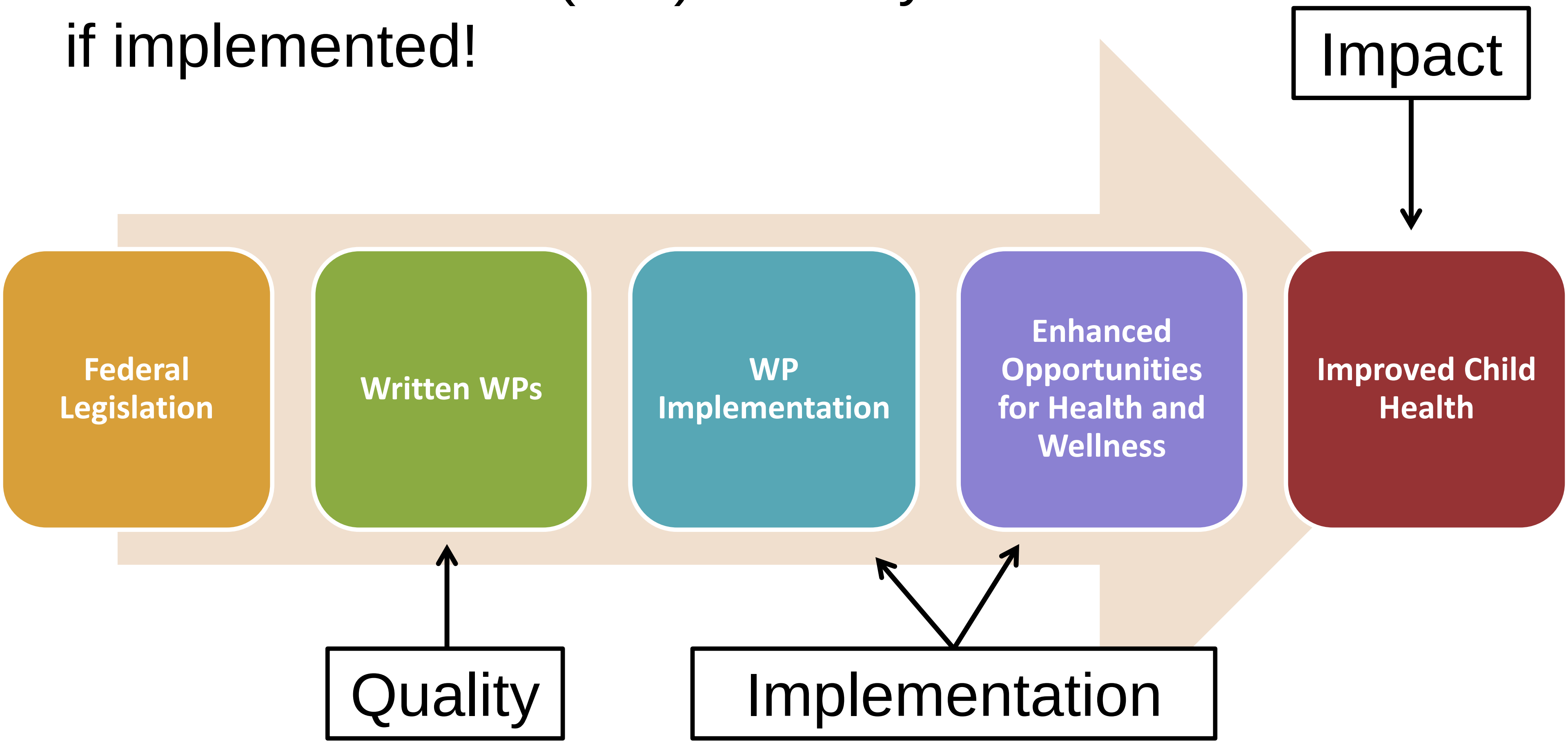
Maureen M. Black, PhD, and Erin R. Hager, PhD
Division of Growth and Nutrition, Department of Pediatrics, University of Maryland School of Medicine



Childcare

- 30-40% children < age 6 attend childcare centers or family care
- Average 30 hours/week, multiple meals
- AAP, APHA, National Resource Center for Health & Safety in Child Care – standards
- State regulation
- National Assn of Child Care Resources & Referral Agencies
  - Water available
  - No forcing to eat
  - No food rewards
  - Limit screen time
  - Limited sugar sweetened bev
  - Limited low nutrient dense foods
  - Breastfeeding support & breast milk
  - Daily physical activity

Wellness Policies (WP) are only effective if implemented!



THANK YOU

Bottle Feeding: Influence on Weight, Weight Gain, and Later Obesity

Karen A. Bonuck, PhD

NIH Workshop on Prevention of Obesity in Infancy and Early Childhood, Oct. 30- Nov. 1, 2013

(Christel Hyden, EdD, post-workshop supplemental slides)

Bottle-Feeding: Early Rapid Growth and Obesity in Early Childhood

- Bottle Feeding: Guidelines, Definitions, Prevalence
- Data: Link to Rapid Growth & Obesity
- Hypotheses: Bottle Role in Obesity
- Factors: Demographics & Beliefs
- Interventions: FYCS & Others
- Issues & Future Research

Prolonged Bottle Use

- AAP: Introduce cup at 6 months; bottle-wean by 15 months
- Bright Futures: "Drinking from a cup" is a developmental milestone for 12 month olds
- WIC: Failing to begin & complete weaning by 12 – 14 months are nutritional risks
- AAPD: Wean from bottle by 12 months

Inappropriate Bottle Use

- Use of bottle to feed juice
- Bottle-propping/unrestricted use
- Bed- or nap-time bottle
- Adding food to bottle
- Adding any sugar-containing liquid

- (WIC Priority 4: Inappropriate Nutrition Practices for Infants)

Prevalence: Prolonged Bottle Use

Bottle Use, Duration	White	Black	Mexican-American
<12 Months	38%	45%	21%
13-23 Months	45%	41%	42%
24-48 Months	17%	14%	37%

(Brotanek, APAM, 2005 from NAHNES III)

Prolonged/ Inappropriate Bottle Use: Demographics

- At 2 years:
  - Ethnicity: 37% Hispanic v 15% Black or White
  - Education: < HS 32% v 16% College grad (mom)
  - Income: 26% lowest v 18% highest
  - 9 m W/L: not significant

- (Gooze J *Peds* 2011, ECLS “regular use of bottle”)

Prolonged Bottle Use & Obesity Risk: Cross-sectional data

- *Fragile Families*- bedtime bottle at 3 yrs, doubles obesity odds

- *Bronx, NY WIC studies:*

- *Study #1* Among n=95 Hisp/AA, 63% use bottles, range 3-10/day:

		Bottles (YES)	Bottles (NO)	
>85% BMI	18-56 m	56%	41%	($p<.06$)
>95% BMI	18-56 m	39%	29%	($p<.05$)

- *Study #2 Among n=150, 60% use bottles, median = 5/day*

		Bottles (YES)	Bottles (NO)	
>85% BMI	12-36 m	27%	11%	($p<.11$)
	37-60 m	27%	36%	($p<.74$)
>95% BMI	12-36 m	19%	0%	($p<.02$)
	37-60 m	20%	24%	($p<1.0$)

- [Kimbro, AJPH, 2007; Bonuck Clin Peds 2002; Bonuck, MCN, 2010]

Prolonged Bottle Use & Obesity Risk: prospective data

Early Childhood Longitudinal Study-

Bottle @ 2 yrs → obesity @ 5.5 yrs , OR= 1.33

[Gooze, J Peds, 2011]

NHANES III- 3% increased odds of higher BMI group, w/each extra month bottle use, among 3-5 year olds (<85%, 85%-95%, > 95%)

[Bonuck, Clinical Peds.2004]

Bottle-feeding Effects on obesity Risk: Hypotheses

- Infant Hunger & Satiety Cues (Infant)
- Maternal Behavior (Caregiver)
- Bottle Contents: Formula v. Breast-milk (Milk)
- Bottle: As Vessel for Extra Calories (Vessel)
  - Prolonged bottle feeding

Infant Hunger & Satiety Cues

- Infants born with ability to self-regulate intake
- Feeding directly at breast is ‘infant controlled’
- Infant controls suckling flow
- Infant disengages from breast when full

- *Bottle-feeding either milk or formula does not provide these opportunities*

Maternal Behavior

- <u>Responsive Feeding</u>: Caregivers may ignore/be unaware of infant or toddler cues
- <u>Bottle as Visual Cue</u>: Caregiver may see remaining milk/formula as 'cue' to empty bottle
- <u>Weight Gain</u>: Mistaken belief that rapid weight gain is good, may impel bottle-emptying behavior
- <u>Sleep</u>: "A full baby sleeps better"

Bottle v. Milk Type: Effects on Feeding & Weight Gain in First Year of Life

- Infant Feeding Practices Study-II (FDA & CDC)
- Longitudinal study of feeding practices, 0-12 mos
- Participants completed up to 10 mailed surveys
- Mother report of infant wt at recent health visit
- Includes data on:
  - milk type (human v not)
  - % feedings by bottle
  - Weight gain in 1st year

Bottle Use – *Not Milk Type per se* – Affects Bottle/Cup "Emptying"

Intensity of bottle use or feeding type, 0-6 mos.	OR, emptying bottle, 7-12 mos.	95% CI
Each 10% increase, *overall bottle* intensity	1.09	1.05-1.13
Each 10% increase, *formula feeding* intensity	1.09	1.05-1.13
Each 10% increase, *expressed milk* feeding intensity	1.15	1.04-1.27

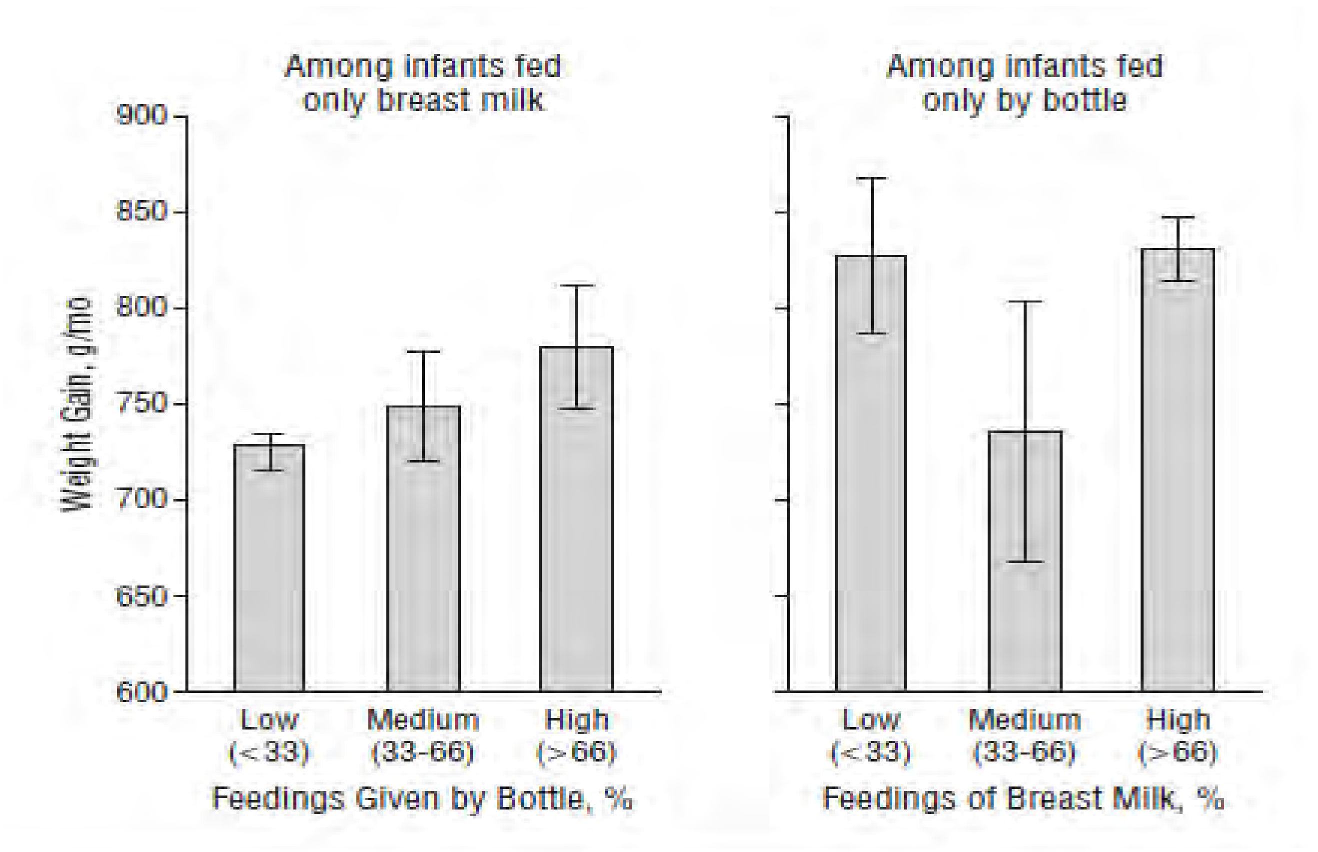
(Li et al, Pediatrics 2010)

Bottle Feeding and Weight Gain: 1st Year of Life (li et al APAM 2012)

Table 3. Multilevel Analyses of Linear Monthly Weight Gain for Each Feeding Category Compared With Infants Fed at Breast Only for 1899 Infants[a]

Group No./Feeding Category	No.	Weight Gain, g/mo	95% CI
1/Breastfed only (reference)	936	0	
2/Breastfed and human milk by bottle	1108	10.11	–8.72 to 26.88
3/Breastfed and nonhuman milk by bottle	1518	45.15	30.00 to 60.30
4/Human milk by bottle only	34	88.83	13.19 to 164.47
5/Human and nonhuman milk by bottle	107	37.18	–5.06 to 79.42
6/Nonhuman milk by bottle only	2016	71.25	56.03 to 86.47

Weight Gain by Milk Type & Bottle



(Li et al. APAM 2012)

Bottle Contents: Formula v. Breastmilk

- Early Protein Hypothesis:
  - European multi-center trial of healthy formula fed infants, breastfed comparison group
  - Randomized to low v. high protein formula
  - At 24 mo, weight-for length z scores in lower protein formula group was 0.20 (0.06, 0.34) *lower* than higher protein group…*and did not differ from breastfed group* *(Koletzko, AJCN, 2009)*

Among women who bottle feed, 76% are using the bottles for formula. Just 24% put human milk in bottles. (IFPS)*

Prolonged/ Inappropriate Bottle Use: Reasons

- Reasons: convenience/avoid crying, won't fall asleep, chubby baby is good, to get enough milk
- Knowledge gaps: when & why to wean at 1 year, links to IDA/anemia, milk needs of 1+ year old
- Incorrect beliefs: 2 yrs good age to wean, > 2 cups milk/day is good

(Brotanek, *Academic Peds*, 2009)

Interventions: Responsive Feeding

- WIC Bottle-Feeding Practices
  - RCT of > 800 formula-fed, 1 month olds
  - Messages: aware/respond to infant cues & not fill > 6 oz
  - Result: No effect on practices or infant growth
- Primary Care RCT of Bottle-Weaning
  - RCT of 251, all feeding, 9 month visit, 1 week protocol
  - Earlier cup use= 9 vs. 12 months
  - Earlier bottle weaning = 12 vs. 16 months
  - ≠ affect primary outcomes = iron & > 16 oz milk

  * No measures of sippy cups, diet or weight

(Kavanagh, 2008 JNEB; Maguire 2010Pediatrics)

Feeding Young Children Study (FYCS)

RCT of WIC based bottle-weaning intervention:

- 1st Aim= Reduce bottle use
- 2nd Aim= Reduce rate of children > 85% weight-for-length
- 3rd Aim= Observational study of diet changes
- Sample= 12 month olds drinking 2+ bottles/day

Feeding Young Children Study (FYCS)

Measures:

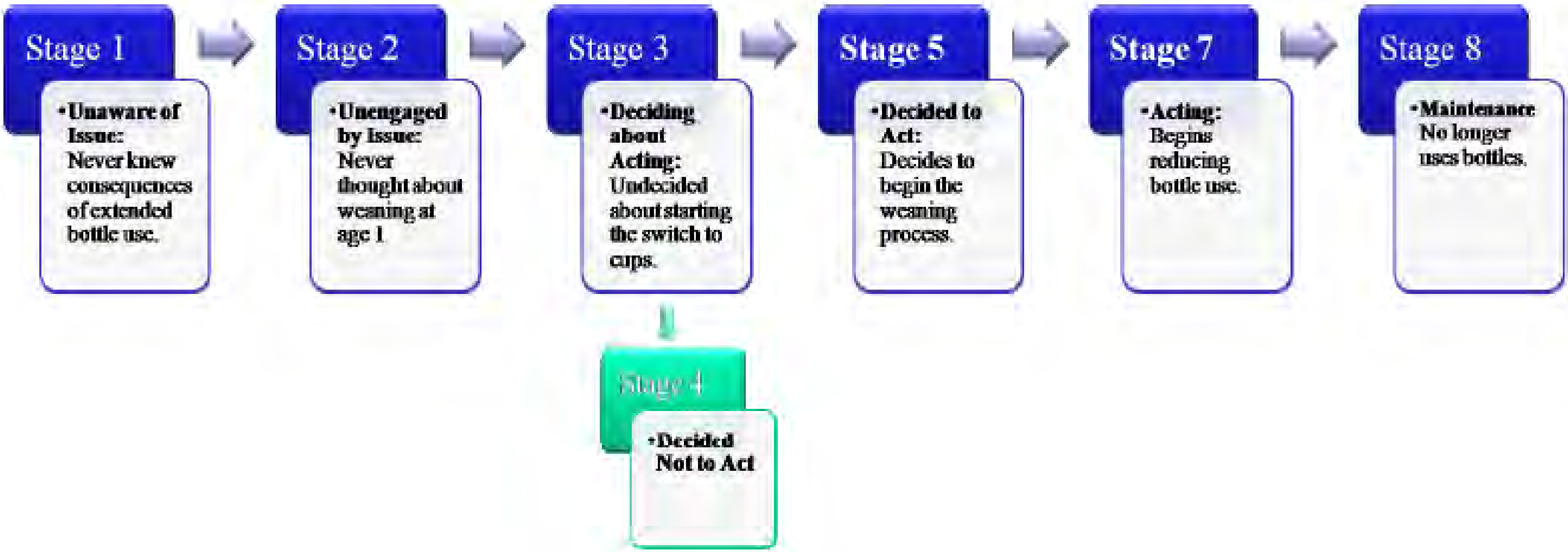
- NDSR 24-h recall on diet & energy intake @ 15, 18, 21, 24 mos
- Assessed drinking container as: bottle, sippy cup, cup, other
- Research-based weight-for-length

About This Tool

Underlying Theoretical Model

For behaviors with known risks & benefits, discussing behavior change "trade-offs" makes sense. Alternatively, lack of awareness of risks and benefits can dampen engagement in the change process. We posit that WIC clients are unlikely to appreciate the *full* gamut of potential risks (dental caries, overweight, iron deficiency anemia) of bottle use past 1 year of age, along with the potential benefits (e.g., improved speech & swallowing skills) of timely weaning.

Our conceptual framework, the Precaution Adoption Process Model (PAPM) outlines a pathway from 'lack of awareness' to 'adopting or maintaining a healthy behavior.' The PAPM is uniquely apt, given the relative lack of awareness of the above consequences of prolonged bottle use. Here is a brief summary of the PAPM, and how it would apply to bottle weaning:



FYCS Design & Messages

- WIC-nutritionist counseling
- Focus on continued bottles as risk for:
  - Iron Deficiency Anemia - excess calcium blocks iron
  - Early Childhood Caries- most common peds condition
  - Weight gain- “healthier” rate

<u>Remember:</u>

Milk and juice are okay,

in the right amount and in the right way.

What to Expect: Eating

What are your concerns about [child] drinking milk from a cup?

Parent Concern	Sample Responses
"I'm afraid my child won't drink enough milk."	*At first, [child] may not.* *Child will soon take milk from a cup.* *1 year olds don't need more than 16 ounces a day.* *(see Educational material: Calcium)*
"The milk will spill."	*Use a lidded cup filled only halfway.*
"I'm afraid my child won't eat enough."	*The amount and type of food children eat varies.* *They don't eat a square meal.* *They eat what tastes good.* *Think about what your child eats over a week or so to judge if s/he is getting enough.*

Golden rule of feeding children: Parent provides, child decides.

Using cups develops the tongue, jaws and lips. This results in good swallowing skills. Over time, they'll get better at chewing and can enjoy the same foods that the rest of your family eats.

Other Sources of Calcium

1 – 3 year olds need up to 16 oz of milk

Calcium in these foods = calcium in 16 oz of milk

One slice of cheese =
8 Oz milk

Bottle Calories Add Up:

FYCS: Baseline Characteristics

Child Demographics (n=295)	
Age, months	12.6$\pm$0.48
Gender-Male	48.1%
Non-Hisp. White/ Other Non-Hispanic Black Hispanic Bi- or Multiracial	6% 17% 62% 15%

FYCS: Baseline Characteristics

Child Anthropometrics (n=295)	
Weight, kg	10.1$\pm$1.3
Weight for length z-score	0.56$\pm$1.2
Weight for age z-score	0.55$\pm$1.1
Length for age z-score	0.33$\pm$1.2
>= 85th percentile weight for length	35%
>= 95th percentile weight for length	20%

Parent Perception of Child Weight	
Underweight	6%
Right Size	89%
Overweight	6%

FYCS: Baseline Characteristics

Family Characteristics (n=295)	
Adult Age	28.3$\pm$7
Education High School or higher	72%
Mother born in US	56%
Father born in US	48%
No child care	68%
1 or more sibling	57%

FYCS: Beverage Consumption

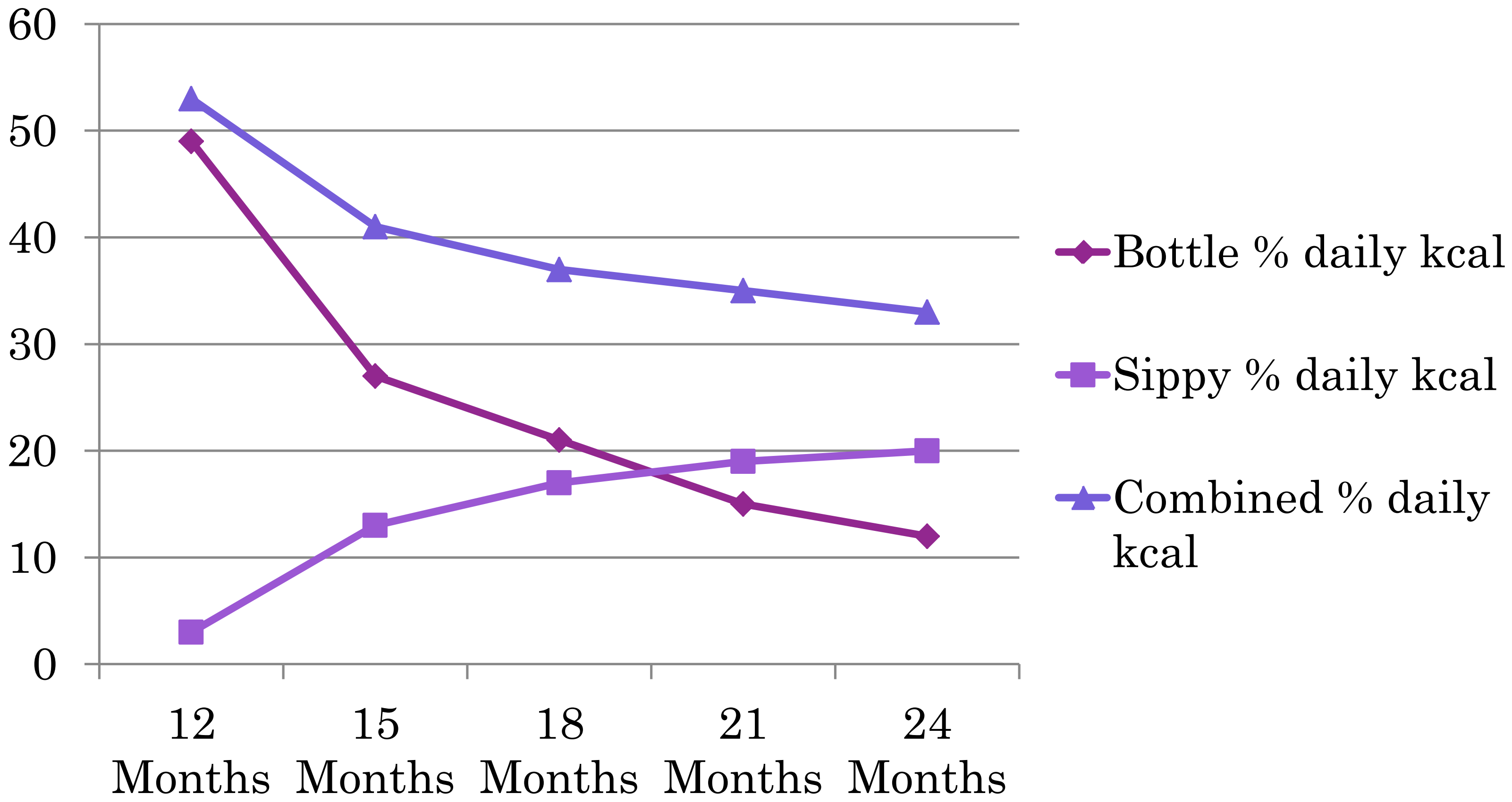
- Bottle and sippy cup contents =
  - 52% of energy intake at age 1 year
- Bottle and sippy cup contents =
  - 33% of energy intake at 2 years

FYCS: Weight, Bottles, & Energy

OR= compared to reference (Controls)	Effect Size	95% CI	P value
Weight-for-length	OR= 1.02	0.05-2.00	0.95
Any bottles	OR= 0.23	0.08-0.61	0.01
# Bottles	OR= 0.71	0.57-0.90	0.01
% Energy via milk bottles	OR= 0.36	0.18-0.74	0.01
Total daily kcal intake	B= -1.15	SE= 0.57	0.04

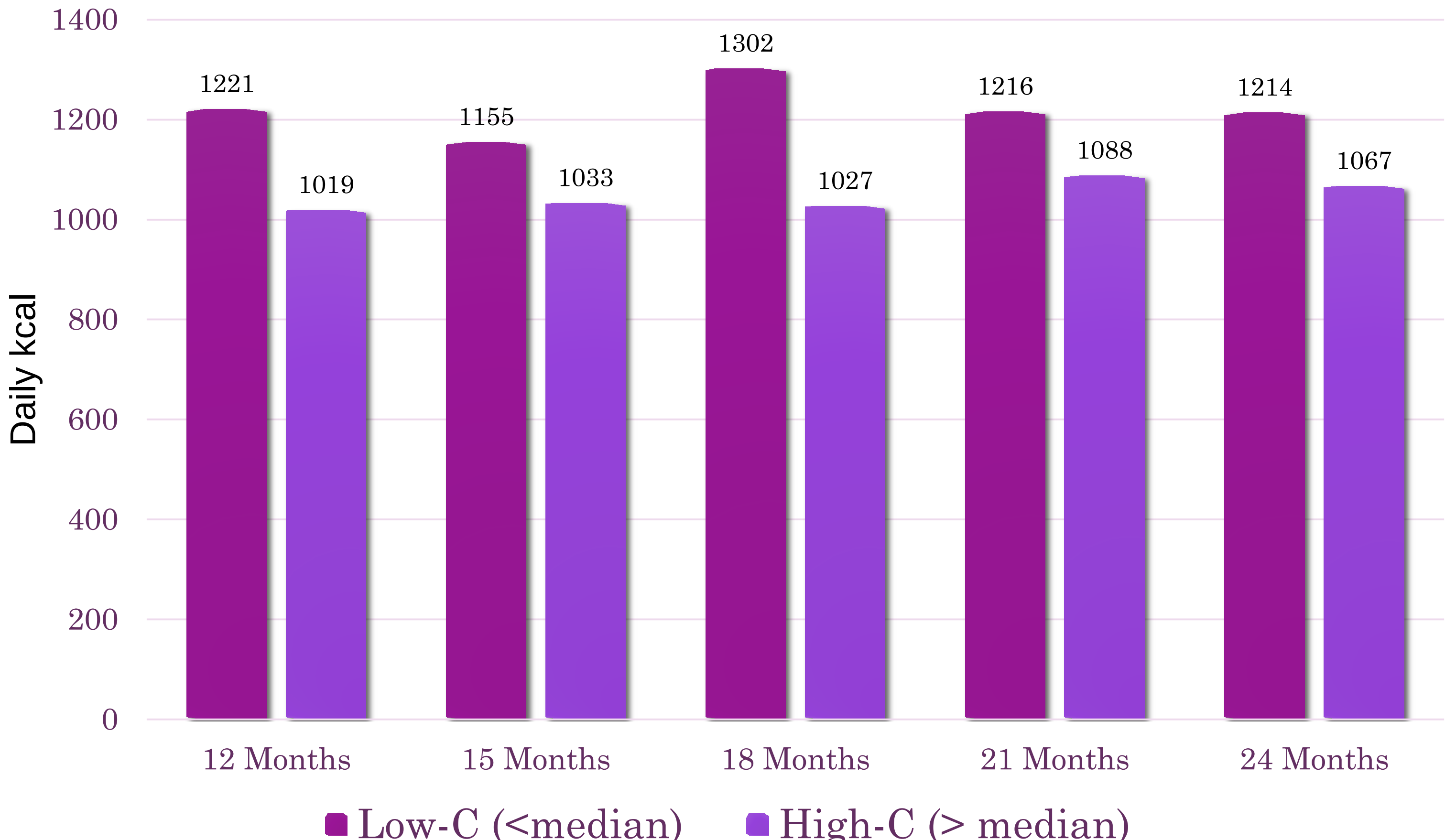
(Bonuck, J Peds, , October 30 2013)

Bottle + Sippy % Energy in FYCS: 2+ bottle/day at 12 mos.



(Ben Avraham, unpublished)

FYCS: Energy (kcal)/day, by % Energy From Containers (bottle + sippy)



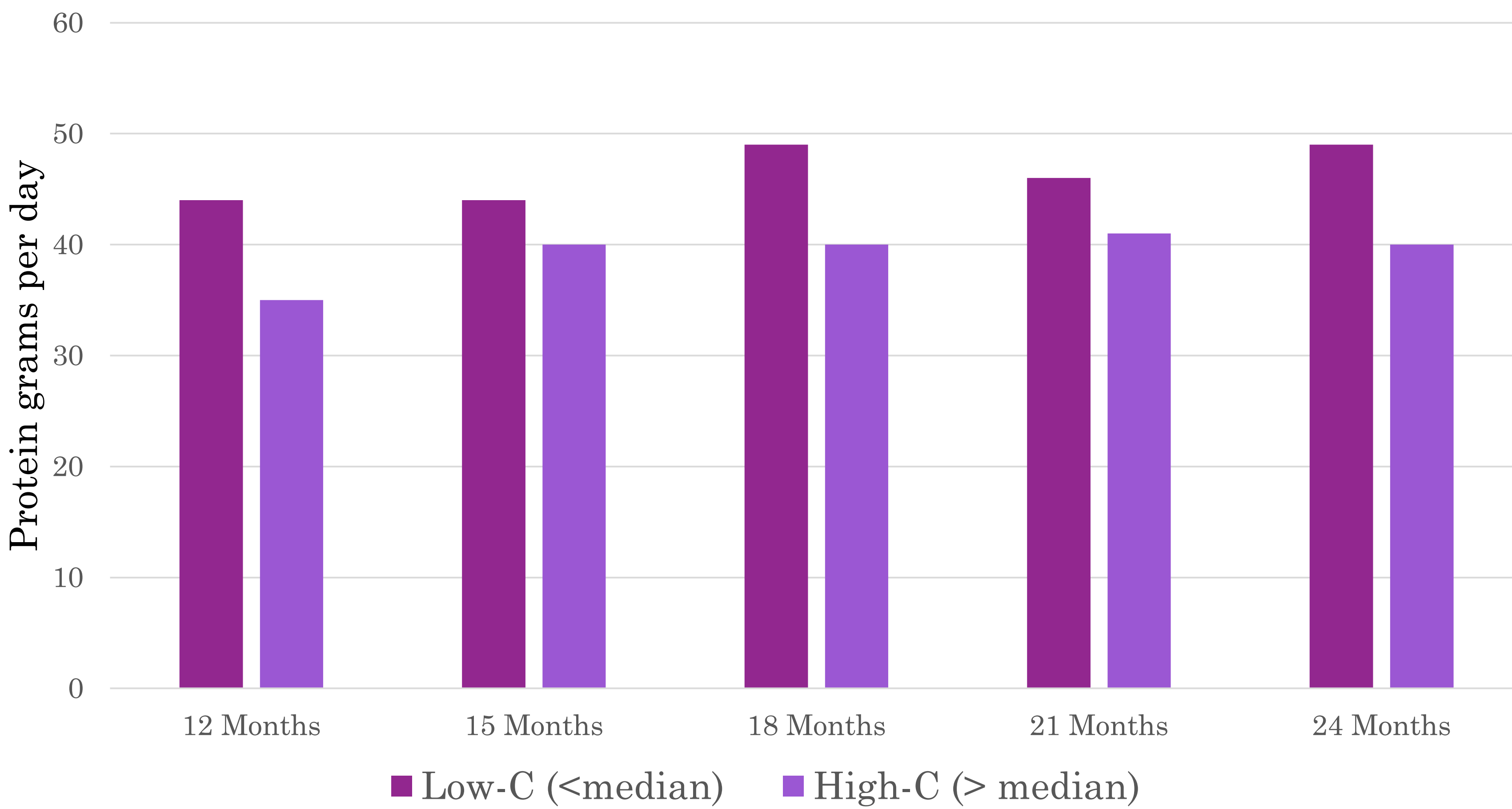
(Ben Avraham, unpublished)

FYCS: Baseline Bottle Use & Energy by Weight Status

N=286 total Mean (sd)	Normal Weight (<85% W/L) n=186	Overweight (≥ 85% W/L) n=100	P
W/L Z score	-0.13 (0.82)	1.8 (0.62)	.00
Kcal/day	1105 (345)	1085 (350)	0.65
Milk cups/day	2.4 (1.7)	2.1 (1.7)	0.39
Kcal via bottles/day	518 (223)	531 (204)	0.63
Kcal per bottles/day	118 (34)	123 (36)	0.30

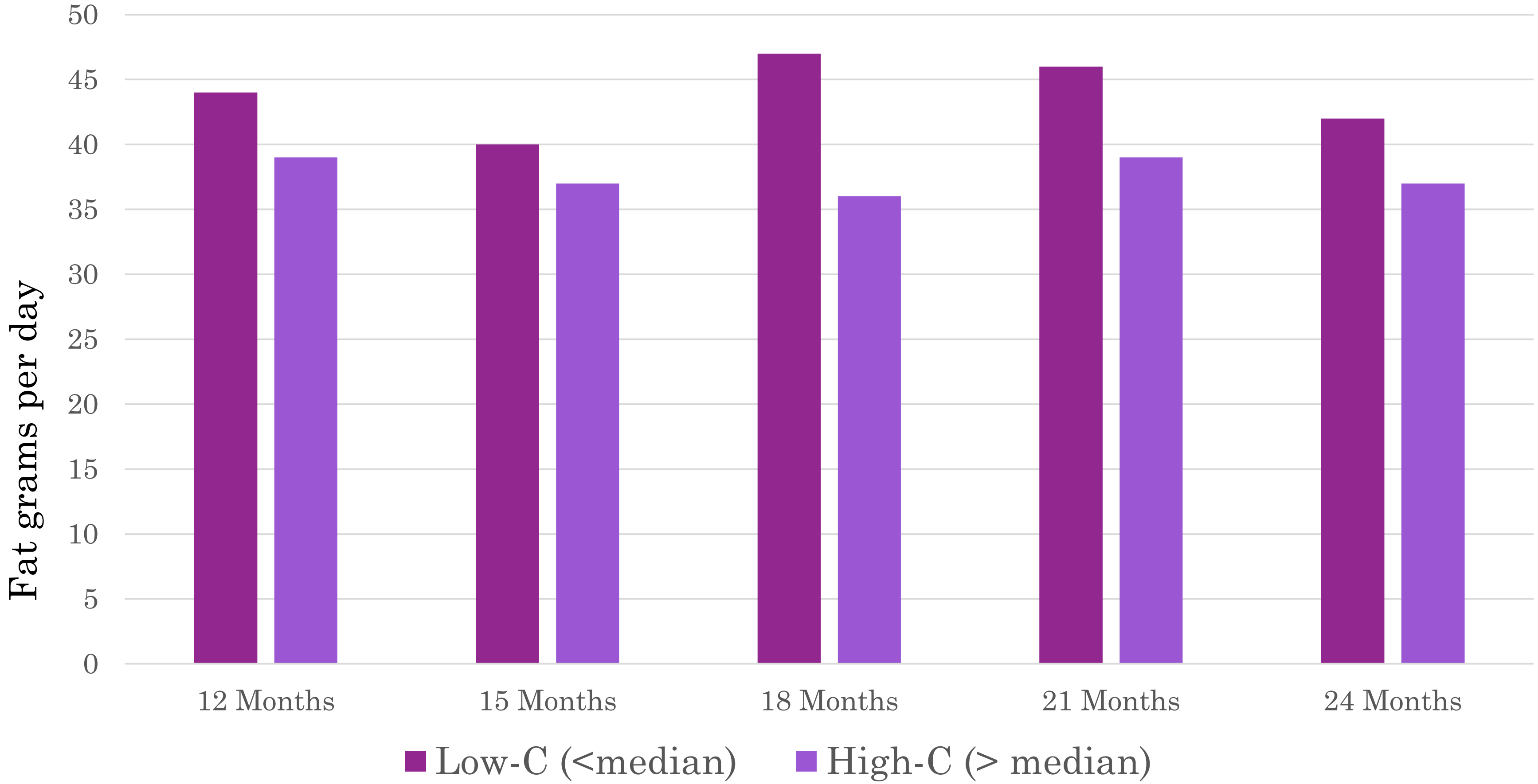
No differences in any bottle use, dietary, or energy variables.
Set point theory?

FYCS: Protein by % Energy From Containers (bottle + sippy)



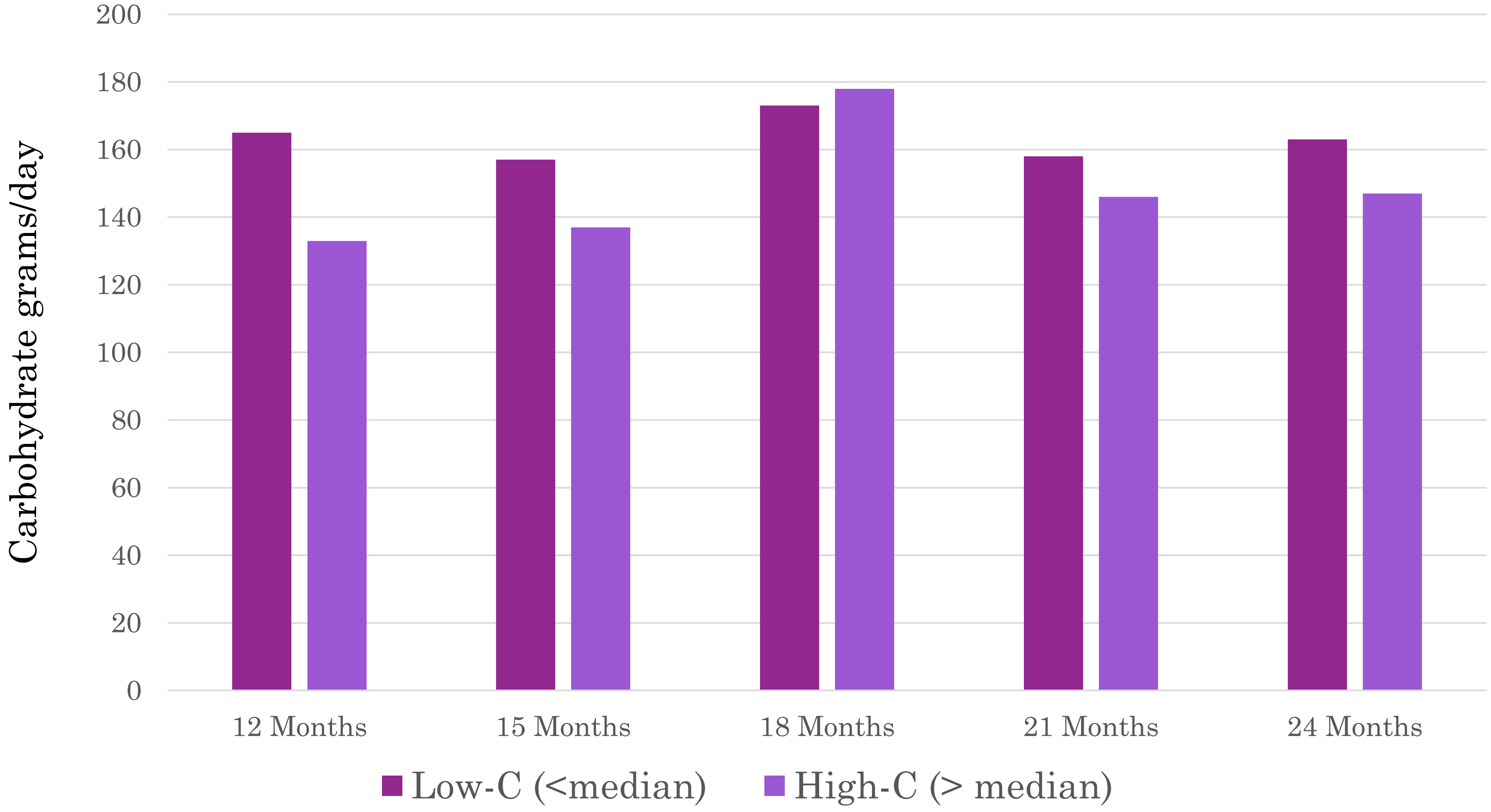
(Ben Avraham, unpublished)

FYCS: Fats/d by % Energy From Containers (bottle + sippy)



(Ben Avraham, unpublished)

FYCS: Carbohydrates by % Energy From Containers (bottle + sippy)



(Ben Avraham, unpublished)

Bottle & Sippy Cups: Vessel for Extra Calories

- Extraction of 3,105 records of milk, formula, non-dairy milk by vessel (bottle, sippy)

Base Beverage

+

Addition(s)

Bottle & Sippy Cups: Vessel for Extra Calories

- 39 single ingredient and combination recipes

+

Bottle & Sippy Cups: Vessel for Extra Calories

- 61% of caregivers ever added solid or sweetener

Bottle & Sippy Cups: Vessel for Extra Calories

	Child Age at Dietary Recall			
	12-14 m	**15-17 m**	**18-20 m**	**21+ m**
# beverages	1348	657	512	588
% with additions	**35%**	**36%**	**35%**	**32%**

Bottle & Sippy Cups: Vessel for Extra Calories

	Child ethnicity (n=298)			
	Hispanic	Non-Hispanic Black	Non-Hispanic white/ Asian/Other	Bi/ Multiracial
% beverages with additions				
None	37.6	36.7	42.1	43.2
<50%	32.8	34.7	21.1	27.3
>50%	29.6	28.6	36.8	29.5

Bottle & Sippy Cups: Vessel for Extra Calories

4%

37%

43%

8%

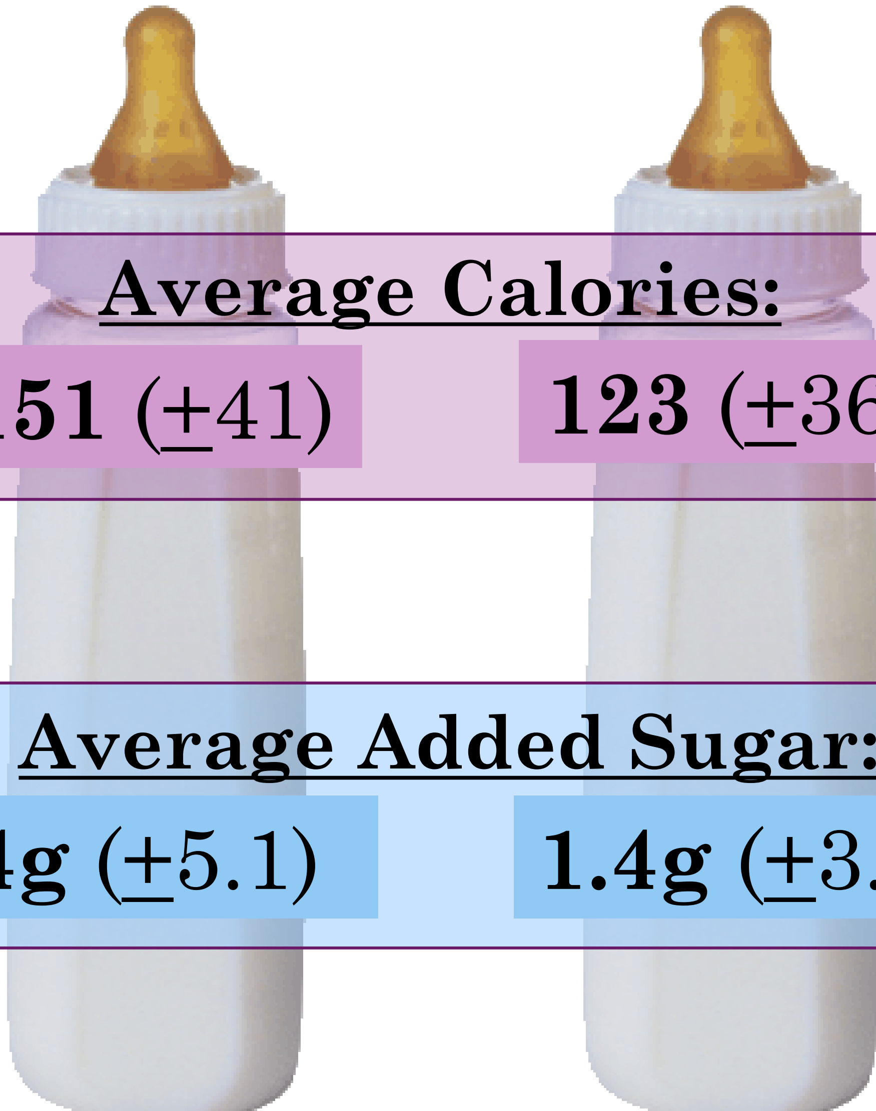
8%

Bottle & Sippy Cups: Vessel for Extra Calories

	Child ethnicity (n=298)			
	Hispanic	Non-Hispanic Black	Non-Hispanic white/ Asian/Other	Bi/ Multiracial
Ingredient(s)*				
Baby food only	4.2	4.2	5.8	5.8
Flavoring only	32.7	55.2	33.9	38.5
Cereal only	43.9	32.9	48.8	45.5
Cereal plus flavoring/other	10.4	2.8	5.4	3.2
All other	8.8	4.9	6.2	7.1
Total	100	100	100	100

*p<.05

With Additions | ***Without* Additions**



Average Calories:

151 ($\pm$41) | **123** ($\pm$36)

Average Added Sugar:

4g ($\pm$5.1) | **1.4g** ($\pm$3.7)

Limitation/Challenge


Nuby





Playtex

Next Steps

- Develop- schema for classifying drinking vessels of children through 2 or 3 years of age

- Collect- data on vessel type in national dietary intake surveys (e.g., NHANES, IFPS, FITS)

- Analyze- in studies on related outcomes (IDA/anemia, ECC), associations between vessels + diet + weight data

Issues To Be Addressed

- Sippy Cups: Lack guidance on use; they replace bottles in 2nd year of life and beyond
- Liquid vs. Solids: Lack guidelines on balance, in 2nd half of first year of life, and beyond
- Vessel + Contents: Providers & parents often unaware of this combination

Questions?

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Measurement of Body Composition in Infants and Young Children

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Body Composition in Infants and Young Children

During this period of rapid growth, substantial changes in normal body composition occurs.

Growth involves not only quantitative changes in body size, but also qualitative changes.

Chemical maturation of body tissues: mineral, protein, water and lipid content of body changes with age at markedly different rates.

Body Composition Assessment

Reference 3-C or 4-C

Body Wt	=	FAT	Water	Protein	Mineral

Basic 2-Compartment Model

Body Wt	=	FAT	***FFM*** (fat-free mass)

In 2-C model, chemical component or physical property of FFM is measured to estimate FFM using a conversion factor, and then *FM* = Weight – *FFM*.

Due to chemical maturation, the conversion factors are not constant.

Body Composition Assessment

Four-Compartment (4-C) "*Reference*" Model
Weight = Fat + Water + Protein + Mineral

Classical "Reference Infant" model (Fomon et al, *Am J Clin Nutr* 1982)
Constructed model from literature values for birth to 10 years

Contemporary Reference Infant model (Butte et al, Pediatr Res 2000)
Healthy term infants (n=76) at 0.5, 3, 6, 9, 12, 18, 24 months
Longitudinal study design=> individual variation

Body Composition Methods

Method	#	Compartment	
Isotope dilution	2C	Total body water	Deuterium or oxygen-18
Bioelectrical impedance or spectroscopy	2C	Total body water Fat free mass	Secondary method-requires calibration against another method
Air-displacement plethysmography	2C	Body density Body volume	
Dual-energy X-ray absorptiometry	3C	Lean tissue mass Fat mass Bone mineral content	
Whole body counting	2C	Body cell mass Fat free mass	Total body potassium
Magnetic resonance imaging	2C	Fat mass Fat free mass	
Multicompartment models	3C 4C	Fat mass Fat free mass	TBW, body vol, protein, BMC

Isotope Dilution (^{2}H or ^{18}O)

Fick principle states that volume of distribution of a substance (D) is equal to the amount of that substance present in the body divided by its concentration

$$D \text{ (moles)} = V \times [D]$$

$$V = D/[D]$$

TBW computed from amount of isotope given (D), isotope enrichment in body fluid and dose dilution (A):

$$\text{TBW (kg)} = \frac{D \times A \times E_{\alpha}}{a \times E_{d} \times 10^{3}}$$

Since negligible water associated with FM, FFM is computed applying the hydration constant of FFM:

$$\text{FFM (kg)} = \text{TBW}/H$$

Isotope Dilution (^2H or ^{18}O)

Dosages (oral or IV)

- 0.04 g/kg of ^2H_2O at 99.8%
- 0.6 g/kg of $H_2{}^{18}O$ at 10% ^{18}O

Sampling - urine, saliva, breath water vapor or blood

- Equilibrium method - baseline, 3-6 h post-dose sampling
- Zero-time extrapolation method – 5-10 d multiple sampling

Gas isotope ratio mass spectrometry (GIRMS):

- Conversion H_2O to H_2 – zinc reduction method
- H_2O-CO_2 exchange method
- Isotopic abundance measurements

Alternative analytical techniques:

- Infrared spectrometry, NMR, gas chromatography

Isotope Dilution (^{2}H or ^{18}O)

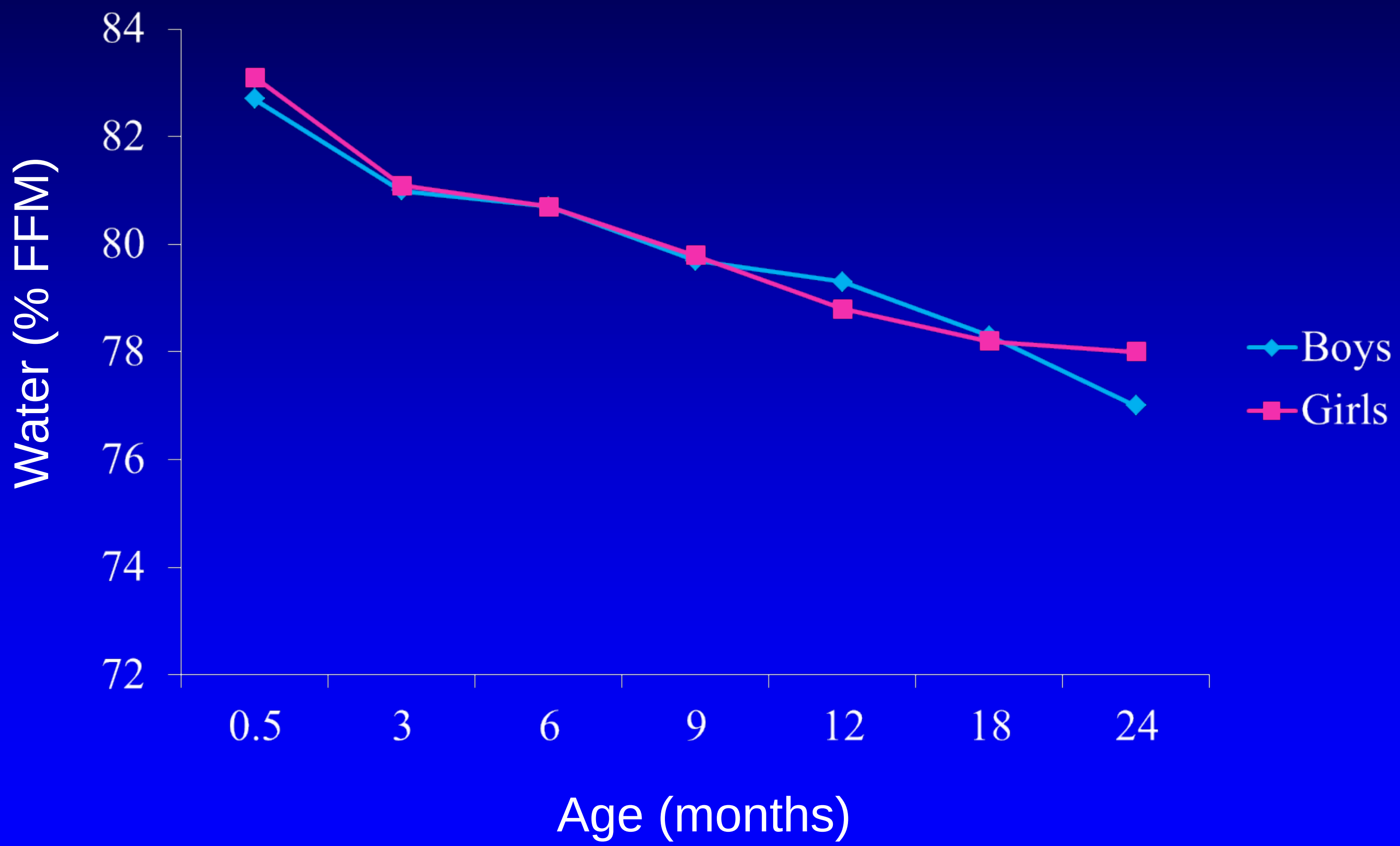
Advantages

- No radiation
- Field administration
- Shipped for centralized analysis
- ^{2}H and ^{18}O isotope ratio measurements by GIRMS accurate and precise

Disadvantages

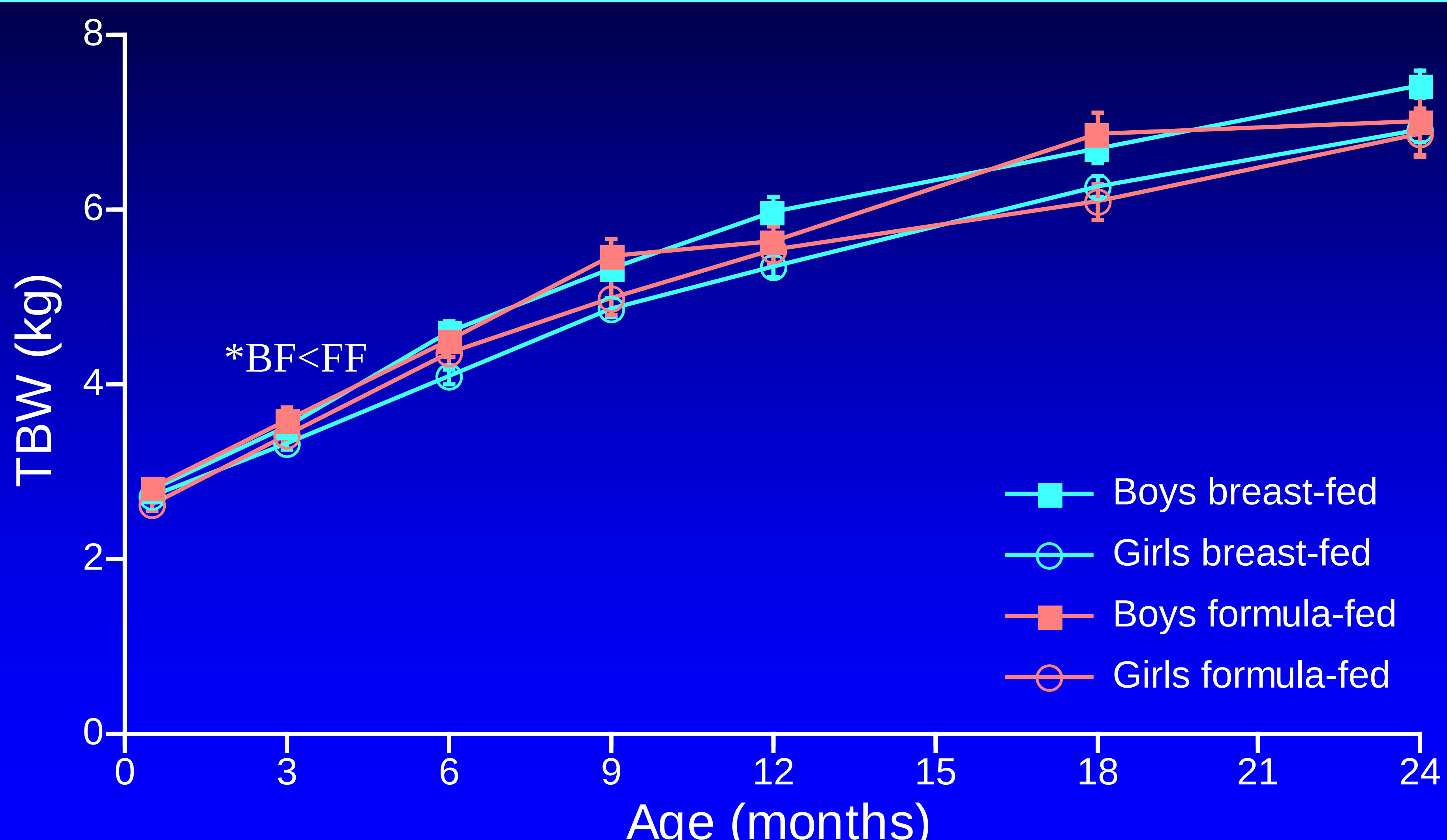
- Analytical errors due to administration of isotope dose, timing of samples
- Hydration of FFM varies with age

Hydration of FFM



Butte NF *et al.* Pediatr Res 47:578-85, 2000

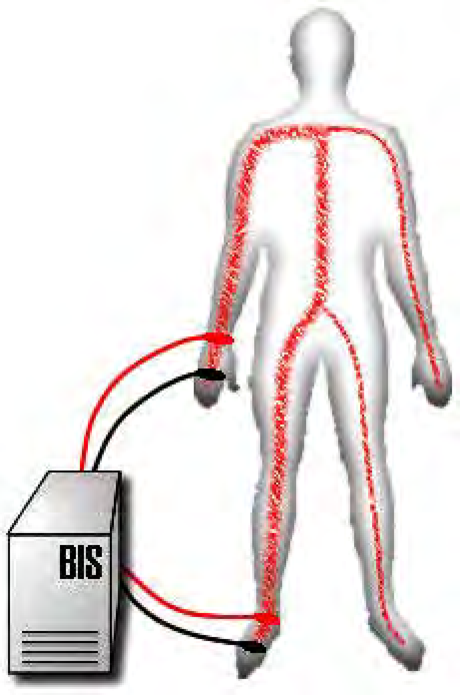
Total Body Water



Butte N. Pediatr 106;1355-66, 2000

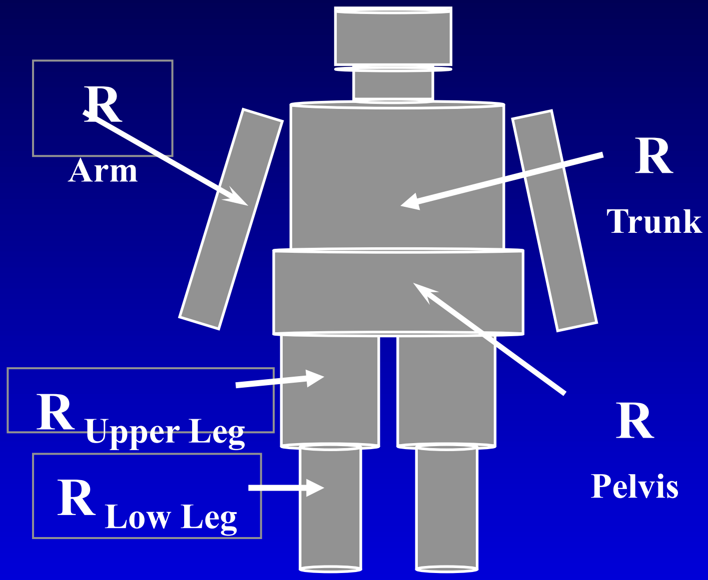
Bioelectrical Impedance Analysis (BIA) and Bioelectrical Impedance Spectroscopy (BIS)

- BIA and BIS are widely used methods for estimating body composition - relatively simple, quick, and noninvasive.
- BIA determines the electrical impedance of body tissues to the flow of a small alternating current
- Secondary method requiring calibration with more direct method
- Many equations for specific populations have been developed to estimate TBW and thereby FFM as a function of impedance, weight, height, gender, and age.
- Equations require independent validation



Bioelectrical Impedance Analysis (BIA) and Bioelectrical Impedance Spectroscopy (BIS)

- Limitations
  - Some studies show BIA provides little benefit over anthropometry alone
  - Hydration and composition of adipose differs in infants vs. adults counter to assumption that fat is nonconductive
  - Affected by body position, hydration status, consumption of food and beverages, ambient air and skin temperature, recent physical activity
  - Classification of populations, not individuals



$$\text{Volume}_{\text{conductor}} = \rho\, Ht^2 / R$$

Air-Displacement Plethysmography (ADP)

- Theory: whole-body densitometry
- BOD POD measures body mass and volume

  Density = Mass/Volume

Knowing the density of fat and FFM, the relative proportions of body fat and FFM are calculated from body density

- BOD POD for adults and children >6 y/o

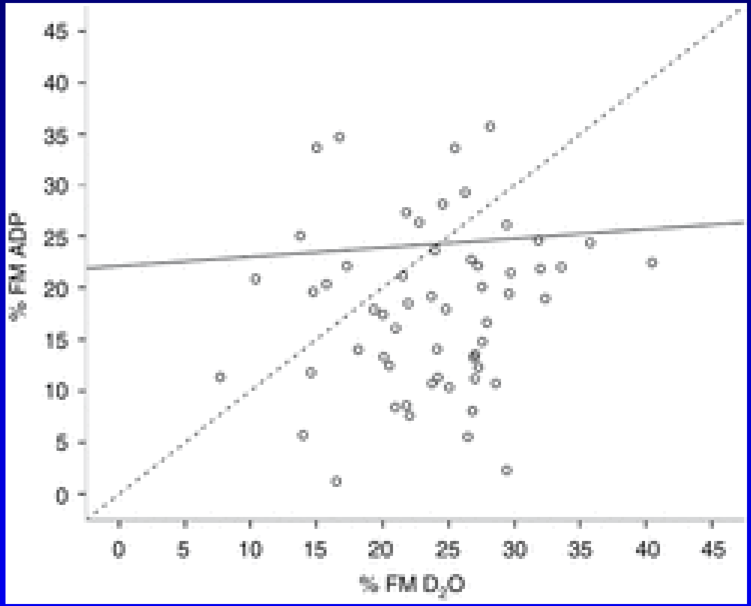
- BOD POD GS with Pediatric Option

  FDA approved for children > 2 y/o

  Applicable for children as small as 12 kg

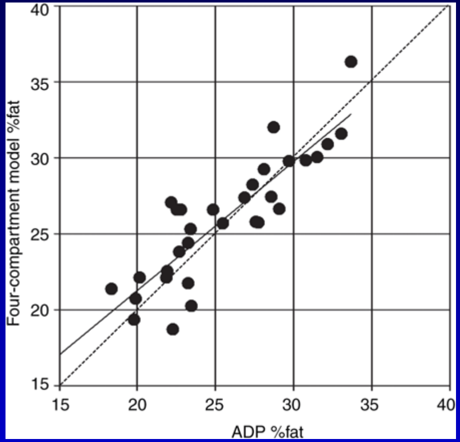
Air-Displacement Plethysmography (ADP)

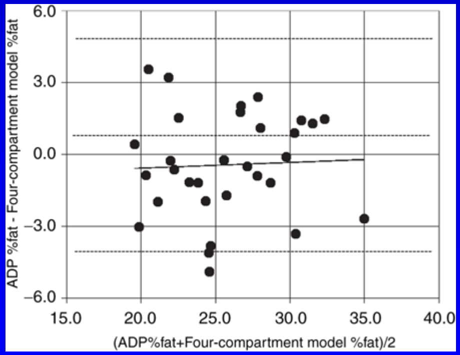
- Rosendale RP and Bartok CJ. *Pediatr Res* 71:299-303, 2012.
  - 72 children 6-48 mo (12.2 kg)
  - BOD POD, Pediatric option
- ADP vs. ^2H_2O Dilution
- Results:
  - %FM by ADP (17.9%) vs. ^2H_2O (23.7%) (p=0.001)
  - SEE exceeded 6% FM
- Conclusion:
  - ADP is not accurate method for measuring body composition in young children



Air-Displacement Plethysmography (ADP)

- Fields DA and Allison DB
  Obesity 20:1732-7, 2012.
  - 31 children 24-72 mo (17.5 kg)
  - BOD POD, Pediatric option
- ADP vs. 4C: ${}^2H_2O$ Dilution and DXA
- Results:
  - %FM by ADP (25.6%) vs. 4-C (26.0%)
  - SEE = 2.1% FM
- Conclusion:
  - ADP is accurate, precise, reliable method for measuring body composition in young children 2-6 y of age





Note: Phase I: 32 children 6-24 mo tested, movement and crying affected reliability of measurements

Air-Displacement Plethysmography (ADP)

- Possible explanations for discrepancy in study results
  - Instrumentation
    - Rosendale used modified BOD POD (earlier prototype)
    - Fields used BOD POD with Pediatric Option
  - Thoracic volume equations differed in two papers
  - Age and weight range
    - Rosendale validation, half children were younger than 2 y/o
    - Fields validation, all children > 2 y/o
  - Movement and crying – errors due to temperature and volume changes
    - Rosendale included subjects irrespective of behavior
    - Fields excluded subjects if movement and crying intense
      - Error substantial (7.2% FM) if crying
  - Development Solution: Reduced chamber volume, and air circulation and temperature control systems for children <2 y/o

Air-Displacement Plethysmography (ADP)

PEA BOD

Infants weighing less than 8 kg (< ~6 months of age)
Larger tray for infants up to 10 kg now being validated
Remaining gap is ~2 kg or 6 and 24 months of age between PEA BOD and BOD POD

PEAPOD Measurement

Daily QC calibration: < 10 min.

Weight (~ 6-10 sec)

Volume (2 min)

Air-Displacement Plethysmography (ADP)

- Validation of PEA POD
  - Ellis KJ (2007)
    - 49 term infants, 6 wk old
    - ADP vs. 4-C: ^2H_2O, TBK, DXA
    - %FM ADP (16.9%) vs. 4-C (16.3%) ($p=0.62$) SEE=1.4%
  - Roggero P (2012)
    - 70 preterm, <4 wk old, 31 wk GA
    - ADP vs. $H_2{}^{18}O$
    - %FM ADP (5.7%) vs. $H_2{}^{18}O$ (6.0%) ($p=0.53$) SEE=2.1%

- PEA POD provides reliable, accurate and immediate assessment of %FM in infants in research and clinical settings
- Limitation: sick infants with alterations in hydration

Dual-Energy X-ray Absorptiometry (DXA)

Theory: Based on attenuation of dual x-rays (40 and ~ 80-100 keV), bone pixels can be separated from non-bone pixels, and the relative fat content of the non-bone pixels can be estimated.

Infant < 10-15 kg

Bone	Non-bone soft tissues

FAT	LTM (lean tissue mass)

3-Compartment Model

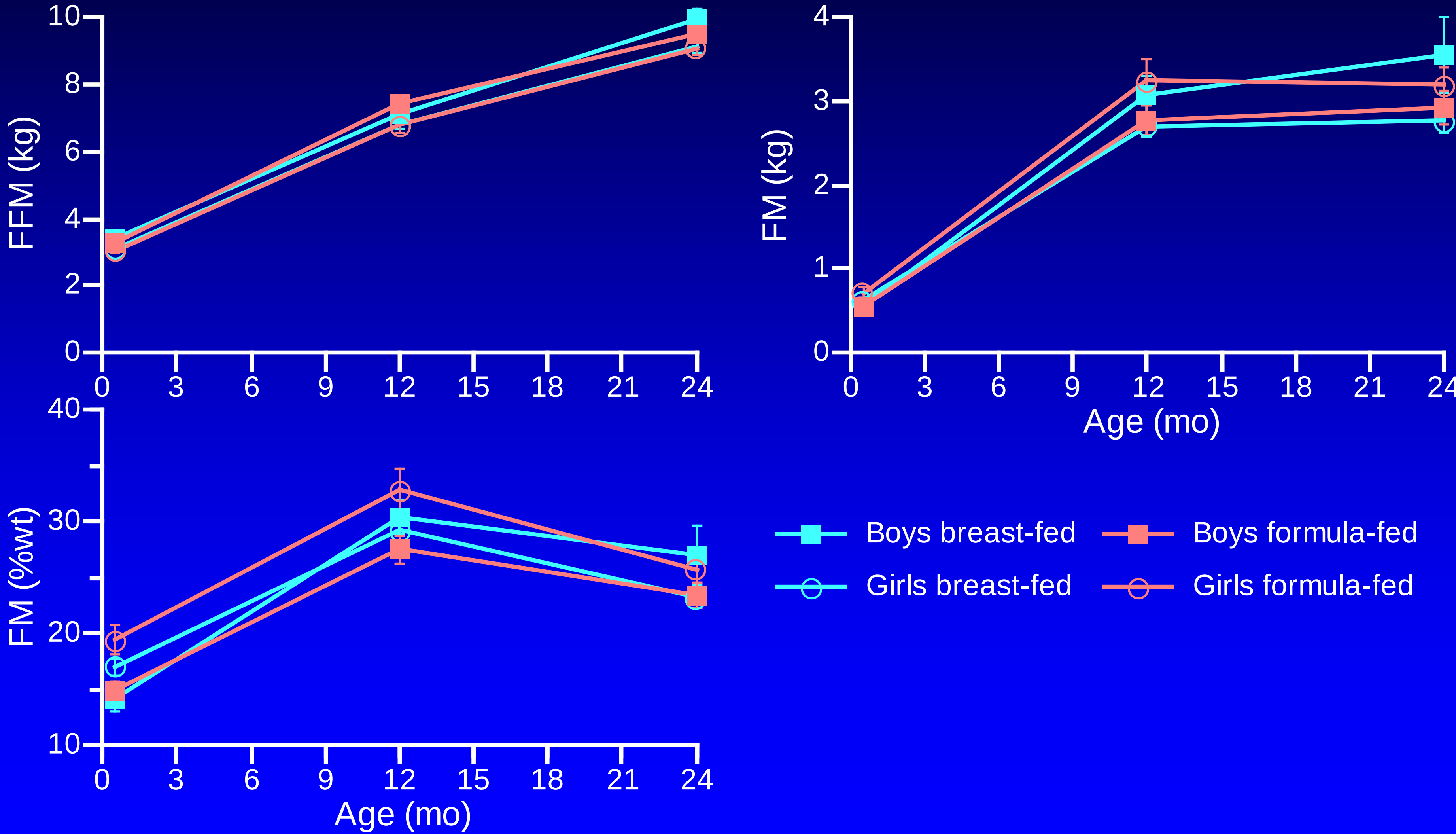
$$Wt_{DXA} = Fat + LTM + BMC \text{ (Bone Mineral)}$$

Dual-Energy X-ray Absorptiometry (DXA)

- Although DXA is considered a "criterion" method, it has limitations
- FFM and FM values dependent on DXA hardware and software versions
  - Hologic software v11.2 vs. v12.1 (Shypailo et al. Obesity 2008)

    -3 y/o Δ%FM 8% in girls and 4% in boys
- Disjunction between infant and adult scanning modes
- Radiation exposure (less than 1 millirem)
- Sensitive to child movement

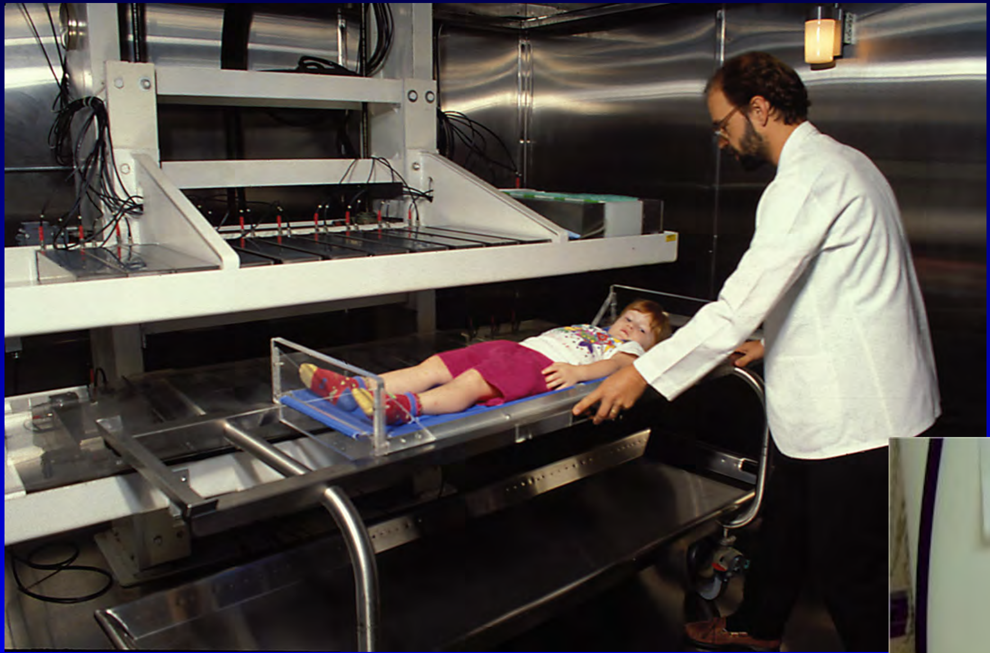
Body Composition Based on DXA



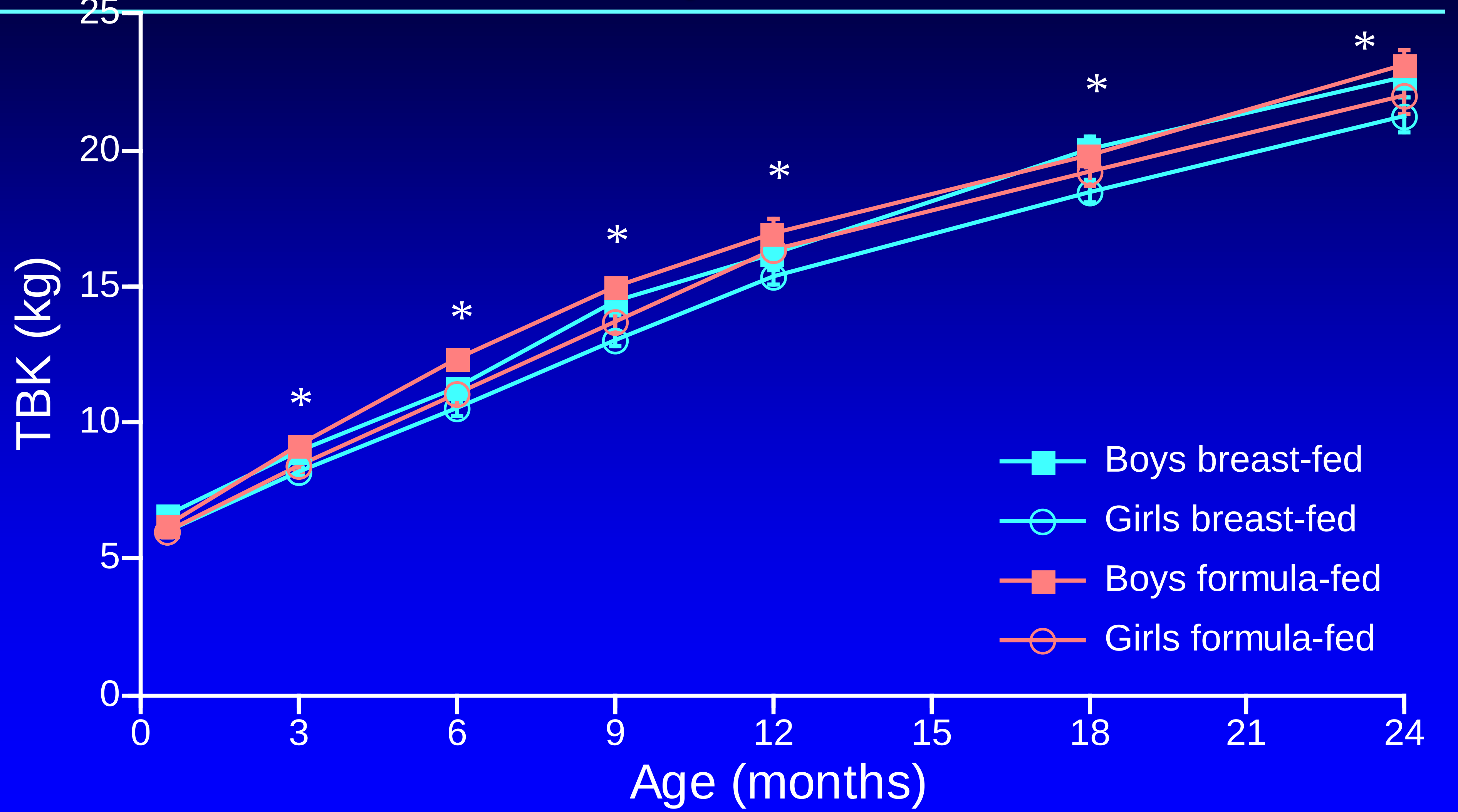
Total Body Potassium (TBK)

- Whole body counting of naturally occurring ^{40}K
- ^{40}K makes up ~0.012% of body potassium and emits a high-energy γ-rays (1.46 MeV)
- More than 98% body's K is in body cell mass, actively metabolizing tissues
- TBK can be converted to body cell mass (BCM) and FFM using age- and sex-specific conversion factors

CNRC Whole Body Counters - TBK



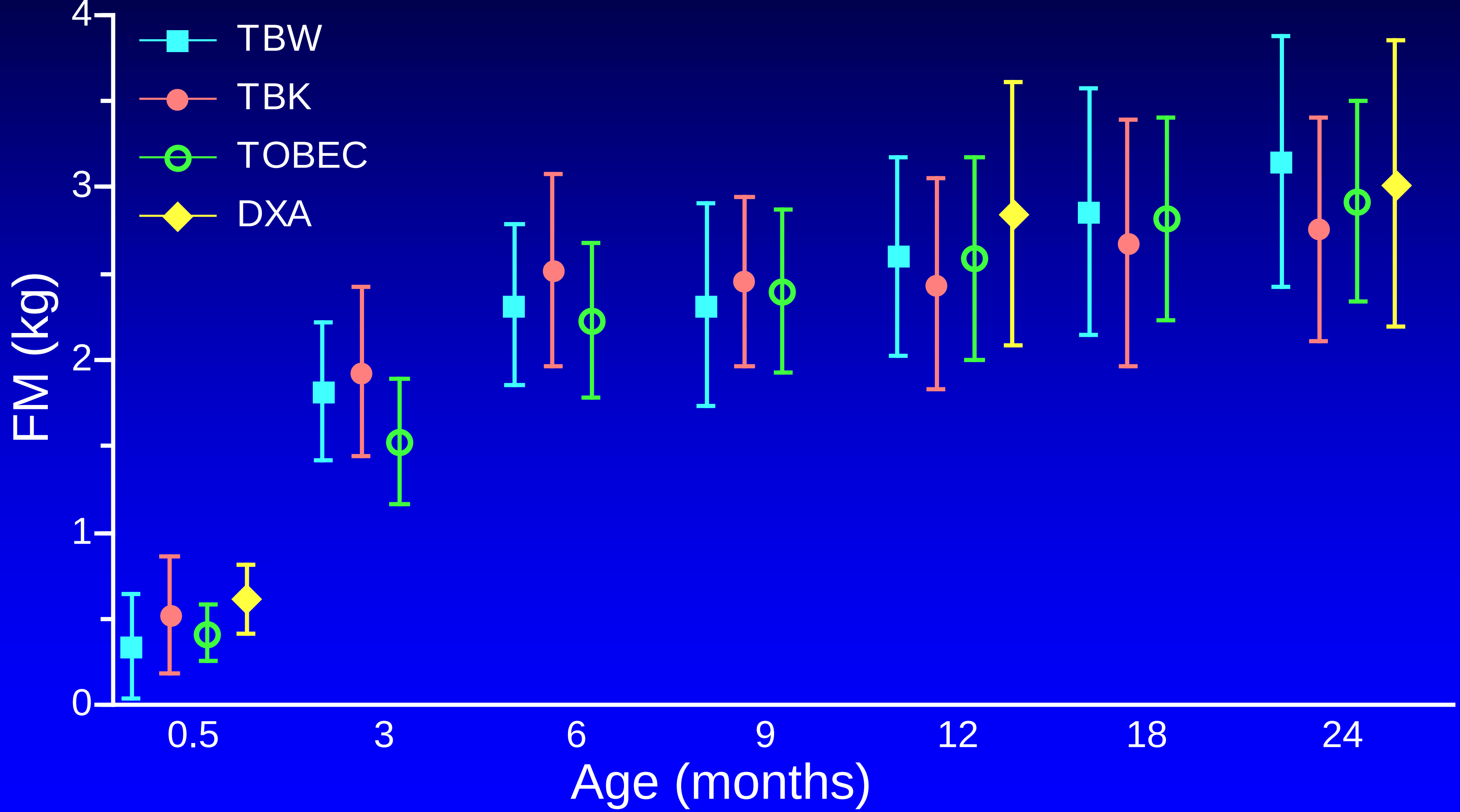
Total Body Potassium



Magnetic Resonance Imaging (MRI)

- MRI can be used to visualize and estimate volume of internal body structures: SAT, VAT, organs
- Few MRI studies measuring FM in infants
  - Olhager E et al. Pediatri Res 2003; 54:906-12
  - Uthaya S et al. Horm Res 2004; 62:143-8.
- Limitations:
  - Calculation of FM from adipose tissue volume depends on the fat content of adipose tissue
    - Neonates 33-45% to 58-69% at 6-9 mo, 75% adults (Baker 1969)
  - Sedation or significant restraints; small movements during the scan can degrade the accuracy of the reconstruction images

Estimation of FM Based on TBW, TBK, TOBEC and DXA



Butte N. JPGN 1999;29:184-189

Multicompartment Methods

- Contemporary Reference Infant Body Composition Model
  - Measured chemical components of fat free mass: total body water, total body potassium and bone mineral content
  - Estimated fat free mass and fat mass from a 4-C multicomponent model
  - Examined patterns of change and chemical maturation of body composition during the first 2 y of life
  - Evaluated effects of age, gender and feeding mode on body composition

Butte NF, Hopkinson JM, Wong WW, Smith EO, Ellis KJ. Body composition during the first 2 years of life: an updated reference. Pediatr Res 47:578-85, 2000.

Multicomponent Body Composition Model

FFM = Protein + TBW + BMC + Nonosseous mineral + Glycogen

Assumptions:

1. Protein is derived from ratio of 461 mgN/mEq K;
2. [K] in ICW and ECW is equal to 4 and 150 mEq/kg;
3. Minerals in ECW and ICW are 9.4 and 9.0 g/kg H_2O;
4. When DXA not available,

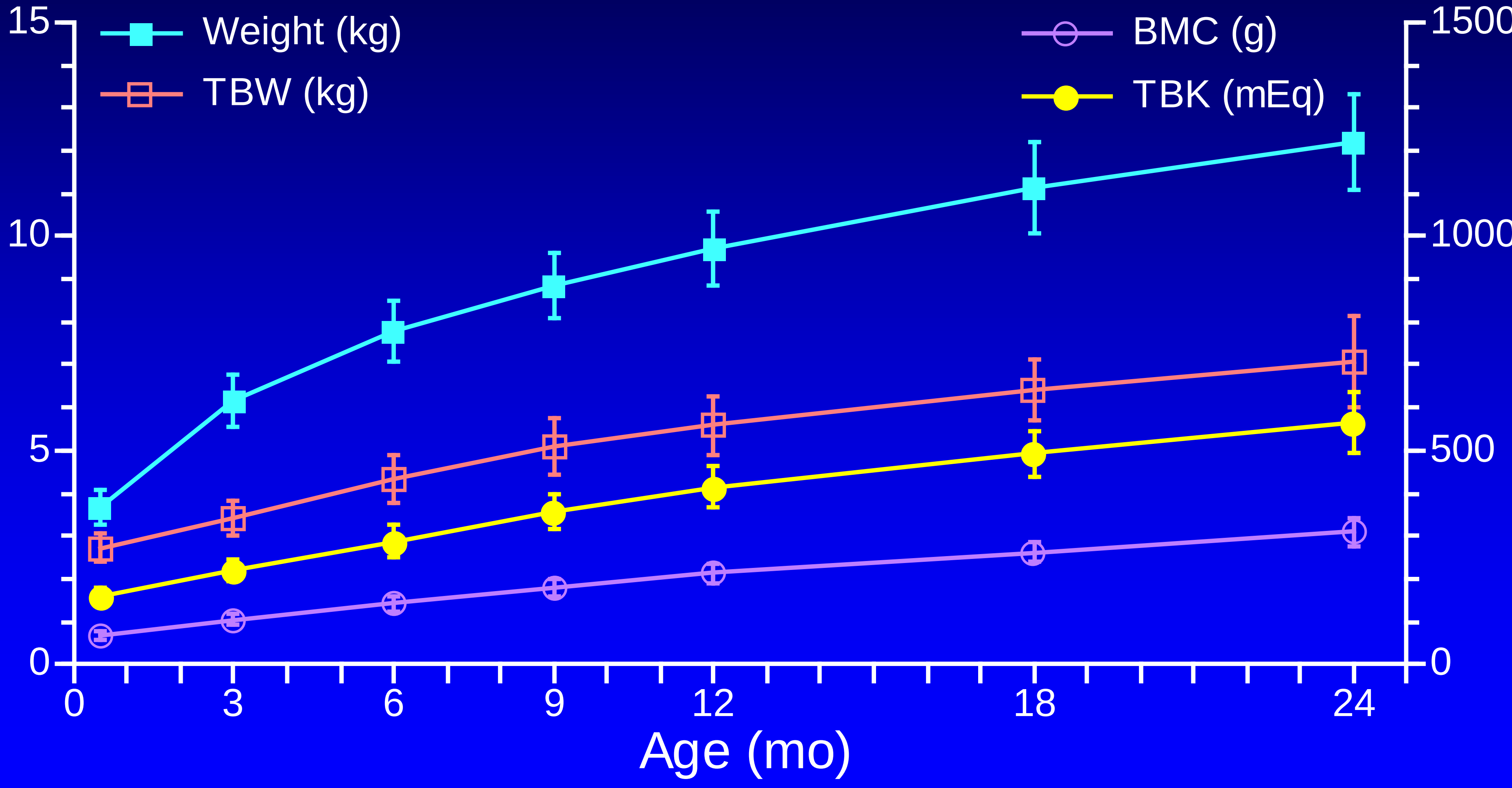
   BMC = -5.3 + 2.0 Age + 0.468 TBK R^2= 96%;

5. Glycogen is equal to 0.45% body weight.

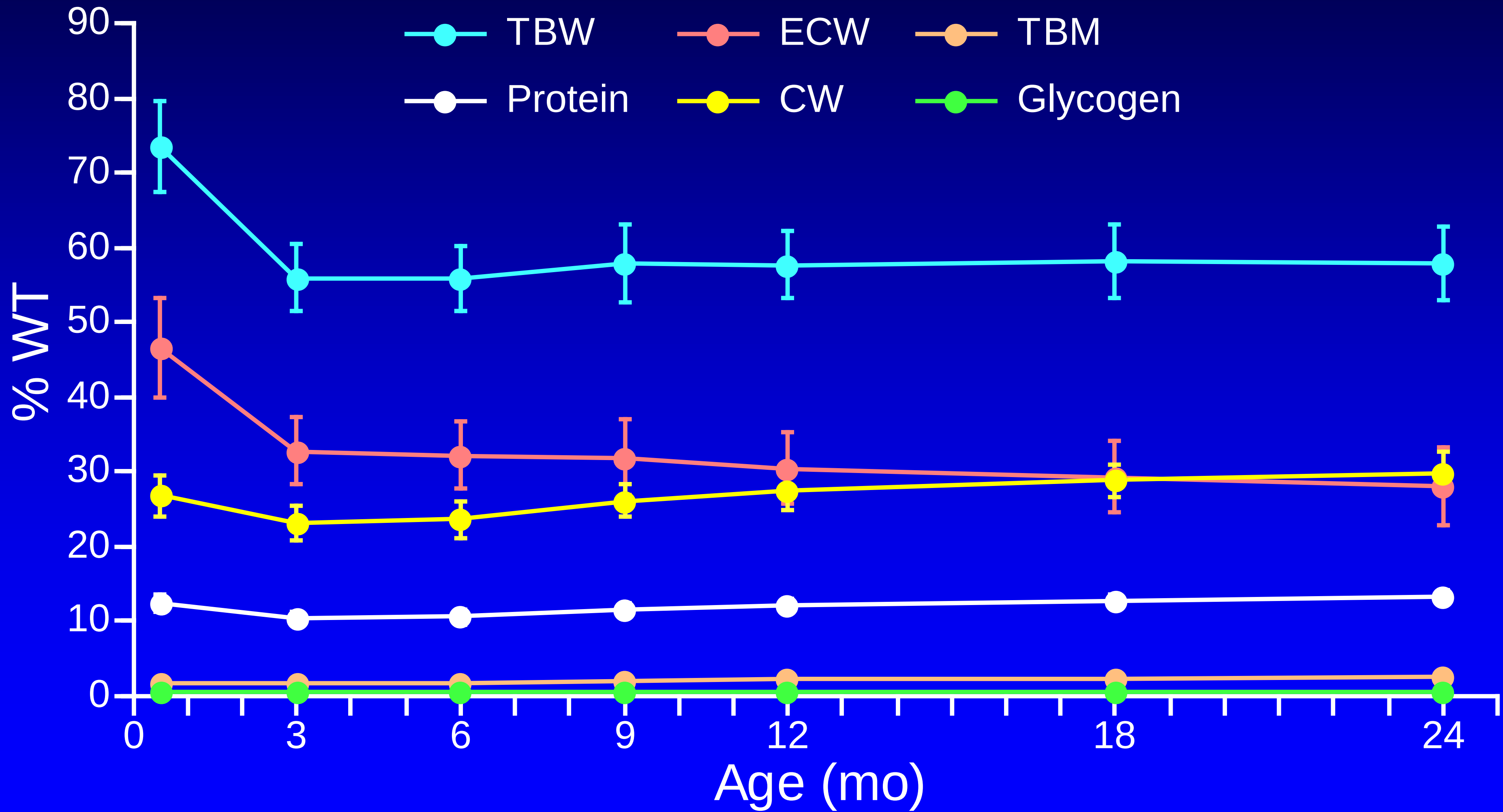
Multicomponent Body Composition Model

ECW (kg)	= 1.027 x TBW (kg) - 0.00685 x TBK (mEq)
ICW (kg)	= TBW (kg) - ECW (kg)
Protein (g)	= TBK (mEq) x 0.461 x 6.25
Glycogen (g)	= 0.0045 x Weight (kg) x 1000
EC nonosmin (g)	= 9.4 x ECW (kg)
IC nonossmin (g)	= 9.0 x ICW (kg)
Nonossmin (g)	= EC nonossmin (g) + IC nonossmin (g)
FFM (kg)	= TBW+Protein+Glycogen+BMC+Nonossmin
FM (kg)	= Weight - FFM

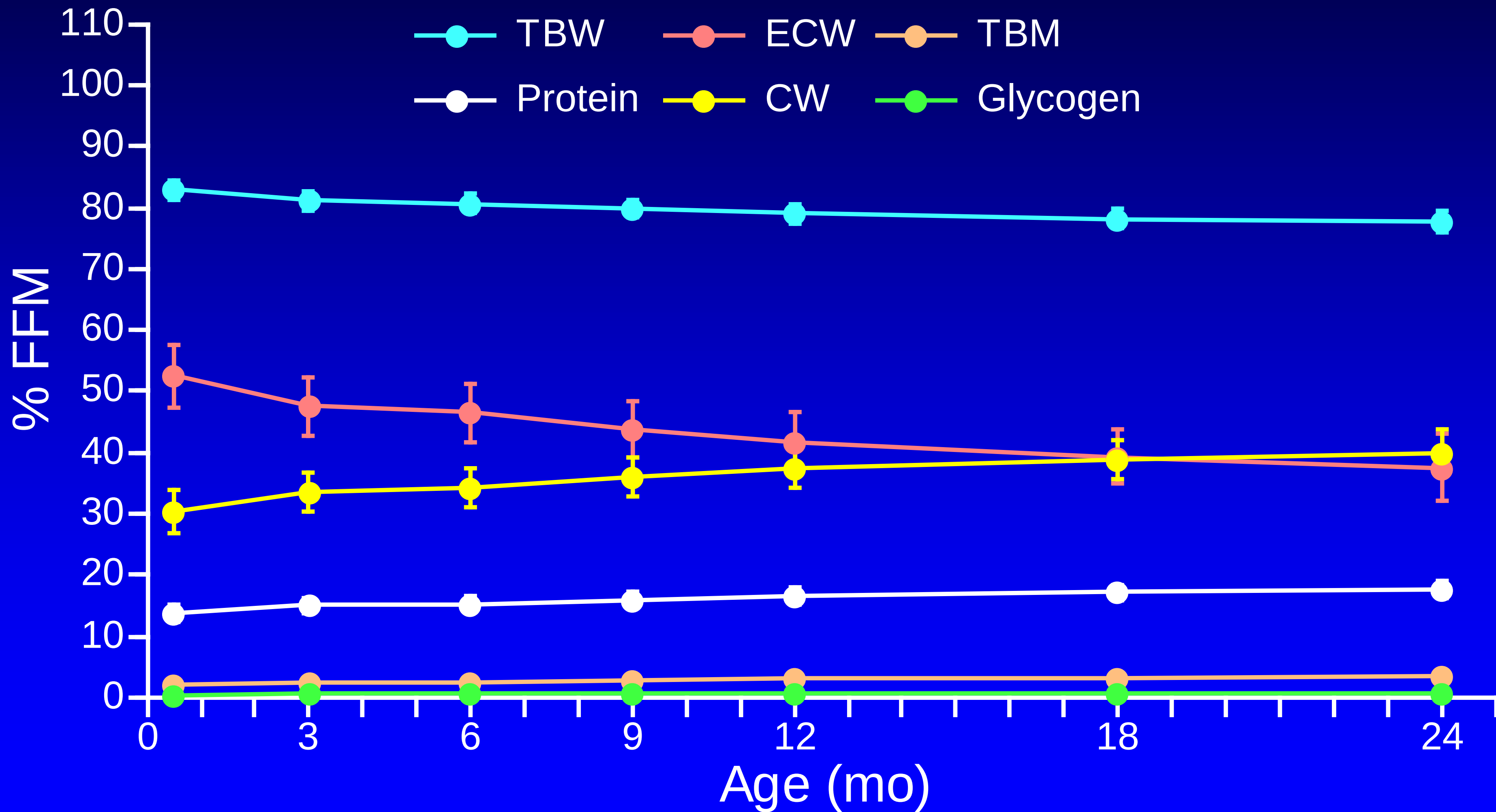
Weight and Chemical Components Used to Estimate Body Composition of Infants



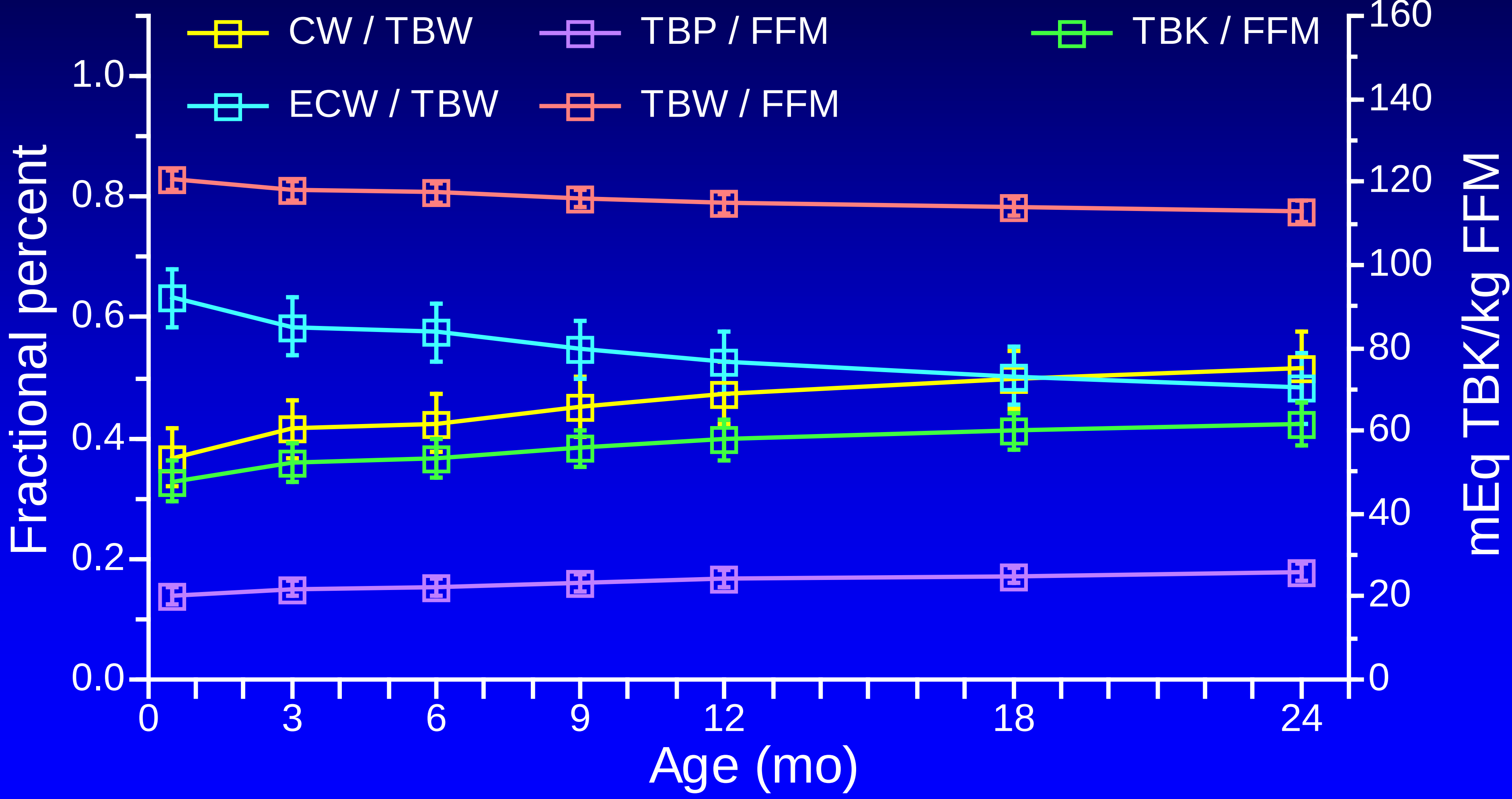
Chemical Components as a Percentage of Weight



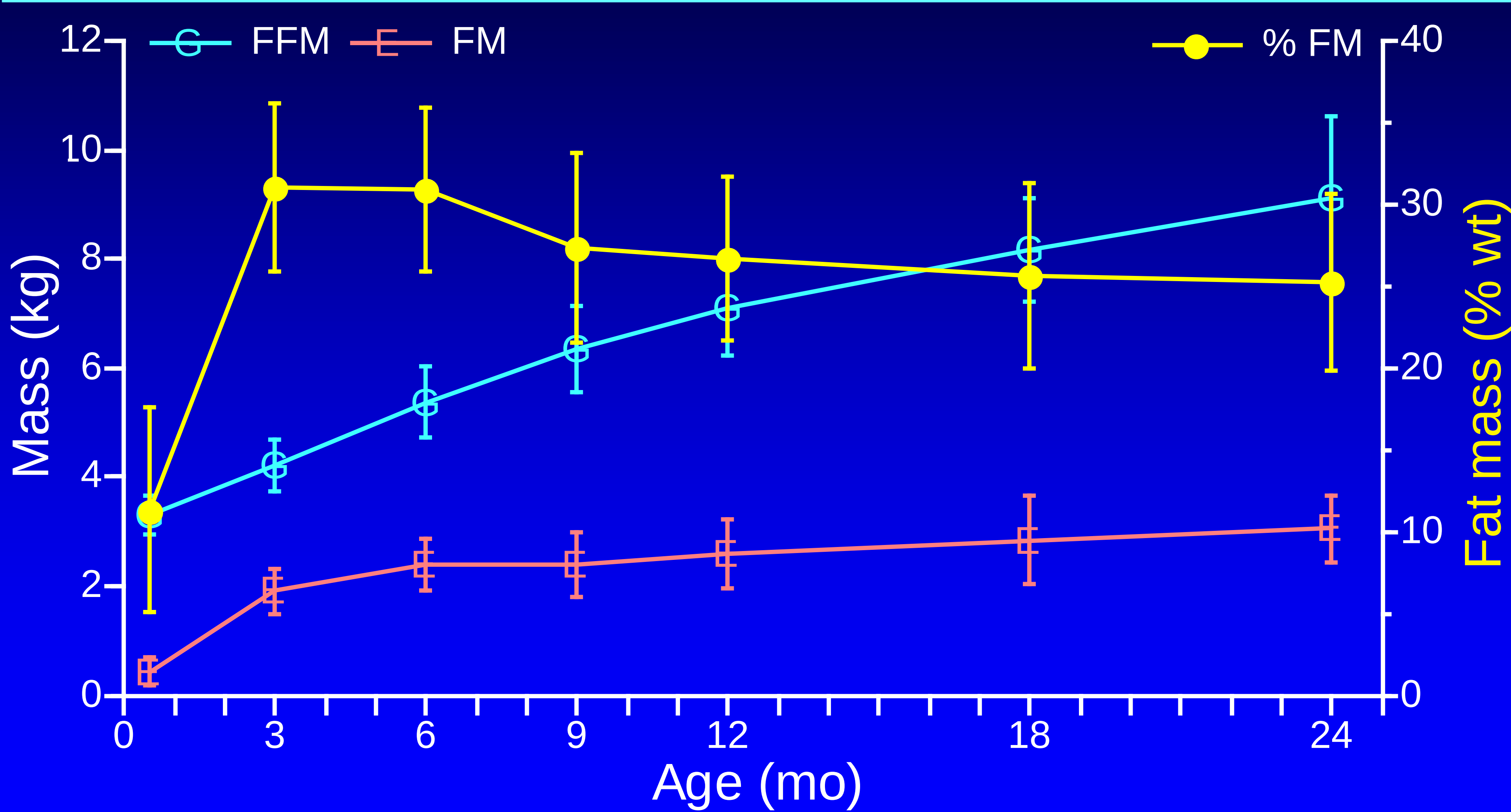
Chemical Components as a Percentage of FFM



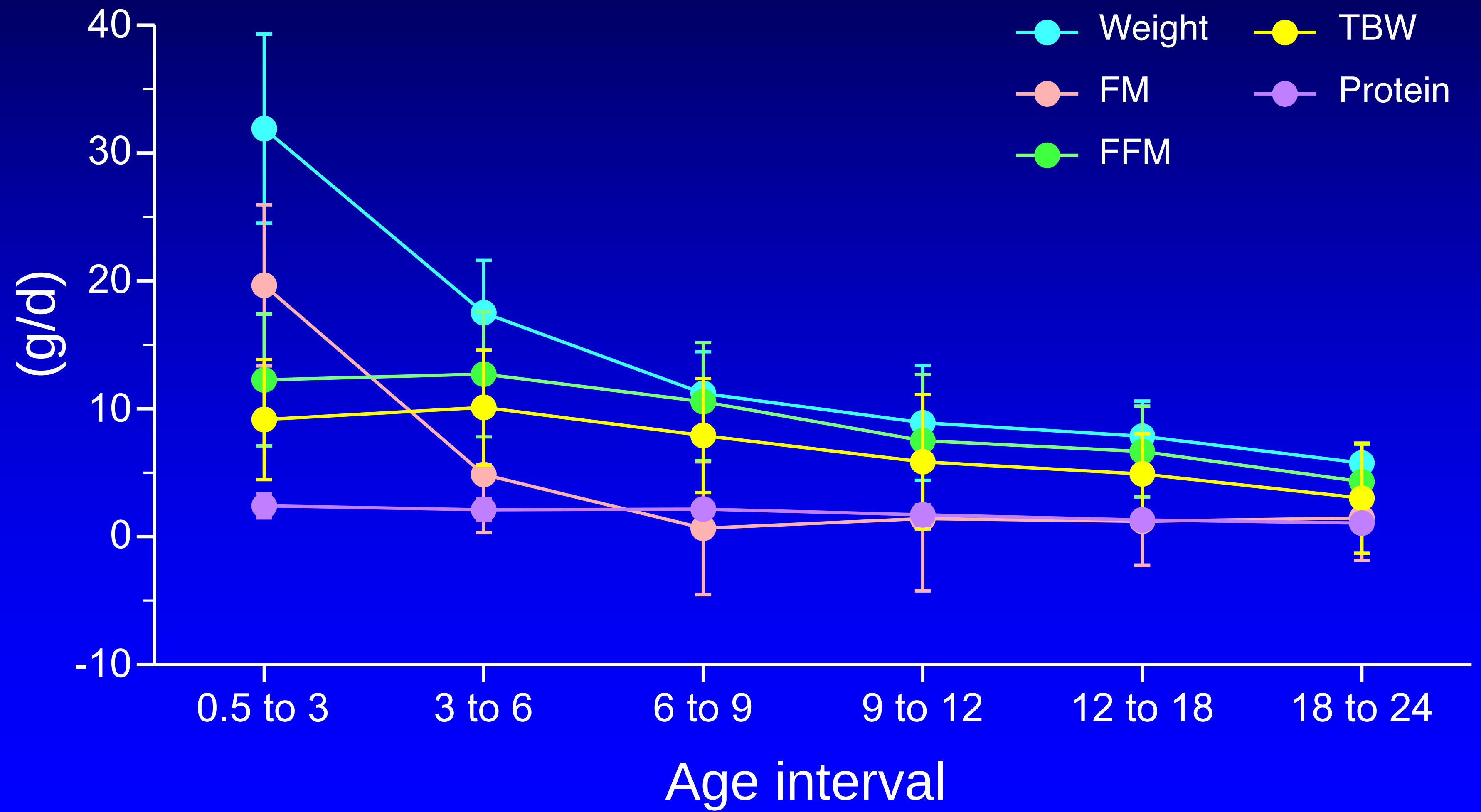
Constants for Conversion of Chemical Components to FFM



Fat Free Mass and Fat Mass Estimated from Multicomponent Model



Incremental Growth Rates

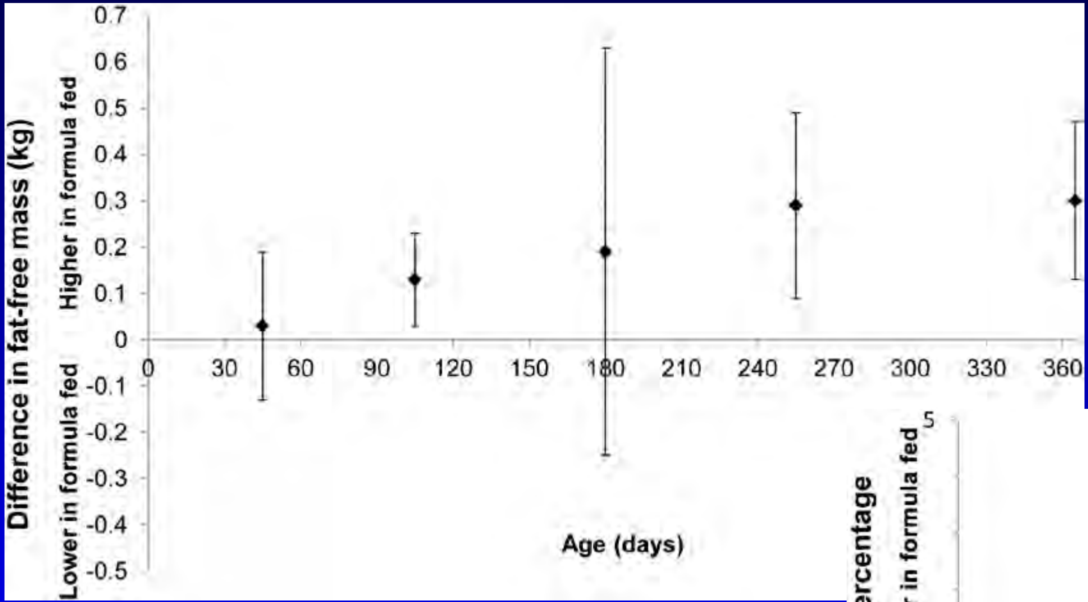


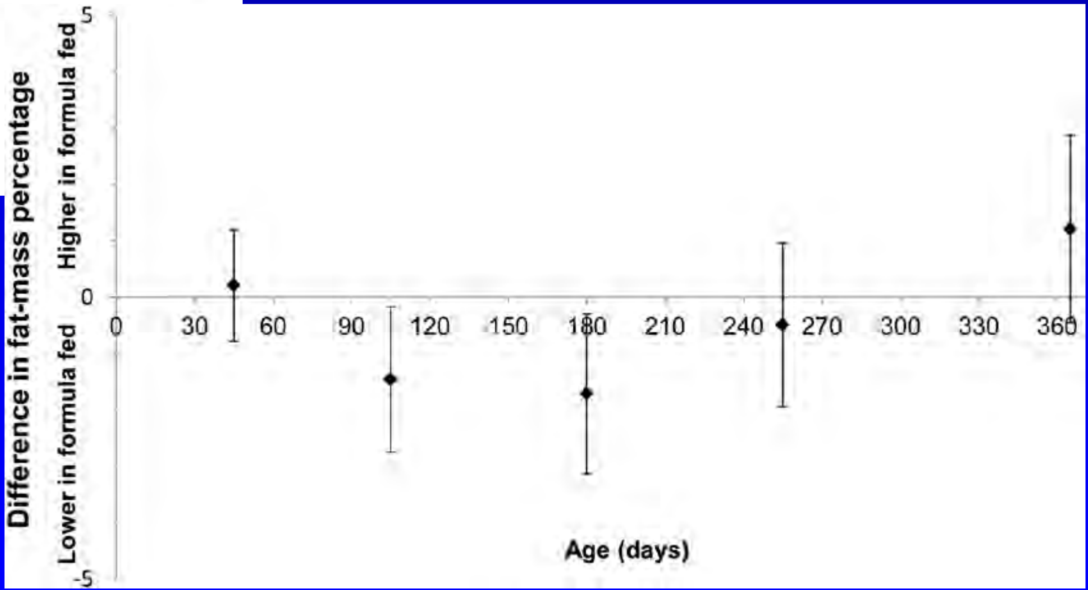
Effect of Breastfeeding vs. Formula Feeding on Body Composition

- Meta-analysis of 11 studies that examined body composition of healthy, term infants
- Outcomes: FFM, FM or %FM of BF and FF
- Findings:
  - FFM higher at 3-4 mo, 8-9 mo and 12 mo in FF than BF infants
  - %FM lower at 3-4 mo and 6 mo in FF than BF infants
  - Trend towards higher %FM in FF infants at 12 mo ($p=0.16$)

Gale C. AmJClinNutr 2012;95:656-69.

Effect of Breastfeeding vs. Formula Feeding on Body Composition





Gale C. AmJClinNutr 2012;95:656-69.

Body Composition Methods

Method	#	Compartment	
Isotope dilution	2C	Total body water	Deuterium or oxygen-18
Bioelectrical impedance or spectroscopy	2C	Total body water Fat free mass	Secondary method-requires calibration against another method
Air-displacement plethysmography	2C	Body density Body volume	Gap in weight/age coverage
Dual-energy X-ray absorptiometry	3C	Lean tissue mass Fat mass Bone mineral content	Instrument and software dependent
Whole body counting	2C	Body cell mass Fat free mass	Total body potassium
Magnetic resonance imaging	2C	Fat mass Fat free mass	
Multicompartment models	3C 4C	Fat mass Fat free mass	TBW, body vol, protein, BMC

Summary

- Measurement of body composition of infants and young children must take into account chemical maturation of FFM
  - Decrease in the hydration of FFM, attributable to decrease in ECW
  - Increase in potassium content
  - Slight increase in protein and calcium content
- Patterns of change in body composition in first 2 years of life
  - Curvilinear patterns seen for TBW, TBK, BMC, FFM and FM
  - %FM increased markedly between 0.5 and 3-6 months, then gradually declined
- Available methodologies can be applied with an understanding of their theoretical basis and limitations

RAISING THE BAR: ENGINEERING OPTIMIZED BEHAVIORAL INTERVENTIONS FOR INCREASED PUBLIC HEALTH IMPACT

Linda M. Collins, Ph.D.
The Methodology Center
Penn State

Presented at the Workshop on the Prevention of Obesity
in Infancy and Early Childhood
National Institutes of Health
November 1, 2013

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The Methodology Center
advancing methods, improving health

Behavioral interventions can be engineered to meet specific criteria.

This will set the bar for effectiveness, efficiency, and scalability.

We then can keep raising the bar, and behavioral interventions will keep improving incrementally.

Outline

- A few definitions
- Developing behavioral interventions: Business as usual
- Engineering behavioral interventions: The Multiphase Optimization Strategy (MOST)
- OK, so how do you do this? An example
- Imagine…

Definition: behavioral intervention

- A program aimed at modifying behavior for the purpose of treating or preventing disease, promoting health, and/or enhancing well-being.
- Examples:
  - —Clinic-based smoking cessation
  - —Weight loss/management program
  - —School-based drug abuse prevention
- Note that according to this definition, most behavioral interventions are treatment packages made up of multiple components.



Definition: Intervention component

- *Any aspect of an intervention that can be separated out for study*
  - Parts of intervention content
    - e.g.: segments in the curriculum of a family-based weight management intervention program
  - Features that promote compliance/adherence
    - e.g.: use of mems caps on medication
  - Features aimed at improving fidelity
    - e.g.: 800 number for program delivery staff to call with questions

More about intervention components

- Can impact
  - Effectiveness
  - Efficiency
  - Economy
  - Scalability
  - Sustainability
- Some may be pharmaceutical
- Can be defined at any level: individual, family, school, etc.

Outline

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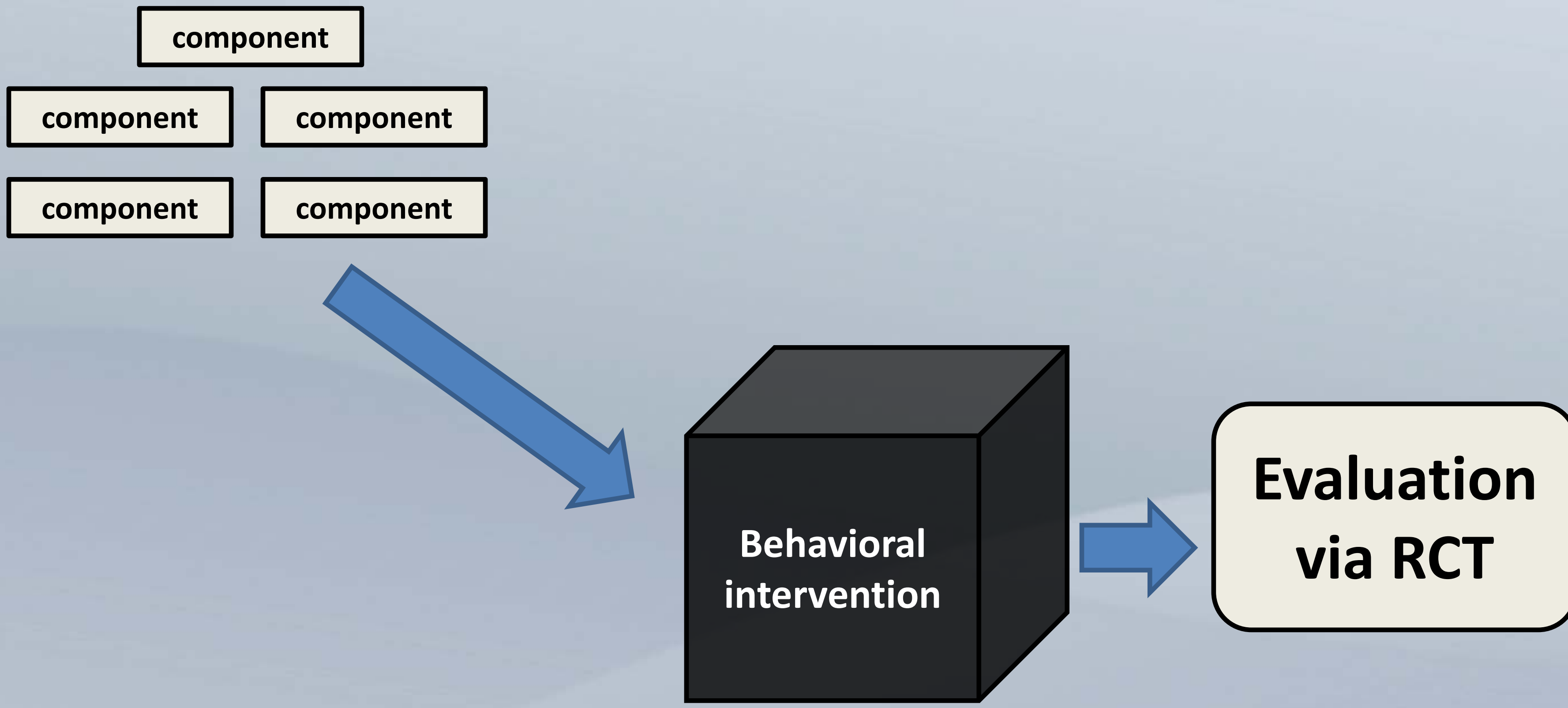
How behavioral inventions are typically developed

- Intervention components are chosen based on scientific theory, clinical experience, etc.
- Combined into a treatment package
- Package is evaluated via a randomized controlled trial (RCT)
- The *treatment package approach*

Treatment package approach



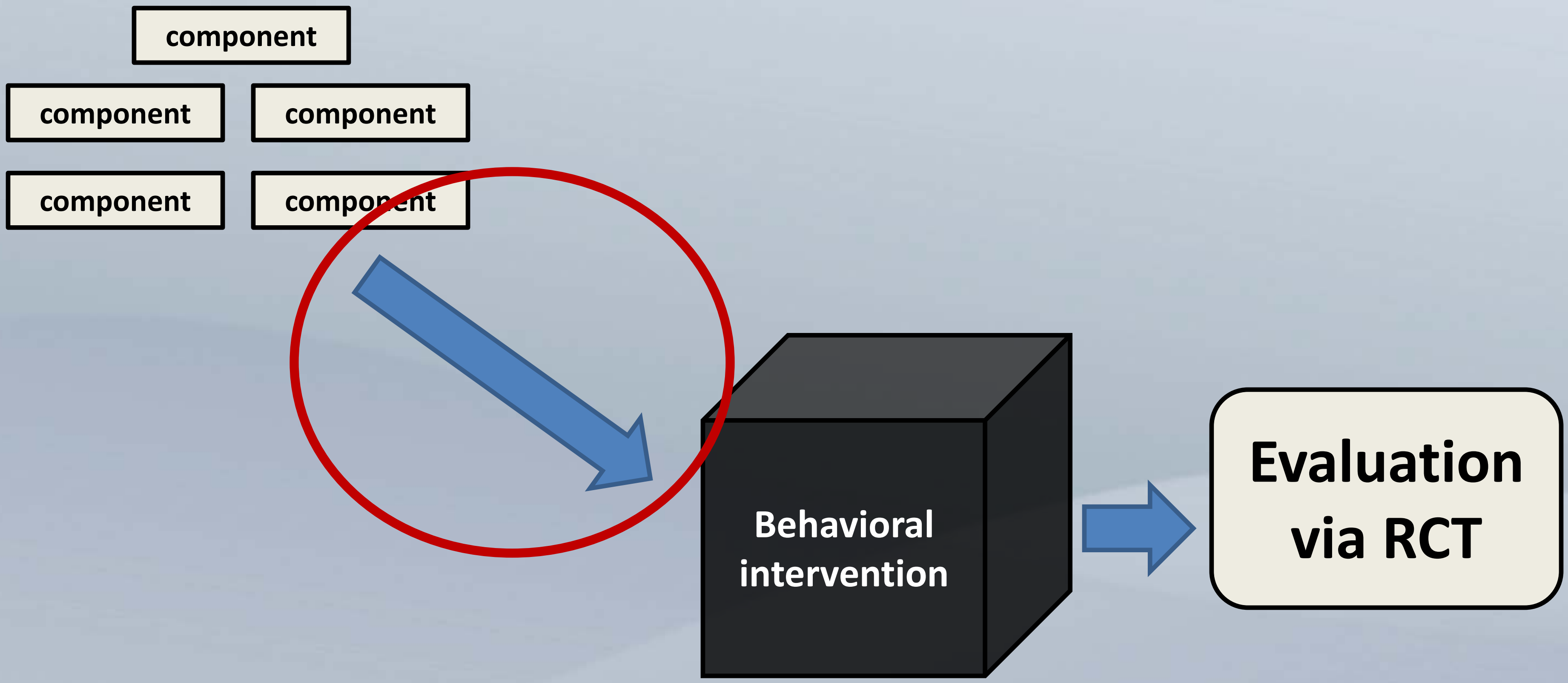
What's wrong with evaluating a treatment package via an RCT?

Absolutely nothing!

The RCT is designed to tell us

- Whether a treatment package performs better than a control or comparison
- Whether one treatment package performs better than another

Treatment package approach



The RCT does not tell us

An RCT that finds a <u>significant</u> effect DOES NOT tell us

- Which components are making positive contributions to overall effect
- Whether a component's contribution offsets its cost
- Whether all the components are really needed
- How to make the intervention more effective, efficient, scalable, and sustainable

What the RCT does not tell us

An RCT that finds a non-significant effect DOES NOT tell us

- Whether any components are worth retaining
- Whether one component had a negative effect that offset the positive effect of others
- Specifically what went wrong and how to do it better the next time

What's the alternative?

- When engineers build products they take an approach that is
  - Systematic
  - Efficient
  - Focused on the clear objective of <u>optimizing</u> the product
- Can we borrow ideas from engineering…
- … and build optimized behavioral interventions?

Outline

- A few definitions
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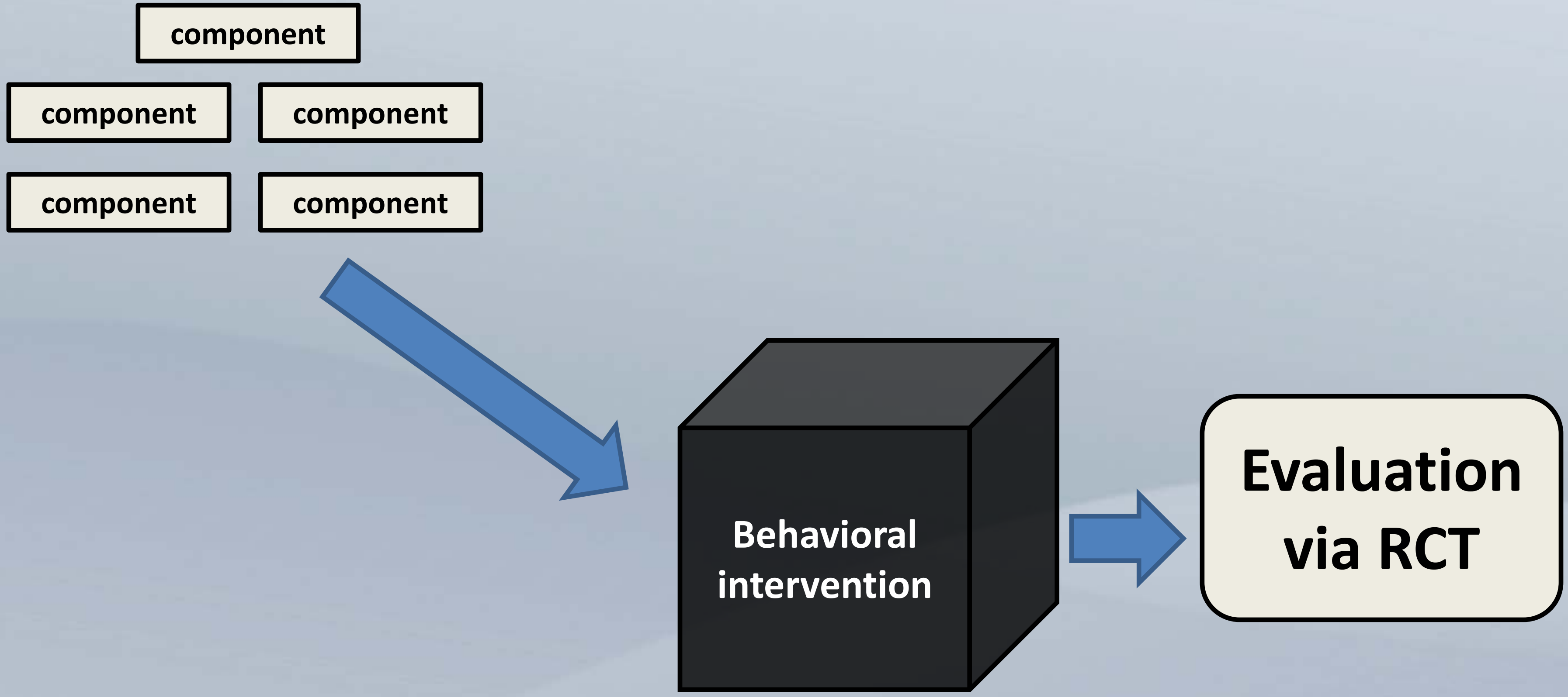
- Imagine…

The Multiphase Optimization Strategy (MOST)

- An engineering-inspired framework for development, optimization, and evaluation of behavioral interventions
- Using MOST it is possible to engineer a behavioral intervention to meet a specific optimization criterion

Collins, Murphy, Nair, & Strecher, 2005; Collins, Murphy, & Strecher, 2007; Collins, Baker, Mermelstein, Piper, Jorenby, Smith, Schlam, Cook, & Fiore, 2011

Treatment package approach



Treatment package approach

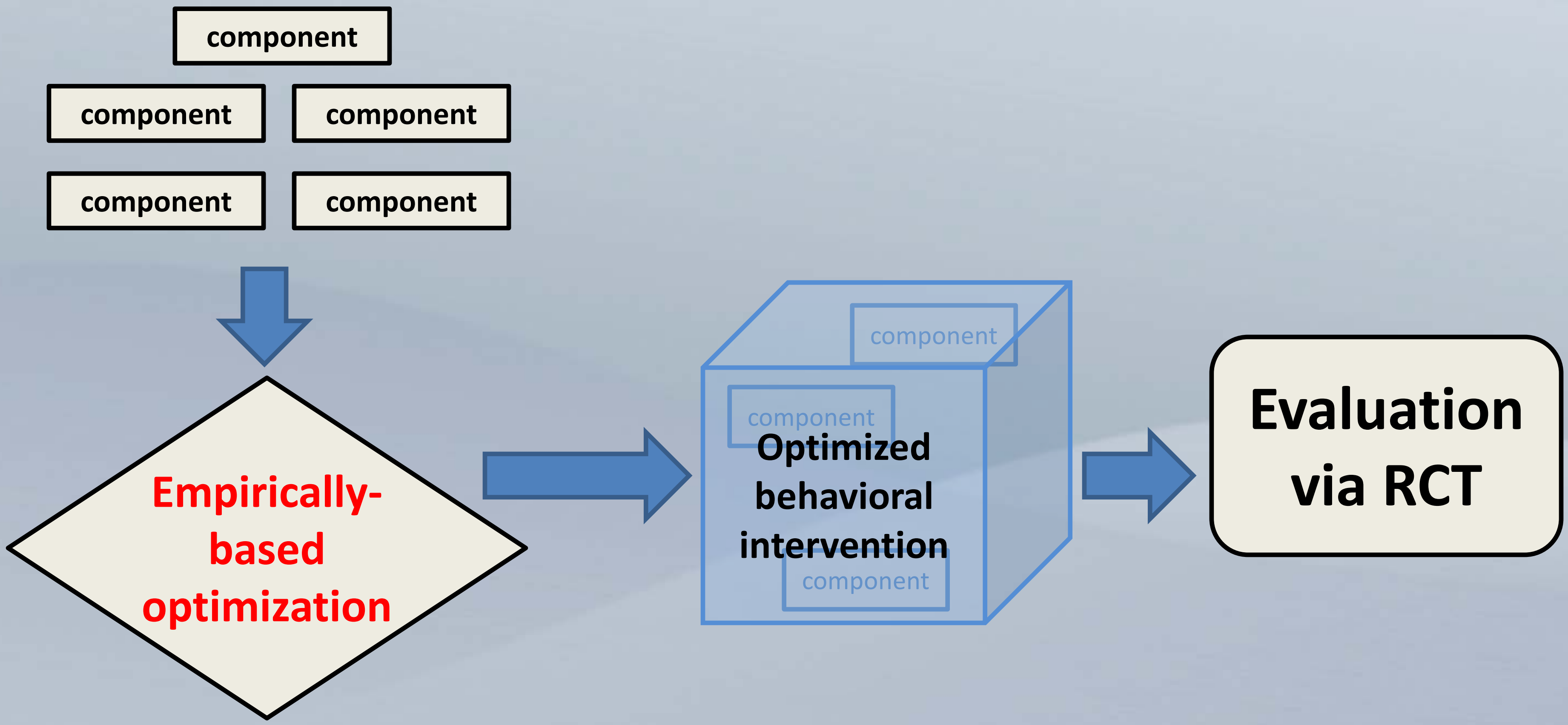
component

component component

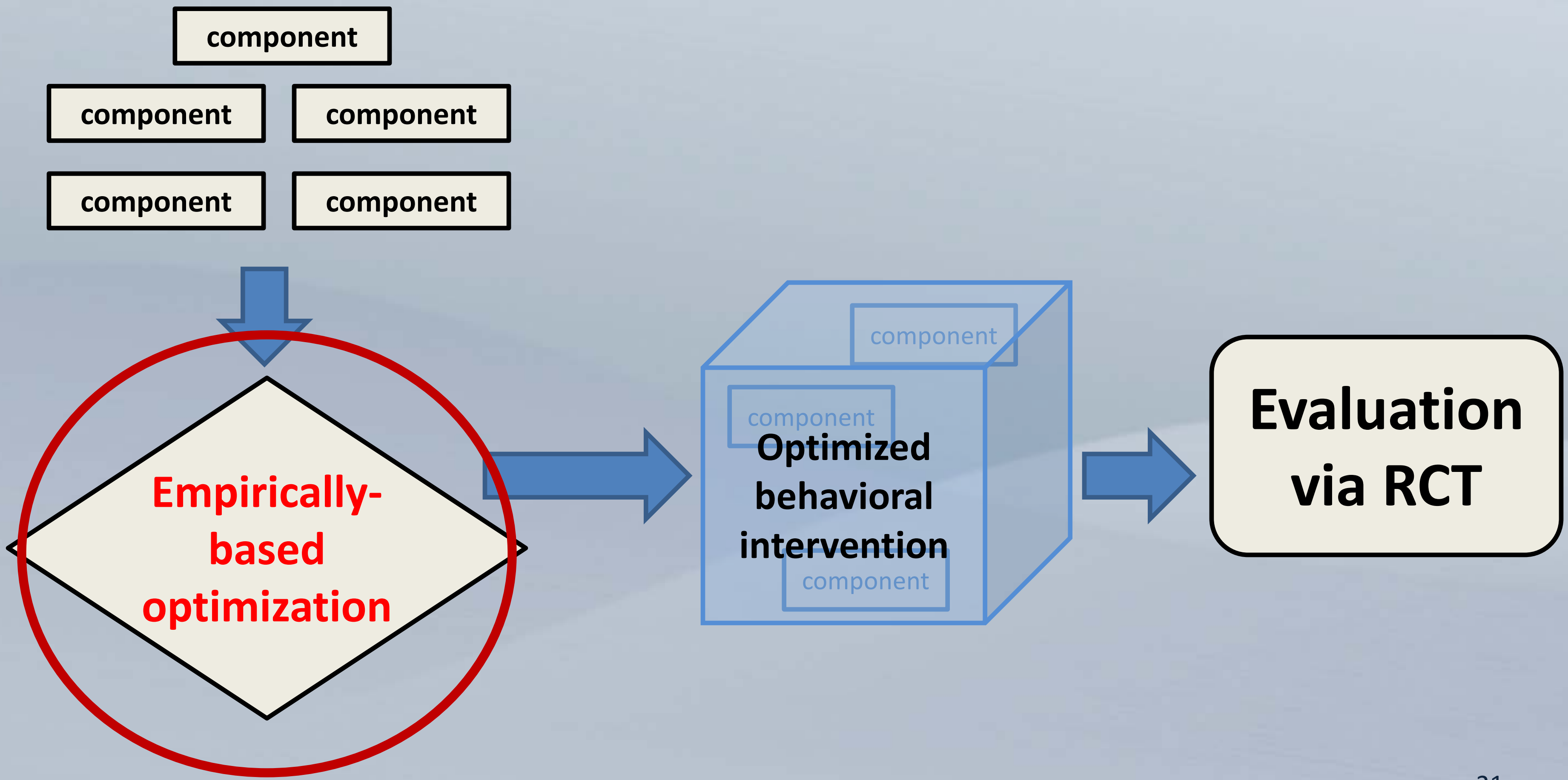
component component

Evaluation via RCT

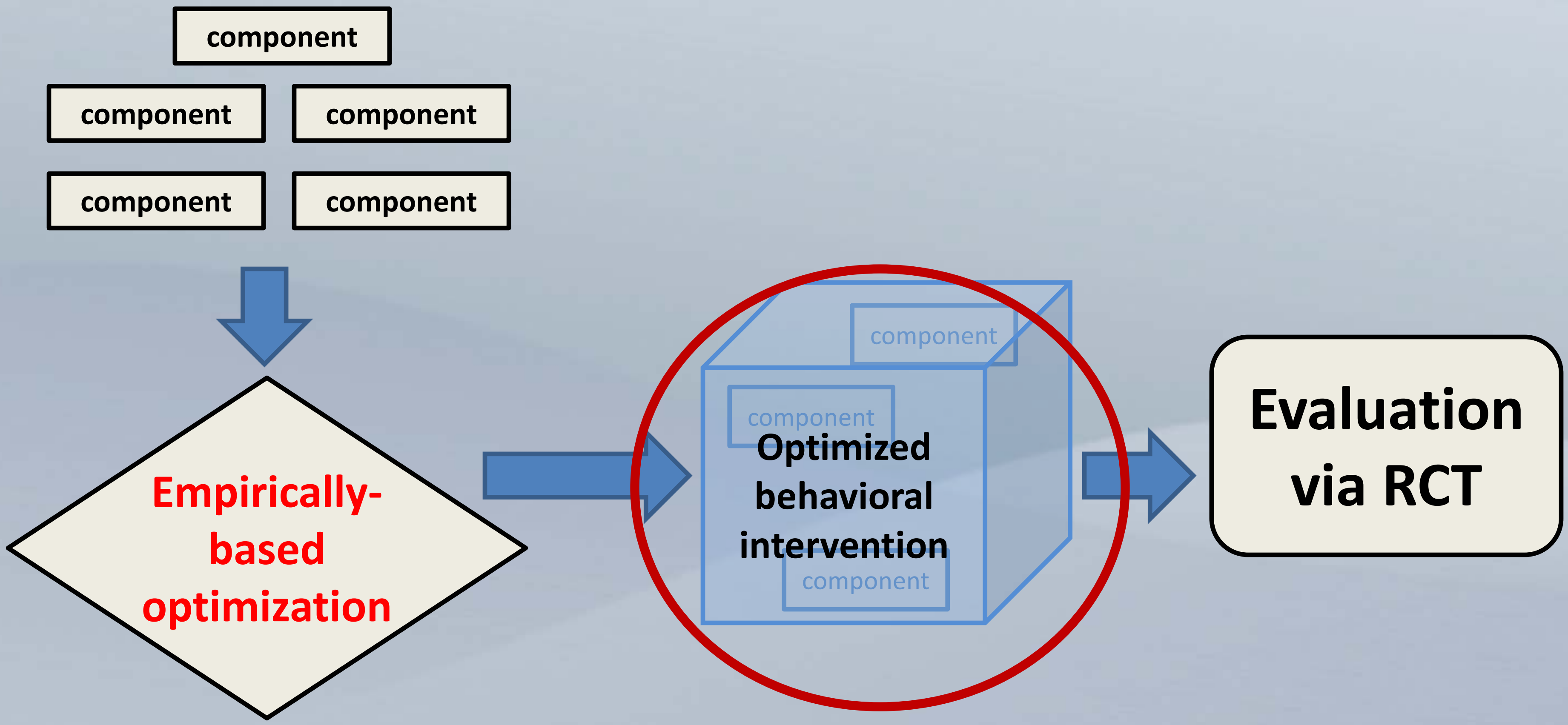
Multiphase Optimization Strategy (MOST)



Multiphase Optimization Strategy (MOST)



Multiphase Optimization Strategy (MOST)



Definition: Optimization

- "*The process of finding the best possible solution… subject to given constraints*" (The Concise Oxford Dictionary of Mathematics)
  - —Optimized does not mean best in an absolute or ideal sense
  - —Instead, realistic because it includes constraints
- Optimization always involves a clearly stated <u>optimization criterion</u>

Selecting an optimization criterion

- Your definition of “best possible, given constraints”
- This is the goal you want to achieve
- Once achieved, it is the bar that sets a standard for later efforts

One possible optimization criterion:

- Efficient intervention with no “dead wood”
- CONSIDER a school-based obesity prevention program.
  - Suppose: The investigators want to be confident that every component is necessary to reduce waste of time and money.
  - Achieve this by selecting only active intervention components.

Another possible optimization criterion

- Most effective intervention that can be delivered for ≤ some $$
- CONSIDER a health care setting based intervention to prevent excessive gestational weight gain.
  - Suppose: Insurers say they will pay for an intervention that costs no more than $500/person to deliver, including materials and staff time.
  - Achieve this by selecting set of components that represents the most effective intervention that can be delivered for ≤ $500.

Other possible optimization criteria

- Cost-effectiveness
- A criterion based on a combination of cost and time
- Most effective without exceeding a specified amount of time to implement
- Most effective without exceeding a specified level of participant burden
- Or any other relevant criterion

Fundamental principle: *Resource management principle*

- Conduct research to gain the most scientific information relevant to the research questions at hand, without exceeding available resources.
  - This is what I need to find out: ______
  - These are the resources I have: ______
  - HOW CAN I MANAGE MY RESOURCES STRATEGICALLY TO FIND OUT WHAT I NEED TO KNOW?

Evaluation and optimization: Both important; not the same thing.	Evaluation: Is the intervention's effect ***statistically significant***?	
Optimization: Is the intervention the *best possible, given constraints*?	No	Yes
No	May wish to optimize using effect size as criterion	Intervention can probably be improved
Yes	Different intervention strategy needed	What we should be aiming for

Outline

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- Imagine…

Example of MOST: "Opt-in" weight reduction intervention study

Objective: Develop a highly effective weight reduction intervention aimed at adults

Bonnie Spring
Northwestern University

Funded by NIDDK.

Program official: Christine Hunter

Opt-in theoretical model

Core Intervention
- Education
- Goal Setting
- Skill Building
- Tech Tools

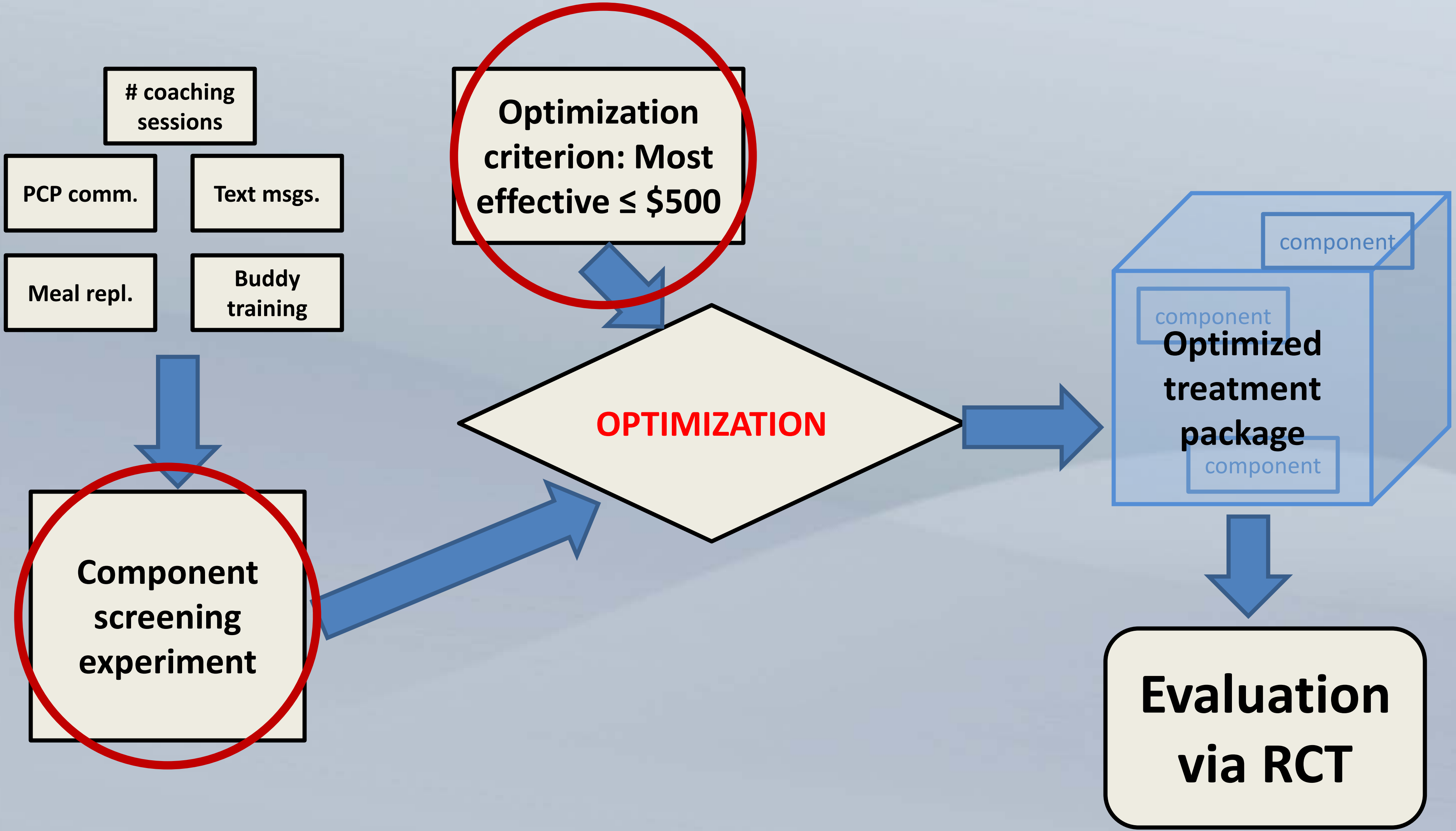
Experimental Components
1. Phone Coaching (12 v 24)
2. Text Messages (Y v N)
3. PCP Communication (Y v N)
4. Buddy Training (Y v N)
5. Meal Replacements (Y v N)

Social Cognitive Mechanisms
- Self-Efficacy
- Self-Regulation
- Supportive Accountability
- Facilitation

Adherence

Weight Loss

MOST as implemented in opt-in



The component screening experiment

- Purpose: efficient screening of intervention components
  - Weed out underperforming components
  - Get a sense of magnitude of each component's effect
  - Examine whether effect of a component is augmented or reduced in presence of another
- This information is then used to optimize the intervention
- Choice of the most efficient design is critical

The component screening experiment

- To select a design, consider several, and examine
  - The scientific information each will provide
    - And whether that information is what you want!
  - What each design costs
    - Number of subjects
    - Number of experimental conditions
- NOTE that the starting point is <u>the resources you have</u>

Comparison of four experimental design options for Opt-In

Design	*N* to achieve power ≥ .8	Number of experimental conditions	Can interactions be examined?
Option 1: Five individual experiments	2,800	10	No
Option 2: Comparative treatment	1,680	6	No
Option 3: Factorial experiment	560	32	Yes, all
Option 4: Fractional factorial experiment	560	16	Yes, but only selected

Using data from the experiment to optimize

- Conduct an analysis of variance, obtain estimates of effects of each of the components
- Use this information to select components to include in the intervention
  - Discard components that do not perform adequately
  - Use size of effects in combination with other data (e.g. cost) to select components that will make up optimized intervention

Status of Opt-In project

- Just went into the field about one month ago
- Premeasures and randomizing subjects to experimental conditions

After we have optimized and evaluated this intervention

- We will have set a bar for adult weight loss interventions
- Our work will establish which components work…
- …and what is the best combination under $500 pp
- Future work (by us or others) can build on this to develop
  - equally effective for less money
  - OR more effective for $500
  - OR "Here is a more meaningful optimization criterion:____"

Outline

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- OK, so how do you do this? An example
- Imagine…

Imagine the state of the art if MOST were widely implemented

- Every evidence-based intervention is optimized, so it is the best possible, given specific constraints.

Imagine the state of the art if MOST were widely implemented

- Every evidence-based intervention is immediately scalable
  - because important implementation constraints have been included in the optimization criterion.

Imagine the state of the art if MOST were widely implemented

- It is known which intervention components work, so interventions are transparent.
  - A coherent base of scientific knowledge is accumulating.
- Once a component screening experiment has been conducted, the ANOVA is made public, so if desired others can optimize using a different criterion.

Imagine the state of the art if MOST were widely implemented

- Every time a behavioral intervention is optimized, a clear bar is set for effectiveness, efficiency, and economy.
- Any new intervention must demonstrate that it is incrementally better than the preceding one, and specifically in what ways.

Imagine the state of the art if most were widely implemented

- **In this way the bar is raised with each new evidence-based intervention.**
- There is incremental progress over time, with interventions steadily gaining public health impact.

Behavioral interventions can be engineered to meet specific criteria.

This will set the bar for effectiveness, efficiency, and scalability.

We then can keep raising the bar, and behavioral interventions will keep improving incrementally.

For more information:

http://methodology.psu.edu/ra/most

This web site has

- suggested reading
- FAQ
- Advice for people writing grant proposals involving MOST

LMCOLLINS@PSU.EDU

Recent Publications

Caldwell, L.L., Smith, E.A., Collins, L.M., Graham, J.W., Lai, M., Wegner, L., Vergnani, T., Matthews, C., & Jacobs, J. (2012). Translational research in South Africa: Evaluating implementation quality using a factorial design. *Child and Youth Care Forum, 41,* 119-136.

Chakraborty, B., Collins, L.M., Strecher, V., and Murphy, S.A. (2009). Developing multicomponent interventions using fractional factorial designs. *Statistics in Medicine, 28,* 2687-2708.

Collins, L.M., Baker, T.B., Mermelstein, R.J., Piper, M.E., Jorenby, D.E., Smith, S.S., Schlam, T.R., Cook, J.W., & Fiore, M.C. (2011). The Multiphase Optimization Strategy for engineering effective tobacco use interventions. *Annals of Behavioral Medicine, 41,* 208-226.

Collins, L.M., Chakraborty, B., Murphy, S.A., & Strecher, V. (2009). Comparison of a phased experimental approach and a single randomized clinical trial for developing multicomponent behavioral interventions. *Clinical Trials, 6,* 5-15.

Collins, L.M., Dziak, J.R., & Li, R. (2009). Design of experiments with multiple independent variables: A resource management perspective on complete and reduced factorial designs. *Psychological Methods, 14,* 202-224.

Dziak, J.D., Nahum-Shani, I., & Collins, L.M. (2012). Multilevel factorial experiments for developing behavioral interventions. *Psychological Methods, 17,* 153-175.

Development from Birth to 24 Months: Considerations for Earliest Obesity Prevention

Sheila Gahagan, M.D., M.P.H

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SCHOOL OF MEDICINE

Presenter Disclosures
Sheila Gahagan

No relationships or conflicts of interest to disclose

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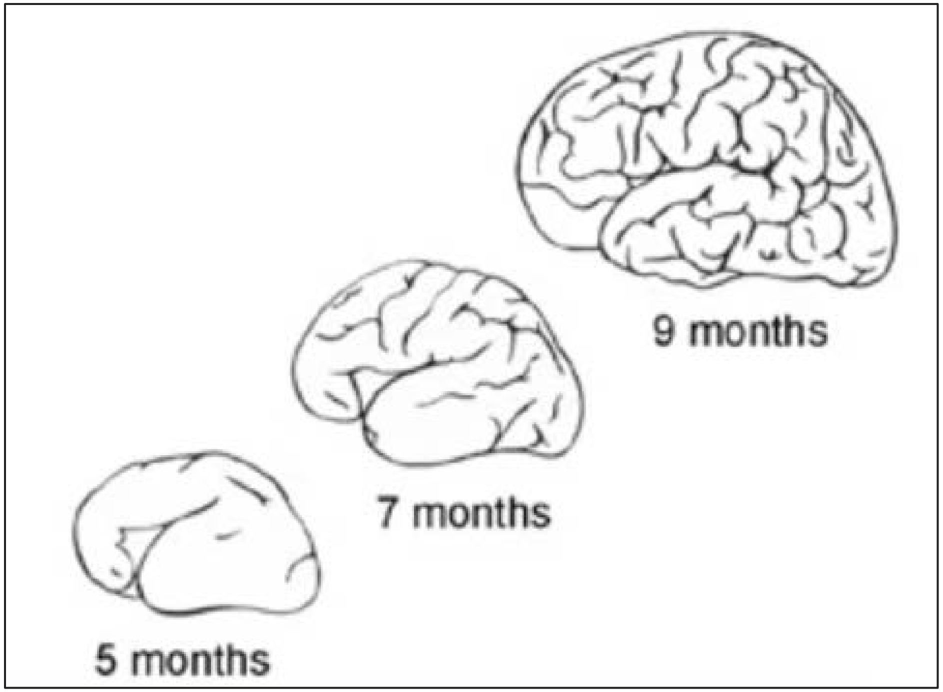
Goal and Overview

- Evolving neurodevelopment: birth - 24 months
- Relationships to early obesity prevention
- Informed by:
  - Neuroscience
  - Child development



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Developmental Domains

- Sensory
- Gross Motor
- Fine Motor
- Language
- Cognitive
- Socio-emotional

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Assessing Development

- Partitioned for assessment
- Driven by brain; reinforced by experience
- Overlapping and interacting
- Milestone - median - wide standard deviation

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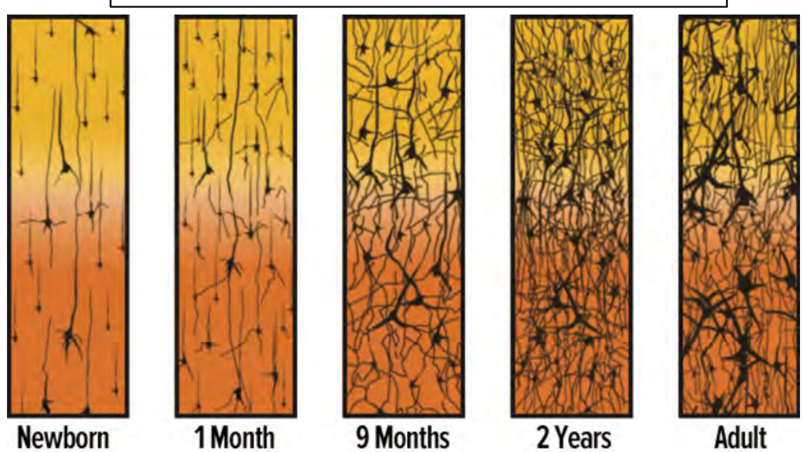
Brain Development

- Newborn nervous system
  - Neuronal cells present but immature
  - Myelination far from complete
  - Axon development continues into adolescence
    - corpus callosum
    - corticospinal tract

Synapse Density over time



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Newborn

- Follow a face
- Turn head toward sound
- Move body to rhythm of language
- Mimic
  - tongue protrusion
  - mouth opening
  - puckering of the lips

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Sensory

- Vision – fix and track
- Hearing
  - Turn to voice
- Taste and smell
  - Present early in gestation
  - Newborns
    - pleasure to sweet
    - aversion to bitter
    - neutral to salt
  - Discrimination and preferences develop and change

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Developmental Variation: 25th-75th %ile



Domain	Task	Months
Gross Motor	Walks independently	11.0 – 14.5
Fine Motor	Pincer grasp	9.5 – 12.5
Language	Combines 2 words	14 – 22
Socio-emotional	Plays ball	9.5 – 13.5

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Development – early obesity risk?

- Gross Motor
- Fine Motor
- Language
- Cognitive
- Socio-emotional

Development – early obesity risk?

- ENVIRONMENT
  - Obesogenic
    - High levels of passive activities
    - Low levels of activity
    - High caloric density foods
  - Impoverished
    - Lack of developmental stimulation

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Relevance for research

- Child development expertise
- Inclusion and exclusion criteria
- Family factors
- Using standardized developmental tools
    - Screening
    - Assessment

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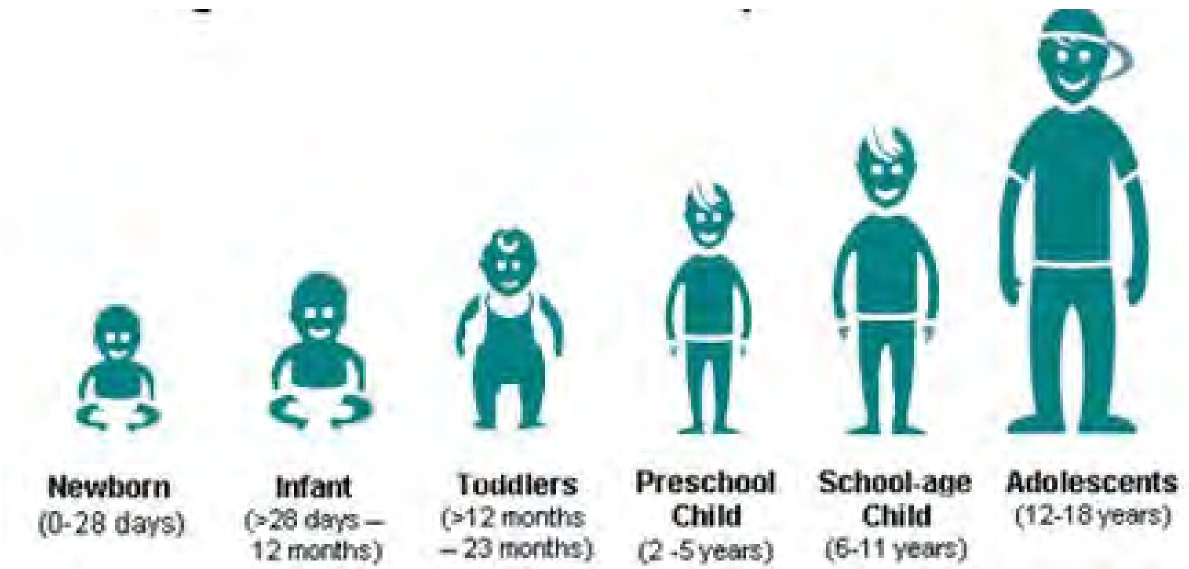
Conclusions

- Opportunities

- Challenges



Thank you!

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Emerging Risk Factors for Later Adiposity

Matthew W. Gillman, MD, SM

John Hancock
DELTA DENTAL
WELCOME TO
FENWAY PARK
AMERICA'S MOST BELOVED BALLPARK
OCTOBER 30, 2013
8:07 PM
WORLD SERIES
ST. LOUIS CARDINALS
GAME 6
BOSTON RED SOX
Beth Israel Deaconess Medical Center
STANLEY
HESS
DUNKIN
DONUTS

Emerging Risk Factors for Later Adiposity

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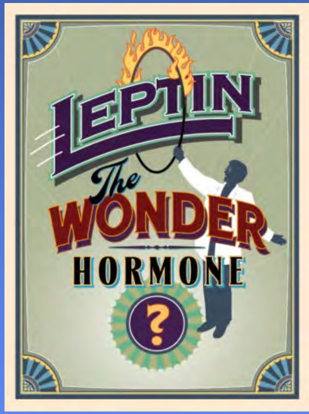

Thanks to…

Faculty, Trainees, & Staff

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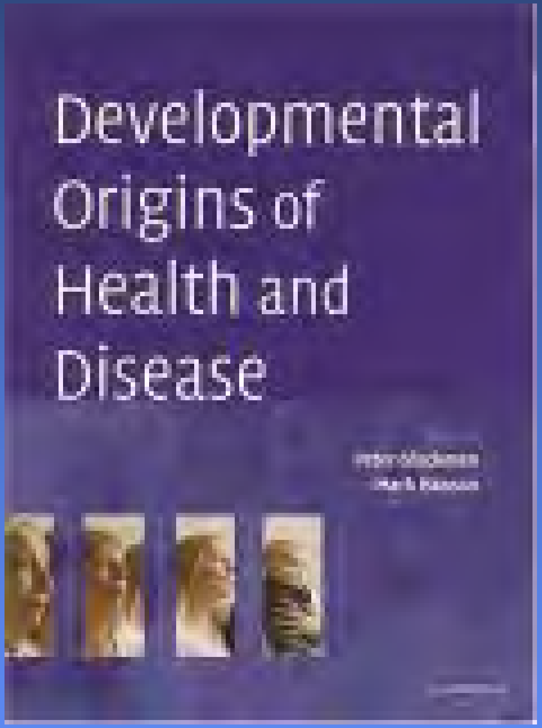
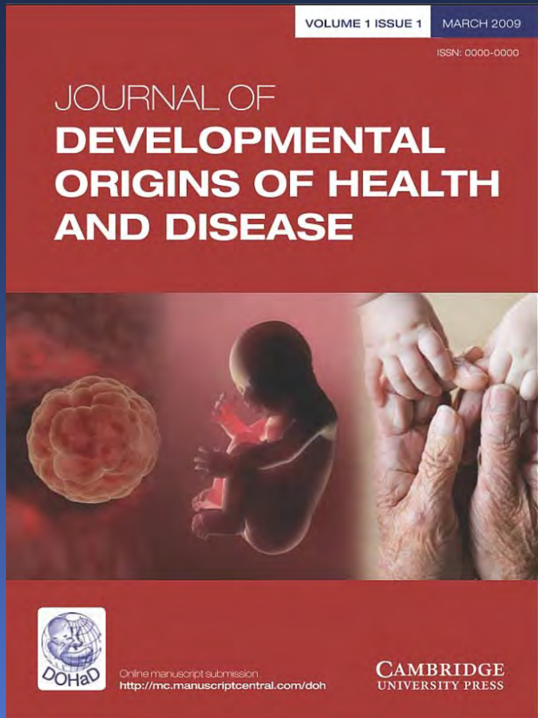
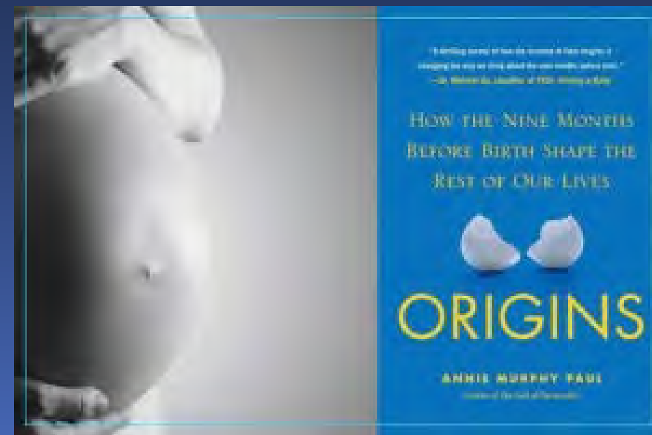
and
Support from NIH, CDC, DHHS
(R01 HD/HL/ES/MD/MH/NR, R03 TW, R18 AE, RC1 HD, R37 HD, P30 HL, U54 CA, K23/24/99 HD/HL/DK/ES)

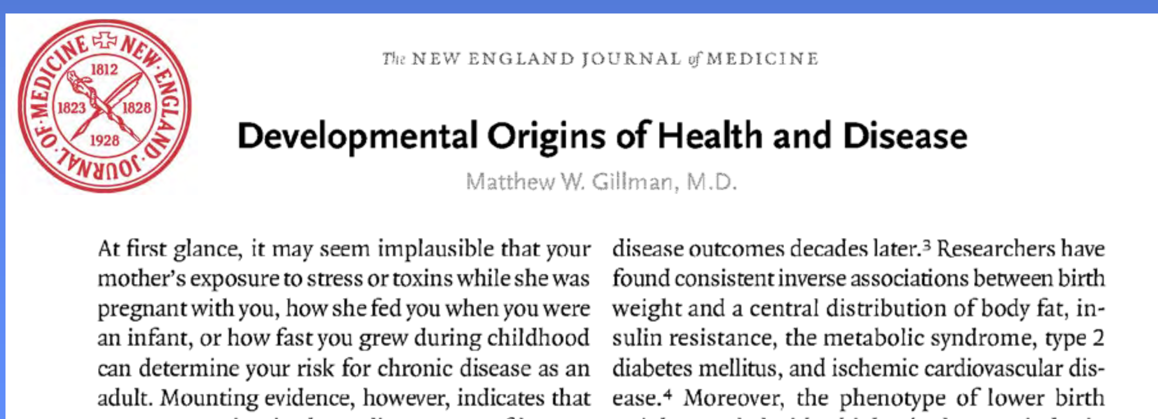
Developmental Origins of Health and Disease

- DOHaD emphasizes prenatal period and early childhood as important periods for development of chronic disease throughout life









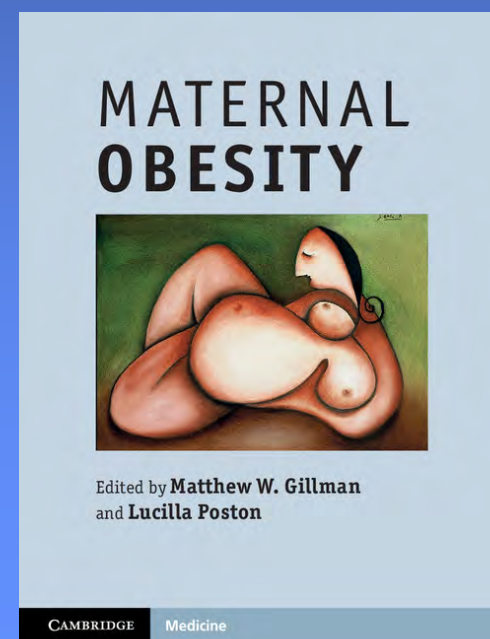
The NEW ENGLAND JOURNAL *of* MEDICINE

Developmental Origins of Health and Disease

Matthew W. Gillman, M.D.

At first glance, it may seem implausible that your mother's exposure to stress or toxins while she was pregnant with you, how she fed you when you were an infant, or how fast you grew during childhood can determine your risk for chronic disease as an adult. Mounting evidence, however, indicates that events occurring in the earliest stages of human

disease outcomes decades later.[3] Researchers have found consistent inverse associations between birth weight and a central distribution of body fat, insulin resistance, the metabolic syndrome, type 2 diabetes mellitus, and ischemic cardiovascular disease.[4] Moreover, the phenotype of lower birth weight coupled with a higher body-mass index in



David J. P. Barker (1938-2013)

Developmental Origins Research

- In animal models, perinatal programming of adult health outcomes well known
- Programming
  - Perturbation at a critical period of development causes alterations with lifelong, sometimes irreversible consequences

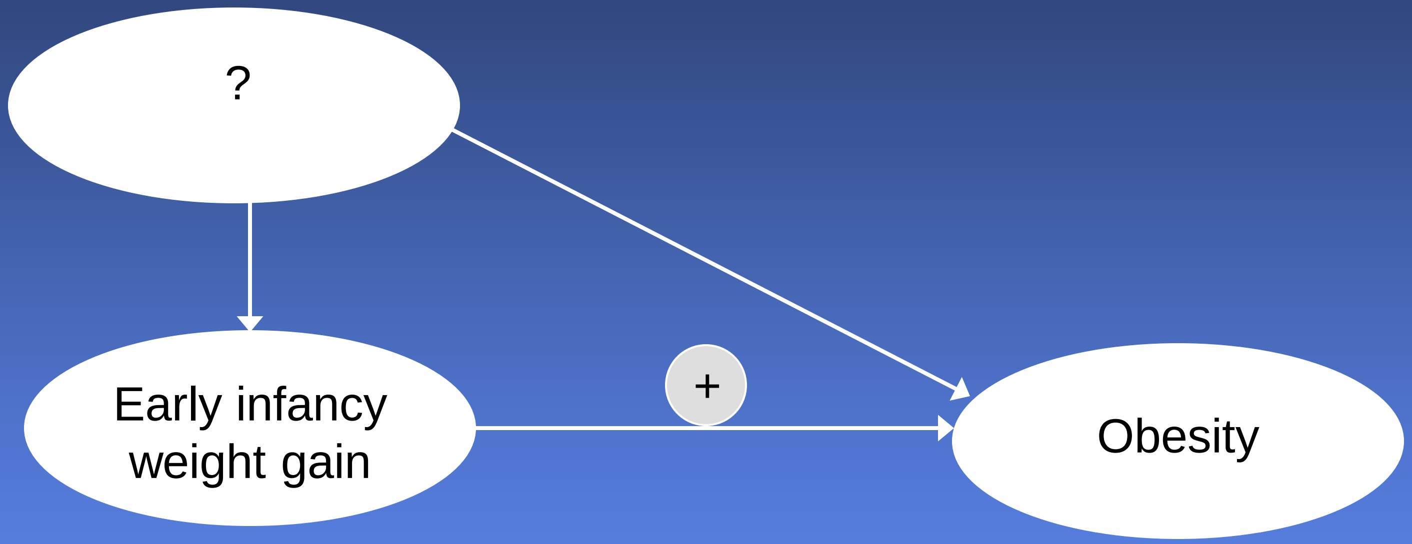
Developmental Origins of Health and Disease (DOHaD)
Animal models

- Chronic health conditions, esp. adiposity and cardio-metabolic consequences, proven in rats, guinea pigs, mice, sheep, pigs, non-human primates
- Relatively easy to induce
  - Diverse interventions in pre- and perinatal period
    - Nutritional, also hormonal, uterine artery ligation, anemia/hypoxia
- Involves environmental alteration of genetic expression, e.g., by epigenetic mechanisms

Rapid Infant Weight Gain

Rapid early infancy weight gain

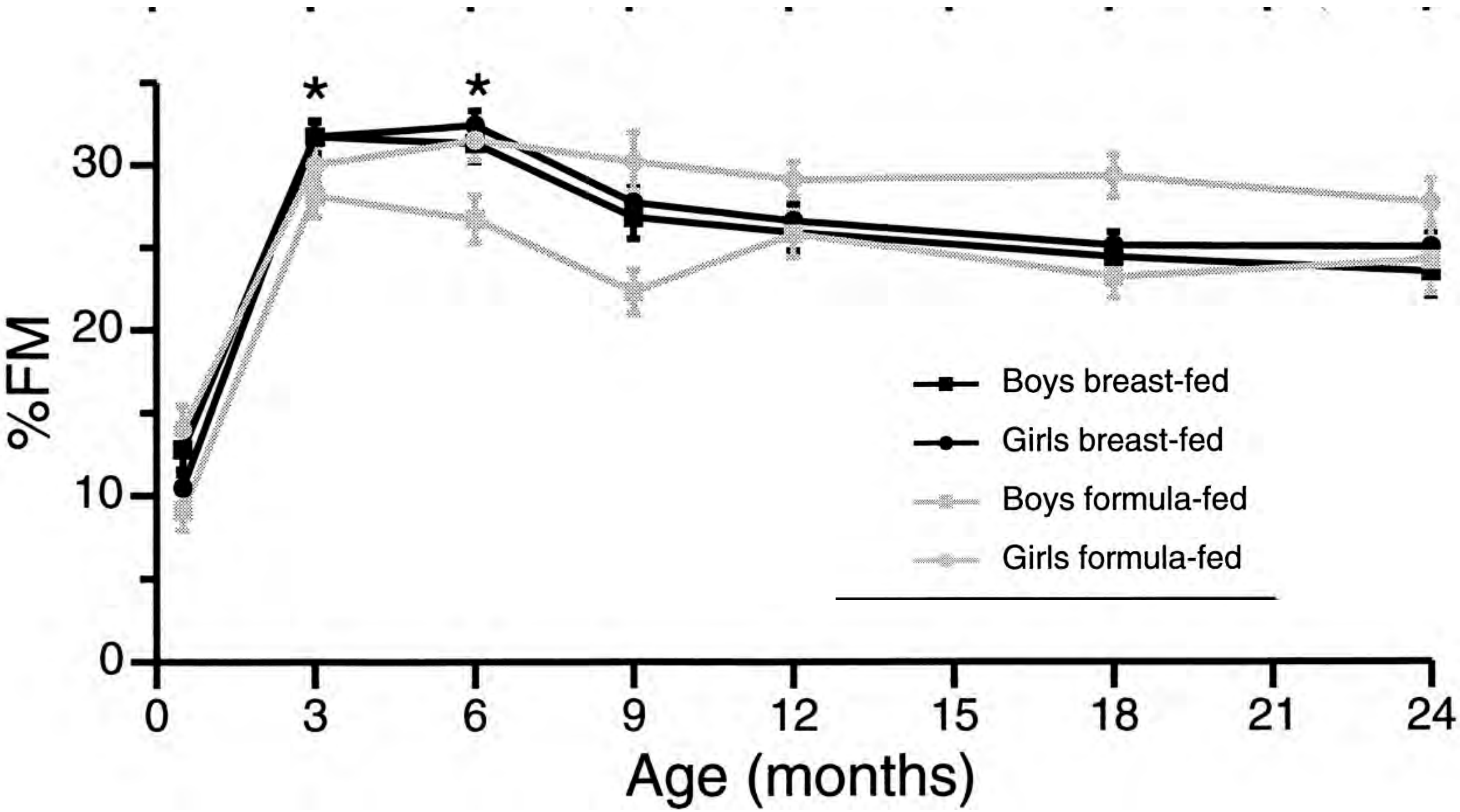
- What does it comprise?
  - Fat, muscle, bone?
- What causes it?


?
Early infancy weight gain
+
Obesity

Breastfeeding?

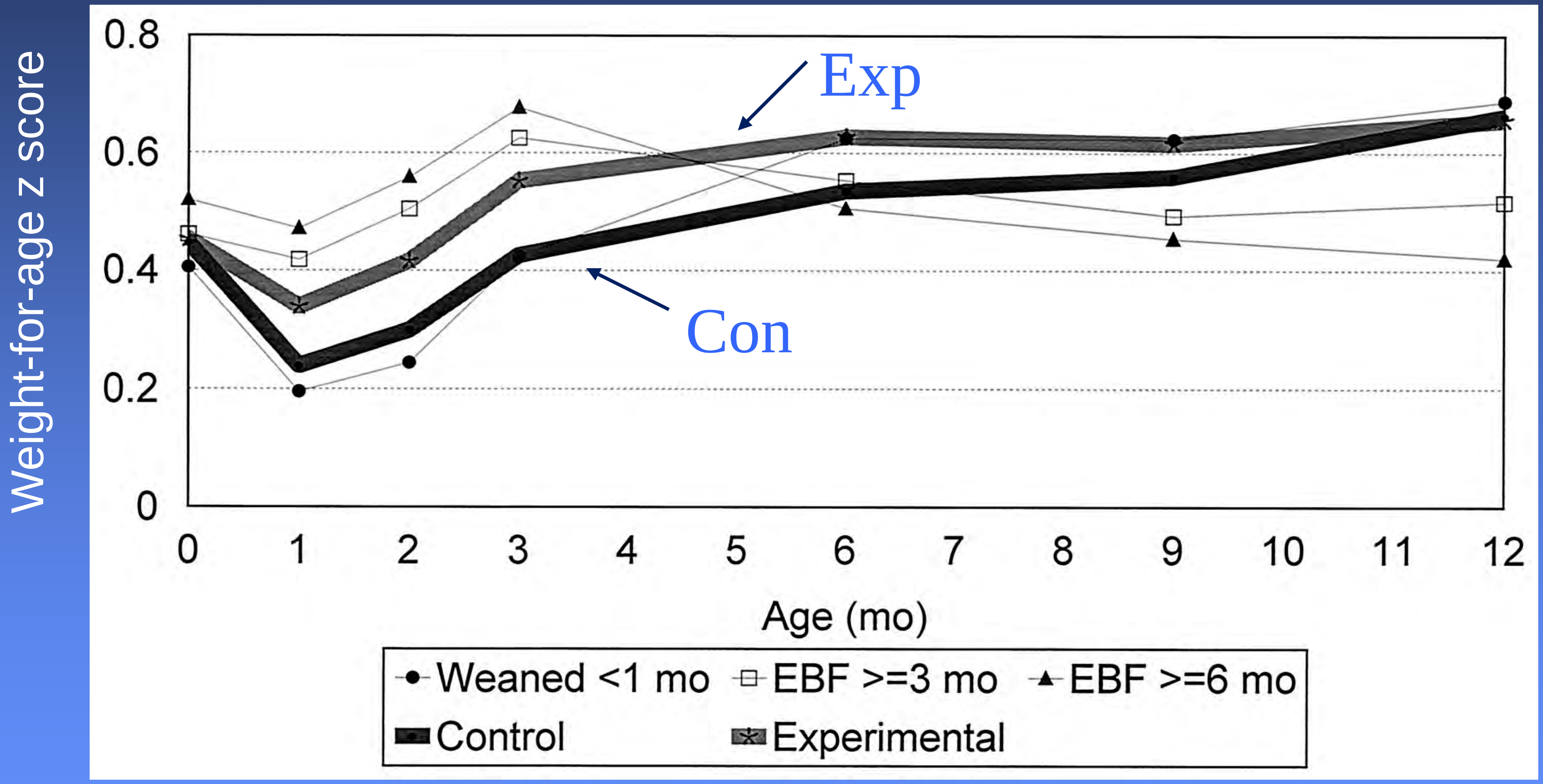
- Everybody “knows”
  - Having been breastfed lowers risk of later obesity
  - Breastfeeding leads to slower infant growth

In early infancy, breast-fed have *higher* fat mass than formula-fed



Butte N F et al. Pediatrics 2000;106:1355-1366

Breastfed babies gain *more* weight in early infancy in both observational and randomized design



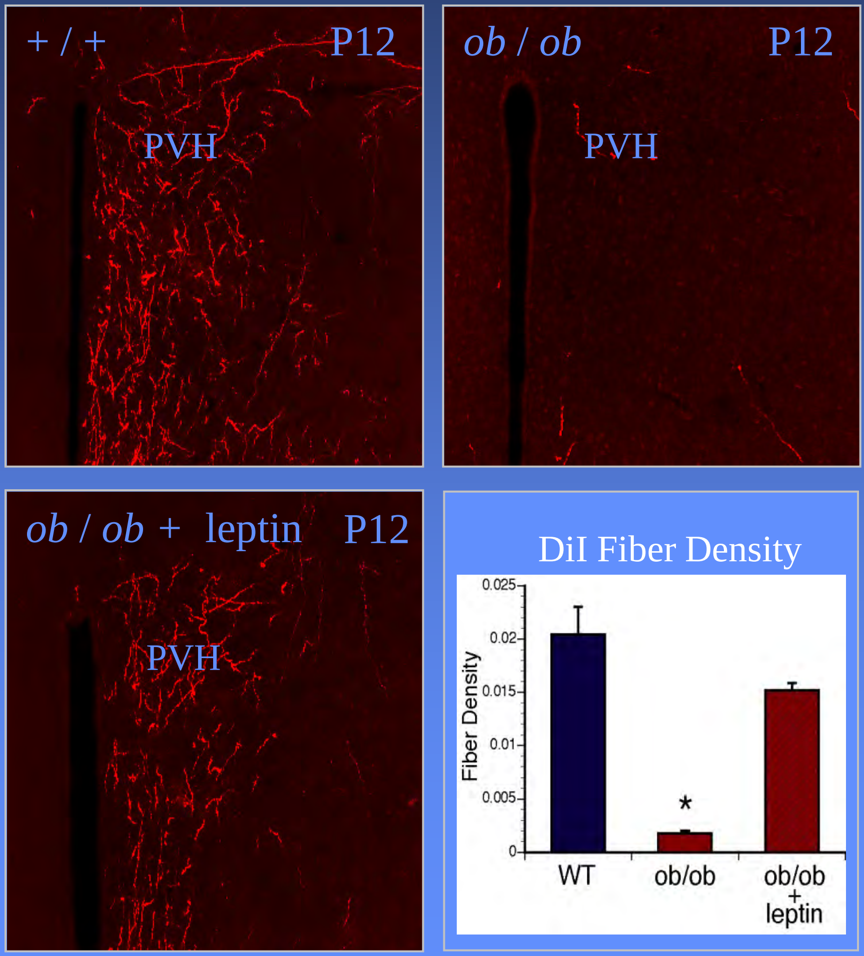
Kramer, M. S. et al. Pediatrics 2002;110:343-347

Rapid early infancy weight gain

- What does it comprise?
  - Fat, muscle, bone?
- What causes it?
  - Not just infant feeding
  - Entrained perinatally?

Critical period for the developmental actions of leptin

Neonatal Treatment

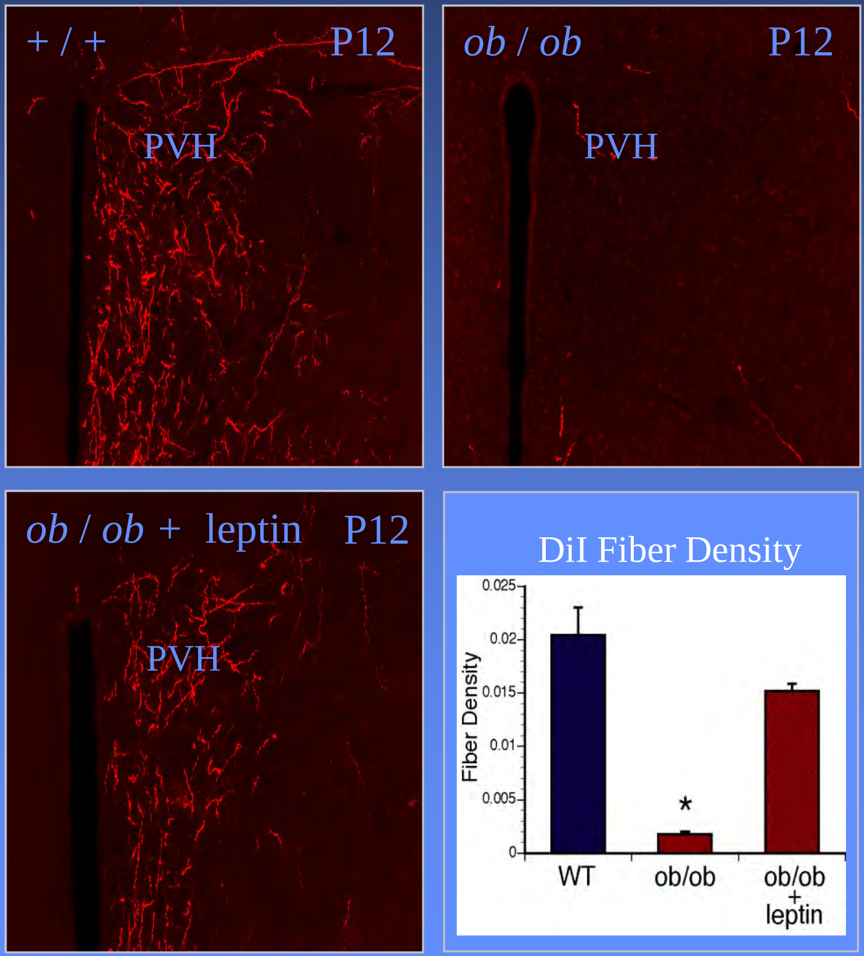


Growth and maturation of hypothalamic neurons responsible for appetite control

Courtesy Sebastien Bouret

Critical period for the developmental actions of leptin

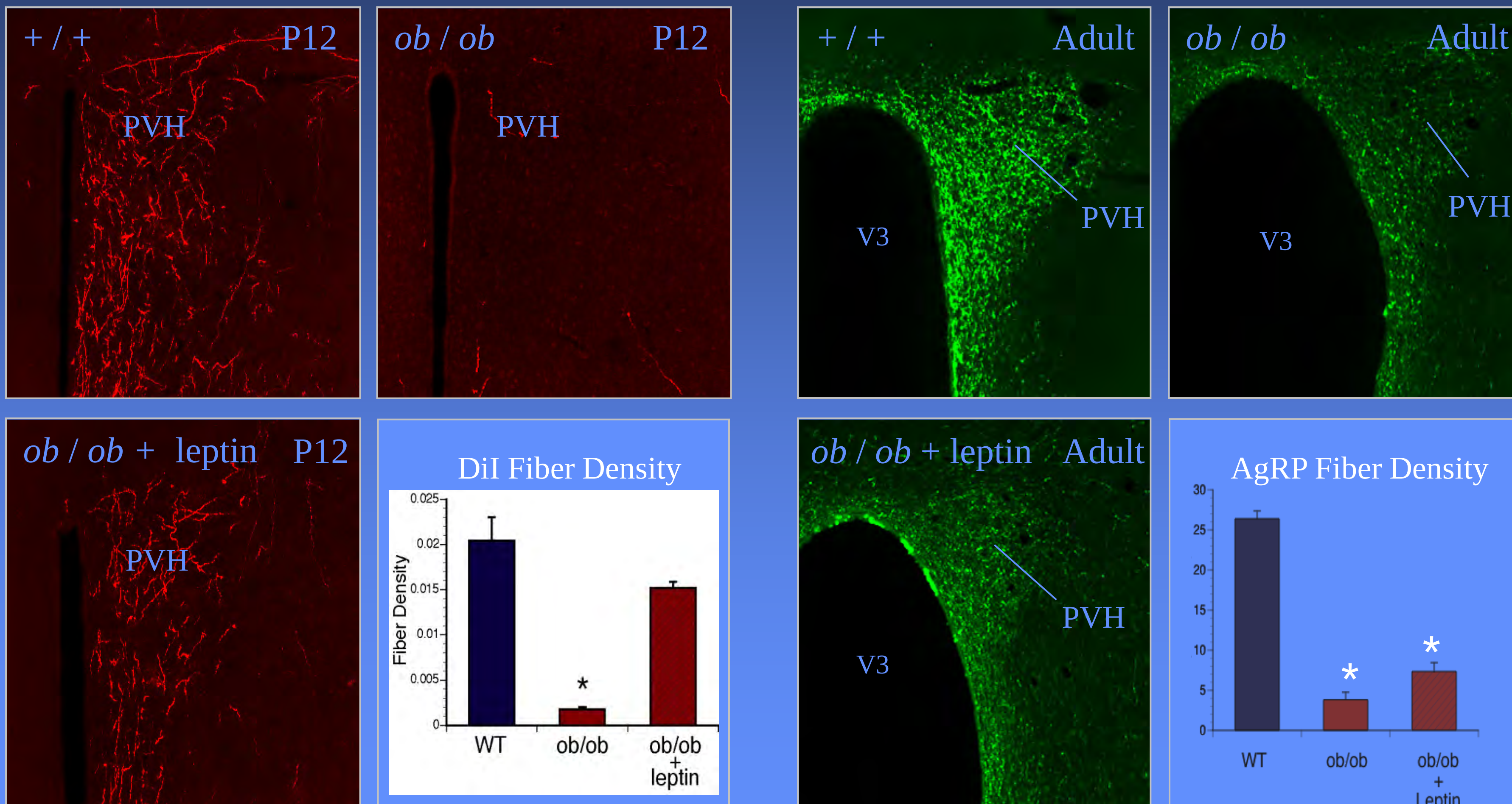
Neonatal Treatment



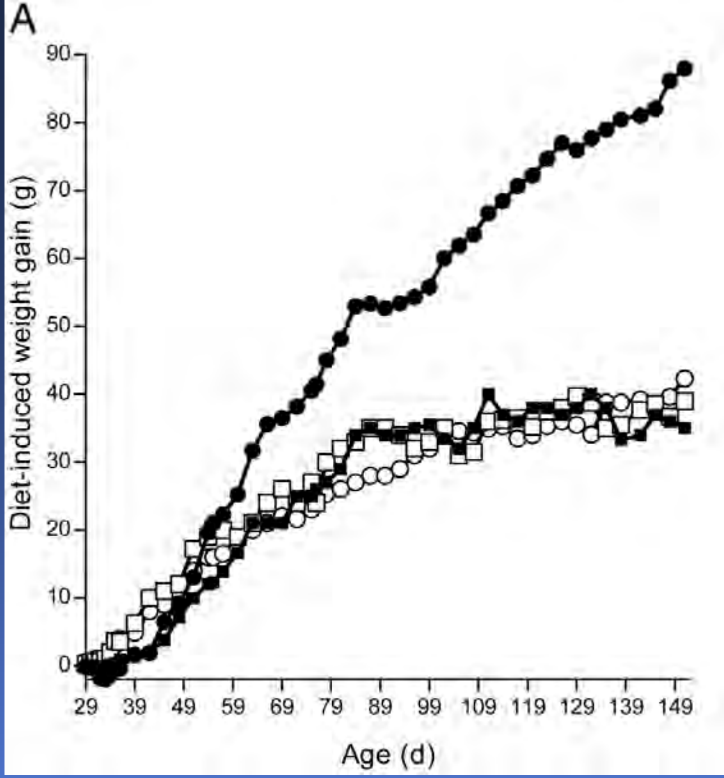
Growth and maturation of hypothalamic neurons responsible for appetite control

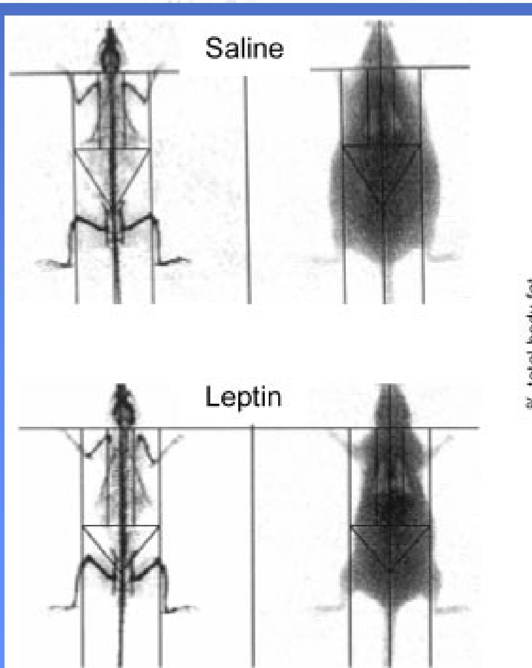
Critical period for the developmental actions of leptin

Neonatal Treatment *Adult Treatment*



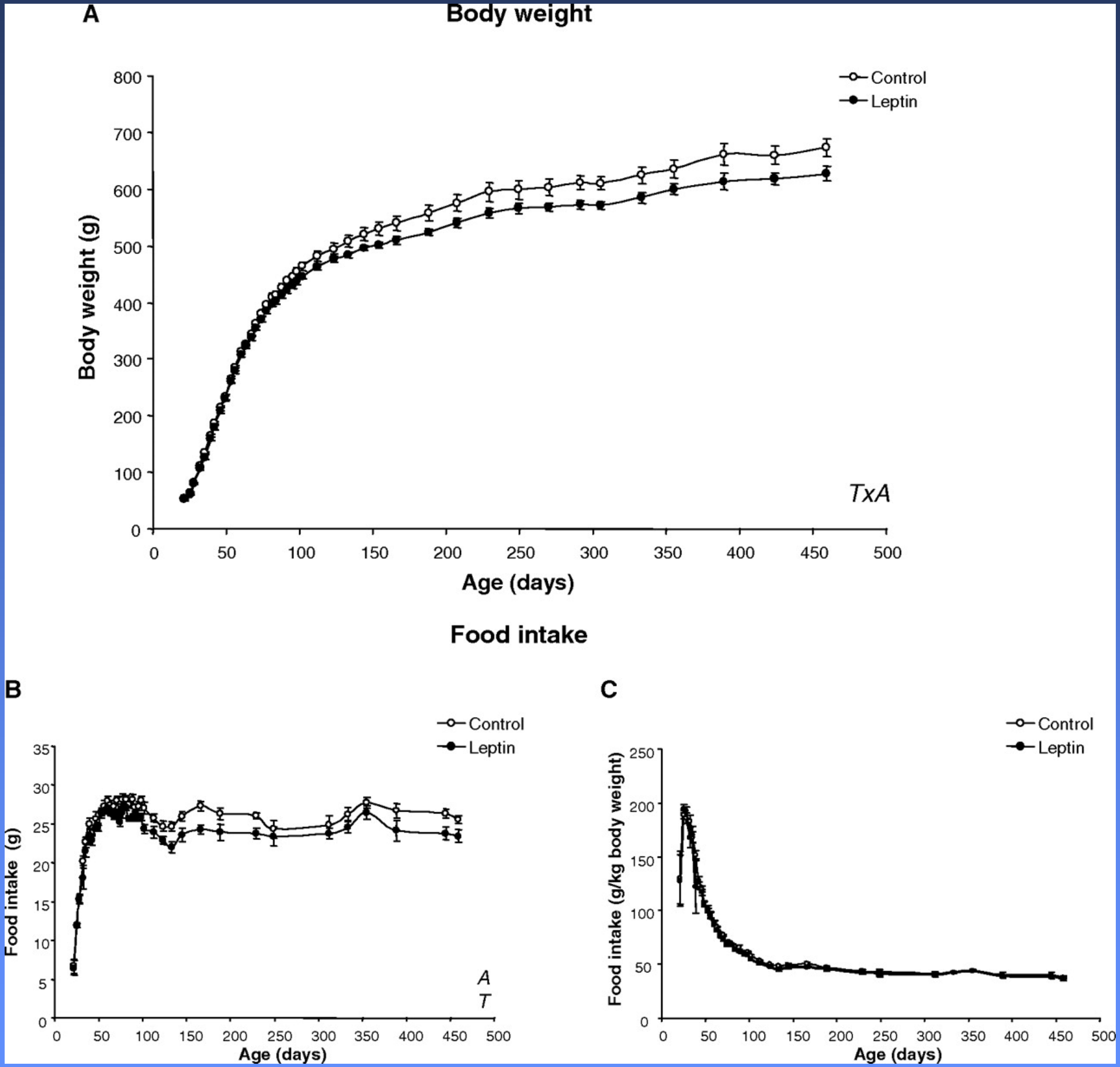
Neonatal leptin administration reverses adiposity and metabolic consequences of maternal prenatal under-nutrition in the rat



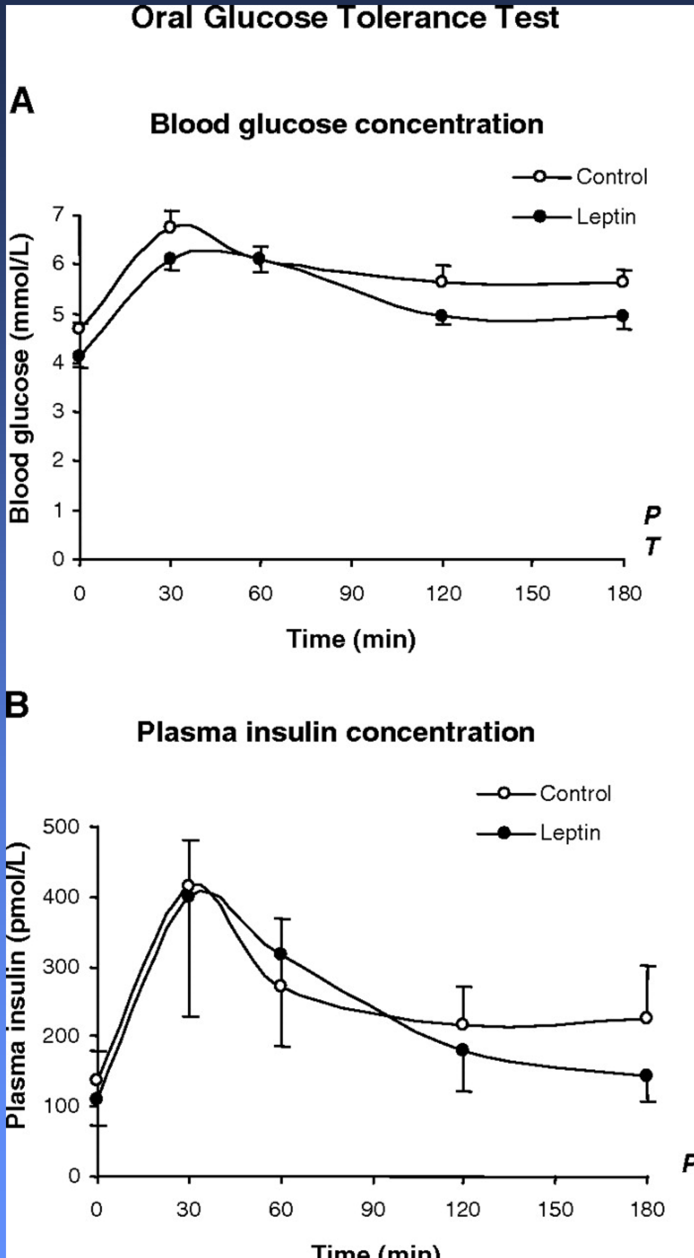


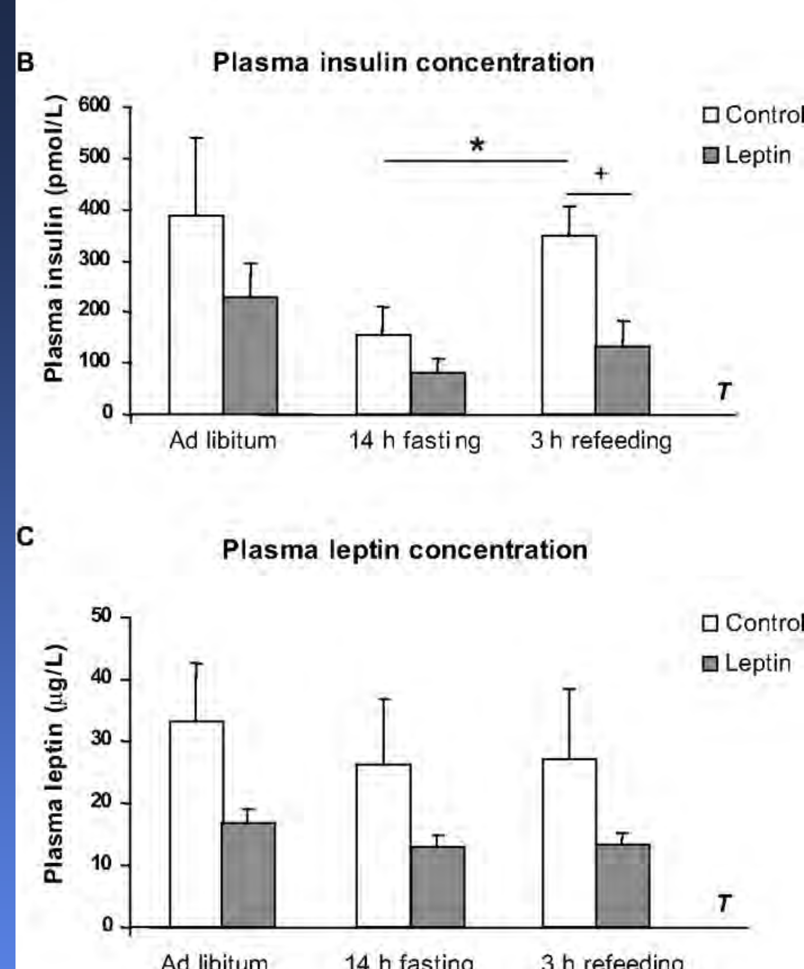
Vickers, M. H. et al. Endocrinology 2005;146:4211

Oral leptin during lactation causes reduced food intake and less weight gain in rats…



Sanchez, J. et al. Endocrinology 2008;149:733-740





…as well as less insulin and leptin resistance

Hypothesis:

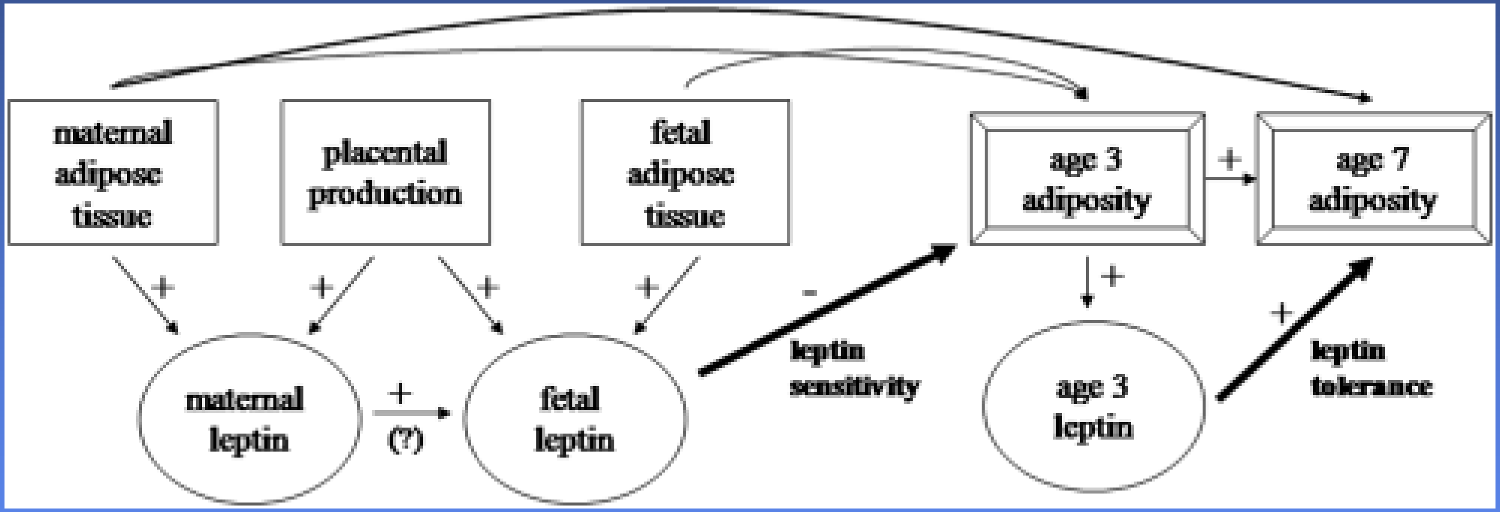
Placental leptin production (reflected in cord blood levels) causes less rapid gain in adiposity in infancy

But later on, tolerance (resistance) occurs, and leptin levels predict faster adiposity gain

Project Viva

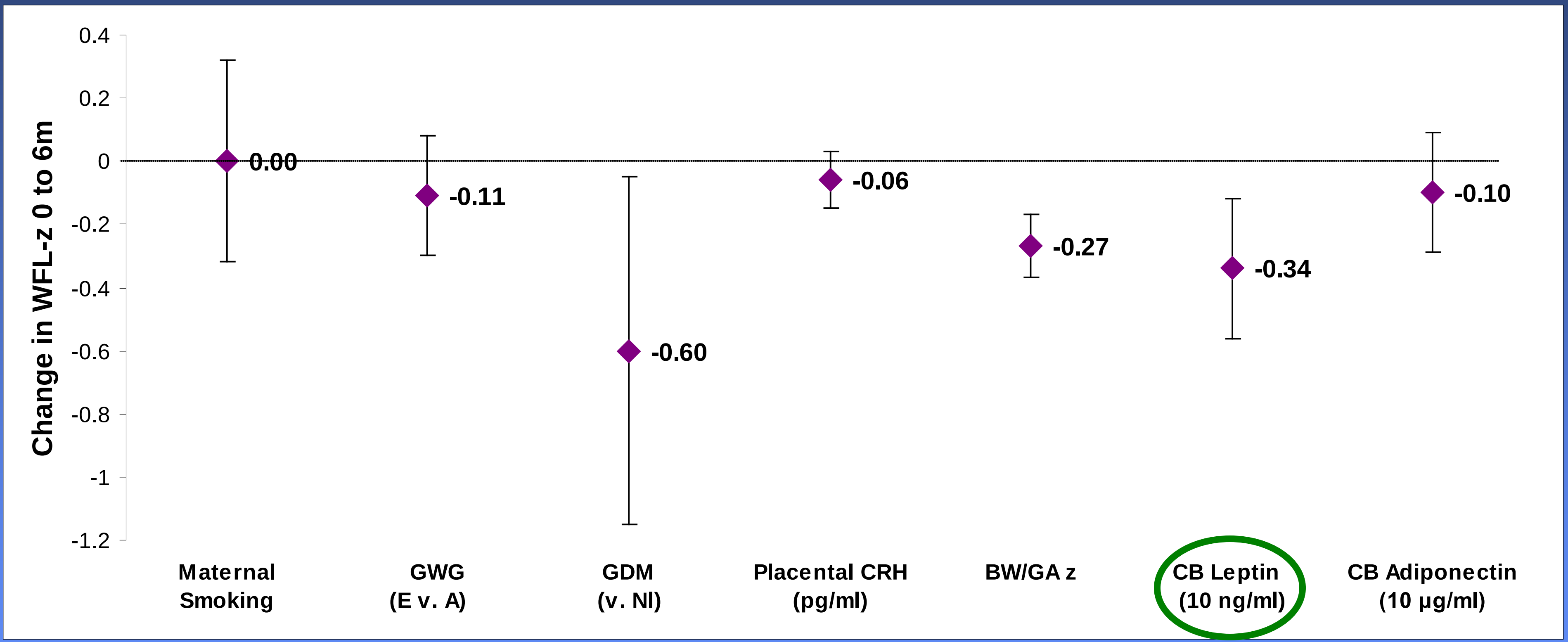
A Study of Health for the Next Generation

Conceptual Model



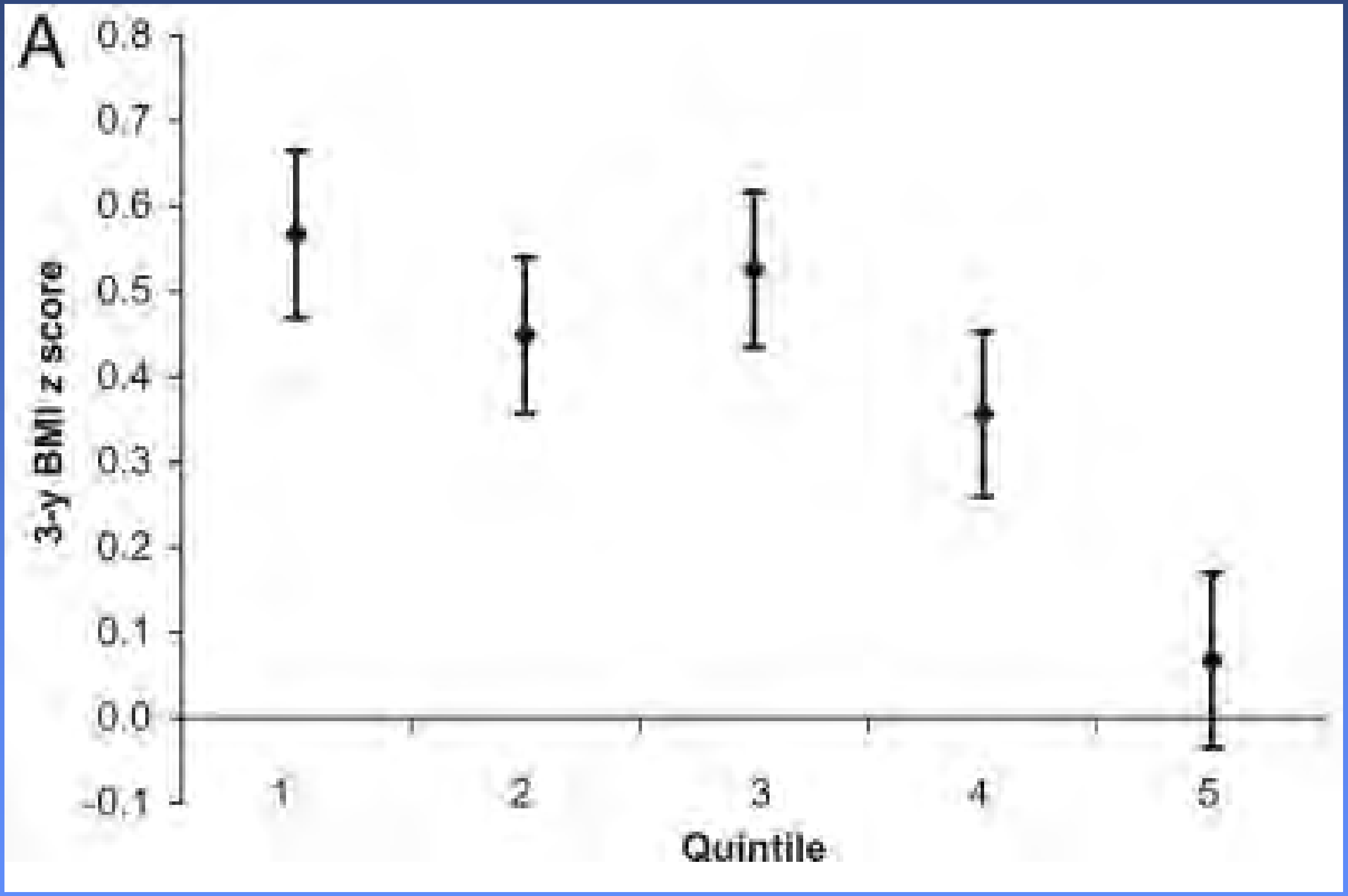
Boeke et al, Obesity 2013;21:1430-7

Predictors of early infancy weight (WFL) gain



M. Parker et al., J Pediatr. 2011;158:227-33

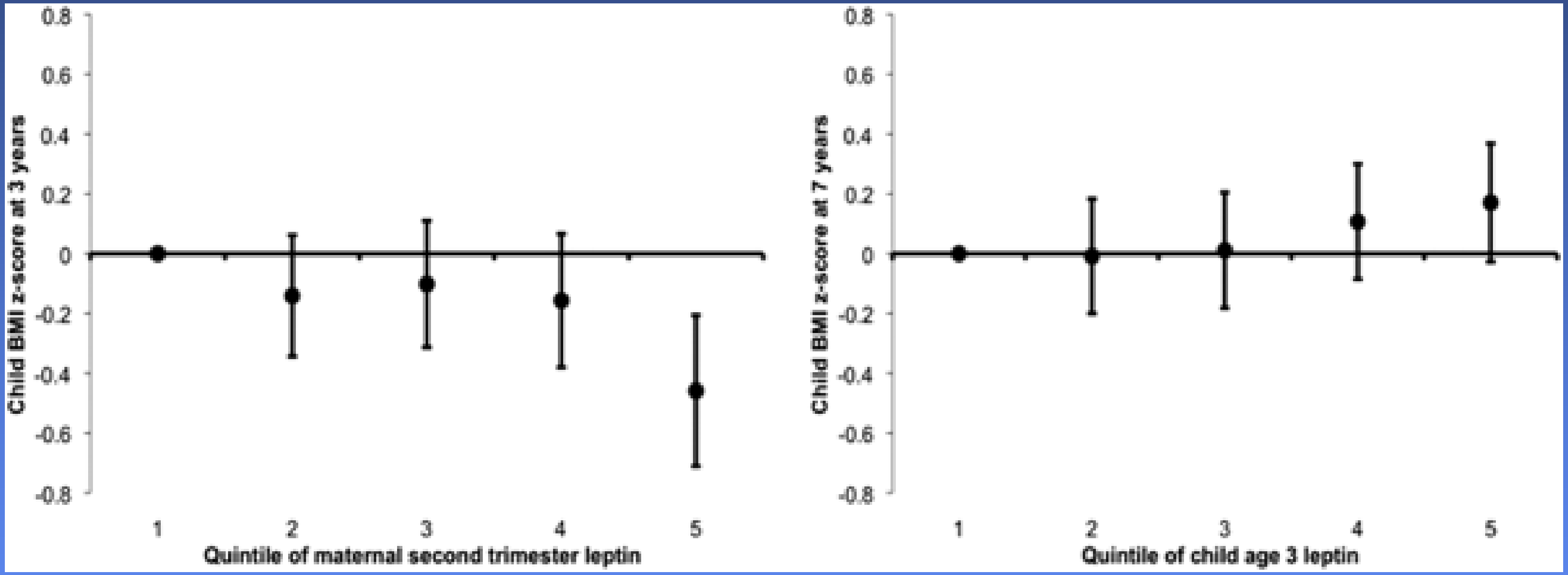
Cord blood leptin predicts lower 3-year BMI z-score



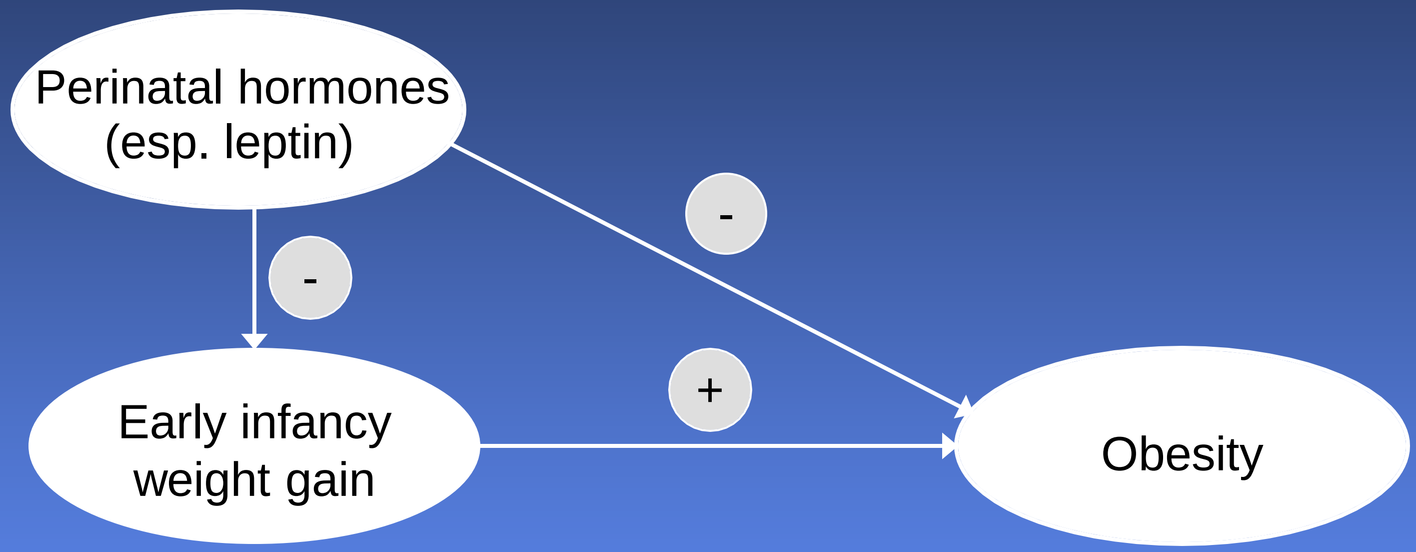
Mantzoros et al. Pediatrics 2009;123:682-689

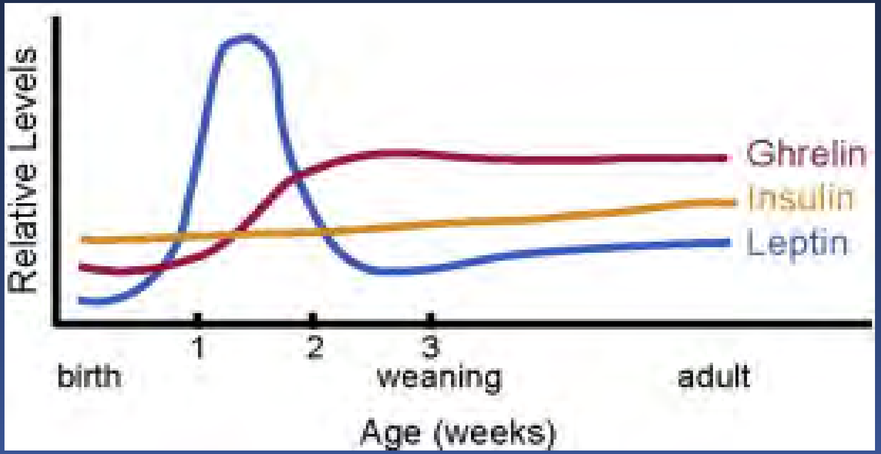
Cord blood leptin predicts lower 3-y (and 7-y) BMI, but age 3 leptin predicts *higher* 7-y BMI

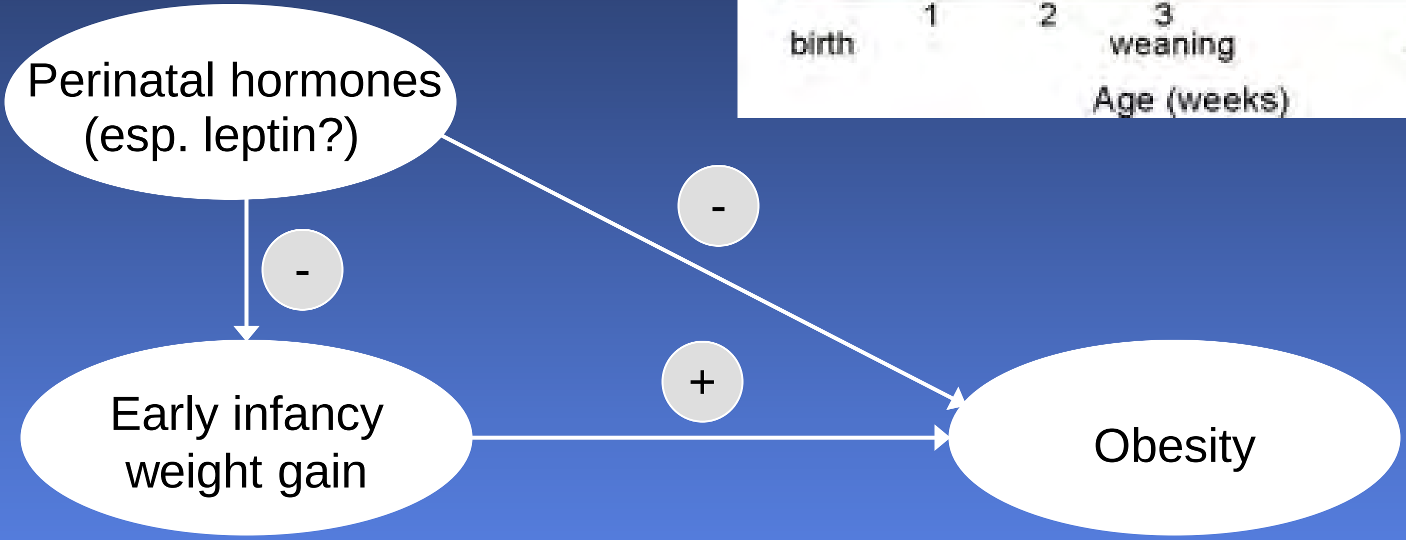
→ early sensitive period of leptin action



Boeke et al, Obesity 2013;21:1430-7


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





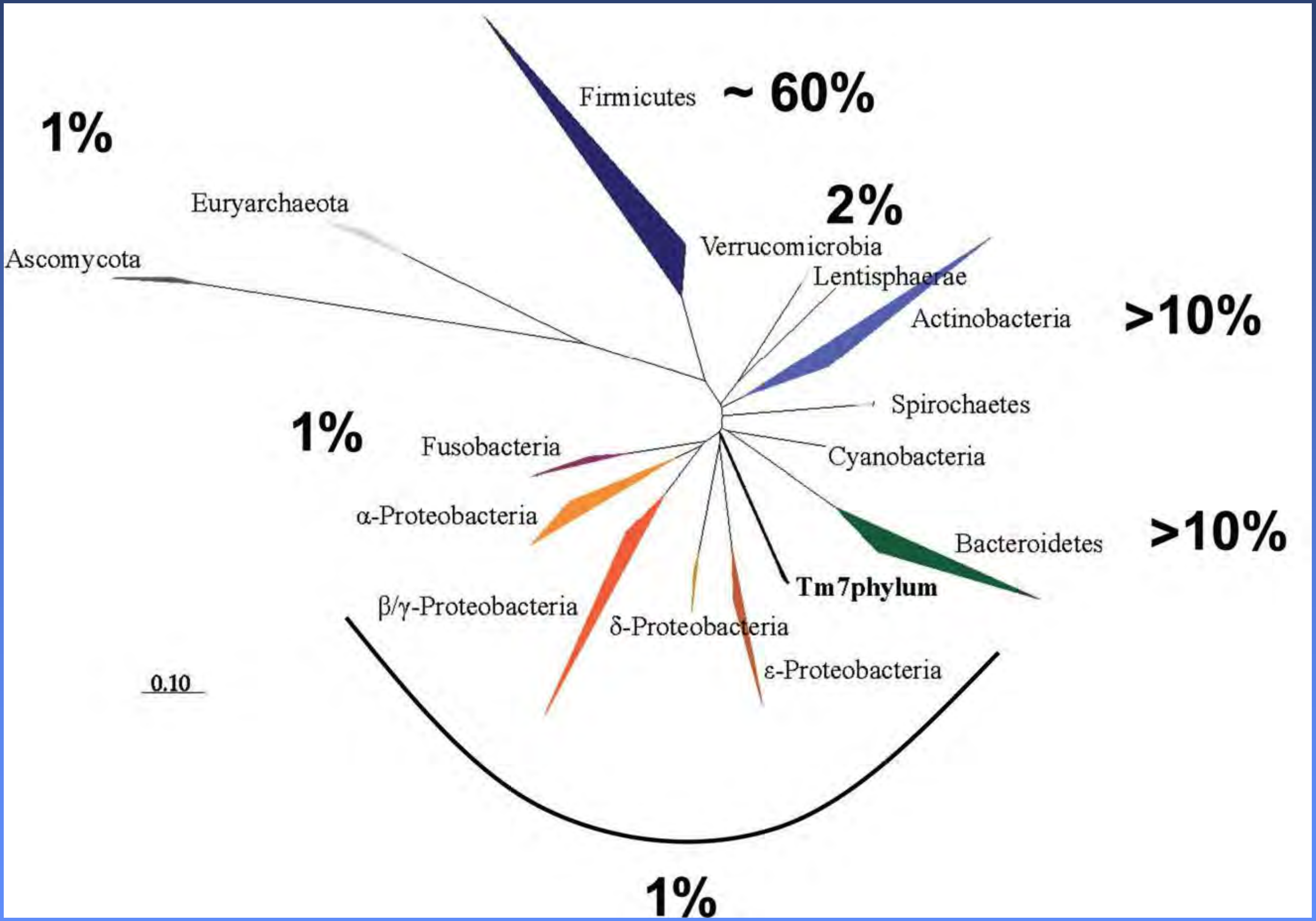
Bouret, Front Neuroendocrinol. 2013 Jan;34(1):18-26.

Perinatal hormonal milieu
Research Needs

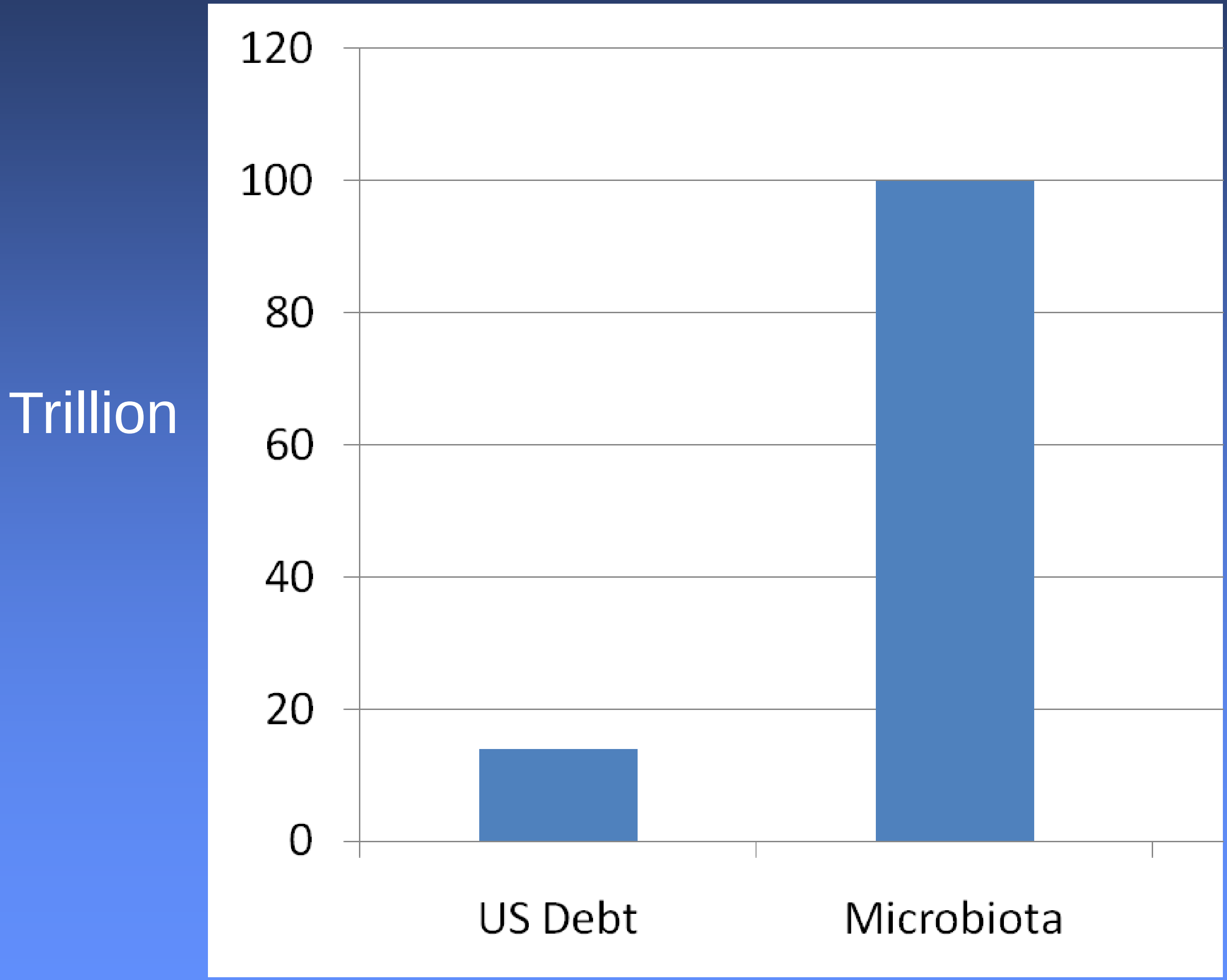
- Multiple hormones
- Systems approaches
  - Feedback loops
- Modifiable determinants


Science
The Gut Microbiota
AAAS

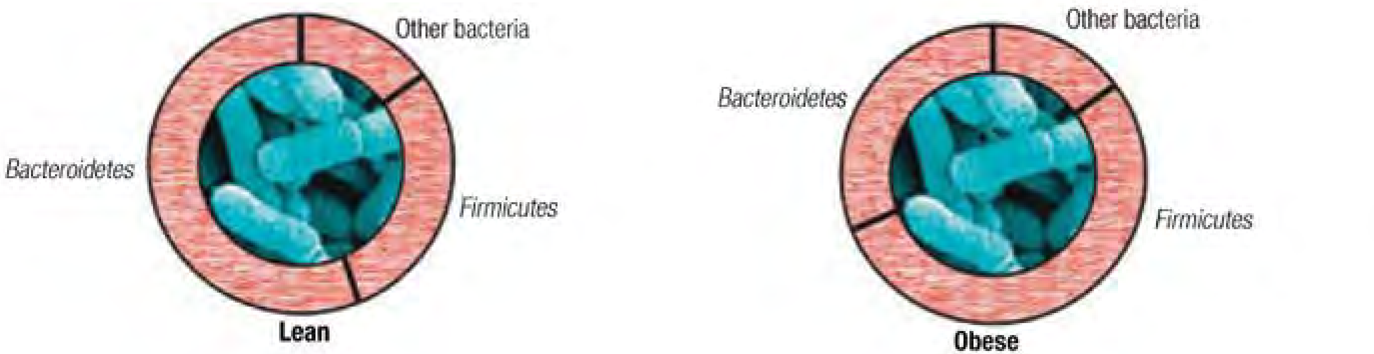
The gut contains >500 species and 95% of the body's 10^{14} cells



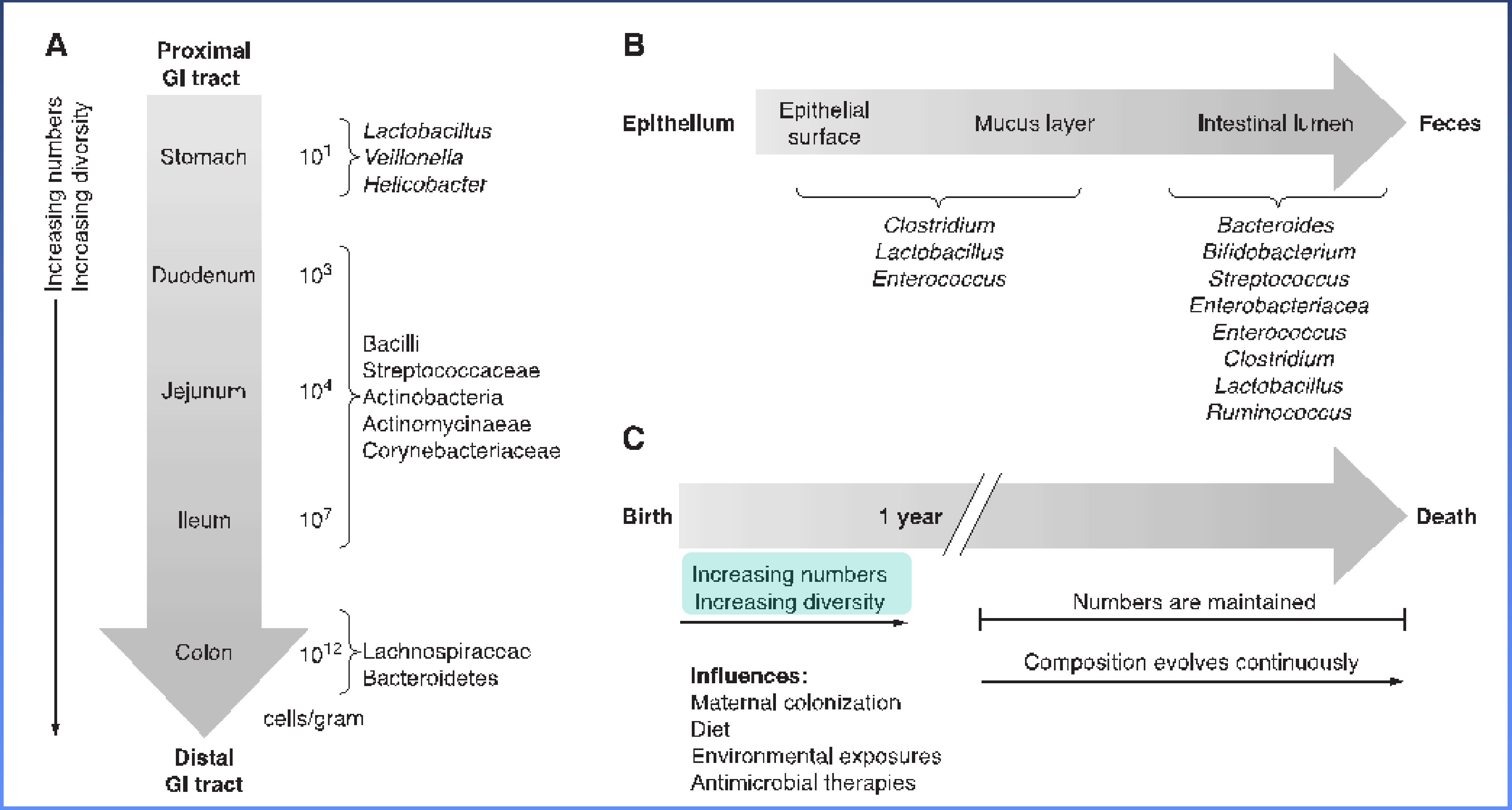
100 Trillion Bacteria
v. only $17.1 Trillion US Debt

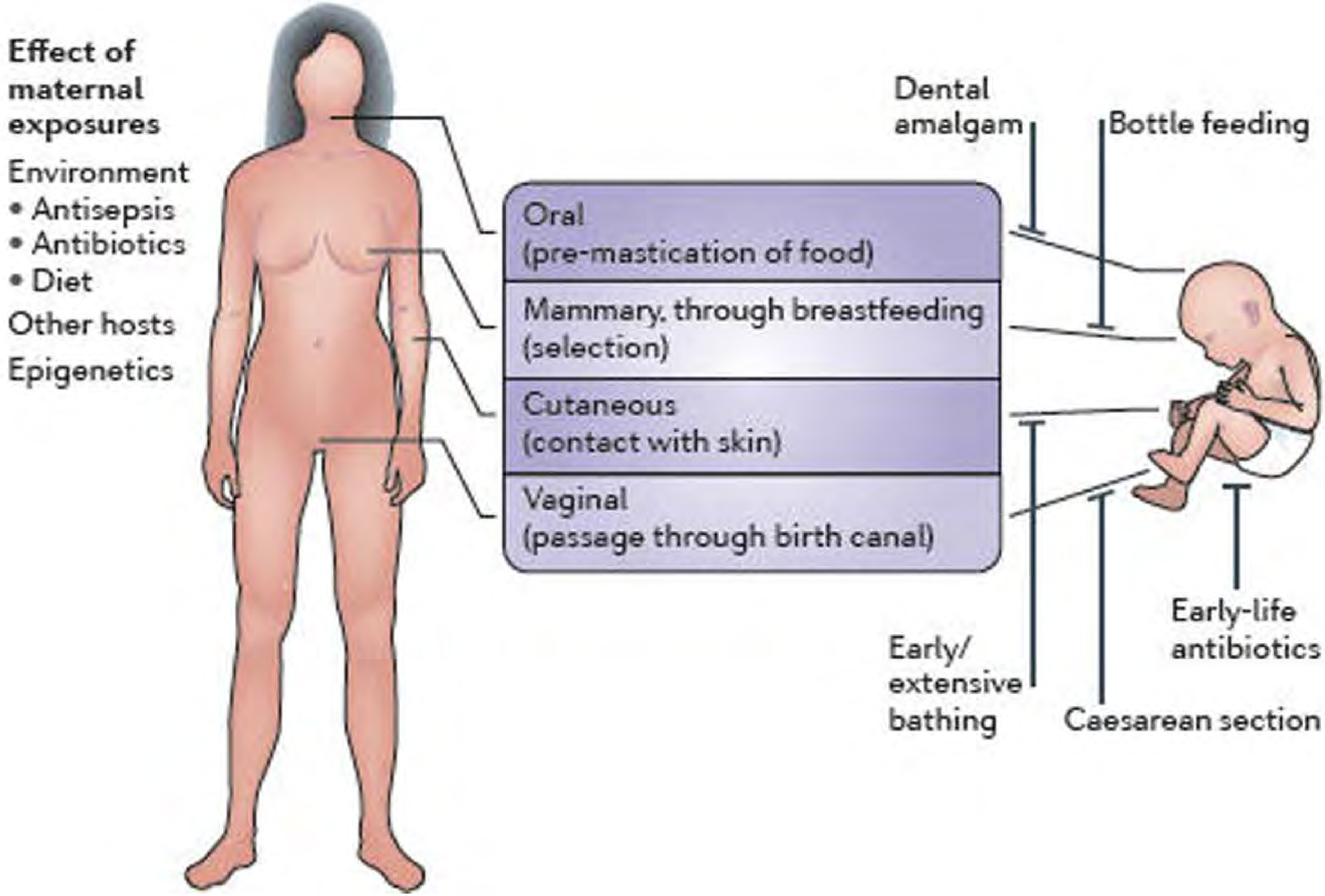


Obese have higher firmicutes:bacteroides than lean



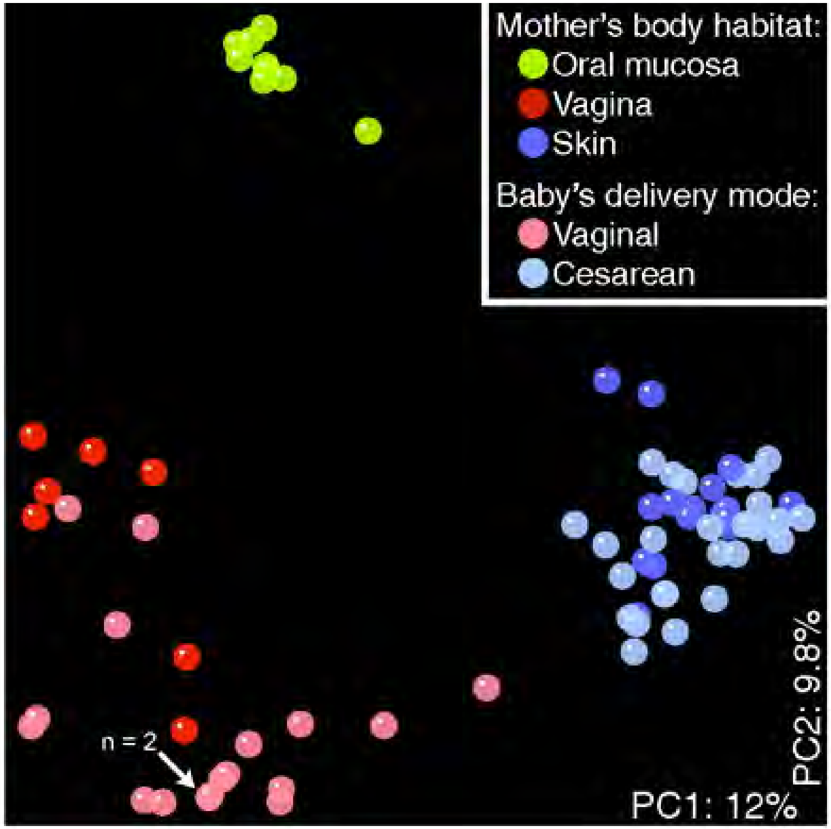
Gut microbiota increase in number and diversity in 1st year of life



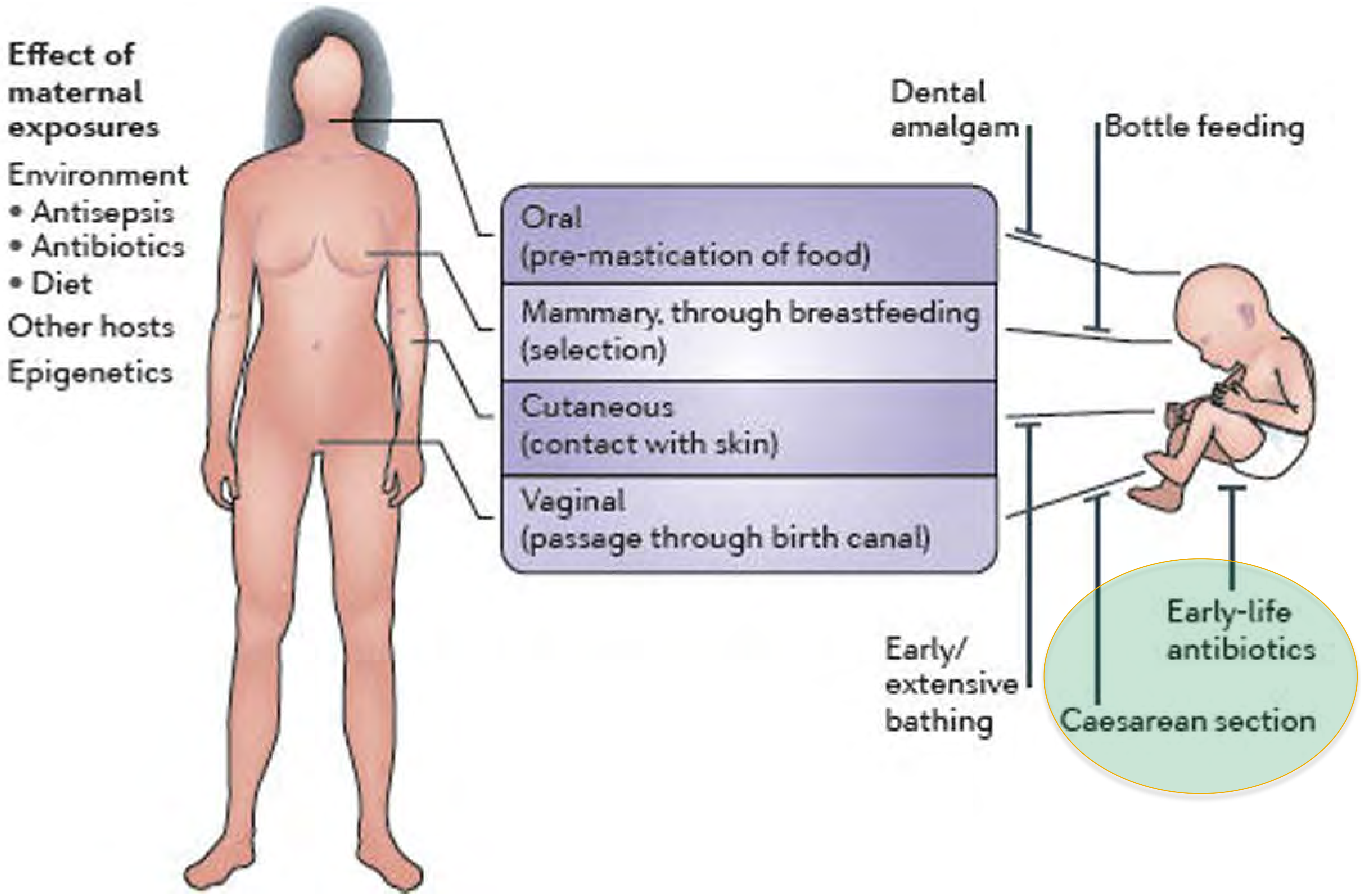


Cho I, Blaser MJ. Nat Rev Genet. 2012 Mar 13;13(4):260-70

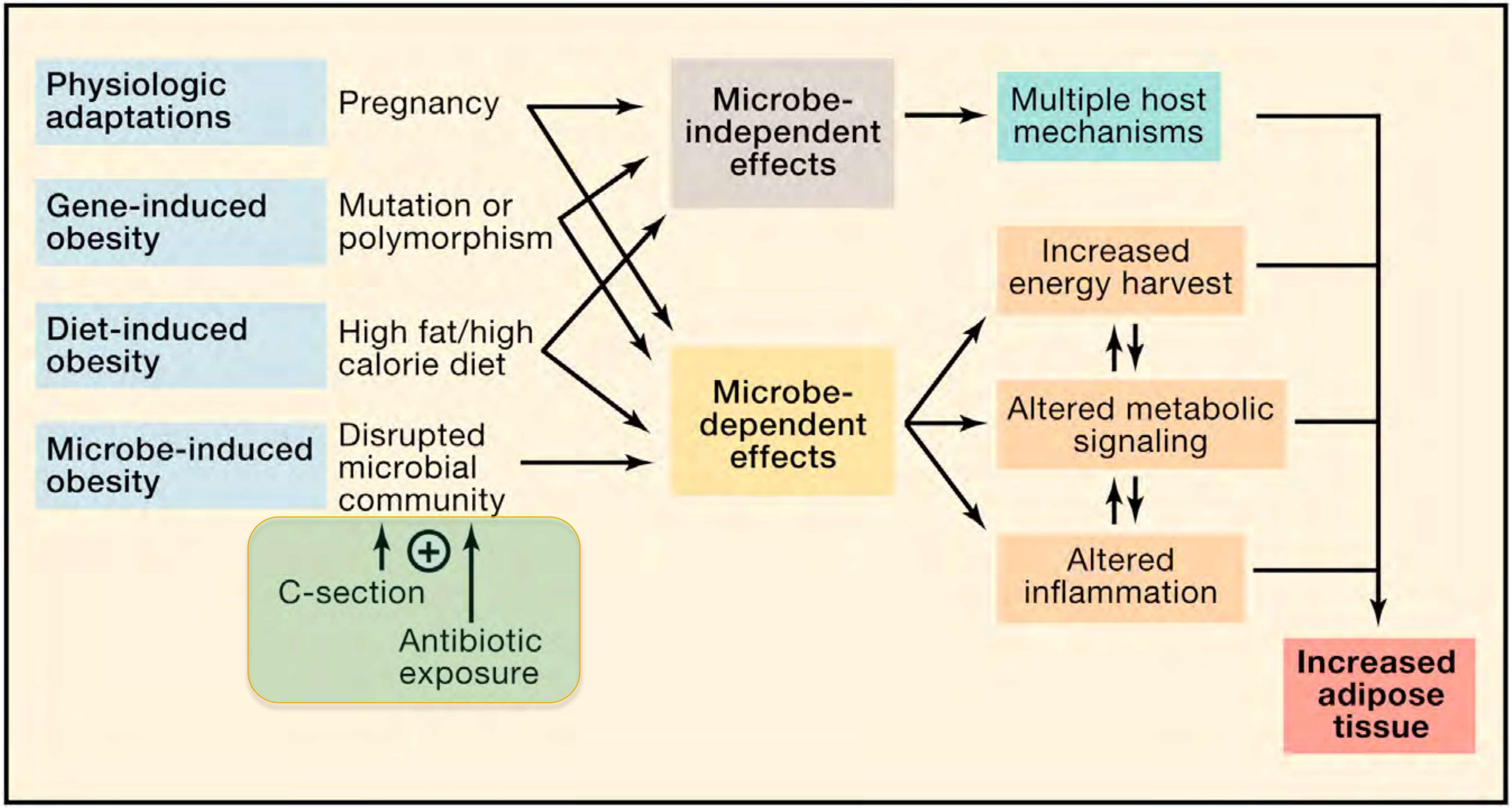
Source of infant gut microbiota different in C-section v. vaginal delivery



Dominguez-Bello M G et al. PNAS 2010;107:11971-11975

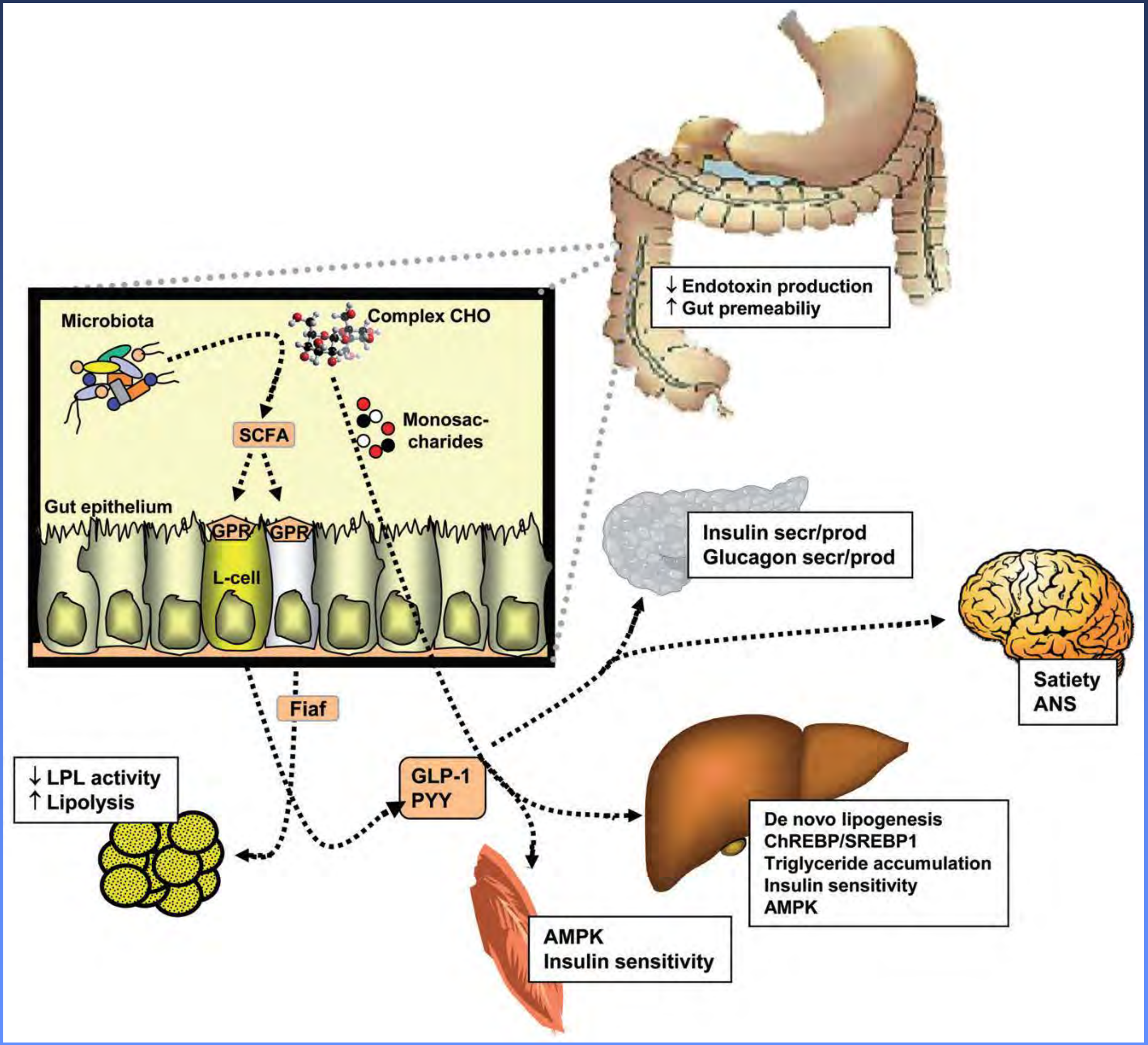


Cho I, Blaser MJ. Nat Rev Genet. 2012 Mar 13;13(4):260-70



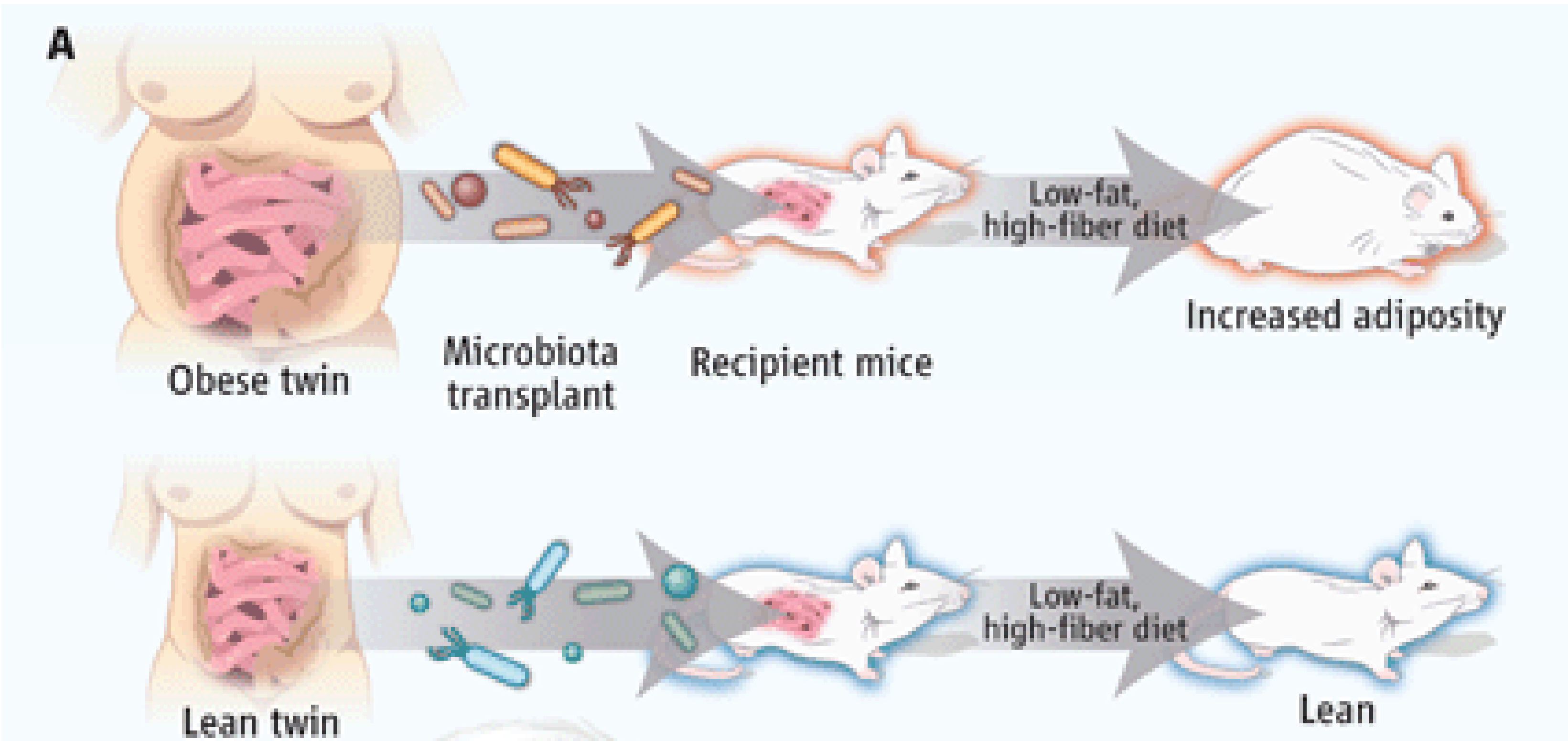
Physiologic adaptations
Gene-induced obesity
Diet-induced obesity
Microbe-induced obesity
Pregnancy
Mutation or polymorphism
High fat/high calorie diet
Disrupted microbial community
C-section
Antibiotic exposure
Microbe-independent effects
Microbe-dependent effects
Multiple host mechanisms
Increased energy harvest
Altered metabolic signaling
Altered inflammation
Increased adipose tissue

Gut microbiota and excess weight gain



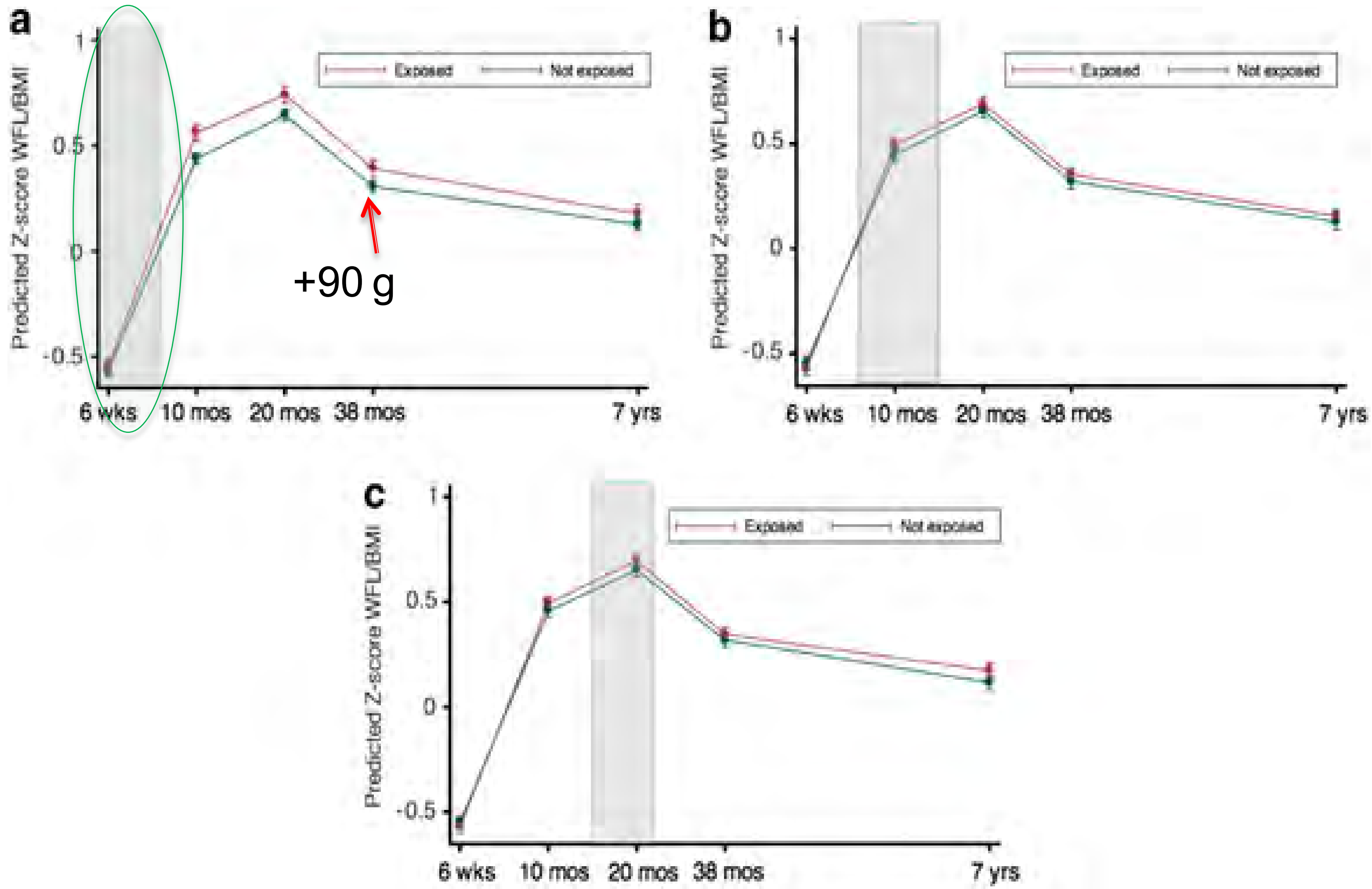
Germ-free mice inoculated with microbiota from obese or lean human twins take on microbiota—and adiposity—characteristics of donor

Associated with changes in serum levels of branched-chain amino acids



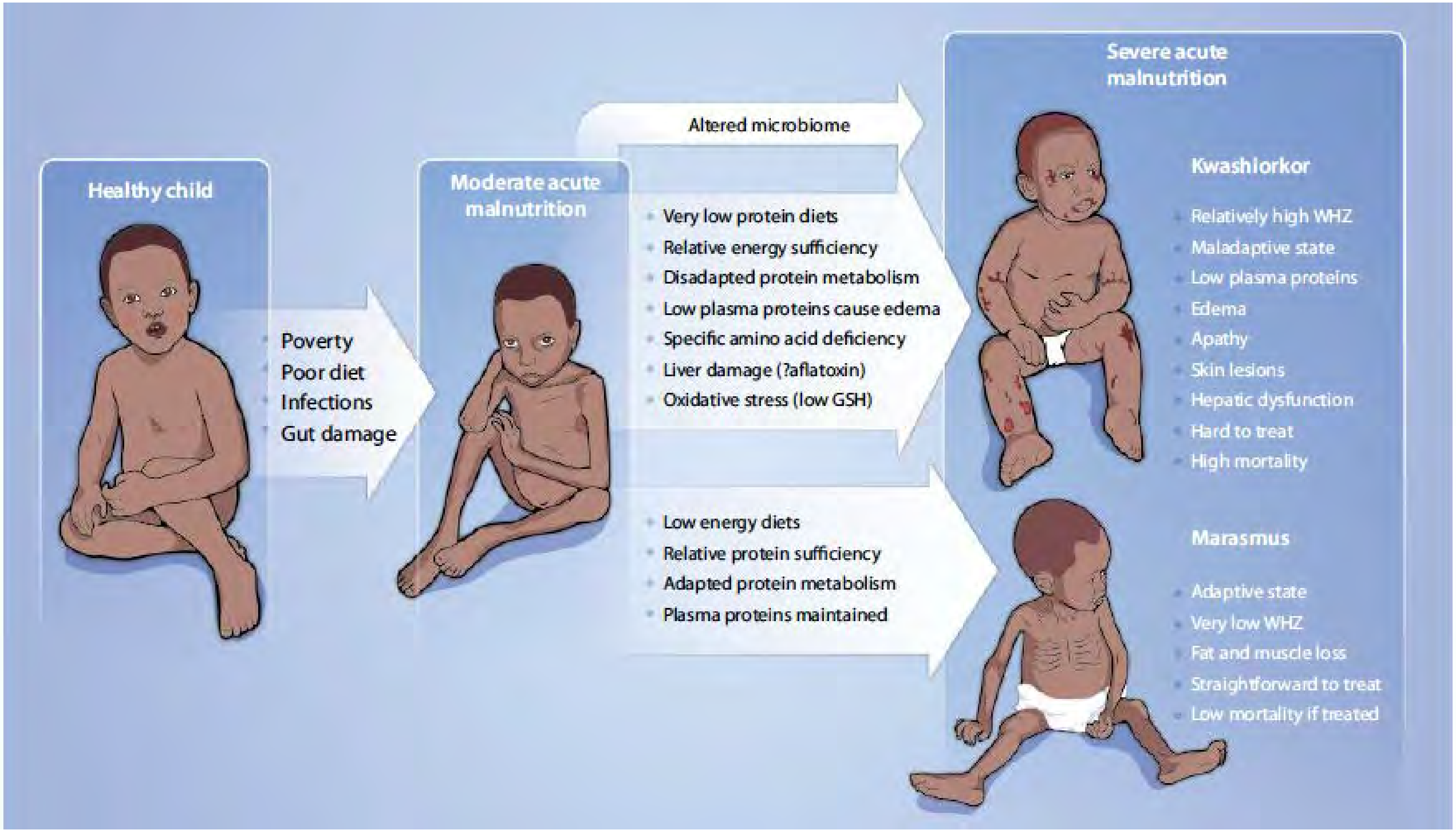
Ridaura et al., Science 6 September 2013; 341(6150): 1241214

Antibiotics in 1st 6 mo Associated with Modestly Higher BMI



[Trasande et al., Int J Obes (Lond).](#) 2013 Jan;37(1):16-23; ALSPAC

Severe acute malnutrition:
Kwashiokor associated with altered microbiome?



Courtesy of Sue Huh

Prentice, Sci Transl Med, 2013

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Antibiotics as Part of the Management of Severe Acute Malnutrition

Indi Trehan, M.D., M.P.H., D.T.M.&H., Hayley S. Goldbach, Sc.B., Lacey N. LaGrone, M.D., Guthrie J. Meuli, B.S., Richard J. Wang, M.D., Kenneth M. Maleta, M.B., B.S., Ph.D., and Mark J. Manary, M.D.

Trehan, NEJM, 2013 Jan 31;368(5):425-35.

Gut Microbiomes of Malawian Twin Pairs Discordant for Kwashiorkor

Michelle I. Smith,[1*] Tanya Yatsunenko,[1*] Mark J. Manary,[2,3,4] Indi Trehan,[2,3] Rajhab Mkakosya,[5] Jiye Cheng,[1] Andrew L. Kau,[1] Stephen S. Rich,[6] Patrick Concannon,[6] Josyf C. Mychaleckyj,[6] Jie Liu,[7] Eric Houpt,[7] Jia V. Li,[8] Elaine Holmes,[8] Jeremy Nicholson,[8] Dan Knights,[9,10]† Luke K. Ursell,[11] Rob Knight,[9,10,11,12] Jeffrey I. Gordon[1]‡

Smith et al. Science 2013; 339:548

Antibiotic treatment improved Kwashiokor recovery and mortality rates

	Placebo vs. Amoxicillin and Cefdinir		
		RR (95% CI)	*P-value*
Overall	Did not recover	1.5 (1.2 – 1.8)	<0.001
	Died	1.7 (1.2 – 2.3)	0.002
Kwashiorkor	Did not recover	1.4 (1.0 – 2.0)	0.06
	Died	2.0 (1.3 – 3.3)	0.005
Marasmus	Did not recover	1.4 (1.0 – 1.9)	0.05
	Died	1.1 (0.6 – 1.9)	0.87

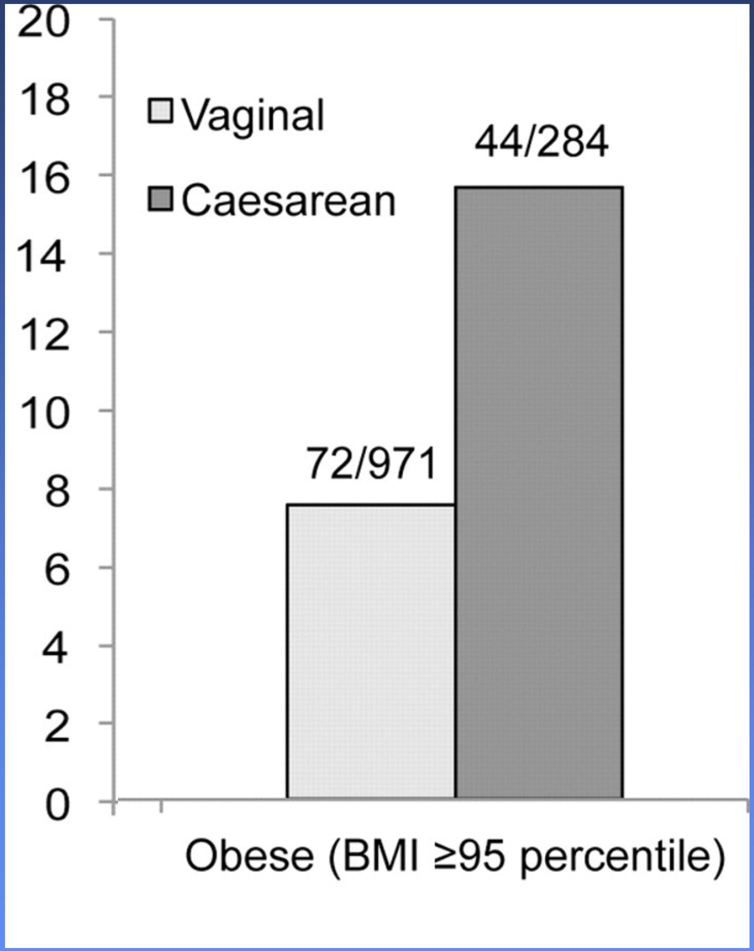
Recovery defined as no edema or WFH z-score >=-2

Trehan et al, NEJM, 2013 Jan 31;368(5):425-35.


THINGS TO KNOW ABOUT HAVING A C-SECTION

C-section associated with 3-y obesity.

Percent obese



Adjusted OR 2.1 (95% CI 1.4, 3.2)

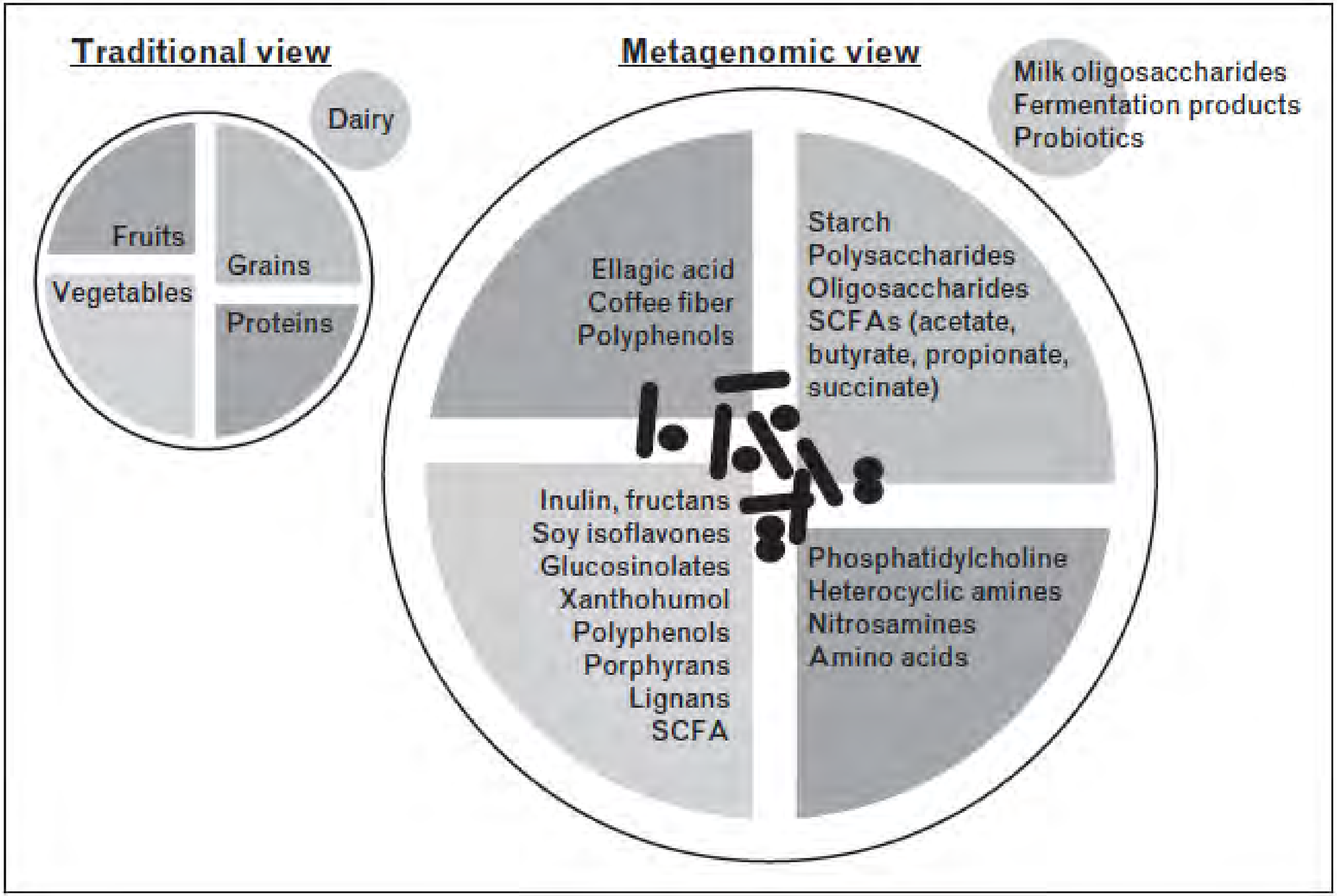
Huh S Y et al. Arch Dis Child 2012;97:610-616

Meta-analyses of cesarean delivery and offspring obesity

- Li et al. [IJO 2013; 37:893–89]
  - 9 studies
  - Pooled OR for obesity 1.33 (95% CI 1.19, 1.48)
- Hyde et al. [2013, unpublished]
  - 21 studies
  - Mean (unadjusted) difference in BMI z-score between CS and VD groups was 0.12 (0.09, 0.16)
    - Mean (adjusted) difference in Project Viva: 0.2 (0.1, 0.3)

Courtesy of Sue Huh

“A metagenomic view of our dinner plate”



Dutton and Turnbaugh, Curr Opin Clin Nutr Metab Care 2012, 15:448–454

Probiotic

- Food with defined viable microorganisms, sufficient amounts of which reach the intestine in an active state
  - Exert positive health effects
- Lactobacilli and Bifidobacteria
- Yogurt, pickled vegetables, tempeh, miso, kefir, kombucha, sauerkraut, soy sauce
- Found in human milk

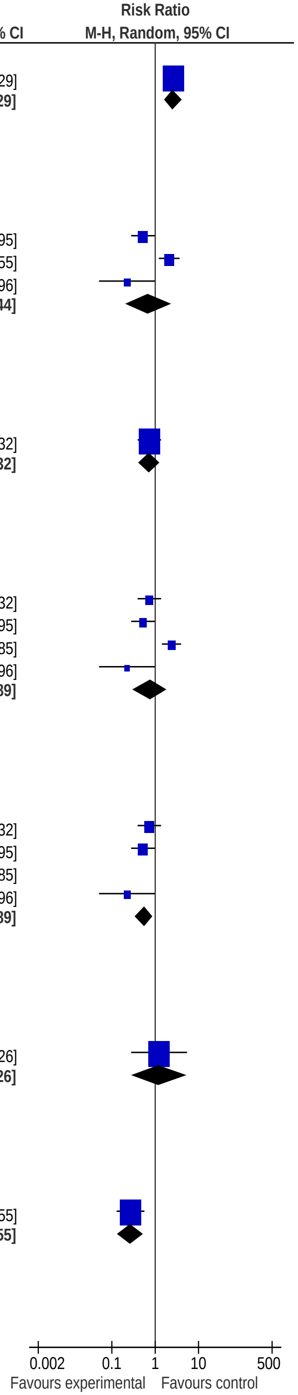
Prebiotic

- Non-digestible, fermentable food ingredient that selectively stimulates growth and/or activity of gut bacteria
  - Exert positive health effects
- Inulin, oligosaccharides
- Found in human milk

Prebiotic


ORANGES
PINEAPPLES
BANANAS
APPLES
AVOCADOS
AZUKI BEANS
MELONS
BROWN RICE
TOMATOES
PUMPKINS
PEAS
Chicory
LEMONS
SWEET POTATOES
JALO BEANS
ROXINHO BEANS
SESAME SEEDS
RYE GRAIN
CARAMBOLA
GUAVA
SOY BEANS
PLUMS (PRUNES)
CASHEW NUTS
CARROTS
GRAPES
CABBAGES
ACEROLAS
KIWI FRUIT
CHICK PEAS
CASSAVA ROOT
GREEN BELL PEPPER
BRAZIL NUTS
SUGAR BEETS
SEAWEED
MATE LEAVES
CINNAMON
WATERMELON
BLACK BEANS
ANISE SEEDS
LENTIL BEANS
LEMON GRASS
OATS
CLOVES
MILLET
COLLARD GREENS
PASSION FRUIT
MANGOES
PAPAYA
CORN
ZEDOARY ROOT
LOTUS ROOT
BARLEY GRAIN
PEARS
TURNIP ROOT
GINGER ROOT

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.6.1 Bb12						
Phuapradit 1999	40	62	14	57	100.0%	2.63 [1.61, 4.29]
Subtotal (95% CI)		**62**		**57**	**100.0%**	**2.63 [1.61, 4.29]**
Total events	40		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.86 (P = 0.0001)						
1.6.2 Bb12 + Str thermophilus						
Correa 2005	13	80	24	77	38.1%	0.52 [0.29, 0.95]
Phuapradit 1999	29	56	14	57	39.5%	2.11 [1.25, 3.55]
Saavedra 1994	2	29	8	26	22.4%	0.22 [0.05, 0.96]
Subtotal (95% CI)		**165**		**160**	**100.0%**	**0.71 [0.20, 2.44]**
Total events	44		46			
Heterogeneity: Tau² = 1.00; Chi² = 16.72, df = 2 (P = 0.0002); I² = 88%						
Test for overall effect: Z = 0.55 (P = 0.58)						
1.6.3 Bb12 + Str thermophilus + L helveticus						
Chouraqui 2004	13	46	17	44	100.0%	0.73 [0.40, 1.32]
Subtotal (95% CI)		**46**		**44**	**100.0%**	**0.73 [0.40, 1.32]**
Total events	13		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.04 (P = 0.30)						
1.6.4 Bb12 (single or in combination - all studies)						
Chouraqui 2004	13	46	17	44	27.5%	0.73 [0.40, 1.32]
Correa 2005	13	80	24	77	27.4%	0.52 [0.29, 0.95]
Phuapradit 1999	69	118	14	57	28.9%	2.38 [1.47, 3.85]
Saavedra 1994	2	29	8	26	16.1%	0.22 [0.05, 0.96]
Subtotal (95% CI)		**273**		**204**	**100.0%**	**0.76 [0.31, 1.89]**
Total events	97		63			
Heterogeneity: Tau² = 0.70; Chi² = 22.20, df = 3 (P < 0.0001); I² = 86%						
Test for overall effect: Z = 0.59 (P = 0.56)						
1.6.5 Bb12 (single or in combination - Phuapradit excluded						
Chouraqui 2004	13	46	17	44	38.7%	0.73 [0.40, 1.32]
Correa 2005	13	80	24	77	38.6%	0.52 [0.29, 0.95]
Phuapradit 1999	69	118	14	57	0.0%	2.38 [1.47, 3.85]
Saavedra 1994	2	29	8	26	22.7%	0.22 [0.05, 0.96]
Subtotal (95% CI)		**155**		**147**	**100.0%**	**0.56 [0.35, 0.89]**
Total events	28		49			
Heterogeneity: Tau² = 0.03; Chi² = 2.40, df = 2 (P = 0.30); I² = 17%						
Test for overall effect: Z = 2.45 (P = 0.01)						
1.6.6 BL999 + LPR						
Chouraqui 2008	4	64	3	59	100.0%	1.23 [0.29, 5.26]
Subtotal (95% CI)		**64**		**59**	**100.0%**	**1.23 [0.29, 5.26]**
Total events	4		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.28 (P = 0.78)						
1.6.7 L salivarius						
Maldonado 2009	7	40	26	40	100.0%	0.27 [0.13, 0.55]
Subtotal (95% CI)		**40**		**40**	**100.0%**	**0.27 [0.13, 0.55]**
Total events	7		26			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.62 (P = 0.0003)						



Probiotic-supplemented formula for preventing gastrointestinal infections

Multiple

Study populations
Entry criteria
Probiotic formulations
Endpoints

Microbiota
Research Needs

- Human studies
  - Longitudinal tissue collection
  - Species, metagenomics, metabolomics
    - Type, diversity, quantity, function
  - Incorporation into observation and experiment
  - Risk and protective factors

'Each living organism has two histories that determine its biology:

an evolutionary history whose duration is in the hundreds of thousands of years, and a developmental history that starts at the time of its conception.'

Hochberg, 2011

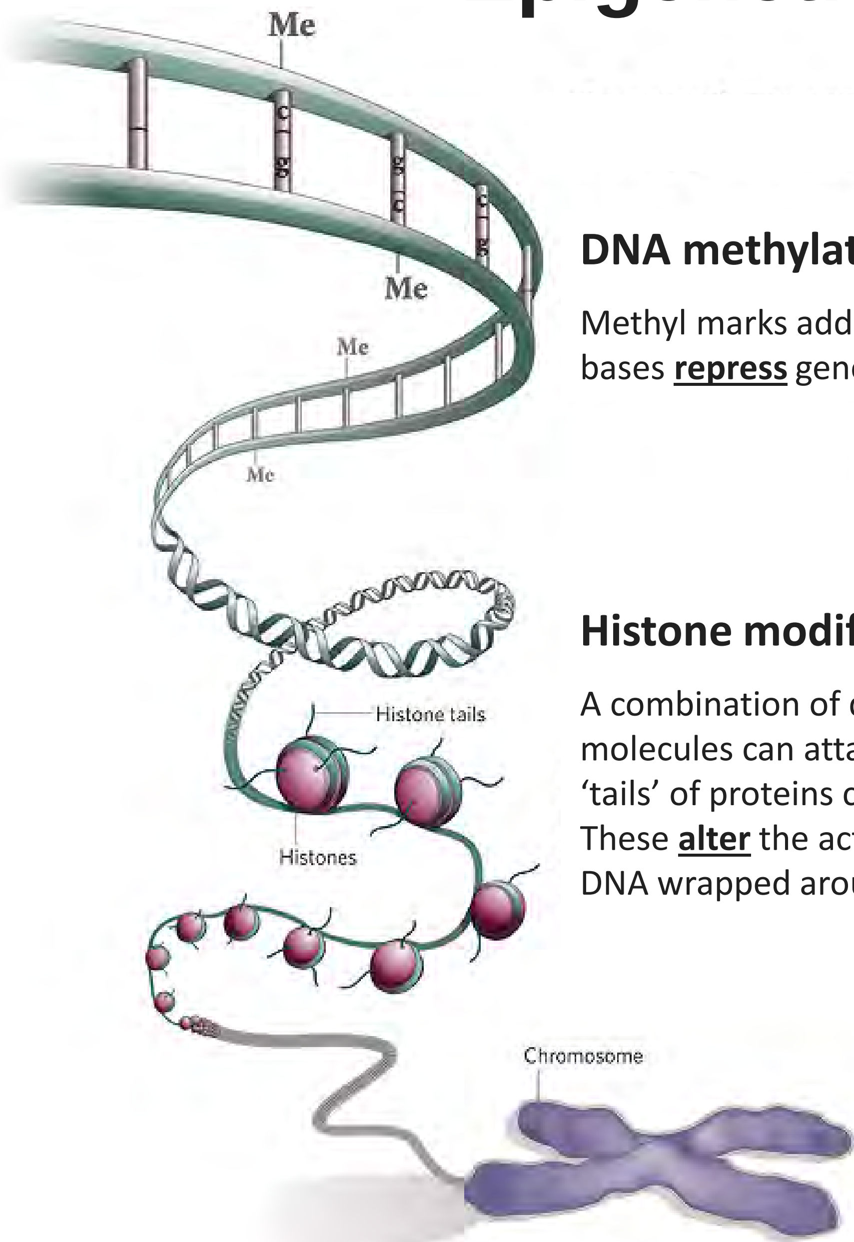
Epigenetics

- Could
  - Unite human and animal data
  - Identify pathways between early life risk factors and later obesity-related outcomes
  - Support causality

Epigenetics

- Programming of gene expression that:
  - does not depend on the DNA code
  - (relatively) stable, i.e., replicated through
    - cell mitosis
    - meiosis, i.e. transgenerational
      - limited evidence in humans

Epigenetic markings

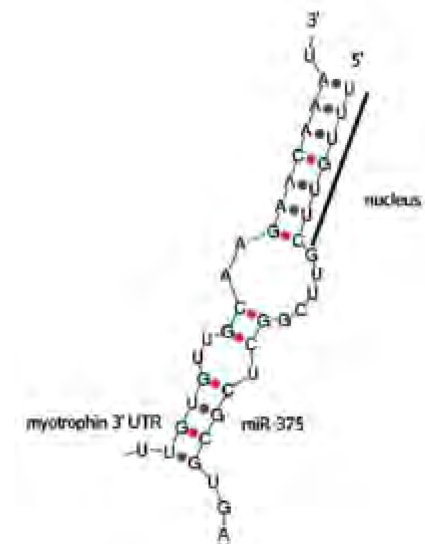


DNA methylation

Methyl marks added to certain DNA bases **repress** gene transcription

Histone modifications

A combination of different molecules can attach to the 'tails' of proteins called histones. These **alter** the activity of the DNA wrapped around them

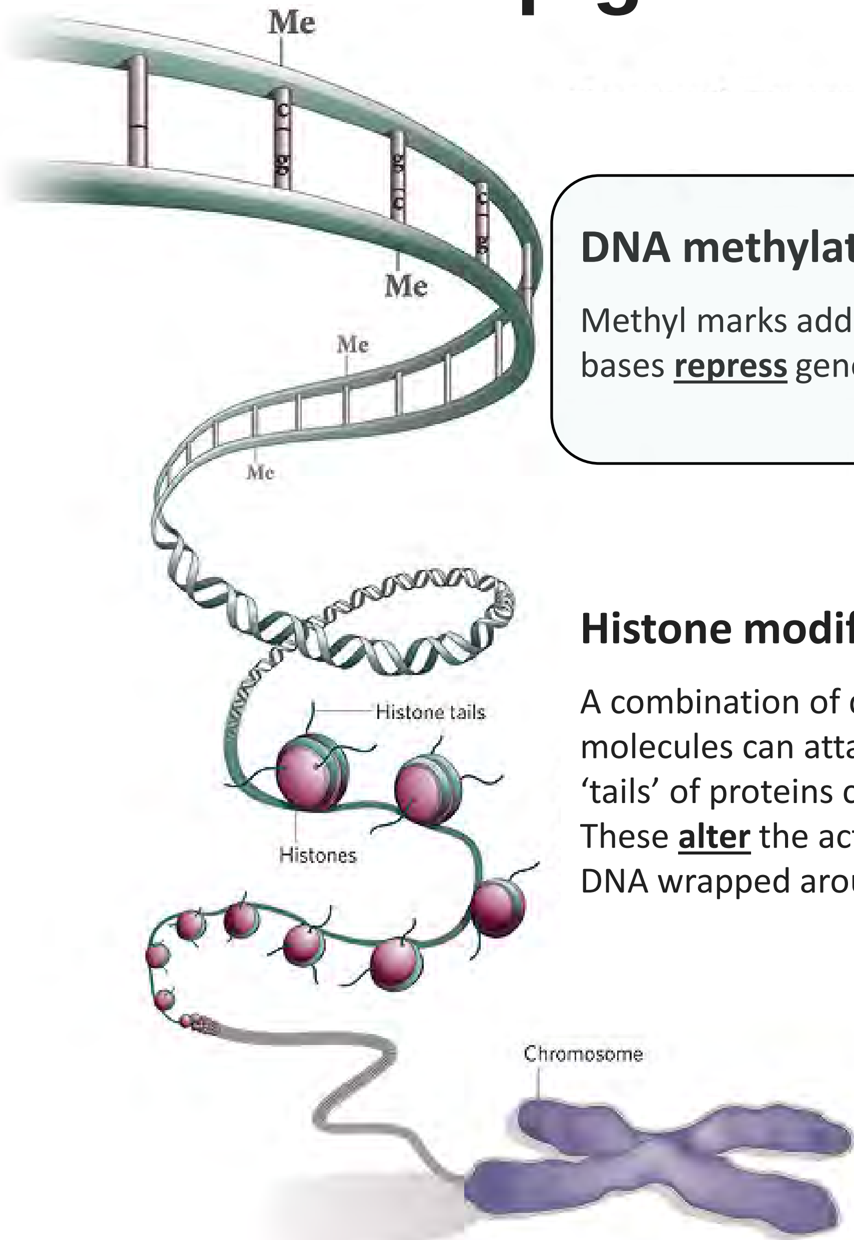


microRNAs

Small non-coding RNAs that **block translation** of messenger RNAs into proteins

Courtesy Andrea Baccarelli

Epigenetic markings



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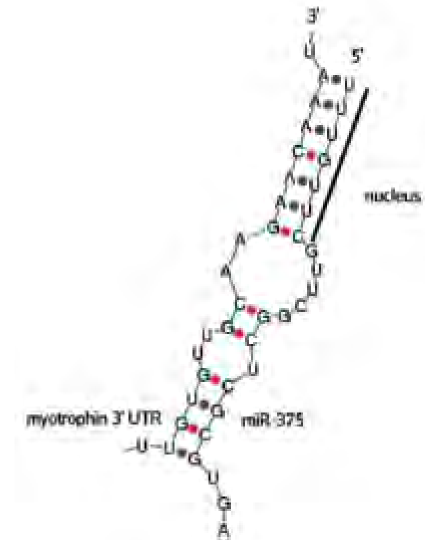
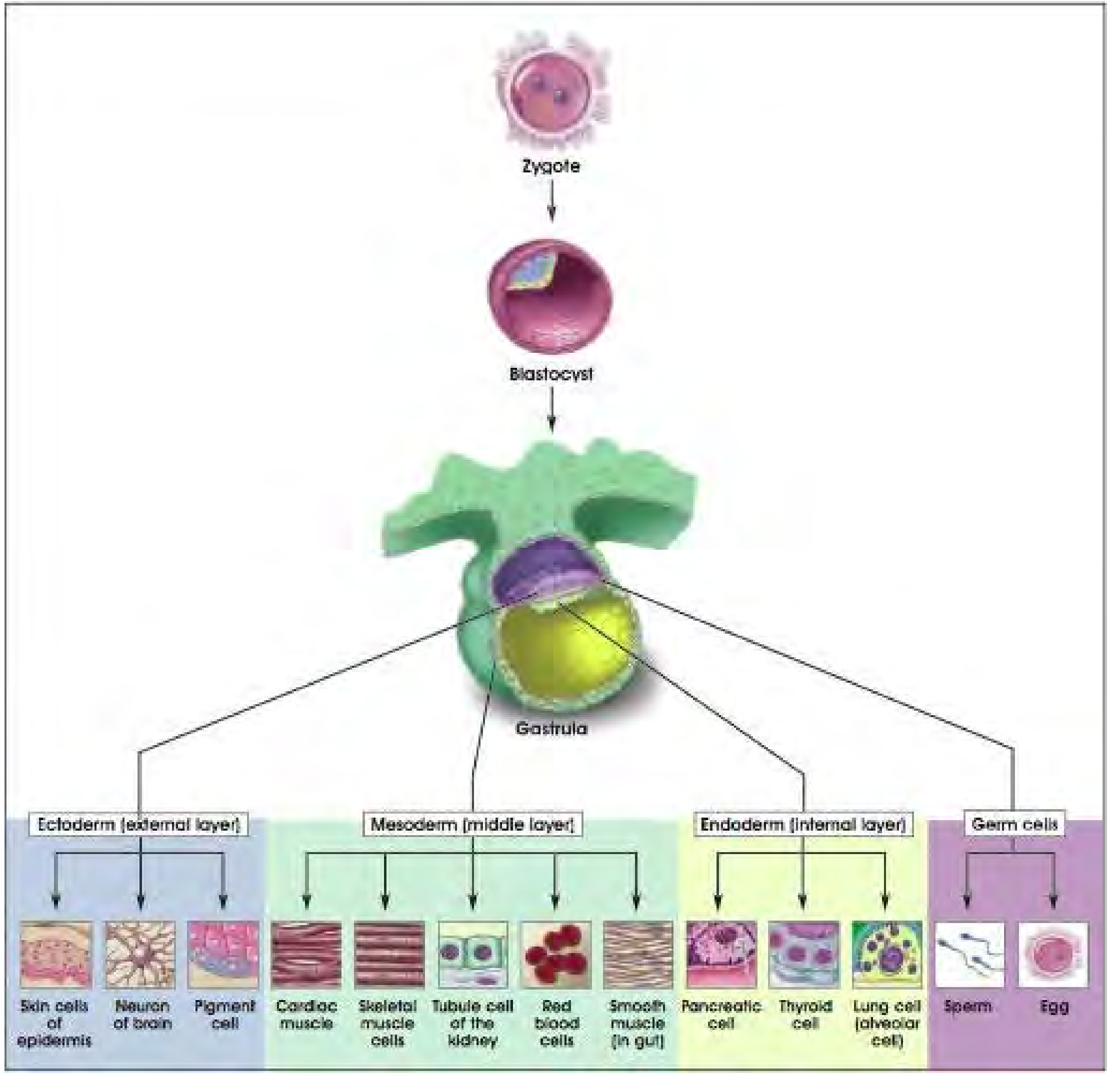


microRNAs

Small non-coding RNAs that **block translation** of messenger RNAs into proteins

Epigenetics

- Programming of gene expression that:
  - does not depend on the DNA code
  - (relatively) stable, i.e., replicated through
    - cell mitosis
    - meiosis, i.e. transgenerational
      - limited evidence in humans
- Epigenetic programming
  - Modifiable, i.e.,can be reprogrammed
    - Especially in early development

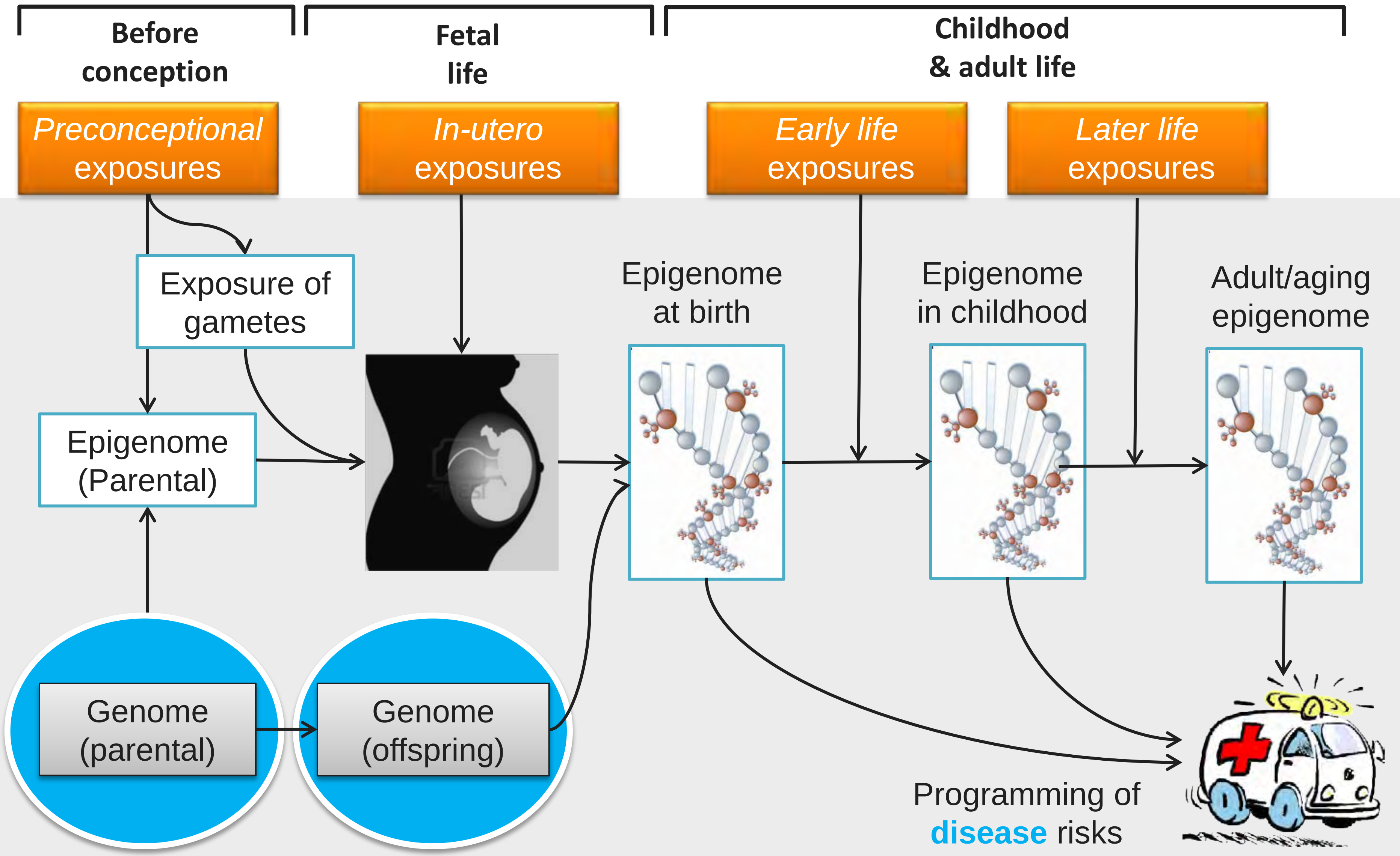


Epigenetics contribute to
tissue differentiation

Same Genotype → Different Phenotype?

Thanks to Rob Waterland

Same Genotype, Different Epigenotype → Different Phenotype



Disease programming throughout the lifecourse

Figure adapted from Fleisch, Wright & Baccarelli, J Mol Endocrinol, 2012

Epigenetics

- Approaches to DNA methylation in epidemiology
  - Candidate-gene
    - Pro—close to function
    - Con—hard to find

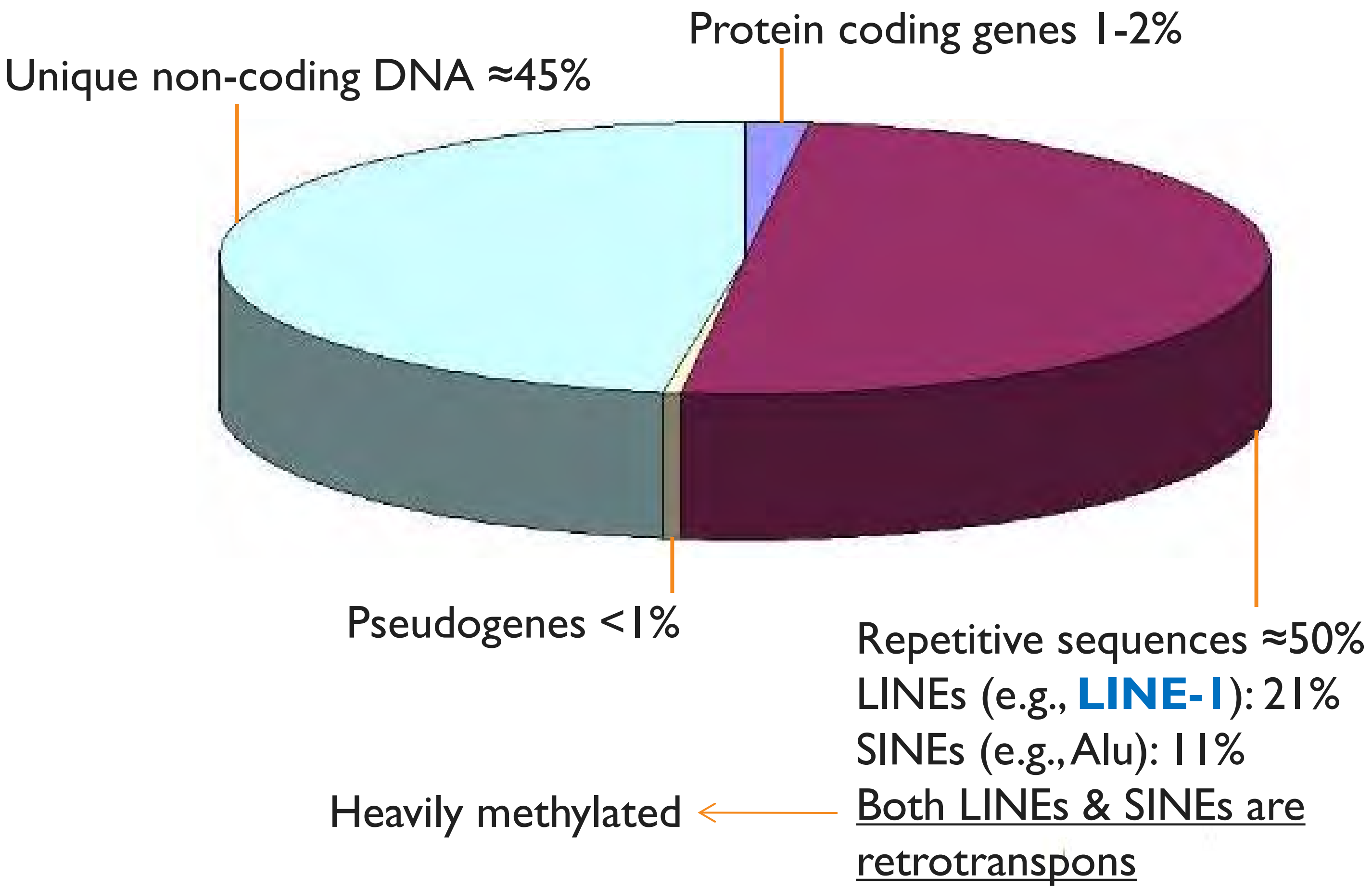
Epigenetics

- Approaches to DNA methylation in epidemiology
  - Candidate-gene
  - Genome-wide
    - Pro—investigate many genes
    - Con—“unbiased,” available platforms focus on promoter regions

Epigenetics

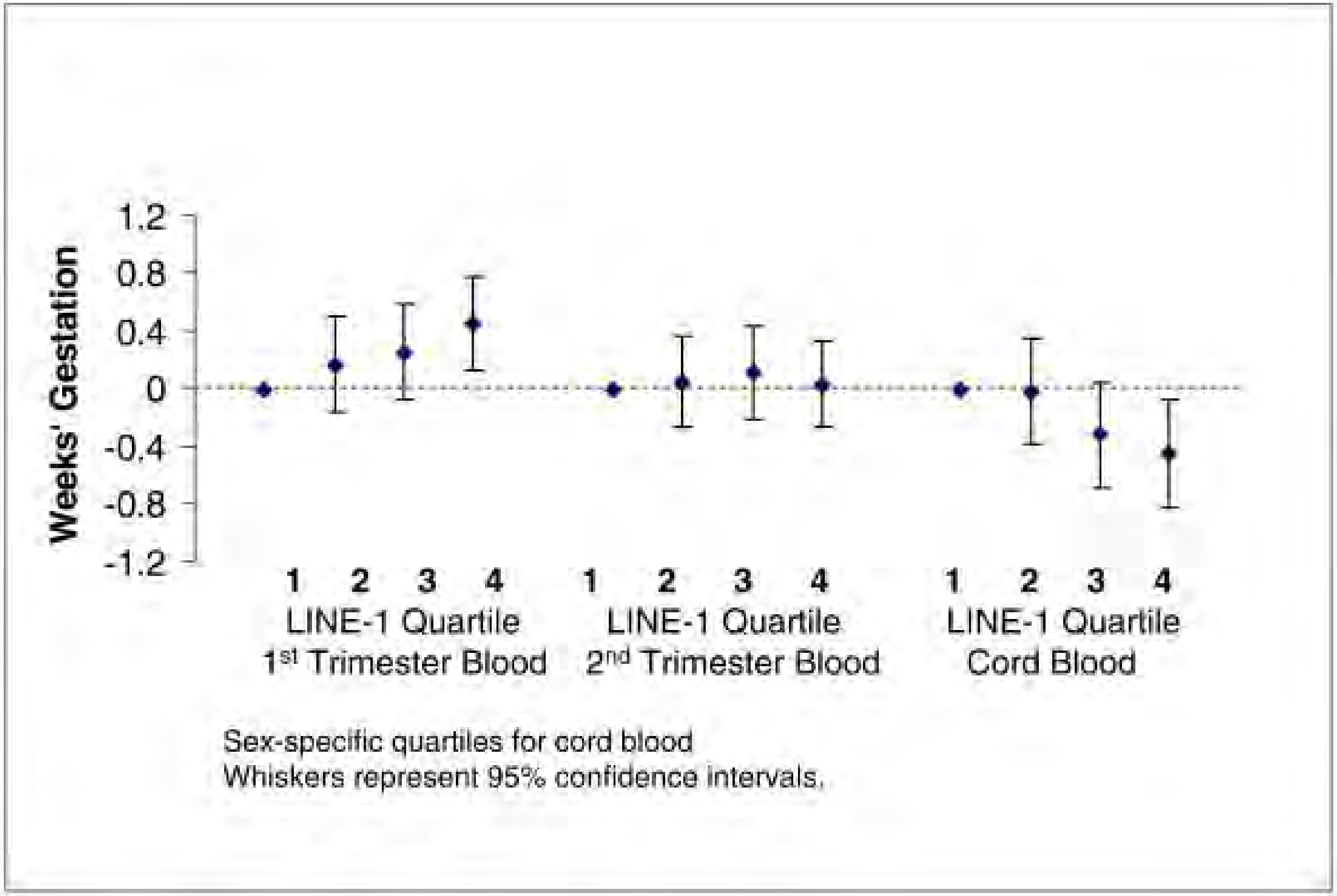
- Approaches to DNA methylation in epidemiology
  - Candidate-gene
  - Genome-wide
  - Global (e.g., LINE-1)
    - Pro—single number
    - Con—single number

Coding & non-coding DNA in the Human Genome



Courtesy Andrea Baccarelli

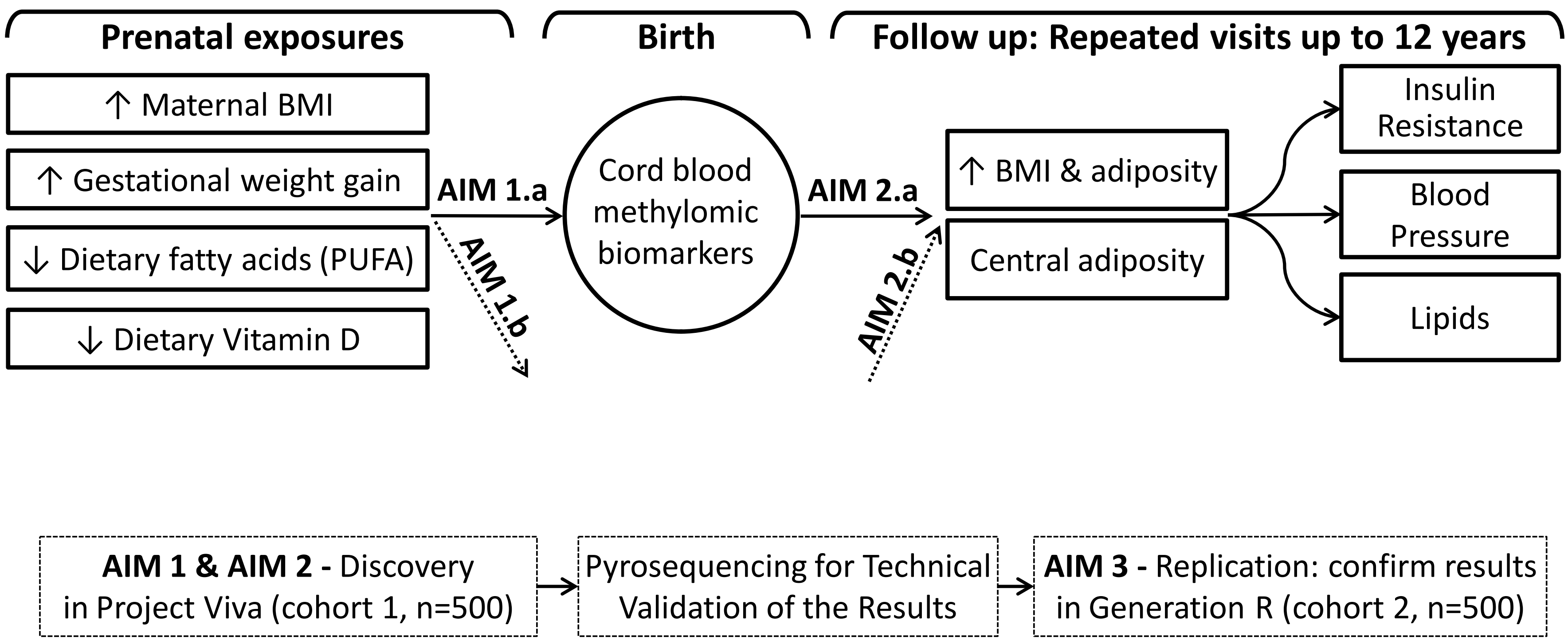
Higher early pregnancy LINE-1 predicted *longer* gestation, but *shorter* gestation was associated with higher LINE-1 in cord blood



Burris et al., J Dev Orig Health Dis. 2012; 3: 173–181

Novel Epigenomic Biomarkers of Prenatal Risk Factors and Childhood Obesity

R01 NR013945 (Baccarelli)
R01 HL111108 (Litonjua, DeMeo)



Novel Epigenomic Biomarkers…

Analytic Logic Model

Stage I - Discovery
Screen ~486K methylation sites
in Project Viva (discovery set)

1. Prenatal obesogenic risk factors

2. Postnatal obesity and related outcomes

Identify exposure biomarkers

Identify risk biomarkers

Cross-reference hits from **1 & 2**

Technical Validation
Validate methylation data by Pyrosequencing

Pathway analysis
Incorporate biological knowledge

Identify methylation markers specific for *prenatal risk factors + postnatal risks*

Explore moderating postnatal behaviors

Stage II - Replication
Screen ~486K methylation sites
in Generation R (replication set)

Repeat all steps above in Generation R

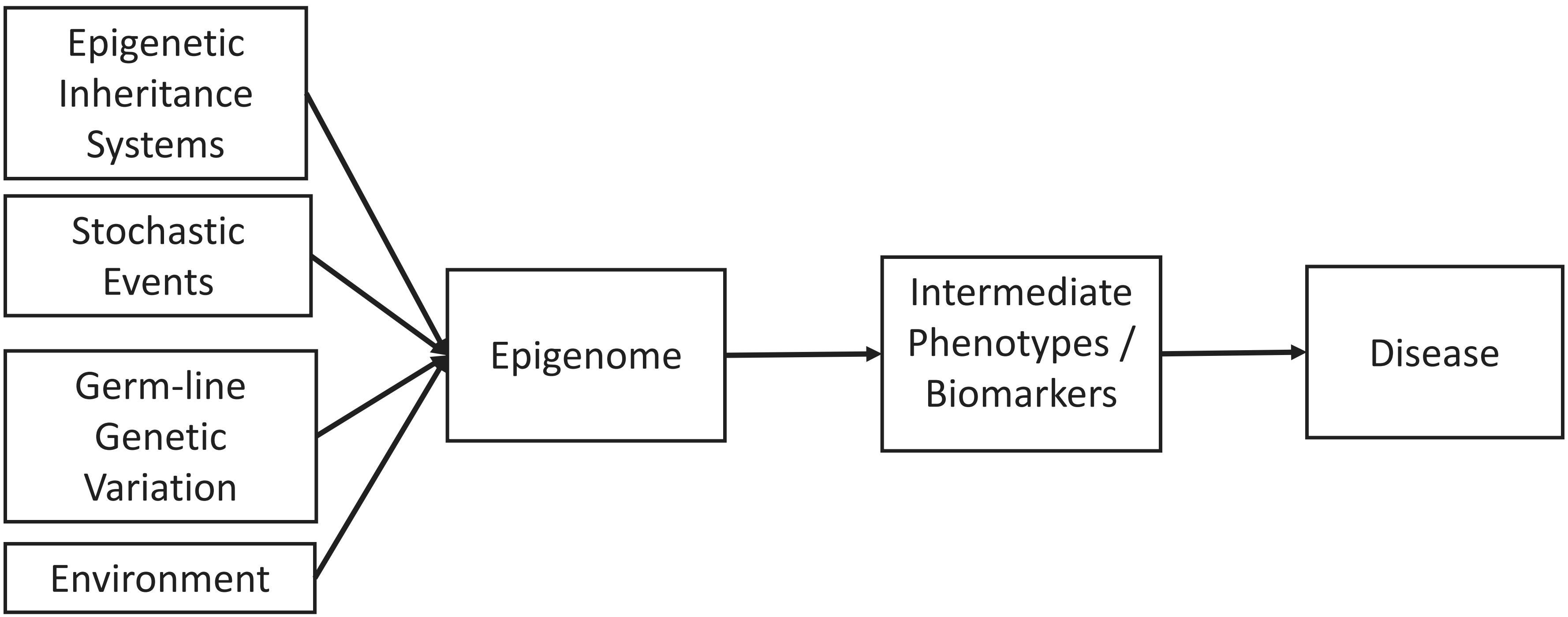
Compare Project Viva and Generation R top-ranked methylation regions

Meta-analize data from the two cohorts to obtain summary estimates

Report final ranks of confirmed DNA methylation loci

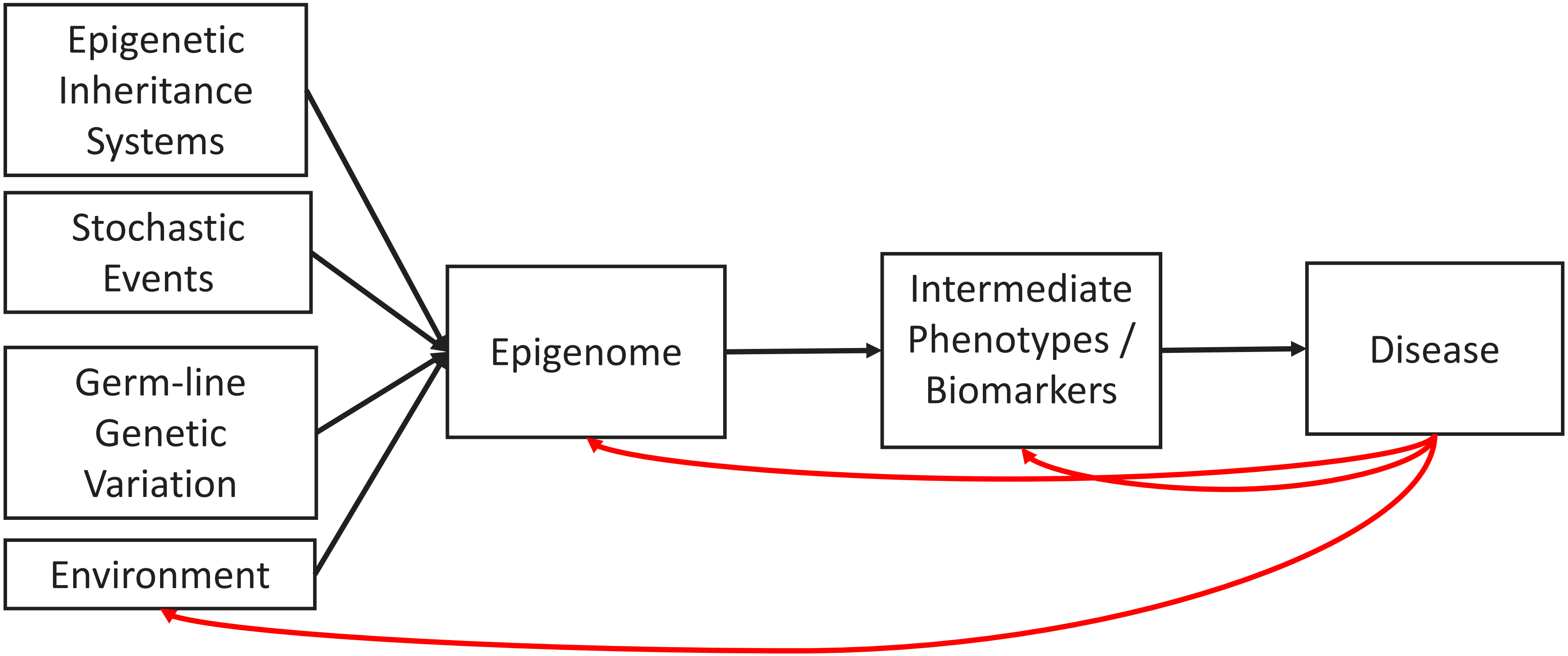

DAMN YOU, EPIGENOME

The ideal world



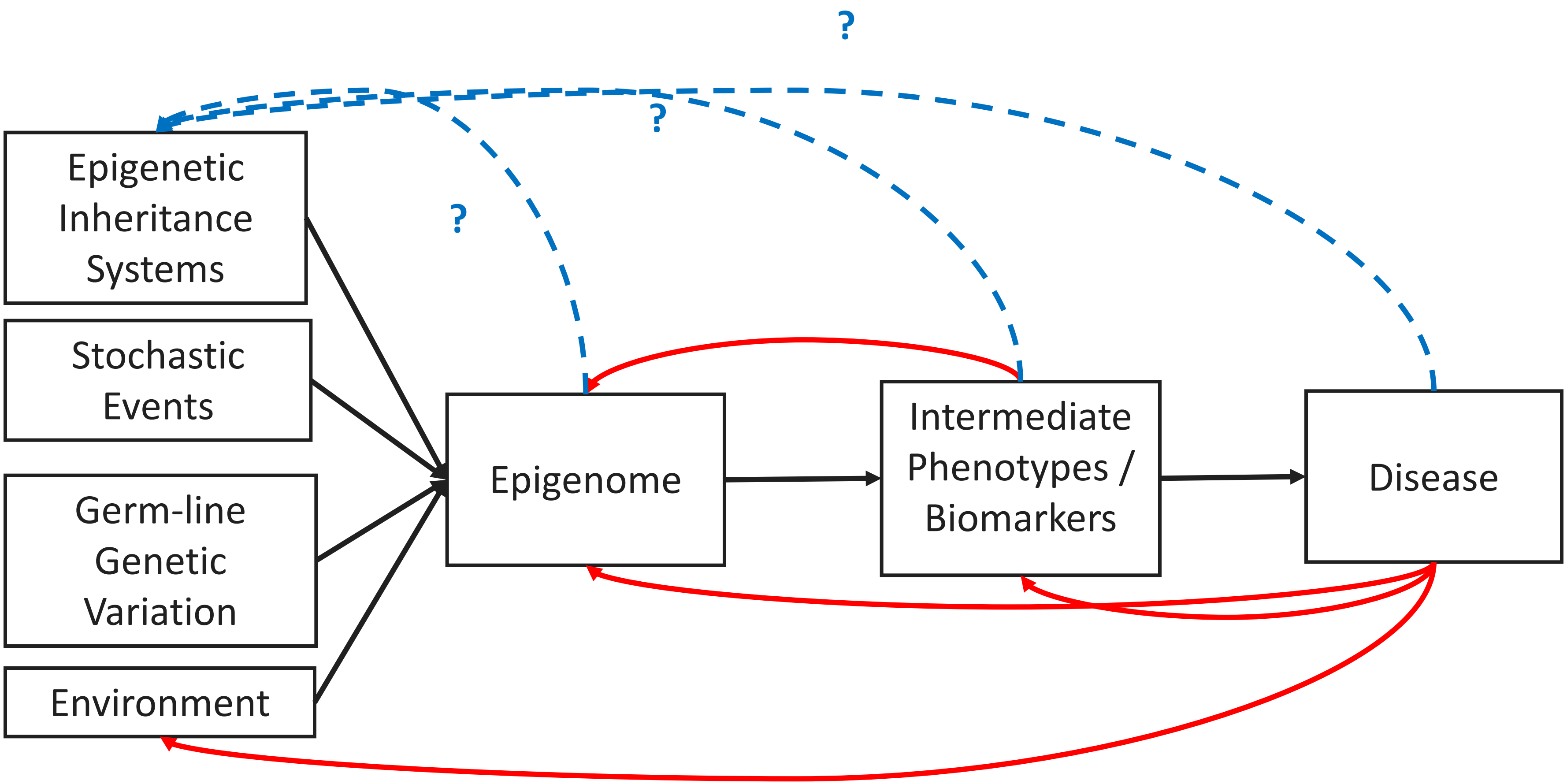
Relton and Davey-Smith Int J Epidemiol 2012

The real world



Relton and Davey-Smith Int J Epidemiol 2012

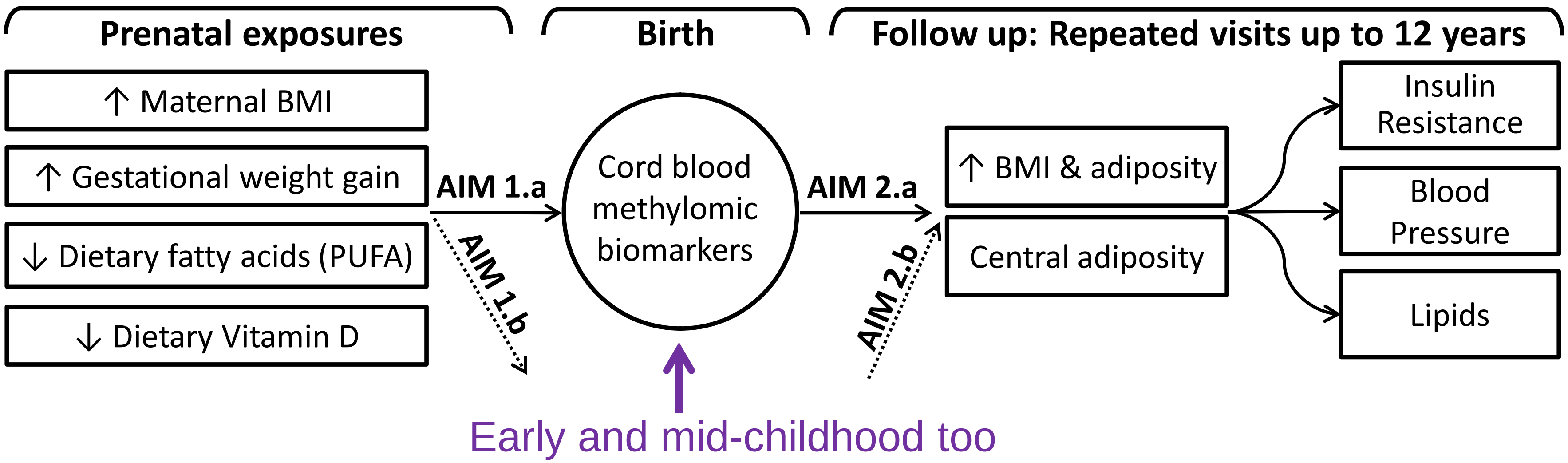
The real world



Relton and Davey-Smith Int J Epidemiol 2012

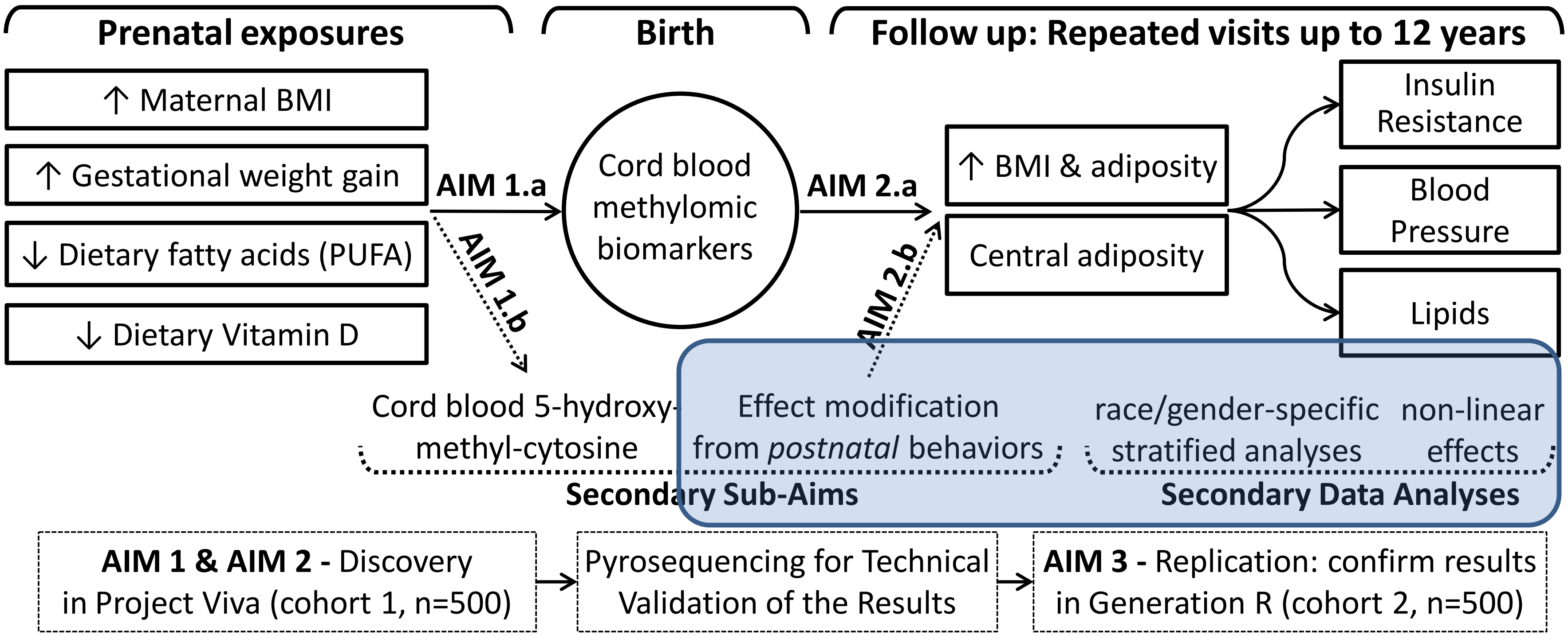
Novel Epigenomic Biomarkers of Prenatal Risk Factors and Childhood Obesity

R01 NR013945 (Baccarelli)
R01 HL111108 (Litonjua, DeMeo)



AIM 1 & AIM 2 - Discovery in Project Viva (cohort 1, n=500) → Pyrosequencing for Technical Validation of the Results → **AIM 3 -** Replication: confirm results in Generation R (cohort 2, n=500)

Novel Epigenomic Biomarkers of Prenatal Risk Factors, and Childhood Obesity



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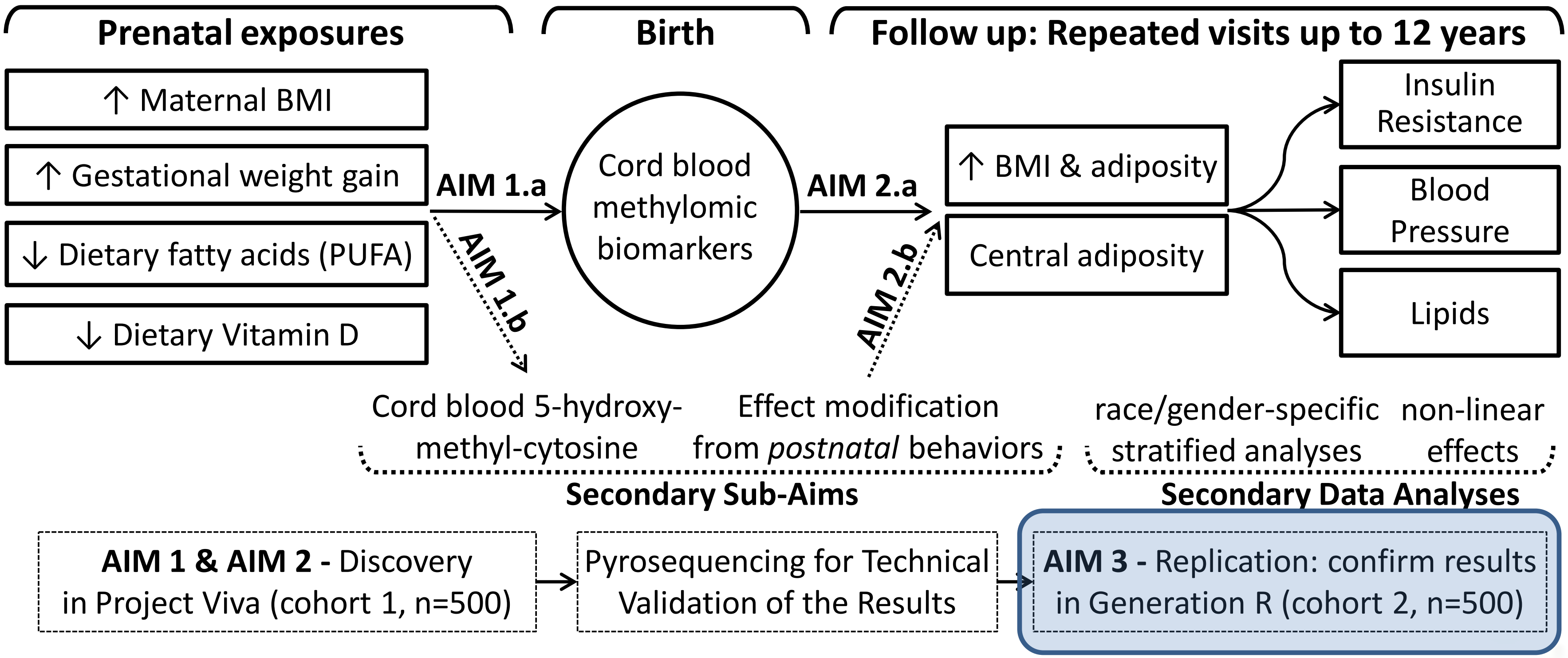


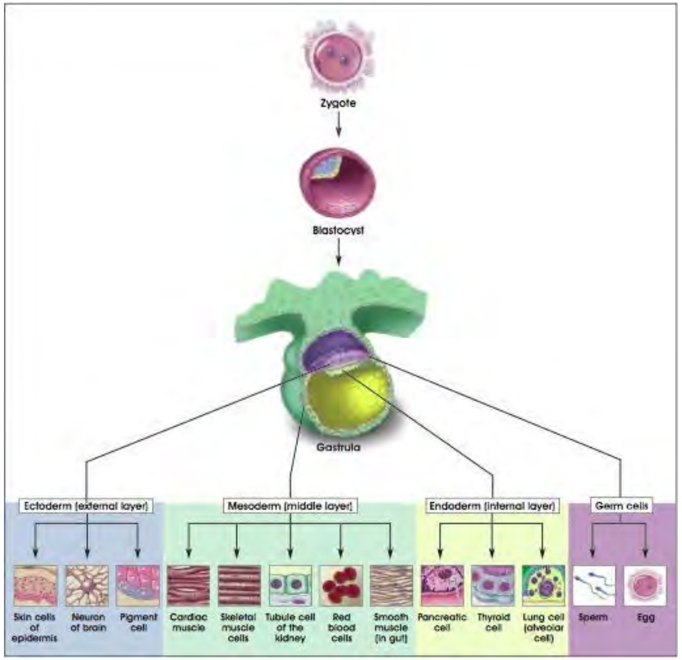
Relationships among increased cord blood DNA methylation at single CpG sites defined by an Illumina GoldenGate probe), gene expression, and indices of body composition

Gene	Symbol	Direction of expression change in high BMI children	Phenotype influenced	Function*
Alkaline phosphatase	*ALPL*	↓	Height	Bone mineralization
Caspase 10	*CASP10*	←	BMI	Apoptosis
Cyclin-dependent kinase inhibitor 1C	*CDKN1C*	↓	BMI, Fat mass, Lean mass	Negative regulator of cell proliferation
Ephrin type-A receptor 1	*EPHA1*	↓	BMI, Fat mass	Development (nervous system)
HLA class II histocompatibility antigen DO beta chain	*HLADOB2*	↓	Fat mass	Antigen presentation
Interferon regulatory factor 5	*IRF5*	←	Height	Cell growth, differentiation, apoptosis
Matrix metalloproteinase 9	*MMP9*	↓	Lean mass	Breakdown of extracellular matrix in tissue remodelling
Myeloproliferative leukemia virus oncogene	*MPL*	↓	Lean mass	Proliferation (bone marrow haemopoietic cells)
Nidogen-2	*NID2*	-	Fat mass	Cell interactions with extracellular matrix; adipogenesis

Relton CL, et al. PLoS ONE 2012;7(3): e31821; 2 UK cohorts

Tissue specificity

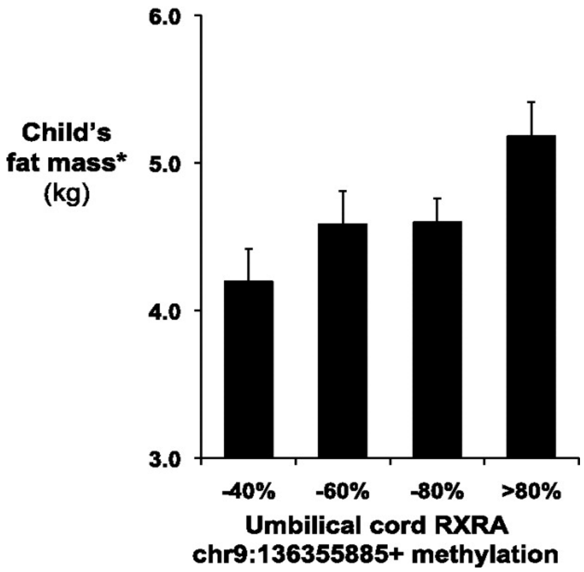
Potentially each tissue or cell type has a specific methylation profile.



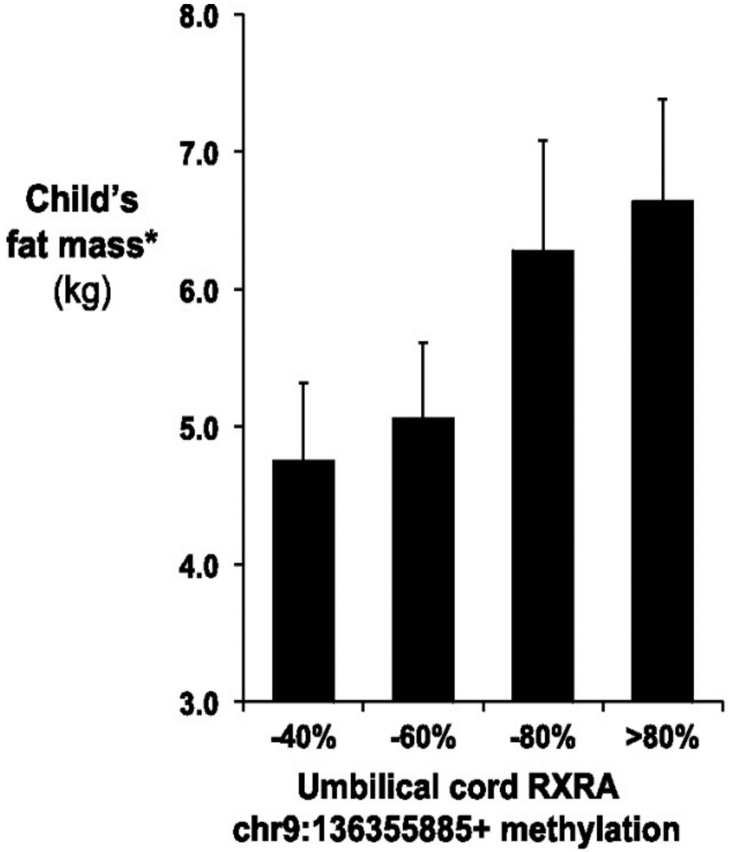
Epigenetics contribute to
tissue differentiation

Courtesy Andrea Baccarelli

Methylation of umbilical cord tissue RXRA chr9:136355885+ associated with child fat mass in 2 cohorts



PAH cohort, age 9 y



SWS cohort, age 6 y

Godfrey KM et al. Diabetes 2011;60:1528-1534

Epigenetics in Childhood Obesity

Moving forward

- Epigenomics
  - Best platforms
  - Approach to bioinformatics, sequencing
- Incorporating into epidemiology
  - Tissue specificity
  - Longitudinal changes
  - Conceptual models
    - Etiology/causal inference
    - Prediction/risk stratification

Overall Conclusions

- Emerging risk factors for obesity
  - Perinatal hormonal milieu
    - No current clinical or public health implications
  - Gut microbiota
    - Avoid unnecessary C-section, infant antibiotics
    - Pre- and probiotics need more evidence
- Epigenetics
  - Common pathway between risk factors and outcomes?
  - May help explain early origins of obesity

'CONGRATULATIONS! IT'S AN OBESITY TIME BOMB...'

Breast Feeding: Influence on Weight, Weight Gain, and Later Obesity

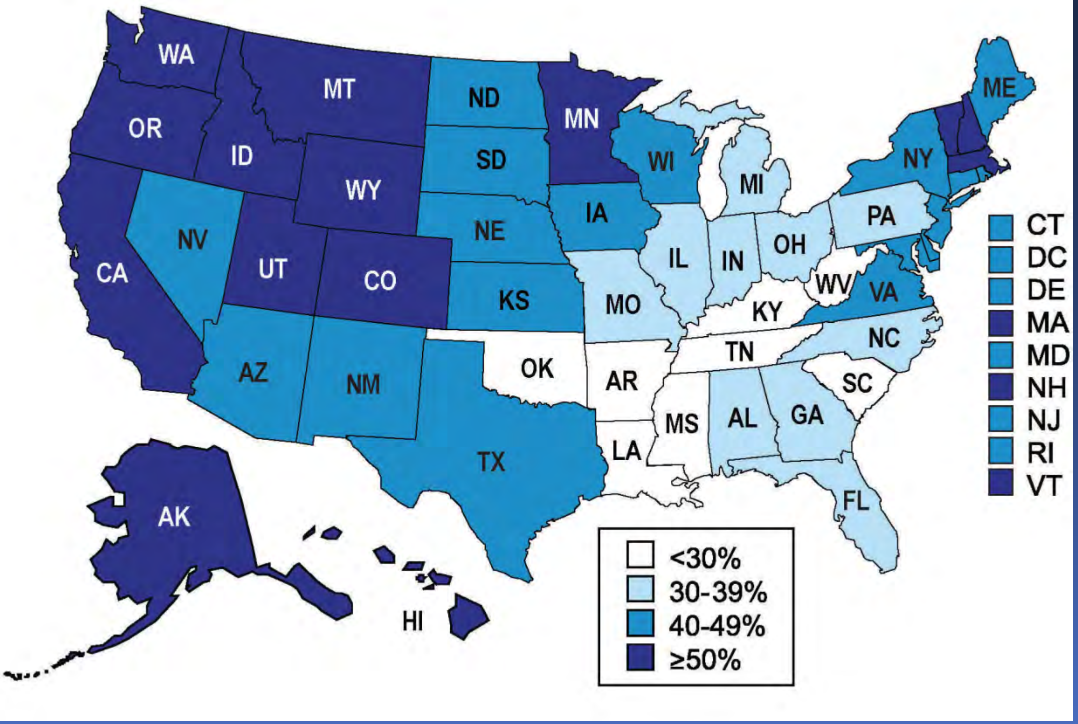
Matthew W. Gillman, MD, SM

Thanks to…

Faculty, Trainees, & Staff

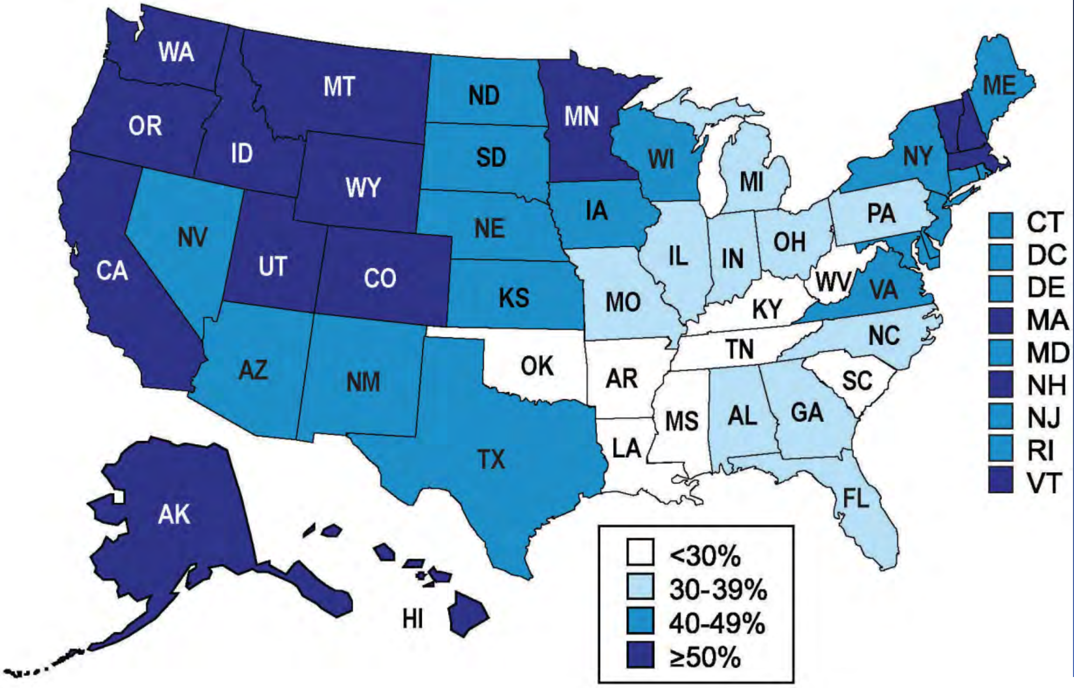
Obesity Prevention Program
Department of Population Medicine
Harvard Medical School/Harvard Pilgrim Health Care Institute

and
Support from NIH, CDC, DHHS
(R01 HD/HL/ES/MD/MH/NR, R03 TW, R18 AE, RC1 HD, R37 HD, P30 HL, U54 CA, K23/24/99 HD/HL/DK/ES)



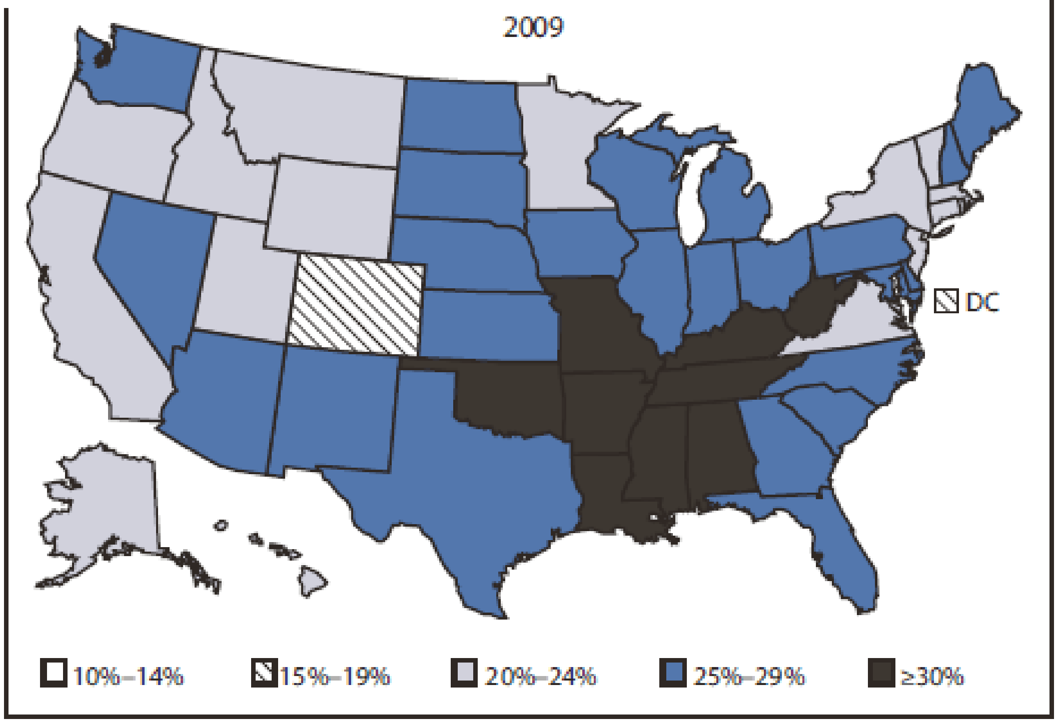
US Breastfeeding Map

(% breastfed at 6 mo in 2007)

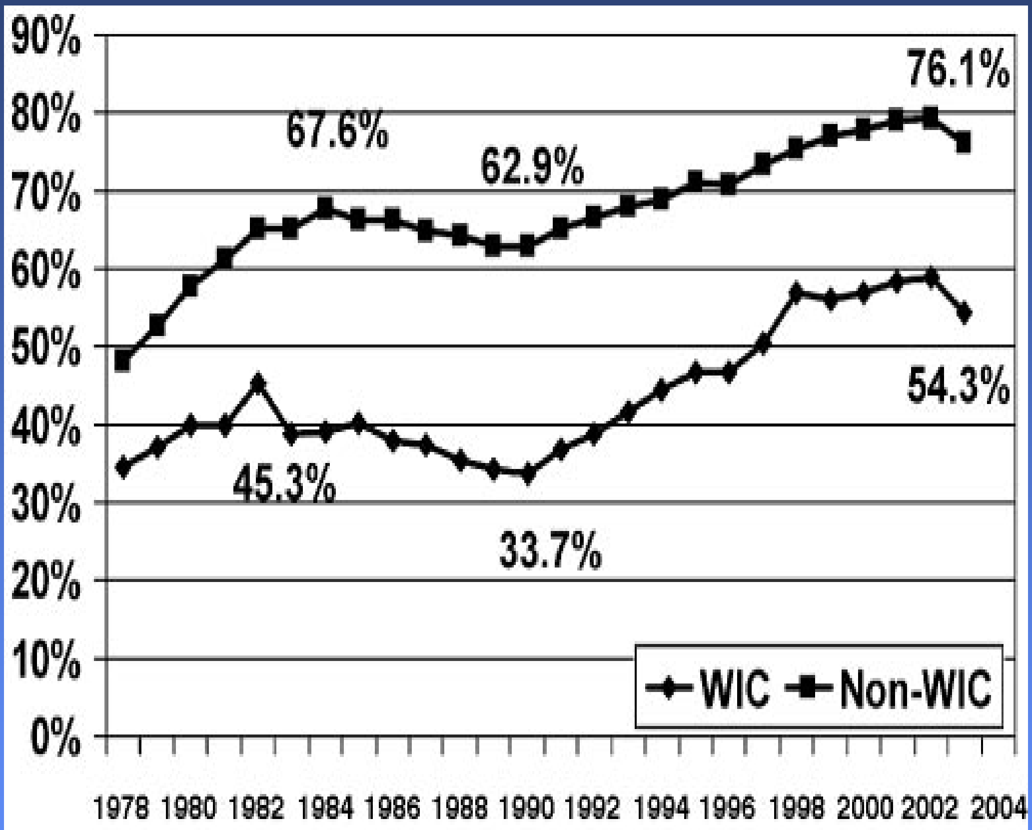


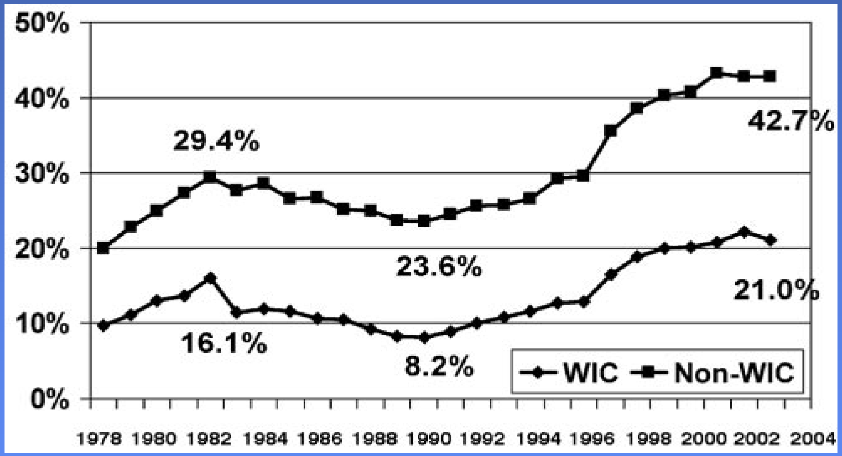
US Breastfeeding Map

...looks a lot like the US obesity map



Breastfeeding initiation and continuation rates lower in WIC than non-WIC children



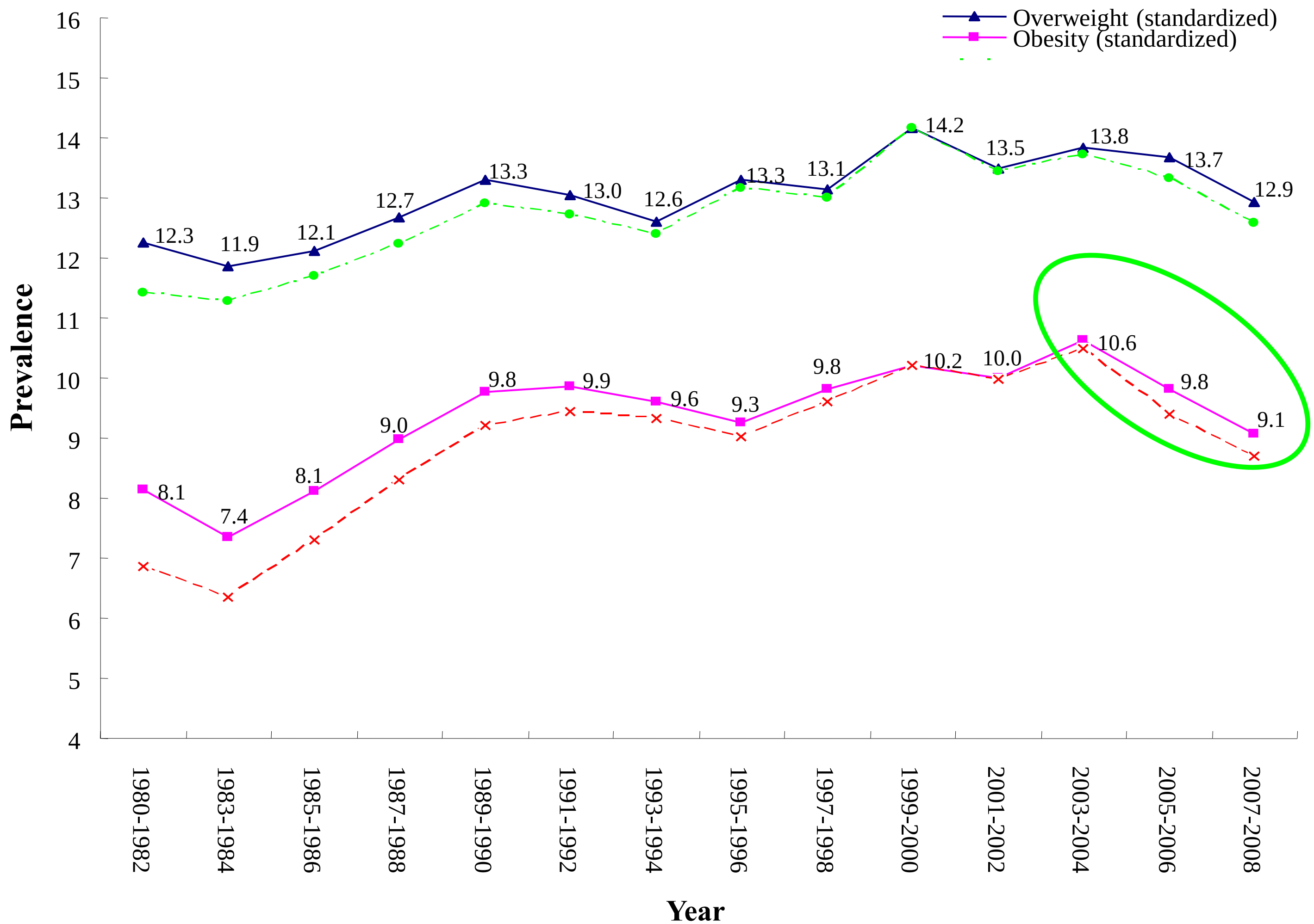


Ryan and Zhou, Pediatrics 2006;117;1136-1146

Downward trend in BMI since 2004 in 0-6-year-olds

… but steeper in higher v. lower SES

Boys

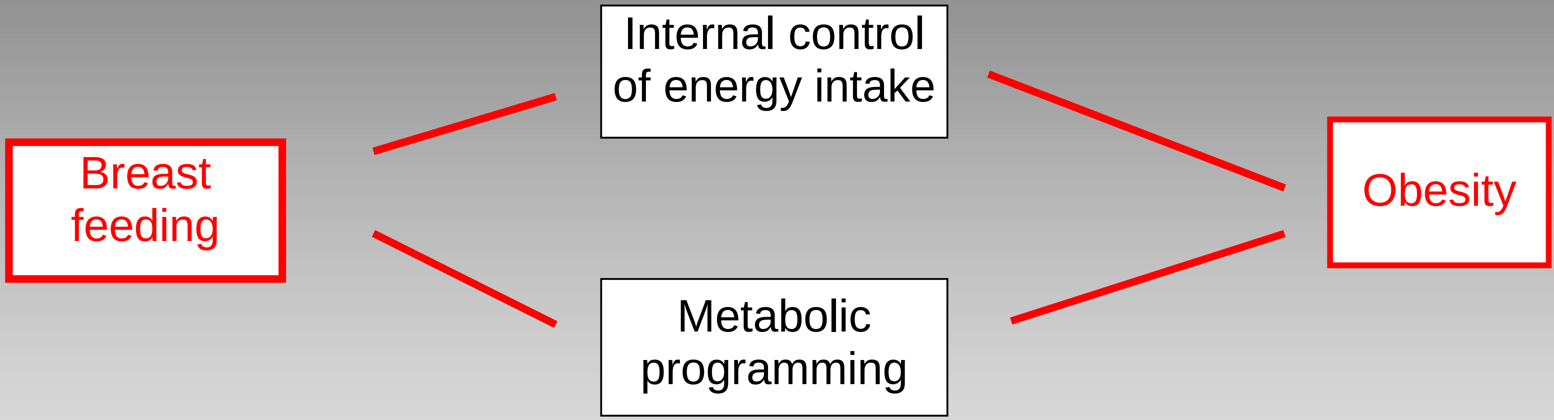


Standardized for age, race/ethnicity, and HVMA site, using the year 1999-2000 as reference

a

X. Wen et al. Pediatrics 2012;129:823-831

- Could increased lactation initiation, duration, exclusivity
  - Reduce overall childhood obesity, and
  - Disparities in childhood obesity?

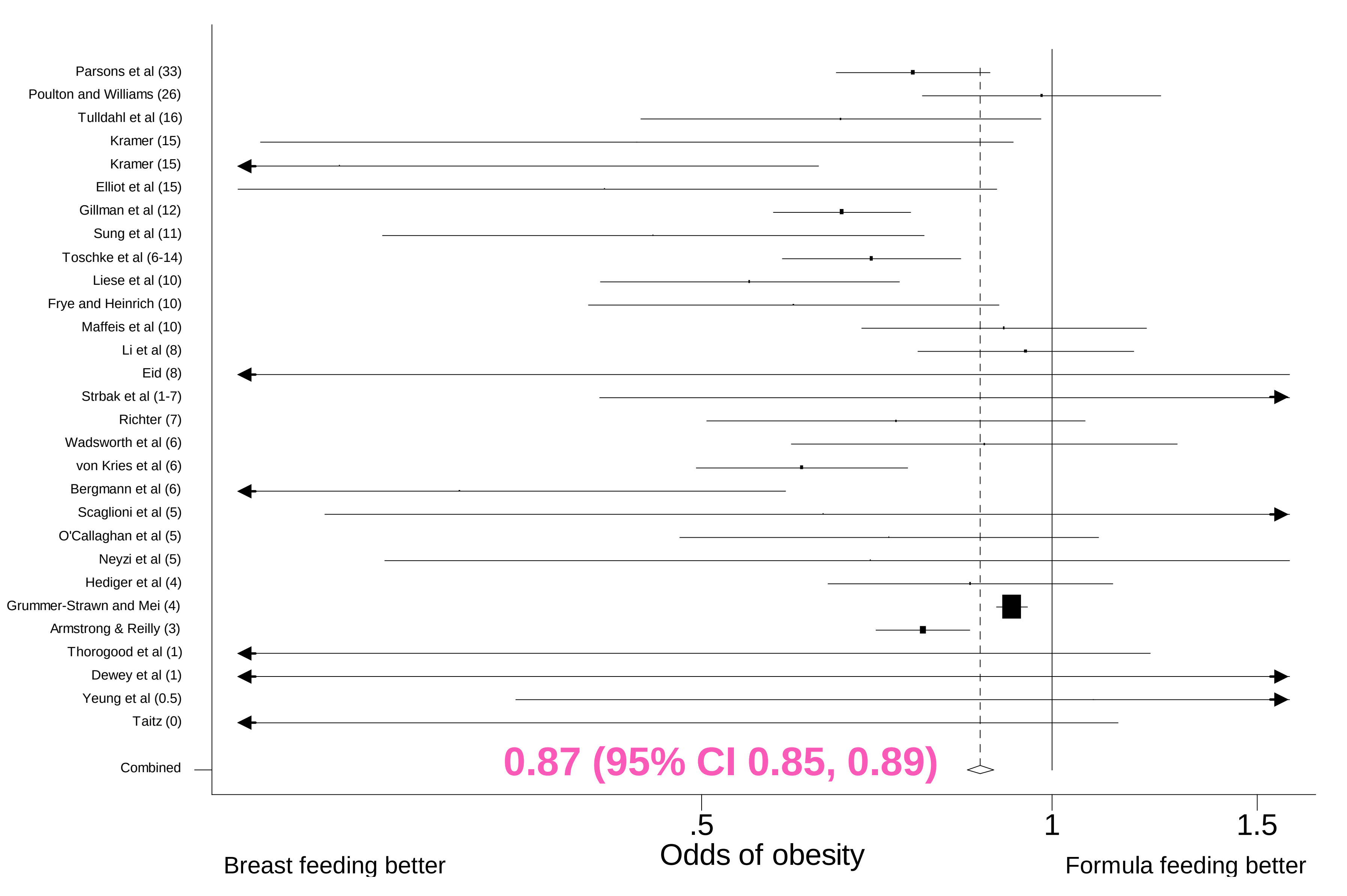


Internal control of energy intake
Breast feeding
Obesity
Metabolic programming

Breastfeeding-Child Obesity

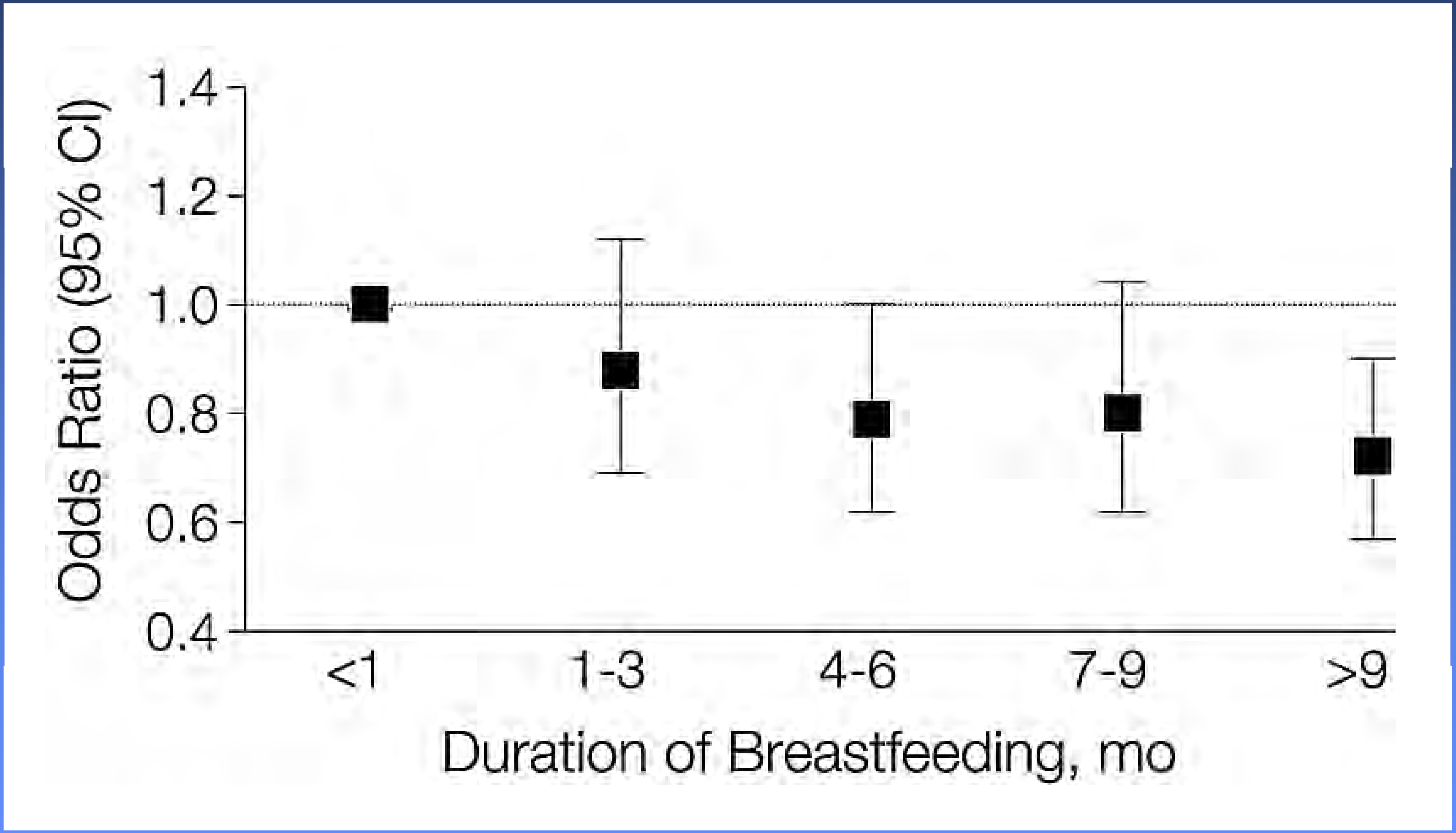
- 3 systematic reviews mid-2000s
- 9-27 studies
- Mostly white, Europe-US

Odds ratio of obesity: Breast v. formula fed



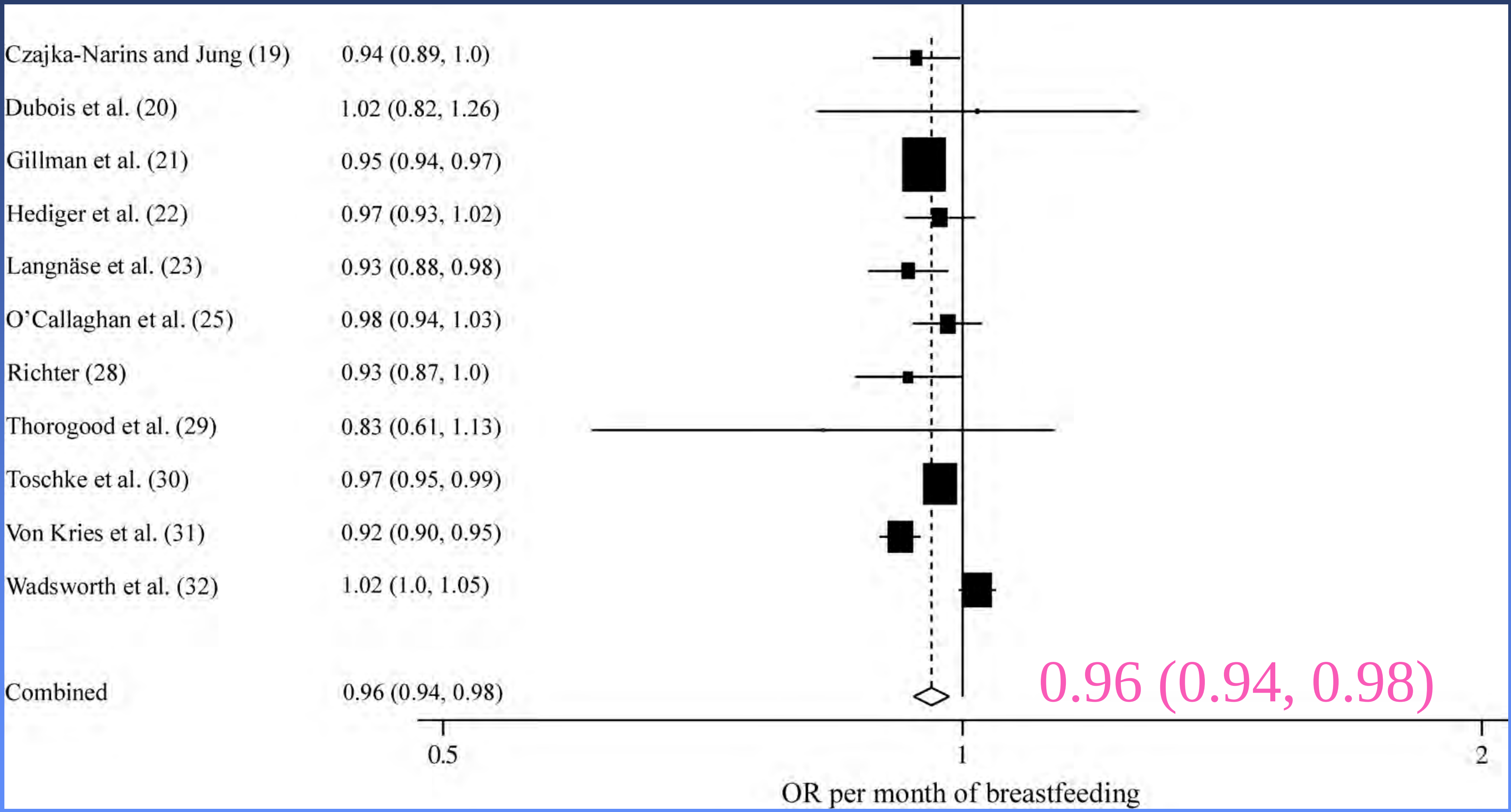
Owen et al, Pediatrics , 2005

Risk of Overweight in Adolescence By *Duration* of Breastfeeding in Infancy



Gillman et al, JAMA 2001; GUTS cohort

Odds ratio of obesity--per month of breastfeeding



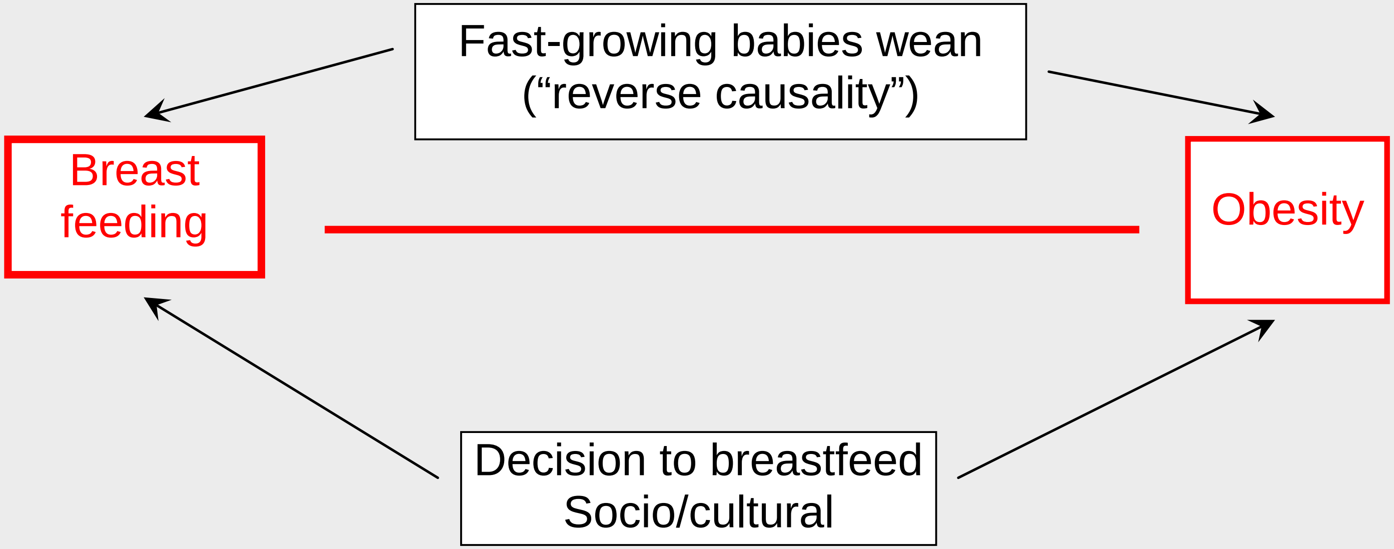
Harder et al. Am. J. Epidemiol. 2005;162:397-403

Breastfeeding-Obesity

- Meta-analyses suggested protection
  - Breastfeeding initiation and duration

Breastfeeding-Obesity

- Does breastfeeding actually *cause* less obesity?


Fast-growing babies wean
(“reverse causality”)
Breast
feeding
Obesity
Decision to breastfeed
Socio/cultural

Breastfeeding-Obesity

- Methods to address residual confounding by shared cultural determinants of both breastfeeding and obesity
  - Careful measurement of confounders
  - Within-family (sib-pair) analyses
  - Cohorts with different confounding structures
  - Explore mechanisms
  - Randomized trials

Breastfeeding-Obesity

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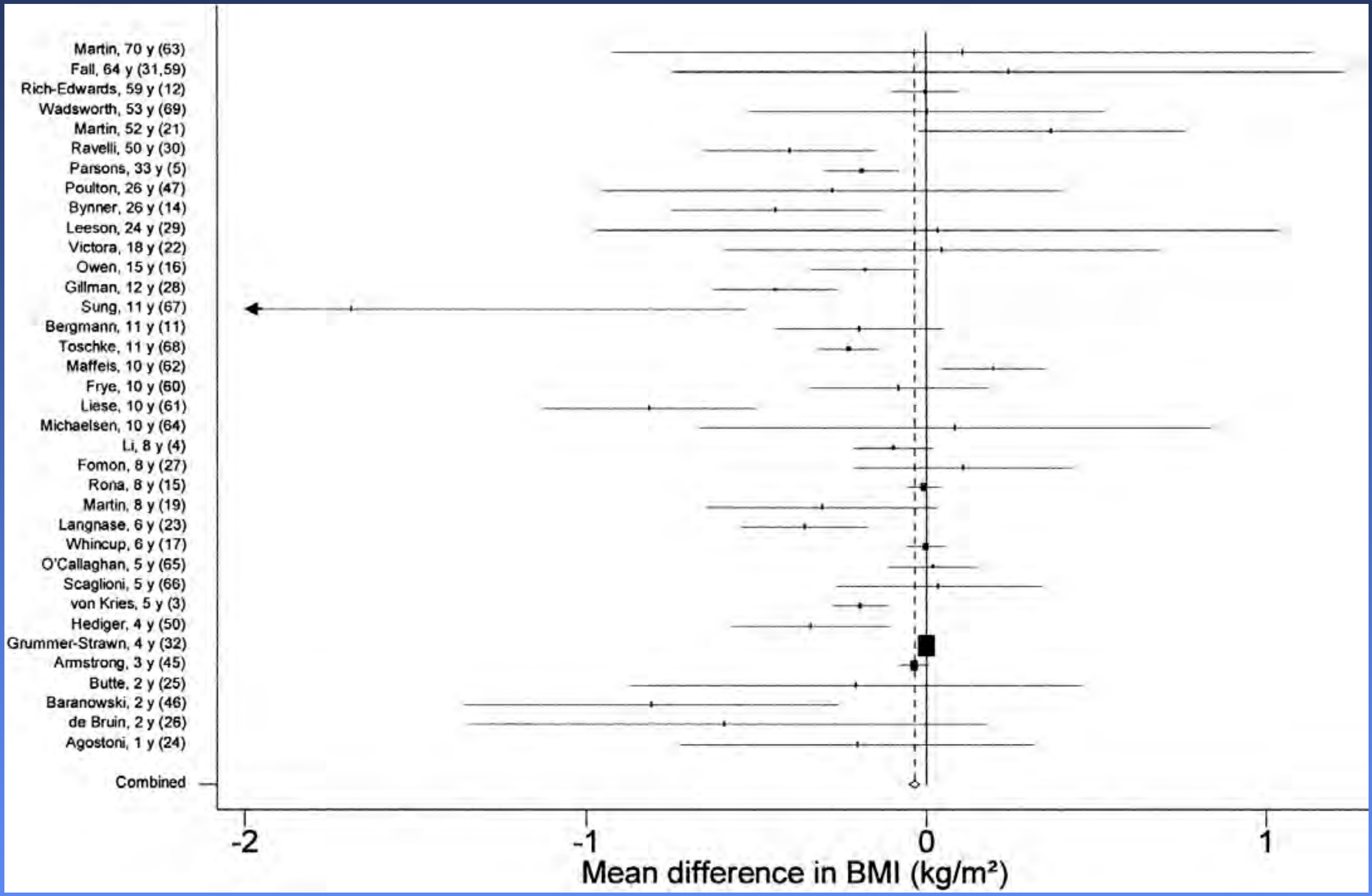
Small mean difference in BMI between breastfed and bottle-fed participants (age-adjusted)

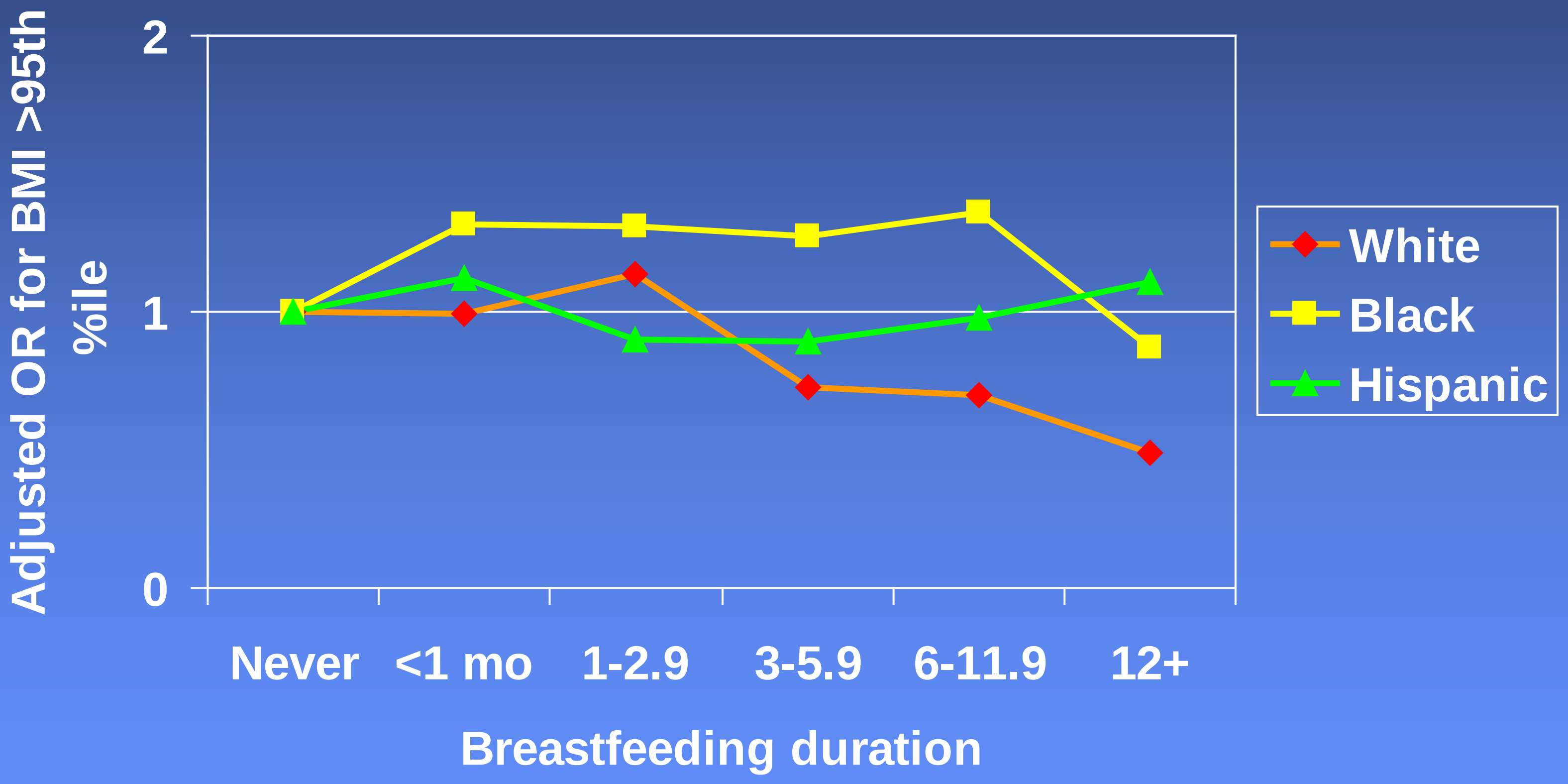


-0.10 (-0.14, -0.06) adjustment for SES, maternal BMI, smoking -0.01 (-0.05, 0.03)

Owen et al. Am J Clin Nutr 2005;82:1298-1307

Breastfeeding Duration and Reduced Obesity at Age 4

Among white, but not black/Hispanic



Grummer-Strawn and Mei, 2004; PedNSS; n = 12,587

Breastfeeding-Obesity

Control for confounding

- One meta-analysis suggests control of confounders explains the association, but
  - Few studies had all the covariates
  - Mean BMI, not % obese
- Weaker or no association in US non-whites
  - And in developing countries
  - Other risk factors overwhelm breastfeeding effect?
  - Different ratios of formula to breast milk?
  - Different formulas in different countries?

Breastfeeding-Obesity

- Methods to address residual confounding by shared cultural determinants of both breastfeeding and obesity
  - Careful measurement of confounders
  - Within-family (sib-pair) analyses
  - Cohorts with different confounding structures
  - Explore mechanisms
  - Randomized trials

Breastfeeding Duration– Obesity
GUTS Sib-Pair Analysis

- Participants
  - 15,341 in whole cohort analysis (JAMA 2001)
  - 5614 sibs
    - with complete data, born after 34 weeks, no medical exclusions, same dad (height)
      - 3242 with same BF duration
  - 2372 with discordant BF duration

Breastfeeding Duration– Obesity

GUTS Sib-Pair Analysis

	Within-family	*Overall*
Model covariates	*OR (95% CI)*	*OR (95% CI)*
Age, sex, Tanner stage	0.94 (0.78, 1.14)	0.87 (0.82, 0.93)
+ BW, parity, energy, activity	0.92 (0.76, 1.11)	0.88 (0.82, 0.94)
+ maternal BMI, smoking, inc.	N/A	0.94 (0.88, 1.00)

Breastfeeding Duration– Obesity

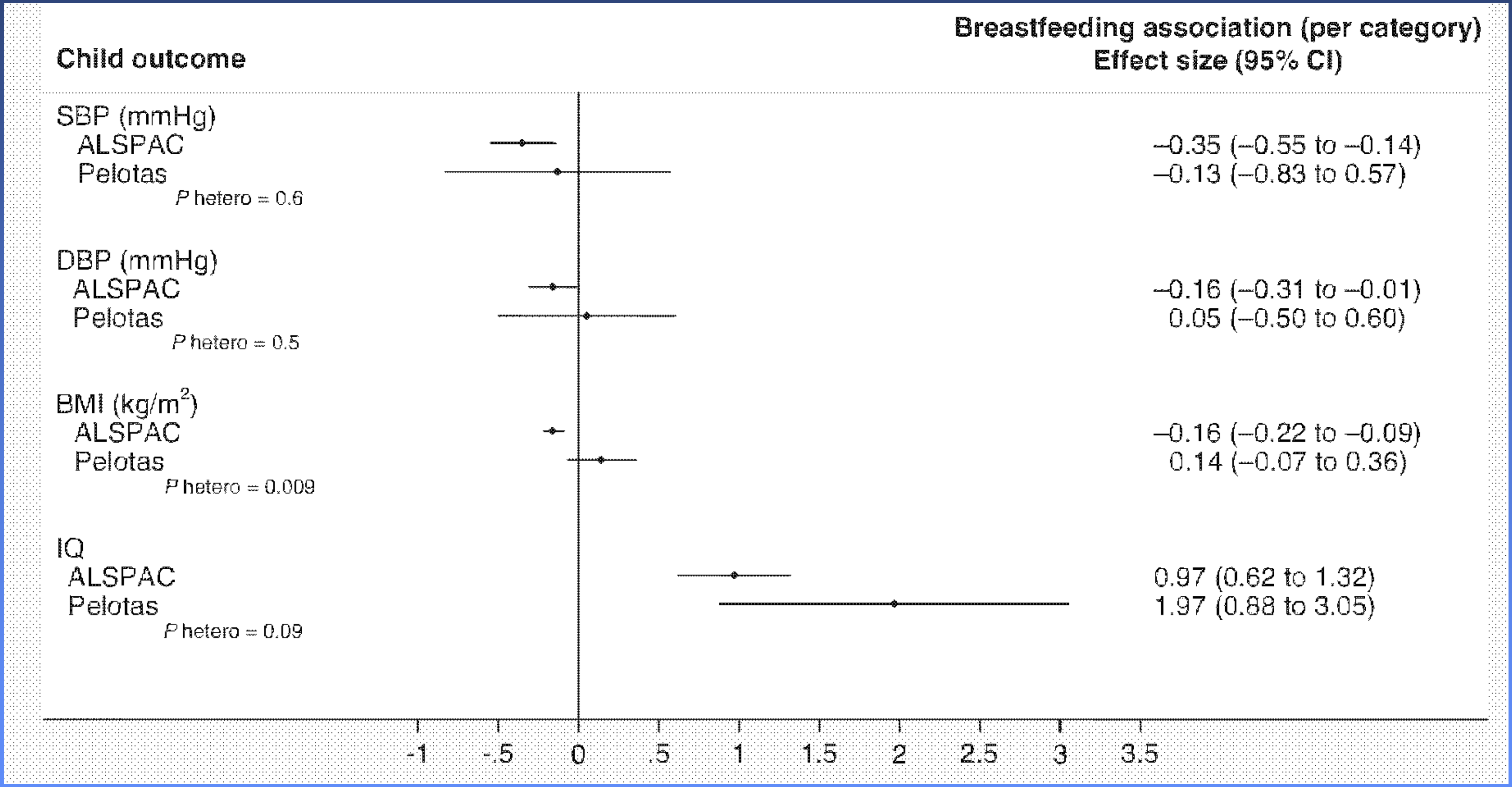
GUTS Sib-Pair Analysis

- Conclusions
  - Within-family association appears equal in magnitude to overall association
  - Tends to support valid relationship
  - But wide confidence intervals
    - Need larger studies of siblings

Breastfeeding-Obesity

- Methods to address residual confounding by shared cultural determinants of both breastfeeding and obesity
  - Careful measurement of confounders
  - Within-family (sib-pair) analyses
  - Cohorts with different confounding structures
  - Explore mechanisms
  - Randomized trials

Breastfeeding duration predicts higher IQ in both ALSPAC and Pelotas, but lower BMI/BP only in ALSPAC, in which breastfeeding is associated with SES



Brion et al, IJE 2011; 40:670

Breastfeeding-Obesity

- Methods to address residual confounding by shared cultural determinants of both breastfeeding and obesity
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  - Cohorts with different confounding structures
  - Explore mechanisms
  - Randomized trials

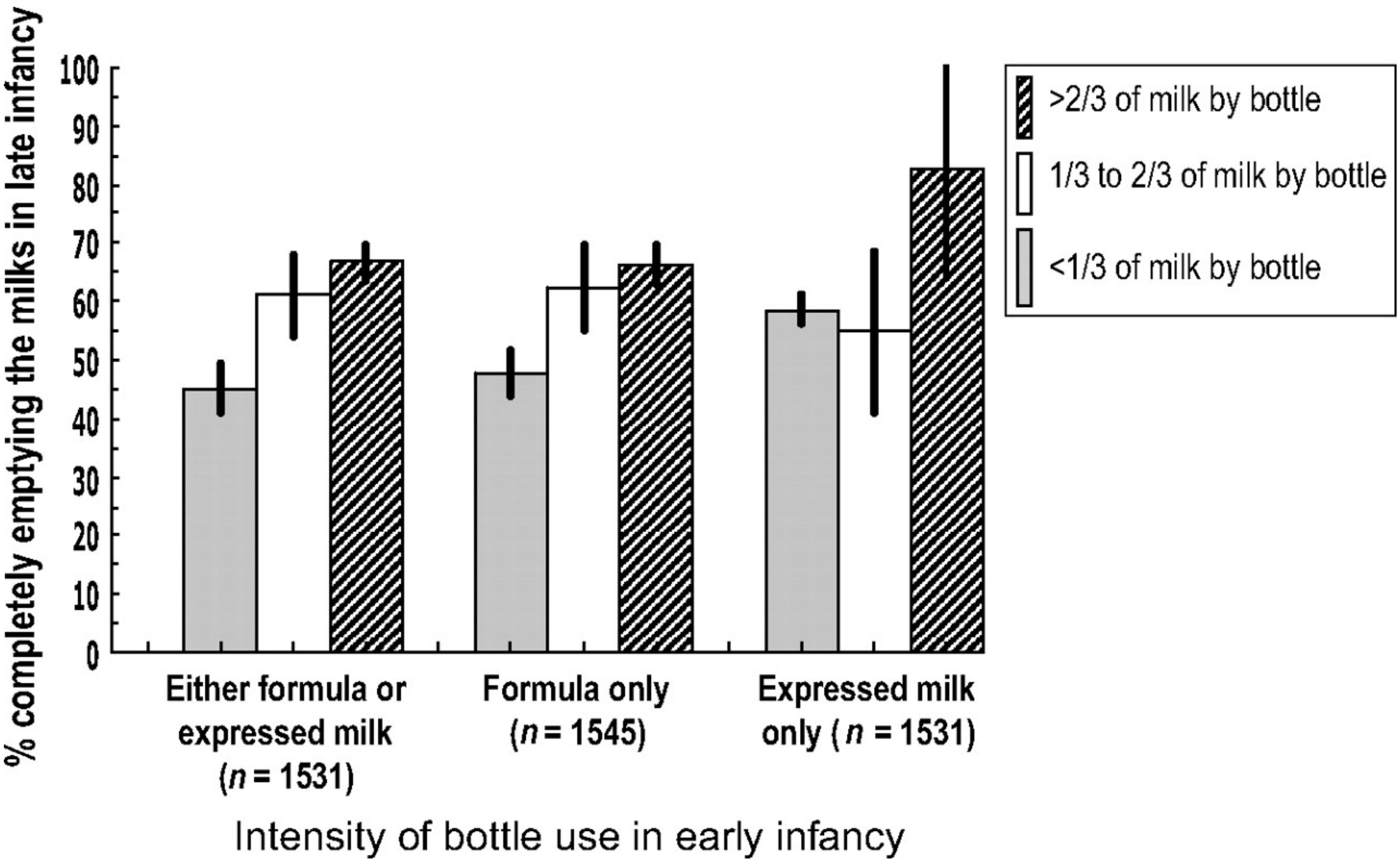
Breastfeeding-Obesity

Mechanisms

Breastfeeding-Obesity
Mechanisms

- Behavioral (breast feeding)
  - → Self-regulation of energy intake
- Metabolic (breast milk v. formula)
  - – Insulin, leptin
  - – Protein

Infants who are bottle-fed in early infancy are more likely to empty the bottle or cup in late infancy



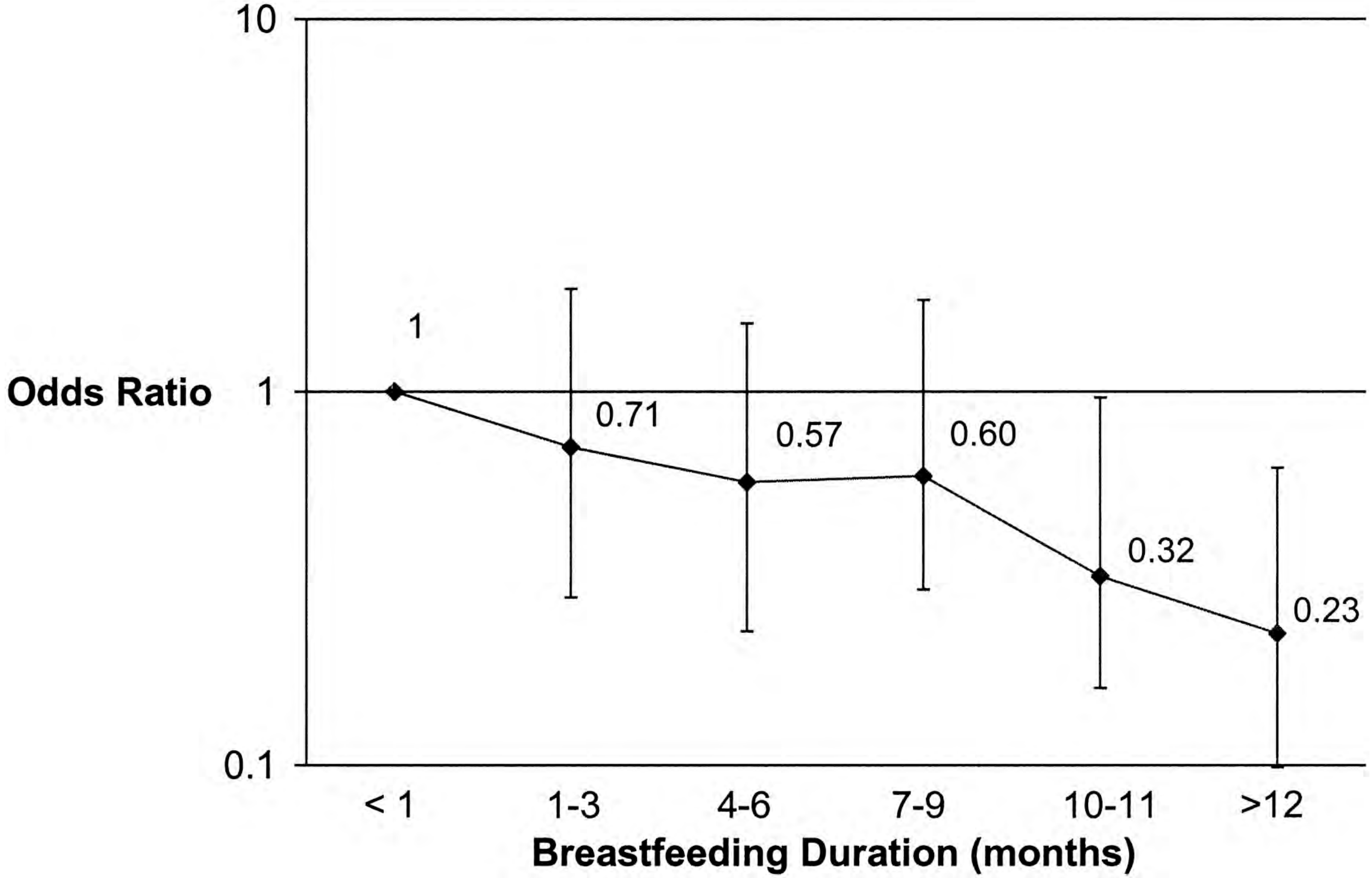
Li R et al. Pediatrics 2010;125:e1386-e1393

Project Viva

- Pre-birth cohort
- At 12 months
  - Restriction domain
    - "I have to be careful not to feed my baby too much"—agree (or strongly) v. disagree
  - Mother's preexisting attitudes collected prospectively in 2nd trimester
    - Concern/worry that baby will
      - Eat too much/not eat enough
      - Become overweight/become underweight

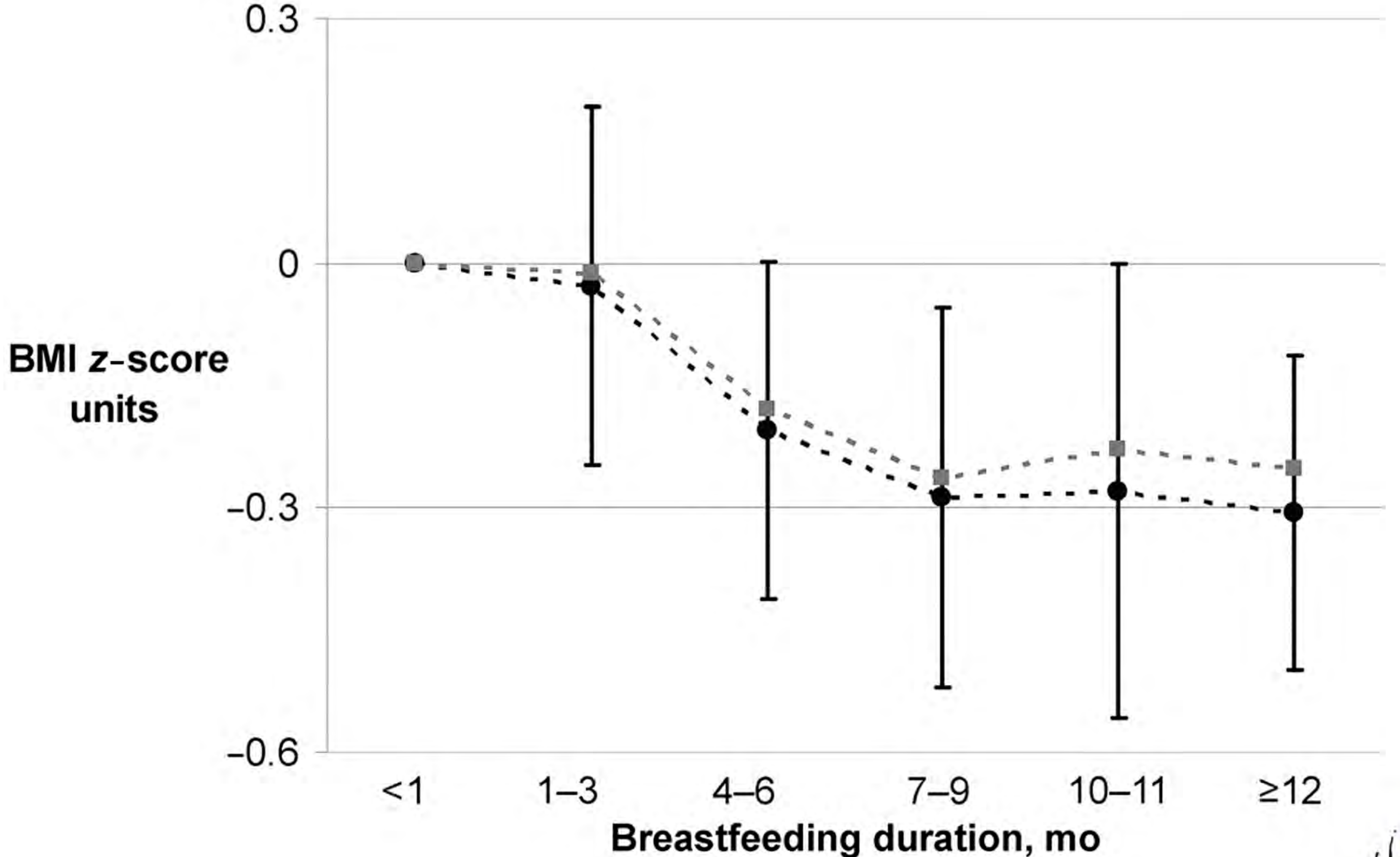
Breastfeeding duration inversely associated with maternal restriction of child's intake at age 1 year

Adjusted for SES, pre-existing maternal concerns, infant WFL



Taveras E M et al. Pediatrics 2004;114:e577-e583

But association of breastfeeding duration with 3-year BMI only partially explained by restriction.



Taveras E M et al. Pediatrics 2006;118:2341-2348

Restriction is not associated with child obesity after adjusting for weight status at the time of measuring restriction

Table 2 Association of maternal feeding restriction at age 1 and obesity-related outcomes at age 3, before and after adjusting for weight-for-length z-score at age 1, among 837 mother–infant pairs

		BMI z-score	SS+TR*	Obesity†
Model	**Predictor**	**β (95% CI)**	**β (95% CI)**	**OR (95% CI)**
M1. Unadjusted	Restriction	0.43 (0.22 to 0.64)	1.03 (0.17 to 1.88)	2.95 (1.60 to 5.42)
M2. M1 + covariates‡	Restriction	0.26 (0.05 to 0.48)	0.95 (0.07 to 1.83)	2.14 (1.02 to 4.46)
M3. M2 + WFL	Restriction	0.00 (−0.17 to 0.18)	0.40 (−0.44 to 1.25)	1.04 (0.41 to 2.62)
z-score at age 1	WFL z-score	0.57 (0.51 to 0.62)	1.22 (0.95 to 1.50)	10.49 (6.01 to 18.31)

Rifas-Shiman et al., Arch Dis Child 2011; 96:265

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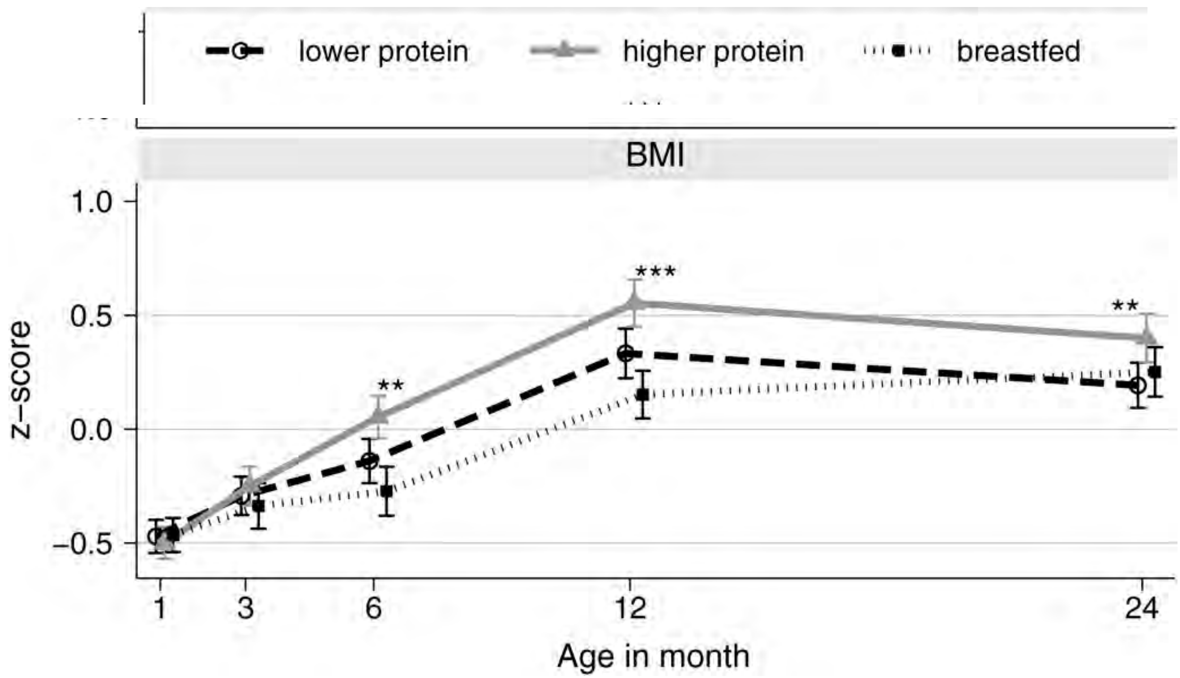
Rifas-Shiman et al., Arch Dis Child 2011; 96:265

RCT of lower protein formula resulted in lower BMI at 24 mo



Koletzko B et al. Am J Clin Nutr 2009;89:1836-1845

BF-Obesity: Is it causal?

- Residual confounding?
  - No! 1 meta-analysis, no ass’n in minorities
  - Maybe! Sib-pair analyses
- Biological effect of breast milk?
- Biological effect of formula?
- Insistence on “finishing the bottle”?
- Reverse causality (smaller infant size leads to supplementation and weaning)?
- Cohorts with different confounding structures?

BF-Obesity: Is it causal?

- Residual confounding?
- Biological effect of breast milk?
  - Maybe… conflicting data on leptin, etc.
- Biological effect of formula?
- Insistence on “finishing the bottle”?
- Reverse causality (smaller infant size leads to supplementation and weaning)?
- Cohorts with different confounding structures?

BF-Obesity: Is it causal?

- Residual confounding?
- Biological effect of breast milk?
- Biological effect of formula?
  - Yes! Protein trial
- Insistence on “finishing the bottle”?
- Reverse causality (smaller infant size leads to supplementation and weaning)?
- Cohorts with different confounding structures?

BF-Obesity: Is it causal?

- Residual confounding?
- Biological effect of breast milk?
- Biological effect of formula?
- Insistence on “finishing the bottle”?
  - No! Restriction doesn’t cause obesity
- Reverse causality (smaller infant size leads to supplementation and weaning)?
- Cohorts with different confounding structures?

BF-Obesity: Is it causal?

- Residual confounding?
- Biological effect of breast milk?
- Biological effect of formula?
- Insistence on “finishing the bottle”?
- Reverse causality (larger infant size leads to weaning)?
  - Yes! One study suggests the opposite: smaller babies wean sooner
- Cohorts with different confounding structures?

BF-Obesity: Is it causal?

- Residual confounding?
- Biological effect of breast milk?
- Biological effect of formula?
- Insistence on "finishing the bottle"?
- Reverse causality (larger infant size leads to weaning)?
- Cohorts with different confounding structure?
  - No! BF predicts higher IQ in ALSPAC and Pelotas, but lower obesity only in ALSPAC

Breastfeeding-Obesity

- Methods to address residual confounding by shared cultural determinants of both breastfeeding and obesity
  - Careful measurement of confounders
  - Within-family (sib-pair) analyses
  - Cohorts with different confounding structures
  - Explore mechanisms
  - Randomized trials

Randomized Controlled Trial

- Randomization to breast v. artificial feeding infeasible/unethical
- But…randomization to BF promotion intervention both feasible and ethical

PROBIT

PROmotion of Breastfeeding Intervention Trial

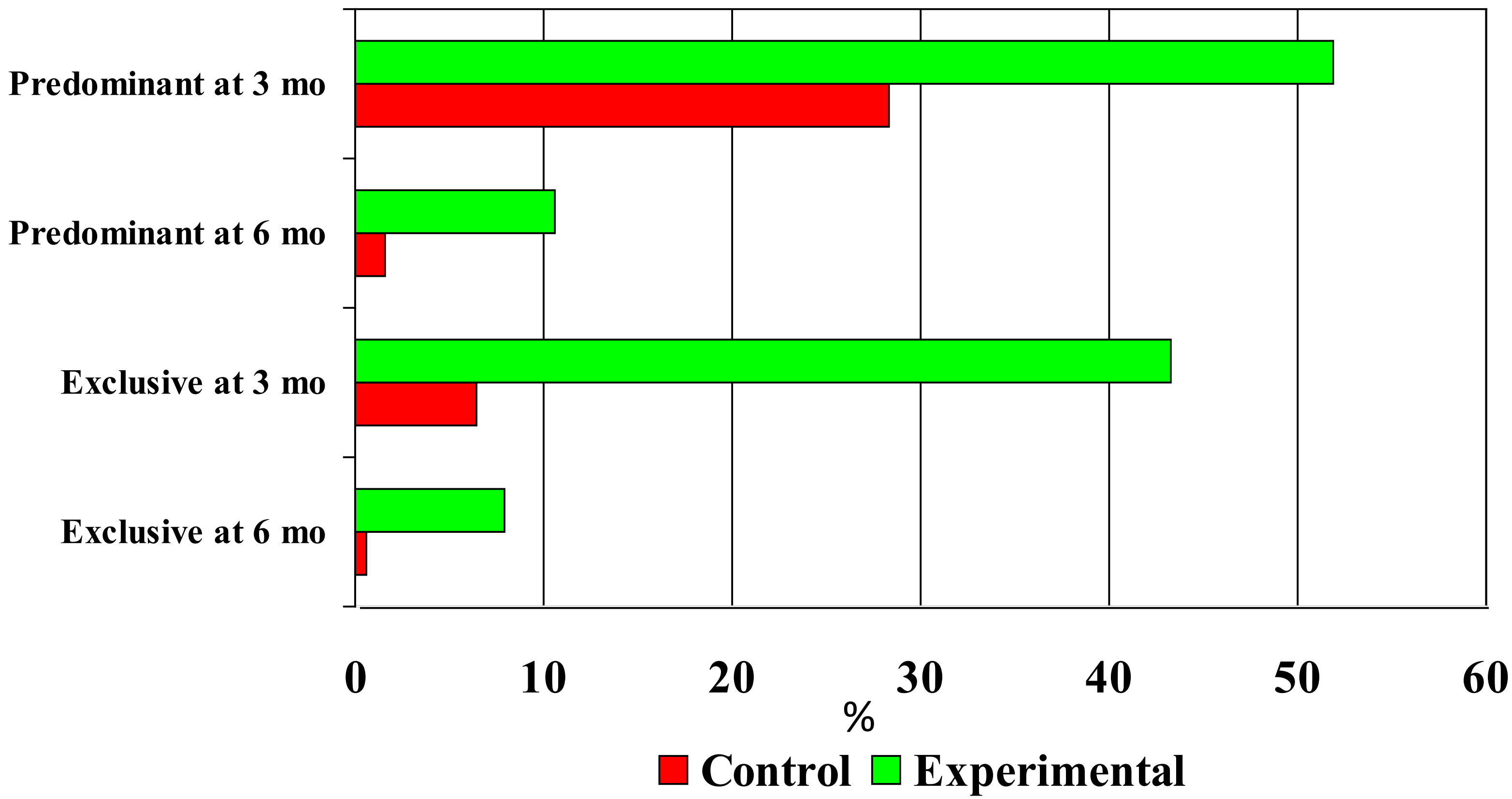
A Cluster-Randomized Trial in the Republic of Belarus


LATVIA
RUSSIA
LITHUANIA
Novopolotsk
Vitebsk
Orsha
Zhodino
Lida
MINSK
Mogilev
Grodno
POLAND
Bobruisk
Baranovichi
Gomel
Brest
Pinsk
Mozyr
UKRAINE

PROBIT Design

- Intervention based on WHO/UNICEF Baby-Friendly Hospital Initiative
- RCT using cluster randomization
  - 31 maternity hospitals
    - 1 pediatric clinic per hospital
- 17,046 healthy newborns
  - $\geq$37 wk, $\geq$2500 g
  - All initiated breastfeeding
- Follow-up to 6.5 years, 11.5 years
  - >80% retention rate

Duration & exclusivity substantially higher in experimental group



PROBIT Anthropometry/BP Results

At age 6.5 years

Outcome	***Experimental***	***Control***	***E-C (95% CI)***
Height (cm)	121.1	120.2	+0.7 (-0.3 to +1.7)
BMI (kg/m^2)	15.6	15.6	+0.1 (-0.2 to +0.3)
Waist Circ (cm)	54.6	54.2	+0.3 (-0.8 to +1.4)
Triceps SF (mm)	9.9	10.0	-0.4 (-1.8 to +1.0)
Subscap SF (mm)	5.9	5.8	0.0 (-0.4 to +0.5)
Systolic BP (mm)	97.8	96.7	+0.2 (-2.9 to +3.3)
Diastolic BP (mm)	57.3	57.8	+0.2 (-1.8 to +2.2)

Kramer et al, Am J Clin Nutr 2007

PROBIT Results for Overweight/Obesity at 6.5 y

Outcome	***Experimental***	***Control***	***OR (95% CI)***
BMI $\geq$85th %ile	13.4%	12.2%	1.1 (0.8-1.4)
BMI $\geq$95th %ile	5.9%	5.0%	1.2 (0.8-1.6)

Percentiles based on CDC 2000 Growth Charts

Breastfeeding Promotion Did Not Reduce Adiposity at 11.5 y

ITT analysis

31 clusters, 13,879 participants

	Groups					Difference, Mean (95% CI)	
	Intervention (n = 7405)		Control (n = 6474)		Intraclass Correlation Coefficient		
Outcome	No.	Mean (95% CI)	No.	Mean (95% CI)		Cluster Adjusted	Further Adjusted for Baseline Factors[a]
BMI, kg[b]	7402	18.32 (18.25 to 18.39)	6464	18.05 (17.97 to 18.12)	0.01	0.19 (−0.09 to 0.46)	0.16 (−0.02 to 0.35)
FMI, kg[b]	7342	3.40 (3.35 to 3.45)	6427	3.24 (3.19 to 3.29)	0.01	0.12 (−0.03 to 0.28)	0.10 (−0.02 to 0.22)
FFMI, kg[b]	7348	14.92 (14.89 to 14.95)	6426	14.83 (14.80 to 14.87)	0.02	0.04 (−0.11 to 0.18)	0.04 (−0.06 to 0.14)
Body fat, %	7345	17.38 (17.20 to 17.56)	6433	16.78 (16.59 to 16.97)	0.01	0.47 (−0.11 to 1.05)	0.36 (−0.09 to 0.81)
Waist circumference, cm	7402	64.68 (64.50 to 64.87)	6471	64.77 (64.58 to 64.97)	0.09	0.30 (−1.41 to 2.01)	0.57 (−1.09 to 2.23)
Triceps skinfold thickness, mm	7399	13.62 (13.47 to 13.76)	6470	14.20 (14.05 to 14.36)	0.13	−0.07 (−1.71 to 1.57)	−0.14 (−1.85 to 1.56)
Subscapular skinfold thickness, mm	7399	9.07 (8.95 to 9.19)	6470	9.16 (9.02 to 9.30)	0.03	−0.02 (−0.79 to 0.75)	−0.14 (−0.88 to 0.60)
IGF-I (z-score)[c]	6668	0.01 (−0.02 to 0.03)	5712	−0.01 (−0.03 to 0.02)	0.02	−0.02 (−0.12 to 0.08)	−0.03 (−0.12 to 0.06)
Hip circumference, cm	7402	78.38 (78.20 to 78.56)	6471	77.38 (77.18 to 77.57)	0.03	0.82 (−0.20 to 1.84)	0.81 (0.09 to 1.53)
Waist-hip ratio	7402	82.56 (82.42 to 82.70)	6471	83.73 (83.59 to 83.88)	0.25	−0.44 (−2.63 to 1.75)	−0.12 (−2.21 to 1.96)
Standing height, cm	7403	150.39 (150.2 to 150.6)	6471	149.16 (149.0 to 149.4)	0.05	0.52 (−0.78 to 1.82)	0.42 (−0.39 to 1.23)
Leg length, cm	7395	72.01 (71.90 to 72.13)	6460	71.28 (71.17 to 71.40)	0.05	0.59 (−0.22 to 1.40)	0.54 (0 to 1.07)
Head circumference, cm	7402	53.61 (53.57 to 53.65)	6471	53.50 (53.46 to 53.54)	0.10	0.20 (−0.18 to 0.58)	0.25 (−0.13 to 0.62)
Mid-upper arm circumference, cm	7399	22.12 (22.05 to 22.18)	6467	21.95 (21.88 to 22.02)	0.03	0.19 (−0.19 to 0.57)	0.18 (−0.13 to 0.49)
BMI ≥85th percentile[d]		1192 (16.1)[e]		910 (14.1)[e]	NA	1.18 (1.01 to 1.39)[f]	1.17 (1.01 to 1.35)[f]
BMI ≥95th percentile[d]		397 (5.4)[e]		304 (4.7)[e]	NA	1.17 (0.97 to 1.41)[f]	1.16 (0.98 to 1.39)[f]

Martin et al., JAMA. 2013;309(10):1005-1013

PROBIT Additional Analyses

	Intention to Treat			Instrumental Variable
	Cluster	***+ Adjusted***	***+ MI***	***(> 6 v. < 3 m exclusive BF)***
N	13,879		17,046	
	β (95% CI)			
BMI, kg/m^2	0.19 (-0.09, 0.46)	0.16 (-0.02, 0.35)	0.16 (-0.03, 0.35)	0.71 (-0.37, 1.79)
	OR (95% CI)			
BMI > 95th %ile	1.17 (0.97, 1.41)	1.16 (0.98, 1.39)	1.11 (0.92, 1.36)	1.80 (0.92, 3.84)

Martin et al., JAMA. 2013;309(10):1005-1013

PROBIT Conclusions

- No effect of prolonged and exclusive BF on stature, adiposity, obesity, BP
- Population with low obesity prevalence
  - Caution in generalizing to other settings
- All mothers intiated BF
  - Does not exclude very early effects
- Observational analysis in PROBIT did not show inverse association

Breastfeeding-Child Obesity

- Earlier studies suggested considerable protection
- More recent studies cast more doubt

Table 1 The '2011 Scorecard'

Gillman, IJE 2011; 40:681

	Supports protective effect of breastfeeding?		
Type of Study	Yes	Maybe	No
Cluster randomized controlled trial of breastfeeding promotion			No effects on anthropometric outcomes at 6.5 or 11.5 years of age, but observational data within the cohort show no (or slightly +) association
Cohort studies, mostly White European descent	Three pooled meta-analyses of (dichotomous) obesity show modest associations, but limited confounder control		One individual-level meta-analysis of mean BMI shows no effect after confounding control, but limited number of studies with sufficient data
Cohort studies in developing countries and racial/ethnic minorities			Many are null, but in some misclassification of exposure may exist
Sib-pair analyses in cohort studies		Three studies suggest effect, but low power	
Comparison of cohorts with different confounding structure			One study suggests that confounding explains observed associations
'Reverse causality?'		A few studies suggest this phenomenon, but could be in opposite direction to hypothesis	
Biological effects of breast milk		Conflicting data on adipokines	
Biological effects of formula	RCTs of high vs low protein (+/– energy) result in more adiposity and related outcomes		
Behavioural effects of nursing	Short-term studies suggest less self-regulation in bottle- vs breast-fed infants		
Ecological analysis			Breastfeeding rates have gone up along with emergence of the obesity epidemic, but that does not rule out inverse individual-level effects

Summarizing evidence for and against the hypothesis that having been breastfed reduces the risk of obesity.

Table 1 The '2011 Scorecard'

Gillman, IJE 2011; 40:681

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Cohort studies in d countries and rac minorities		but in some tion of exposure
Sib-pair analyses in studies		
Comparison of coh ferent confoundi		gests that con- plains observed
'Reverse causality?'		
Biological effects of		
Biological effects of		
Behavioural effects		
Ecological analysis		ates have gone up mergence of the emic, but that e out inverse vel effects

Summarizing evidence for and against the hypothesis that having been breastfed reduces the risk of obesity.

Summary

- Lack of initiation, and lower duration, of BF predicts child/adult obesity
  - Causality in question
  - Measurement?
    - Crude epidemiologic tools
  - Don’t conflate feeding and growth
    - Other determinants of adiposity during infancy

Clinical/Public Health Implications

- Breast feeding is good for other reasons
  - Bonding
  - Increased cognition
  - Prevention of infection/atopy
  - Possible protection against maternal breast cancer
  - Lowers household costs
- No longer justified to actively promote for childhood obesity prevention

Breastfeeding Successes/Challenges

- Overall BF rates rising in US
  - Met Healthy People 2010 goal for initiation
- BF rates lagging among minorities, lower SES
  - Higher rates of obesity
- More effort needed to increase, esp., duration, exclusivity
  - Clinical, public health, policy approaches


MAN, THAT'S GROSS!


May 11, 1998
THE NEW YORKER
Price $3.00

Extra slides

Breastfeeding-Obesity
Clinical/Public Health Implications

- How can breastfeeding be important if initiation rates have risen along with obesity?

Systematic Review #1

- Literature search completed thru 2003
- 3600 references, 96 articles retrieved, 60 of potential relevance
- 27 papers with 28 observations giving crude OR of defined obesity between those breast fed and formula fed
- Preschool age through adult
- 14 with adjustment for potential confounders - SES, parental body size, and smoking

Owen et al., Pediatrics in press

Systematic Review #2

- 954 references, 122 articles retrieved, 72 of potential relevance
- Same 27 papers with 28 observations as in Owen et al.
- Further limited to 9 studies with
  - Age 5-18 years,
  - Outcome as >90^{th}, 95^{th}, or 97^{th} %ile
  - Adjustment for ≥3 of the following covariates
    - SES, parental body size, smoking, birth weight, dietary factors, physical activity

Arenz et al., IJO 2004;28:1247

Characteristics of Studies of Breastfeeding and Later Obesity (n > 1000)

Author	n	Age	Sex	Place	BF/BM Exposure: Dichotomous	BF/BM Exposure: Duration	"Dose response?"
von Kries, 1999	9357	5-6	M/F	Germany	Ever v. never BF	Exclusive BF	Yes
Gillman, 2001	15,341	9-14	M/F	USA	Mostly/only BM v. Mostly/only formula 1st 6 mo.	Any BF	Yes
Hediger, 2001	2685	3-5	M/F	USA	Ever v. never exclusive BF	Exclusive BF	No
Liese, 2001	2108	9-10	M/F	Germany	Ever v. never BF	Any BF; exclusive BF	Yes, both
Armstrong, 2002	32,200	3	M/F	Scotland	BF v. not at 6-8wk	-	-
Toschke, 2002	33,768	6-14	M/F	Czech	Ever v. never BF	Any BF	No (Yes only for > 90th %ile)
Victora, 2003	2250	18	**M**	Brazil	-	Any BF; predominant BF	No, neither
Li, 2003	2584	4-18	M/F	UK	-	Any BF	No
Bergmann, 2003	**480**	6	M/F	Germany	BF ≥ 3 v. < 3 mo.	-	-
Parsons, 2003	9287	**33**	M/F	UK	BF > 1 mo. v. never	-	-
Grummer-Strawn, 2004	177,304	4	M/F	USA	-	Any BF	Yes (whites only)

Breastfeeding Duration– Obesity
GUTS Sib-Pair Analysis

- Within-family analysis
  - Exposure variable
    - Breastfed longer or shorter than mean of sibship (avg. differential 3.7 mo)
  - Outcome
    - BMI exceeding 85^{th} %ile for age and sex
- Compared with overall (not within-family) analysis
  - Continuous BF duration exposure variable (per 3.7 mo)

Statistical Analysis

- Based on intention to treat
- MIXED and GLIMMIX in SAS: multilevel models account for clustering within polyclinics
- Models permit inference at individual level
- Multivariate models
  - Include stratum- (geographic region, urban vs rural) and individual-level covariates
  - Results virtually identical to simpler models

PROBIT II

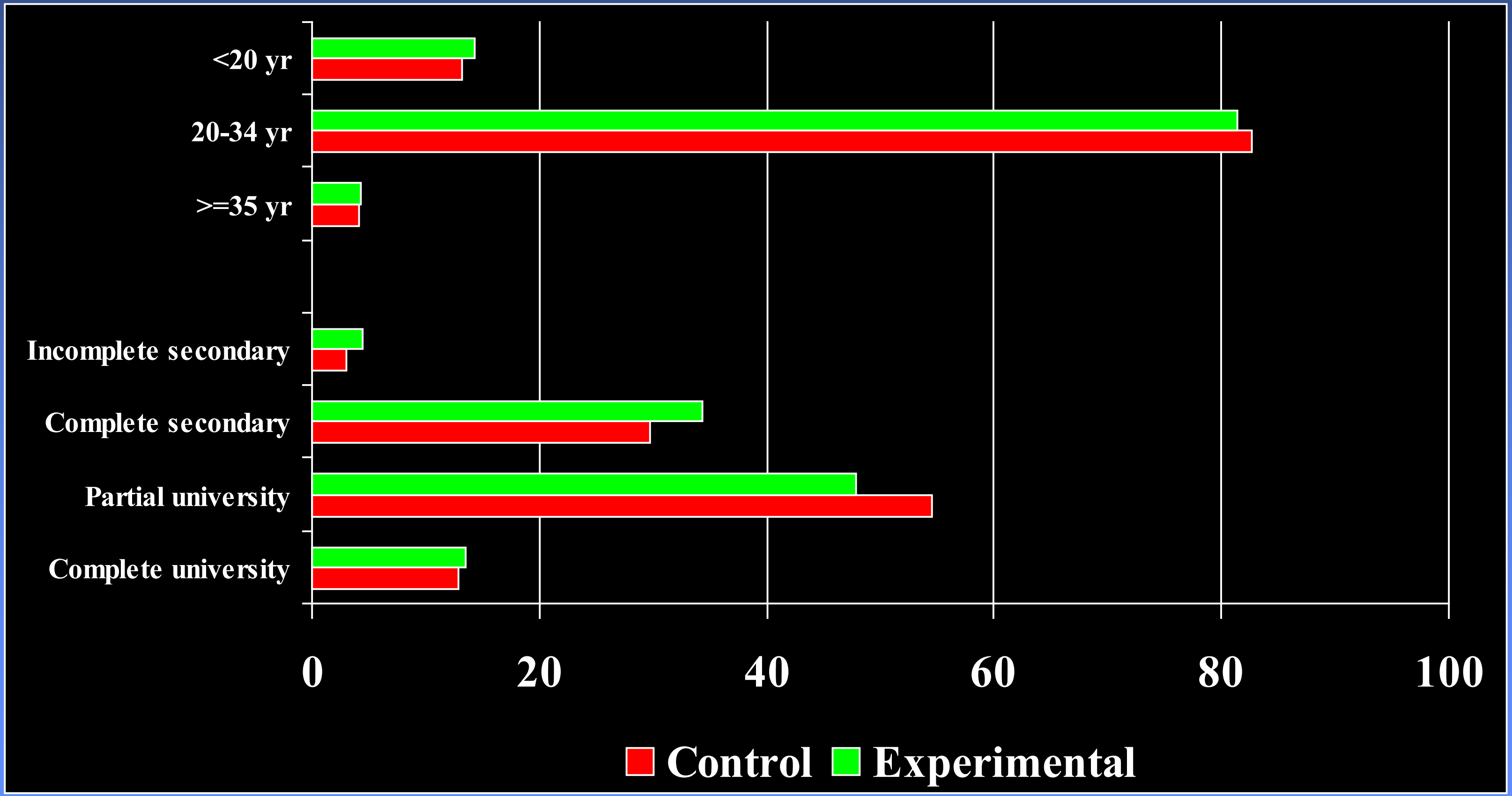
- PROBIT resulted in 2 cohorts that differed substantially in exclusivity/duration of BF
  - These cohorts were created by ***randomization***, not choice of mother or doctor
  - This enables ***strong causal inferences*** with respect to BF effects on long-term outcomes
- PROBIT II: a unique scientific opportunity
- Funded by CIHR in 2002
- Data collected December 2002 to April 2005

PROBIT II: Objective

- To examine the causal relation between prolonged/exclusive BF and important health outcomes at early school age (6.5 years)
  - ***Growth (including height and adiposity)***
  - ***Blood pressure***
  - Allergy, asthma, hay fever, and atopic eczema
  - Cognitive ability (IQ, academic performance)
  - Behavior
  - Dental health
- n=13,889 followed up (81.5% of randomized)

Baseline Comparison (%)

Experimental (n=7,108) vs Control (n=6,781)



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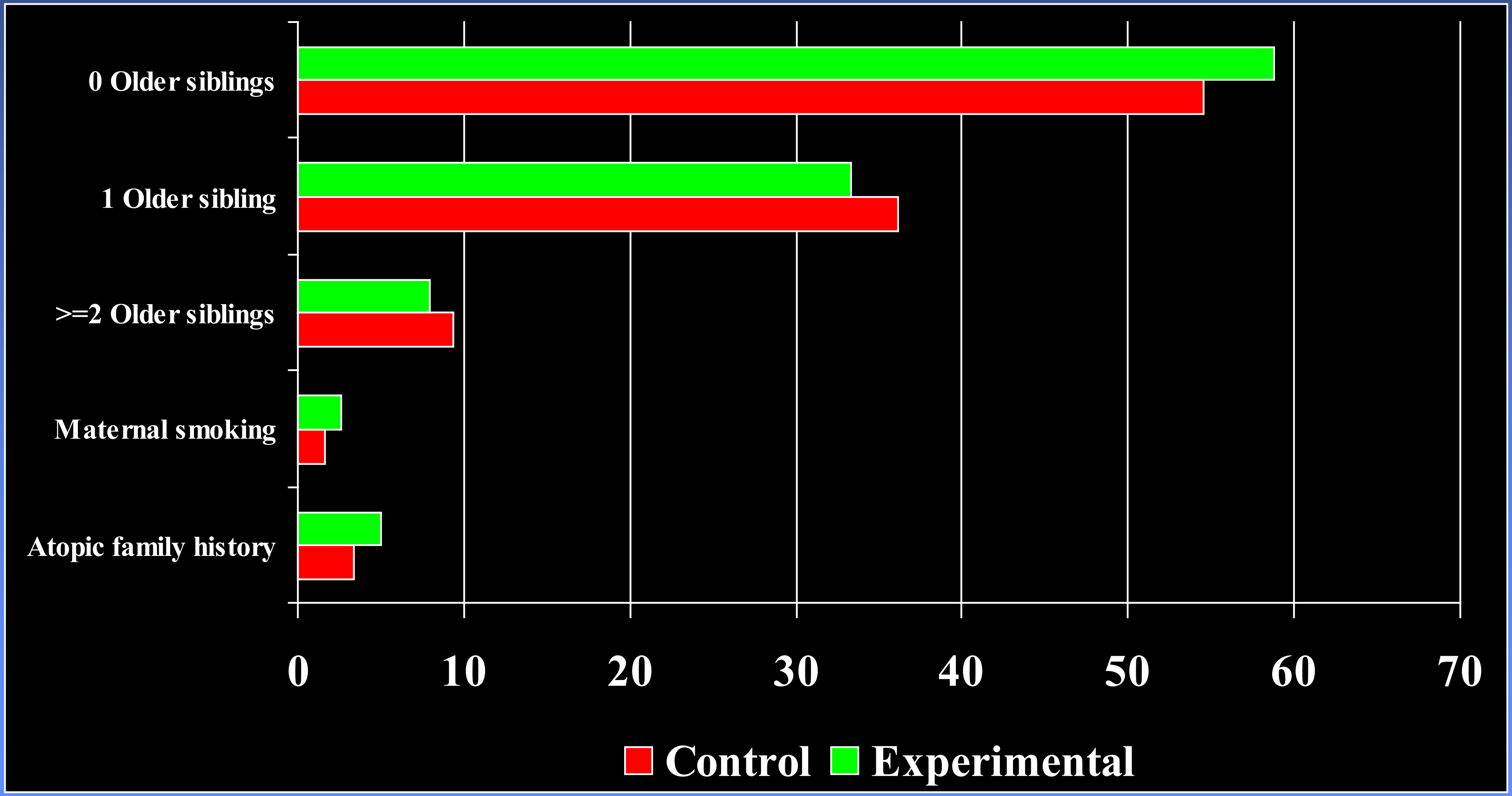
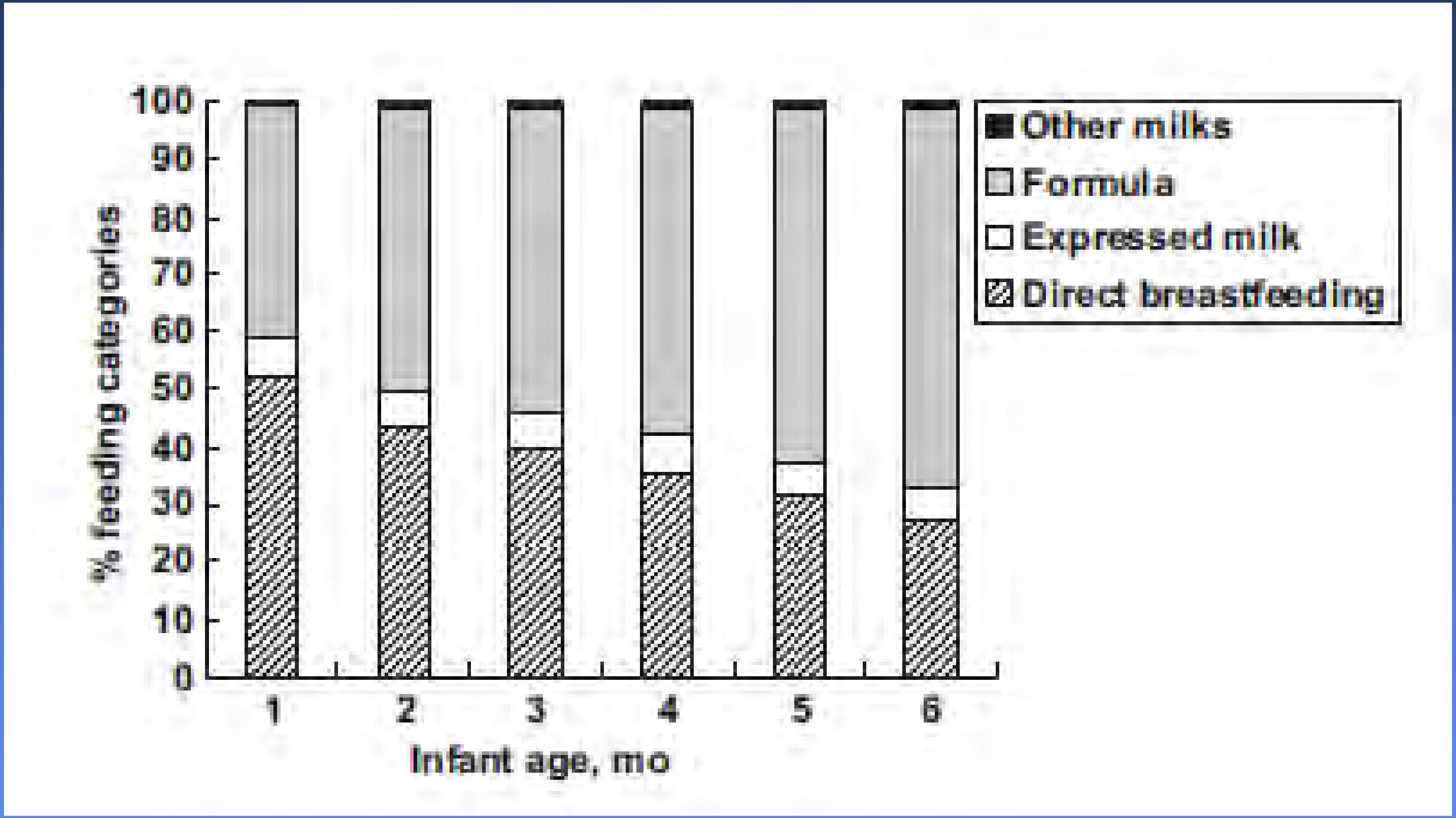


Data Quality

- Anthropometric, BP measurements in duplicate
- BP measured using digital oscillometric device
- Blinding of study pediatricians was infeasible
- 5 children per pediatrician randomly selected for audit (total n=190)
- Audit: 18 (5-33) mo after primary data collection

Audit Results

Anthro/BP	r (95% CI)



R. Li et al., Pediatrics 2010

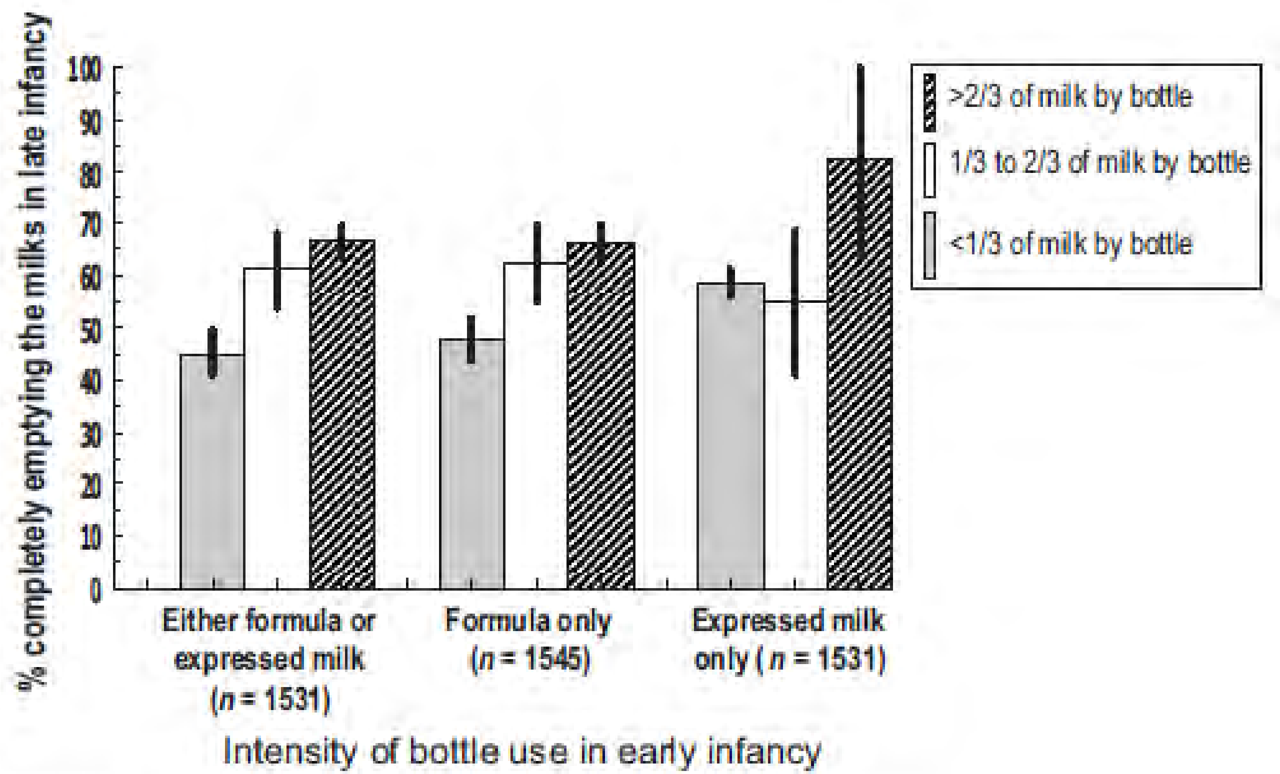
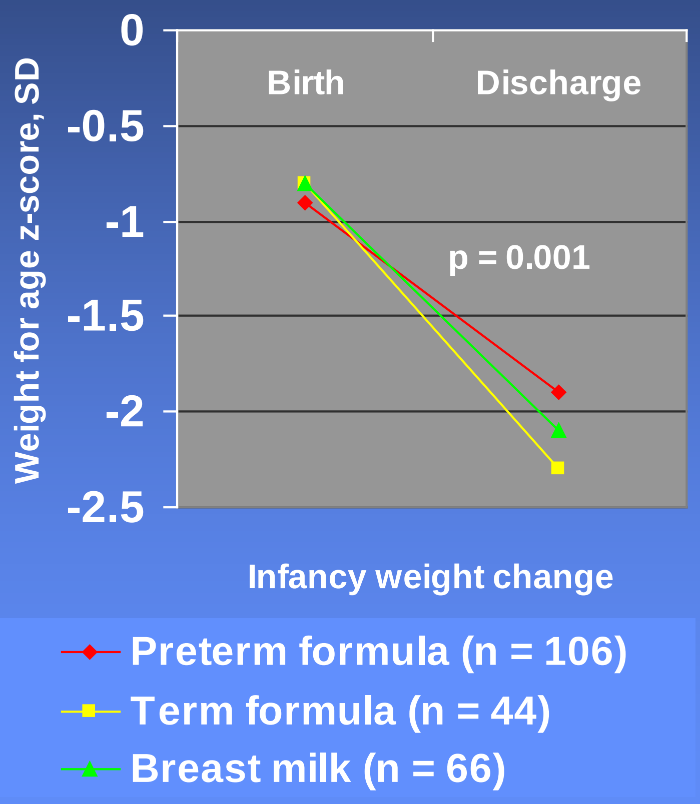


FIGURE 2

Percentage of infants completely emptying the milk in the bottle or cup in late infancy according to intensity of bottle use in early infancy. A confidence interval of 95% is indicated by the line on each bar.

R. Li et al., Pediatrics 2010; 125:s1386

Breast Milk, Early Growth, and Insulin in Adolescents



Singhal et al., Lancet 2003

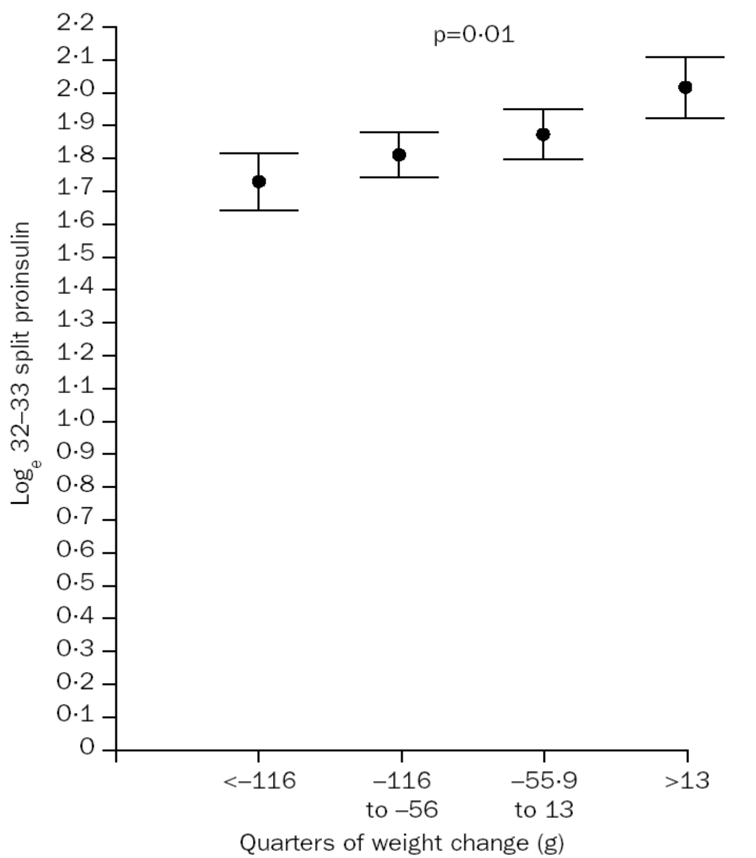


Figure 2: **Fasting 32–33 split proinsulin concentrations according to quarters of the distribution of weight change in the first 2 postnatal weeks in adolescents born preterm**
Data analysed by linear regression. Error bars are 95% CI.

Breastfeeding-Obesity

Can It Explain Infant Growth Findings?

- Faster early infant growth associated with later obesity
- Breastfeeding leads to slower infant growth
- RCTs of premies suggest long-lasting beneficial effects of breast milk
- But epidemiologic studies suggest clear effect of breastfeeding on obesity only after 4-6 months duration

Breastfeeding-Obesity

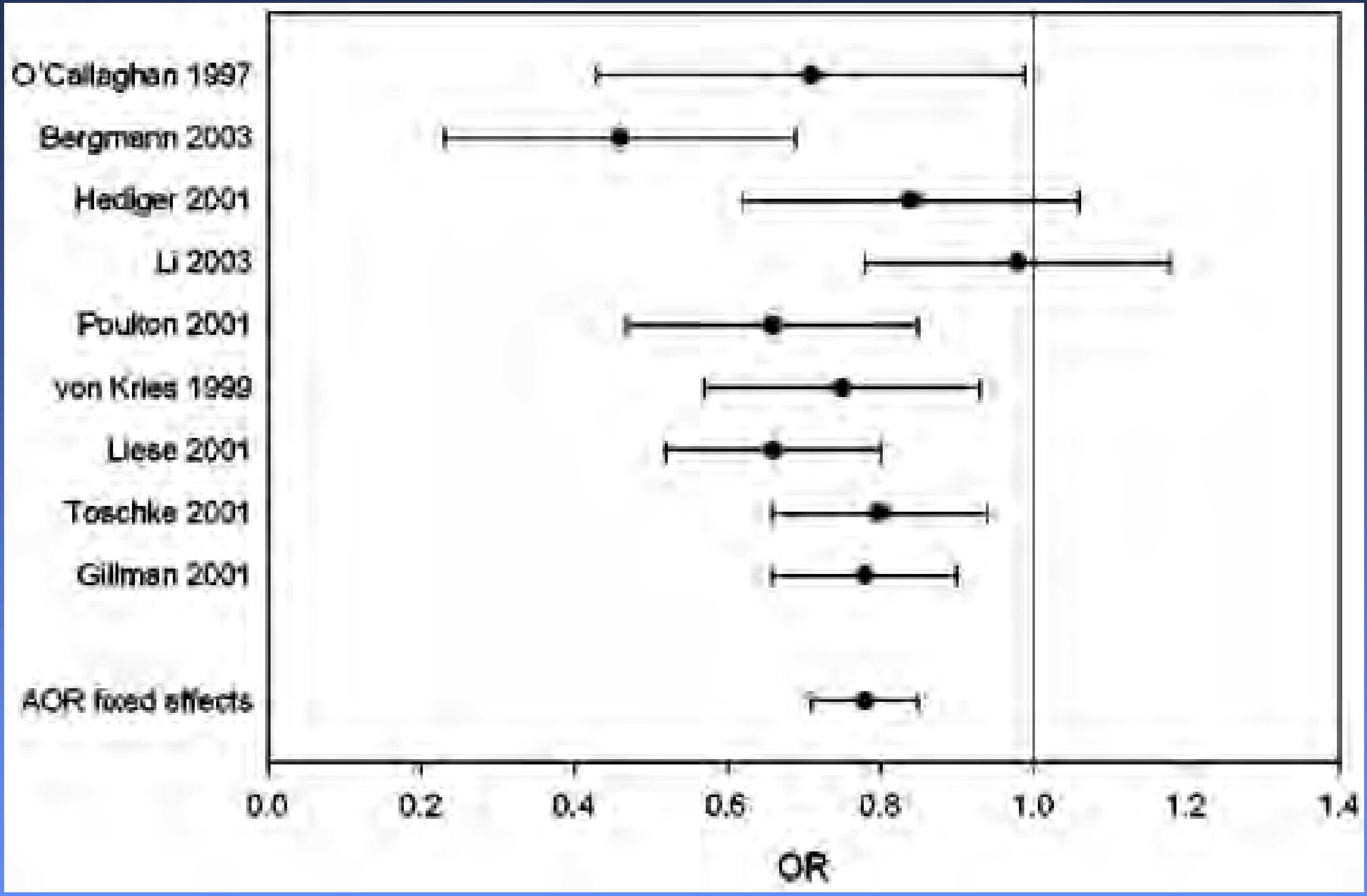
Can It Explain Infant Growth Findings?

- Faster early infant growth associated with later obesity
- Breastfeeding leads to slower infant growth
- RCTs of premies suggest long-lasting beneficial effects of breast milk
- But epidemiologic studies suggest effect of breastfeeding on obesity only after 4-6 months duration
- Jury still out

Today

- Breastfeeding effects
  - On child's obesity
  - On mother's obesity/CVD/DM
- Maternal obesity and breastfeeding success
- Trends in breastfeeding in US
- Intergenerational cycle?
  - Maternal obesity → lower BF → child obesity…
- Clinical, public health, research implications

Odds ratio of obesity: Breast v. formula fed



Adjusted Odds Ratio 0.78 (95% CI 0.71, 0.85)

Arenz et al., 2004

Maternal Obesity and Reduced Breastfeeding Success

- Obese mothers
  - Initiate BF at lower rates
  - Have shorter durations
- Reasons?

Maternal Obesity and Reduced Breastfeeding Success

- Psychosocial factors
  - Lower SES, lower intention to BF
  - Possible body image dissatisfaction

Maternal Obesity and Reduced Breastfeeding Success

- Anatomic
  - Large breasts
  - Hard to latch

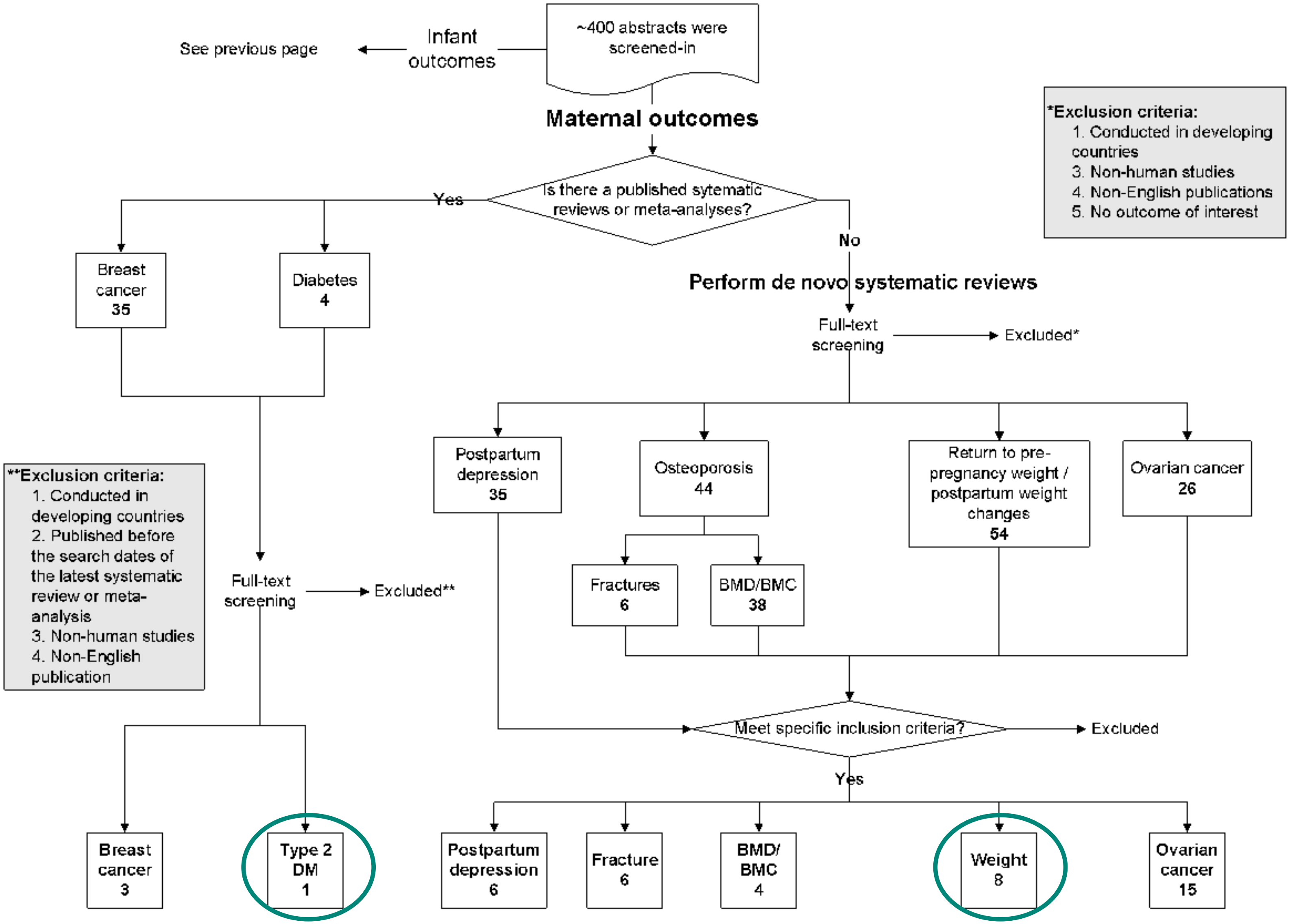
Maternal Obesity and Reduced Breastfeeding Success

- Biological
  - – Poor lactogenesis
  - – Related to prolactin response?
  - – In cows, childhood overfeeding reduces lactation performance
    - Timing of obesity in humans never examined

Maternal Obesity and Reduced Breastfeeding Success

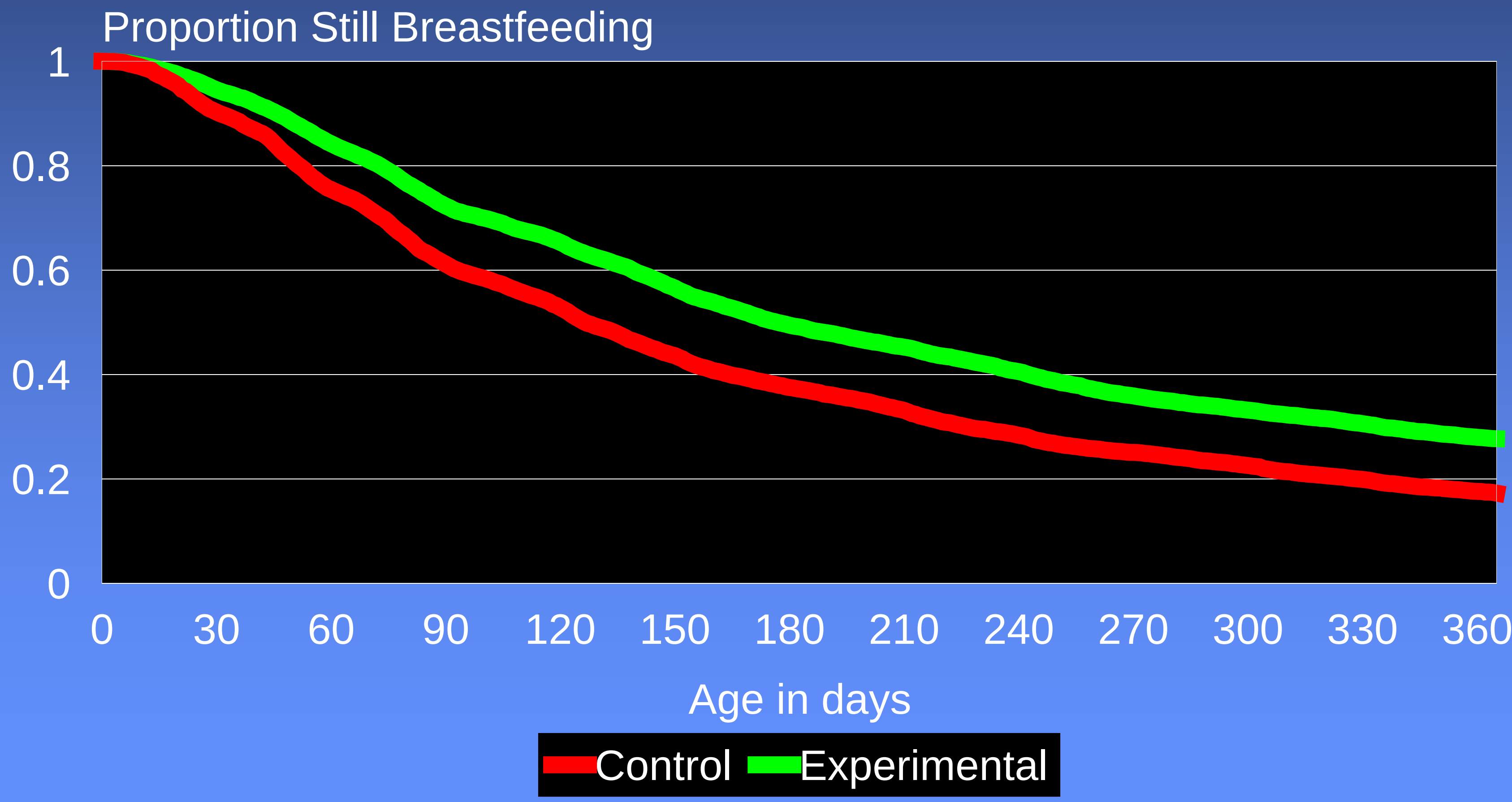
- Medical Conditions
  - Gestational diabetes
  - Cesarean section
  - Macrosomia

Figure 5. Primary studies available to assess the relationship between breastfeeding and maternal health outcomes.



A total of 43 unique studies were included for updates of maternal outcomes

Duration of Breastfeeding



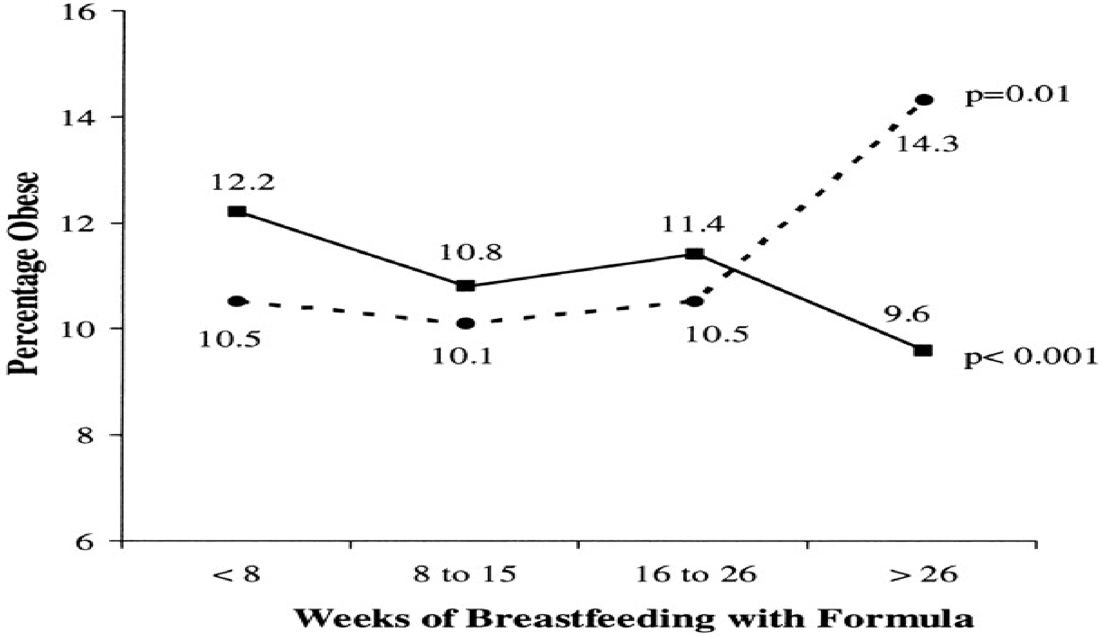
CDC Breastfeeding Report Card
August 2010

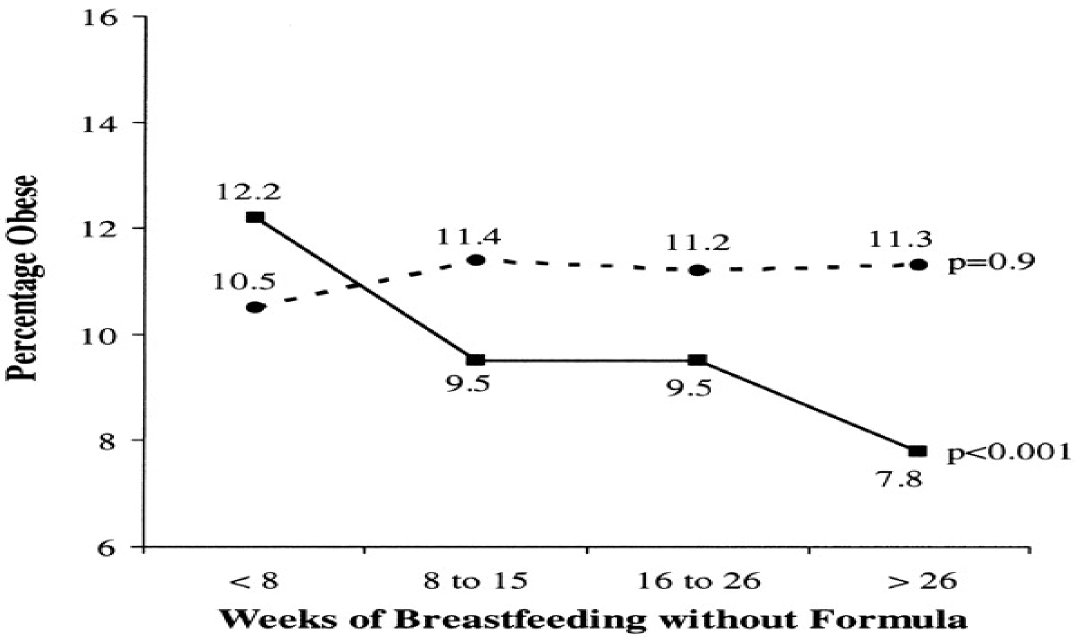
Percent of live births occuring at facilities designated as Baby Friendly (BFHI)	Percent of breastfed infants receiving formula before 2 days of age	Number of IBCLCs* per 1,000 live births	State legislation about breastfeeding in public places
3.78	25.4	2.40	49

State legislation mandating^ employer lactation support	Number of state health department FTEs** dedicated to breastfeeding	Breastfeeding coalition with public website	State child care center regulation supports lactation
16	96.79	42	12

Lactation and Type 2 Diabetes

- 1 study of 2 US cohorts (N > 150,000)
  - Longer duration of lifetime breastfeeding associated with reduced risk of T2DM among parous women without history of GDM.
  - RR 0.84 (0.78-0.91)
  - Nurses' Health Studies—generalizability?





Breastfeeding Duration and Obesity

At Age 4, By race

Black = dashed line

White = solid line

Bogen et al, 2004

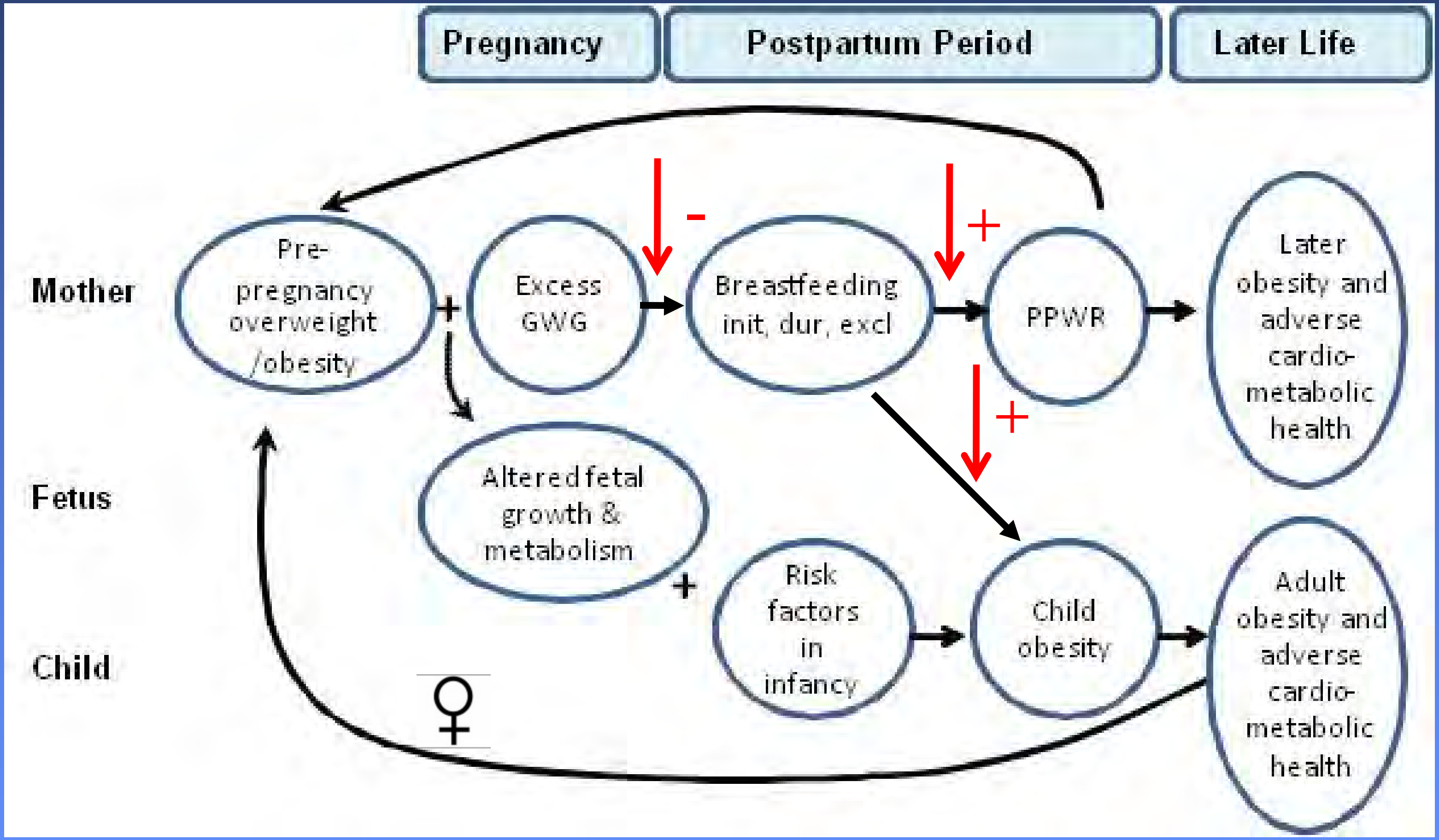
Ohio WIC; n = 73K

Project Viva

A Study of Health for the Next Generation

- Prospective cohort study of pregnant women and their offspring
- Recruitment 4/99-7/02
  - Enrolled in early pregnancy
  - Interviews/questionnaires, medical records, examinations, biomarkers
  - 2128 deliveries

Today



Pregnancy
Postpartum Period
Later Life
Mother
Fetus
Child
Pre-pregnancy overweight /obesity
+
Excess GWG
-
Breastfeeding init, dur, excl
+
PPWR
+
Later obesity and adverse cardio-metabolic health
Altered fetal growth & metabolism
+
Risk factors in infancy
Child obesity
Adult obesity and adverse cardio-metabolic health
♀

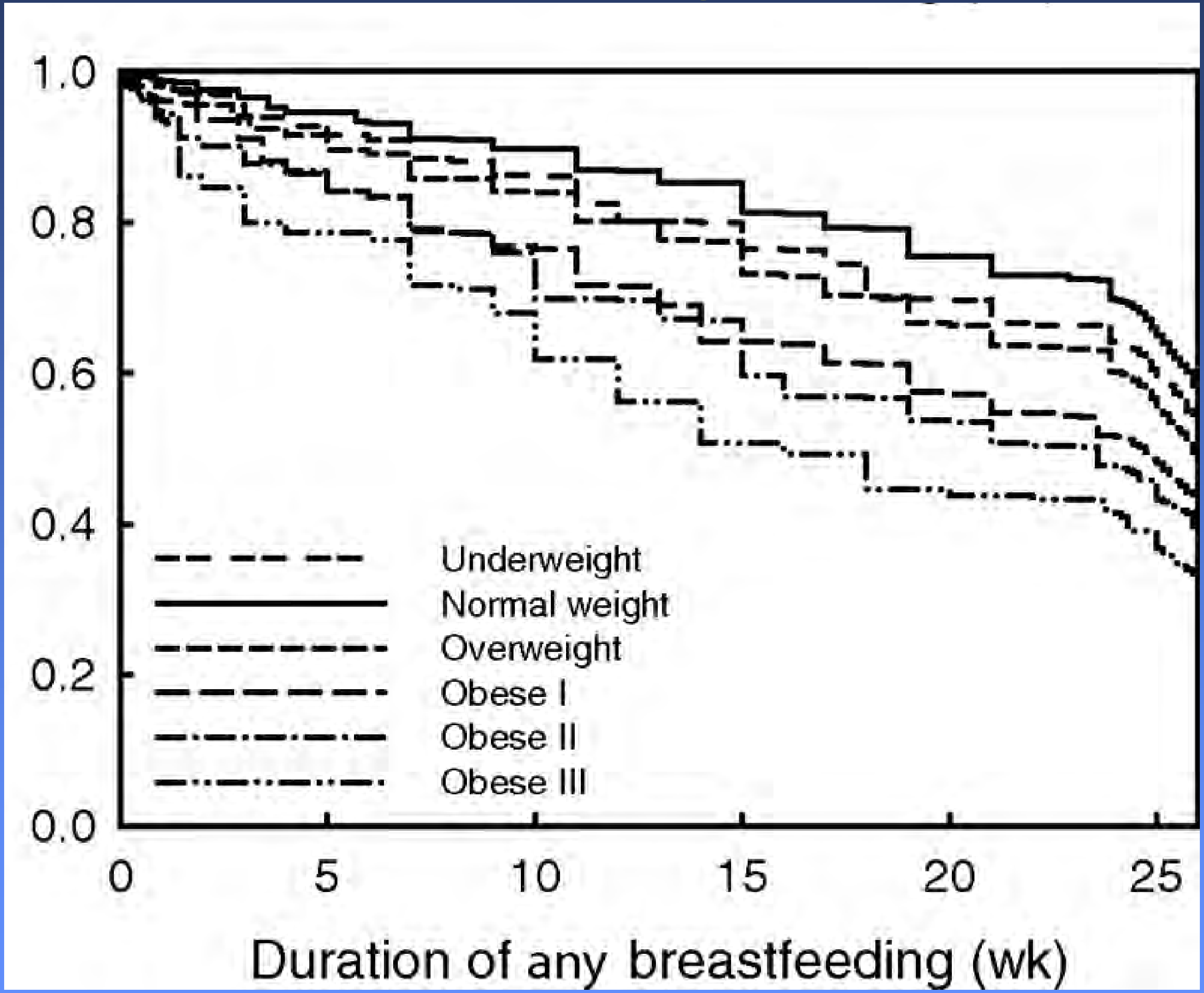

May 11, 1998
THE
NEW YORKER
Price $3.00

Maternal Obesity and Reduced Breastfeeding Success

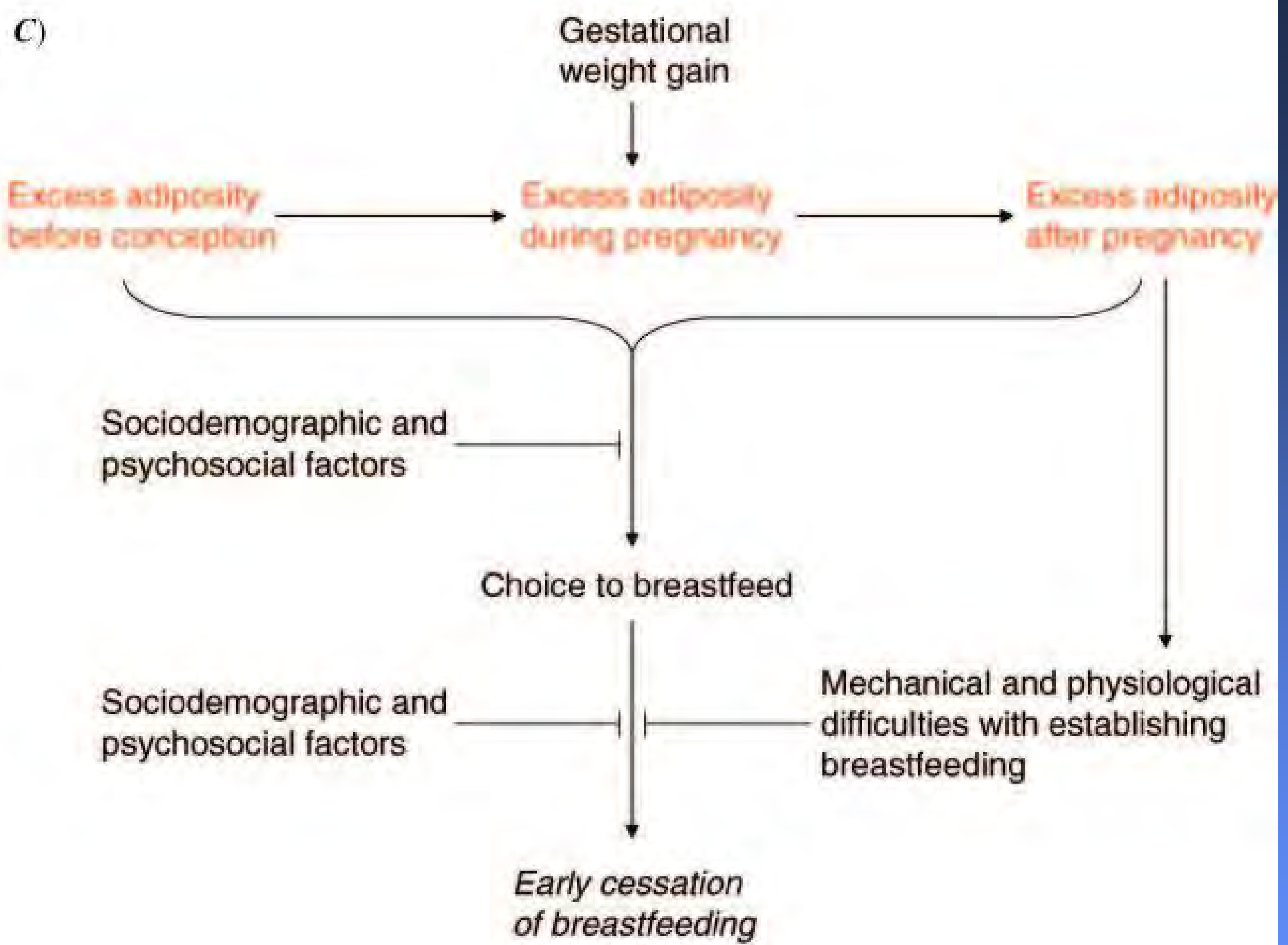
- Systematic review of 13 observational studies
- Obese mothers
  - Initiate BF at lower rates
  - Have shorter durations

Wojcicki, J Womens Hlth 2011; 20:341

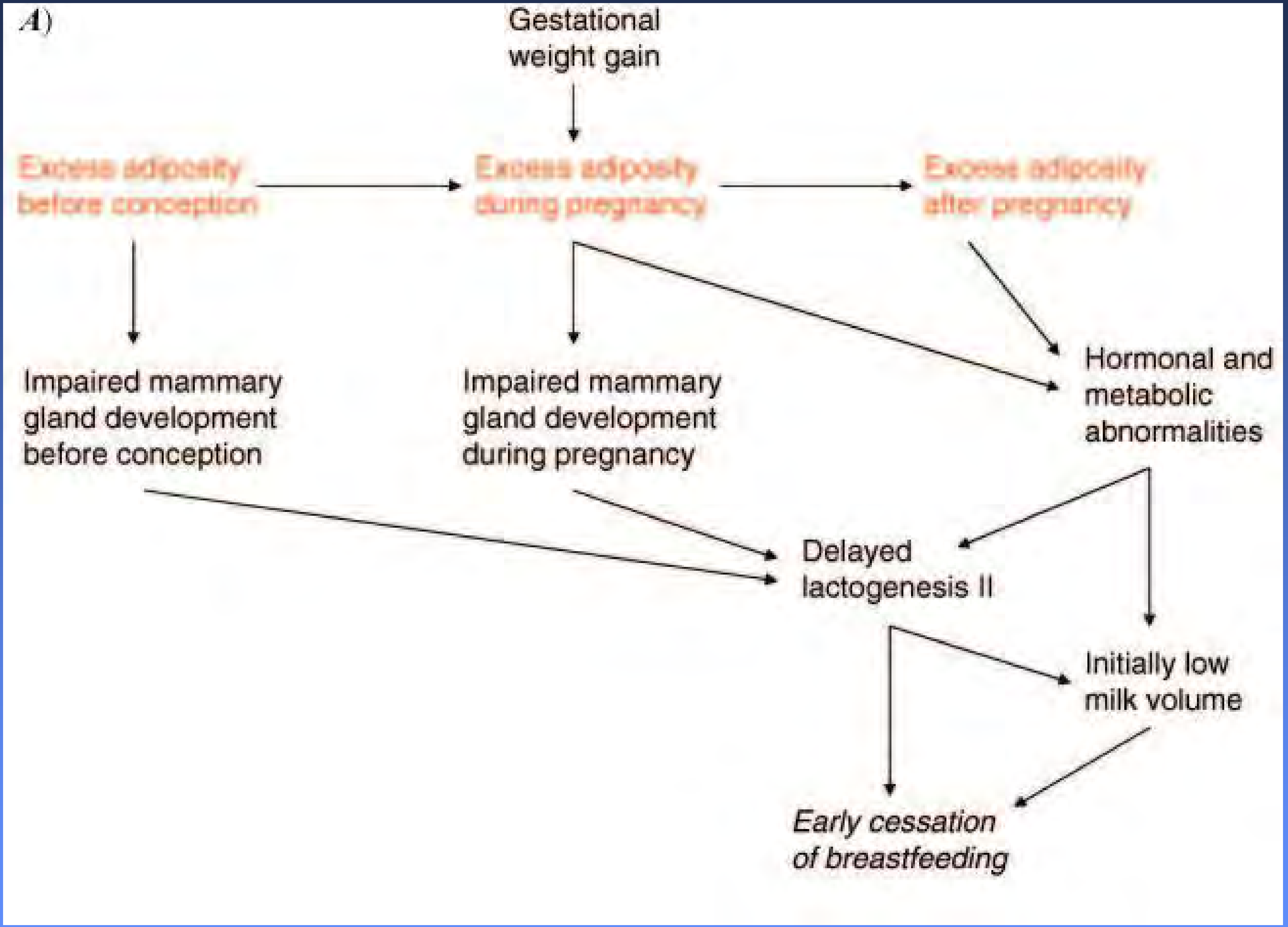
Heavier Danish mothers terminate breastfeeding earlier

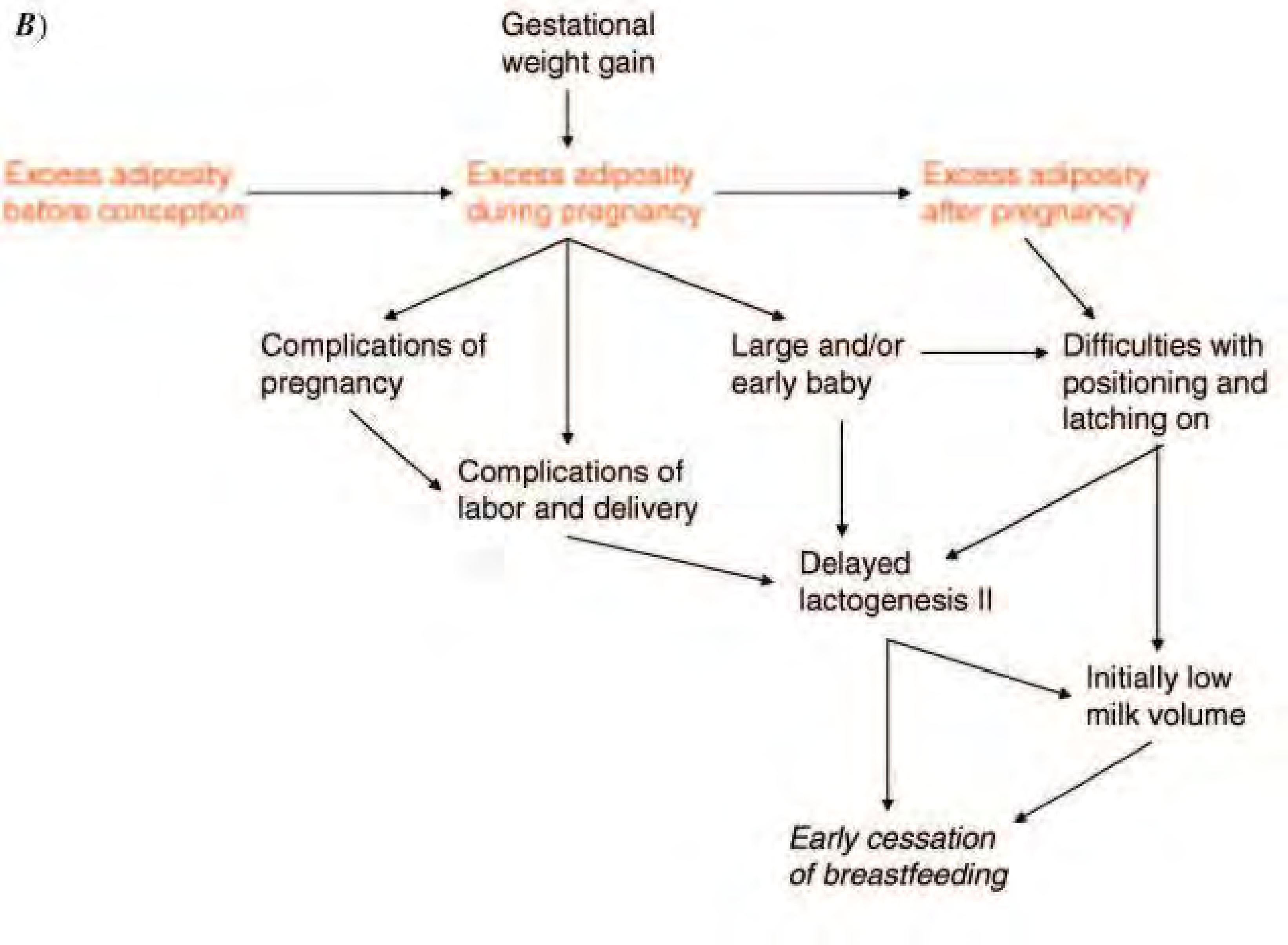


Baker J L et al. Am J Clin Nutr 2007;86:404-411



Rasmussen KM. 2007.
Annu. Rev. Nutr. 27:103–21


A)
Gestational weight gain
Excess adiposity before conception
Excess adiposity during pregnancy
Excess adiposity after pregnancy
Impaired mammary gland development before conception
Impaired mammary gland development during pregnancy
Hormonal and metabolic abnormalities
Delayed lactogenesis II
Initially low milk volume
Early cessation of breastfeeding


B)
Gestational weight gain
Excess adiposity before conception
Excess adiposity during pregnancy
Excess adiposity after pregnancy
Complications of pregnancy
Large and/or early baby
Difficulties with positioning and latching on
Complications of labor and delivery
Delayed lactogenesis II
Initially low milk volume
Early cessation of breastfeeding

Maternal Obesity and Reduced Breastfeeding Success

- Even after controlling for BF intention

  RR for delayed onset of lactogenesis

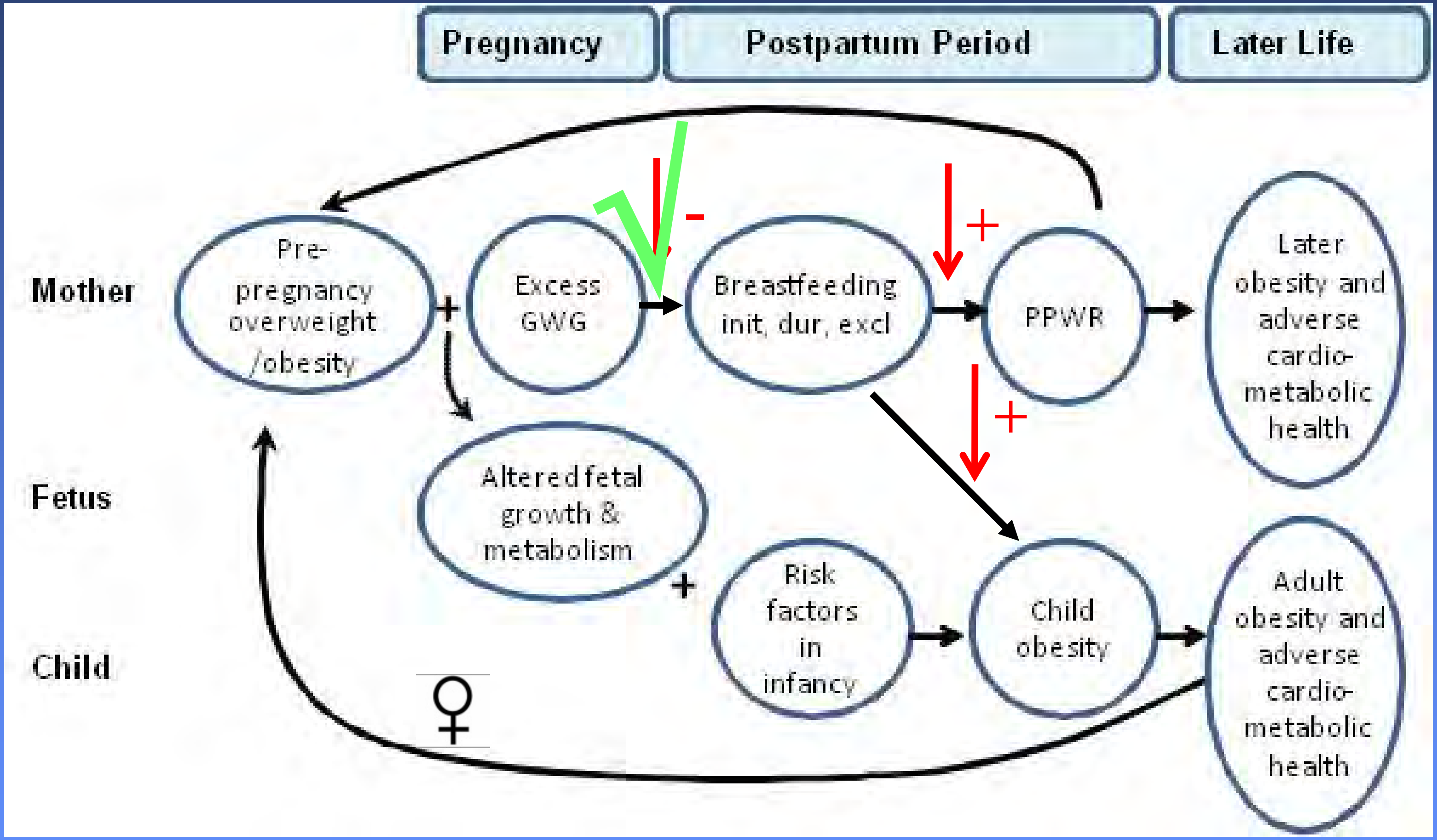
  1.52 (1.13, 2.11) for obesity

  1.40 (1.05, 1.92) for overweight

- Other factors
  - Older maternal age
  - Higher birth weight
  - Early BF success
  - Nipple pain

Nomsenn-Rivers et al., Am J Clin Nutr 2010; 92:574-84

Today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Altered fetal growth & metabolism
Risk factors in infancy
Child obesity
Adult obesity and adverse cardio-metabolic health
+
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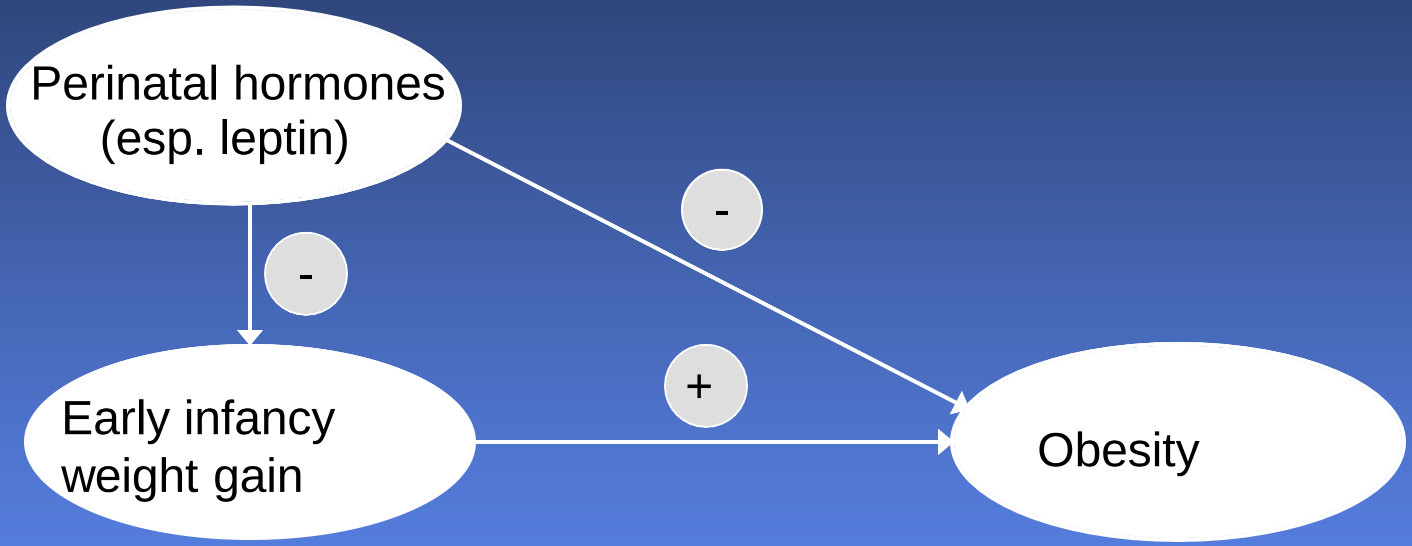
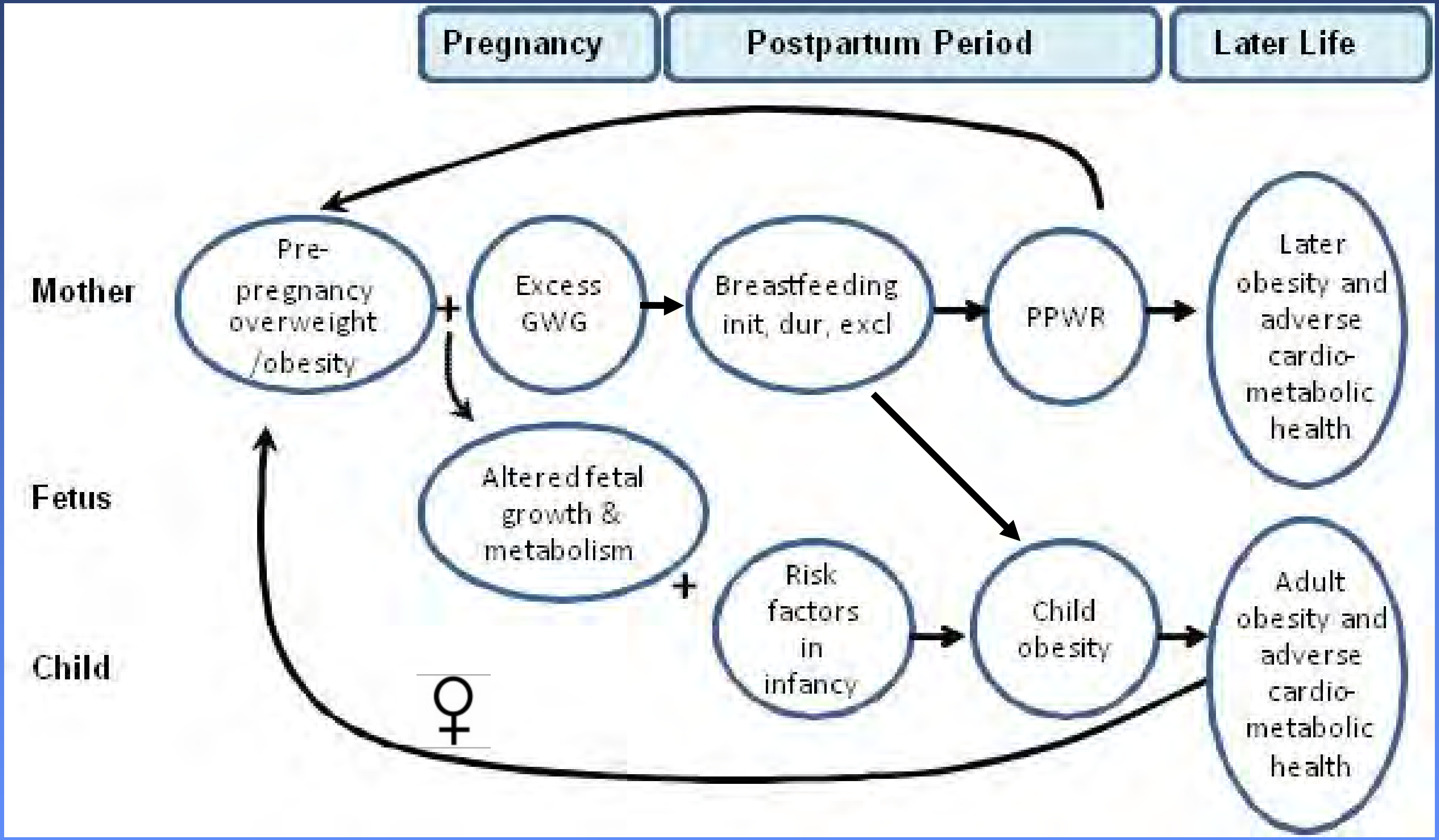

Perinatal hormones (esp. leptin)
-
-
+
Early infancy weight gain
Obesity

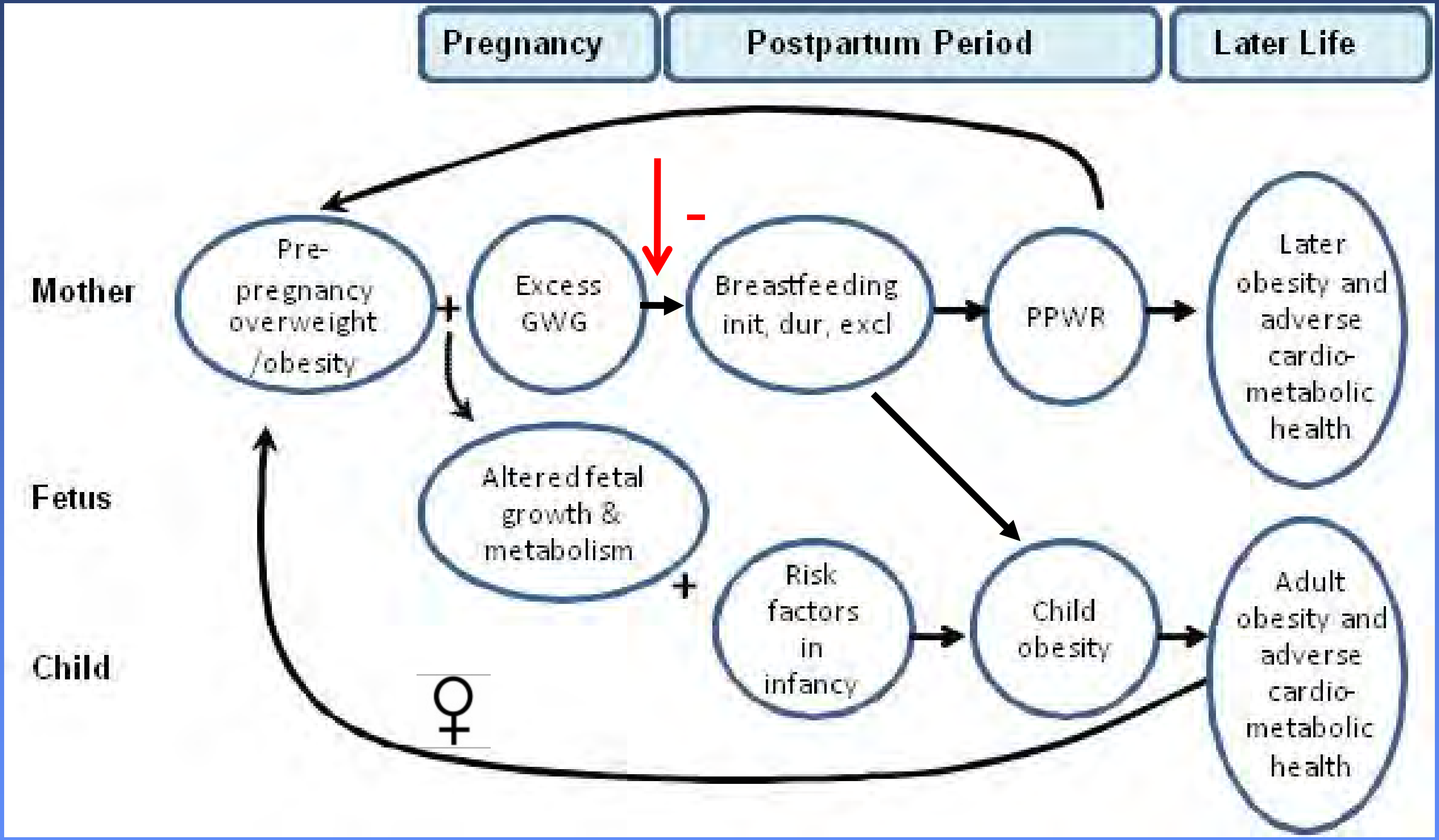
A new look at infancy

- Weight (adiposity?) gain in early infancy predicts later outcomes
- Perinatal hormonal milieu important
- It’s not all infant feeding

Intergenerational cycles of breastfeeding-obesity?



Intergenerational cycles of breastfeeding-obesity?



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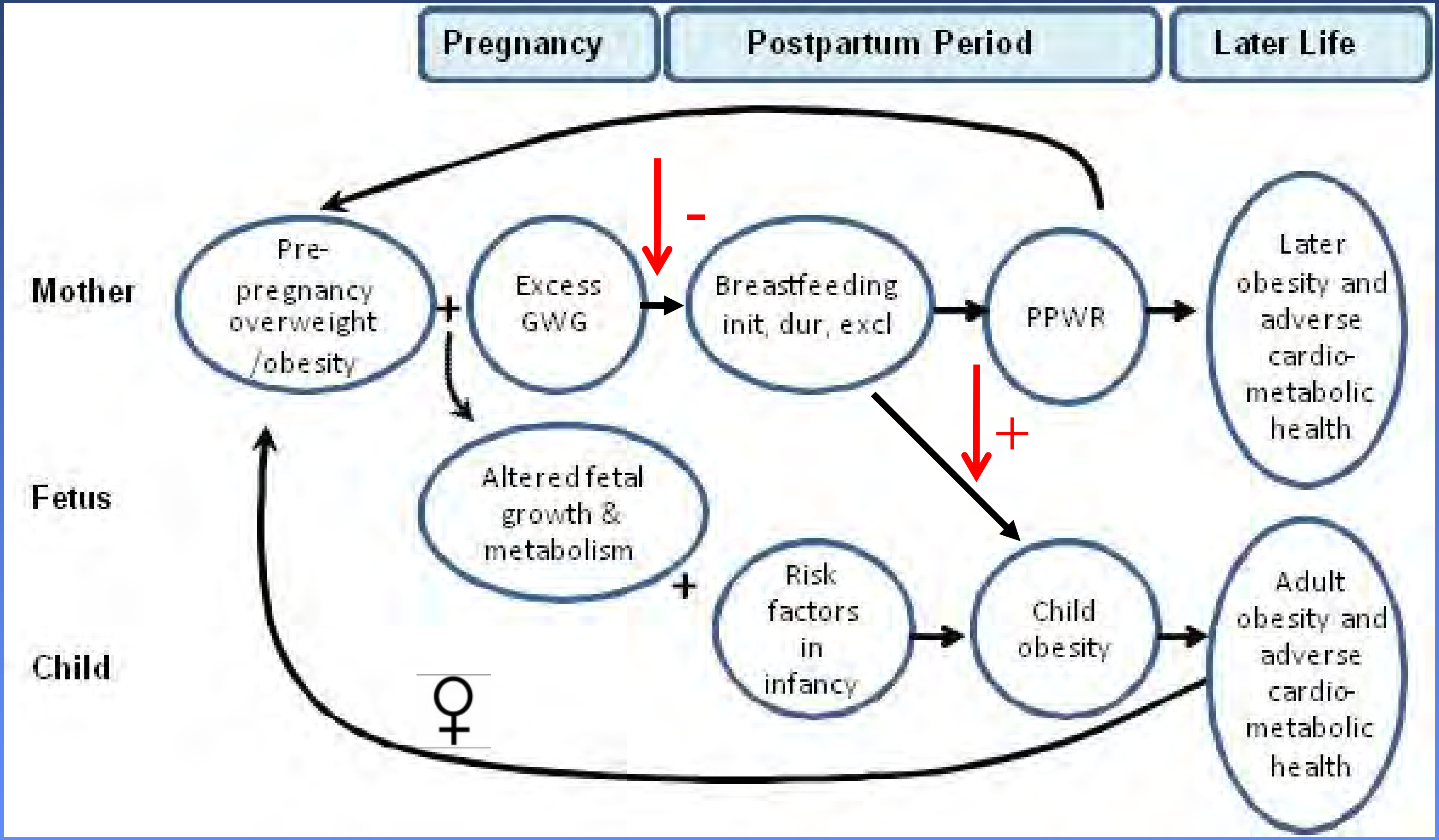

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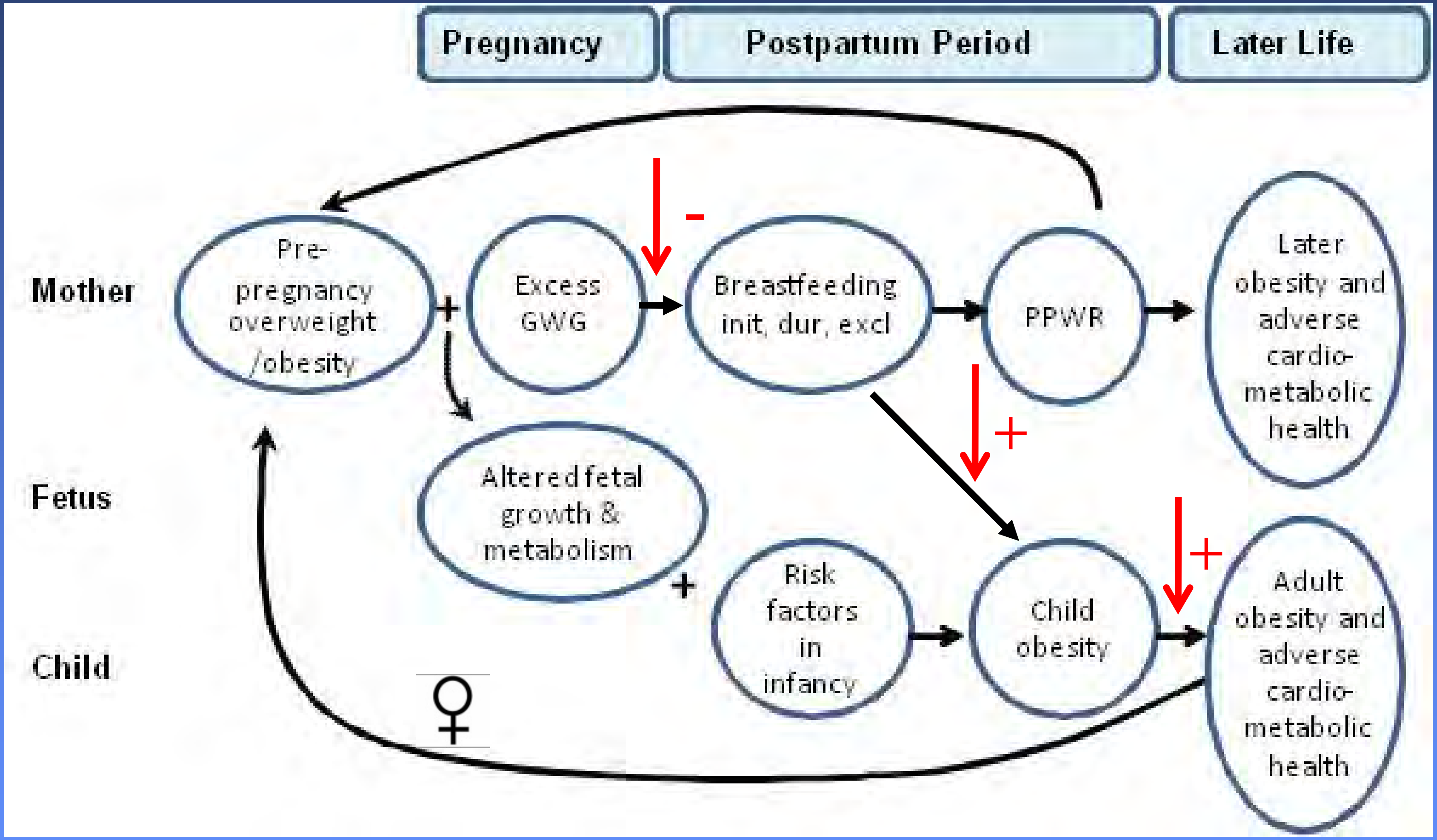

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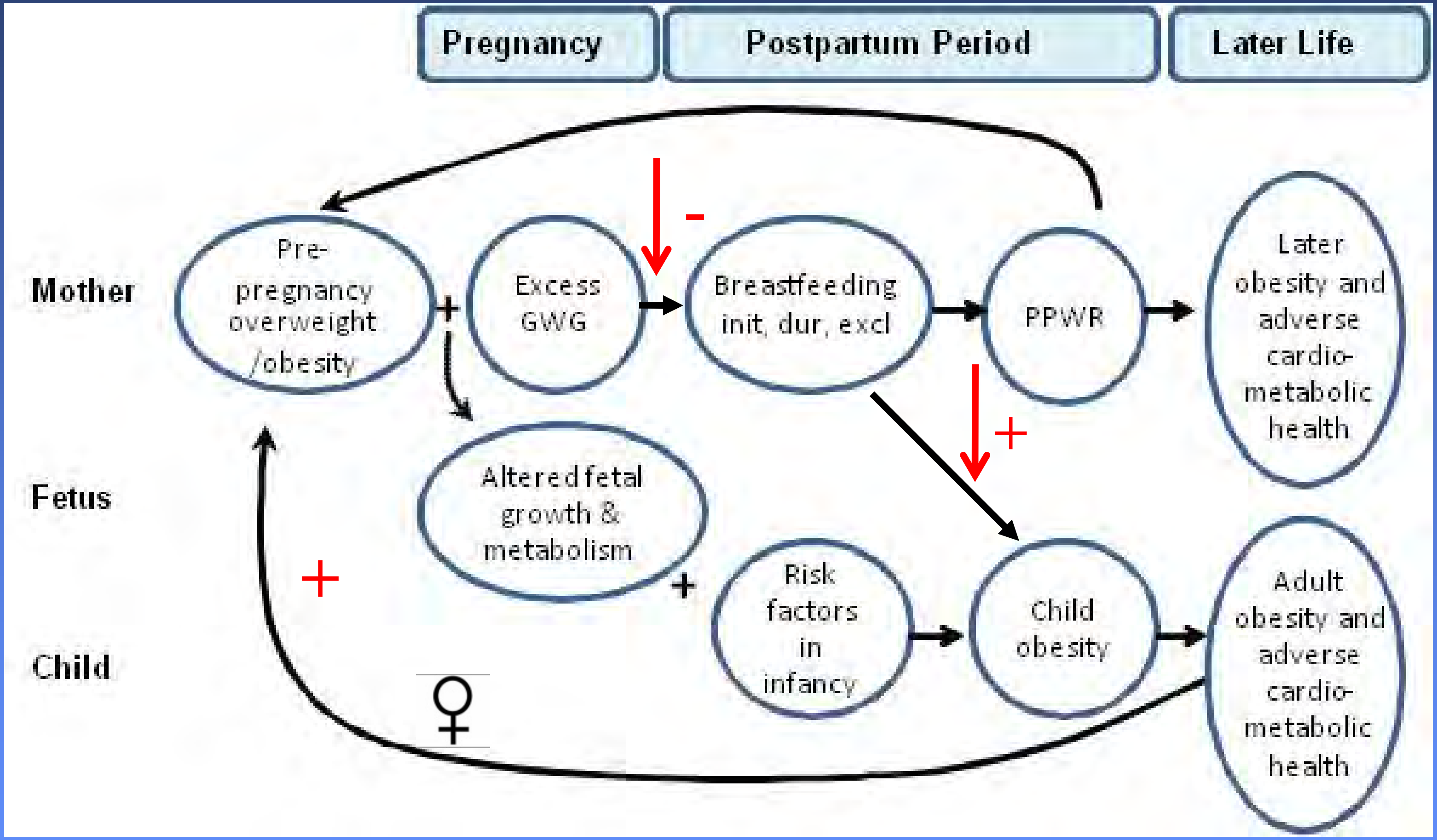

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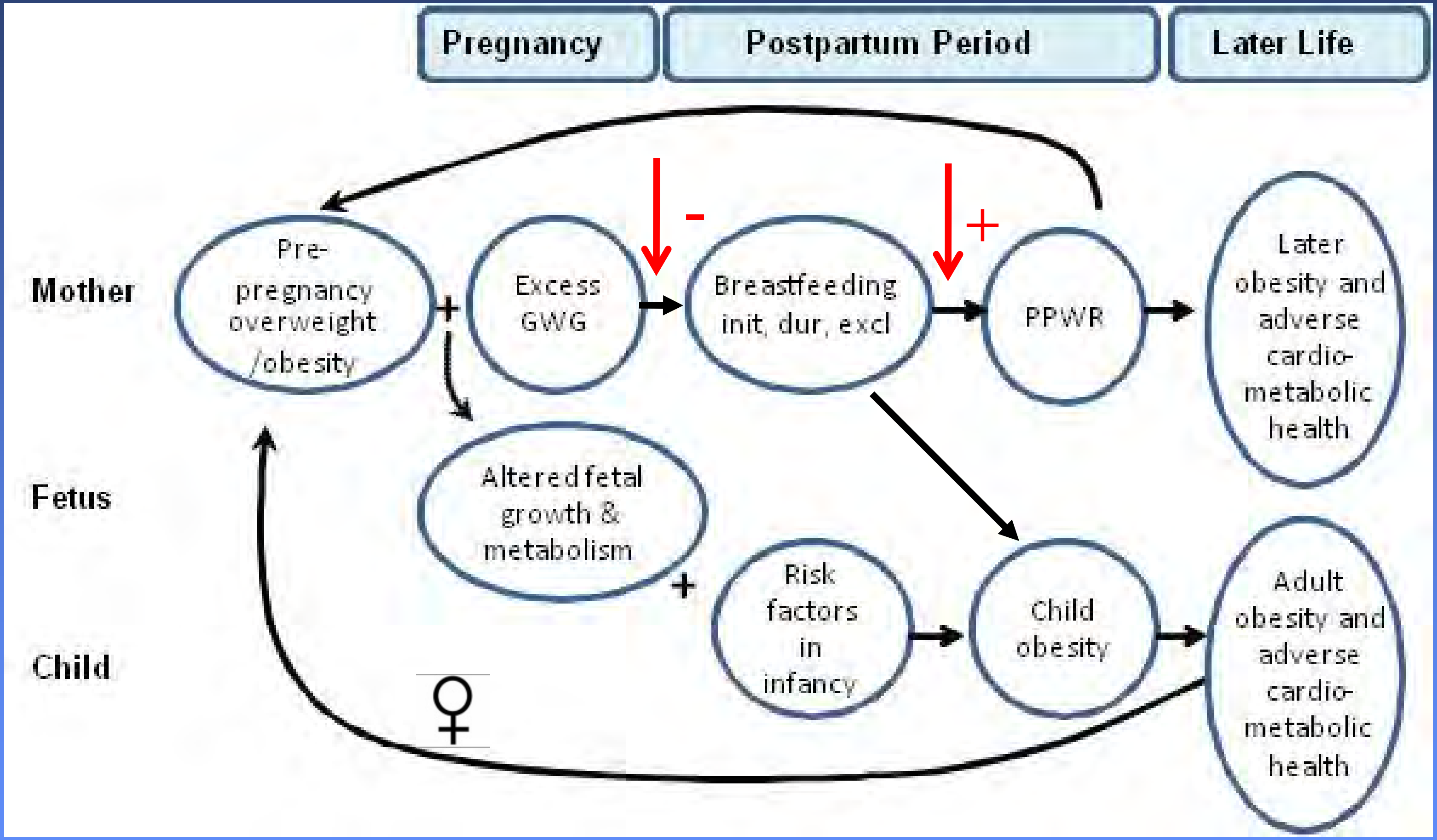

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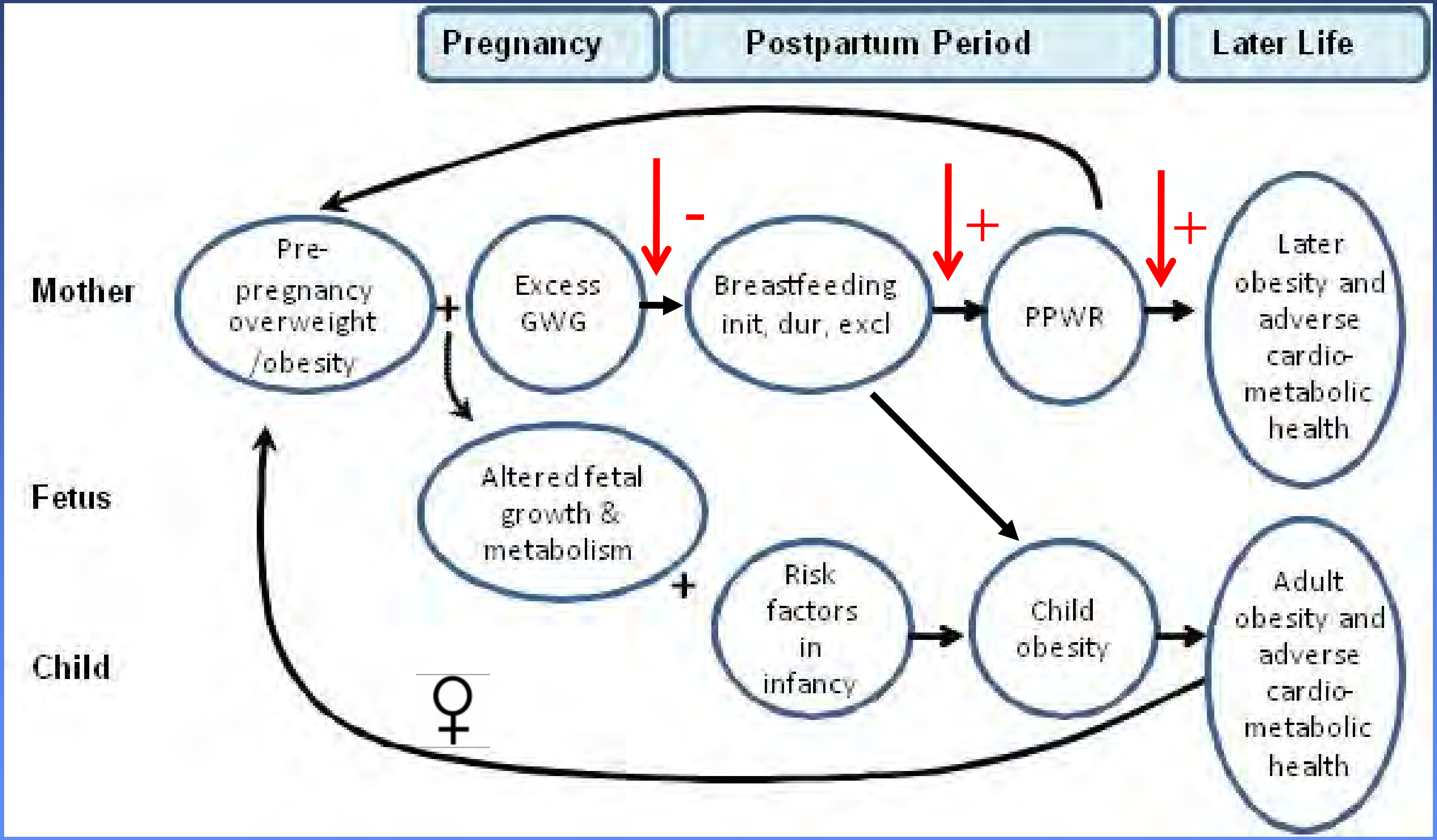
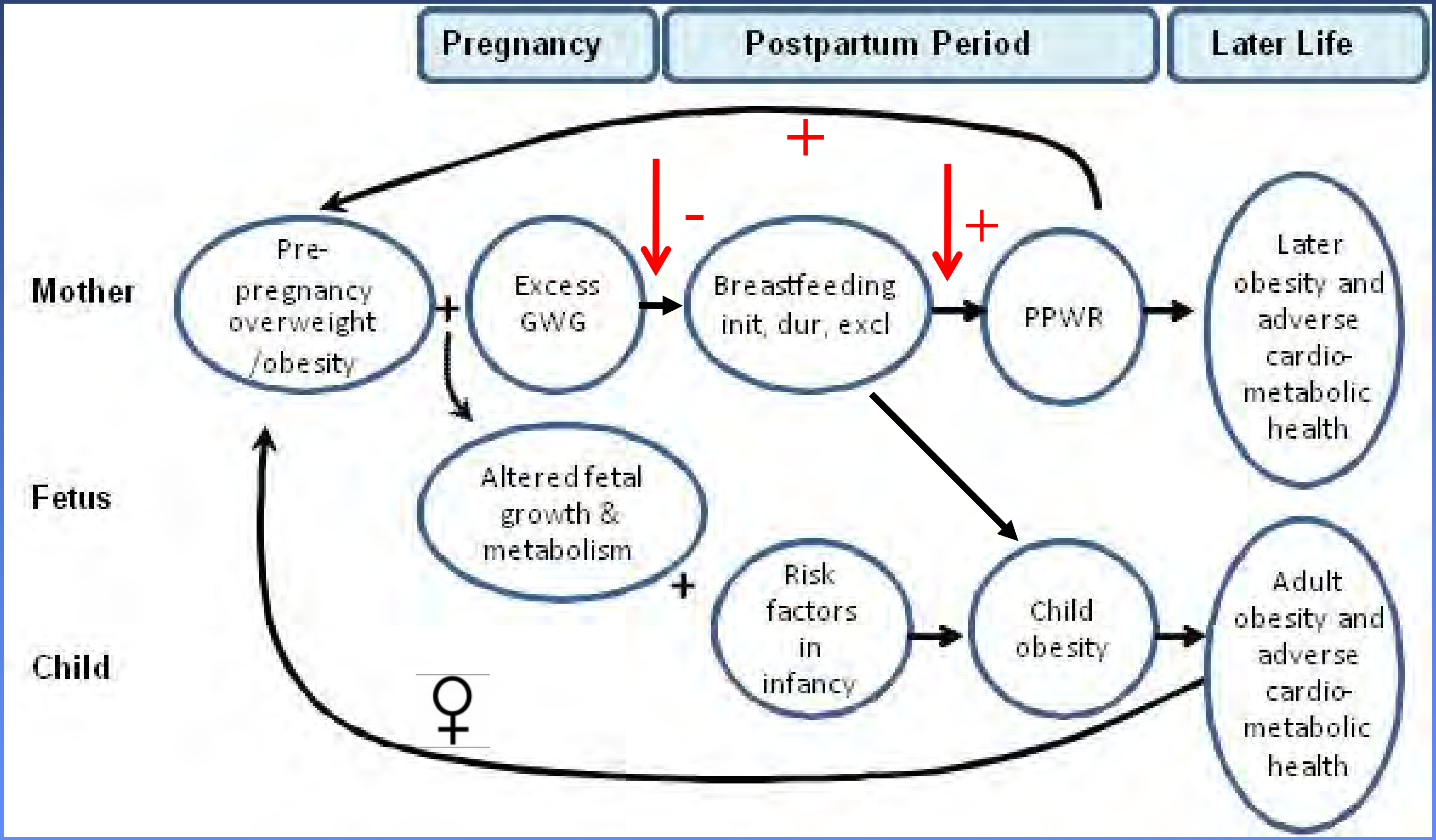
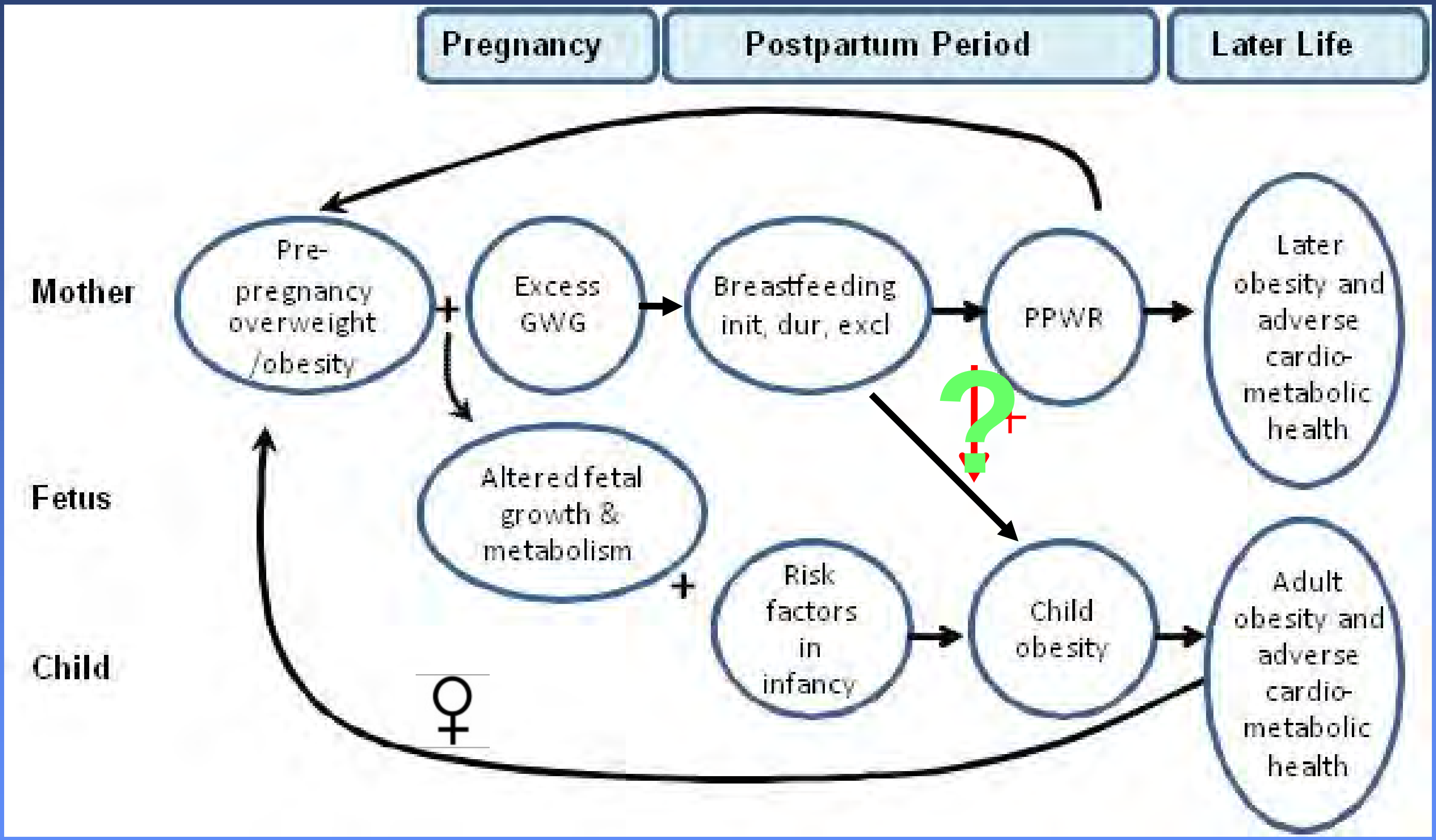


Intergenerational cycles of breastfeeding-obesity?

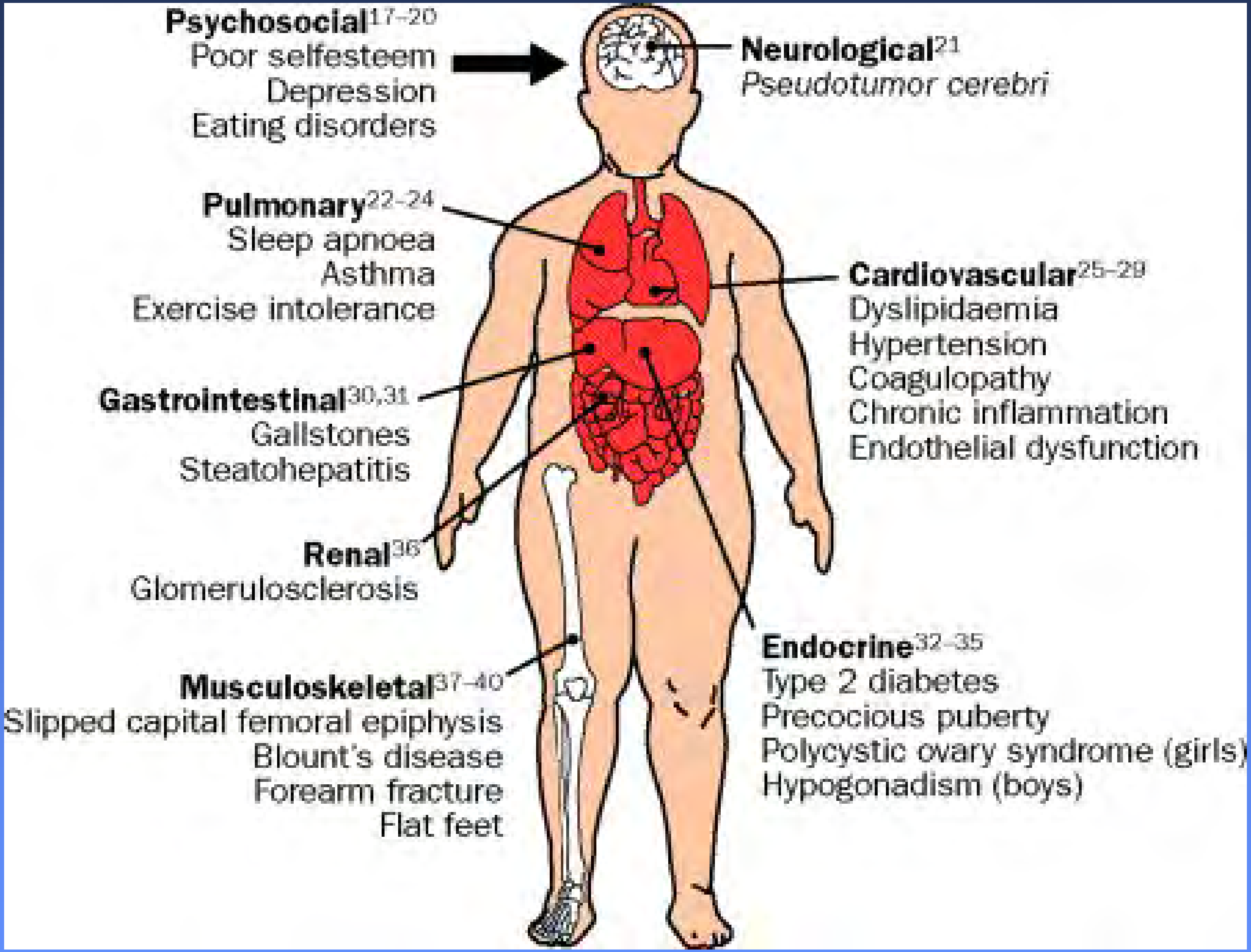


Today

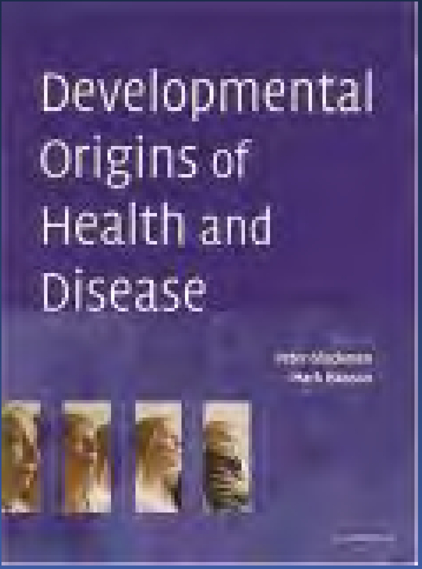


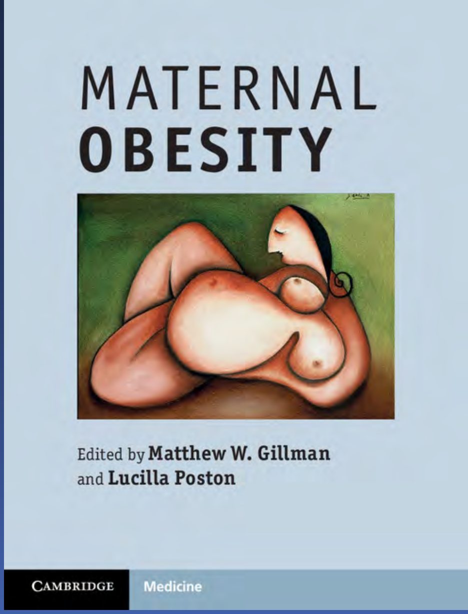
Pregnancy
Postpartum Period
Later Life
Mother
Fetus
Child
Pre-pregnancy overweight /obesity
+
Excess GWG
Breastfeeding init, dur, excl
PPWR
Later obesity and adverse cardio-metabolic health
Altered fetal growth & metabolism
+
Risk factors in infancy
Child obesity
Adult obesity and adverse cardio-metabolic health
?
♀

Medical Complications of *Childhood* Obesity



Ebbeling et al., Lancet 2002





DOHaD

Developmental origins

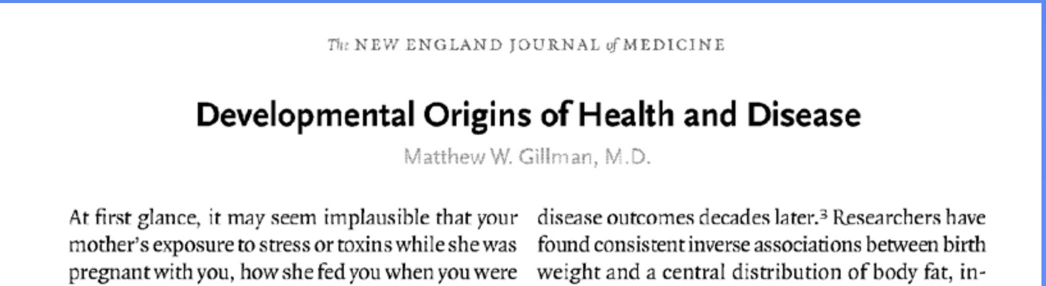
Life course approach

Barker hypothesis

1^{s} 1000 days

Fetal basis

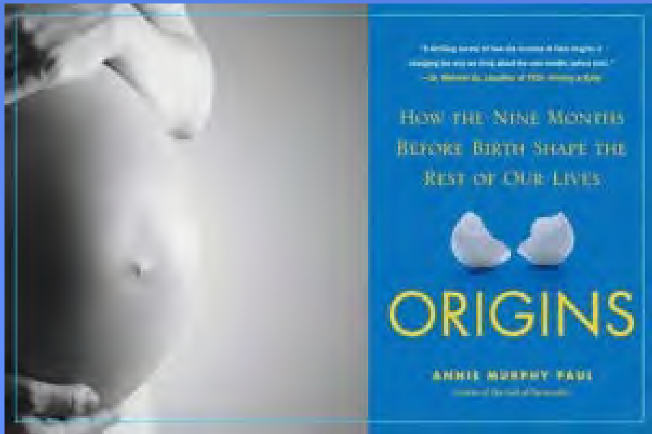
Early origins


The NEW ENGLAND JOURNAL of MEDICINE

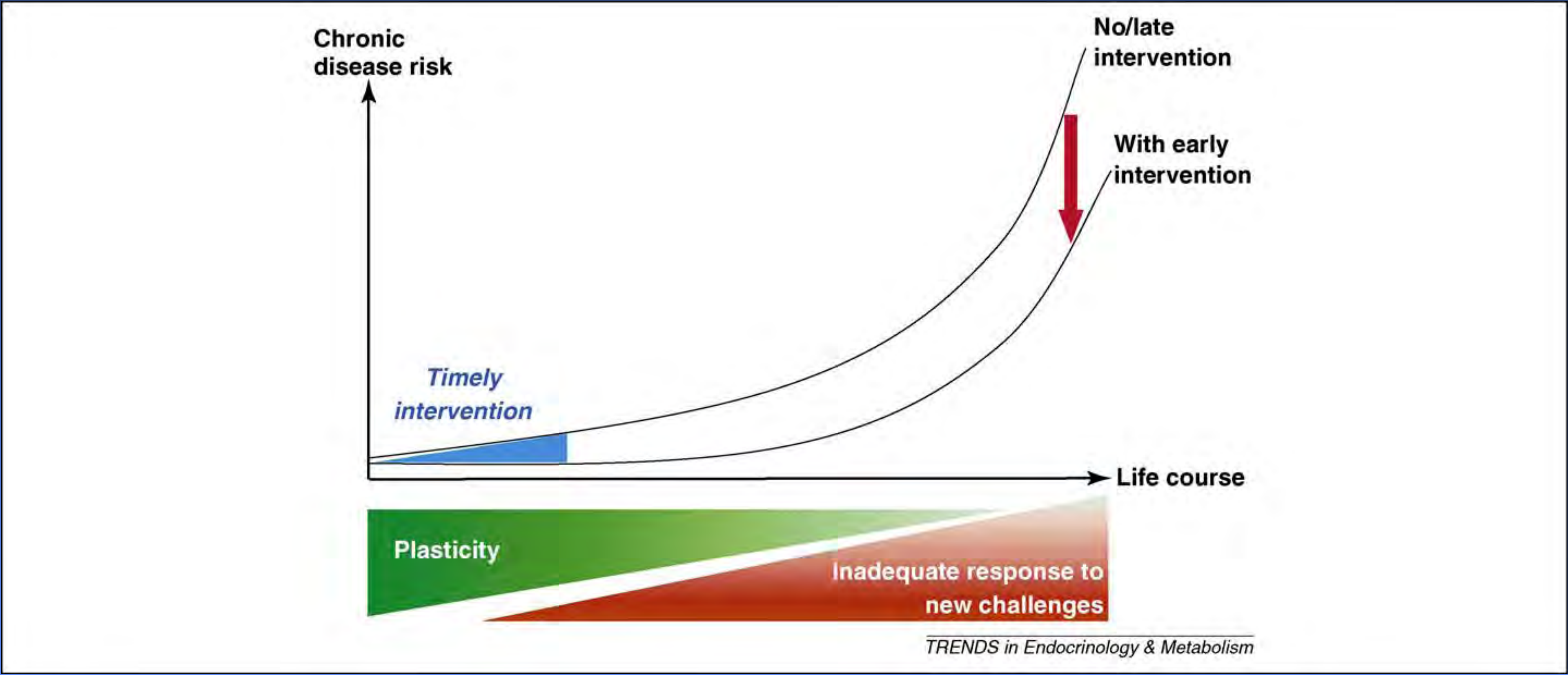
Developmental Origins of Health and Disease

Matthew W. Gillman, M.D.

At first glance, it may seem implausible that your mother's exposure to stress or toxins while she was pregnant with you, how she fed you when you were disease outcomes decades later.[3] Researchers have found consistent inverse associations between birth weight and a central distribution of body fat, in-

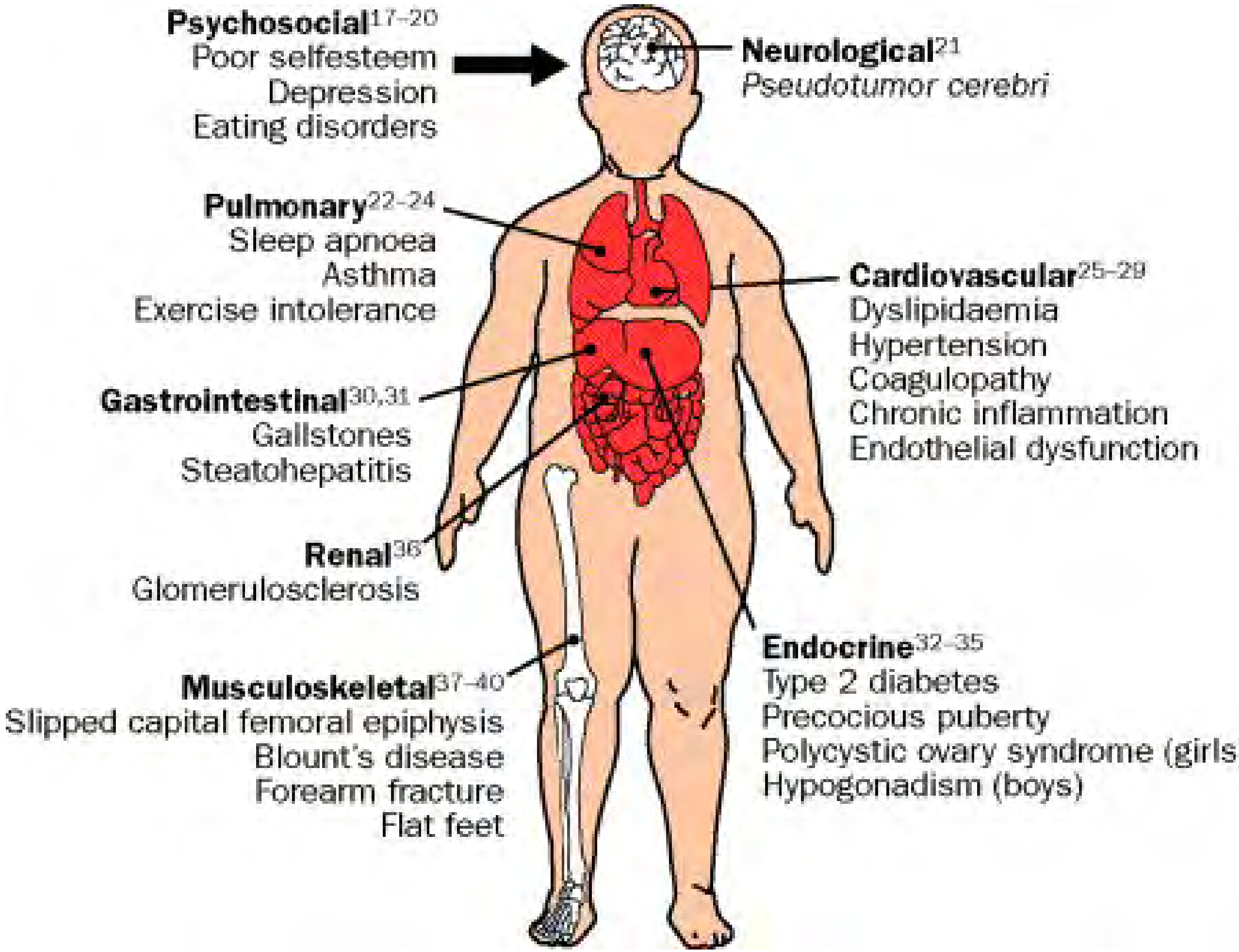


Why Early Intervention Makes Sense



Godfrey et al., Trends Endocrinol Metab 2010 ; 21:199-205

Medical Complications of *Childhood* Obesity



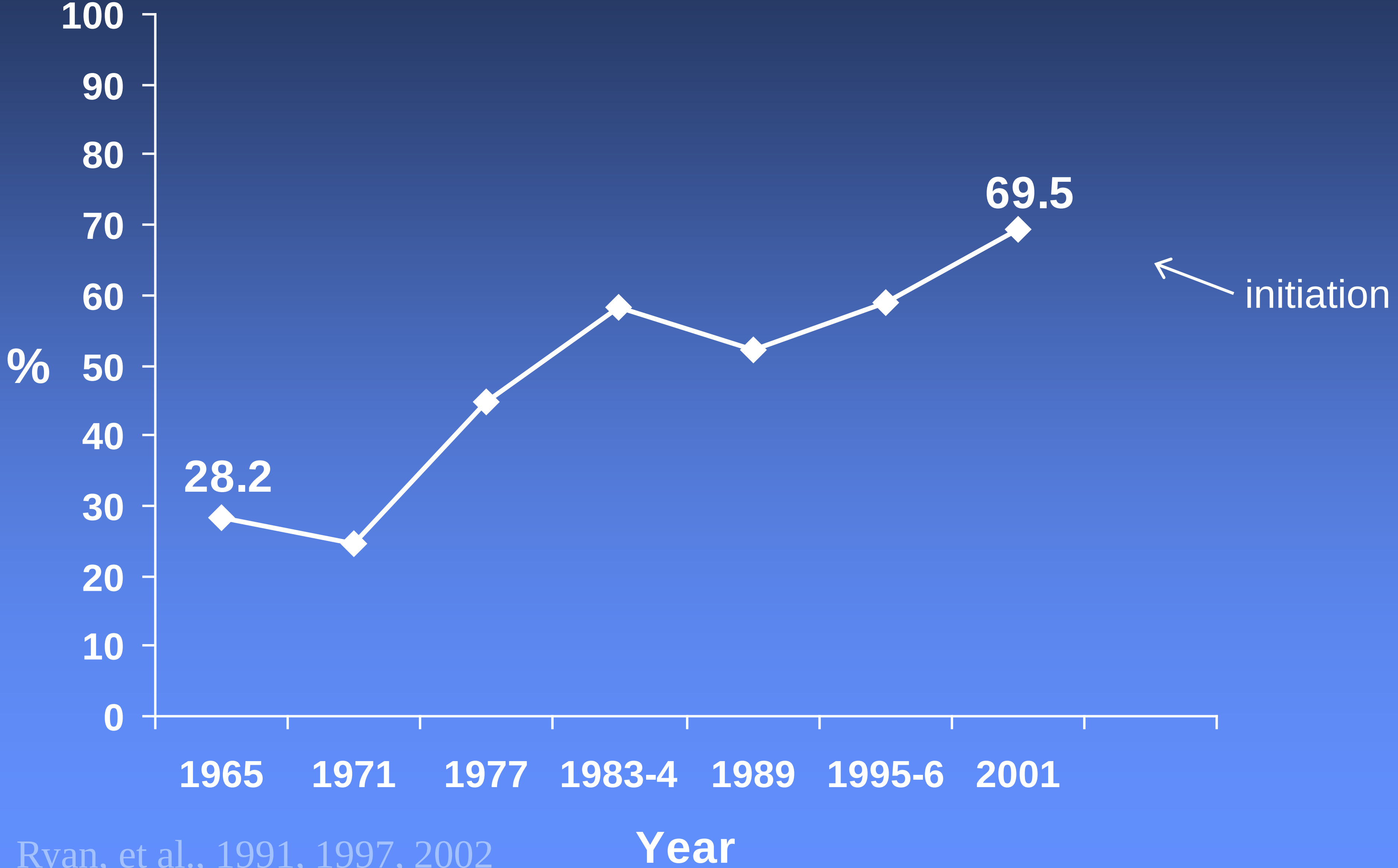
Ebbeling et al., Lancet 2002

Today

- Infant feeding and childhood obesity
  - Liquid feeding
    - Human milk v. formula….lactation v. bottle
    - ~~Formula content~~ (J. Mannella, K. Michaelsen)
  - Introduction of solid (complementary) foods
    - Timing
    - ~~Content~~ (few data)
  - ~~Parent-infant feeding interaction~~ (L. Birch)
    - Restriction

US Breastfeeding Trends 1965-2001

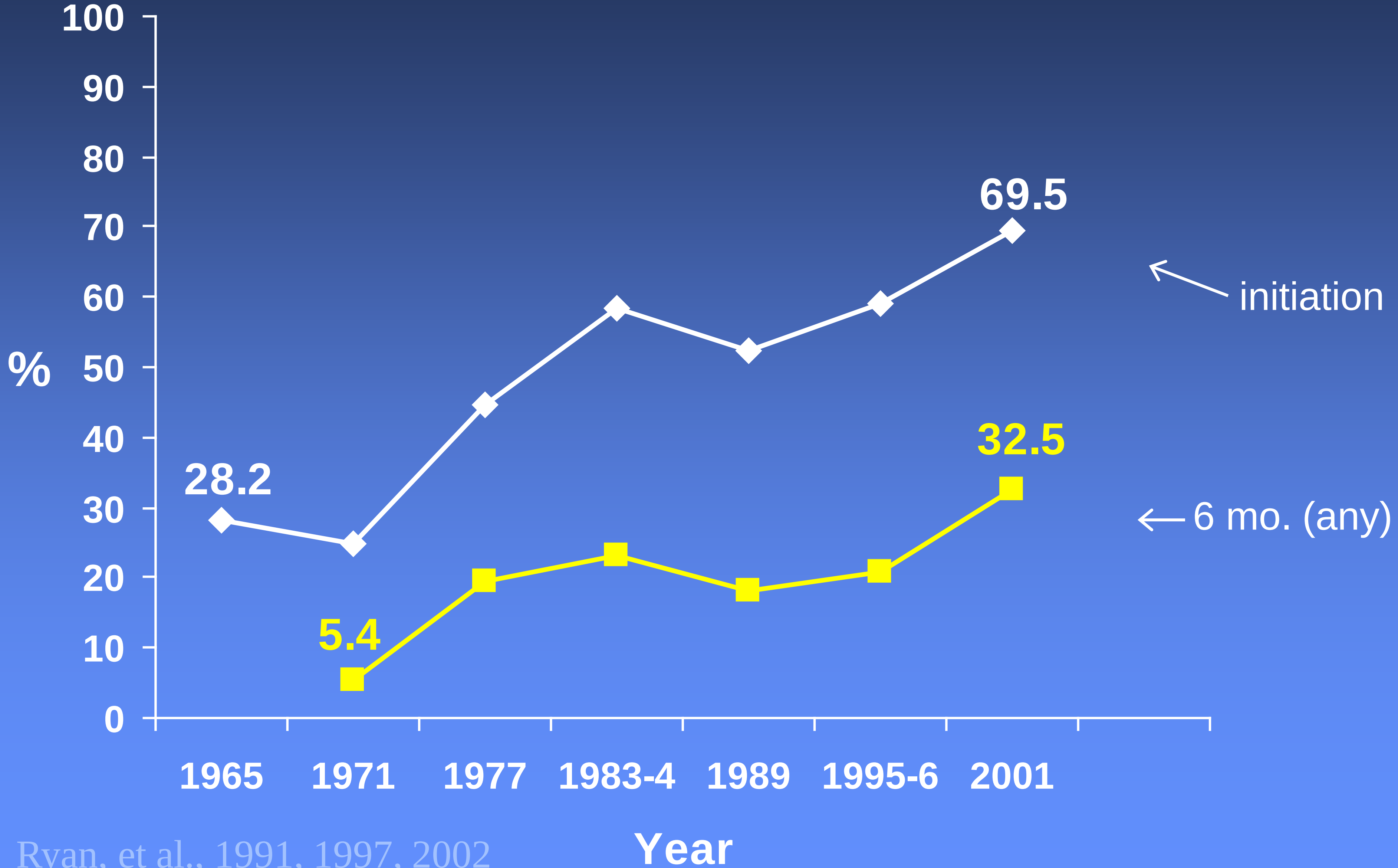
Ross Labs Mothers Survey



Ryan, et al., 1991, 1997, 2002

US Breastfeeding Trends 1965-2001

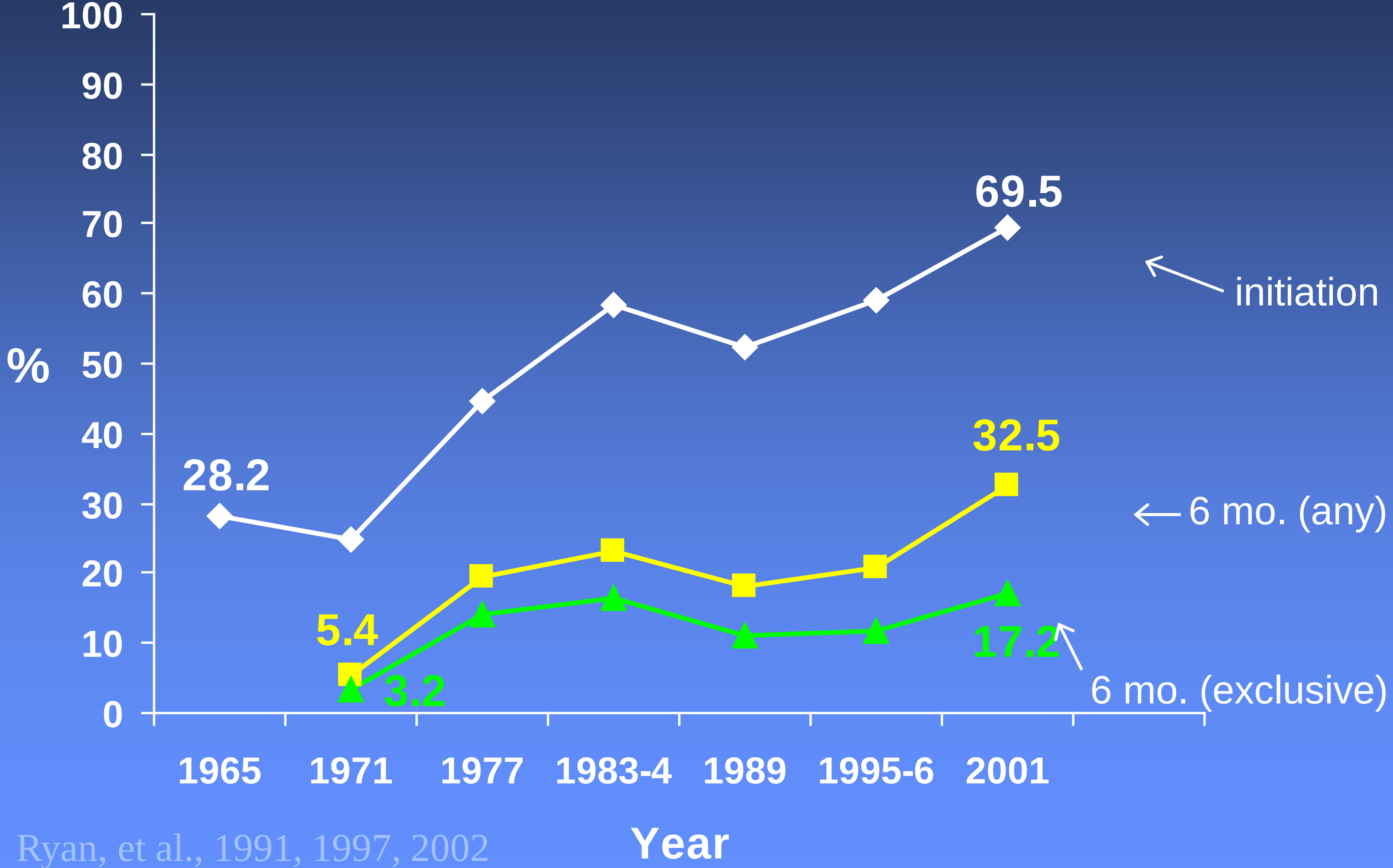
Ross Labs Mothers Survey



Ryan, et al., 1991, 1997, 2002

US Breastfeeding Trends 1965-2001

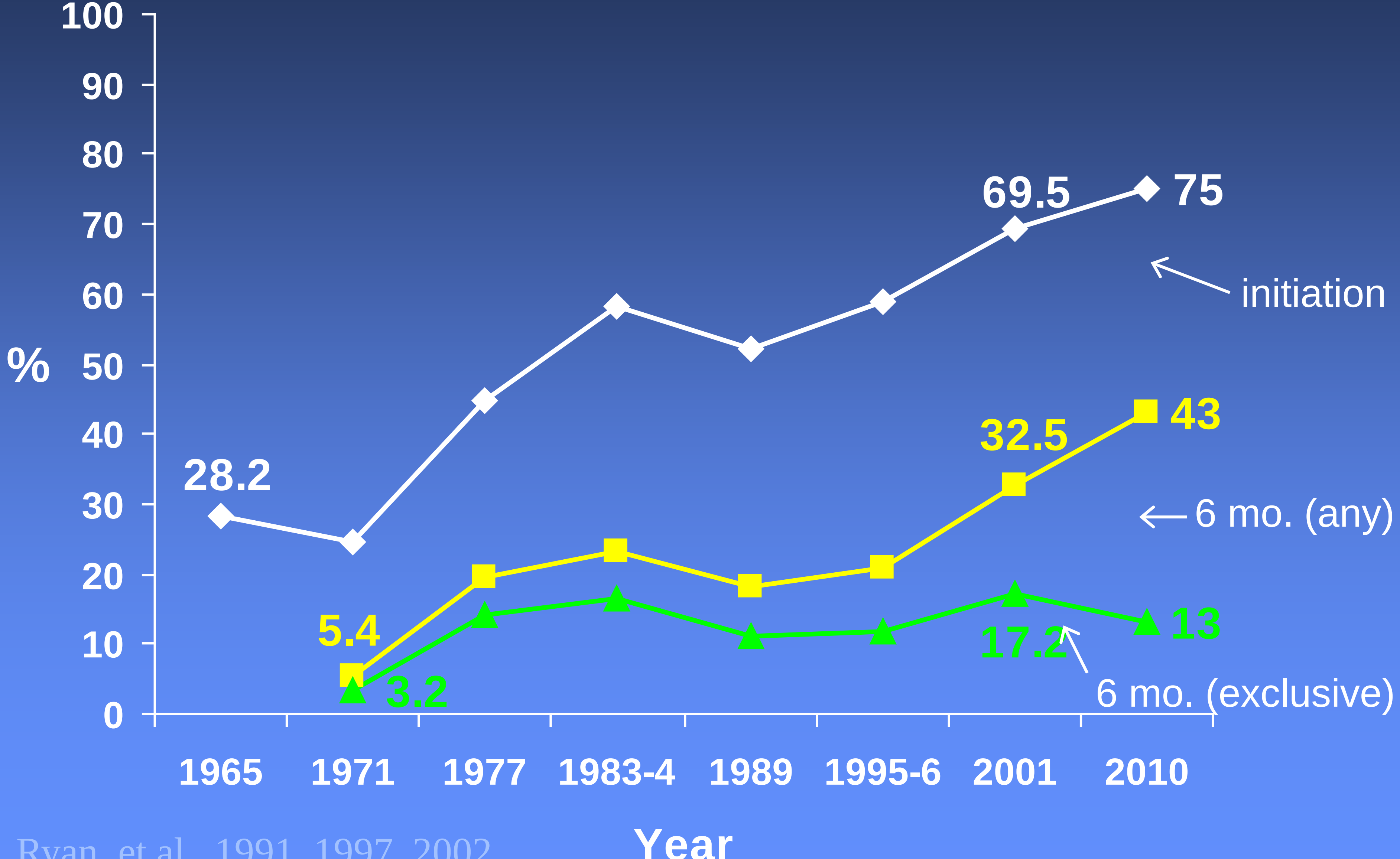
Ross Labs Mothers Survey



Ryan, et al., 1991, 1997, 2002

US Breastfeeding Trends 1965-2001

Ross Labs Mothers Survey + ***new CDC data***



Ryan, et al., 1991, 1997, 2002

US Breastfeeding Trends 1965-2001

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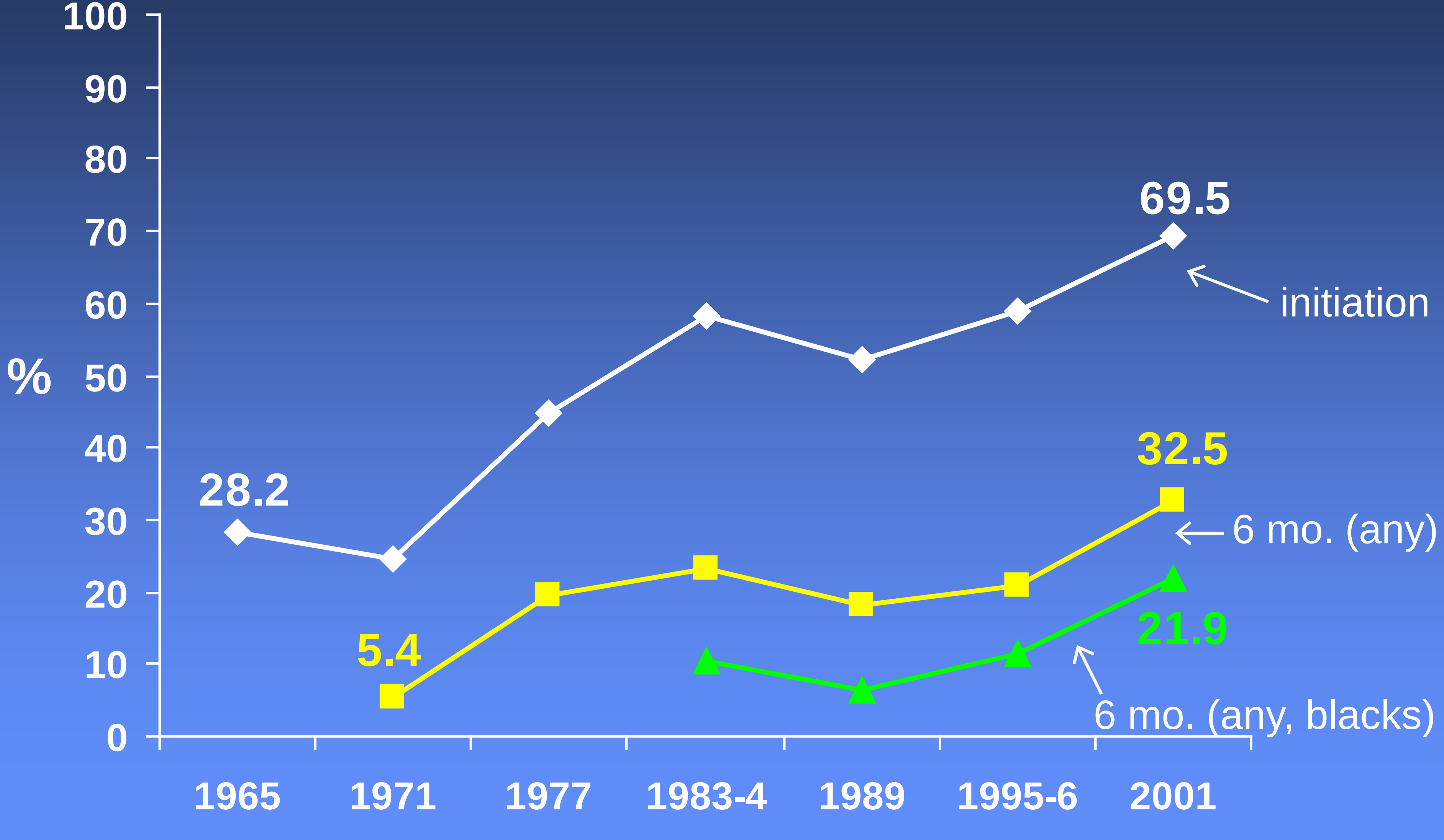
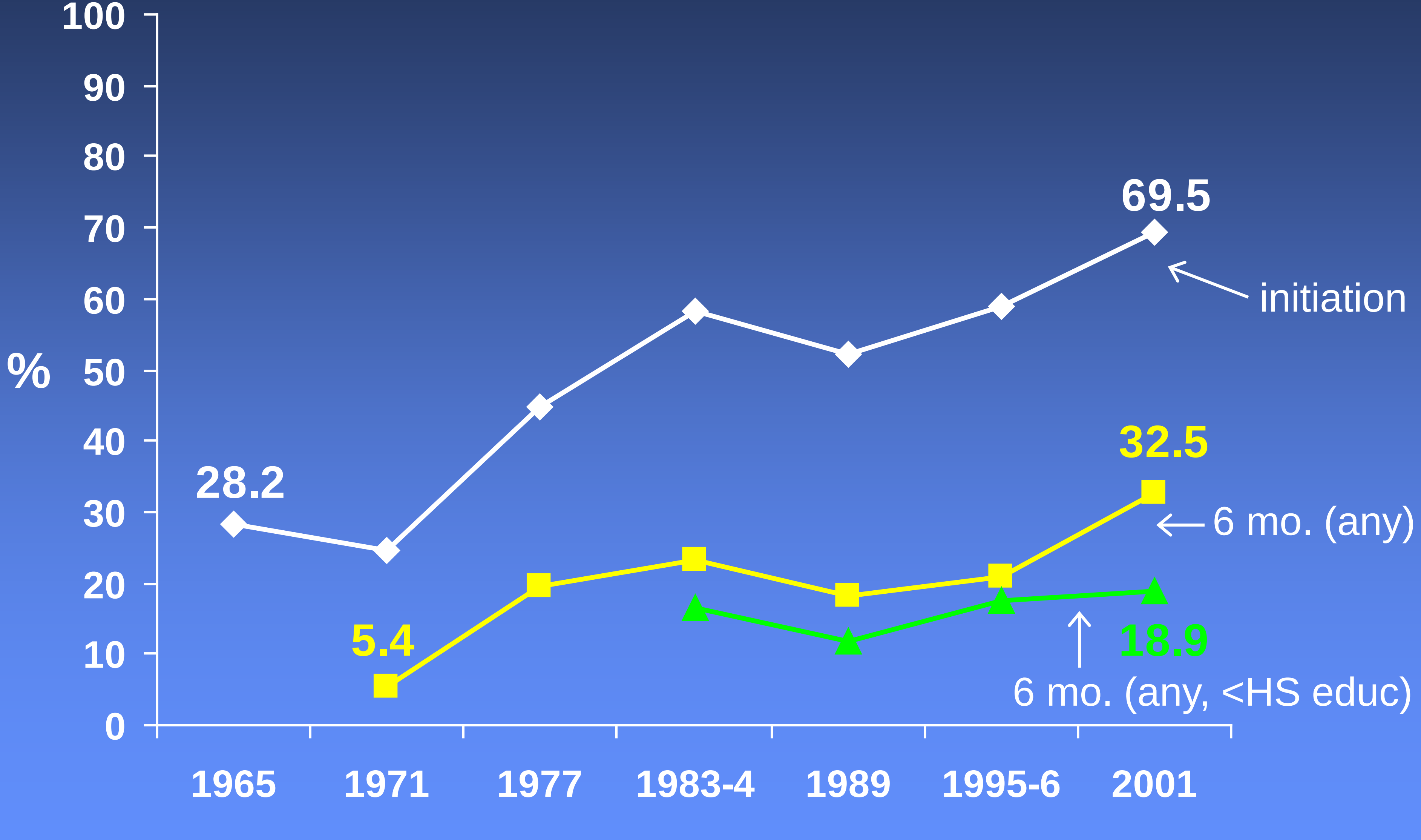


Ryan, et al., 1991, 1997, 2002

US Breastfeeding Trends 1965-2001

Ross Labs Mothers Survey

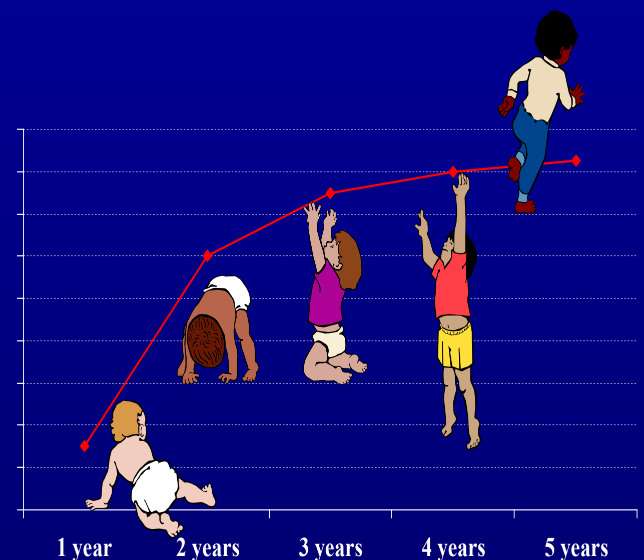


Ryan, et al., 1991, 1997, 2002

Measurement of Weight and Linear Growth in Infants and Young Children

October 31, 2013

Workshop on the Prevention of Obesity in Infancy and Early Childhood



Laurence M. Grummer-Strawn
Nutrition Branch
Division of Nutrition, Physical Activity, and Obesity

Background

- Child growth monitored to:
  - Assess adequacy of nutrition and care
  - Screen for adverse genetic or hormonal conditions
  - Assist in disease diagnosis
  - Identify childhood obesity

- Growth charts are a key tool used to interpret growth measurements

Background

- NCHS 1977 growth reference used worldwide until 2000
- CDC 2000 growth reference for children aged 0-19.9 years
- WHO 2006 international growth standard for children aged 0-4.9 years

Reference vs. standard

- A **reference** describes how children do grow in a particular time and place (descriptive)

- A **standard** describes how children should grow, regardless of time or place (prescriptive)

Reference vs. standard

- Reference is easier to explain, esp. using percentiles
- Reference gives point of comparison, but does not imply value judgments
- Standard defines what is normal or physiological

CDC 2000 growth reference

- Describes growth in the U.S. in the 1970s and 1980s
- Based on nationally representative data
- VLBW infants excluded

WHO International Growth Standard

- Optimal Nutrition
  - Breastfed infants
  - Appropriate complementary feeding
- Optimal Environment
  - No microbiological contamination
  - No smoking
- Optimal Care
  - Immunization
  - Pediatric routines

→ Optimal Growth

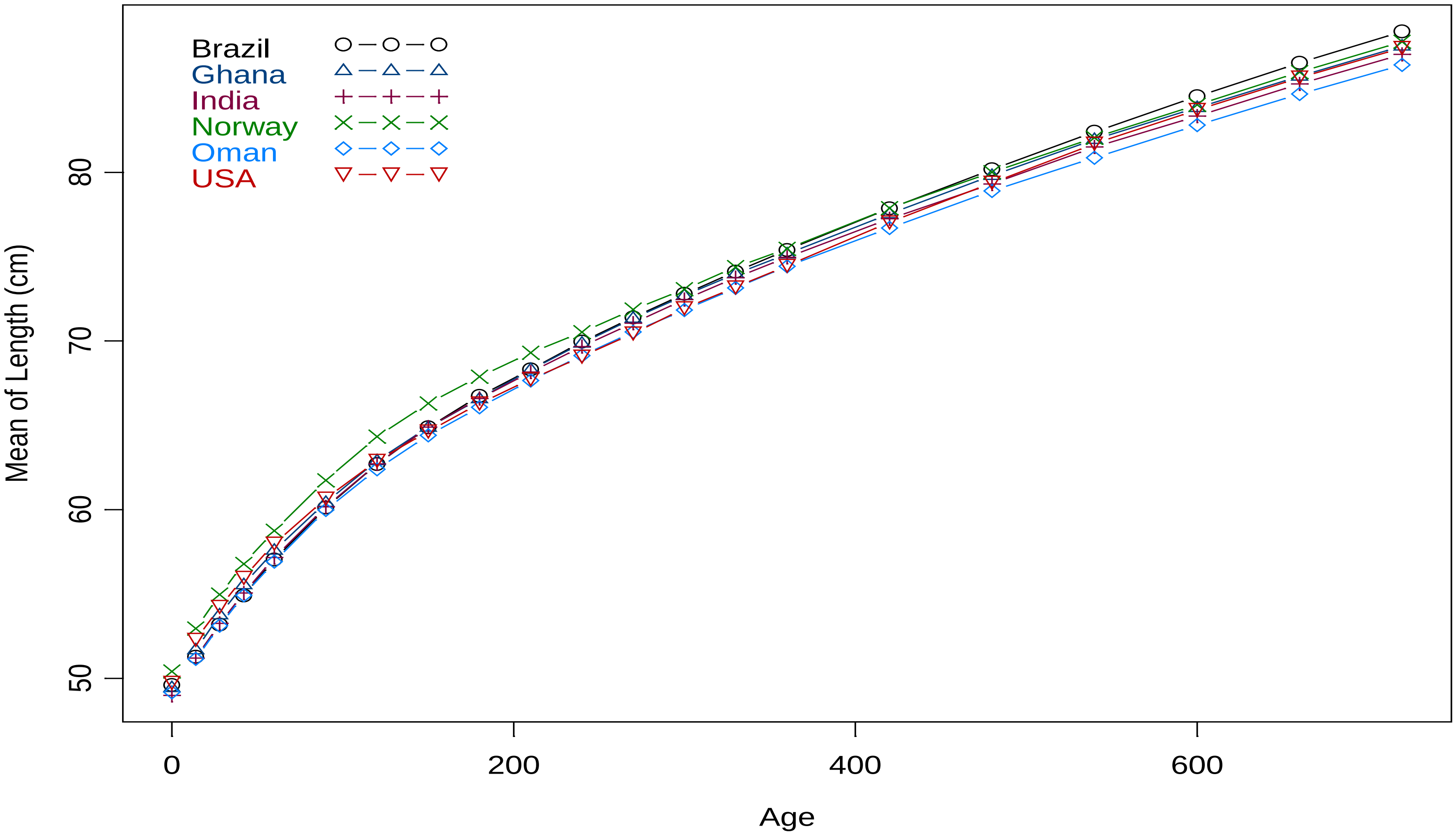
WHO International Growth Standard

- Communities selected for:
  - High socio-economic status
  - Altitude <1500 meters
  - Breastfeeding support systems
  - At least 20% following feeding recommendations
  - Low mobility
  - Collaborating institutions to collect data
- Subjects selected for:
  - No health, environmental or economic constraints on growth
  - Mother willing to follow feeding recommendations
  - Term, singleton birth
  - Lack of significant perinatal morbidity
  - No smoking mothers (before and after delivery)

WHO International Growth Standard

- Data collected in:
  - Davis, CA, United States
  - Pelotas, Brazil
  - Oslo, Norway
  - South Delhi, India
  - Muscat, Oman
  - Accra, Ghana
- Hypothesis was that children throughout the world will grow similarly if exposed to optimal circumstances

Mean length from birth to 24 months for the six WHO sites



WHO International Growth Standard

- Attained growth
  - Weight-for-age
  - Length/height-for-age
  - Weight-for-length/height
  - Body mass index-for-age
  - Mid-upper arm circumference-for-age
  - Triceps skinfold-for-age
  - Subscapular skinfold-for-age
  - Head circumference-for-age
- Growth velocity
  - Weight
  - Length/height
  - Head circumference
  - Arm circumference
  - Body mass index

Key methodology differences (Birth-2 yrs)

WHO	CDC
Longitudinal data	Cross-sectional data • NHANES I, II, & III • National Birth Certificates • MO & WI Birth Certificates • Fels data, PedNSS data
Frequent data collection • biweekly 0-8 weeks • monthly 2-12 months • bimonthly 14-24 months	No data between birth and 3 months • mathematical models used
Feeding requirements • exclusive/predominant breastfeeding ≥ 4 months • complementary feeding by 6 months • continued breastfeeding ≥ 12 months	No feeding requirements • ~50% ever breastfed • ~33% breastfeeding at 3 months
18,973 observations	4,697 observations

Smaller methodology differences at 2-5 yrs

WHO	CDC
Cross-sectional data	Cross-sectional data
Feeding requirements • Breastfed at least 3 months	No feeding requirements
Stop at age 5	Continuous with curves up to age 20
Overweight children (above +2SD) excluded	No data exclusions
6,669 observations	9,894 observations

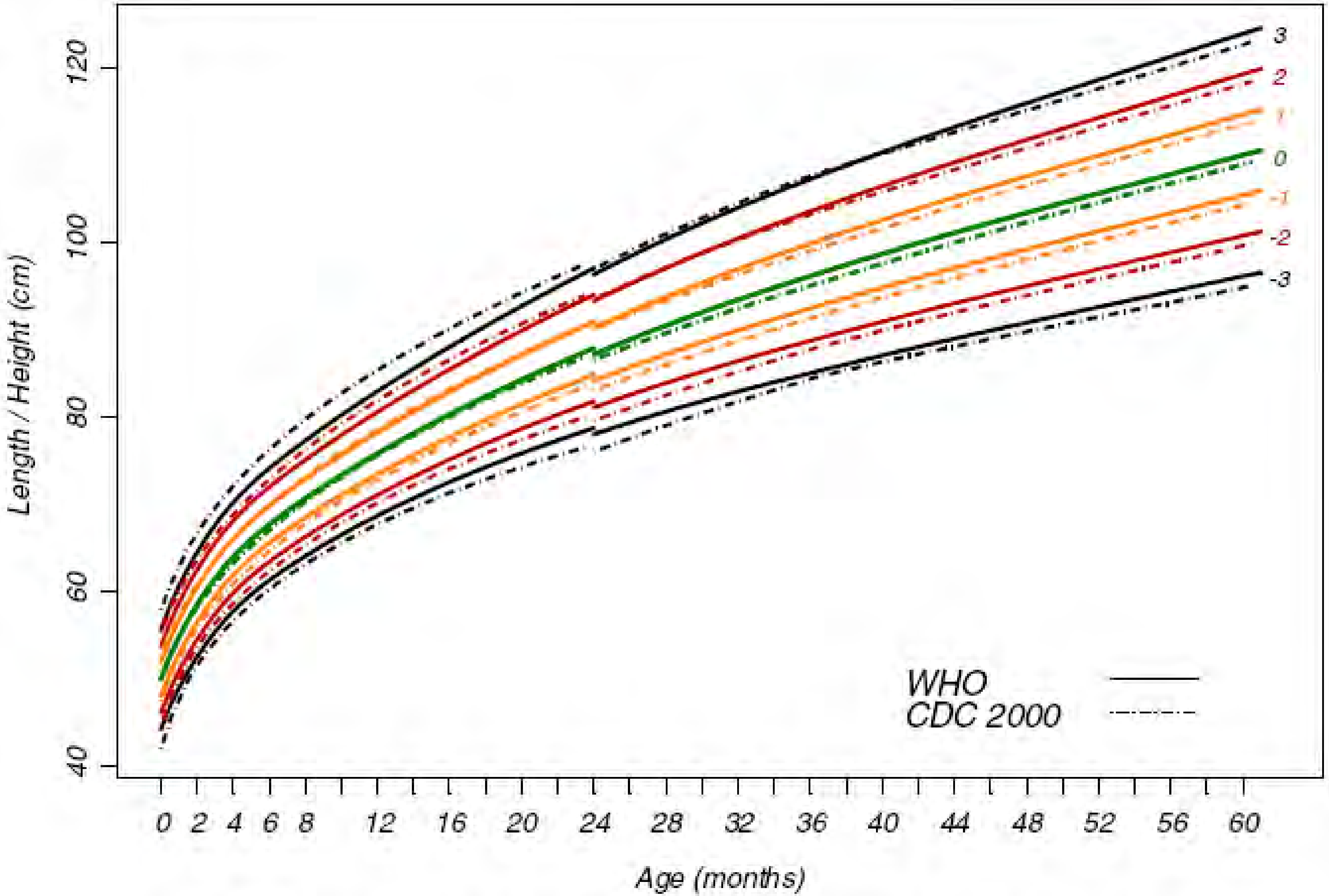


Figure 16 Comparison of WHO with CDC 2000 length/height-for-age z-scores for boys

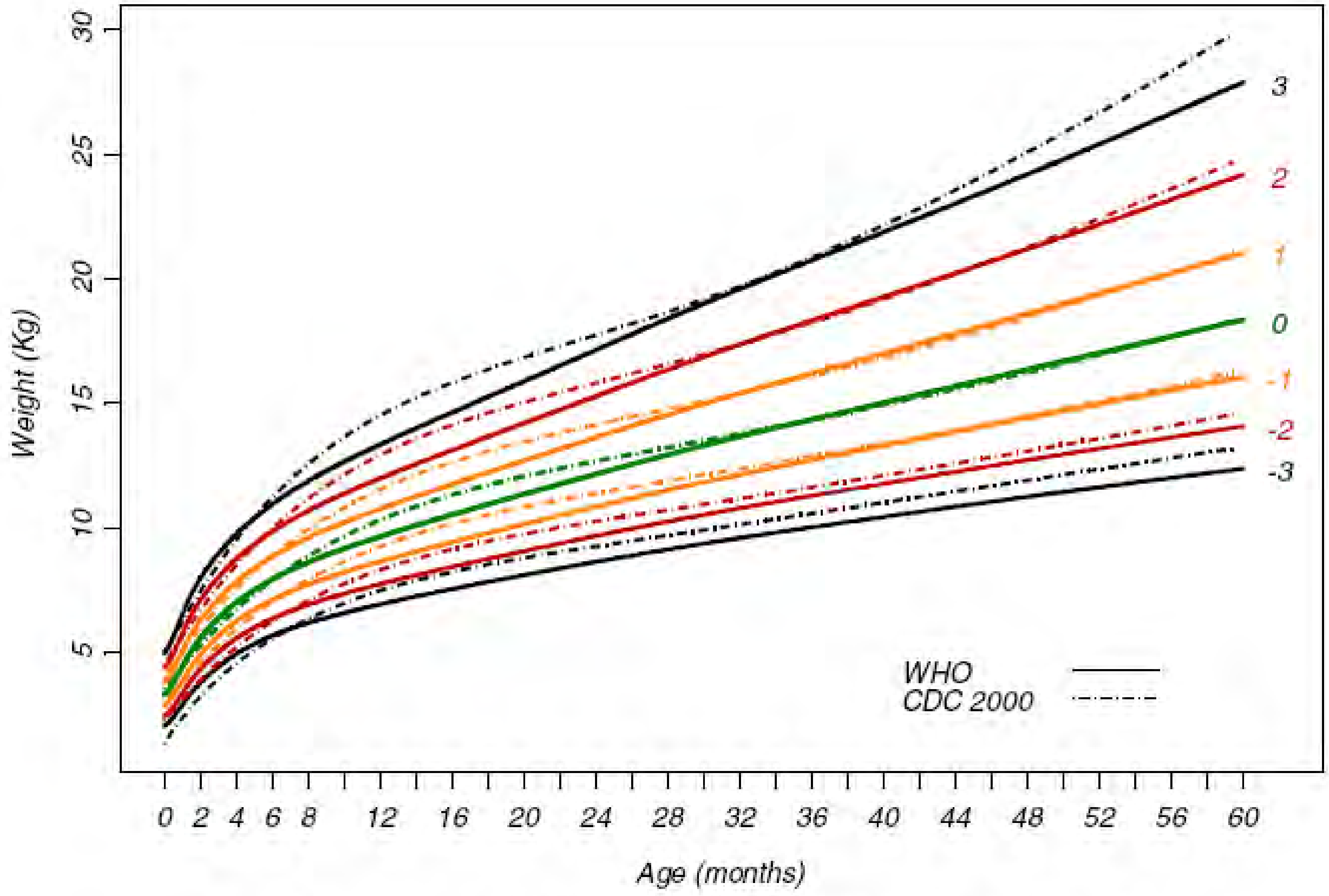


Figure 46 Comparison of WHO with CDC 2000 weight-for-age z-scores for boys

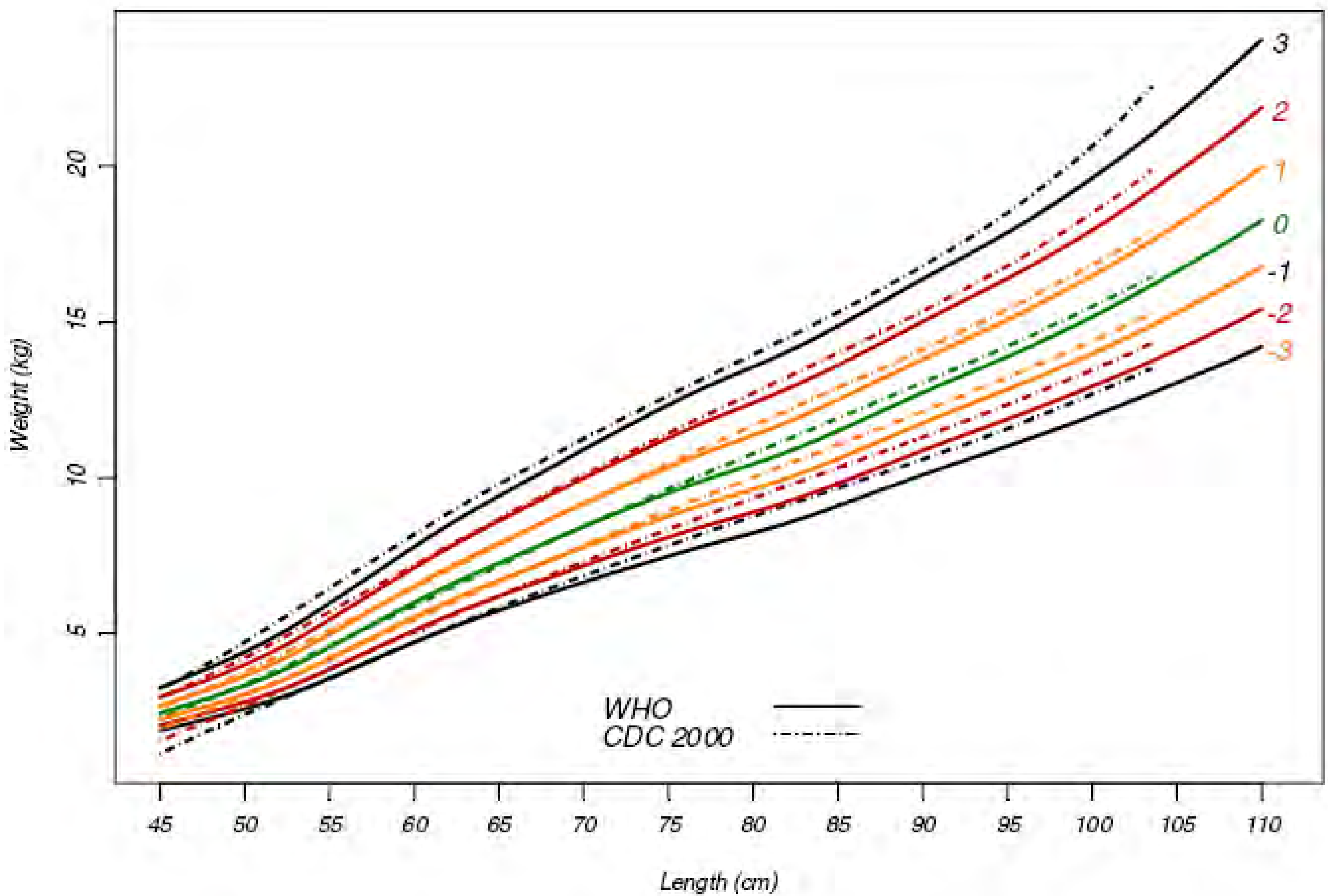


Figure 77 Comparison of WHO with CDC 2000 weight-for-length z-scores for boys

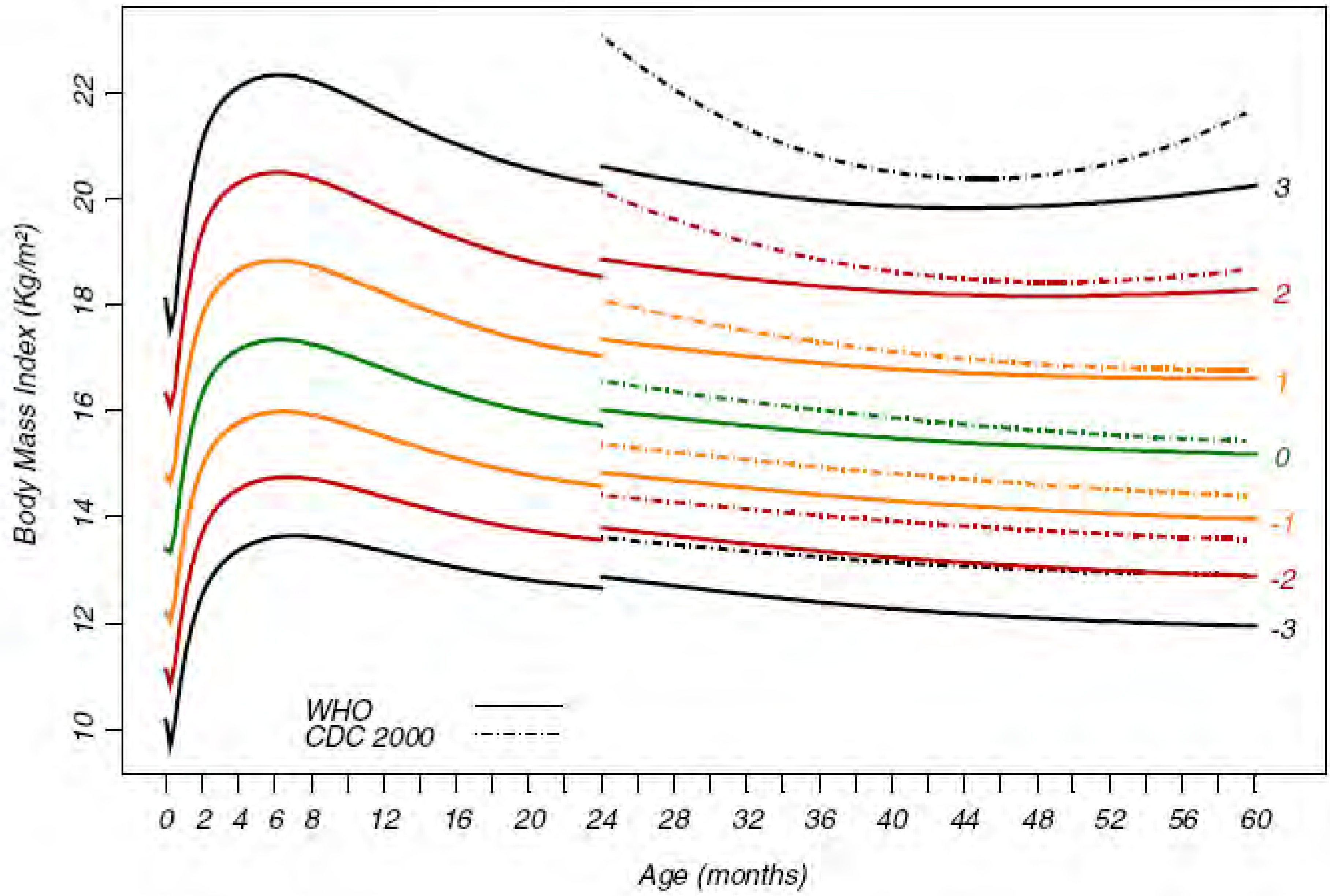


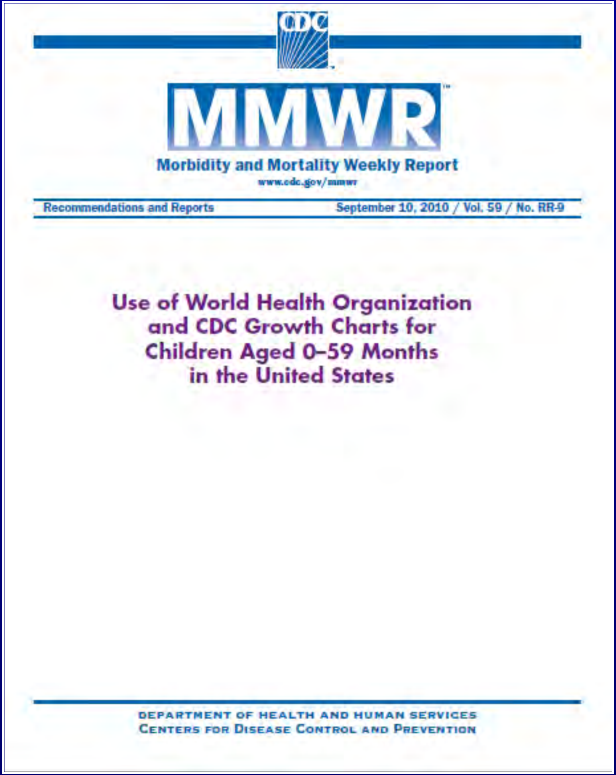
Figure 115 Comparison of WHO with CDC 2000 BMI-for-age z-scores for boys

Recommendations for the U.S.

- Expert panel was convened June 29-30, 2006
- Sponsored by CDC/NIH/AAP
- Considered
  - Rationale for standard vs. reference
  - Methods in construction of both curves
  - Statistical comparisons between the curves
  - Implications for breastfed as well as formula-fed infants
  - Practicalities of using multiple charts
- AAP board voted to recommend use of the WHO charts from birth-2 years, but continued use of the CDC charts from 2-5 years.

Use of World Health Organization and CDC Growth Charts in the United States

- CDC recommends that health care providers:
  - Use the WHO growth standards to monitor growth for infants and children ages 0 to 2 years of age in the U.S.
  - Use the CDC growth charts for children age 2 years and older in the U.S.



MMWR

Morbidity and Mortality Weekly Report

www.cdc.gov/mmwr

Recommendations and Reports — September 10, 2010 / Vol. 59 / No. RR-9

Use of World Health Organization and CDC Growth Charts for Children Aged 0–59 Months in the United States

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

Rationale for recommending WHO at 0-23 months

- Clinicians use growth curves as a standard—must judge growth as abnormal or unhealthy.
- WHO curves based on high quality longitudinal study.
- CDC curves based on very little data birth-3 months and combine very distinct datasets at different ages.
- Concern that children 3-18 months are inappropriately evaluated for failure-to-thrive, when WHO charts indicate that growth is normal.

Rationale for recommending WHO at 0-23 months

- Concerns over using formula-fed reference for breastfed children (2/3 in CDC charts not breastfed beyond 3 months.)
- AAP has said that breastfed child is the "normative model for defining optimal health".
- Intake of breastfed child is used for setting DRIs
- Separate charts for breast- and formula-fed babies are impractical (continuum of mixed feeding, varying durations)

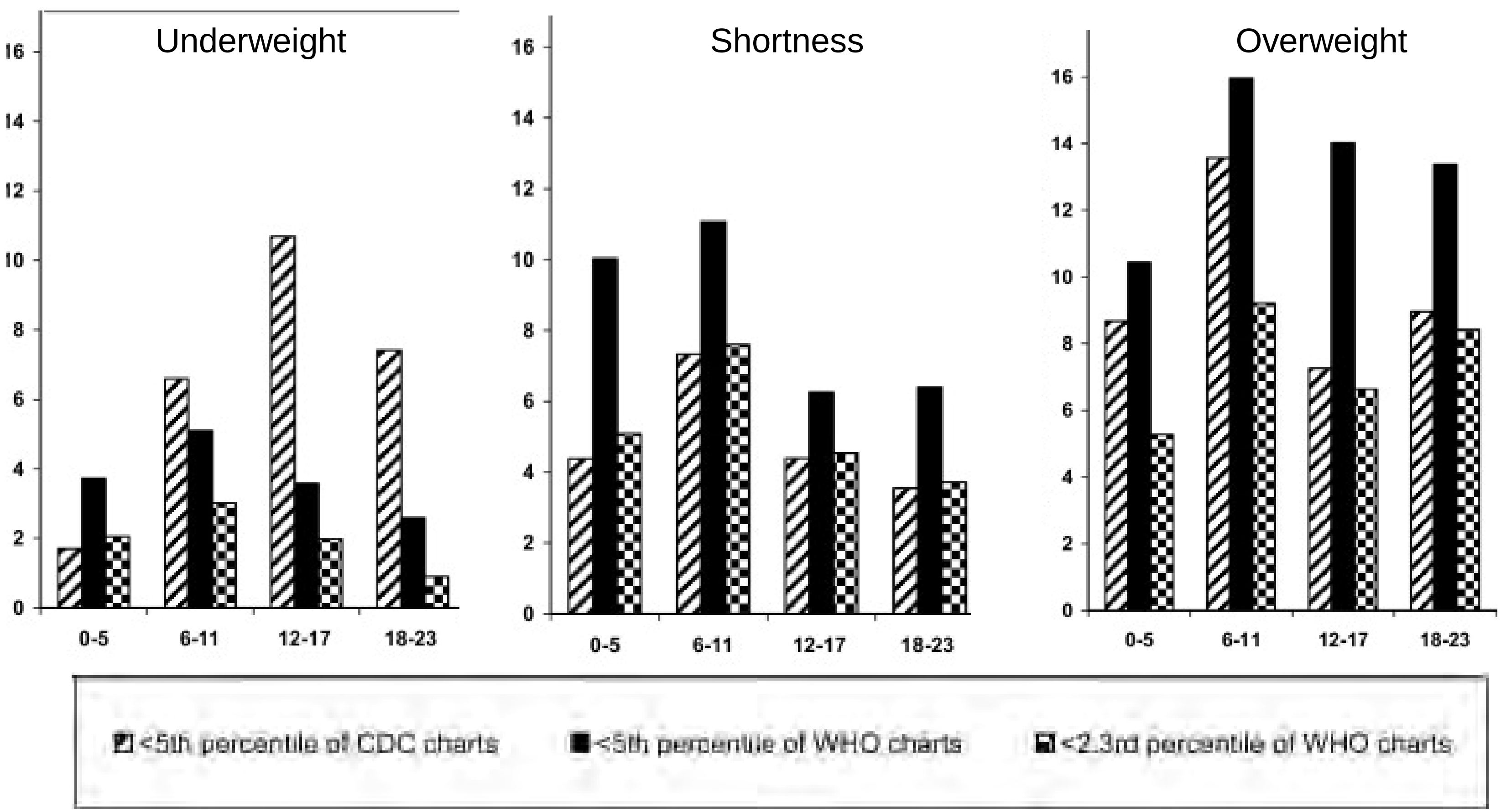
Rationale for not recommending WHO at 24-59 months

- Methodology similar between the WHO and CDC curves.
- Use of the WHO curves for <5 yrs and then CDC curves >5 years would require that clinicians switch curves.
- Switching curves at 2 years of age matches switch from recumbent length to standing height.

Cutoffs

- WHO recommends cutoffs at -2 SD (2.3rd percentile) and +2SD (97.7th percentile)
- In U.S., 5th and 95th percentiles more commonly used
- Because WHO standard measured healthy children under optimal conditions, the more extreme cutoffs may be appropriate
  – Prevalence of stunting and overweight more similar using WHO cutoffs on WHO charts

Comparison of the prevalence of underweight, shortness and overweight based on the CDC 2000 and the WHO 2006 growth charts, NHANES 1999-2004 for children aged 0-59 months.



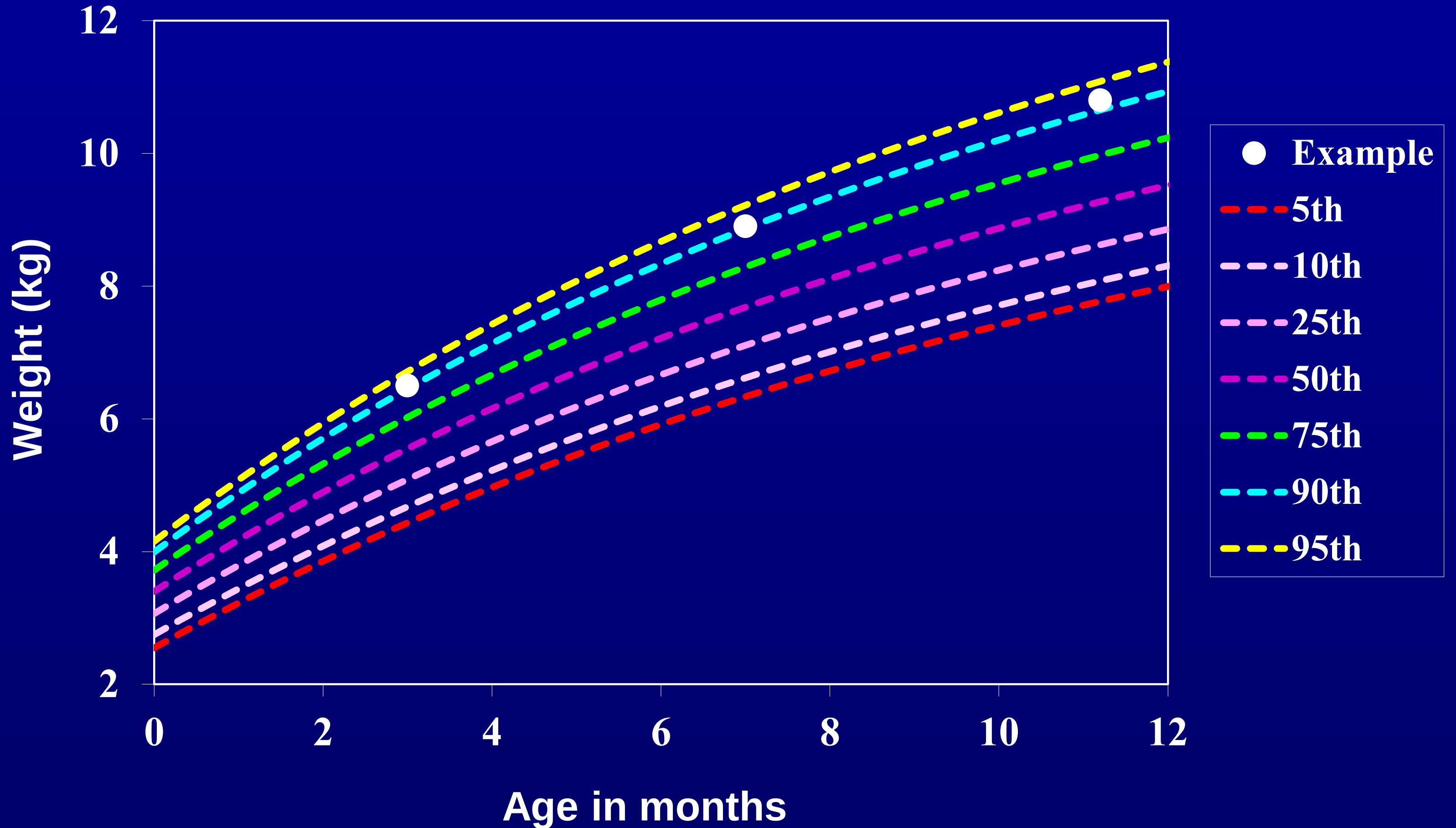
Recommendation on Cutoffs

- The WHO cutoffs should be used with the WHO growth charts
  - 2.3rd and 97.7th percentile
- The traditional CDC cutoffs should be used with the CDC growth charts
  - 5th and 95th percentile

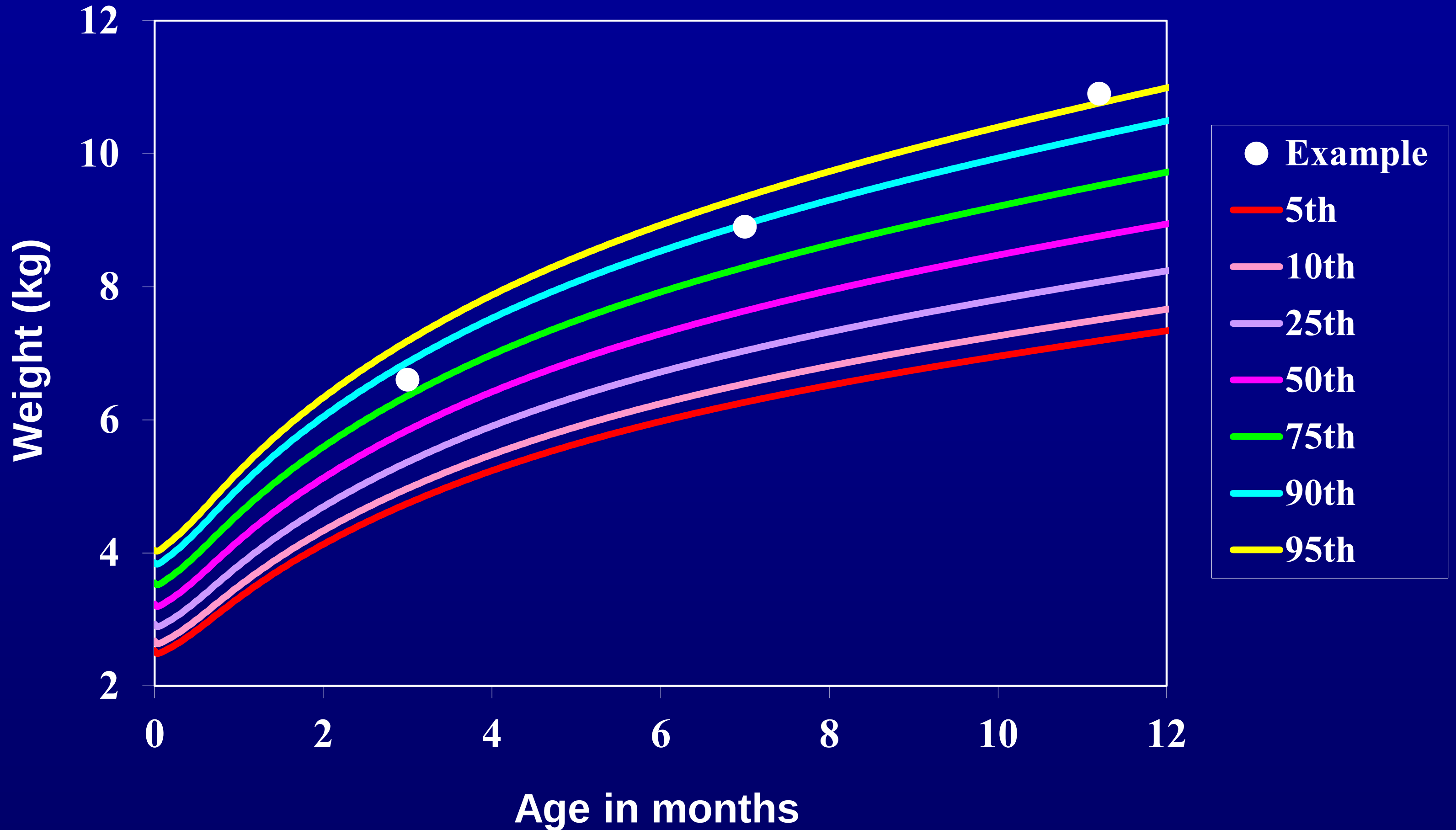
Key Clinical Differences

- More infants will be identified as growing “too fast” on weight-for-age

Weight-for-age, Girls 0-12 mos, CDC reference



Weight-for-age, Girls 0-12 mos, WHO reference



Key Clinical Differences

- More infants will be identified as growing “too fast” on weight-for-age
  - More likely for formula-fed
- Fewer will “fall off” weight-for-age charts from 3-18 months
- Fewer infants will be identified as underweight

CDC Recommendation on Research Priorities

- Clinical consequences of using WHO curves instead of CDC curves (+ & -)
- Use of BMI in infants and toddlers
- Health outcomes associated with different growth patterns and cutoffs

Infant Growth and Later Obesity

- Systematic review by Baird et al. 2005
  - 11 of 18 studies found “infant obesity” assoc. with later obesity (ages 3 to 35 years)
  - 7 of 10 studies found infant weight gain assoc. with later obesity (ages 4 to 20 years)
- Pooling of 5 birth cohort studies (Adair et al. 2013)
  - 1 SD increase in height gain to age 2 y increased odds of overweight in adults by 24%
  - 1 SD increase in relative weight gain to age 2 y increased odds of overweight in adults by 51%

Use of Growth References in Research

- No CDC recommendations

- Longitudinal studies closely spanning 24 months should use consistent reference with consistent cutoffs

- Change in reference or cutoffs is less problematic for longer term follow-up

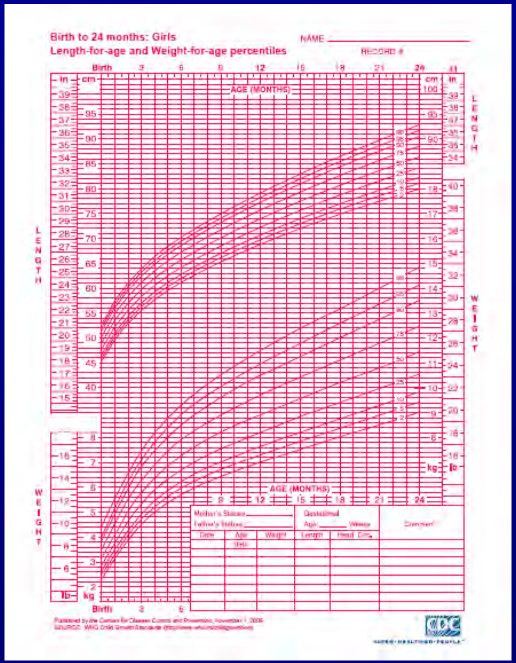
Use of Growth References in Research

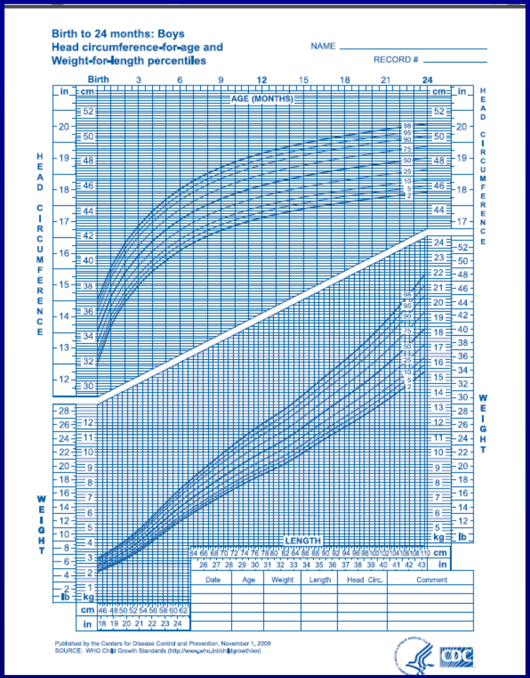
- Switch from length to stature at 24 months is critical
- Difference between WHO and CDC curves is most pronounced in tails (greater impact for prevalences than z-score shift)
- Tracking BMI only possible in WHO curves
- CDC Weight-for-Stature designed to be continuous with Weight-for-Length

Summary

- Numerous advantages of WHO charts for birth to 2 years
- WHO charts are intended for all infants (not just breastfed)
- Patterns of weight gain substantively different in WHO charts

Thank you!





www.cdc.gov/growthcharts

www.cdc.gov/nccdphp/dnpao/growthcharts/who/index.htm

Complementary Feeding: Influence of When, What & How

Nancy F. Krebs, MD, MS
University of Colorado School of Medicine

NIH Workshop:
Prevention of Obesity in Infancy and Early Childhood
October 30–Nov 1, 2013

Outline

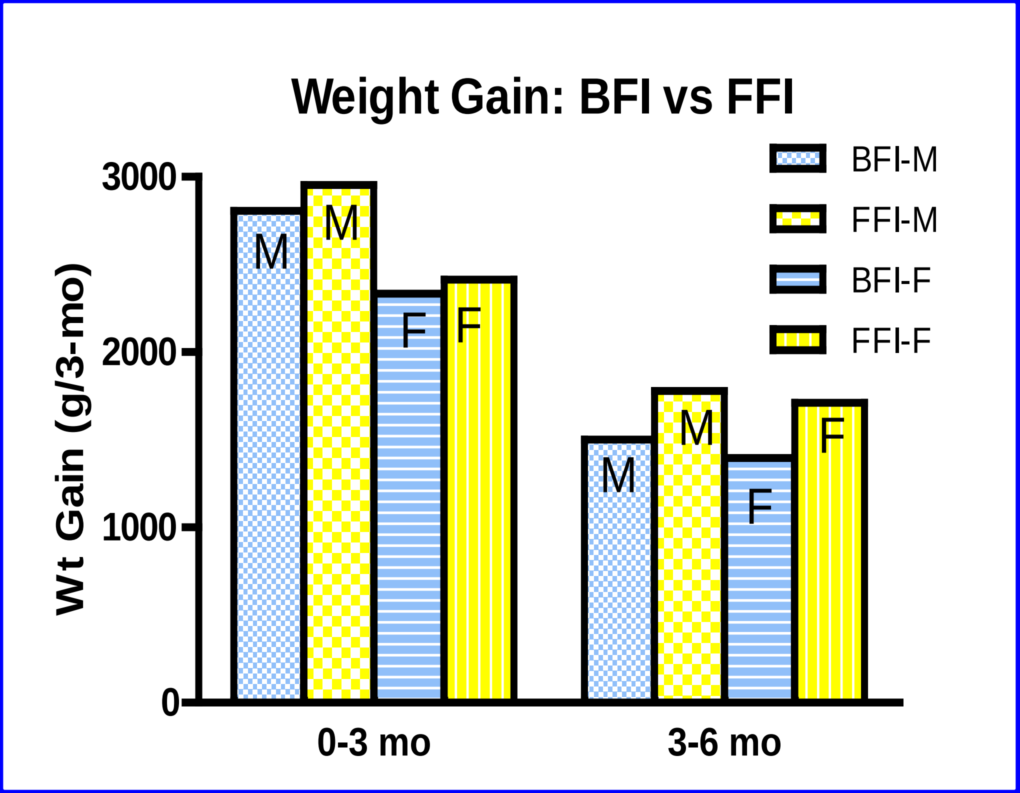
- When: does timing of introduction of CF matter for risk of later obesity?
- What: Do the types of CF make a difference?
- [How: Does the interplay of parent-infant dynamics impact obesity risk?]

When

Complementary Feeding: Timing

- Early (< 4 mo) introduction of CF ***not*** consistently associated with later ow/ob
  - No effect (Burdette, et al, 2006)
  - Delayed intro CF $\rightarrow \downarrow$ ow/ob at **10 yr** (Seach, 2010)
  - Late CF (vs duration BF) protective (Schack-Nielsen, 2010)
  - 2 large cohort studies increased risk of ow/ob at **3 yr**
    - Effect *only* in formula fed infants (Huh, 2011)
    - Increased infant weight gain if BF < 20 wk (Baker 2004)
- Modest impact; persistence?

Differences in Growth: BF *vs* FF DARLING Study



- (N = 46 & 41/group)
- Wt Δ 0-3 mo:
  BFI ≈FFI
  FFI> BFI thereafter
- 12 mo, BFI 0.65 kg < FFI

Growth differences between FFI vs BFI disappeared after adjust for intro CF & cow milk

[Dewey et al, Pediatr, 1992]

European Formula Study

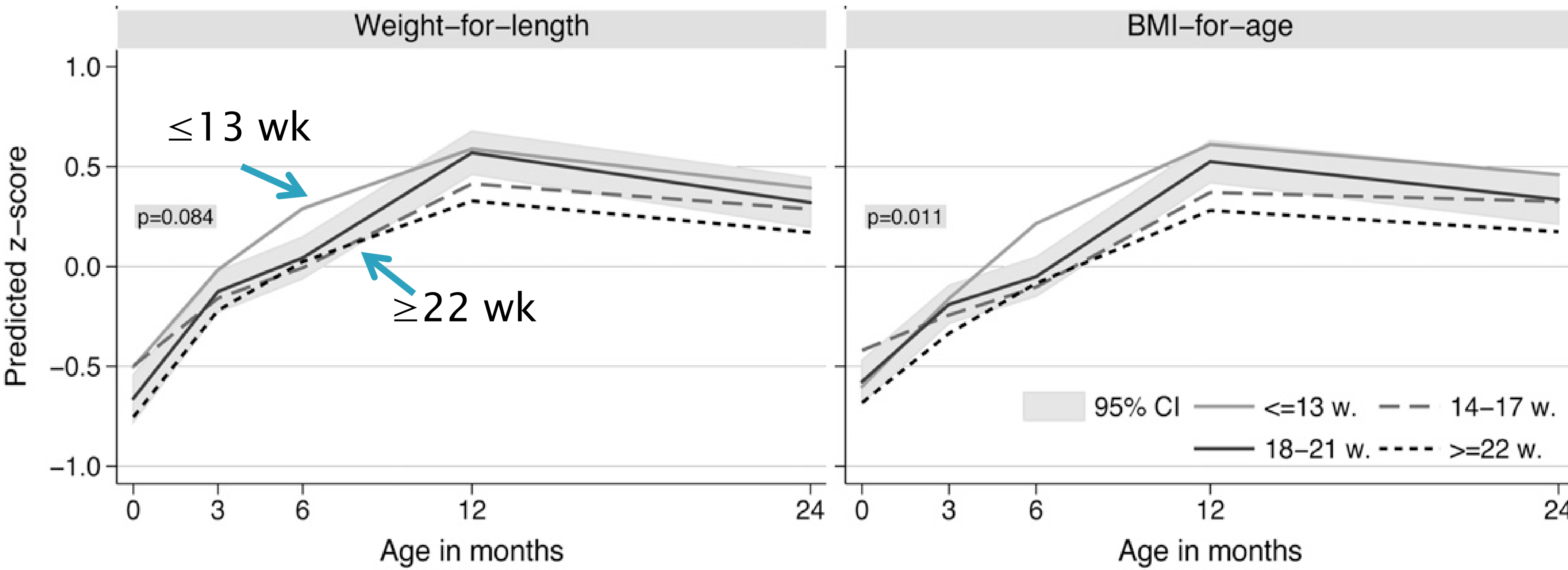
- Large randomized study in Europe comparing effect of different protein content formulas ("low" ~ 1.8 vs "high" 2.9 g/100 kcal) (n > 1000

  [Koletzko, AJCN, 2009]

- Timing of introduction of CF from trial:
  - ≤ 13 wk, 14–17 wk, 18–21 wk, ≥ 22 wk
  - 1090 subjects, 76% w/ data on CF; 61% to 24 mo
  - Early CF were lighter at birth; "caught up" (2–6 mo)

  [Grote, AJCN, 2011]

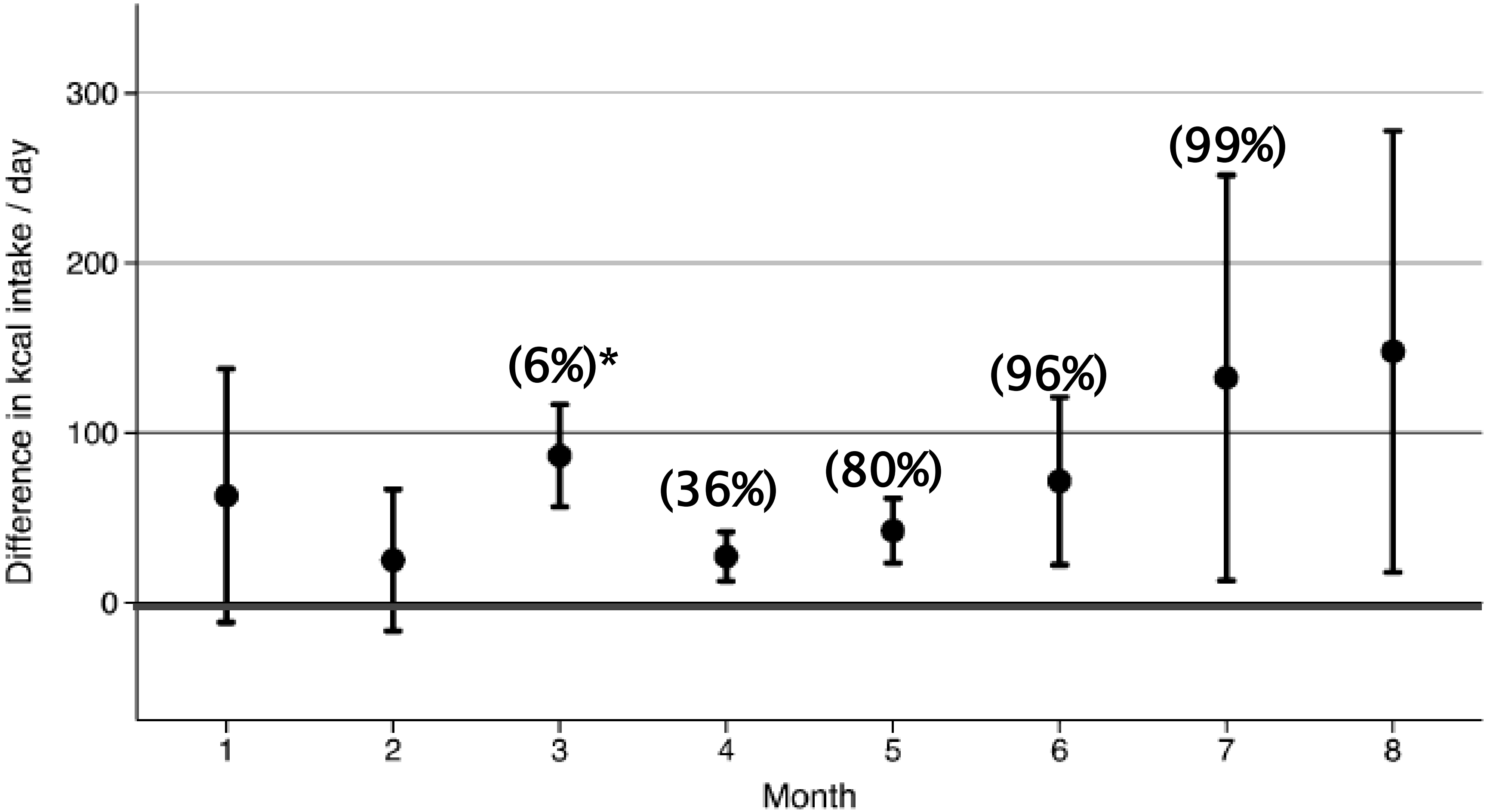
Timing of CF & Growth: 2-24 mo



- "Earliest" vs "Latest" CF grew faster & heavier
- WAZ & BMI significantly greater, not WLZ, not LAZ
- ***After 12 mo, no difference***

[Grote 2011]

Additional Energy from CF



Difference in Energy intake – kcal from CF by month for (+) vs (–)

- *% of subjects getting CF*
- ***After 12 mo, no difference in kcal intake, early vs late***

[Grote et al, AJCN 2011]

Complementary Feeding: Timing

- Early **(< 4 mo)** introduction of CF ***not*** consistently associated with later ow/ob
  - Historically, CF << 4-6 mo
  - Some studies indicate positive assoc w/ early weight gain – especially in **formula fed** infants
- Difference in response between BFI & FFI: *very different regulation of supply/production*
- Risk of early introduction greater in FFI & FFI tend to receive CF earlier
- Overall, effect on growth is modest; longer term effects unclear

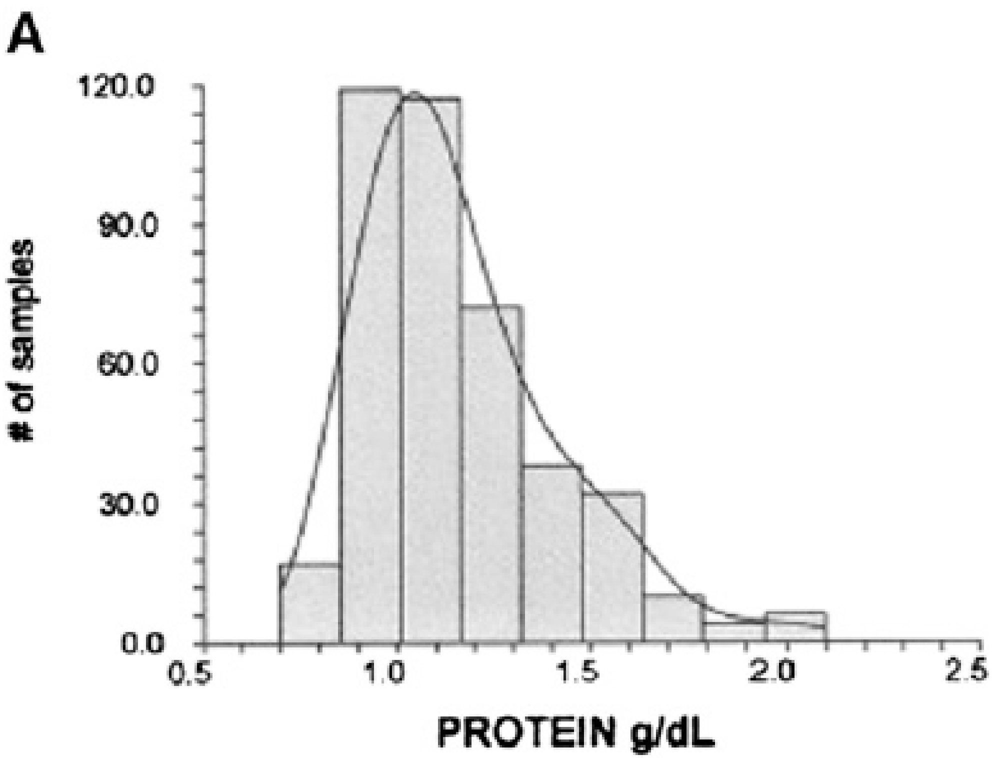
What

Effects of Macronutrient Intake on Infant Weight Gain: FAT

- Both HM & infant formulas ~ 50% energy from fat, but *fat content of HM much more variable; (fat accretion = normal!)*
- AAP Recommendations: transition to 30–40% → 20–30% by 2 yr
- FITS study:
  - Median fat intake of US infants w/in range
  - **~ 25% fat intake < recommended; 3% > recommended**
- Quality of fats (SFA, *trans,* LC-PUFA) important to metabolic & developmental status; few trials w/ CF
- *No data indicate adverse outcomes from fat intake w/in recommended range*
- ***Epidemiologic data do not identify fat intake as risk factor***
  - Lower fat (< 30% kcal) intake safe (STRIP)
  - If weight gain excessive, safe to ↓ fat intake to → ↓ energy intake

Effects of Macronutrient Intake on Infant Weight Gain: PROTEIN

- High protein intake associated w/ ↑ wt gain & ↑ adiposity, but…qualifiers!



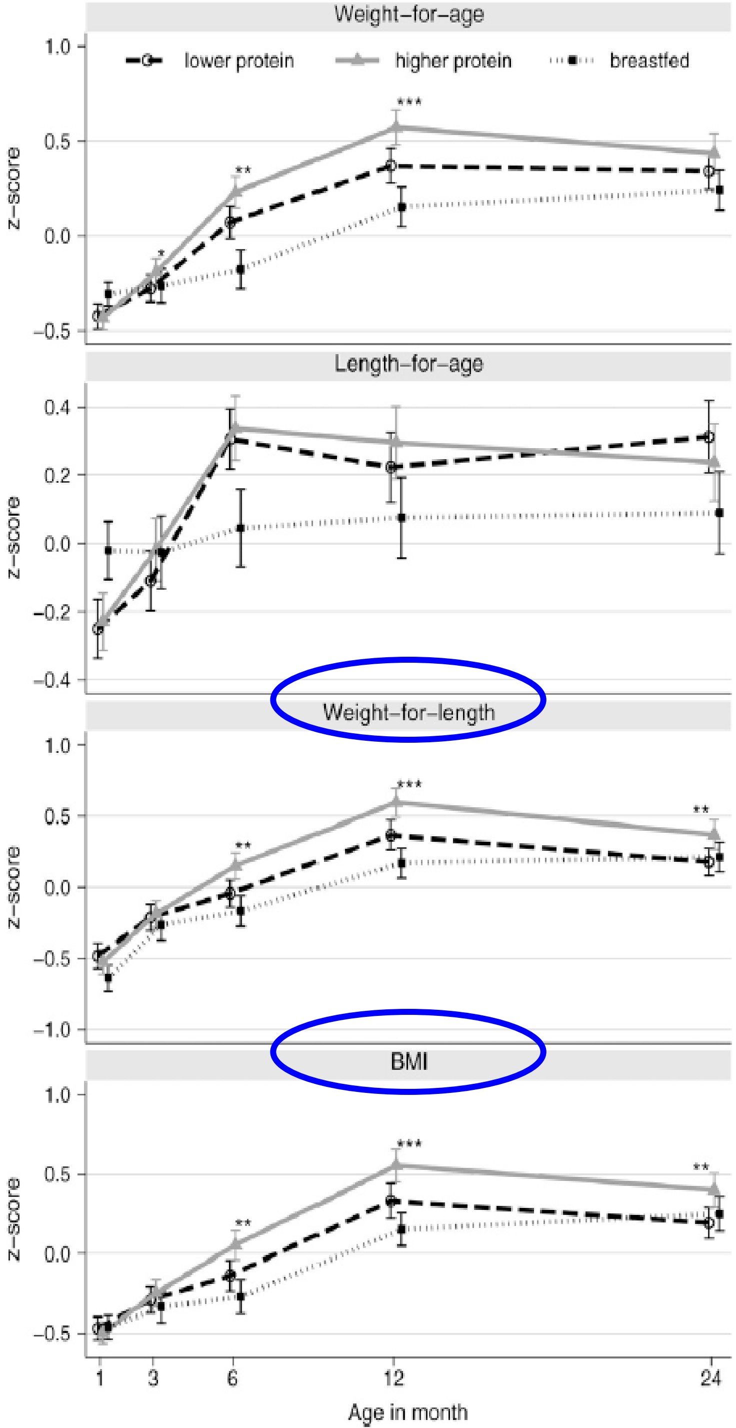
Protein content of HM
~0.9–1 g/dL
↓'s over time
↑ whey : casein
Protein in CMB formula
> 1.6 g/dL
stable
casein > whey

[Stam, AJCN,2013]

Effects of Macronutrient Intake on Infant Weight Gain: PROTEIN

- Large randomized study in 5 Europe comparing effect of different protein content formulas:
  - 2 – 5 mo: 1.2 vs 2.0 g/dL (7 vs 11% energy)
  - 5–12 mo: 1.6 vs 3.2 g/dL (8.8 vs 17.6% energy)
- Caloric density equivalent between formulas
- Observational comparison group of BFI
- Growth followed x 24 mo
- n > 1000

[Koletzko, AJCN, 2009]



High vs Low Protein Formula on 2-24 mo Growth

- **High protein** group:
- ↑ wt gain & wt/ht by 6 mo
- Divergence 2-6 mo, peaked at 12 mo, persisted

- Low protein (vs high) ≈ BFI

- *Subgroup, high protein α ↑wt gain, adiposity, & BMI at 6, 12, 24 mo*

Koletzko, AJCN, 2009]

Effects of Protein in CF (vs formula): Infant Weight Gain

- Mechanism of enhanced growth unclear
  - IGF-1 axis & ↑ insulin documented
- Susceptibility:
  - 9-12 mo trial of cow milk (vs formula) → ↑ IGF-1 but *no effect on growth*; short duration, but also had more BFI
    - *[Larnkjaer, EJCN 2009]*
- 8 yr old children: dairy, *not meat*, associated w/ ↑ IGF-1
- **Recommendation: Protein ≤ 15% energy, late infancy & toddlers**
- FITS: median protein:
  9% (6-11 mo) & 15% (12-24 mo)

Meat as CF Source of Protein for BFI

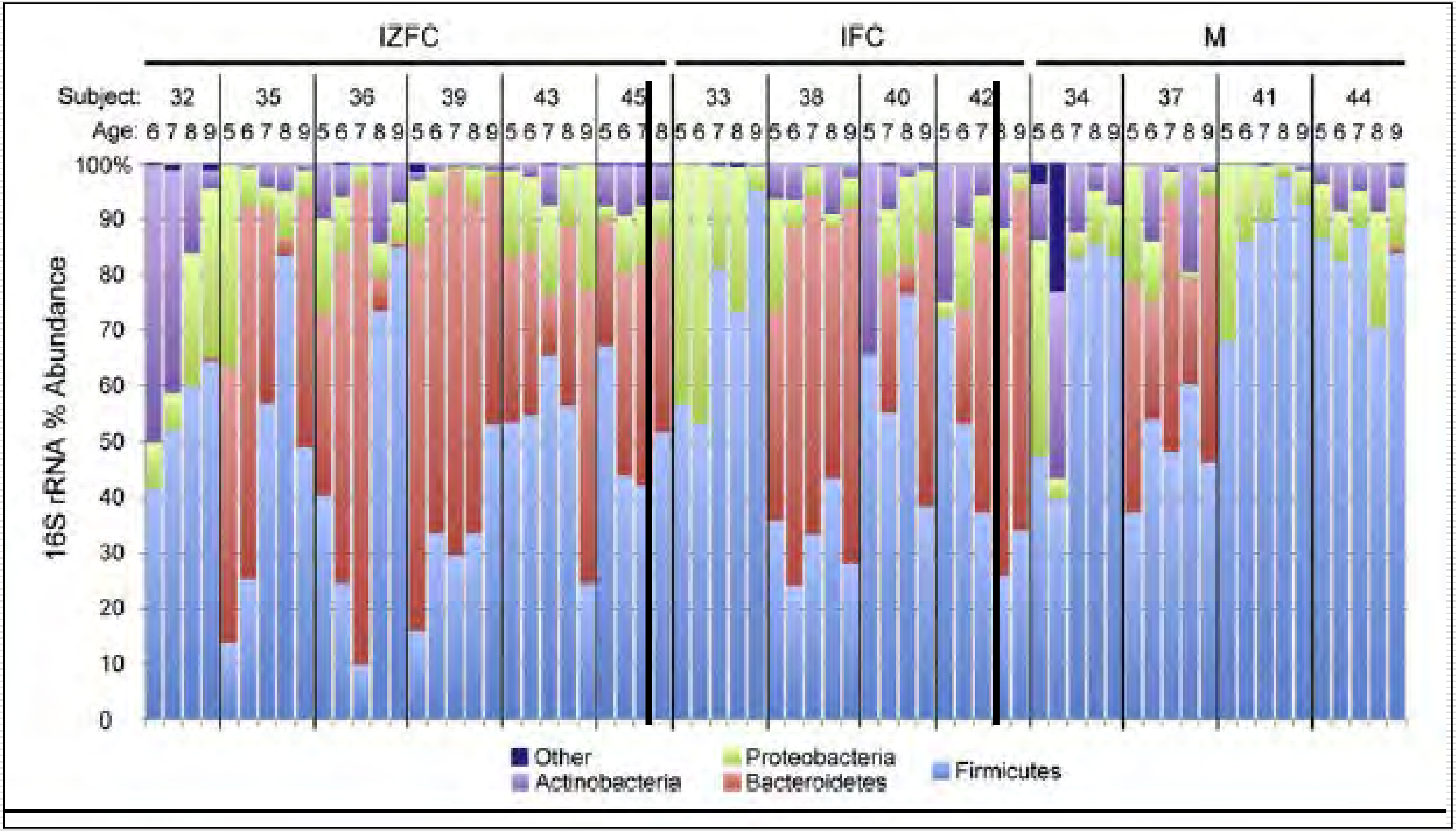
- Older BFI dependent on CF to meet iron & zinc needs
- Animal flesh foods are the richest “natural” source
  (vs Fe- fortified cereal as the vehicle)
- Denver exclusively/only BFI randomized to infant **cereal** or **meat** as first & predominant CF (+ F/V) at 5 mo
- Protein intakes: (6-9 mo)
  - Cereal (n= 28): 8-11% kcal
  - Meat (n=14): 24% kcal
- Total energy intake not different
  - 9 mo: HM + CF: protein 2.9 vs 1.6 g/kg/day (M vs C)
- WAZ ↑MEAT, ↓ in CEREAL ($p=0.05$); WLZ – n.s.; WC n.s.

[Krebs, AJCN, 2012 + unpublished]

Is Fe fortification equivalent to meat consumption?

Do FC choices affect the enteric microbiome?

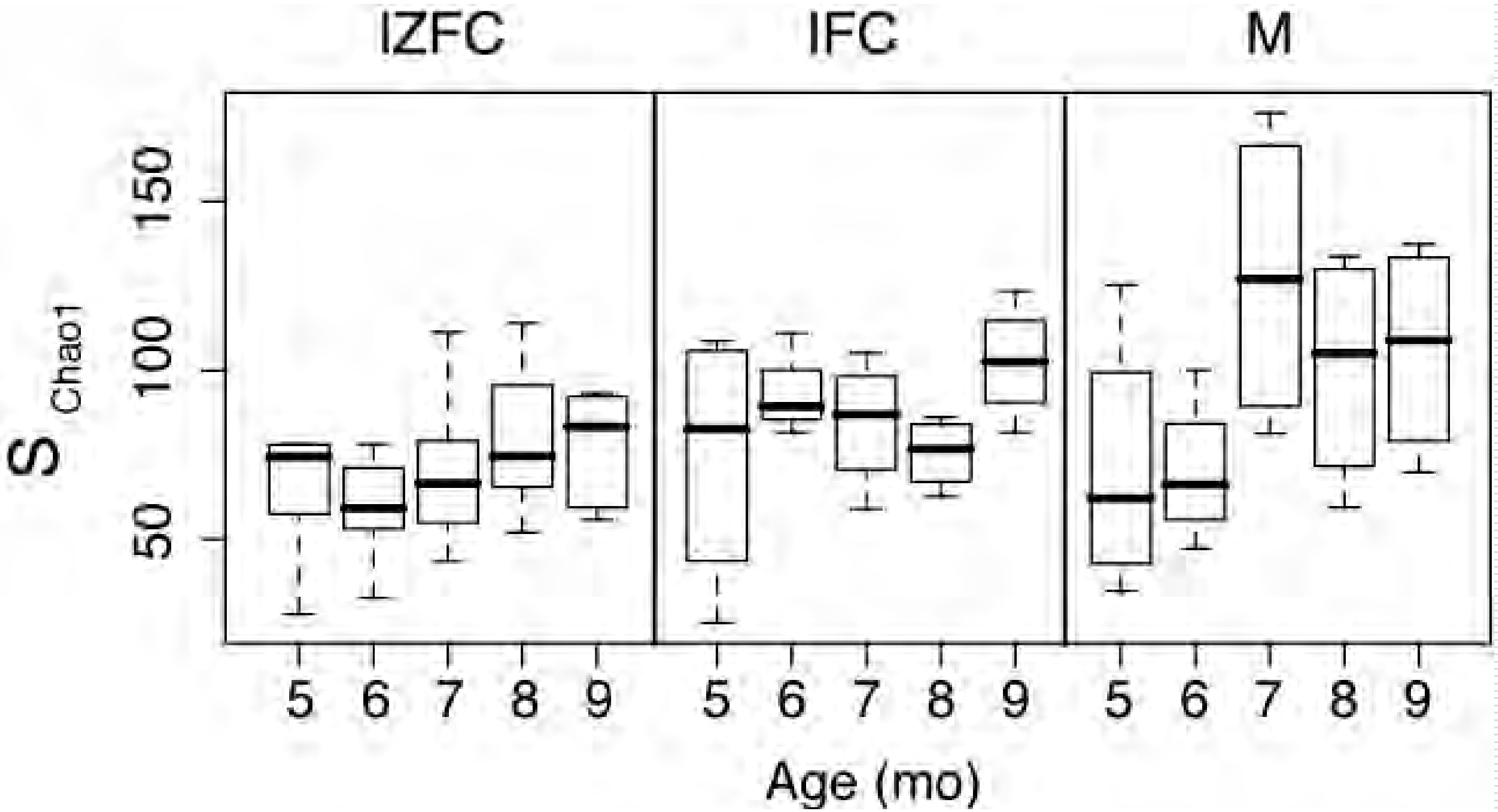
Longitudinal variation in abundances of bacterial phyla



+ *Longitudinal differences by group*

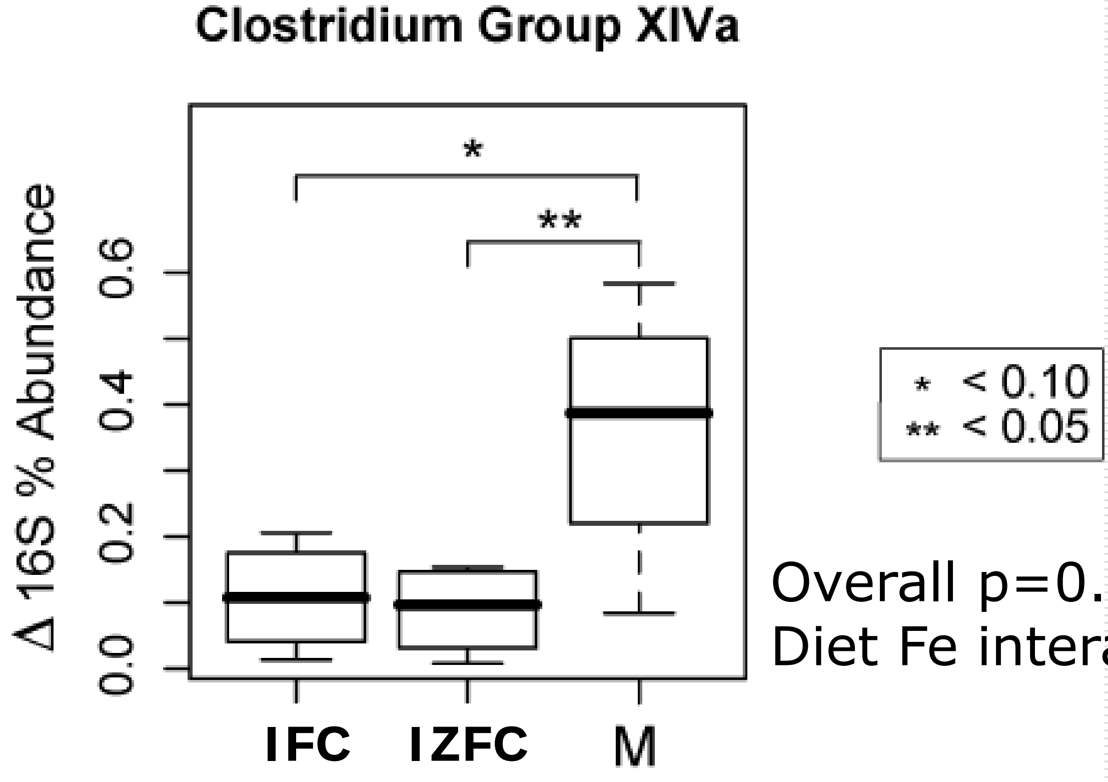
[Krebs, J Peds, 2013]

CF & MB: Species Diversity



More species diversity in M group than either of the Fe-fortified cereal groups. *[Krebs, J Peds, 2013]*

Iron fortification vs meat:
Effects on ***enteric microbiome***



Overall p=0.004;
Diet Fe interaction p=0.01

- *↑ abundance Clostridium in meat group, +interaction w/ diet Fe*

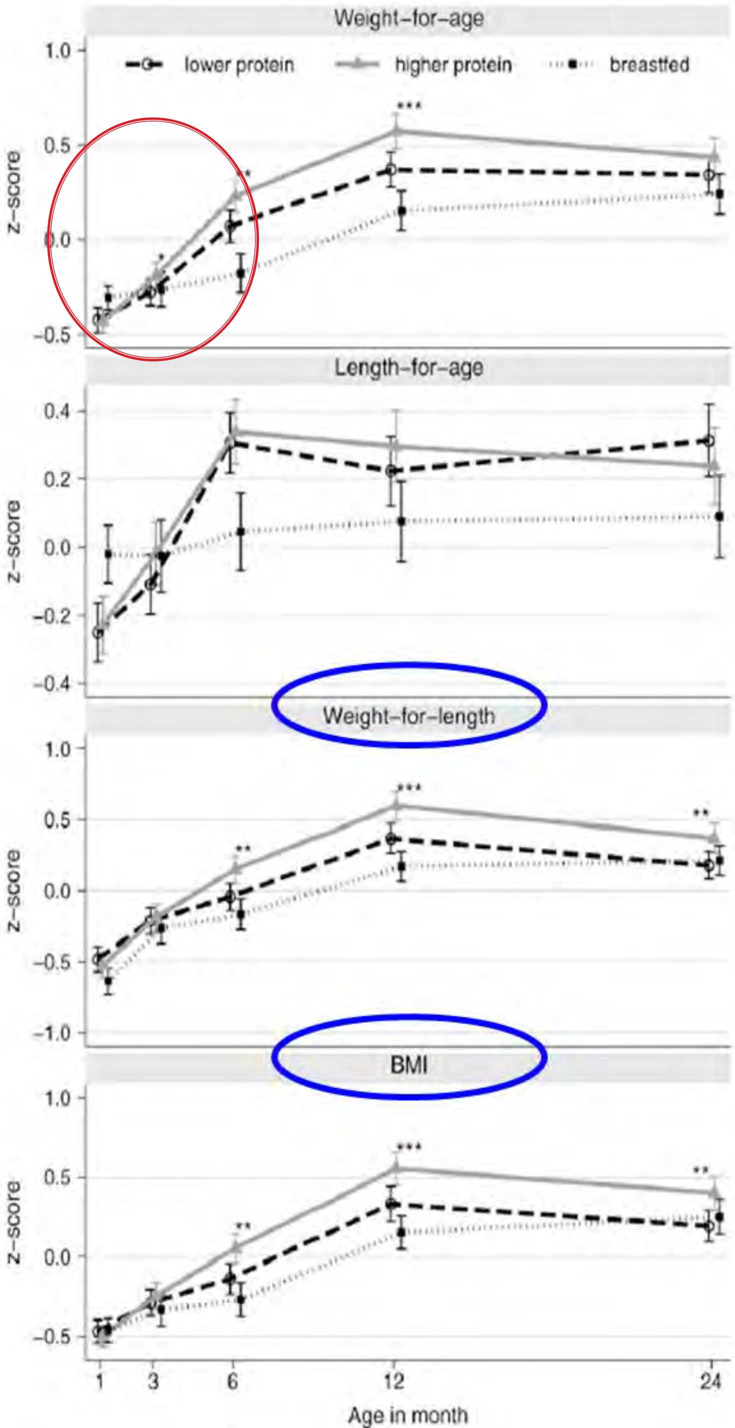
[J Peds, 2013]

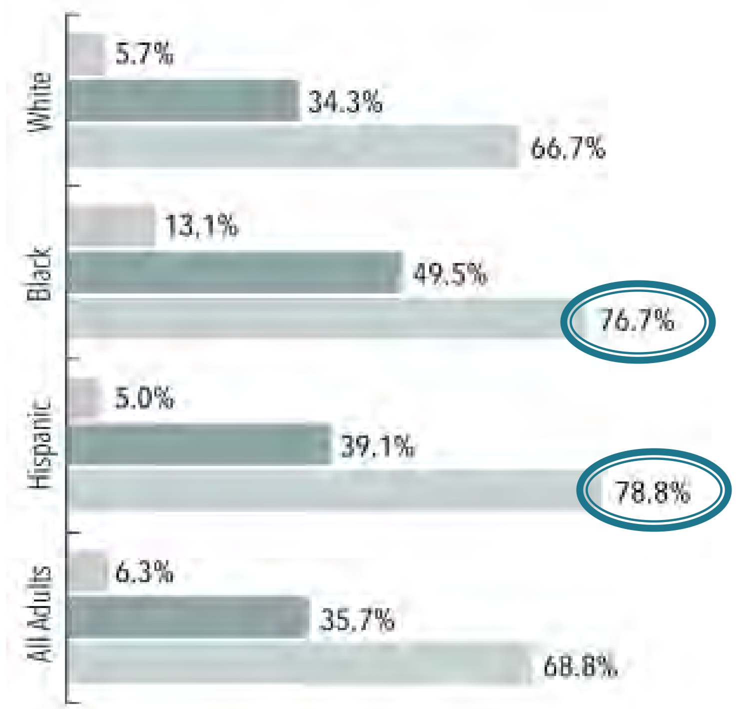
Back to Timing…

Risky Weight Gain is *before* CF

What is driving rapid early gain?

Does the fact that 64% of US women are ow/ob matter?





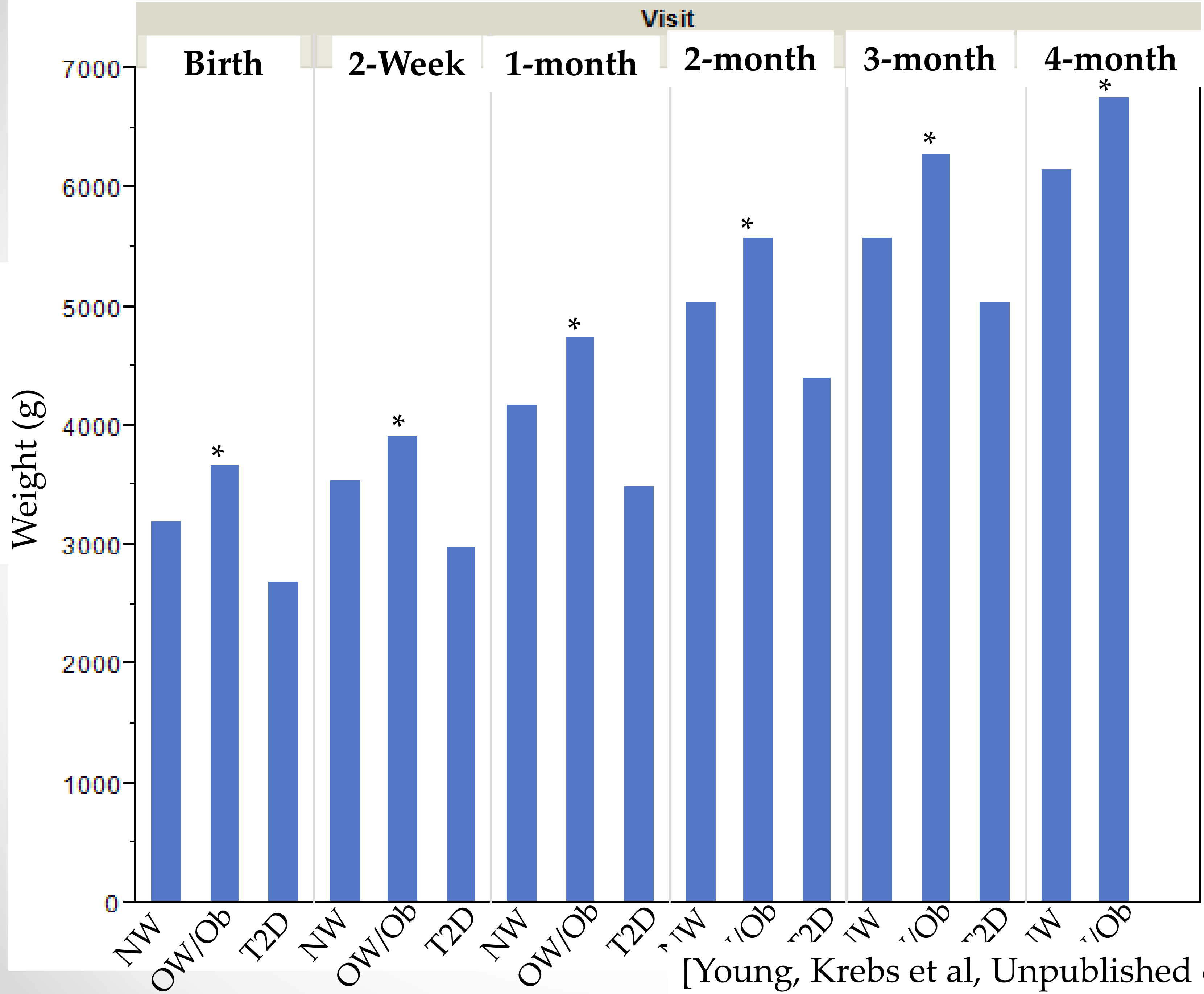
Overweight or Obesity ■ Obesity ■ Extreme obesity Source: NHANES, 2009-2010

Postnatal Impact of Maternal Obesity

- Changes in **human milk** composition
  - Fat content
  - Hormones (insulin, leptin, adiponectin, ghrelin)
  - Inflammatory cytokines; oxidant/anti-oxidant balance
- Changes in **milk production**/lactation success
- For all its protective factors, human milk may also reflect **maternal pathology** (e.g. diabesity) & influence postnatal infant outcomes

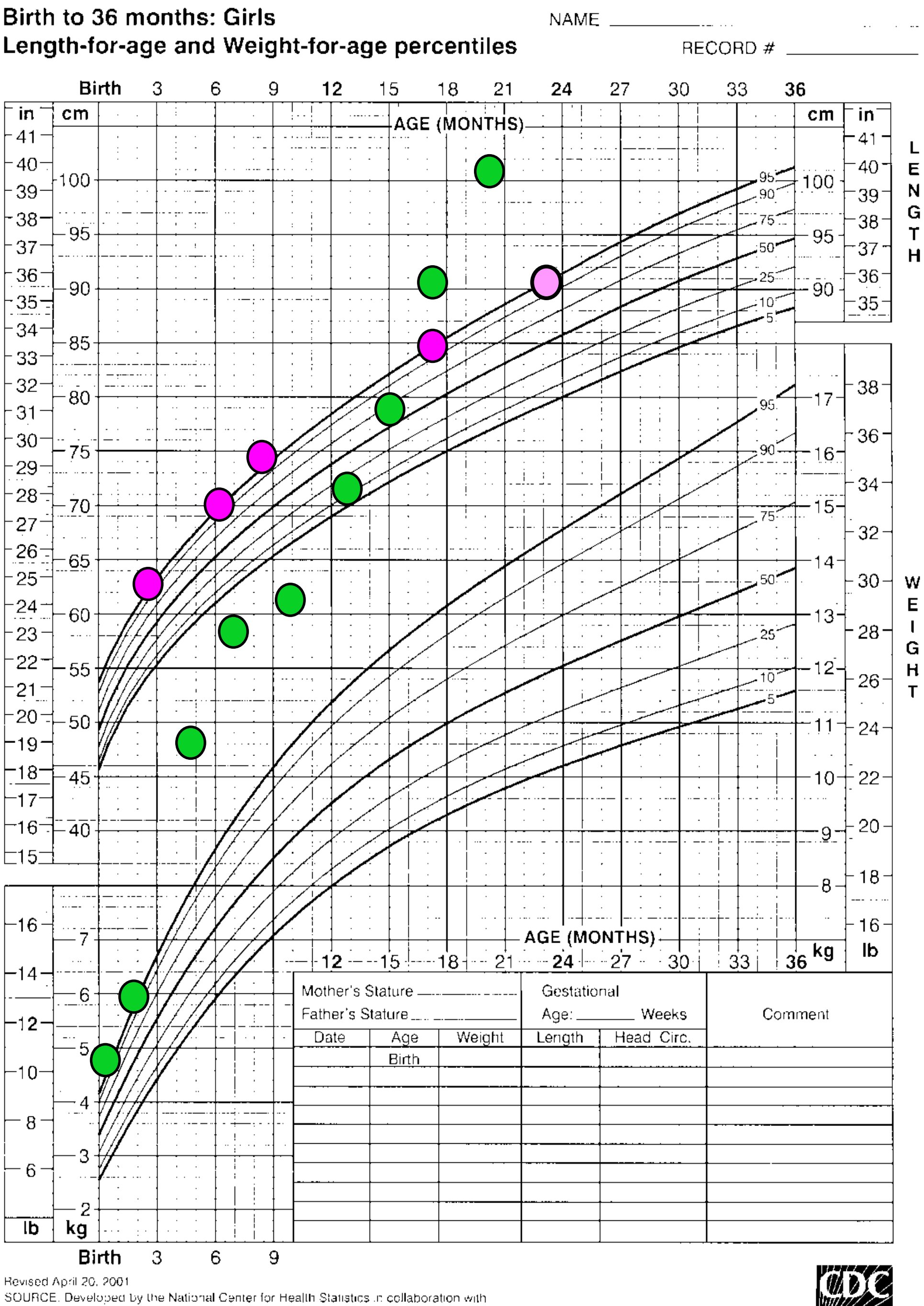
<u>Current work</u>:

- Comparisons of milk, infant growth & body composition, MB: lean vs obese vs T2DM mothers, *all breastfeeding* (w/moderate success!)



[Young, Krebs et al, Unpublished data}

A word about micronutrients

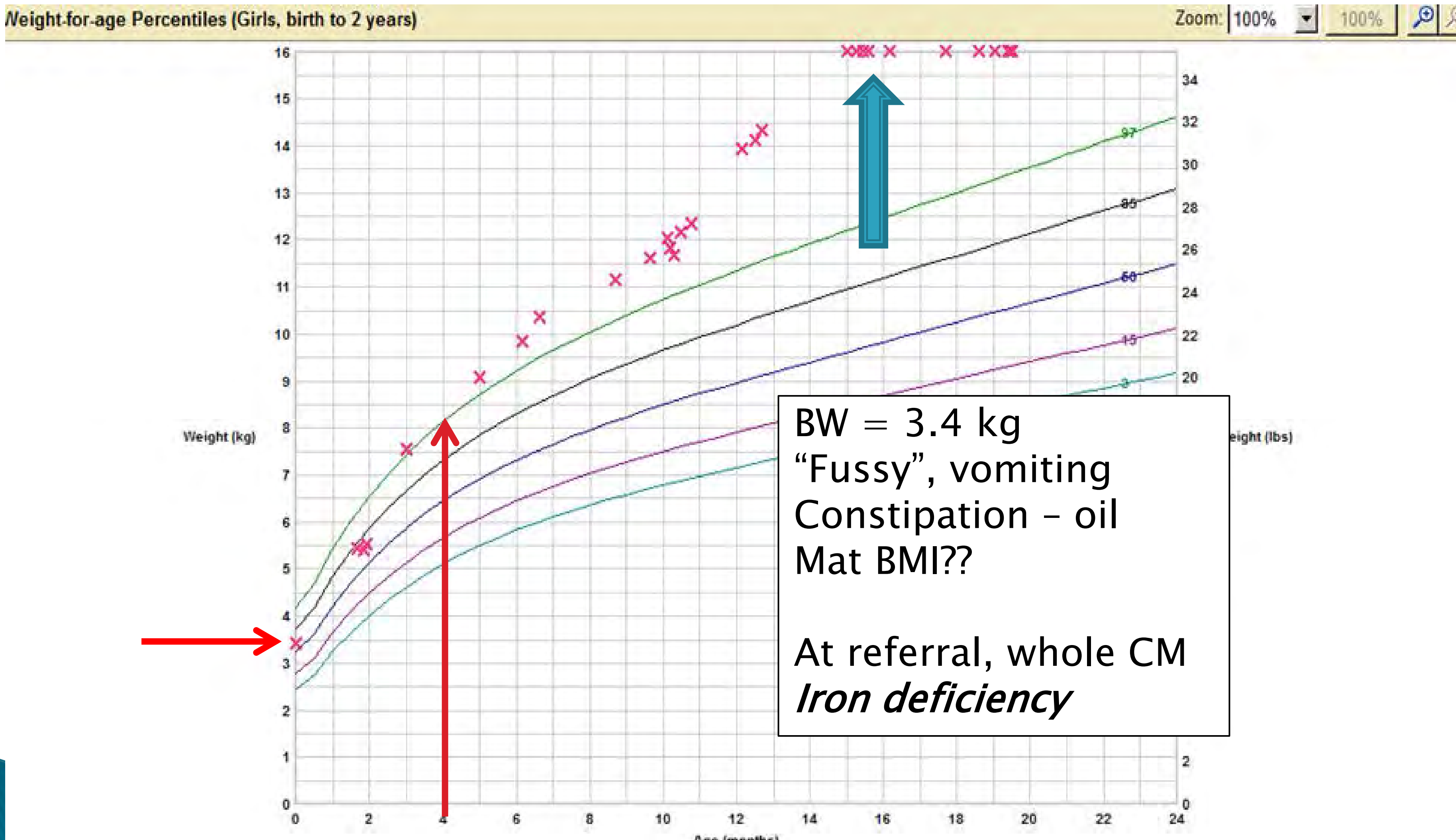


Obese Toddlers

Large from birth

- Excessive whole milk intake (~ 60 oz/d); grazing on bottle
- Large portions, 2nds
- **Iron deficiency**

Obese Toddlers



BW = 3.4 kg
"Fussy", vomiting
Constipation – oil
Mat BMI??

At referral, whole CM
Iron deficiency

Iron Deficiency in Obese Older Infants/Toddlers

- Risk factors:
  - Maternal gestational diabetes → ↓ ferritin in infant
  - Rapid weight gain
  - Wean to cow's milk
  - Obesity → ↑ inflammation → ↑ hepcidin
- How does this relate to obesity?

ID → Poor "executive function" social/emotional wariness; Shorter attention span Sleep Problems → Disturbed Mo-Child Interaction/feeding ↓ Altered Growth – ↑ (or ↓)

Short & Long-Term Health Outcomes

Diet & Nutritional Status

- Prenatal Endowment
- Breastfed vs. formula fed & Duration
- Micronutrient needs
- *CF quality & quantity*
    - ***New tastes & textures***
    - ***Neophobia***
    - ***Self-feeding***
    - ***Preferences***

Developing Infant-Child

- ↓ Growth rate
- ↑ Activity
- Gross & fine motor develop
- ↑autonomy/independence
- ↑ Distractibility
- Temperament

Parent & Environment

- Maternal Nutrient Status
- Caregiver Attentiveness
- Caregiver Feeding Style
- Meal & home routines & structure

[Young & Krebs, Current Pediatr Rep, 2013]

Summary

- **WHEN:**
  Early (< 4 mo*)* introduction of CF risk for excessive wt gain, **FFI > BFI**
- **WHAT:**
  – Protein: effects most potent early, infant feeding status (BF vs FF), and source
  – Types of CF may have unanticipated effects
  – Iron deficiency not rare in ow/ob toddlers
- **HOW:**
  – Complex interactions among diet/nutrition, infant's development & parent/home

Knowledge Gaps

- Critical windows for "risky weight gain"?
- Body composition differences & prediction of later risk?
- Impact of dietary & feeding choices on growth & metabolic status
- Does the CF period offer opportunity to modulate risk?

Recruitment, Retention and Design Issues in Intervention Research With Infants and Young Children

Julie Lumeng, MD

UNIVERSITY OF MICHIGAN

Overview

- Recruitment success
- Public perception
- Evidence base for strategies
- Potential barriers
- Our own experience

Recruitment Success

- Of 114 trials funded in the UK
  - 31% reached recruitment targets
  - recruitment start delayed in 41%
  - early recruitment problems identified in 63%

AM Macdonald, Trials, 2006

Public Perception of Research in Children

C.S. Mott Children's Hospital National Poll on Children's Health

University of Michigan C.S. Mott Children's Hospital

- 2000 US households
- Web-based survey
- Weighted to reflect population estimates from US census

http://mottnpch.org

- Have you ever been asked to have your child participate in research?
  - 92% no

- Would you allow your child to participate if the risks were small?
  - 25% yes

May 2008, Mott Children’s Hospital National Poll on Children’s Health

Why Not?

- Too high a chance for harm 73%
- Don’t want my child to be a guinea pig 60%
- Not appropriate for children to participate 41%
- Disease does not affect my child 36%

May 2008, Mott Children’s Hospital National Poll on Children’s Health

Why yes?

- Risk of harm small 42%
- Disease runs in the family 32%
- Research would help other children 27%

May 2008, Mott Children’s Hospital National Poll on Children’s Health

Public Perception of Obesity as a Health Problem for Children and Obesity Research

"How big of a problem are the following health issues for children and teens in your own community?"

“Big Problem”

1. Childhood obesity
2. Drug abuse
3. Smoking and tobacco use
4. Bullying
5. Stress
6. Alcohol abuse
7. Child abuse and neglect
8. Teen pregnancy
9. Internet safety
10. Depression

August 2013, Mott Children’s Hospital National Poll on Children’s Health

Differences by Race

- White #1
- Hispanic #1
- Black #6
  - Smoking and tobacco use
  - Drug abuse
  - School violence
  - Sexually transmitted infections
  - Teen pregnancy

August 2013, Mott Children's Hospital National Poll on Children's Health

“For each type of research, please rate how important you think it is towards improving children’s health.”

July 2011, Mott Children’s Hospital National Poll on Children’s Health

“Very Important”

1. Childhood cancers
2. Diabetes
3. Birth defects and genetic problems
4. Causes of infant deaths
5. Transplants for cancer and other diseases
6. Safety of medications
7. Heart problems
8. Safety of Vaccines
9. Improving quality of health care
10. Obesity

September 2013, Mott Children’s Hospital National Poll on Children’s Health

Evidence Base for Strategies

Improving Recruitment into RCT's

- Effective:
  - Telephone reminders
  - Opt-out (vs. opt-in) consent
  - Open design: participants know which treatment they are receiving

S Treweek, *Cochrane Reviews*, 2010

Improving Recruitment into RCT's

- No strong evidence:
  - Audiovisual or paper booklet information
  - Changes to consent process
  - Questionnaire plus trial invitation

S Treweek, *Cochrane Reviews*, 2010

Retention Methods for Population-Based Cohort Studies

- Incentives (2-13%, depending on value)
- Reminder letters (12%) and calls (5%)
- Repeat questionnaires 12%
- Alternative modes of data collection 24%

CL Booker, *BMC Public Health*, 2011

Obesity Prevention Trial in Infants

- 2870 mothers approached
  - – 76% agreed to later contact
  - – 24% could not be reached
  - – 44% agreed to participate
- Reasons for non-consent
  - – time commitment 60%
  - – return to work 27%
  - – lack of interest 19%
  - – no need for feeding advice 12%

LA Daniels, *Int J Behav Nutr Phys Act*, 2012

Parenting Intervention

- 36% agreed to participate
  - Main effect of compensation (about $15-20) for attending intervention sessions (46% vs. 26%)
  - No main effect of individual or group setting (40% vs. 32%)
- Once families attended the first session, no main effect of payment or setting
- Short term intervention effects not moderated by payment

Heinrichs, *Journal of Primary Prevention*, 2007

Predictors of Retention into Treatment Programs for Child Behavior Issues

- No effect
  - Phone call reminders
- Positive effect
  - Address practical barriers
  - More education of home visitor
  - Helping families cope with life stressors
  - Identifying and matching families' motivations to treatment structure and activities

Ingoldsby, *J Child Family Studies*, 2010

Potential Barriers to Recruiting into Studies of Childhood Obesity

“What does the word obese mean to you?”

- “Fat. Heavy. Disgusting.”- Overweight, white
- “Obese is very, very fat, kind of grotesque, um . . . someone that has completely let themselves go.”- Obese, white
- “Overweight is somebody that you can tell that is fat, lazy, and is not active at all.” - Normal weight, white
- “I think it’s like, kind of big, lazy . . . they want to eat a lot.”- Obese, biracial
- “Not caring about yourself anymore and really not taking initiative.” –Obese, black
- “I think the majority of the [obese] people are probably miserable with themselves.” –Obese, white

S Ellis, JC Lumeng, *J Nutri Educ Behav,* 2013

“What causes a child to be overweight?”

- “I definitely blame overweight children on the parents. One hundred percent . . .I think it’s because they’re not educated, because they don’t know any better, because they’re feeding them things that are making [them] overweight and not giving them a healthy diet . . . a lot of parents just don’t care. I mean, honestly, there’s a lot of parents that just don’t care…I think children are overweight because of parents neglecting to do their jobs the way that they should, and [not] caring about their weight and their health.”   --- *mother and child normal weight*

- “[Children are overweight] if they have a parent that just lets them sit around and eat and watch TV.” --- *mother and child obese*

- “The mothers give them Twinkies, candy and ice cream and – everyday, this is an everyday thing -- cookies and, you know, to me that’s what causes a child to be overweight.” --- *mother and child obese*

How were you fed growing up? Are you doing it the same or different for your children?

- “Dinner, what it is with me and [my child] is nothing like it was with my family. When I was a kid we didn’t have dinners like that. ‘Here’s a hot dog. Here’s a sandwich. Eat it.’ You know? It’s kinda like that. Not with me and my daughter. I make dinner. I don’t throw a hot dog at her and say, ‘Here you go. Eat that. You’re good.’ No. I don’t do that. I just feel I wasn’t…I wish things would have been different for me, but it wasn’t.” --- *mother and child obese*

- “My dad raised me by himself. Um, and he had a gambling problem. There was a bar just down the road. So, from like, 10 and up, um -- I don’t remember much from 10 and down -- I fed myself. I always make sure my kids have breakfast, lunch, and dinner. My dad never did that, he, just, fend for yourself really, so, that’s, that’s one thing I do. I make sure that they eat and I make sure that we eat together.” --- *mother obese, child weight status unknown*

A Kalinowski, JC Lumeng, *J Nutri Educ Behav,* 2011

Recruitment Strategy: “Your child is overweight or obese. We’d like to invite you to be in our study.”

What parent hears: “You and/or your child are lazy and unmotivated and you are a bad parent. We’d like you to be in our study.”

The Challenge:

- In order to embrace a goal to change behavior, one has to believe the behavior could be improved
- Forces a parent into the current public framing they have been “lazy” or a “bad parent” and is too difficult to reconcile
- Intense stigma is a major barrier

Parents already feel competent and don’t feel their parenting needs to change

	% agree
I would make a fine model for a new parent.	90%
I meet my own personal expectations for caring for my child.	95%
I am comfortable and familiar with being a parent.	100%
I am confident that I can manage my child’s behavior	96%

Meaning of “Health” across SES Groups

- Low Income
  - Sense of well-being
  - Sense of self-worth
  - “Feeling well”
- Middle, Upper Income
  - Exercising often
  - Eating well
  - “Combatting” obesity

Warin, *Sociology of Health and Illness,* 2008*;* Smith et al*, Appetite’,* 2010*;* Inglis, *Appetite,* 2005

Our Own Experience

Retention

- Quarterly phone calls to update contact information ($10)
- Compensation rates at about $20/hour
- Repeated expressions of gratitude for participating
- Contact 8-9 times per year (newsletters, holiday gift bag, birthday card/book)
- Call back 1 week later to ask how the study visit went
- Check ins with participants when new staff are hired to see “how the study visit went”
- 1-800 number manned all day by friendly, organized staff

Essential Characteristics for Field Staff

- Able to adhere to a repetitive protocol but also think on your feet and problem solve
- Able to function as a researcher and not an interventionist (we are not changing the world today)
- Able to interact with study participants with respect and enthusiasm
- Able to view the environments they witness with an anthropologist’s interest

Caring for the Staff

- Quarterly retreats
- PI is available by telephone/page 24-7 for CPS calls/concerns
- Regular debriefing and feedback about challenging situations
- If errors are made, “change the process” don’t punish the individual

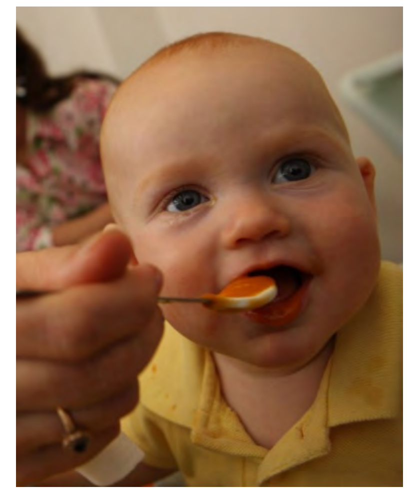
Summary

- Parents do not want their children to be obese.
- Parents want to be good parents.
- It has been a lifelong struggle for many mothers.
- “Tell me something I don’t already know.”
- “Don’t tell me to have more self-control or try harder.”

NIH Workshop on Prevention of Obesity in Infancy and Early Childhood
Bethesda MD
October 30- November 1, 2013

Early Experiences:
Impact on Flavor Learning and Growth



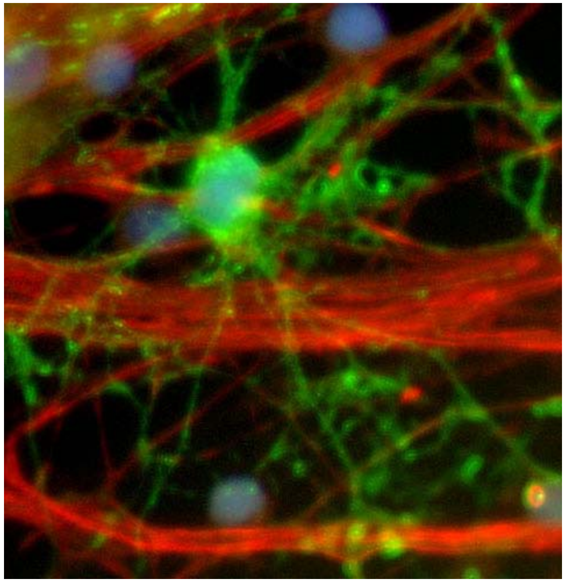



Julie A. Mennella, PhD
Monell Chemical Senses Center

Disclosure: NIH grants HD37119, HD0723201 and DC01128

Function of Nervous System

- Store information and produce adaptive behaviors that reflect prior experience.
- Functioning is established, and many behaviors are best learned, early in life
  - early sensory experiences sculpts neuronal circuits
  - maturation of the senses, at functional and morphological levels, often depends upon proper stimulation during well-defined periods of development.



V. Shukla; 2008 NICHD Image Competition Entry: Section on Nervous System Development and Plasticity (http://retreat.nichd.nih.gov/pastretreats/2008/2008images.html)

Early life exposures (both social and biological) explain trajectories of health in adulthood, decades later.

Outline of Talk

- Part 1: Importance of early life for development of food preferences
  - Basic biology of taste world of children
  - Insights into vulnerabilities of current food environment
  - How children learn to like new foods
  - Breastfeeding vs formula feeding
- Part 2: Importance of early life for growth
  - Not all formulas are alike
    - Food preferences
    - Satiation properties
    - Growth trajectories

Part 1:
Importance of early life for development of food preferences

What we eat early in life is important.

- New foods more likely accepted early (<3 years of age) as opposed to later in life;
- Food preferences formed during the first years of life predict what's actually eaten;
  - children eat what they like.
- Dietary patterns track from early to later childhood;
- Once preferences formed, difficult to change.
- Where you start influences where you end up!

Birch, 1994
Resnicow et al., 1998
Skinner et al., 2002;
Cooke et al., 2004;
Nicklaus et al., 2004;
Pearson et al., 2011
Mikkila et al., 2004, 2005, 2007

Even before their 2nd birthday, many children are developing the same eating habits that plague adults:

- too few fruits and vegetables
- too much sugars
  - 16% of total caloric intake comes from added sugars (Ervin et al., 2012)
- too much salt
  - Estimated average intake of sodium for those ≥2 years is ~3,266 mg/day
  - High sodium intake begins early
- Many illnesses of modern society are, in part, the consequence of poor food choices.

Feeding Infant and Toddler Studies (FITS)
Fox et al., *JADA* 2004
Heird et al., *JADA* 2006
Mennella et al., *JADA* 2006
Siega-Riz et al., *JADA* 2010
Ziegler et al., *JADA* 2006

- How can we account for patterns of food choice that seem antithetical to health, and for the difficulties in changing them?
- How do individuals and society manage the rich abundance of food that now characterizes this evolutionary blink of an eye we find ourselves in?

Several factors conspire to predispose children to consume diets that may lead to obesity:

- Inborn, evolutionarily driven taste preferences;
- Detection of salt and sweet is associated with powerful hedonic appeal, especially among children.
- Learning to like foods begins early.

Ontogeny of Taste: Accumulating Knowledge Base

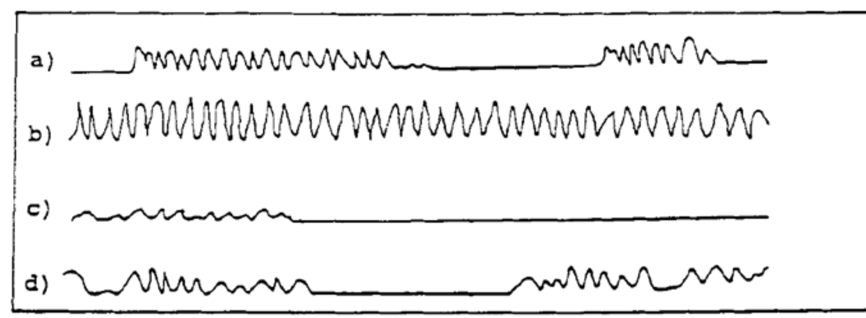
- Children are born with a well-developed taste system that by the last trimester of pregnancy capable of conveying information to the CNS
- Information is made available to systems organizing a variety of consummatory and reflex-like behaviors;
- Inborn responses that change and mature throughout development.

Sweet:
“Oldest Reward”

Steiner, Glaser, Hawilo and Berridge,
Neurosci Biobehav Rev, 2001

- Within hours of birth, infants exhibit a strong preference for sweet tastes.
- Convergence of findings
  - Intake
  - Suckling patterning
  - Facial expressions
  - Heart rate
  - Calming/decrease crying
- Remains heightened and acts as analgesic during childhood
- Taste signal for mother’s milk and energy

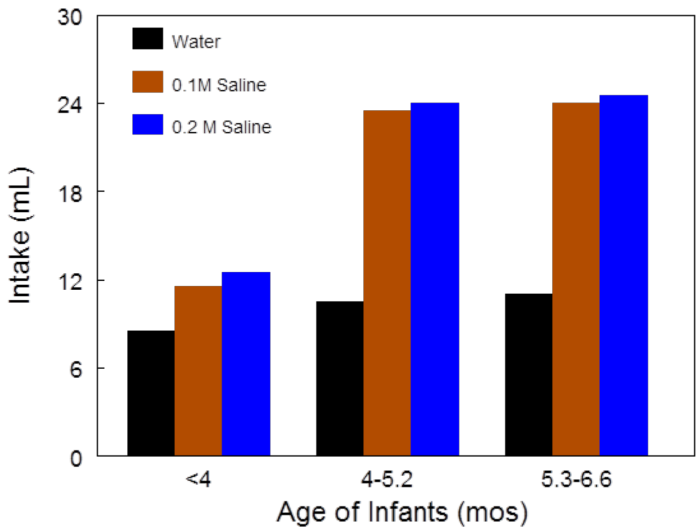
Term and Preterm Infants



Sucking curves generated by term (a: latex nipple; b:sucrose nipple) and preterm (25-36 wks gestational age) c: latex nipple; d: :sucrose nipple) infant. Maone et al., 1990

Salt:
"Primordial Narcotic"

- Salt taste preference is first observed after 4 months of age
- Convergence of findings
  - Intake
  - Suckling patterning
- Remains heightened during childhood
- Taste signal for needed minerals; Liking attracts to sodium, needed for fluid balance and nerve conductance and signal for other minerals needed for bone growth.



Evidence of Developmental Plasticity:

- Early exposures to sweet liquids and sweetened foods or starchy table foods (which are high in sodium) leads to greater preference during childhood
  - Beauchamp and Moran, 1982, 1984; Pepino and Mennella 2005
  - Liem and Mennella, 2002; Liem and De Graaf, 2004
  - Stein et al., 2012
- Children learn to prefer flavors associated with higher carbohydrate content
  - Birch et al., 1990
- The context in which the taste experience occurs is an important factor and through familiarization, children develop a sense of what should, or should not, taste sweet or salty.

Two potential strategies:

Change the stimulus

or

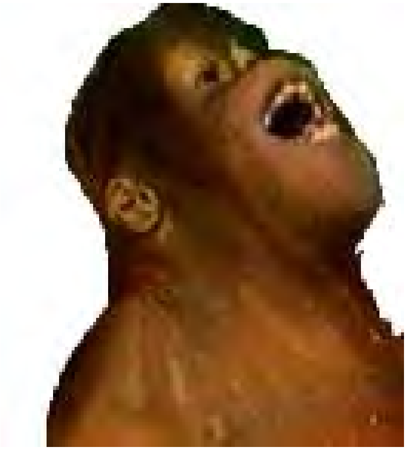
Change the person

Gaps in Knowledge

- Change requires a social, political, and economic food environment.
- Science tells us that the struggle parents have in modifying their children's diets to comply with recommendations has a biological basis.
- Understanding the basic biology that drives the hedonic dimension of sweet and salty taste and learning to like the complex flavors of foods illustrates their vulnerability to the current food environment.
- No evidence-based research on how to decrease sweet and salt taste preferences in children.

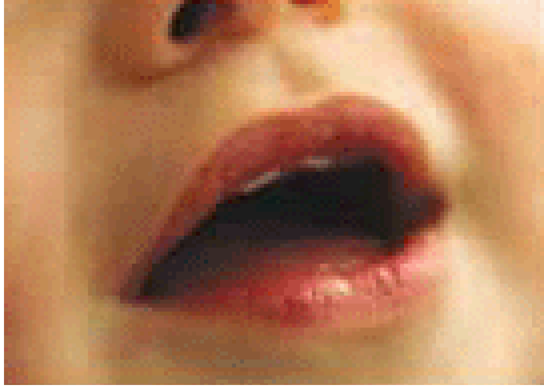
Bitter:
“Taste of Poison”

- Ability to taste bitter compounds, and widespread tendency to reject them among many species, is an adaptation:
  - protects animals from consuming toxic compounds and being poisoned
  - protects the plant producing chemicals from being eaten
- ~ 25 different T2R discovered - substantial degree of sequence diversity and variation;
- Sensitivity to some bitters is enhanced during childhood
  - *Pediatrics* 115:e216-22, 2005
  - *BMC Genetics* 11: 60, 2010



Courtesy of K. Berridge
Steiner, Glaser, Hawilo and Berridge, *Neurosci Biobehav Rev*, 2001

- We cannot easily change the basic ingrained biology of avoiding bitterness and liking sweets to get children to prefer broccoli to candy.
- If this is the bad news, the good news arises from knowledge gained from our experimental research on how, beginning very early in life, sensory experience can shape and modify flavor and food preferences.
- Our biology is <u>not</u> necessarily our destiny!



How do we learn to like foods:
Have mom eat 'healthy' foods
during pregnancy and breastfeed.

Uniqueness of Sensory Experiences

- Psychophysical analyses revealed variety of flavors from maternal diet are transmitted.
- Infants can detect the flavors in amniotic fluid and milk.
- Flavor memories are formed.
- Fundamental feature of mammalian flavor learning

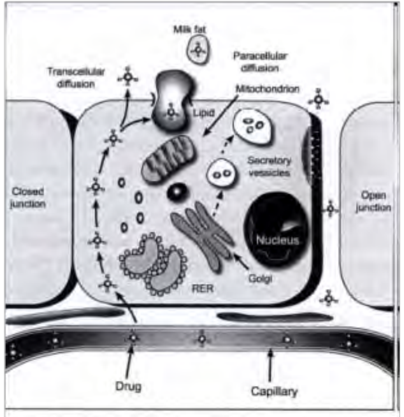
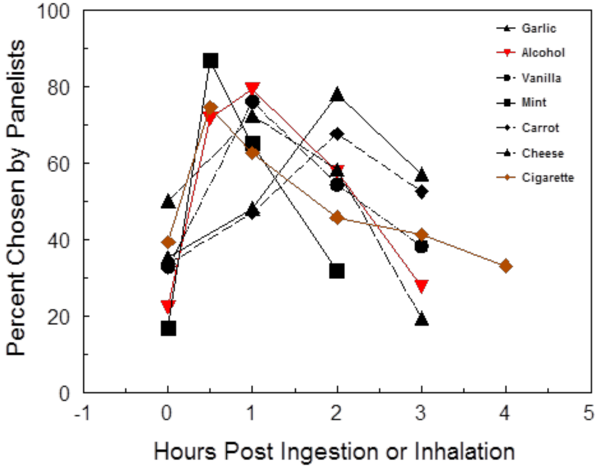


Figure 2. Diagrammatic representation of the pathways of milk secretion and the way in which drugs in plasma may traverse the lactocyte and enter milk.



Review: Mennella, JA. The chemical senses and the development of flavor preferences in humans. In: Hartmann PE, Hale T (eds). Textbook on Human Lactation. Texas: Hale Publishing, 2007: 403-414.

Fundamental Feature of Mammals

"It's not innate knowledge. It's learned and part of their culture."
F. Provenza

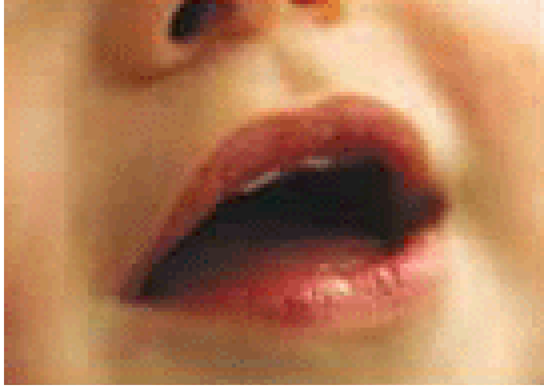
- Learning about foods begins before foraging.
- Young experience flavors of diet of their mothers- the foods she likes, or at the very least, has access to.
- By following their mothers, young animals learn
  - What plants to avoid
  - What plants to eat occasionally
  - When plants are at their peak nutritional content

Research of Provenza, Galef, Hudson, Bilko and others

First exposure to flavors of foods begins before first 'taste' of food

- Infants can detect flavors;
- Experience during late prenatal as well as early neonatal (first 3 months) facilitates enjoyment of a food;
- Mothers who eat more fruits or vegetables have infants who are more accepting at weaning
- Mother's milk is a flavor bridge
  - Continuity in flavor experiences
- Repeated exposure building on the familiar.

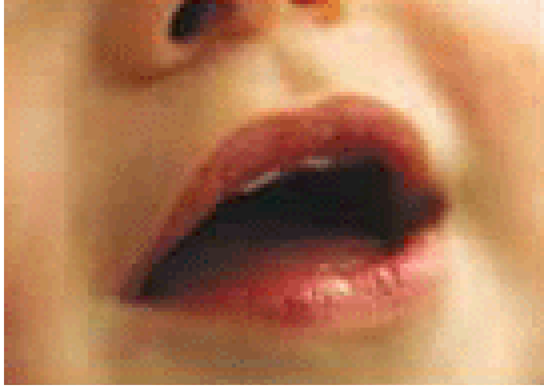
Pediatrics, 1994; 2001, 2007
Am J Clin Nutr, 2001
Physiol Behav, 2008



Differences between breastfed and formula fed infants:

- Formula lacks flavors of maternal diet and variety
- Breastfeeding confers an advantage for initial acceptance of fruits and vegetables.

Breastfeeding confers an advantage but <u>only</u> if mother eats the food.



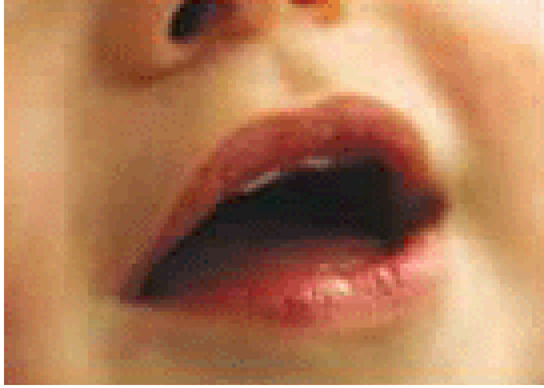
Differences among formula fed infants: *timing and duration of experience*

Formula Feeding: Not a homogenous group

- Formula feeding, a new human innovation in feeding infants.
- Types of formulas differ in composition and flavor profile
  - Cow milk based (CMF)*
  - Soy
  - Partial hydrolysate
  - Extensively hydrolysate formulas (ePHF)*
- Randomized clinical trials: There is a sensitive period after which infants are no longer open to developing an appreciation for these flavors.

Future Directions

- Our previous experiments demonstrated that <u>what</u> a mother eats during the first 4 months of lactation can influence her child's food preferences.
- The overarching goal of our new research (Grant HD37119) is to conduct a randomized clinical trial to specify the <u>timing</u> and effects of the sensitive period for flavor learning in breast milk.



How do we learn to like foods:
Both breast and formula fed infants learn!

Learning about Food

- Presence of a food in the environment does not ensure that the animal will learn to eat particular food.
- Rather, food preferences increase with <u>repeated exposures</u> and <u>variety</u> and are strongly influenced by the conditions in which the exposure occurs.

Summary of Experimental Research: 6-12 months

Type of Exposure	Target Food	Result	Reference
8 days of repeated exposure	Pears	Increased acceptance of pears; no effect on acceptance of novel vegetable (green beans)	Mennella et al., 2008
8 days of repeated exposure	Peaches	Increased acceptance of peaches	Forestell and Mennella, 2007
9 days of repeated exposure	Carrots	Increased acceptance of carrots	Gerrish and Mennella, 2001
10 days of repeated exposure	Bananas or peas	Increased acceptance of target food; seen as early as 1st day of exposure	Birch et al., 1998
8 days of repeated exposure	Green beans	Increased acceptance of green beans	Sullivan and Birch, 1994; Mennella et al., 2008; Forestell and Mennella, 2007
8 days of between-meal variety	Peaches, prunes, apples	Increased acceptance of novel fruit (pears); no effect of acceptance of novel vegetable (green beans)	Mennella et al., 2008
9 days of between-meal variety	Peas, potatoes, squash	Increased acceptance of novel vegetable (carrots) and meat (chicken)	Gerrish and Mennella, 2001
8 days of between-meal variety	Squash, spinach, carrots	Increased acceptance of carrots and spinach; increased acceptance of novel vegetable (green beans)	Mennella et al., 2008
8 days of between- and within-meal variety	Squash/peas, carrot/peas, squash/spinach	Increased acceptance of carrots and spinach; increased acceptance of novel vegetable (green beans)	Mennella et al., 2008
10-20 days of between- and within- meal variety	Pureed, lumpy and diced *vs* pureed and diced apple sauce	Increased acceptance of diced apples in those who experienced more complex textures.	Lundy et al., 1998

Gaps in Knowledge

- Can’t focus on feeding children separately from caregivers. Mothers feed their children the foods that they like and enjoy.
- Mechanisms? recent evidence in adults found relationship between diet and levels of messenger RNA for one of the bitter taste receptor gene (Lipchock et al., AJCN, 2013)
  - Is expression fixed early in life? Does it may change with development? Does diet drive expression or is it the reverse? Is timing important?
- Research needed to: 1) improve dietary habits of women during pregnancy and postpartum; and 2) understand how infants learn to like foods (timing and duration

Part 2:
Importance of early life for growth

Early Programming

- Rapid rates of growth during the first year of life increase risks for later obesity and a number of diseases.
- Infancy - one time in life when predominantly milk-based diet
  - Breast milk (gold standard)
  - Formula (many different types)
- Not all milks are alike
  - Breast milk is the gold standard
  - By 4 months, 60% are being fed formula either as sole milk source or part of mixed feed (Grummer-Strawn et al., 2008).

Growth during Infancy

Several studies have shown that formula-fed infants are larger than breastfed infants by the end of the first year of life

- Koletzko et al (2009)
  - Europe:
  - 1138 infants
- Kramer et al (2004)
  - Republic of Belarus
  - 16,755 infants
- Agostoni et al (1990)
  - Italy
  - 119 infants
- Dewey et al (1993)
  - United States
  - 80 infants

Breastfeeding *vs* Formula Feeding

- Differences in rate of growth can be attributed to the <u>behaviors</u> of formula feeding
  - Breastfeeding imparts more control by the infant
  - Mothers overfeed when they feed from a bottle
  - If bottle feeding was the sole culprit in overfeeding, then one would expect breastfed infants to overfeed when breast milk is fed from a bottle. This is not the case (Bartok et al., 2011)!
- Differences in rate of growth can be attributed to <u>composition</u> of the milk
- Both!

- Formula-fed infants are not a homogeneous group. Among formulas for healthy term infants, one of the main distinctions is their protein source and/or degree of protein hydrolysis.

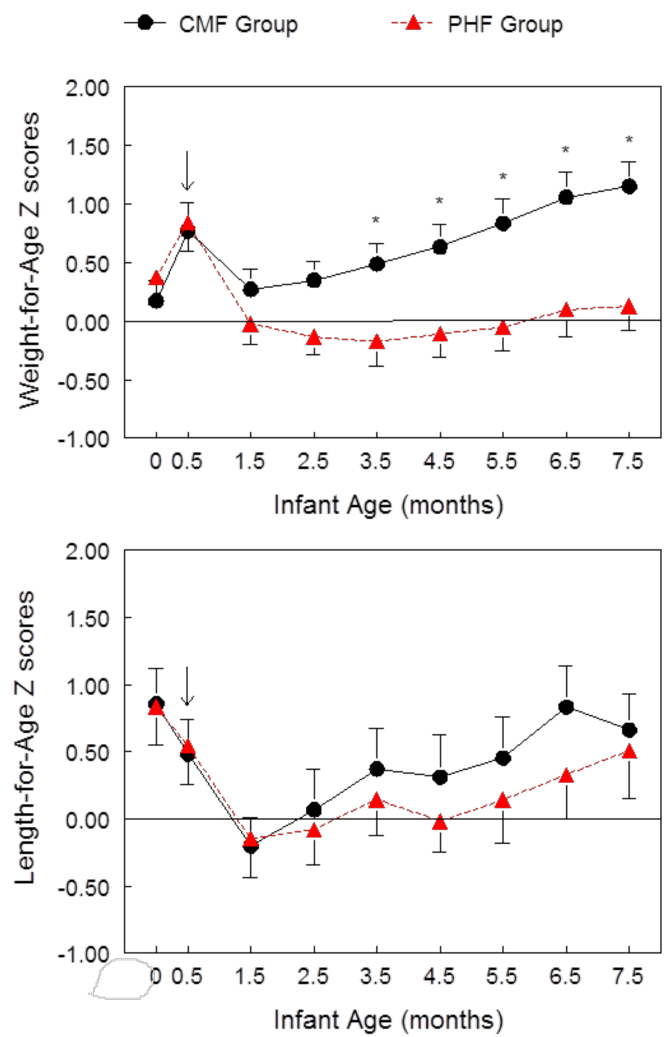
Summary of Growth Studies

Study Population	Age of Infants	Exclusive Formula feeding?	Outcome	Citation
Healthy	1-3 months	yes	No differences	Hauser et al., 1993, Vanderplas et al., 1993
Healthy	1-1.5 months	yes	No difference	Hyams et al., 1995
Healthy	1.5-6 months	No, BF for 6 wks	No differences	Hernell et al., 2003
FHA	0-12 months	No, BF for first 5-6 mos	ePHF<CMF	Rzehak et al., 2009
FHA	0-6 months	yes	ePHF<CMF	Roche et al., 1993
Healthy	0-9 months	yes	ePHF<CMF	Ventura, Beauchamp and Mennella, 2011

CMF=Cow Milk Formula
ePHF=Protein Hydrolysate Formula
BF-Breastfed
FHA=Family history of atopic disease

Not all formulas are alike in terms of growth!

- CMF-fed infants' weight gain was accelerated whereas ePHF-fed infants' weight gain was normative
  - growth differences were attributable to differences in gains in weight, not length
  - Effects did <u>not</u> appear to be mediated by the introduction of solid foods into the infant's diet.
- During monthly assessments, ePHF-fed infants consumed <u>less</u> formula to satiation than did CMF-fed infants (confirmed by other studies).



Pediatrics 127: 110-118, 2011

Mechanisms

Dr. Alison Ventura

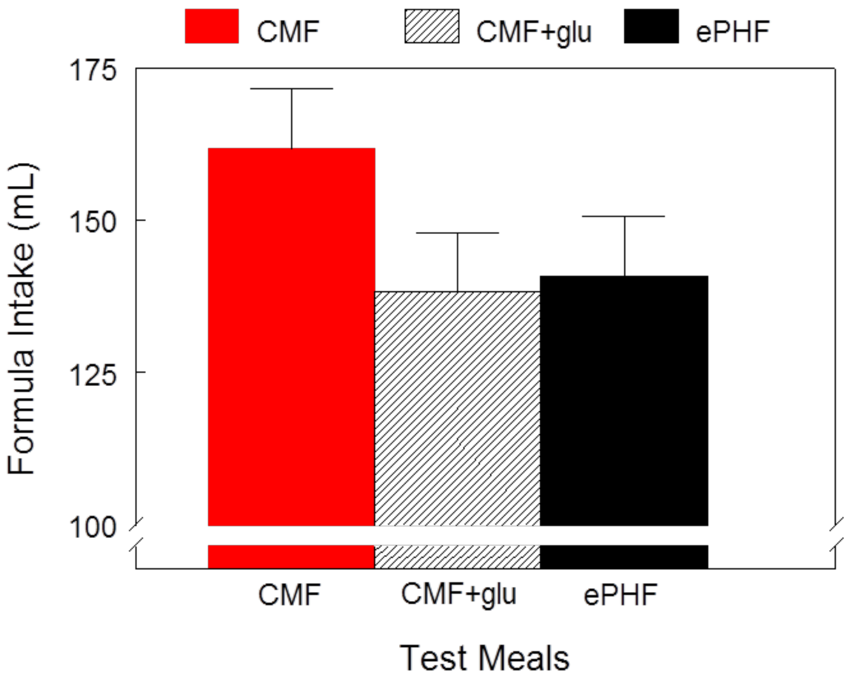
Hypothesis: Differences in the levels of free amino acids are sufficient to produce intake differences when infants feed cow milk formula versus ePHF

- Free glutamate serves as a key signal for satiation in adult and animal studies (Viarouge et al 1992; San Gabriel et al 2007; Niigima 2000)
- Glutamate is the most abundant free amino acid in human breast milk (Agostoni et al 2000)

Goal of postdoctoral fellowship NRSA (F32HD063343) of Dr. Alison Ventura, current Assistant Professor at Drexel University.

Level of one free amino acid was sufficient to produce intake differences

- Within-subject study
- Lowered intakes
- No evidence of compensation for lower intakes at the 2nd formula meal
- Greater satiation
- No difference in activity levels



Ventura, Beauchamp and Mennella, AJCN, 2012

Patterning of behaviors doesn’t change when infants satiate on lower volumes

- Infants (<4 months) start signaling earlier when feeding CMF with free glutamate;
- No difference in number and types of behaviors;
- Remarkable consistency in the types of behaviors infants use during feeding.

Findings

- We cannot consider formula-fed infants as a homogeneous group with respect to <u>satiation</u>.
  - Formula-fed infants can self-regulate intake
  - What is fed to infants in the bottle may be as important as how it is fed to them.
  - What are mechanisms underlying differential growth and flavor preferences? Sensitive periods?

Current Research (HD 0723201)

Co-PI: Jillian Trabulsi, RD, PhD, University of Delaware
Collaborators: Drs. Dale Schoeller, Gary Wu and Virginia Stallings

Dr. Jillian Trabulsi

- Since infants who feed one type of formula (cow milk formula) exhibit more rapid growth than those who feed extensively hydrolyzed formulas or those who breast feed.
- Study aims to determine mechanisms underlying such growth differences to better understand their interrelationships to early growth and obesity risks. Specifically, effect of infant diet composition on
    1. energy intake
    2. energy expenditure
    3. the gut microbiome
    4. satiety and satiation signals

Gaps in Knowledge

- Today's infant formulas differ substantially in macronutrient composition and presence/absence of pre- and pro-biotics.
  - Do these compositional differences affect energy balance and growth?

- As new infant formulas are developed, a common goal of premarket growth and safety trials is to demonstrate a rate of weight gain on the new formula that is comparable to that of breast-fed infants or a currently marketed infant formula over the first 4 months of life
  - to assure formula is suitable during early infancy (a period of rapid growth)
  - because nutrient intake during this time period is mainly attributed to infant formula rather than confounders such as solid foods.
- Problem: many studies do not follow the infants into the 2nd 6 months of life, which is the time in which formula fed infants tend to gain more weight than breastfed infants. Little research on impact of mixed feedings.

NYU School of Medicine
NYU LANGONE MEDICAL CENTER

Bellevue Hospital Center

HHC NEW YORK CITY HEALTH AND HOSPITALS CORPORATION

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Primary Care-Based Early Childhood Obesity Prevention Beginning in Pregnancy

Mary Jo Messito, M.D.
Clinical Assistant Professor of Pediatrics
NYU School of Medicine/Bellevue Hospital Center

Workshop on the Prevention of Obesity in Infancy and Early Childhood
National Institutes of Health October 30 – November 1, 2013

Funding Source: AFRI Program Name: Childhood Obesity Prevention: Integrated Research, Education, and Extension to Prevent Childhood Obesity. Program Code: A2101 Grant/Award #: 2011-68001-30207

Background:

Why intervene in pregnancy and infancy?

- Both rapid infant weight gain and obesity at age 2 are associated with increased risk of later obesity & metabolic co-morbidities
- Initial infant feeding decisions develop during pregnancy
- Feeding styles, attitudes and practices are formed during the first 3 years of life

Taveras 2009, Nader 2006, Stettler 2007 Anzman 2010, Ibaneza 2012, Bonuck 2005

Background:

Why intervene in primary care?

- Potential as a universal platform
  - Frequent visits in pregnancy and infancy
  - Relationship with provider
- Proven impacts of primary care parenting interventions on child development
  - ROR, VIP, Healthy Steps
- Types
  - Enhanced provider counseling
  - ‘Add-ons’ to primary care
- Research on focused primary care-based early obesity prevention is more limited

Mendlesohn 2010 Klass 2009 Needleman 2003, Ciampa 2010 French 2010

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Background:
What increases risk of early obesity?

- Pregnancy:
  - Excess weight gain
  - Diabetes
- Child
  - Diet content
  - Feeding styles
  - Lifestyle behaviors
    - Sedentary and physical activity, screen time, sleep

Glickman 2012, Birch 2011, Oken 2009, Davis 2007, Koplan 2005

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Background:
What impacts obesity-promoting behaviors?

- Increase healthy behaviors
  - Parent knowledge and attitudes
  - Support
- Barriers to healthy behavior
  - Lack of support
  - Parental stressors
  - Many are poverty related

Davis 2007, Gross 2010, Baughcum 2001

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Background:

Disparities in early obesity risk

- Obesity rates up to 40% by age 2 in high risk groups
  - Low SES, Hispanic and African American

- Higher rates of obesity-promoting diets, feeding styles and lifestyle behaviors

Ogden 20002, 2008, 2012, Taveras 2011, Fox 2006

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Aims:

- To determine the impact of ***Starting Early*** - a primary care-based early childhood obesity prevention intervention beginning in pregnancy - on key parent-child outcomes from birth through age 3 years

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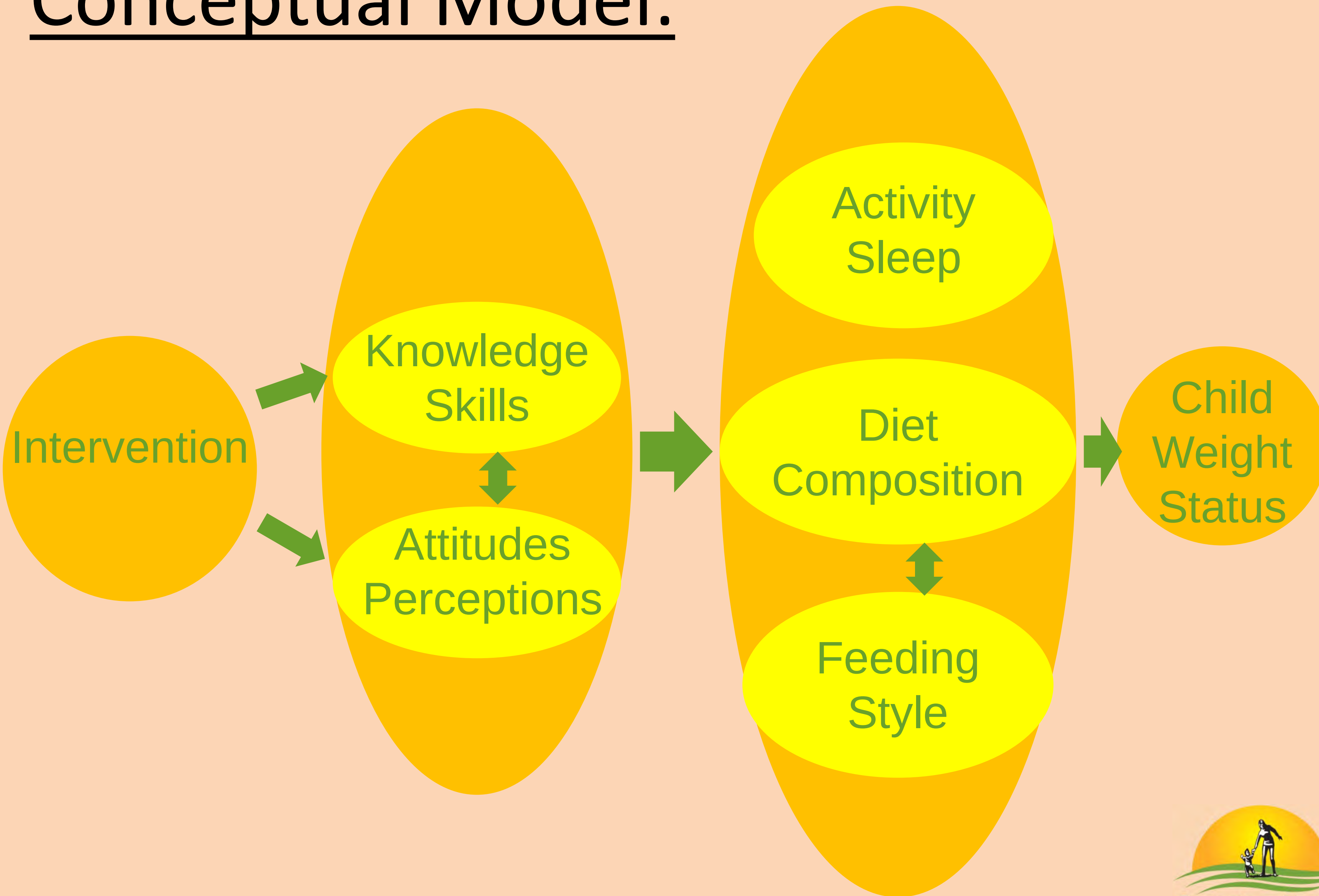
Conceptual Model:



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Study Design:

- Overall Design:
  - Randomized Control Trial
  - Starting Early intervention vs. standard of care
  - 3rd trimester of pregnancy to child age 3 years
- Site:
  - Urban public hospital in obstetric and pediatric clinics
- Enrollment:
  - Consecutive sample of pregnant women
  - Screened for eligibility at initial OB visit
  - Eligibility re-assessed & consent obtained after 26 weeks
  - Randomization after 32 weeks

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Sample:

- Inclusion criteria:
  - ≥ 26 weeks pregnant for consent/enrollment
  - ≥ 32 weeks for randomization
  - Uncomplicated singleton pregnancy
  - Self identify as Hispanic/Latina
  - Spanish or English speaking
  - Planned delivery & pediatric care at study site
- Exclusion criteria:
  - Significant maternal physical or mental illness
  - No working phone contact

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Starting Early Intervention:

- Delivered by bilingual Registered Dietitians (RD)
  - Maternal-child health experience
  - Certified lactation counselors
- Includes:
  - Individual nutrition counseling
  - Nutrition/parenting support groups

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Starting Early Intervention:

- Individual nutrition counseling
  - 3rd trimester
    - Coordinated with OB visits
  - Peri-partum
    - Coordinated with hospital stay
- Offer support for healthy behaviors
- Relationship building

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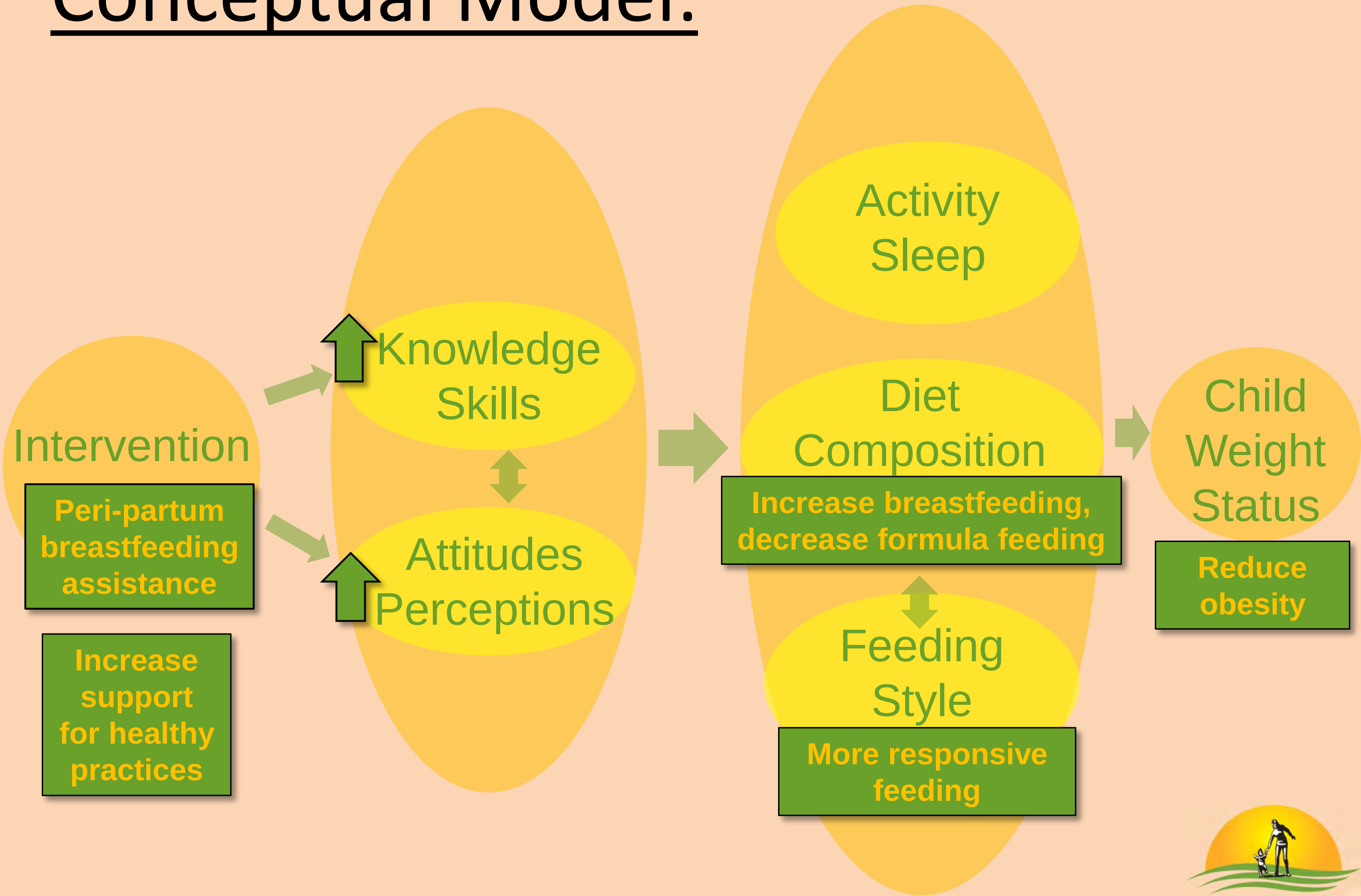
Conceptual Model:



Starting Early Intervention: Nutrition/parenting groups

- Coordinated with every well child visit
- Consistent mother-infant dyads and nutritionist leader at groups
- Support for healthy behaviors
- Content:
  - healthy nutrition
  - responsive feeding
  - parenting skills

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Starting Early Intervention:

Nutrition/parenting groups - Theoretical framework

- Social Learning Theory & Health Belief Model
  - Expert delivers content information
  - Healthy eating and lifestyle habits modeled
    - Meals and child feeding are integral parts of the groups
    - Practice healthy behaviors with mothers and infants
  - Expert and peer support for healthy practices
  - Benefits and barriers explored
  - Collaborative solutions developed

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Starting Early Intervention:

Examples of Group Activities

Tummy time at 1 month

5 S's - How to soothe your baby

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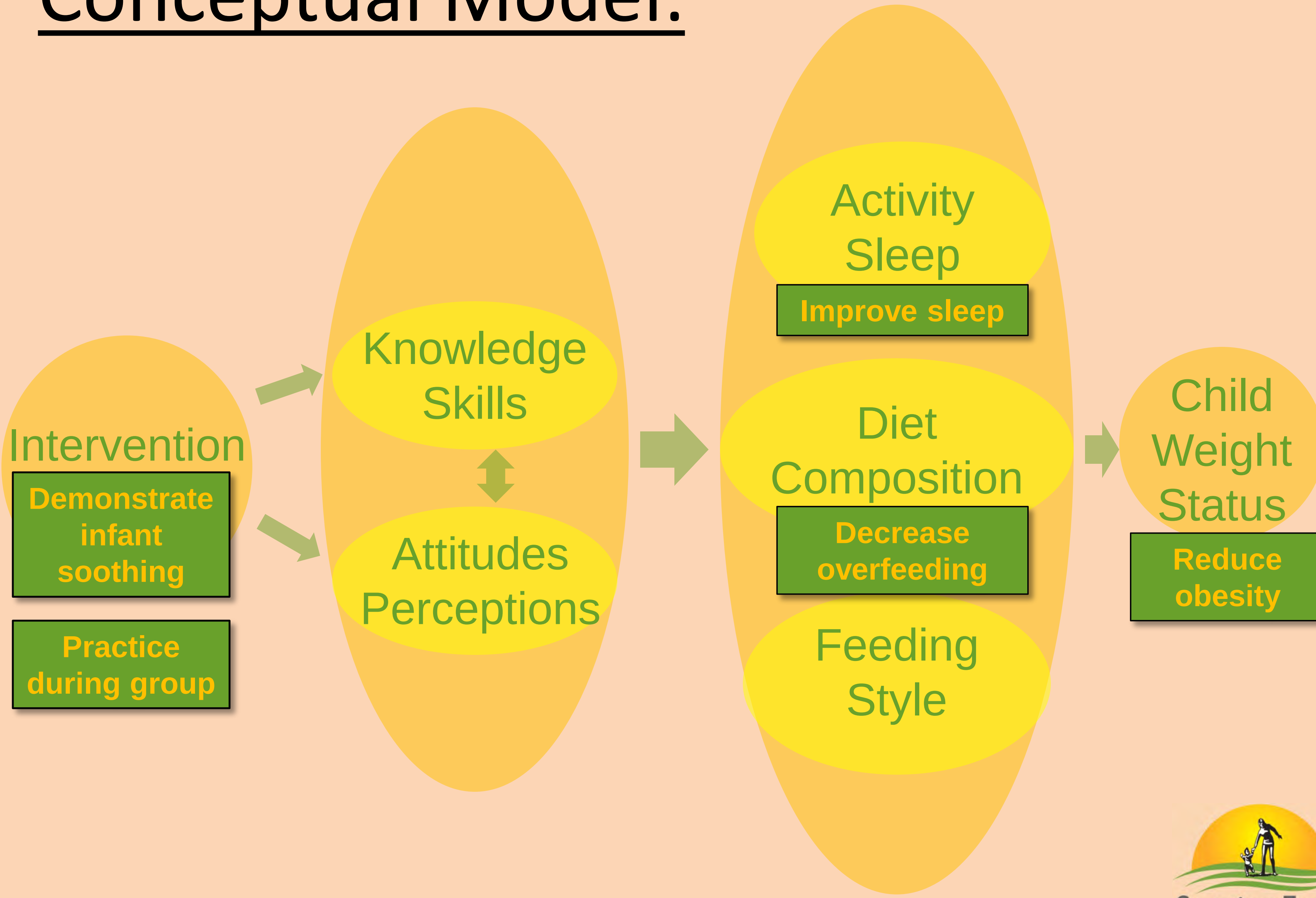
Conceptual Model:



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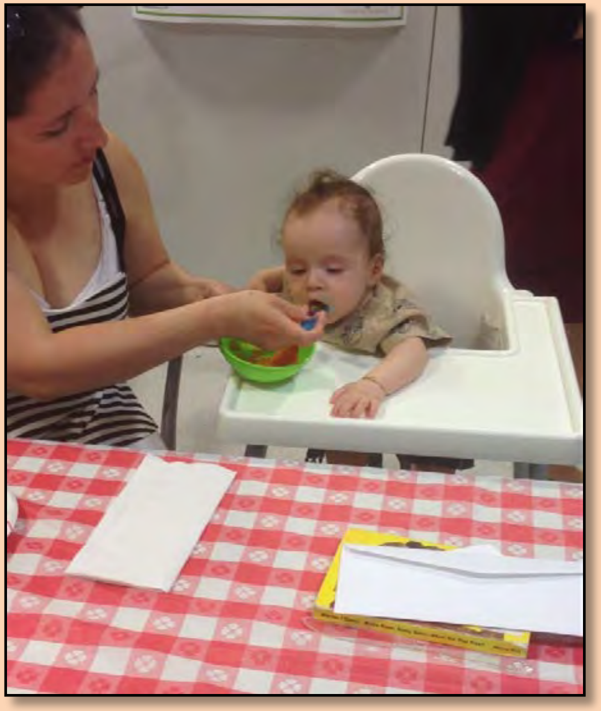
Starting Early Intervention:

Examples of Group Activities

Making baby food at 6 months



Starting solids
at 6 months

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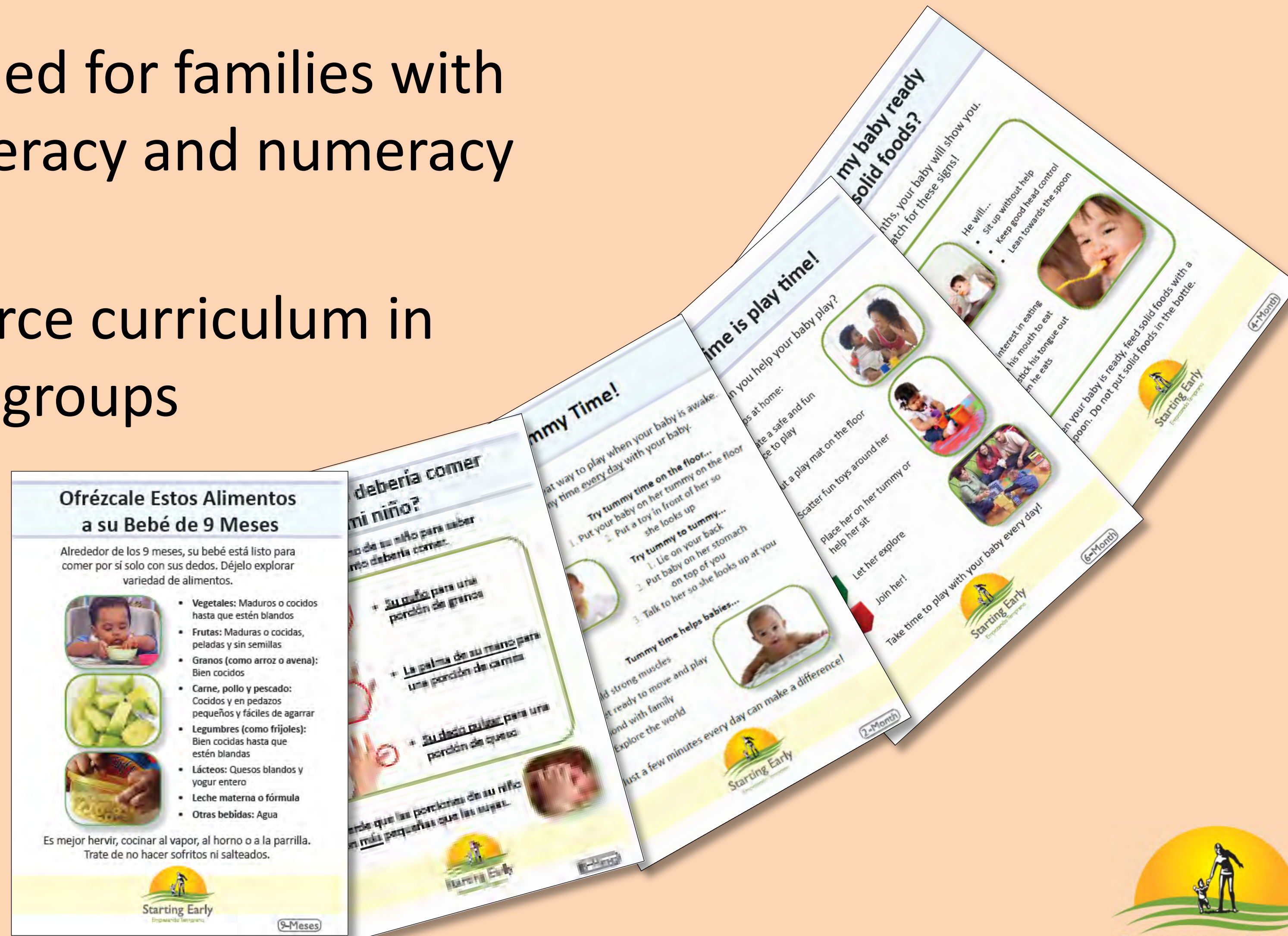
Starting Early Intervention:

Bilingual Plain Language Handouts

- Designed for families with low literacy and numeracy skills
- Reinforce curriculum in family groups



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Starting Early Intervention:

Bilingual Nutritional DVD

- Culturally-specific content
- Stars "real" families from NYC WIC centers
- Found to improve parent nutrition knowledge
- Used in family groups and at home

Scheinmann 2009

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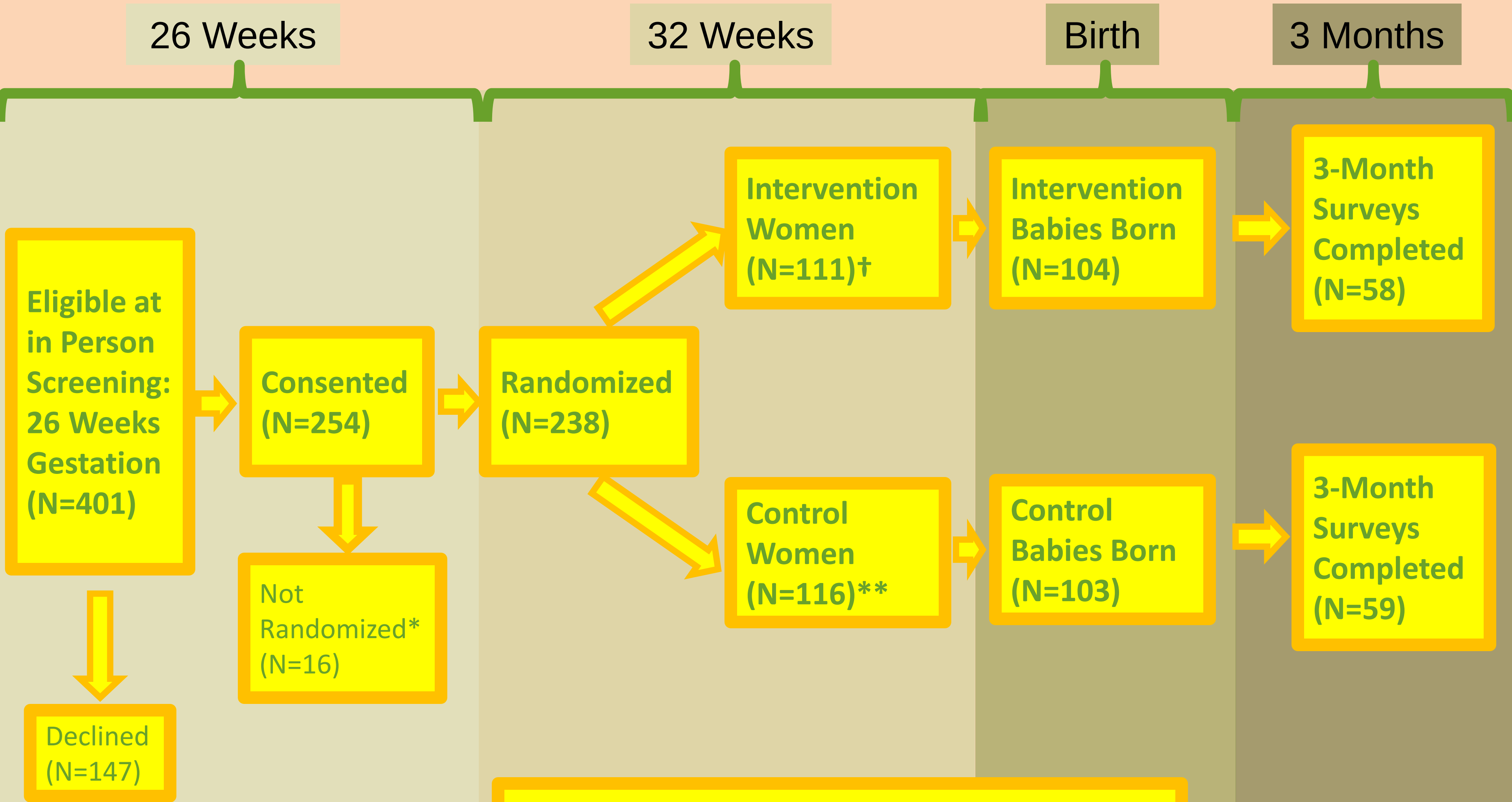
Summary of Assessments at Each Time Point

Assessments	Baseline	3m	10m	19m	25m	36m
Weight/Length or BMI	X	X	X	X	X	X
Diet Composition (Child)		X	X	X	X	X
Diet Composition (Mom)	X				X	X
Nutrition Knowledge	X	X	X	X	X	X
Feeding Styles		X	X	X	X	X
Feeding Attitudes		X	X	X	X	X
Perception of Weight	X	X	X	X	X	X
Physical Activity	X	X	X	X	X	X
Media Exposure	X	X		X	X	X
Sleep	X	X	X	X	X	X
Parenting Stress			X			X
Parenting Styles			X			X
Depression		X			X	

Enrollment Flow Diagram:



*Declined after signed consent, missed visits, other
†1 stillborn, 8 drop outs
**2 drop outs

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Baseline Data:

Demographics

N=238, mean (SD) or n (%)	Intervention	Control	p-value
Age (years)	28 (6.0)	27 (5.9)	0.28
First child	42 (37)	50 (44)	0.34
US born	22 (19)	23 (20)	1.00
Education < high school	44 (39)	33 (29)	0.16
Married/living as married	82 (72)	85 (75)	0.76
Working	26 (23)	31 (27)	0.54

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Baseline Data:

Psychosocial Stressors

N=238, mean (SD) or n (%)	Intervention	Control	p-values
WIC participant	99 (87)	102 (90)	0.68
SNAP participant	41 (36)	42 (37)	1.00
Food insecure	32 (29)	39 (36)	0.29
Serious financial problems	22 (19)	30 (26)	0.27
Depressive symptoms	43 (38)	36 (32)	0.31
History of homelessness	6 (5)	9 (8)	0.60
Victim of a violent crime	7 (6)	10 (9)	0.46

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Baseline Data:

Diet & Lifestyle

N=238, mean (SD) or n (%)	Intervention	Control	p-values
Pre-pregnancy BMI >30	33 (31)	29 (25)	0.31
Daily servings of fruit (cups)*	1.1 (0.8)	1.1 (0.9)	0.67
Daily servings of vegetable(cups)*	1.9 (1.1)	1.9 (1.2)	0.99
Daily sugary drinks (oz)	10 (1.1)	10 (1.1)	0.83
Daily TV time (hours)	3.9 (2.4)	4.3 (2.4)	0.23
No daily physical activity	28 (25)	26 (23)	0.76

*Recommended daily servings:

Fruit = 2 cups

Vegetables = 3 cups

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Design Issues:

Why we chose our design

- Beginning in pregnancy
  - High prevalence early obesity
  - Obesity-promoting behaviors present at birth
- Education and support intervention
  - Low SES immigrant families
  - High level of poverty-related stressors
- ‘Add-On’ to primary care
  - More intensive intervention
  - Resident run, busy urban clinics
  - Time challenged primary care visits

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Assessment Issues:

- Validated measures don't exist, or must be adapted for use in infants
- Self report surveys:
  - Subject to bias
  - Long
- Need for consensus on how and which aspects of feeding interactions to measure
- Planned video-taped assessment of infant feeding interactions on a subsample

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Retention Efforts:

- Selection of dyads most likely to stay for care
- Multiple methods of contact established
- Reimbursement for time
  - intervention attendance and assessments
- Coordination with primary care visits
- Supportive intervention
  - Relationship-based
  - Consistent nutrition and peer groups

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Lessons Learned:

What works

- RDs as intervention leaders
  - Experts with maternal-child health experience
  - Culturally competent
  - Form supportive relationship with participants
- Coordination between obstetric and pediatric services
  - Provider support
  - Buy-in from OB and Pediatrics

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Lessons Learned:

Challenges

- Crossing the *birth line*
  - Balance between loss to follow up and stable sample
  - Unexpected pregnancy outcomes
  - Transience of low SES immigrant families
- Logistics of urban public hospital clinics
  - Problems with resident continuity
  - Frequent provider appointment changes
  - Patient missed appointments
- Diversity of Hispanic community

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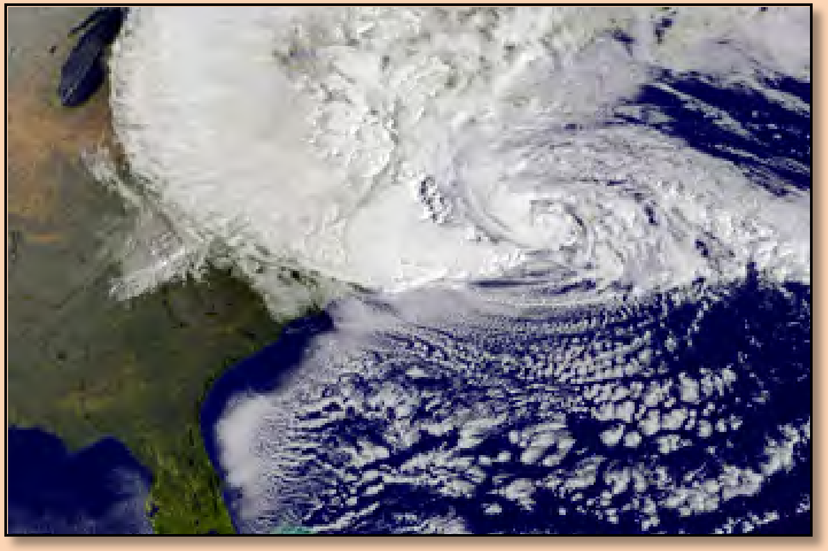
Lessons Learned:

What Doesn't Work

- Super Storm Sandy
- Having the storm of the century close your institution for 4 months!!!



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Potential Impact:

- Reduction in early child obesity
  - Improvement in early feeding patterns
  - Lasting duration of program effect

- Evaluation of potentially scalable intervention
  - Group visits can be cost effective
  - Fits into medical home model

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Conclusions:

- High prevalence of maternal factors linked to child obesity
  - Behaviors potentially modifiable *before* impact on infant growth trajectory
- Primary care-based intervention
  - Acceptable in prenatal care
  - Women will participate
  - Coordination with pediatric and obstetric visits acceptable to families and providers

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Acknowledgments:

Starting Early Team

- Co-investigators
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  - Arthur Fierman, MD
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Sleep in Infancy and Early Childhood

Jodi A. Mindell, PhD
Children's Hospital of Philadelphia
Saint Joseph's University

NIH Workshop – October 2013

Disclosures

- Consultant:
  - Johnson & Johnson (Johnson's Baby)

Questions

- What is the evidence regarding sleep duration and obesity?
- What are mediators of this relationship?
- What parent and infant contextual factors affect sleep duration?
- How modifiable are early sleep patterns?

Evidence indicates that shorter sleep duration is associated with higher weight status across the lifespan

What is and is not known regarding the evidence for this relation in infants and toddlers?

Chen (2008)

- Systematic review
- 17 observational studies
- Shorter sleep duration increased risk of overweight/obesity by 58%
  - Pooled odds ratio = 1.58
  - Each hour increase in sleep, risk decreased by 9%

Chen et al. (2008). *Obesity.*

Monasta (2010)

- Review of reviews (n=22 papers)
- Conclusion: short sleep duration determinant of later obesity in young children (0-5 years)
- Only 2 reviews included sleep duration and weight gain
  - Short sleep duration at 3-4 years assoc at 7 and 10 years (Patel et al., 2008)
  - Chen findings (previous slide)

Monasta et al. (2010). *Obesity Reviews.*

Specific studies

- Taveras et al. (2008)
  - 1401 6-month-olds
  - Infant sleep <12 hours associated with overweight at 3 years

Taveras et al. (2008). *Arch Pediatr Adolesc Med*

Specific studies

- Dev et al. (2013)
  - 329 preschoolers
  - 3 risk factors predicted obesity/overwt
    - Nighttime sleep duration
    - Parent BMI
    - Food restriction for weight control

Dev et al. (2013). *Childhood Obesity*

Specific studies

- Tikotzky et al. (2009)
  - 96 6-month-olds
  - Actigraphic sleep efficiency (*r* = -.23; weight to length ratio)
  - Parental report of nighttime sleep duration (*r* = -.26; weight to length ratio)

Tikotzky et al. (2009). *Journal of Sleep Res*

Not clear cut …

Klingenberg et al. (2012)

- 311 infants
- Cross-sectional and longitudinal study
- No associations found between parent-reported total sleep duration at 9 months, 18 months and 3 years with adiposity at 3 years

Klingenberg et al. (2012). *Pediatric Obesity*

Hiscock et al. (2011)

- Longitudinal study of 7701 children
  - 0-1 year olds followed at 2-3 years
  - 4-5 year olds followed at 6-7 years
- Sleep duration did not predict obesity
  - Concurrent relationship in 6-7 year olds
- Conclusion: “current trials of sleep interventions to prevent or manage obesity in young children may be premature.”

Hiscock et al. (2011). *Arch Dis Child*

And … Wake et al. (2011)

- Outcomes of an infant sleep intervention at 6 years of age
- No differences in rates of child obesity
- Conclusion: “Population-based primary care sleep services seem unlikely to reduce the early childhood obesity epidemic.”

Wake et al. (2011). *Arch Dis Child*

However, in contrast

- 160 families (recruited newborns)
- Added sleep intervention reduced weight-for-length percentiles at age 1 year
- Currently larger scale NIH-funded study

Paul et al. (2013). *Childhood Obesity*.

Prevention of Overweight in Infancy (POI.nz)

- Ongoing study
- 800 families randomized
  - Usual care
  - Food, activity, breastfeeding
  - Sleep
  - Combined

Taylor et al. (2011). *BMC Public Health*.

What is and is not known regarding the possible mediators of this relation?

Possible mechanisms/ mediators

- Decreased physical activity
- Increased caloric intake
- Nocturnal decreases in leptin/increases ghrelin
- Decreased nocturnal release of growth hormone

Focus too narrow

Sleep ≠ sleep duration

Sleep

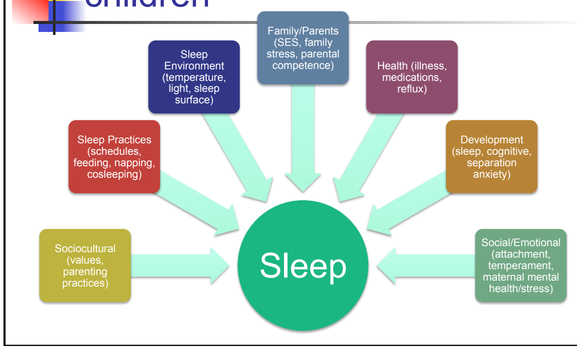
- Duration
  - Nighttime and daytime
  - Total sleep duration
- Bedtimes and wake times
- Sleep disorders (e.g., sleep apnea)
- Night wakings and sleep consolidation
- Parenting practices (sleep ecology)

Sleep disturbances

- May not be sleep duration per se in infants/toddlers; rather sleep disturbances
  - Parents feed to calm overtired-fussy baby
  - Feed as a means to fall asleep/return to sleep
- Reduced nighttime feedings associated with nighttime wakings led to differences in obesity post-treatment.

What parent and infant contextual factors affect sleep duration?

Factors affecting sleep in children

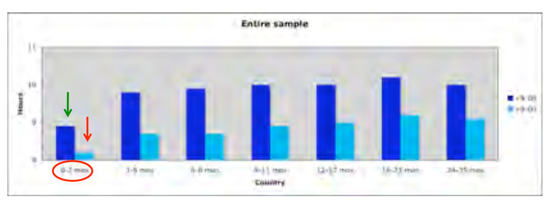


Factors that affect sleep

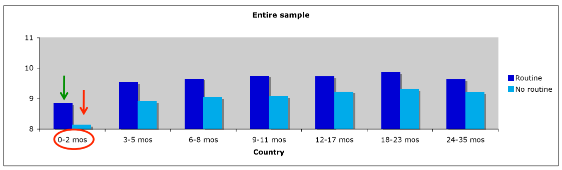
- Global study of 29,287 infants/toddlers
- Predictors of sleep outcomes
  - Nighttime sleep duration

Mindell et al. (2010). *Sleep Medicine*.

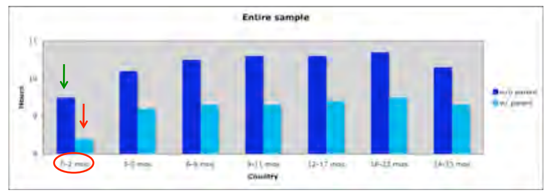
Bedtime <9:00



Bedtime routine



Parental presence



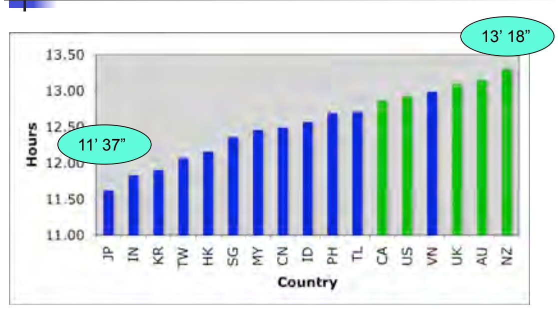
Cross-cultural differences

- Sample (N=29,287)
  - Predominantly Caucasian = 7,960
    - AU, CA, NZ, UK, US
  - Predominantly Asian = 22,315
    - CN, HK, IN, ID, JP, KR, MY, PH, SG, TW, TL, VN
- Ages 0-3 years
- Brief Infant Sleep Questionnaire

Mindell, Sadeh, Wiegand, How, & Goh (2010). *Sleep Medicine.*

Total sleep time

Nighttime sleep + daytime sleep



How modifiable are early sleep patterns?

Standards of practice:
American Academy of Sleep Medicine

- Behavioral treatment of bedtime problems and night wakings in infants and young children
  - Behavioral treatment produces reliable and durable changes (80% of children improve)
  - 94% of studies report intervention was efficacious

Mindell et al. (2006). *Sleep*.
Morgenthaler et al. (2006). *Sleep*.

Efficacy of a bedtime routine

- Methods
  - 405 participants (7-36 months)
  - 1 week baseline; 2 week intervention
  - Prescribed bedtime routine vs usual routine
- Results
  - Reductions in SOL, NWs, parent perception of sleep problems

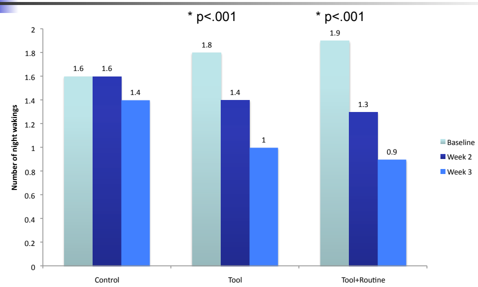
Mindell et al. (2009). *Sleep*.

Internet-based intervention

- 264 mothers and their infants/toddlers (ages 6-36 months)
- 3 week study (randomly assigned)
  - 84 control group
  - 96 internet intervention
  - 84 internet intervention + routine
- All mild to moderate sleep problems

Mindell et al. (2010). *Sleep*.
Mindell et al. (2011). *Journal of Clinical Sleep Medicine*.

Number of night wakings (BISQ)

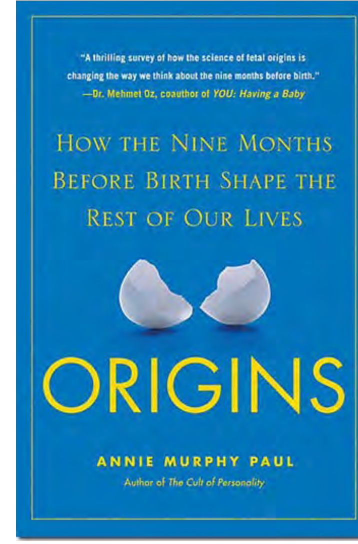


* Brief Infant Sleep Questionnaire

Future studies

- Clearer understanding of the relationship between sleep and obesity in young children (sleep duration and/or sleep disturbances and/or nighttime behaviors)
  - Association or a causal factor
- Assess the impact of sleep interventions on obesity outcomes

Pleasant dreams



Intrauterine determinants of childhood obesity

Emily Oken, MD, MPH

Obesity Prevention Program

Department of Population Medicine

Harvard Medical School and Harvard Pilgrim Health Care Institute

Obesity Prevention PROGRAM

Harvard Pilgrim Health Care Institute

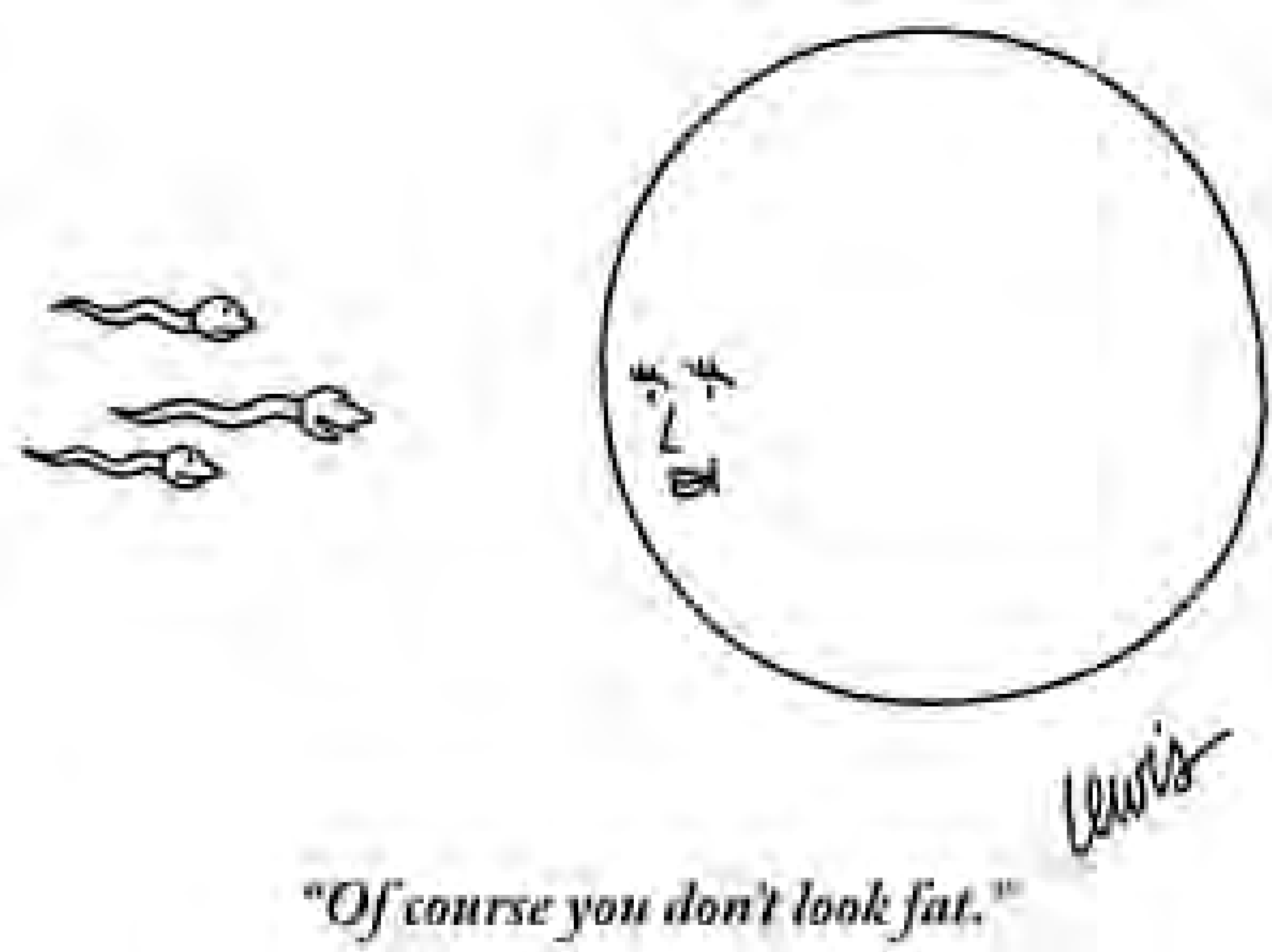
Department of Population Medicine
Harvard Medical School

Overarching questions

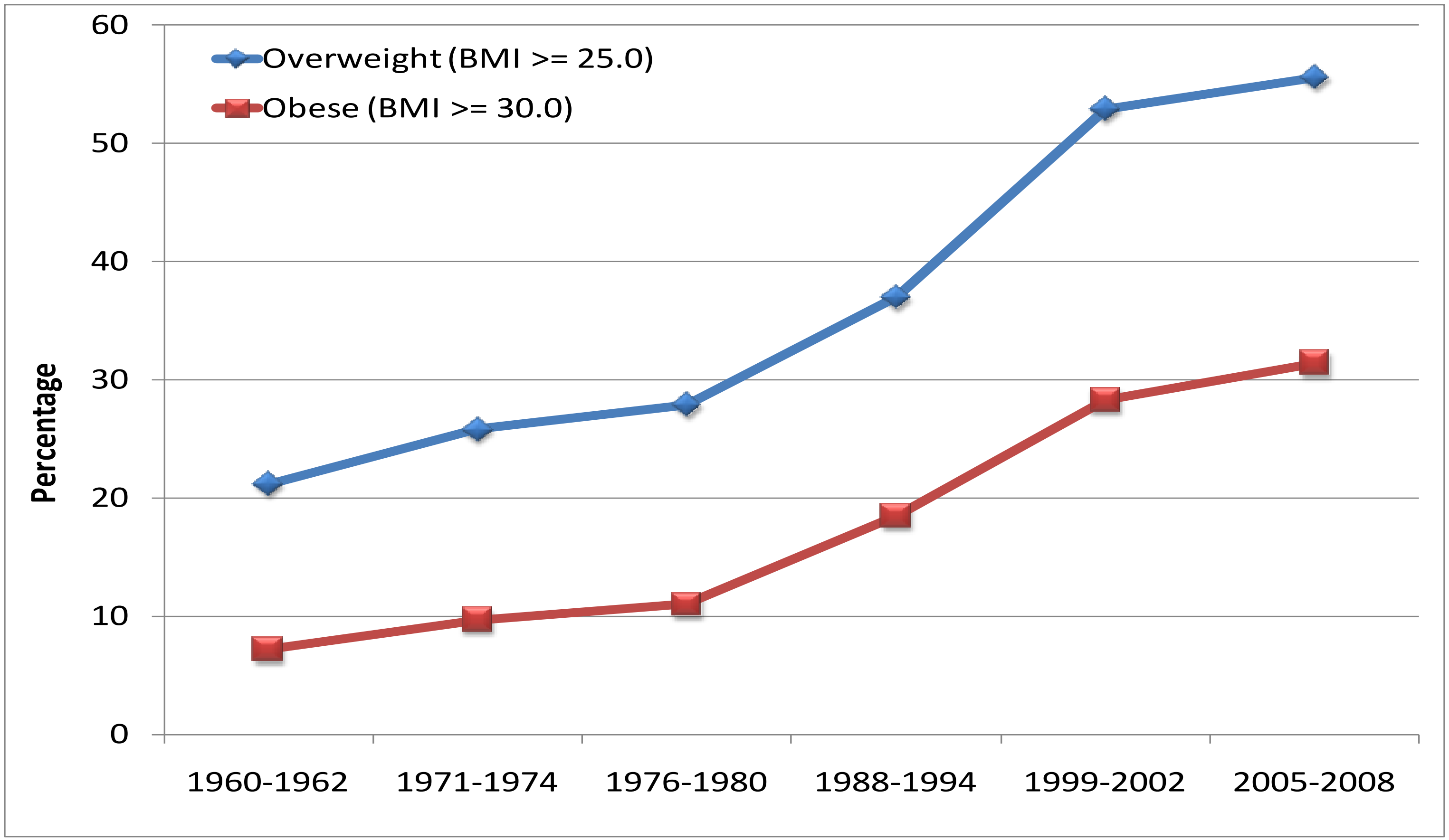
- What intrauterine factors influence child weight and body composition?

  - Which ones are most influential?
    - Of those, which can we alter?
  - Are associations really causal?
    - How do we figure it out?
  - What can we do?
    - Time for intervention? On what?

Maternal obesity



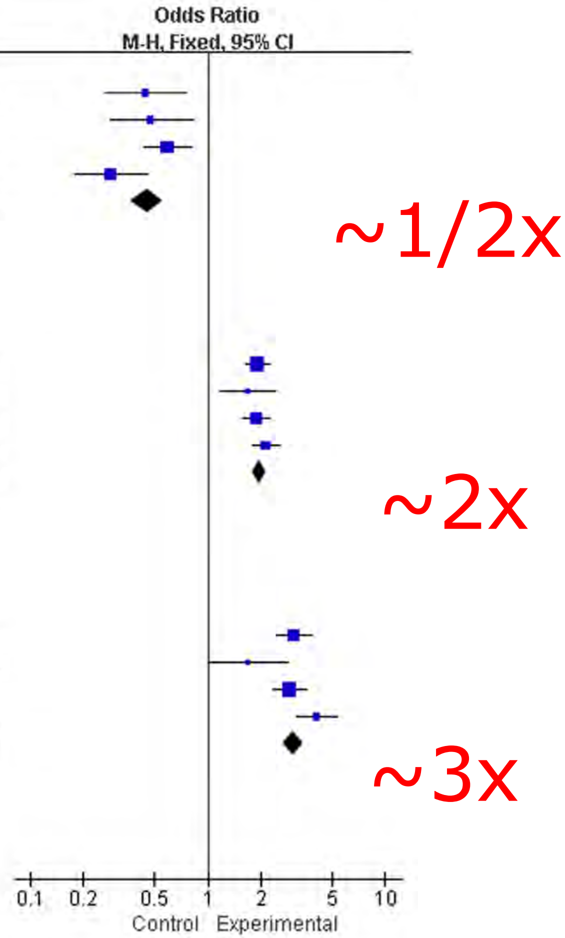
Increase in pre-pregnancy weight



NHANES data

Maternal weight predicts child weight

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1 Underweight vs. Normal						
Padez 2005	16	118	660	2540	15.8%	0.45 [0.26, 0.76]
Gewa 2010	16	180	163	966	14.6%	0.48 [0.28, 0.82]
Margerison Zilko 2012	52	306	789	3108	36.7%	0.60 [0.44, 0.82]
Laitinen 2012	19	459	642	4892	33.0%	0.29 [0.18, 0.46]
Subtotal (95% CI)		**1063**		**11506**	**100.0%**	**0.46 [0.37, 0.56]**
Total events	103		2254			
Heterogeneity: Chi² = 6.99, df = 3 (P = 0.07); I² = 57%						
Test for overall effect: Z = 7.28 (P < 0.00001)						
2 Overweight vs. Normal						
Padez 2005	424	1054	660	2540	38.7%	1.92 [1.65, 2.23]
Gewa 2010	54	211	163	966	7.3%	1.69 [1.19, 2.41]
Margerison Zilko 2012	275	706	789	3108	29.8%	1.88 [1.58, 2.23]
Laitinen 2012	210	856	642	4892	24.2%	2.15 [1.80, 2.57]
Subtotal (95% CI)		**2827**		**11506**	**100.0%**	**1.95 [1.77, 2.13]**
Total events	963		2254			
Heterogeneity: Chi² = 2.06, df = 3 (P = 0.56); I² = 0%						
Test for overall effect: Z = 14.12 (P < 0.00001)						
3 Obesity vs. Normal						
Padez 2005	187	361	660	2540	35.6%	3.06 [2.45, 3.83]
Gewa 2010	22	86	163	966	8.9%	1.69 [1.01, 2.83]
Margerison Zilko 2012	187	376	789	3108	38.5%	2.91 [2.34, 3.62]
Laitinen 2012	94	245	642	4892	17.0%	4.12 [3.14, 5.40]
Subtotal (95% CI)		**1068**		**11506**	**100.0%**	**3.06 [2.68, 3.49]**
Total events	490		2254			
Heterogeneity: Chi² = 9.97, df = 3 (P = 0.02); I² = 70%						
Test for overall effect: Z = 16.72 (P < 0.00001)						



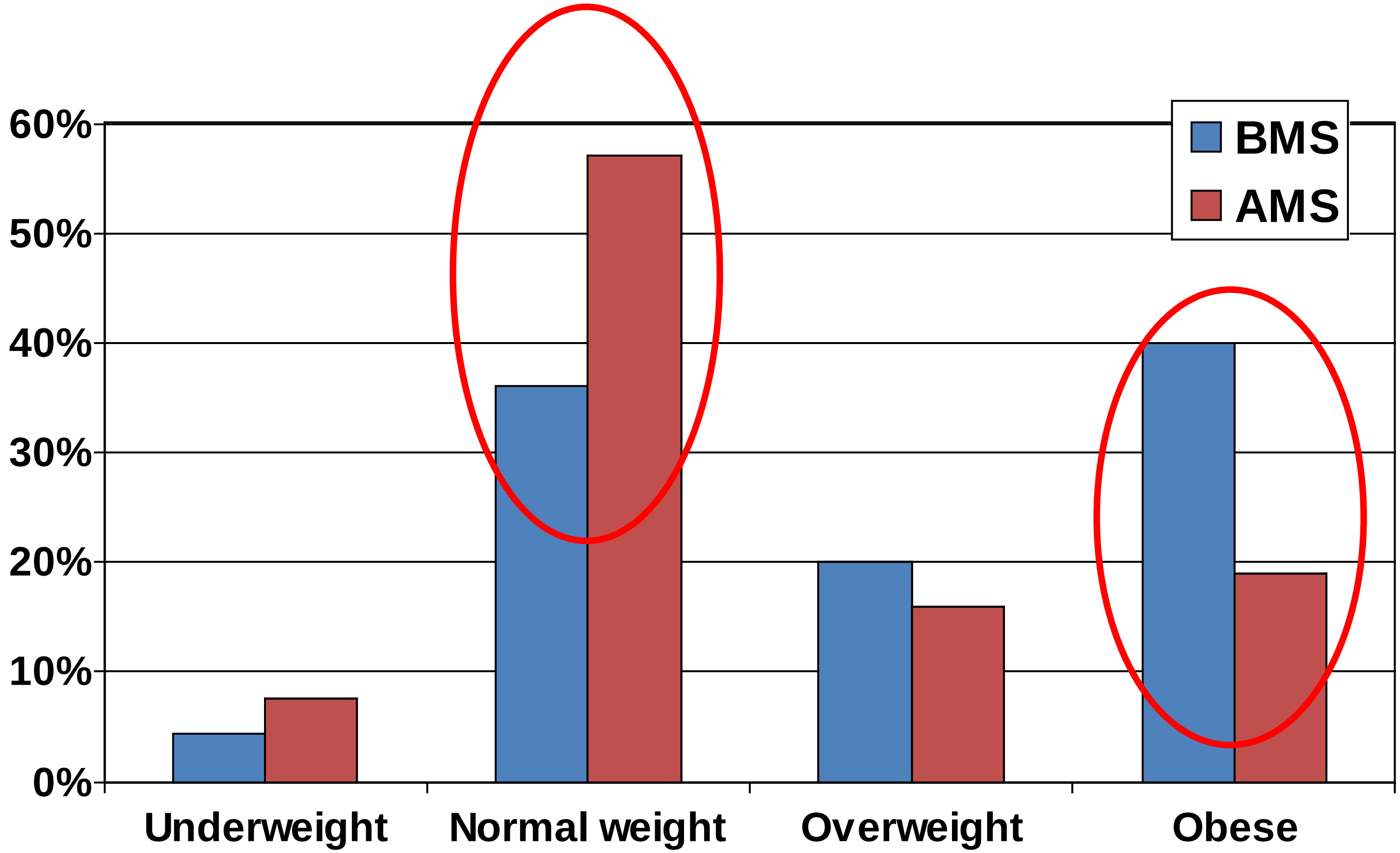
Yu et al. PLOS ONE 2013;8(4): e61627. Meta-analysis

Kids born to obese mothers aren’t just heavier, they are at high cardiometabolic risk

Greater maternal BMI is associated with:

- More overall body fat
- More trunk fat
- Higher insulin
- Greater inflammation

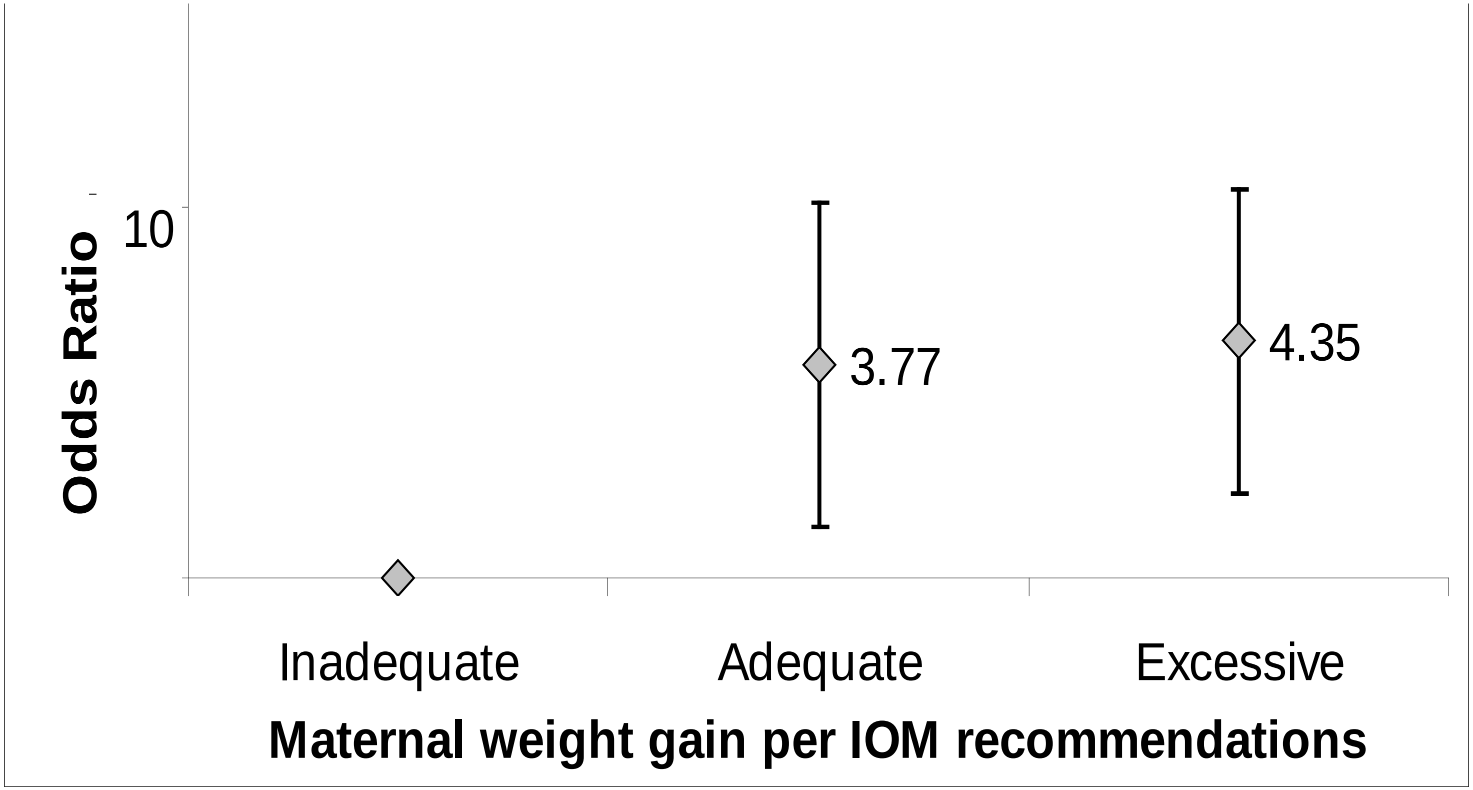
Pre-pregnancy weight and child weight: Is it causal? Pre/post intervention study



Weights of children born before (BMS, n=45) and after (AMS, n=172) maternal weight-loss surgery

Kral JG, et al. Pediatrics. 2006 Dec;118(6):e1644-9

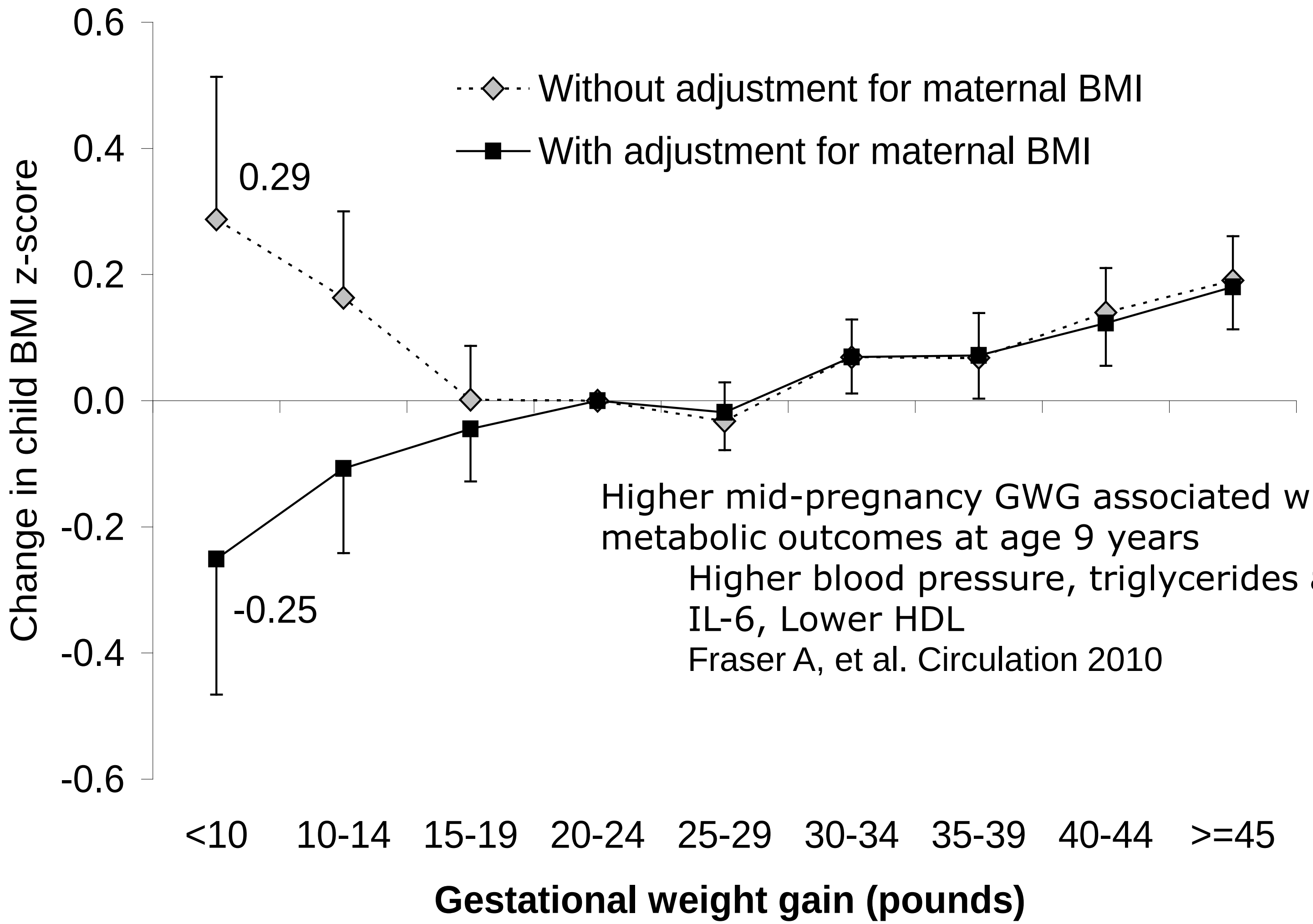
Gestational weight gain and child weight



Adjusted for maternal race/ethnicity, smoking, BMI, socio-demographics, gestational diabetes; paternal BMI; child sex, gestation length, breastfeeding duration

Oken et al., Am J Ob Gyn 2007;196(4):322 e1-8.

Gestational weight gain and adolescent weight



Higher mid-pregnancy GWG associated with metabolic outcomes at age 9 years

Higher blood pressure, triglycerides and IL-6, Lower HDL

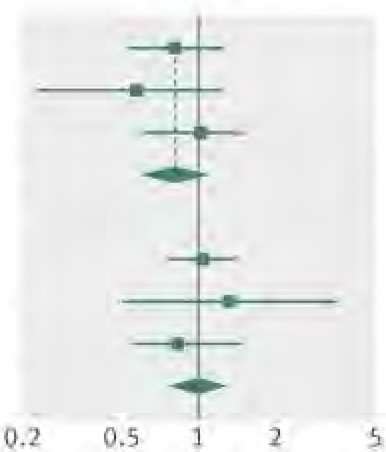
Fraser A, et al. Circulation 2010

Oken et al. 2008

GWG and child weight – is it causal?

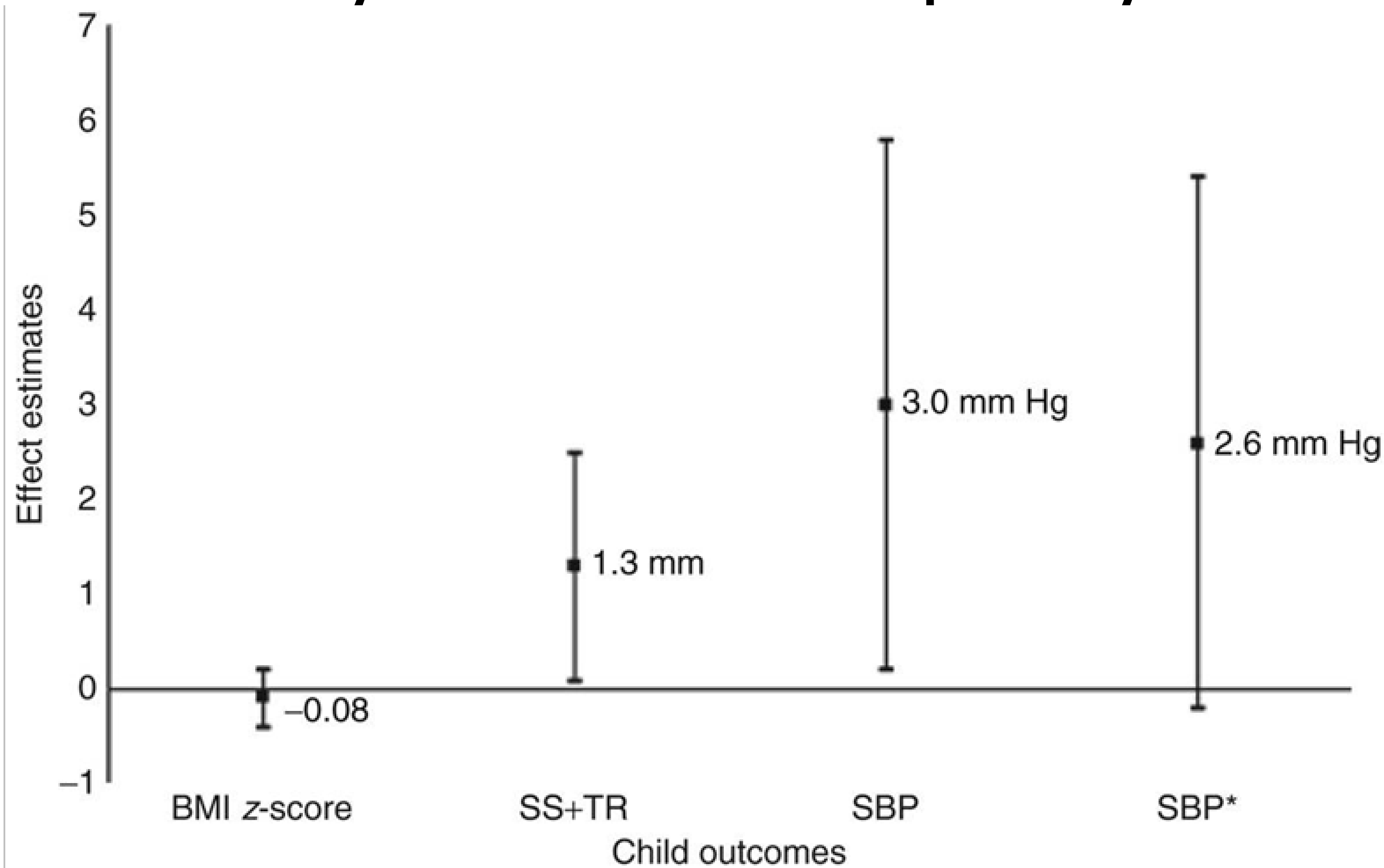
- Meta-analysis of observational studies: Yes
  - 21% increase in obesity risk with excessive GWG (Nehring, Ped Obes 2013)
- Interventions
  - Many ongoing, none with long-term outcome data
  - Difficult to alter GWG!
  - Some evidence for effect on fetal growth

Outcome and intervention	No of studies	No of participants	Relative risk (95% CI)	P value	I^2 (%)	Relative risk (95% CI)
Large for gestational age						
Diet	5	2378		0.26	63	0.78 (0.51 to 1.19)
Physical activity	4	355		0.08	0	0.52 (0.25 to 1.09)
Mixed approach	9	1500		0.72	0	1.05 (0.79 to 1.40)
All	18	4233		0.21	38	0.85 (0.66 to 1.09)
Small for gestational age						
Diet	3	2252		0.91	0	1.02 (0.75 to 1.37)
Physical activity	4	409		0.60	0	1.28 (0.52 to 3.15)
Mixed approach	4	891		0.60	0	0.88 (0.53 to 1.44)
All	11	3552		0.99	0	1.00 (0.78 to 1.28)



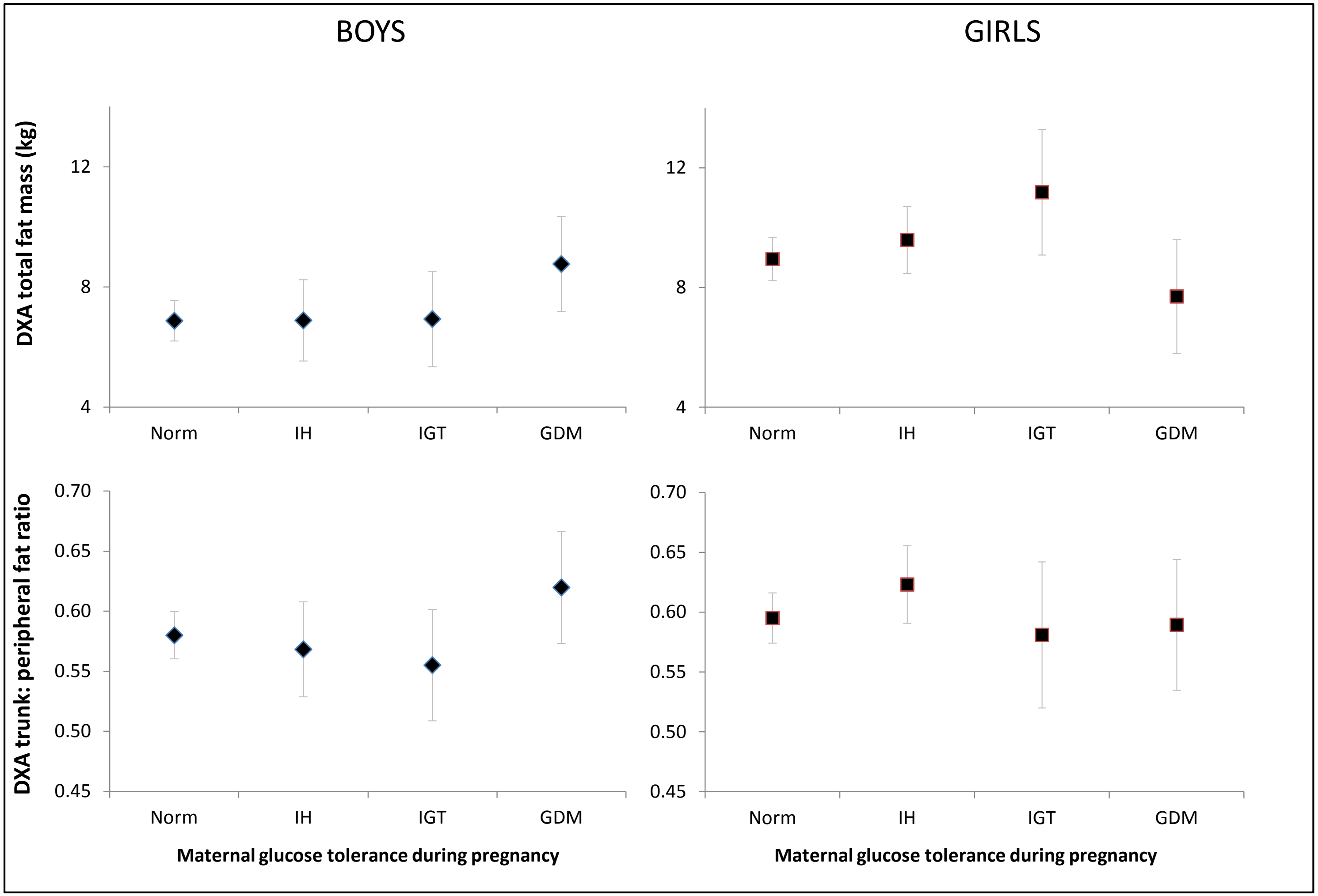
Thangaratinam et al. BMJ 2012

Gestational diabetes and early childhood adiposity



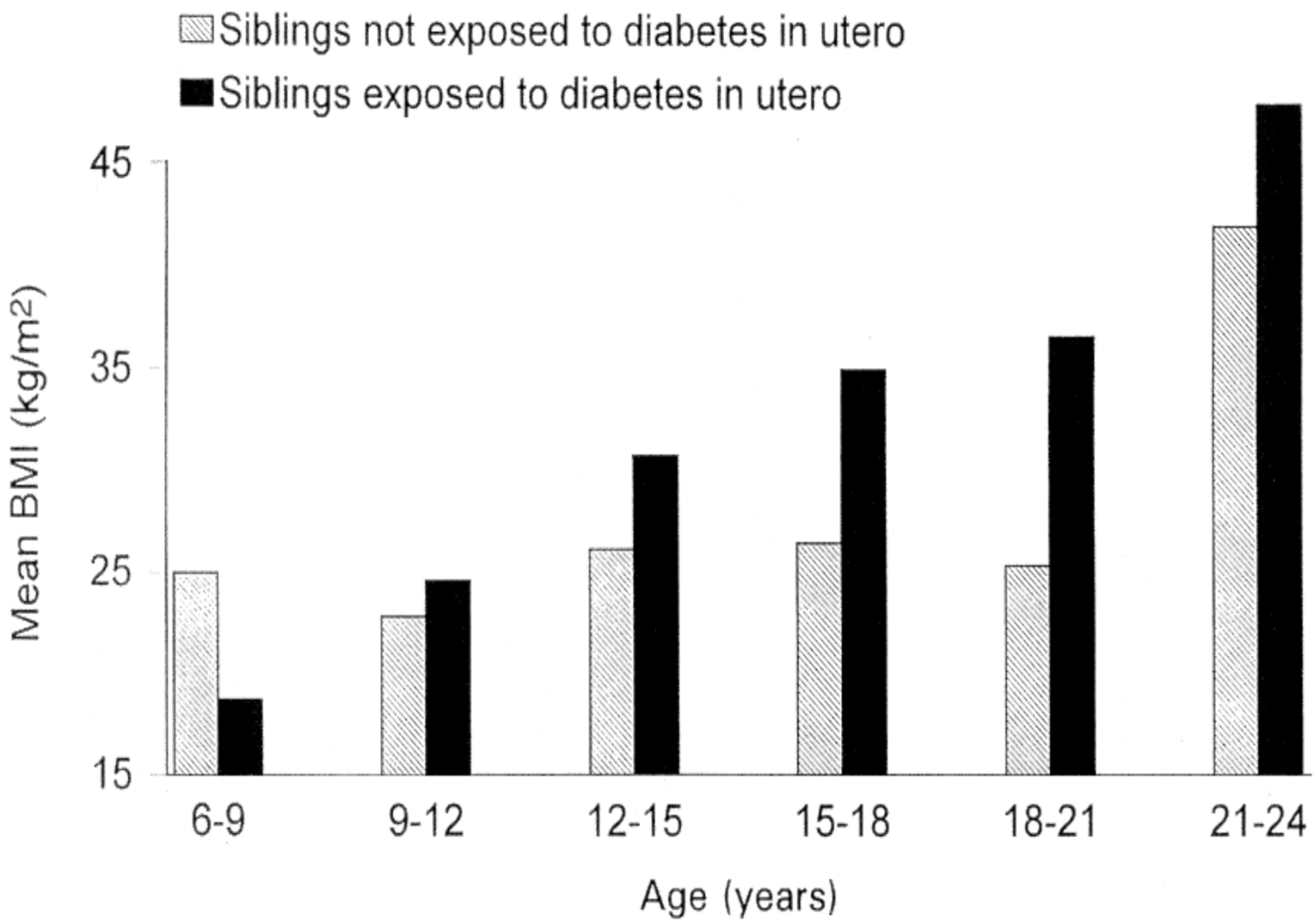
Wright CS, Rifas-Shiman SL, Rich-Edwards JW, Taveras EM, Gillman MW, **Oken E**.
Am J Hypertens 2009;22(2):215-20.

GDM and mid-childhood adiposity sex-specific associations



Regnault N, Gillman MW, Rifas-Shiman SL, Eggleston E, **Oken E.** Diabetes Care 2013.

GDM and child adiposity: Causal? Sibling study



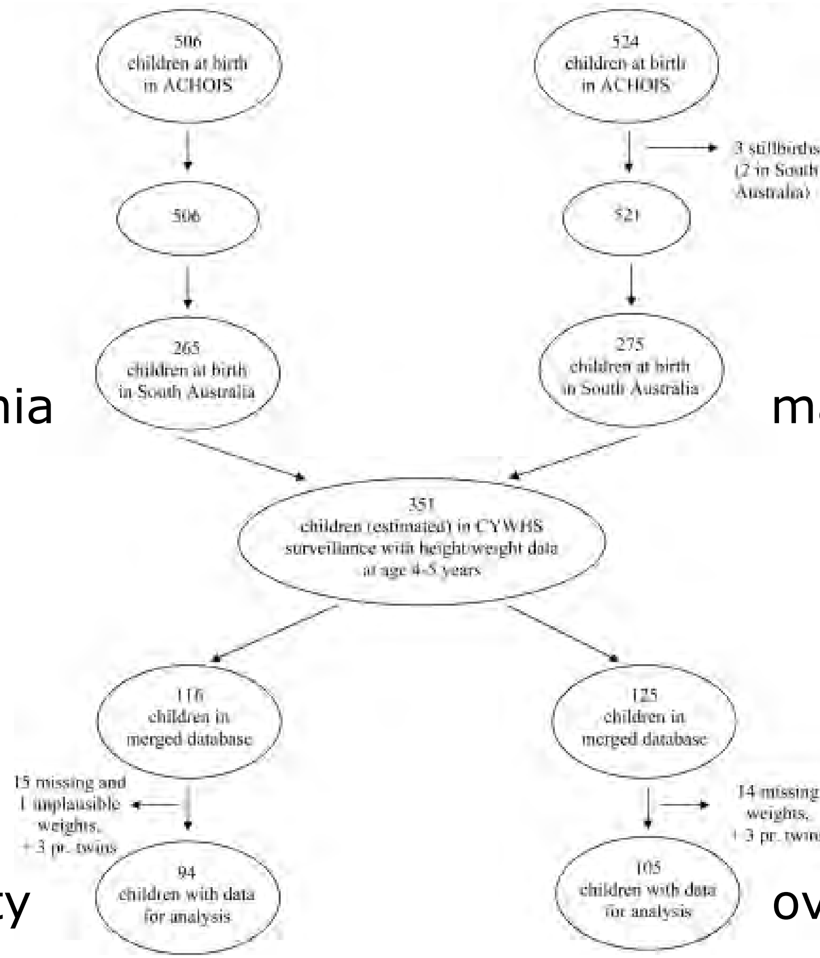
Dabelea et al., Diabetes 2000. 19 Pima families/58 sibs

Follow-up of RCT of GDM treatment

Intervention group Control group

5.3% macrosomia

21.9% macrosomia



33.0% overweight/obesity

27.6% overweight/obesity

RR 1.17
(0.77, 1.78)

Gillman et al. Diabetes Care 2010

Child body weight higher in offspring of mothers with DM

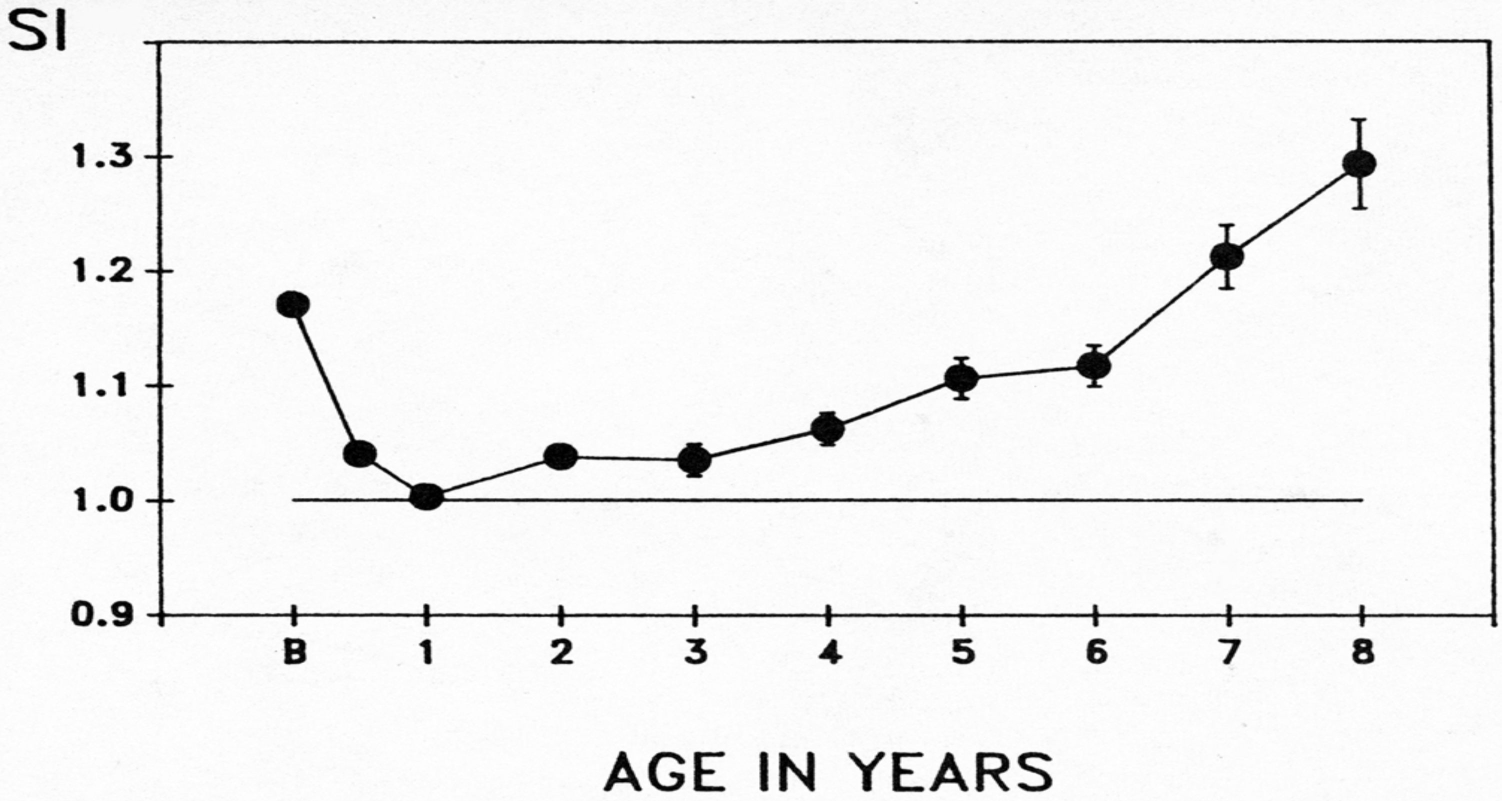


FIG. 3. Symmetry index (SI) (mean ± SEM) in offspring of diabetic mothers from birth to 8 yr of age. SI is greater than expected (1.0) at all ages except 12 mo ($P < 0.05$). Data points are means ± SE.

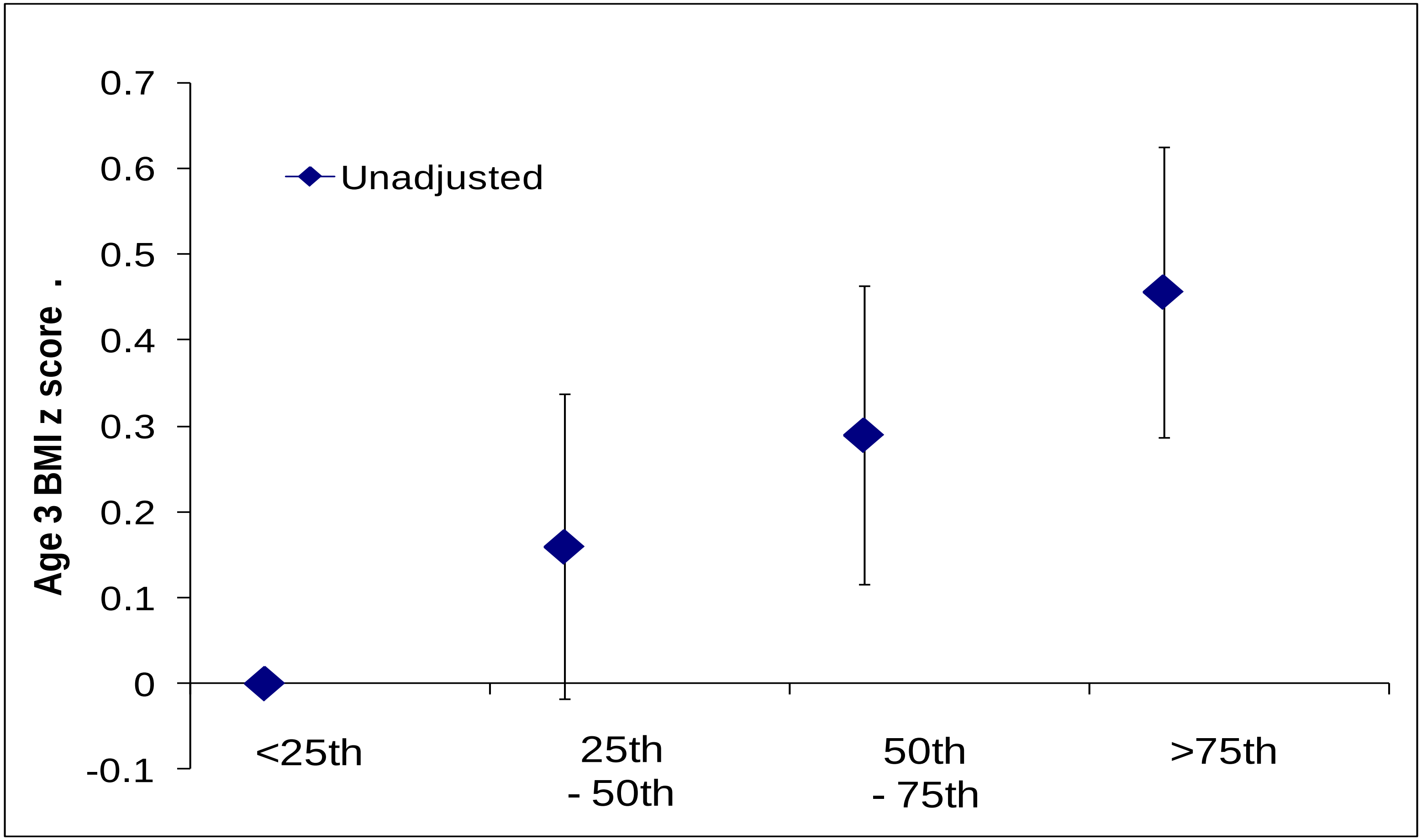
Silverman et al., 1995

Maternal factors and child weight

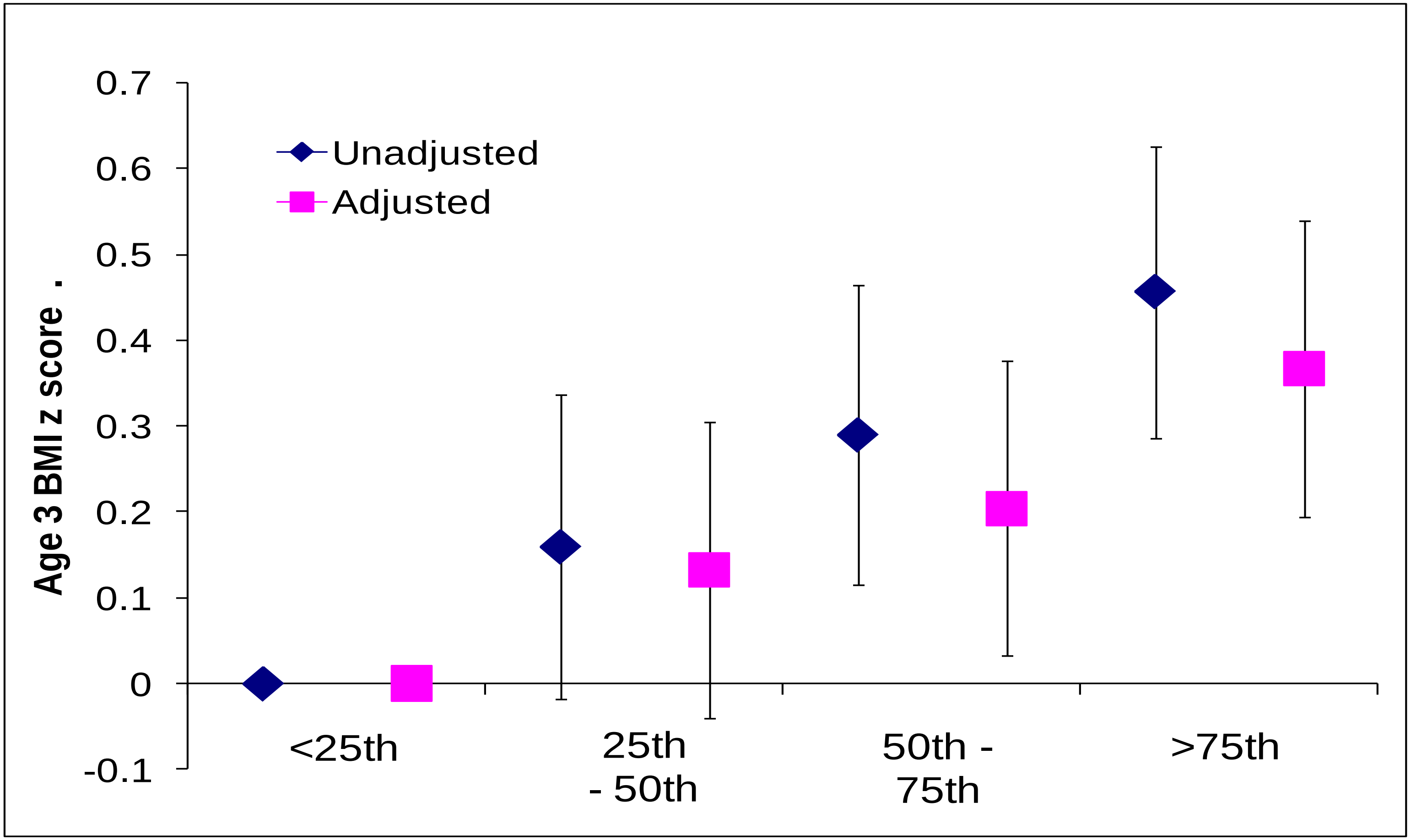
- Maternal obesity
- Gestational diabetes
- Gestational weight gain

All these are associated
with faster intrauterine growth

Fetal growth and later size



Fetal growth and later size – Is it causal? Statistical adjustment



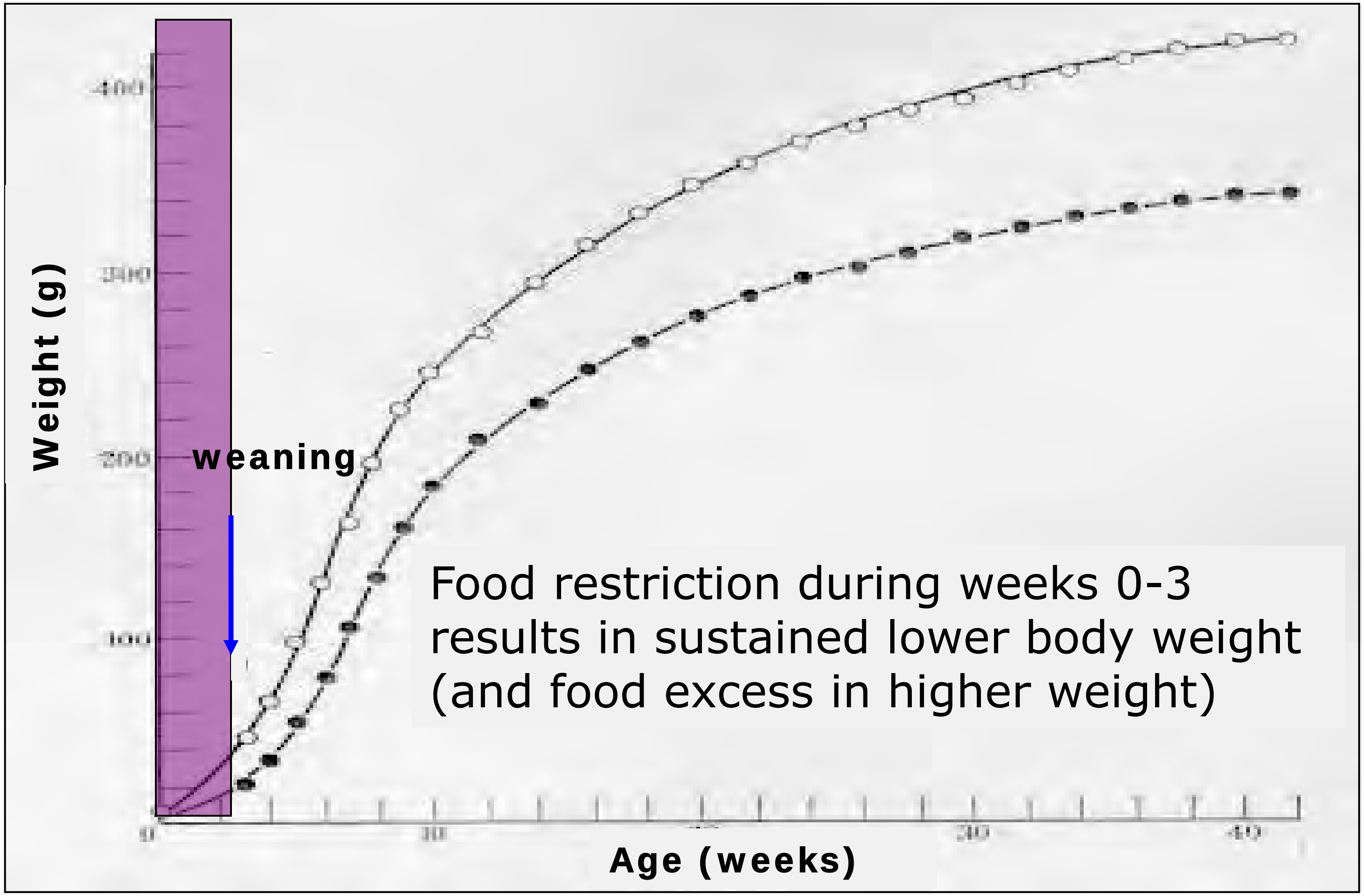
*adjusted for maternal age, race/ethnicity, smoking, marital status, pre-pregnancy BMI, GDM, gestational weight gain; dad BMI, child sex, gestation length, breastfeeding duration

Fetal growth and later size – Is it causal? Animal studies

21 days: Weights 14g, 60g

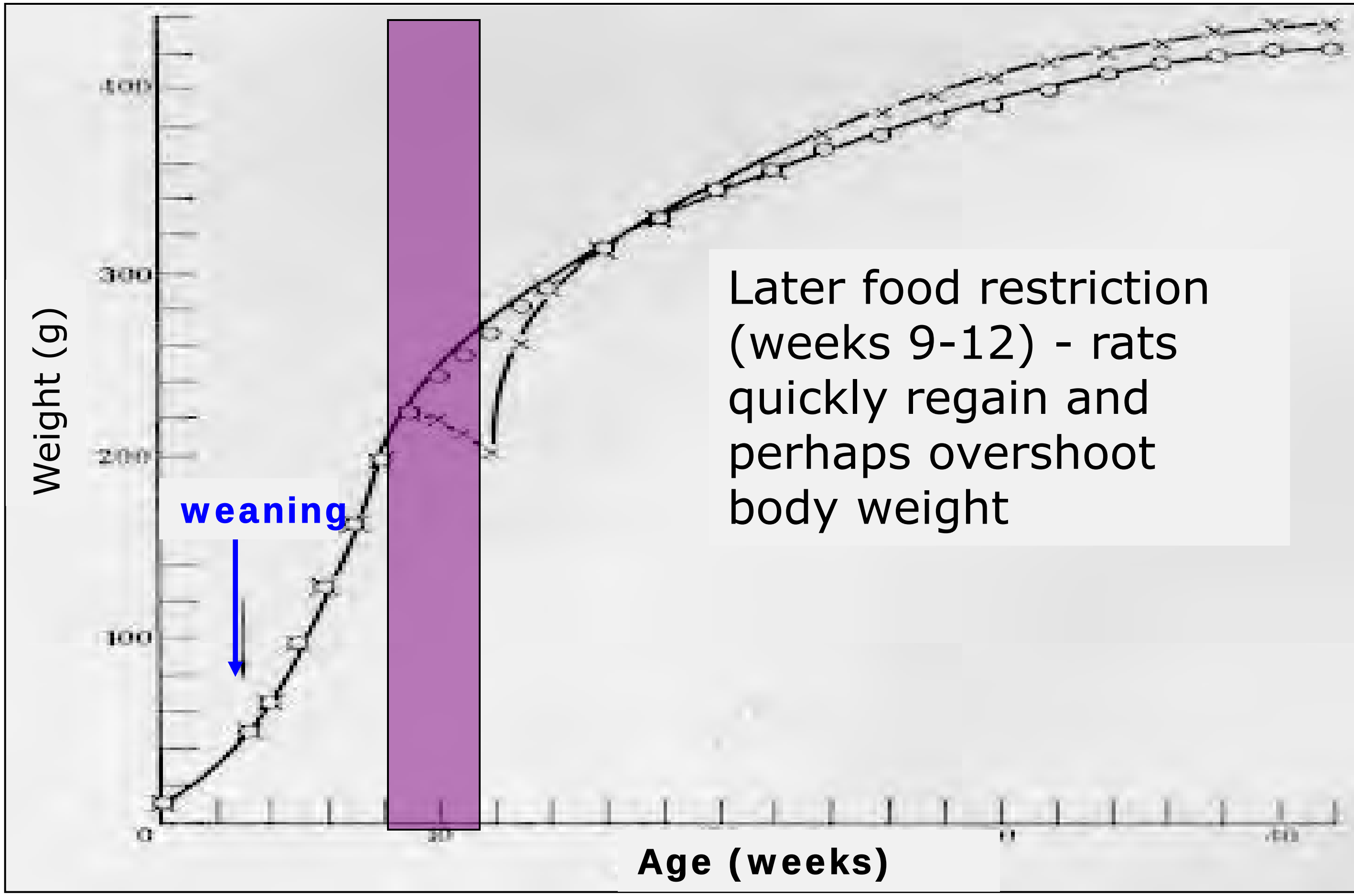
75 days: Weights 86g, 230g

Widdowson and McCance, 1960



21 day period of food restriction

Timing is important



Widdowson and McCance, 1963

21 day period of food restriction

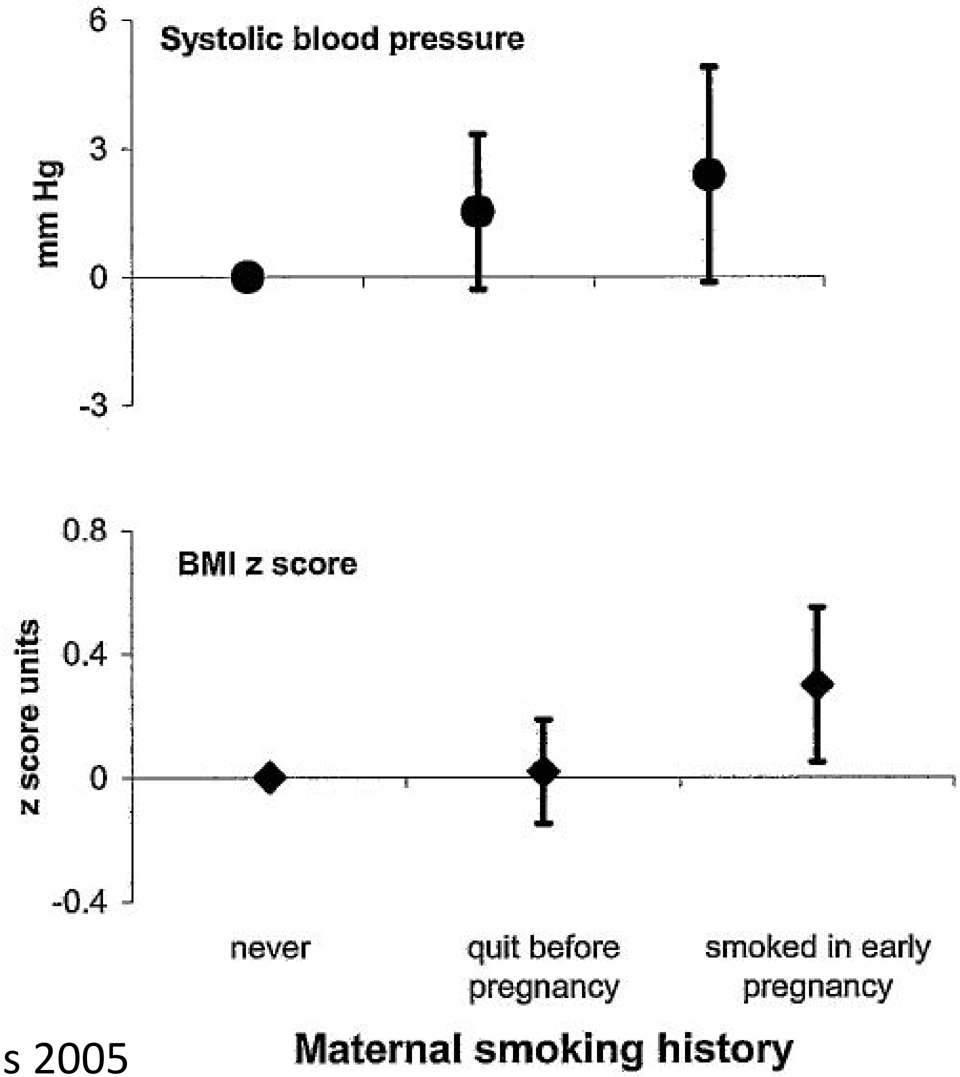
Maternal factors and child weight

- Maternal obesity
- Gestational diabetes
- Gestational weight gain

All these are associated
with faster intrauterine growth ...

Is growth just tracking?

Maternal prenatal smoking – predicts both slower fetal growth and later obesity (also BP)



Oken E et al. Obes Res 2005

Small babies have less muscle, are relatively fatter

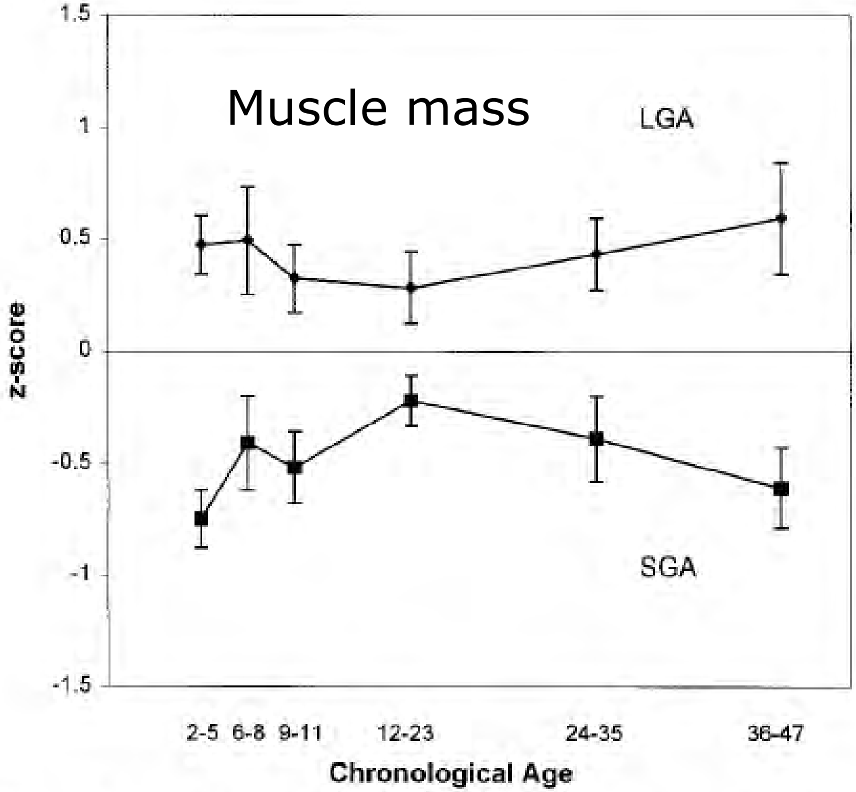


Fig 1. Regression coefficients ± SE in SDU (z-scores) for mid-upper arm muscle area for infants and children born SGA (■—■) and LGA (♦—♦) compared with infants and children born AGA (z-score = 0). All points are statistically different from zero at $P < .05$ with the exception of the 6 to 8 month and 12 to 23 month cohorts for SGA and the 12 to 23 month cohort for LGA.

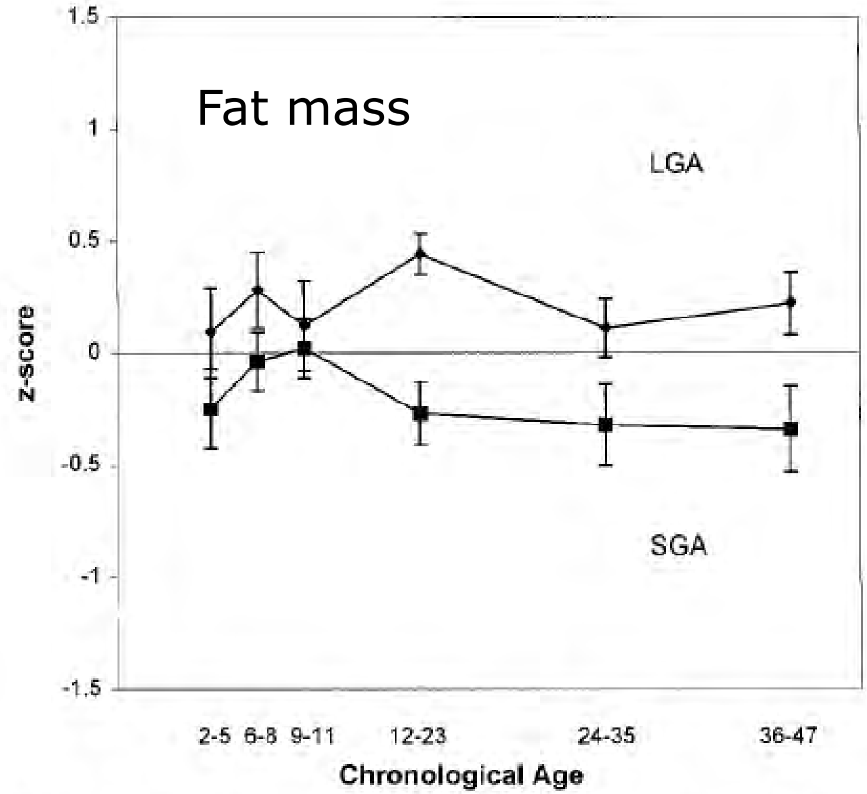
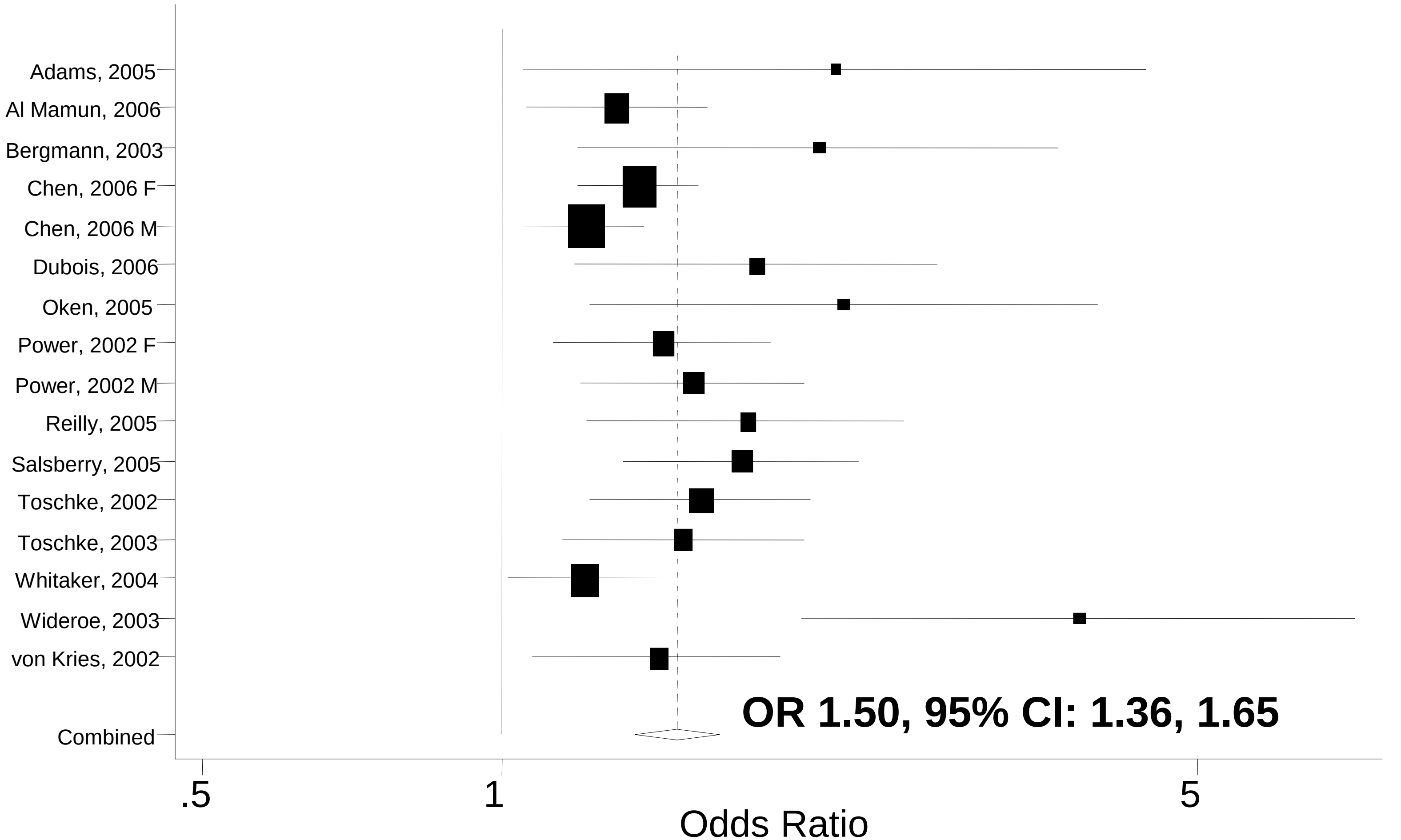


Fig 2. Regression coefficients ± SE in SDU (z-scores) for mid-upper arm fat area for infants and children born SGA (■—■) and LGA (♦—♦) compared with infants and children born AGA (z-score = 0). No point, with the exception of that for infants born LGA at age 12 to 23 months, is statistically different from zero at $P < .05$.

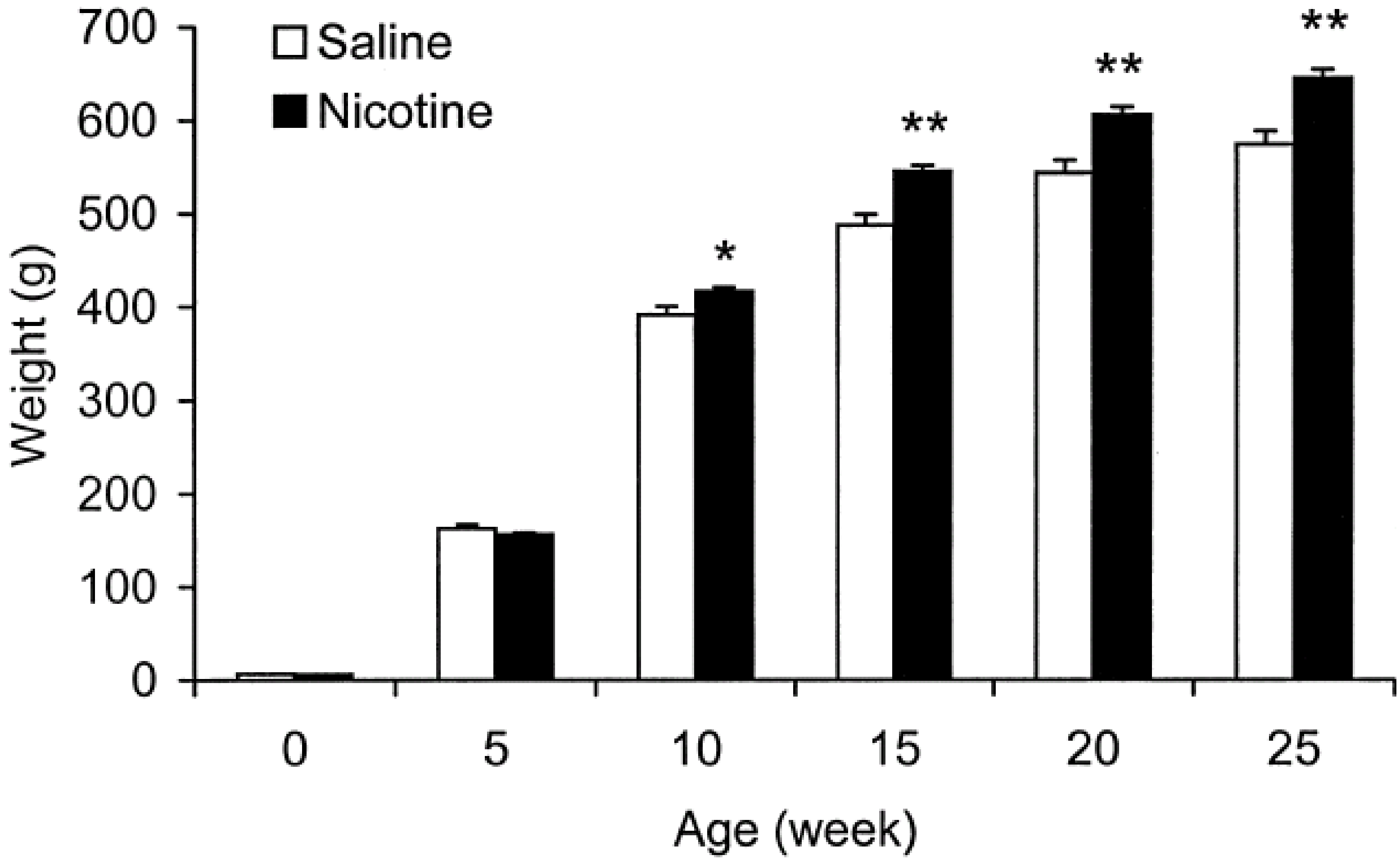
Hediger et al. Pediatrics 1998.

Maternal smoking and child overweight
Is it causal?– meta-analysis



Oken, et al. Int J Obes (Lond) 2008; 32(2):201-10

Maternal smoking and child overweight
Is it causal?– rat study



Gao YJ et al. Obes Res. 2005;13(4):687-92

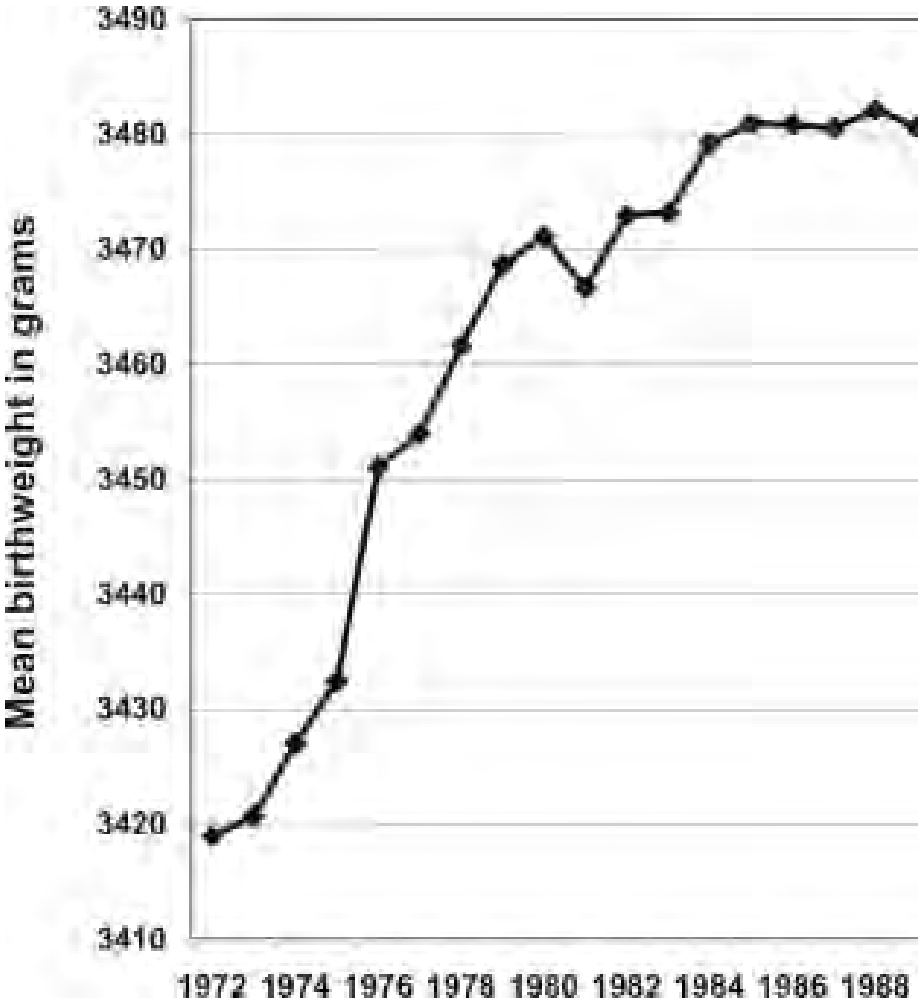
Kids are getting bigger…

Trends in fetal growth

- Contribute to bigger babies
  - Fewer teen births
  - Smoking decreasing
  - BMI increasing
  - GWG increasing
  - Gestational diabetes increasing

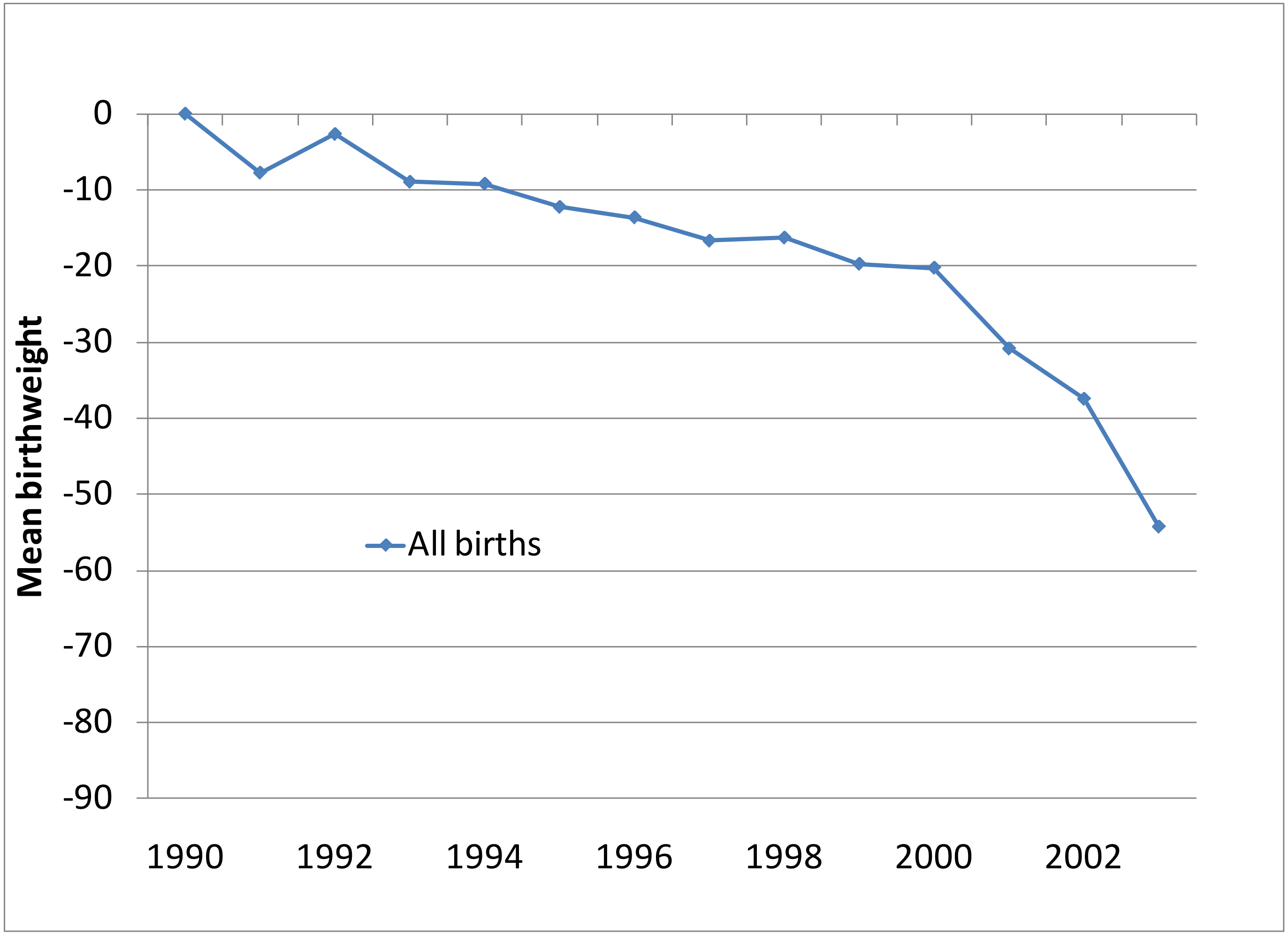
- Contribute to smaller babies
  - More births to older mothers
  - Pre- pregnancy morbidity increasing
  - More preterm births
  - More multiples
  - Assisted Reproductive Technologies

Birthweight among US white, term, singleton births



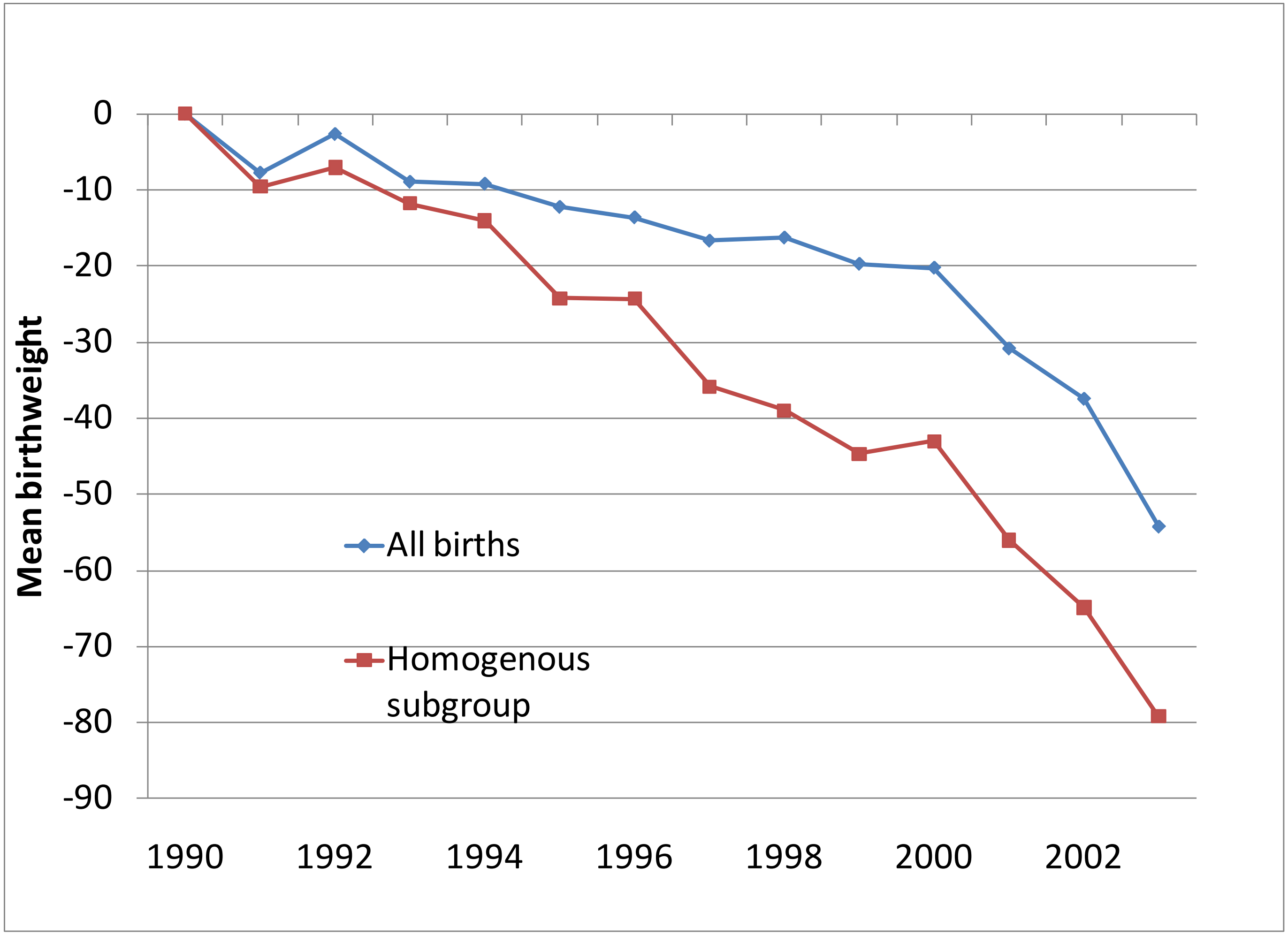
Zhang et al. AJOG August 2010;124.

Birth weight trends since 1990



Oken et al. Obstet Gynecol. 2010 Feb;115(2 Pt 1):357-64

Birth weight trends since 1990 singleton term births



Oken et al. Obstet Gynecol. 2010 Feb;115(2 Pt 1):357-64

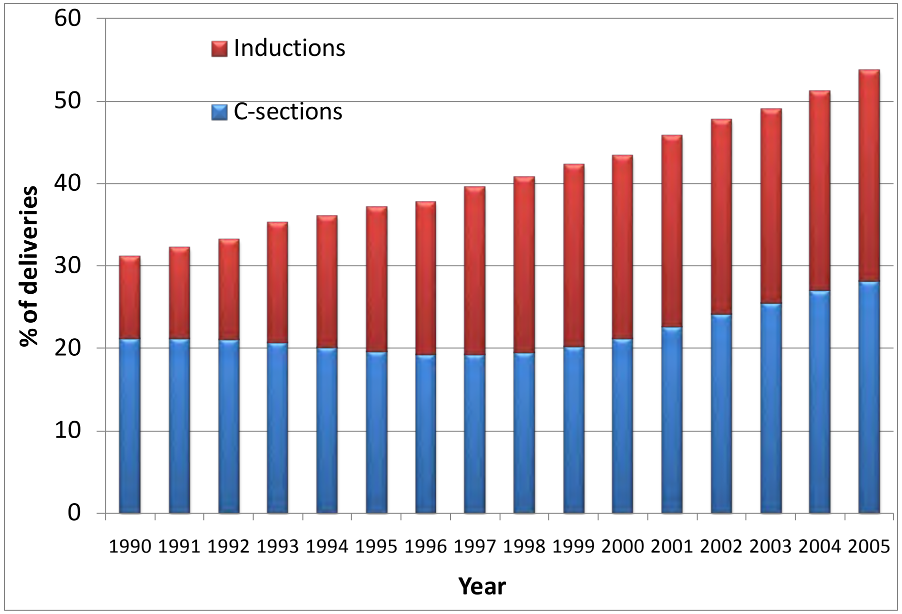
Regression Results – change in BW per year

Covariates	Effect Estimate
None	-3.0 g
+Infant birth order, sex; Maternal age, race, ethnicity, education, prenatal care, smoking, marital status	-3.3 g
+Pregnancy complications, gestational weight gain	-3.7 g
+ csection, induction, ultrasound	-4.2 g
+ gestational age	-1.9 g
+ estimated maternal BMI, height (from NHANES)	-3.5 g

Oken et al. Obstet Gynecol. 2010 Feb;115(2 Pt 1):357-64

Are babies getting bigger?

- No!
  - But you have to read past the headlines
- Why are babies now getting smaller?
  - Gestation length and its contributors



Intervention to reduce elective early term births

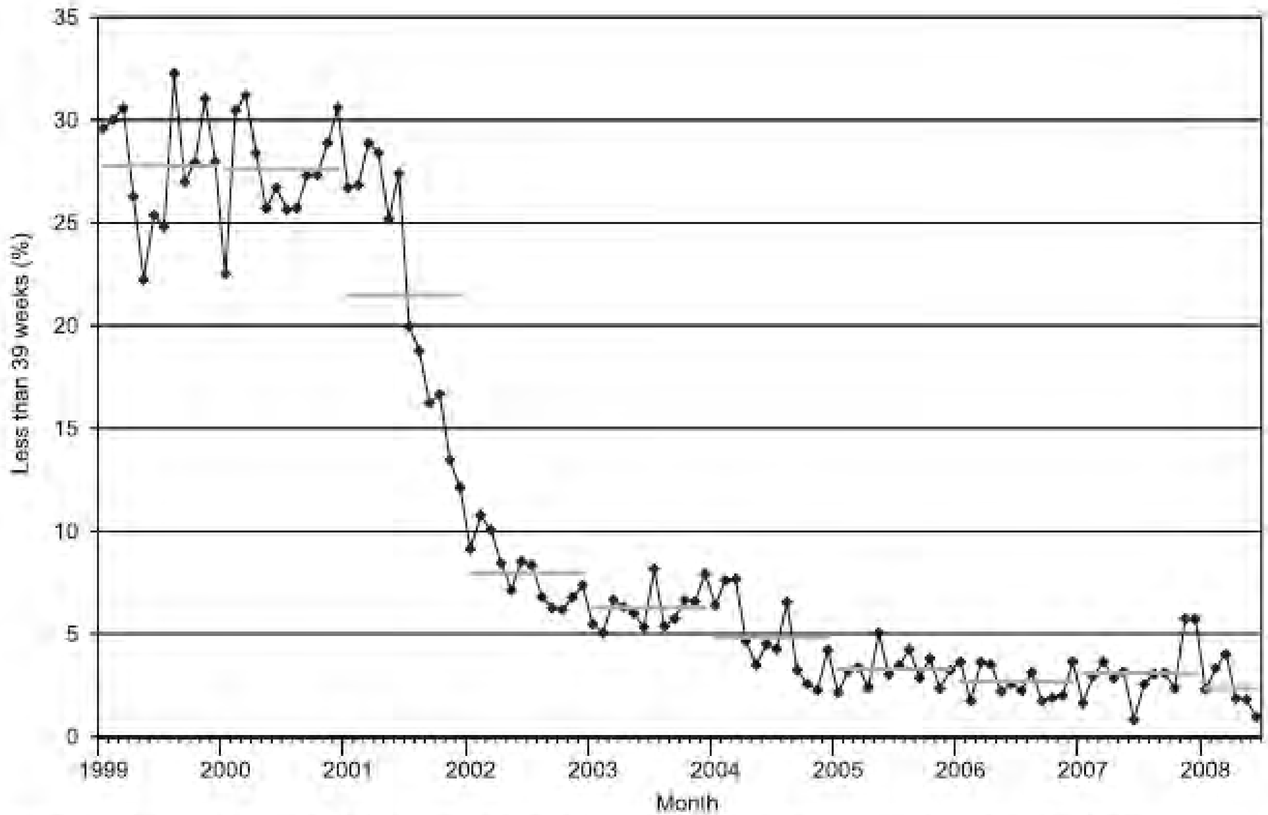
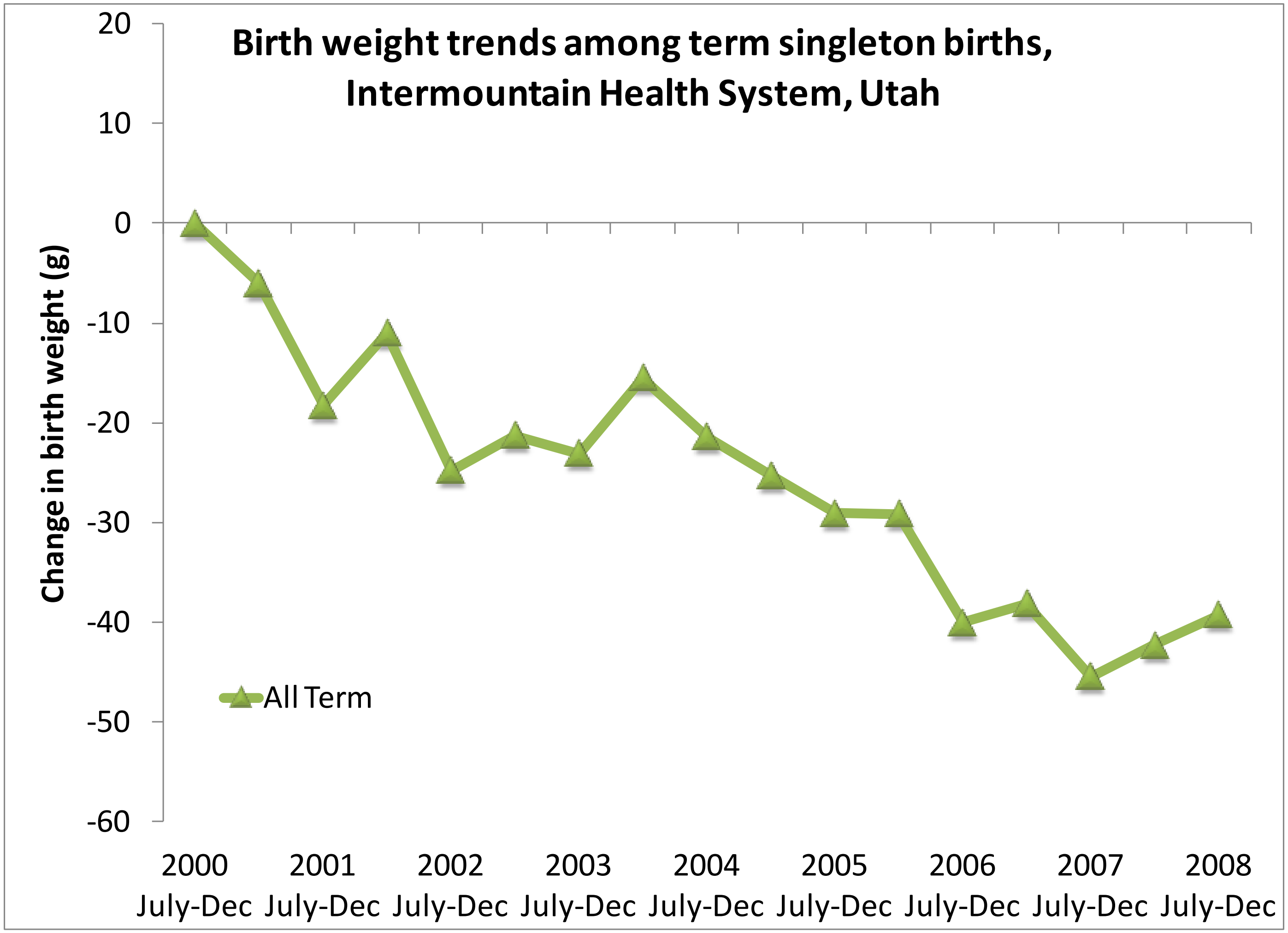


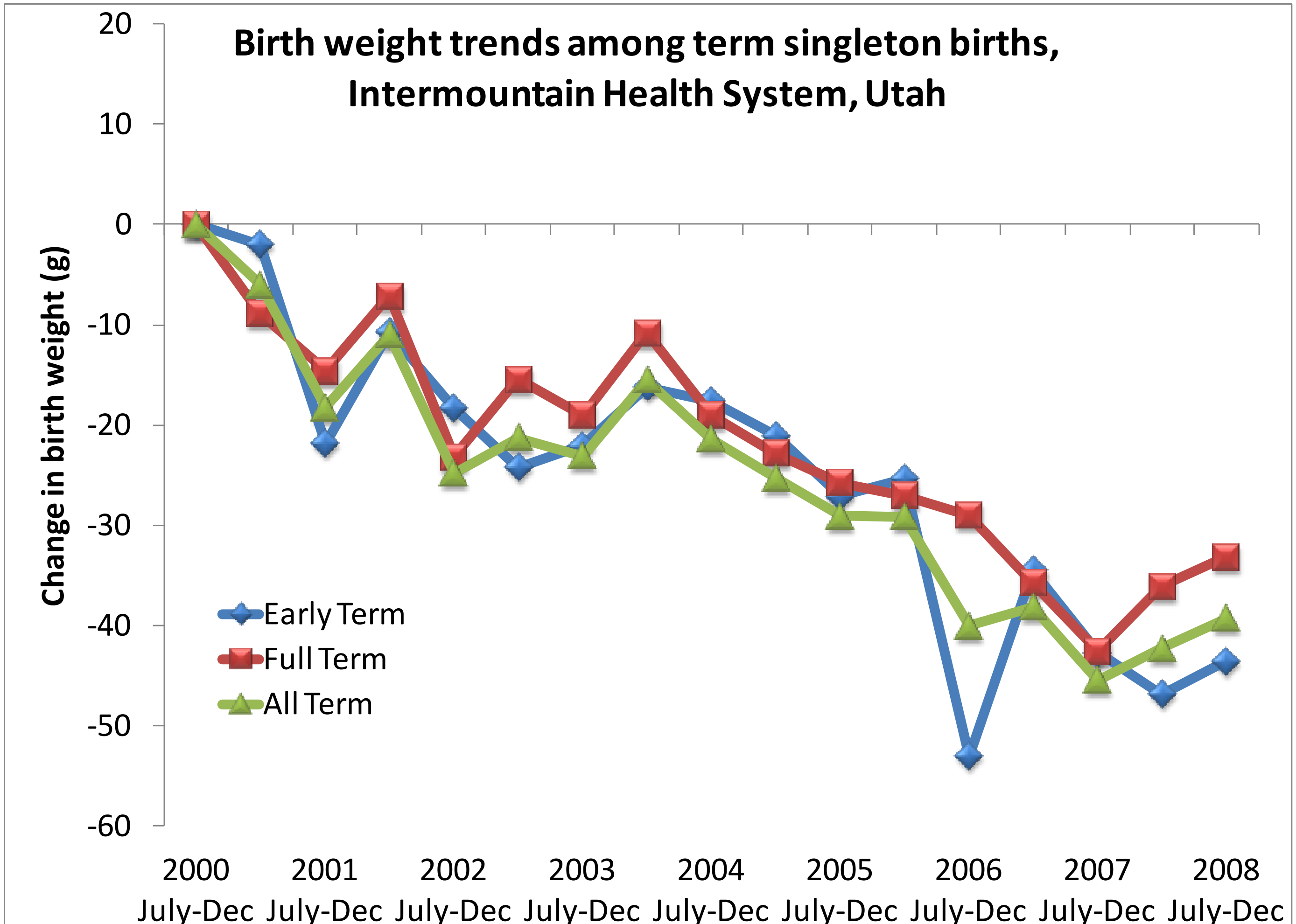
Fig. 3. Percent of elective deliveries before 39 weeks of gestation. Data from Intermountain Healthcare.
Oshiro. Decreasing Elective Deliveries Before 39 Weeks. Obstet Gynecol 2009.

Intervention to reduce elective early term births



Morisaki N, Esplin MS, Varner MW, Henry E, **Oken E**. Obstet Gynecol. 2013 Jan;121(1):51-58.

Intervention to reduce elective early term births



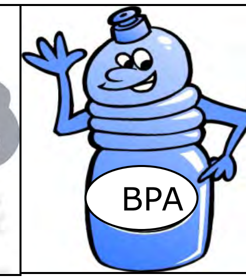
Morisaki N, Esplin MS, Varner MW, Henry E, **Oken E**. Obstet Gynecol. 2013 Jan;121(1):51-58.

Are babies getting bigger? NO

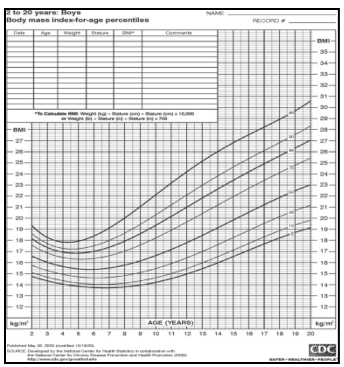
Heaviest Baby

Who:	A baby boy born to Anna Bates (*née* Swan)
Where:	Ohio, USA
Stats:	76 cm (30 in) long, 10.8 kg (23 lb, 12 oz)
When:	19 January 1879

“Intrauterine nutrition” is not only about maternal behaviors

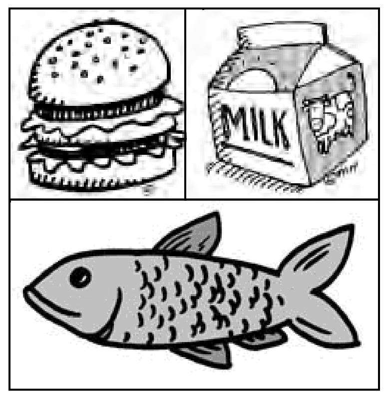


Extrauterine environment

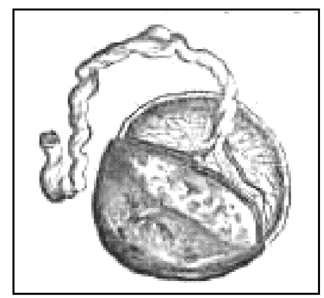


Mom’s own intrauterine and childhood experiences

Mom’s peri-conceptional health



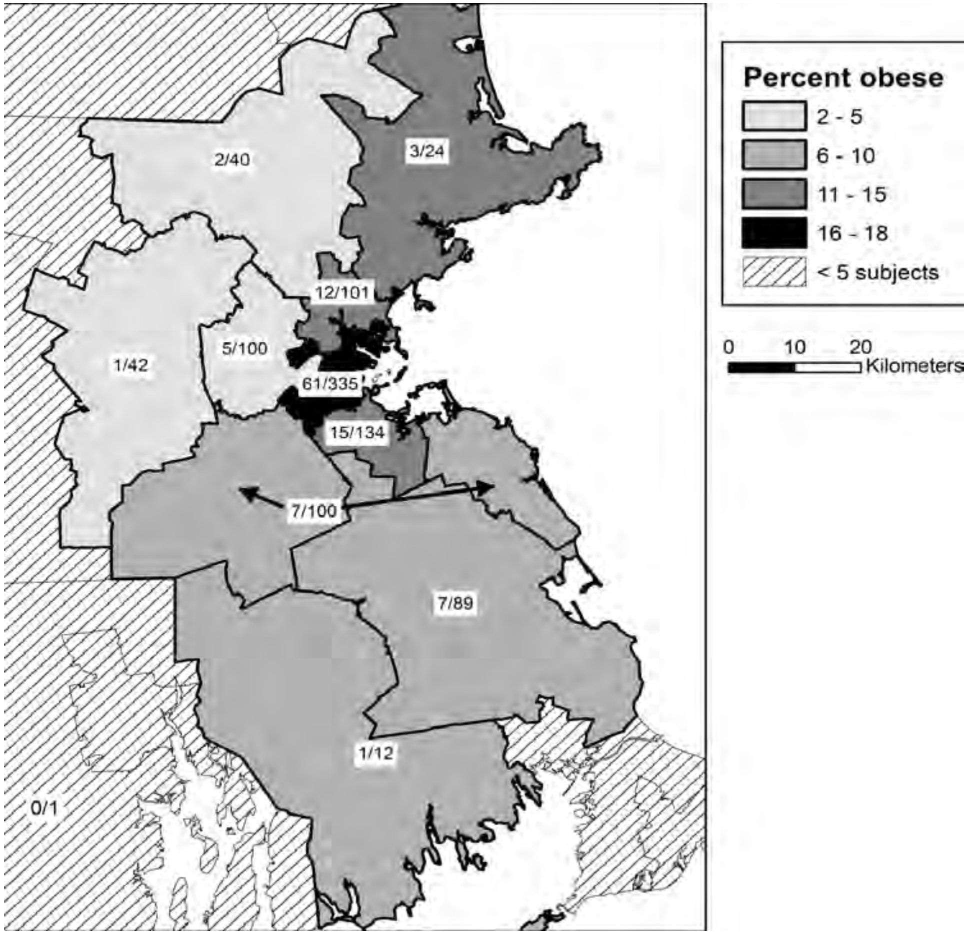
Diet during pregnancy

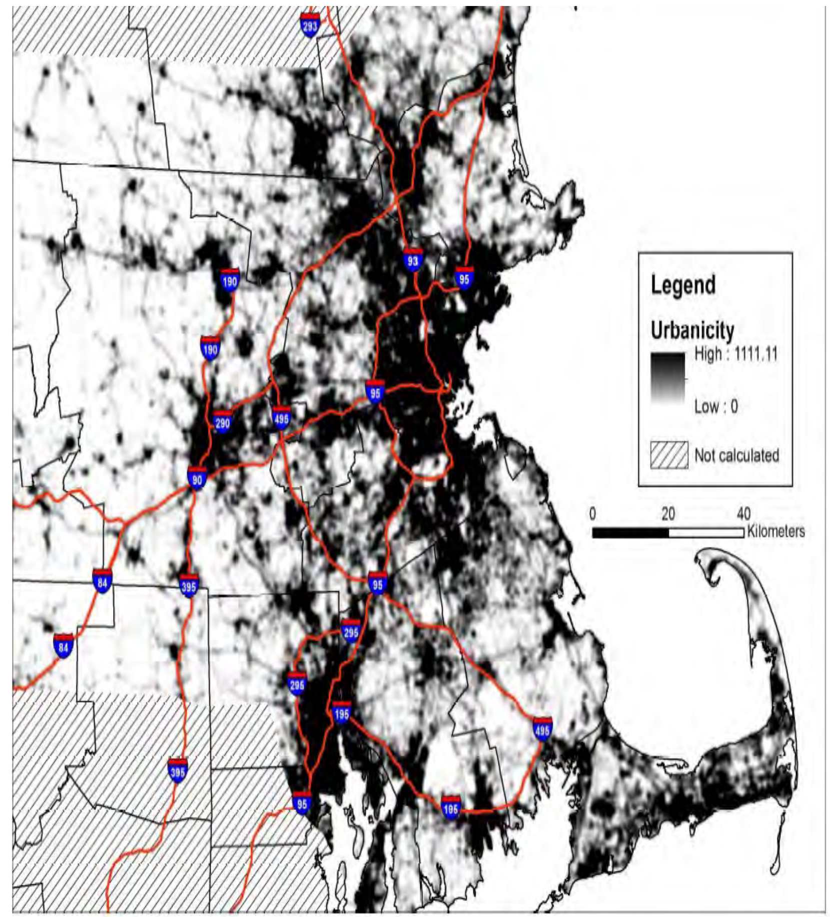


Utero-placental blood flow, placental function

Fetal metabolism

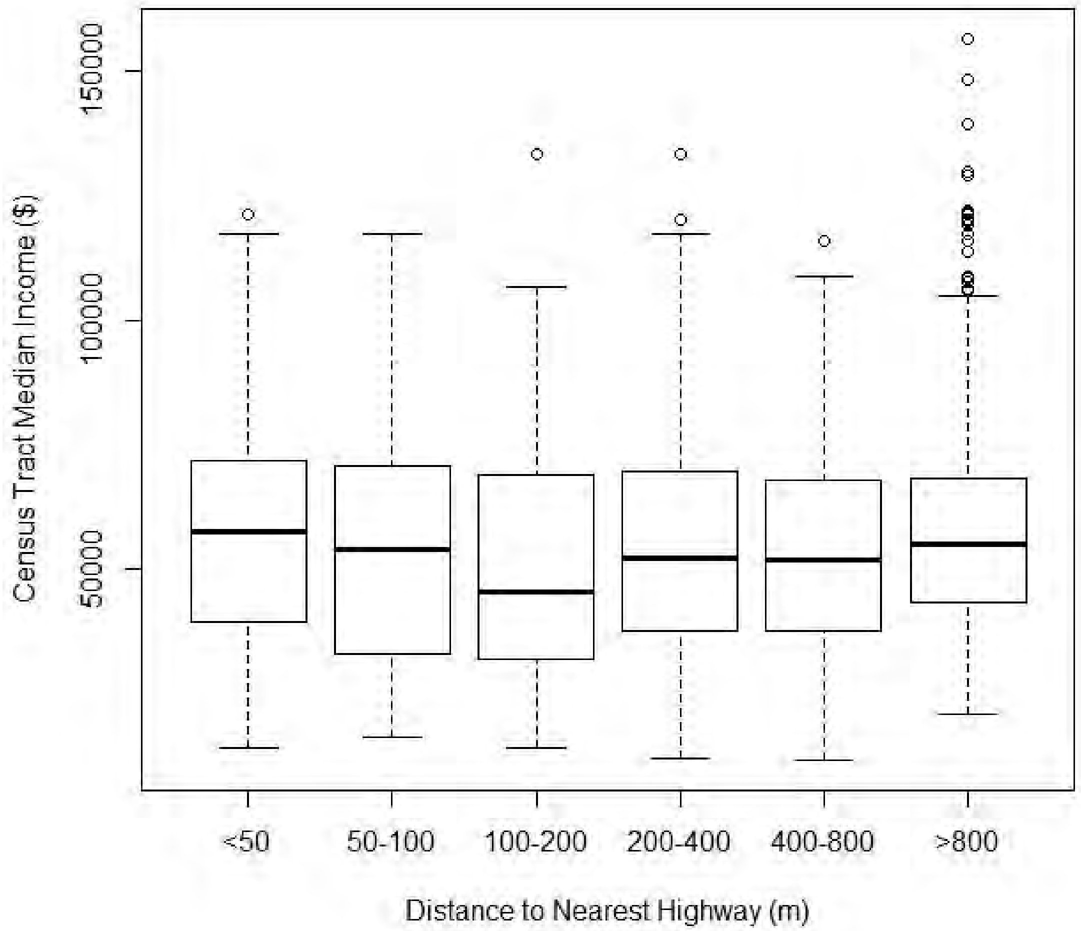
Obesity and urbanicity



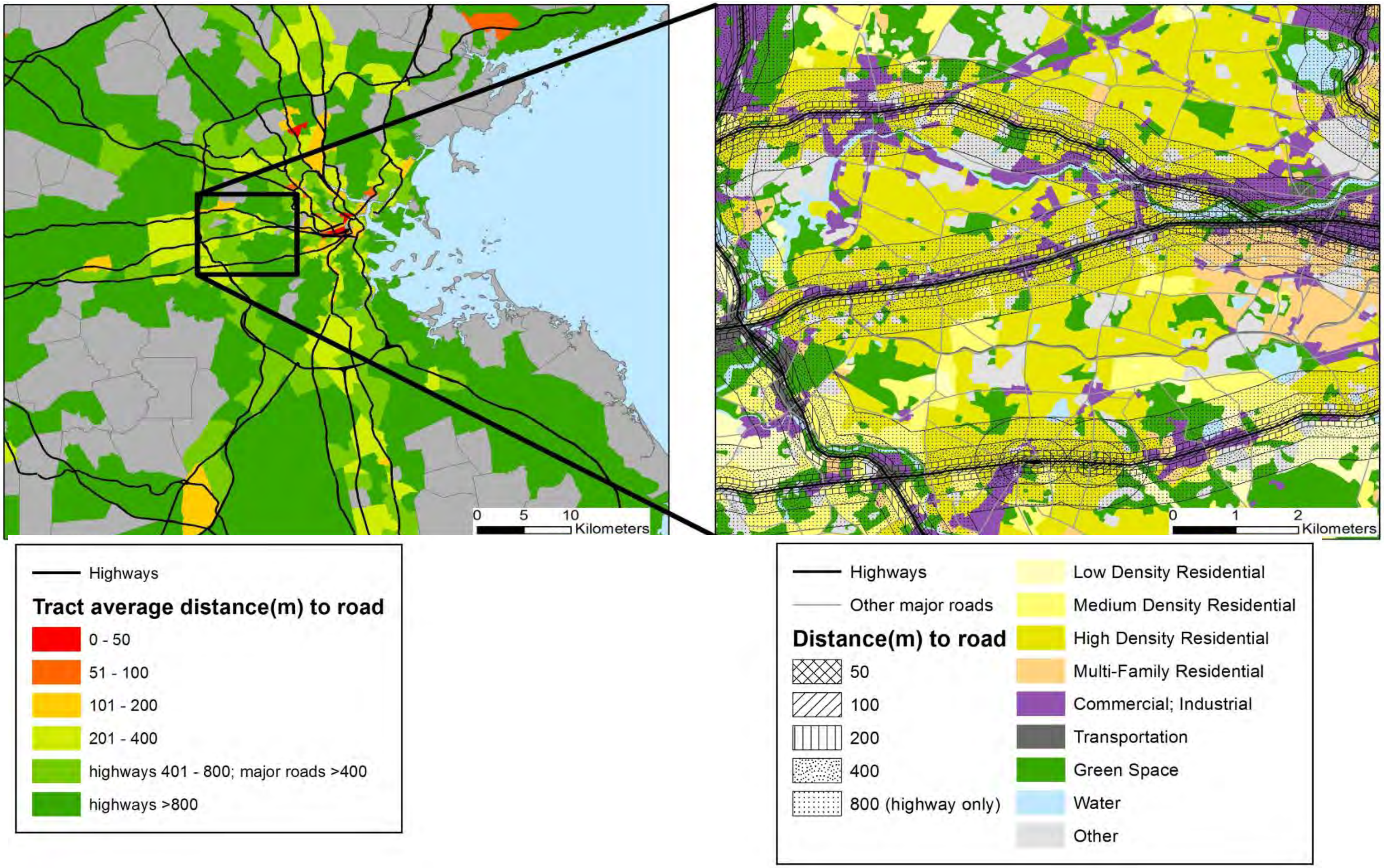


Ratios are # of obese childen/total # of children living in that area

Air pollution and obesity – Is it causal? Look at confounding



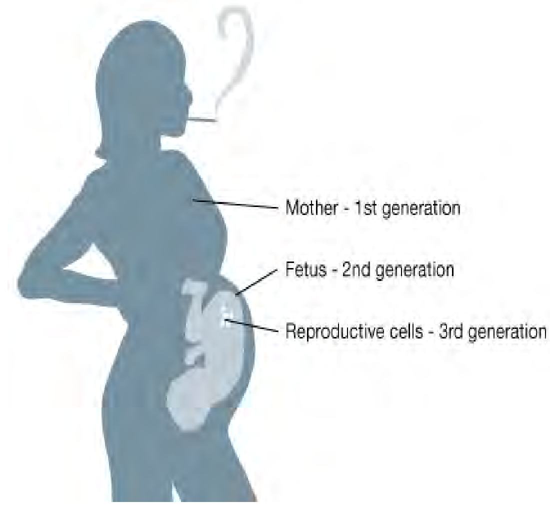
Many in MA live close to highways

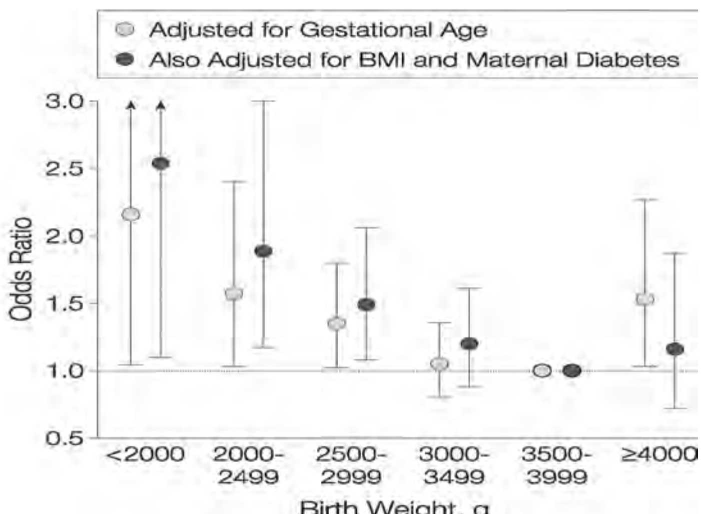


Inter- and trans-generational influences

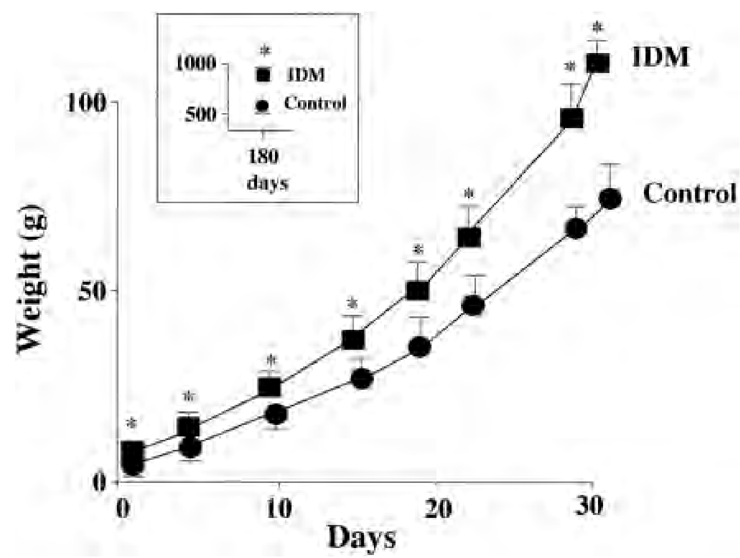
Excess early nutrition in grandmother (pink line) results in shorter lifespan in grandchild

Longevity of grandchild





Innes et al,. JAMA 2002

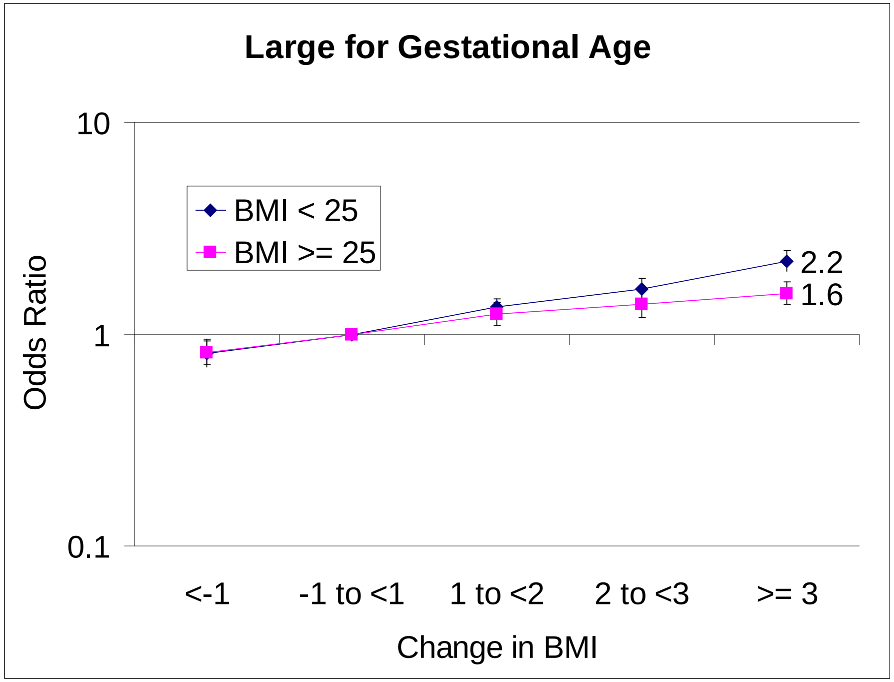


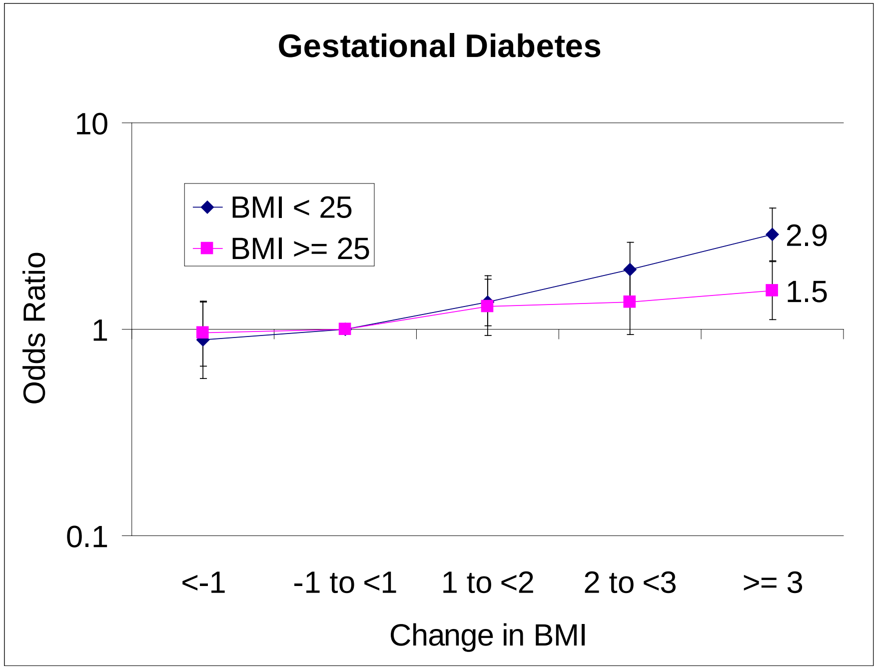
Kaati et al. *European Journal of Human Genetics* (2007) **15,** 784–790

Opportunities for intervention

- Preconceptional counseling
  - Especially in fertility treatment settings
- Gestational weight gain counseling and tracking
- Post-natal weight loss

Inter-pregnancy weight gain and 2nd pregnancy outcomes





Villamor, Lancet 2006;368:1164-70

NIH WORKSHOP
PREVENTION OF OBESITY IN INFANCY AND EARLY CHILDHOOD, 31st Oct 2013

MRC Epidemiology Unit

Factors Affecting Rapid Growth During Infancy

Ken Ong

Programme Leader, MRC Epidemiology Unit, IMS

Paediatric Endocrinologist, Addenbrooke’s Hospital

Affiliated Lecturer, University Dept of Paediatrics

IMS Institute of Metabolic Science

MRC | Medical Research Council

UNIVERSITY OF CAMBRIDGE

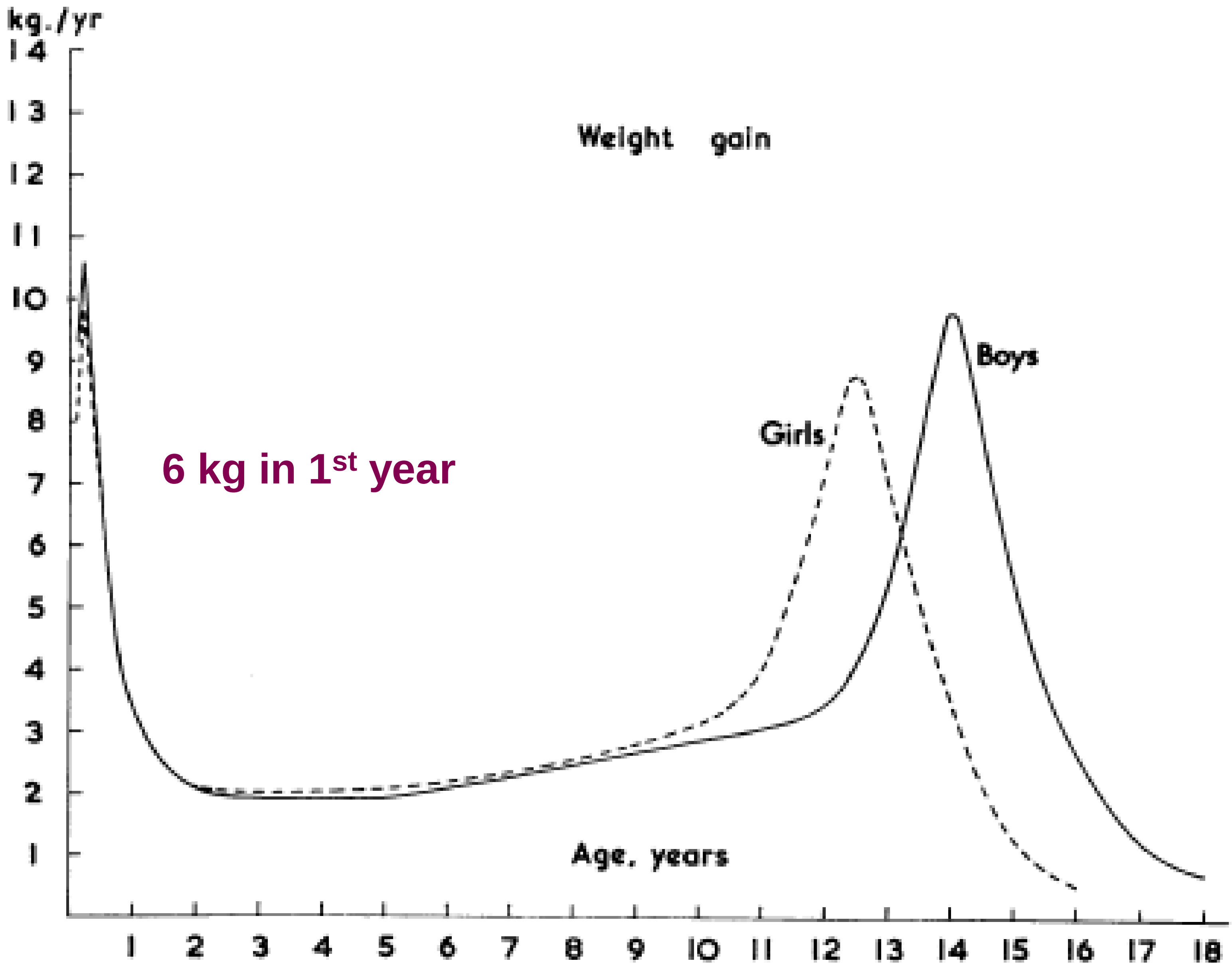
Outline

- Evidence for early rapid growth as a risk factor for obesity
- Metabolic pathways that may mediate these effects
- Potentially modifiable factors in early life
- Relevance of genetic factors

Rapid Infancy Weight Gain and Subsequent Obesity

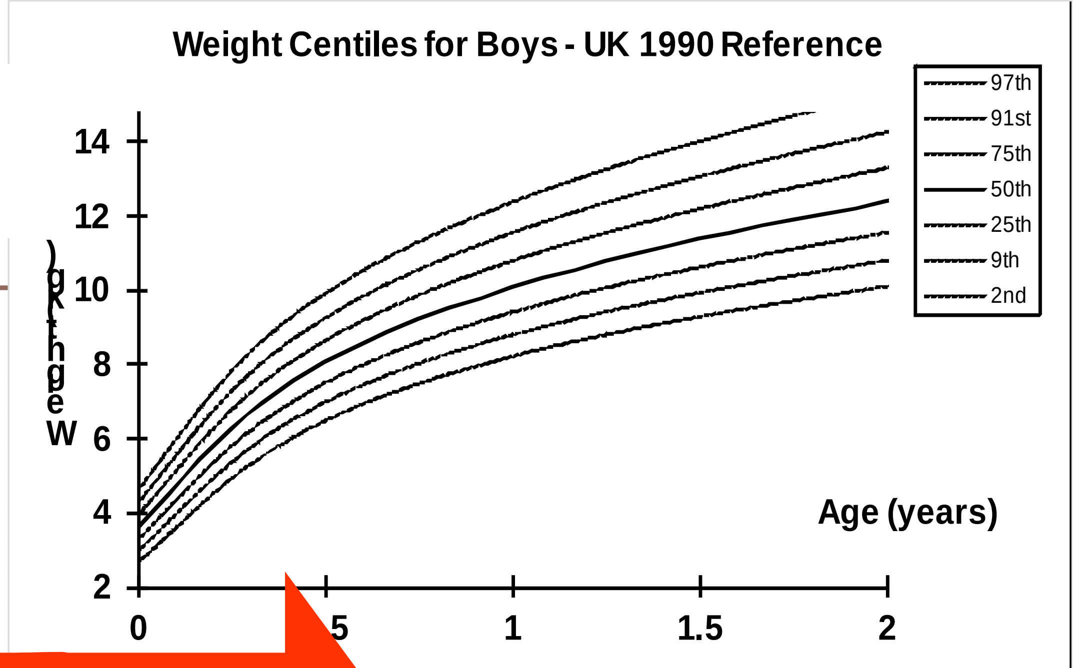
Systematic Reviews:

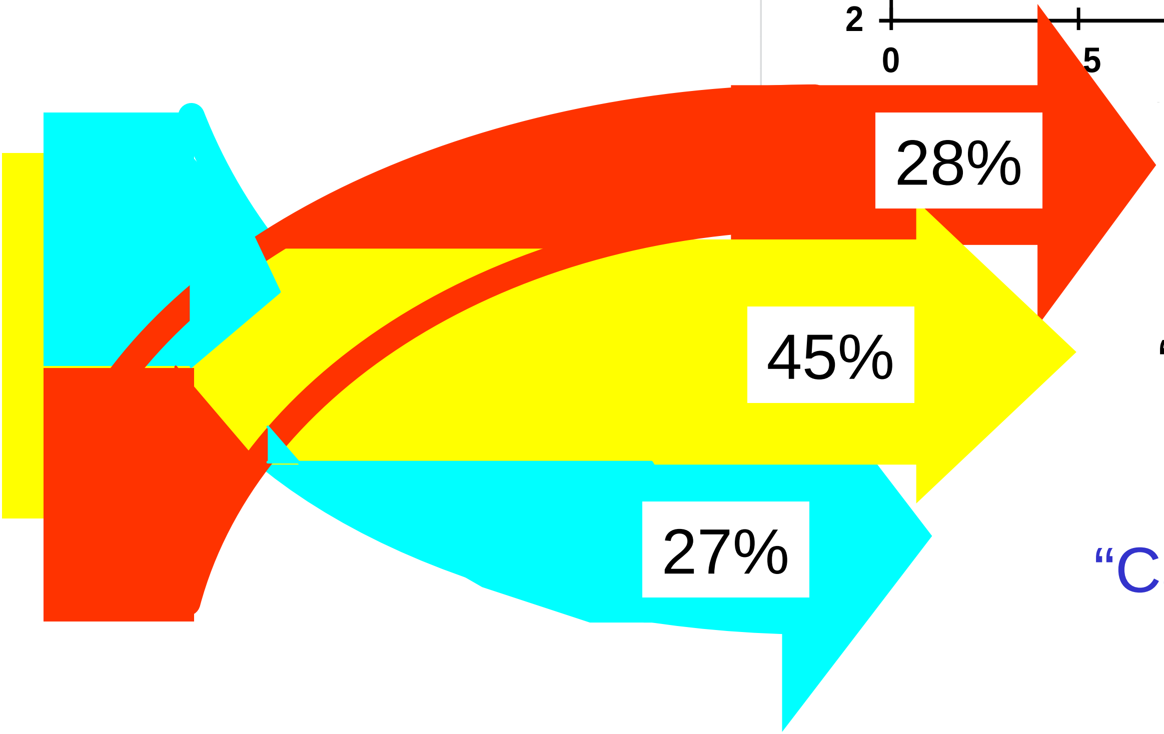
Monteiro & Victora (Obes Rev 2005):	13 studies
Baird et al. (BMJ 2005):	10 studies
Ong & Loos (Acta Paediatrica 2006):	21 studies



6 kg in 1st year

Wide variation in early childhood growth rates





"Catch-up" > +0.67 SDS

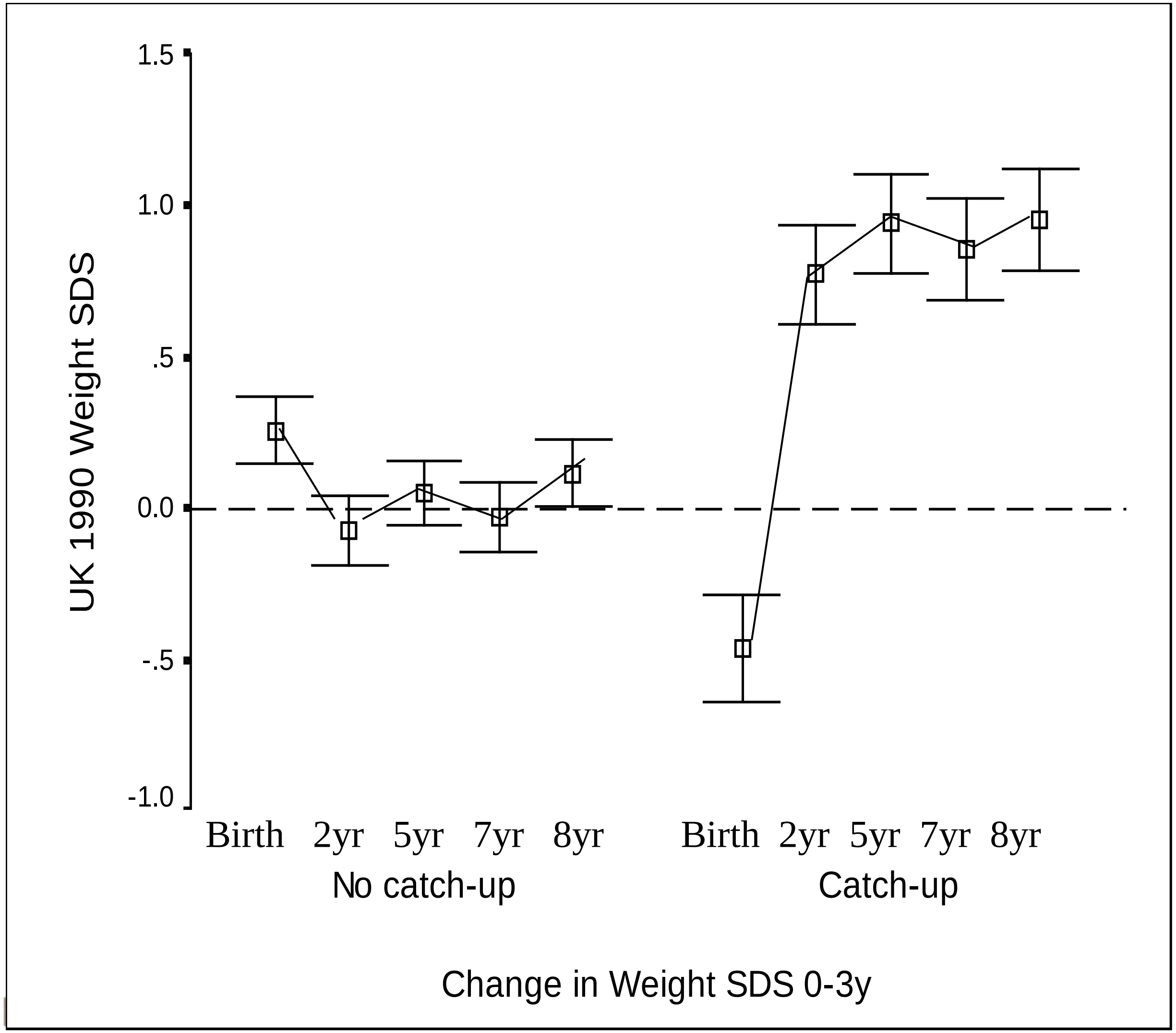
"No-change"

"Catch-down"

Birth *2y* *3y*

Ong et al., *Pediatric Res* 2002

Persisting effects of early postnatal rapid weight gain



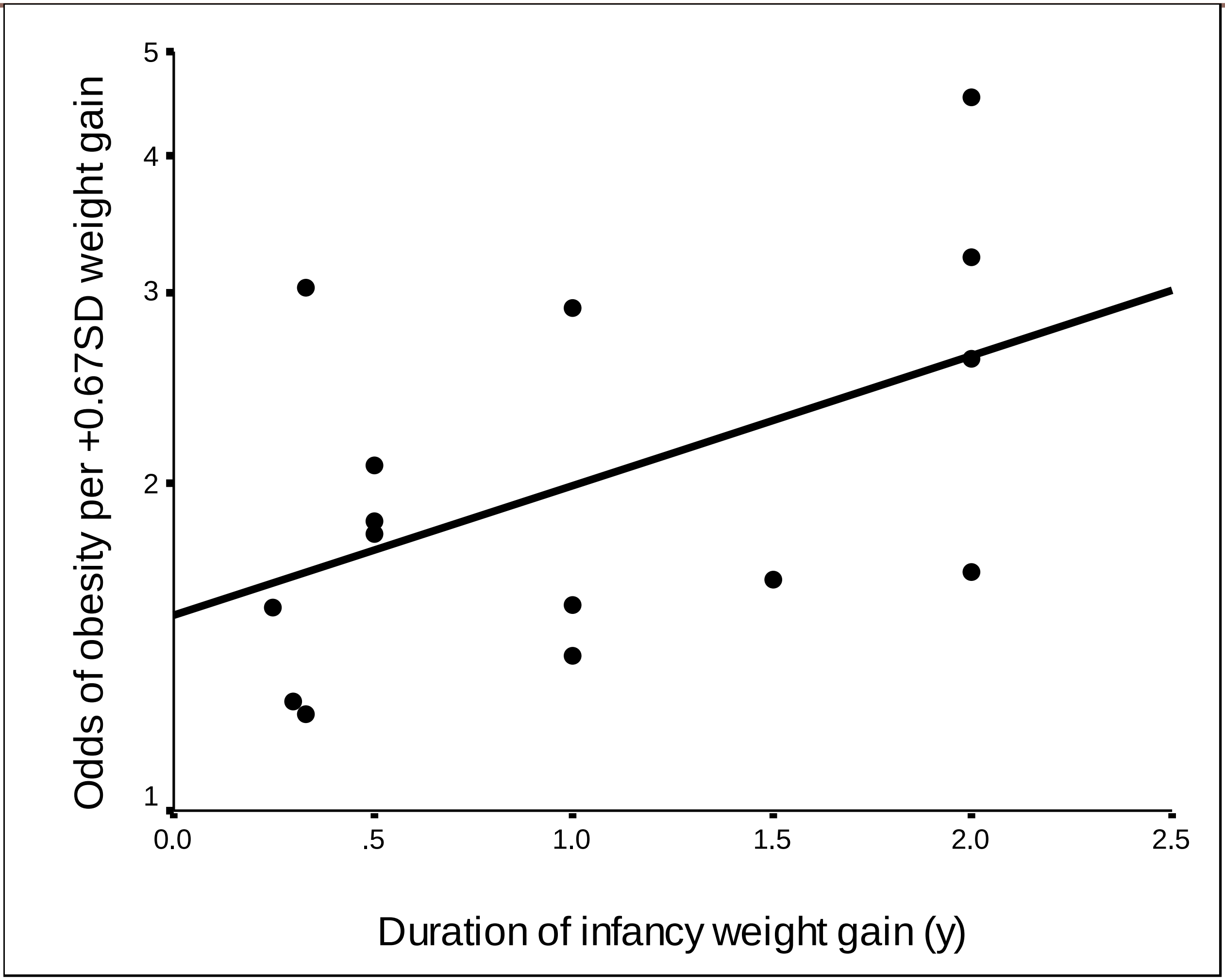
Ong et al. *BMJ* 2000

plus updated ALSPAC data at age 8y

MRC

Infant Weight gain & Childhood Obesity

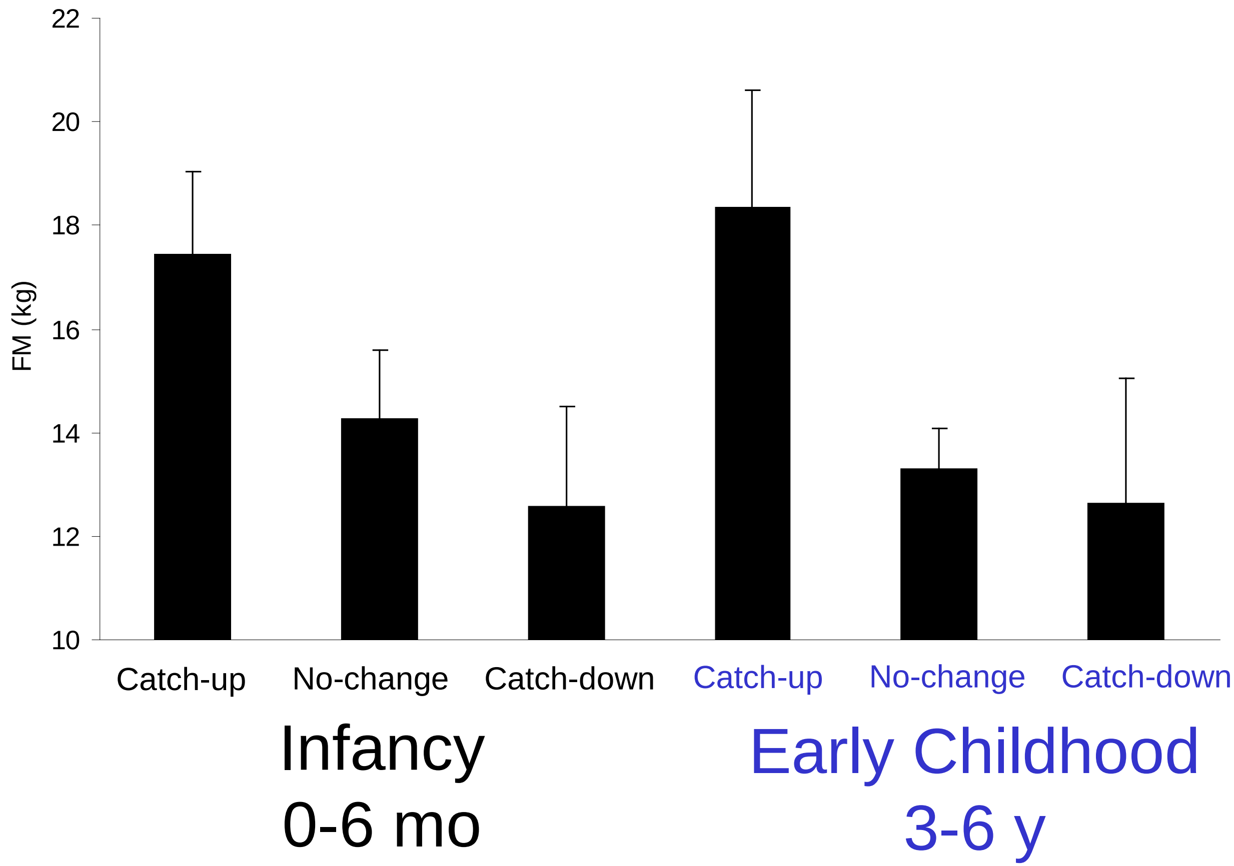
Meta-regression results: Duration of exposure (from birth)



Ong & Loos, *Acta Paediatrica* 2006
Druet & Ong, *Best Pract Res Clin Endo & Metab* 2008

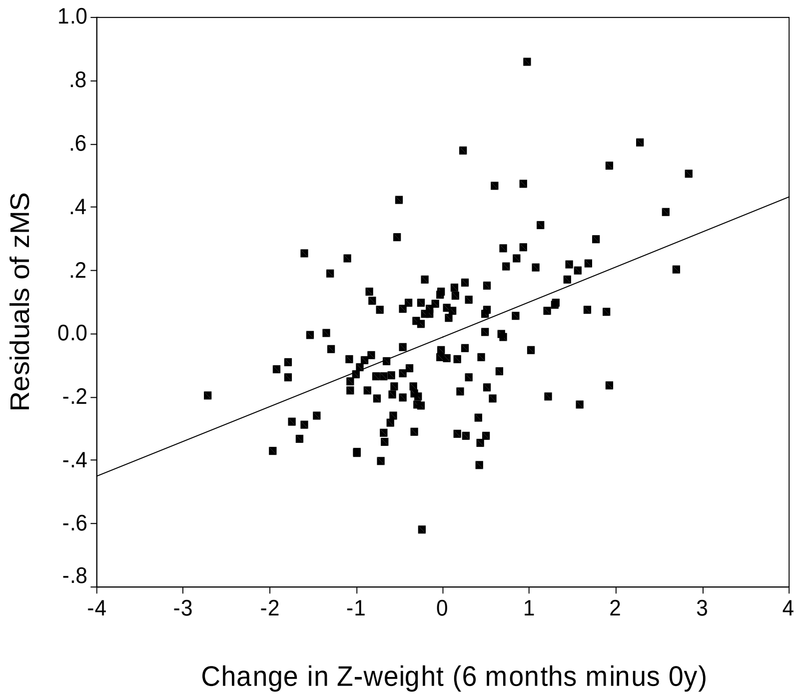
Infant vs. Childhood Weight gain:
Fat mass at 17y

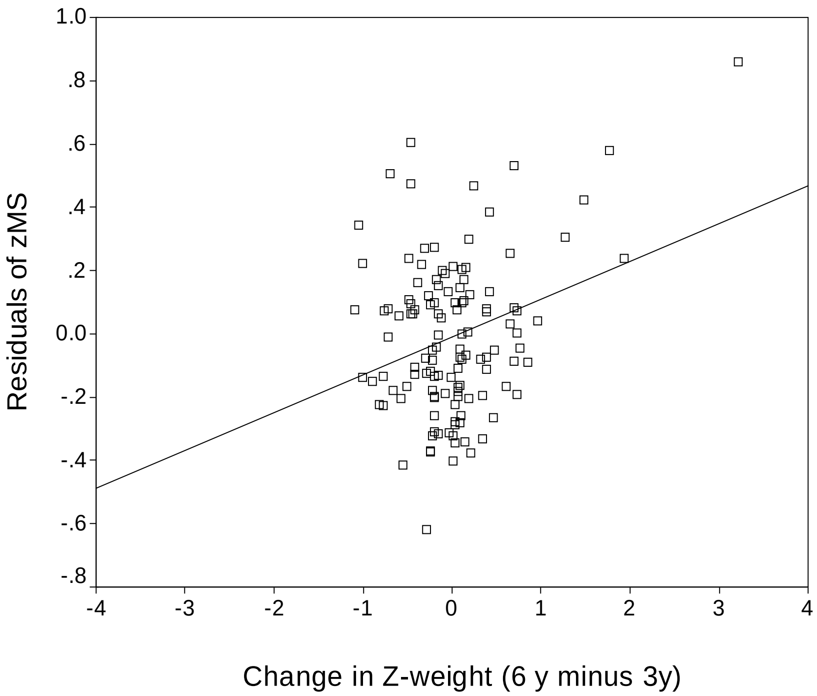
Fat mass
at 17 years



Ekelund et al., *Am J Clin Nutr* 2006

Infant vs. Childhood Weight gain:
Combined Metabolic Syndrome score at 17y





Infancy weight gain
0-6 mo

R-square = 13.7%, P<0.0001

Early Childhood weight gain
3-6 y

R-square = 9.1%, P=0.002

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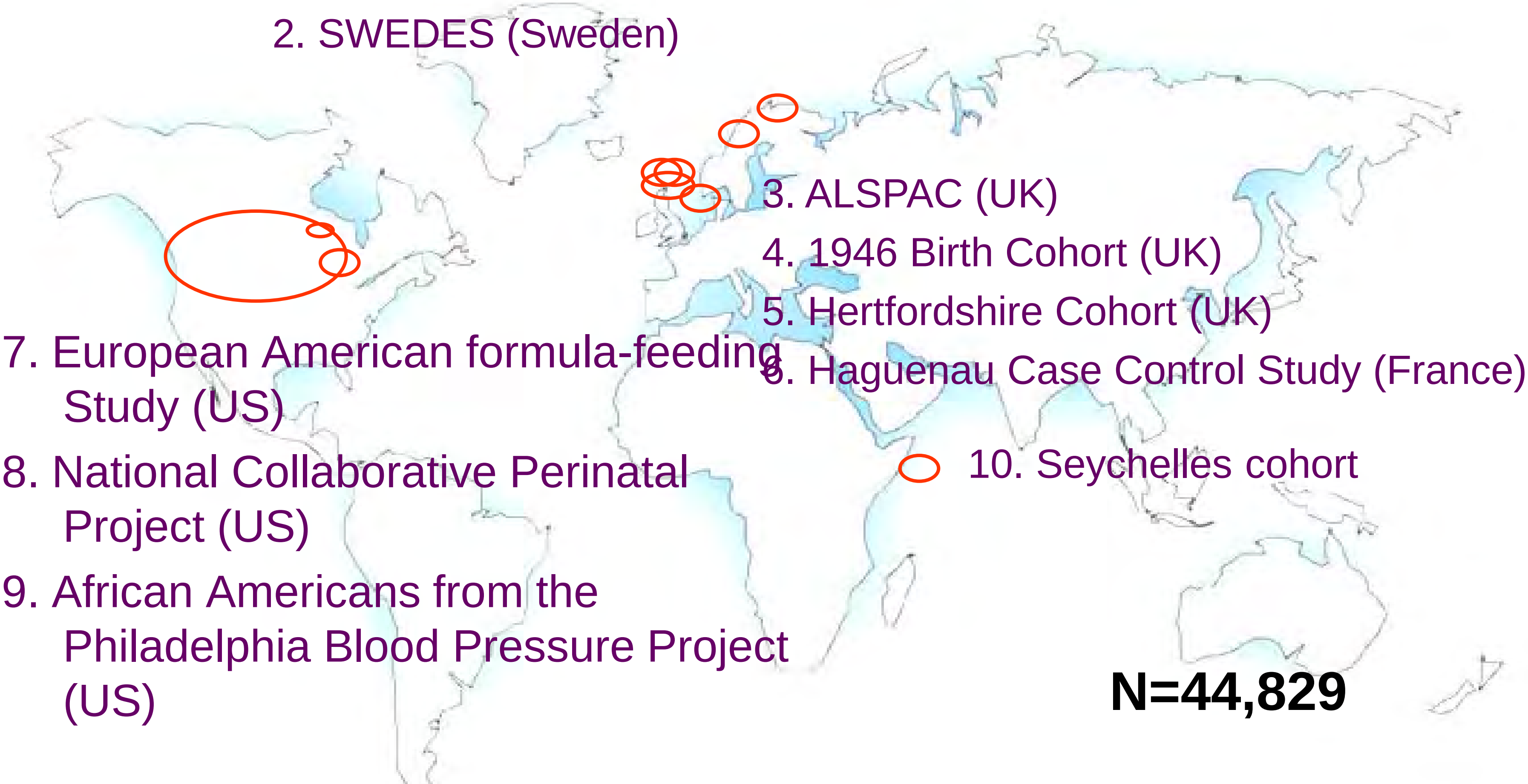
Ekelund et al., *J Clin Endo Metab* 2007

Summary – Infant weight gain & obesity

1. No exclusive window (greatest variation in the first 1-2 years)
2. Threshold?

METRIC collaboration

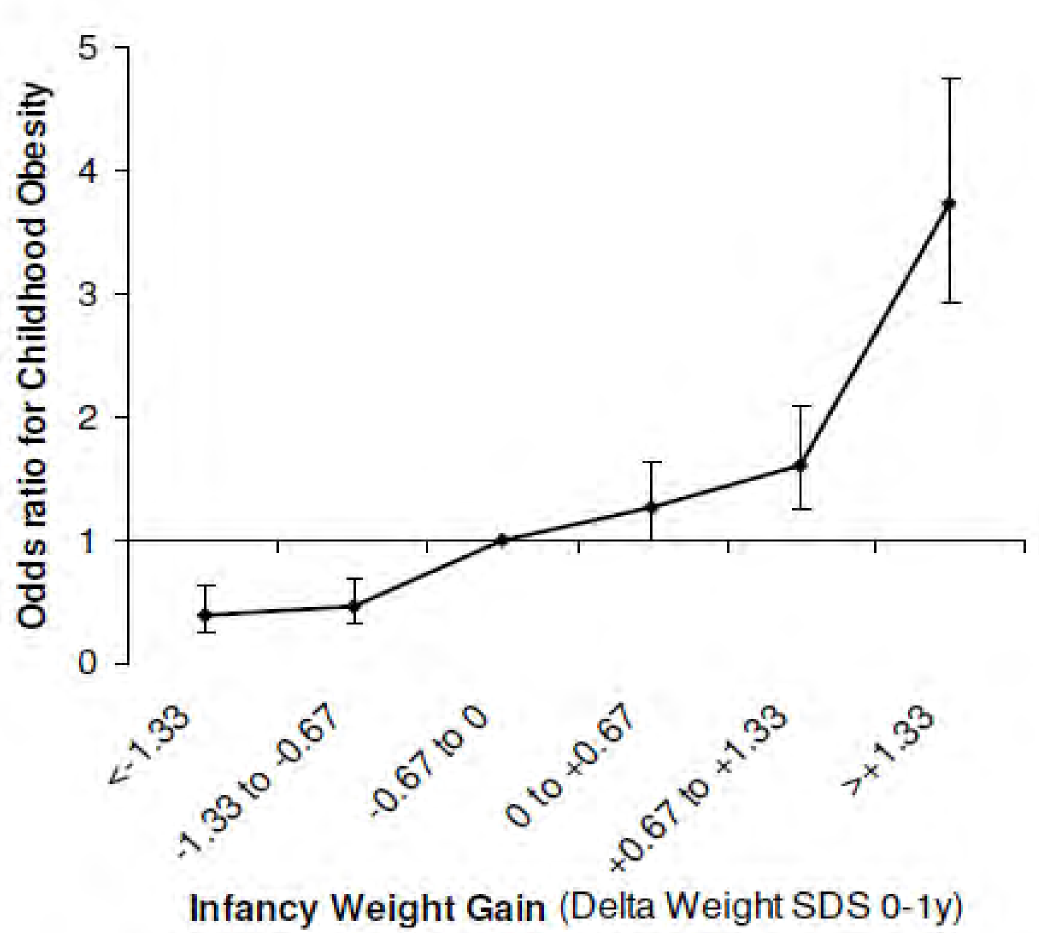
1. Northern Finland 1966 Birth Cohort Study (Finland)
2. SWEDES (Sweden)
3. ALSPAC (UK)
4. 1946 Birth Cohort (UK)
5. Hertfordshire Cohort (UK)
6. Haguenau Case Control Study (France)
7. European American formula-feeding Study (US)
8. National Collaborative Perinatal Project (US)
9. African Americans from the Philadelphia Blood Pressure Project (US)
10. Seychelles cohort



N=44,829

Druet et al, *Paediatric & Perinatal Epidemiology* 2012

Odds ratio for childhood obesity
by infant weight gain 0-1y



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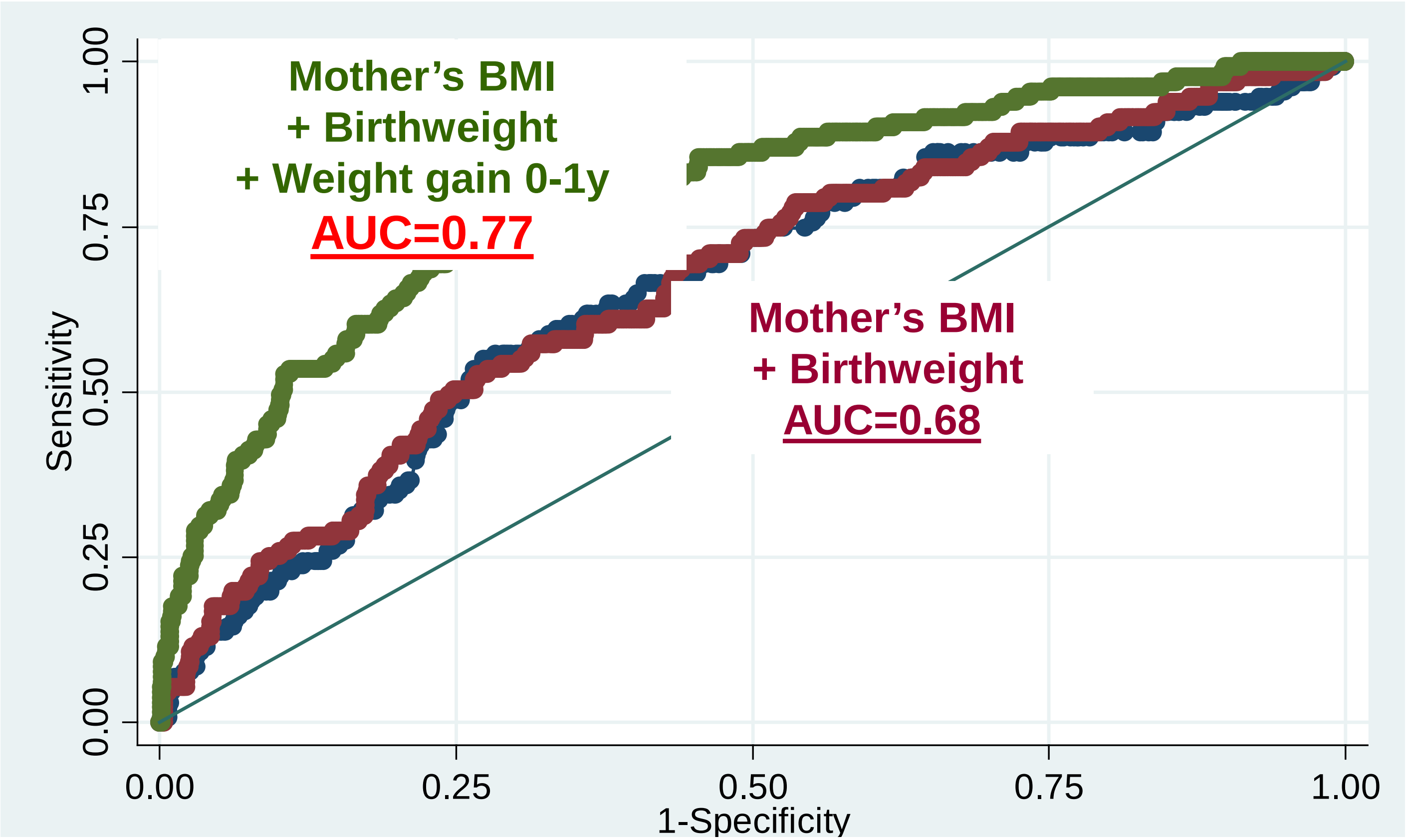
Druet et al, *Paediatric & Perinatal Epidemiology* 2012

Prediction of childhood obesity
by mother's BMI, birth weight and infant weight gain 0-1y



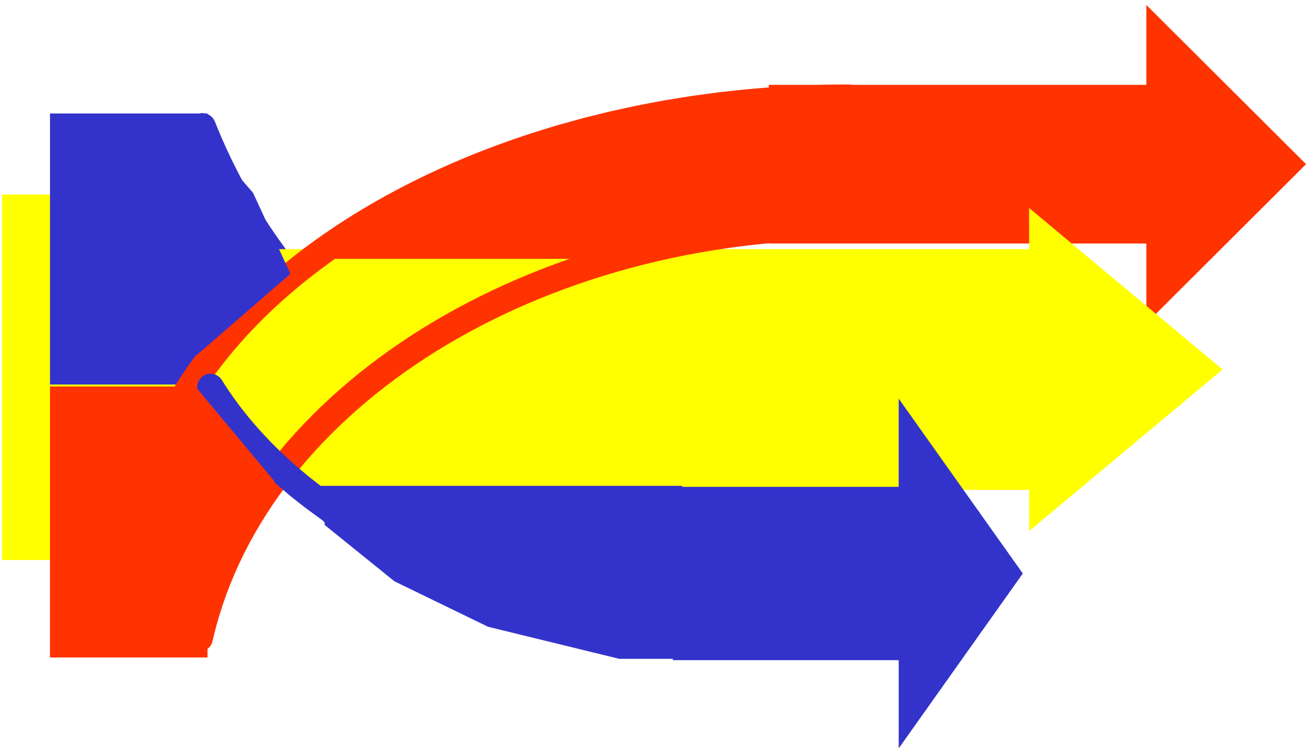
METRIC collaboration: Area under the ROC curve

Druet et al, *Paediatric & Perinatal Epidemiology* 2012

Outline

- Evidence for early rapid growth as a risk factor for obesity
- Metabolic pathways that may mediate these effects
- Potentially modifiable factors in early life
- Relevance of genetic factors

Rapid early postnatal weight gain: Consequences



Obesity
Central Fat
Insulin resistance
IGF-1 levels
Adrenal androgens
Earlier puberty

Birth *2 years* *5 to 8 years*

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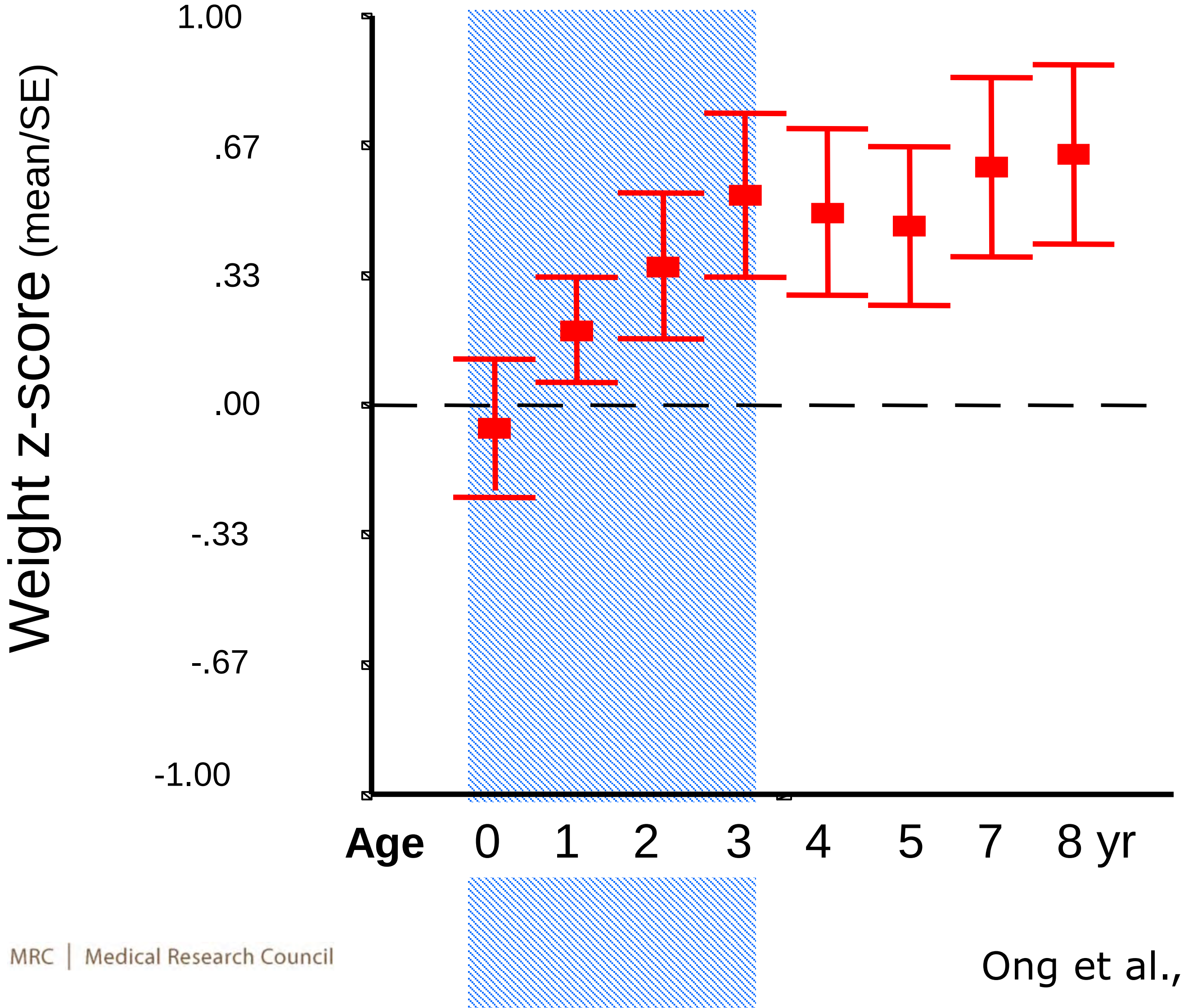
The **most insulin resistant** children (10%) showed rapid early weight gain



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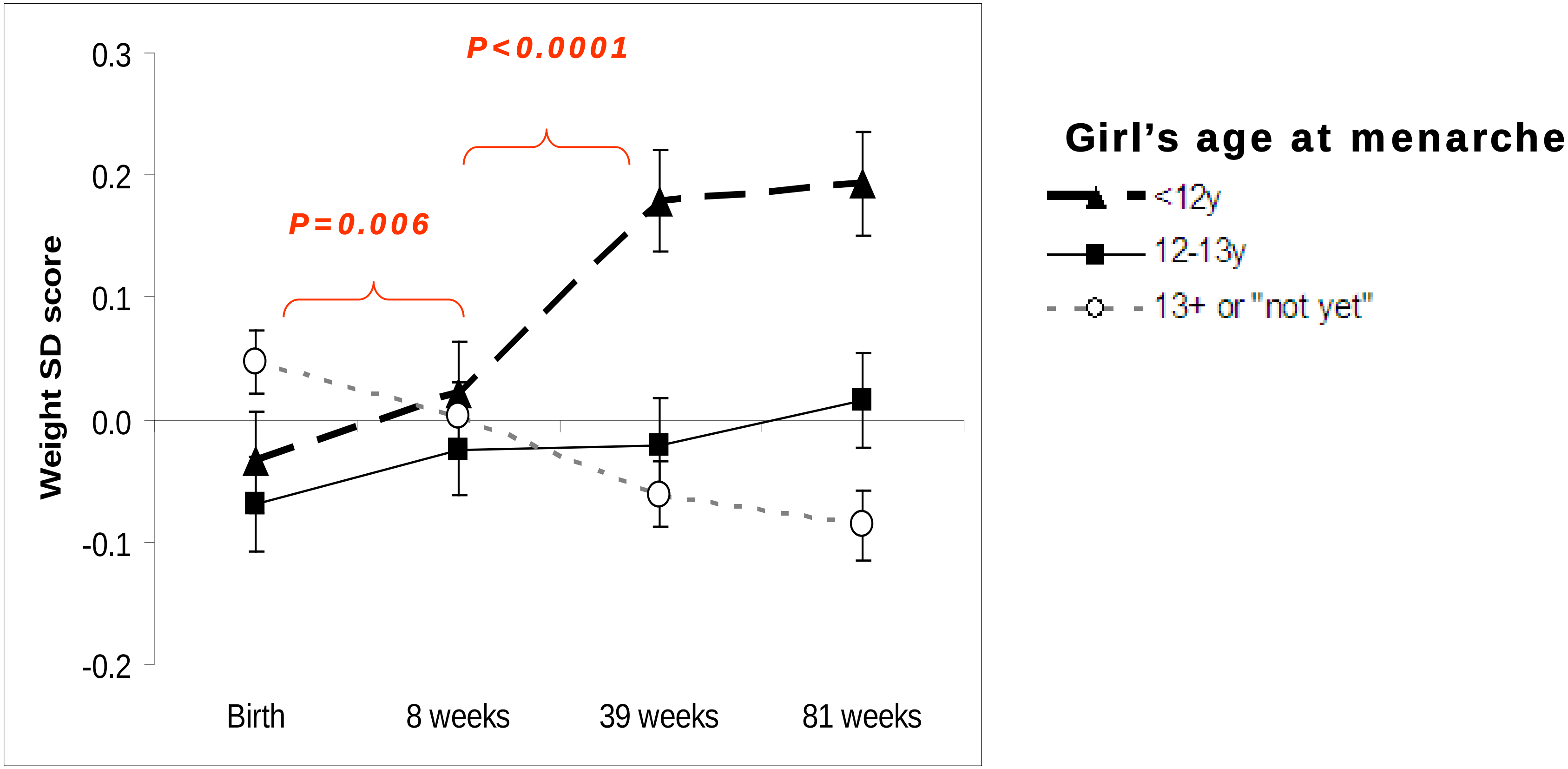
Ong et al., *Diabetologia* 2004

Early menarche in girls related to faster infancy growth

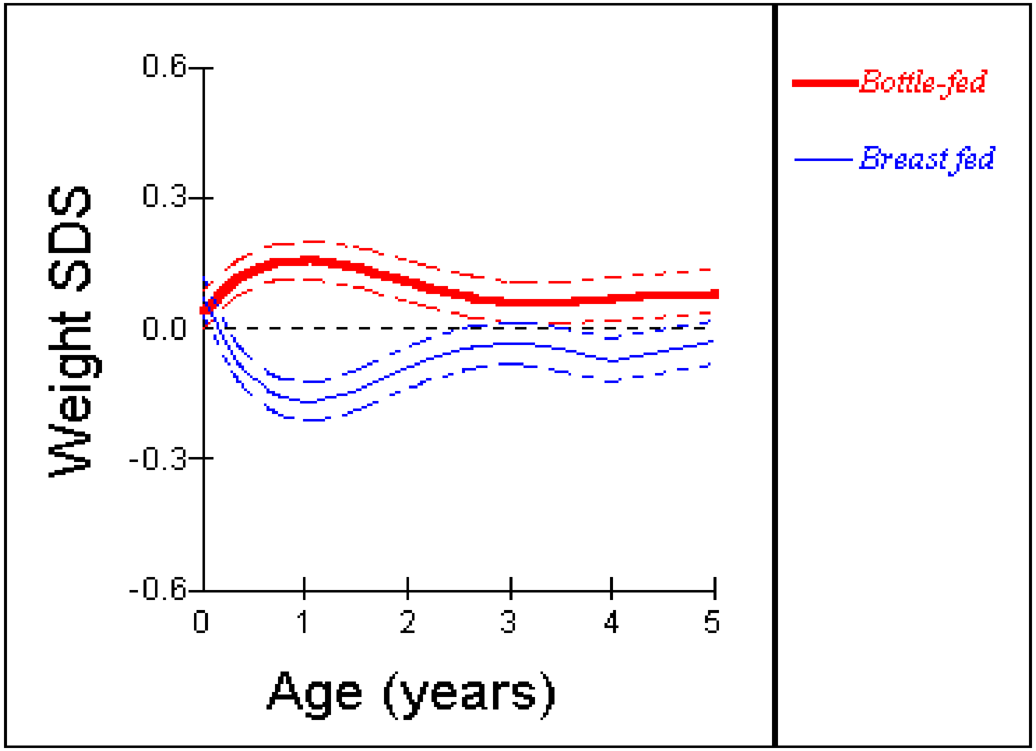


Ong et al. *JCEM 2009*

Outline

- Evidence for early rapid growth as a risk factor for obesity
- Metabolic pathways that may mediate these effects
- Potentially modifiable factors in early life
- Relevance of genetic factors

Formula-fed infants grow faster than breast-fed



Ong et al, *Pediatric Research* 2002

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

A Correction Has Been Published

Myths, Presumptions, and Facts about Obesity

Krista Casazza, Ph.D., R.D., Kevin R. Fontaine, Ph.D., Arne Astrup, M.D., Ph.D., Leann L. Birch, Ph.D., Andrew W. Brown, Ph.D., Michelle M. Bohan Brown, Ph.D., Nefertiti Durant, M.D., M.P.H., Gareth Dutton, Ph.D., E. Michael Foster, Ph.D., Steven B. Heymsfield, M.D., Kerry McIver, M.S., Tapan Mehta, M.S., Nir Menachemi, Ph.D., P.K. Newby, Sc.D., M.P.H., Russell Pate, Ph.D., Barbara J. Rolls, Ph.D., Bisakha Sen, Ph.D., Daniel L. Smith, Jr., Ph.D., Diana M. Thomas, Ph.D., and David B. Allison, Ph.D.

N Engl J Med 2013; 368:446-454 | January 31, 2013 | DOI: 10.1056/NEJMsa1208051

The PROBIT breastfeeding intervention promoted faster infant growth

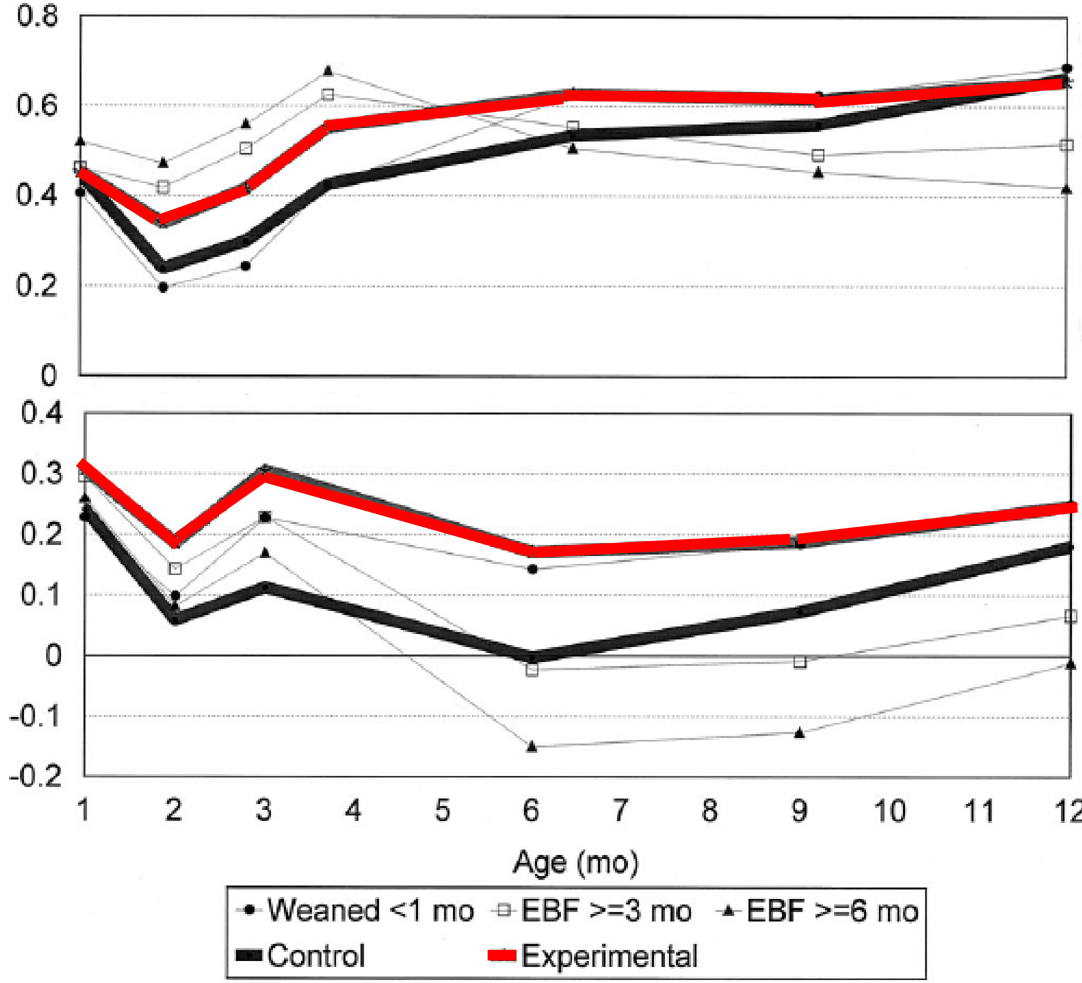


TABLE 2. Effect of Intervention on Weight (g)

Age	Control (*n*)	Experimental (*n*)	Difference	*P* Value
1 mo	4280 (8062)	4341 (8630)	61	.001
2 mo	5170 (7961)	5258 (8459)	88	<.001
3 mo	6047 (8009)	6153 (8620)	106	<.001
6 mo	8042 (7896)	8131 (8509)	89	<.001
9 mo	9451 (7750)	9509 (8339)	58	.002
12 mo	10571 (7918)	10564 (8553)	−7	.726

TABLE 3. Effect of Intervention on Length (cm)

Age	Control (*n*)	Experimental (*n*)	Difference	*P* Value
1 mo	54.63 (8062)	54.79 (8618)	0.16	.258
2 mo	57.57 (7959)	57.89 (8412)	0.32	.030
3 mo	60.63 (8007)	61.13 (8619)	0.50	.001
6 mo	66.90 (7893)	67.36 (8504)	0.46	.002
9 mo	71.62 (7749)	71.93 (8333)	0.31	.039
12 mo	75.75 (7918)	75.93 (8551)	0.18	.226

PROBIT Trial Analysis
Kramer et al, *Pediatrics* 2002

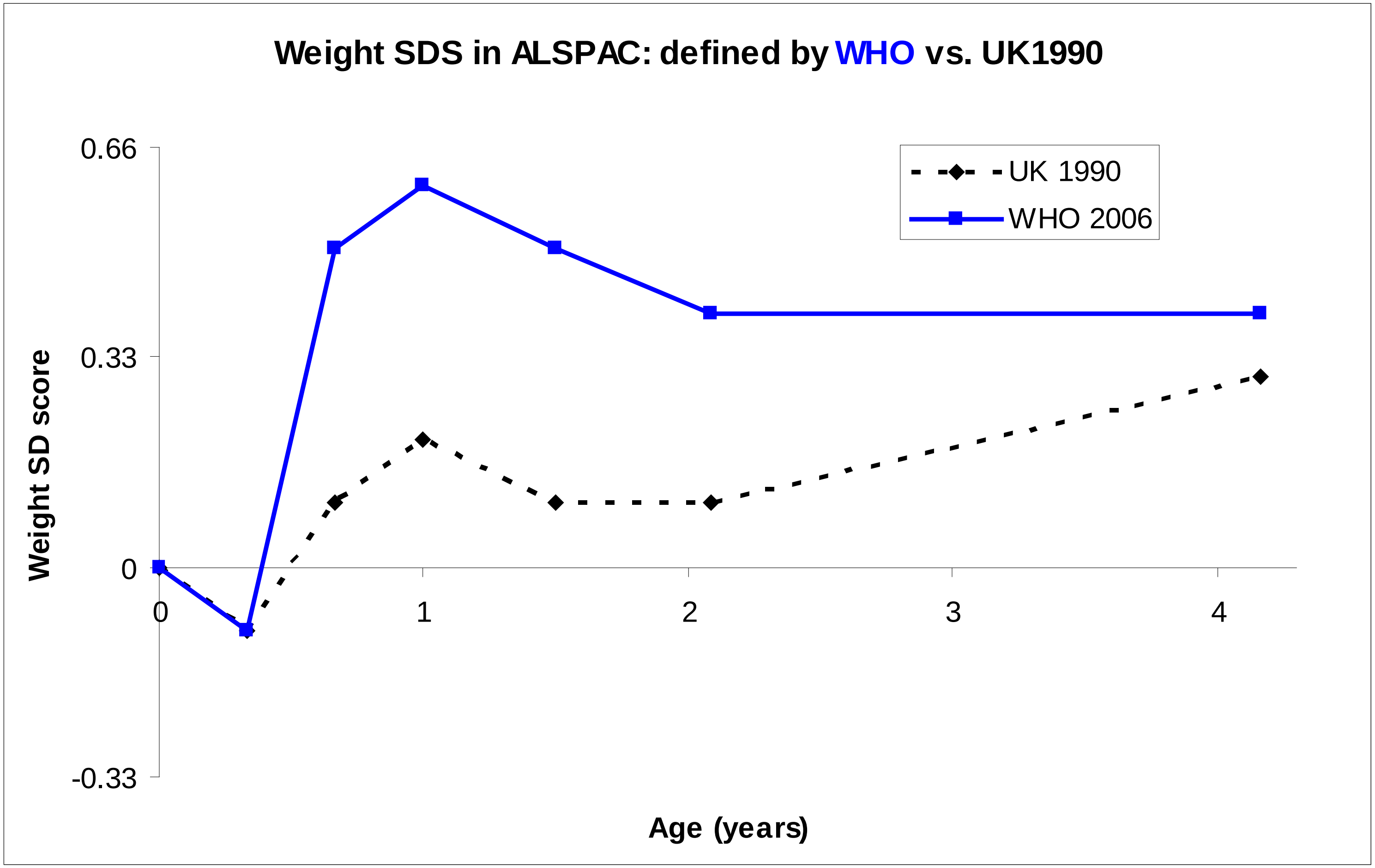
“Breastfeeding and Infant Growth: Biology or Bias?”

“*Conclusions.* Our data, the first in humans based on a randomized experiment, suggest that prolonged and exclusive breastfeeding may actually accelerate weight and length gain in the first few months

Our observational analysis showing …. slower gains with prolonged and exclusive breastfeeding **may reflect unmeasured confounding differences** or a true biological effect of formula feeding.”

Kramer et al, *Pediatrics* 2002

The WHO 2006 Standard: defines optimal growth



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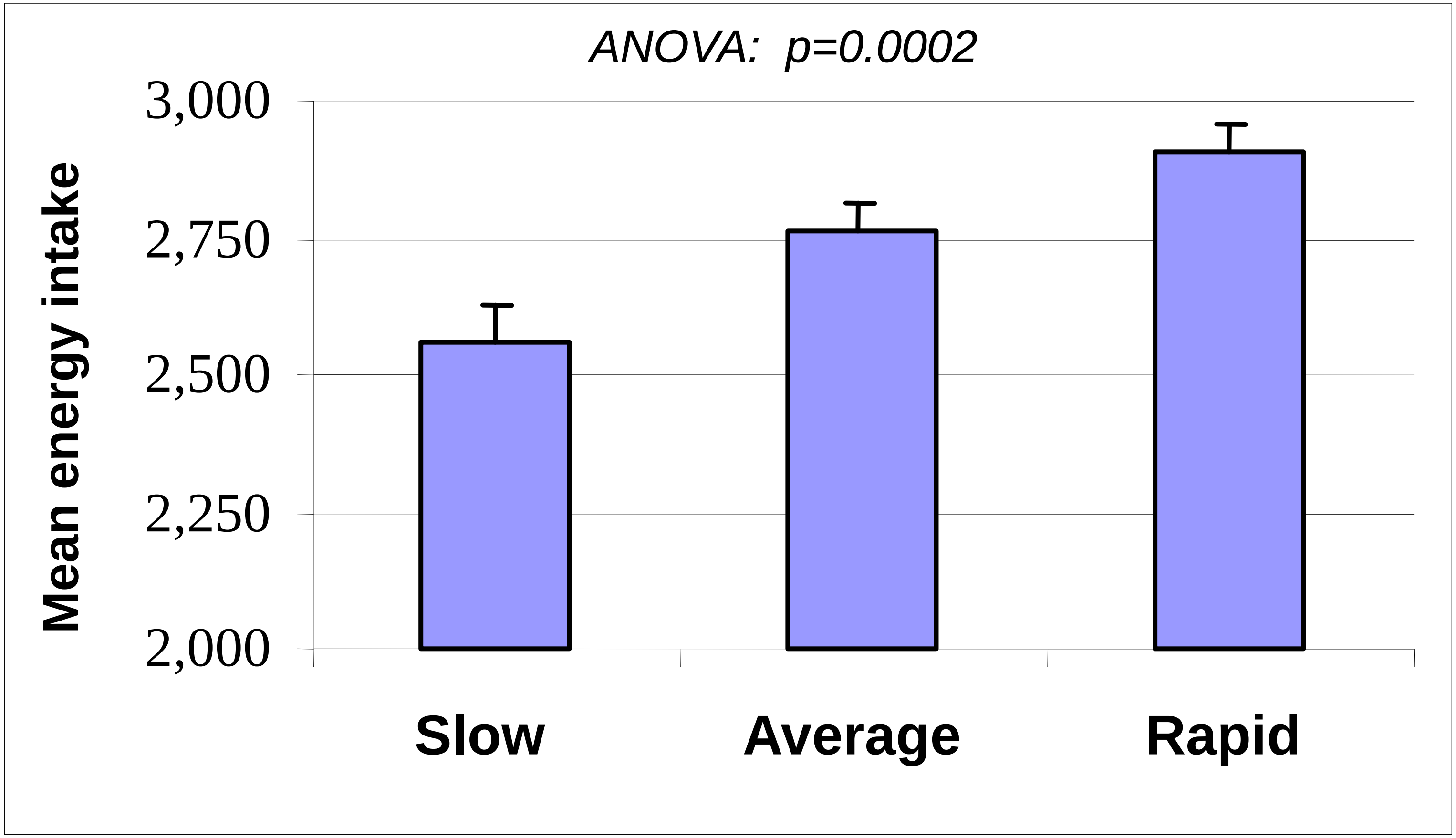
Application of WHO Growth Standards in the UK. *SACN* 2007

Energy intake and weight gain in formula-milk fed infants



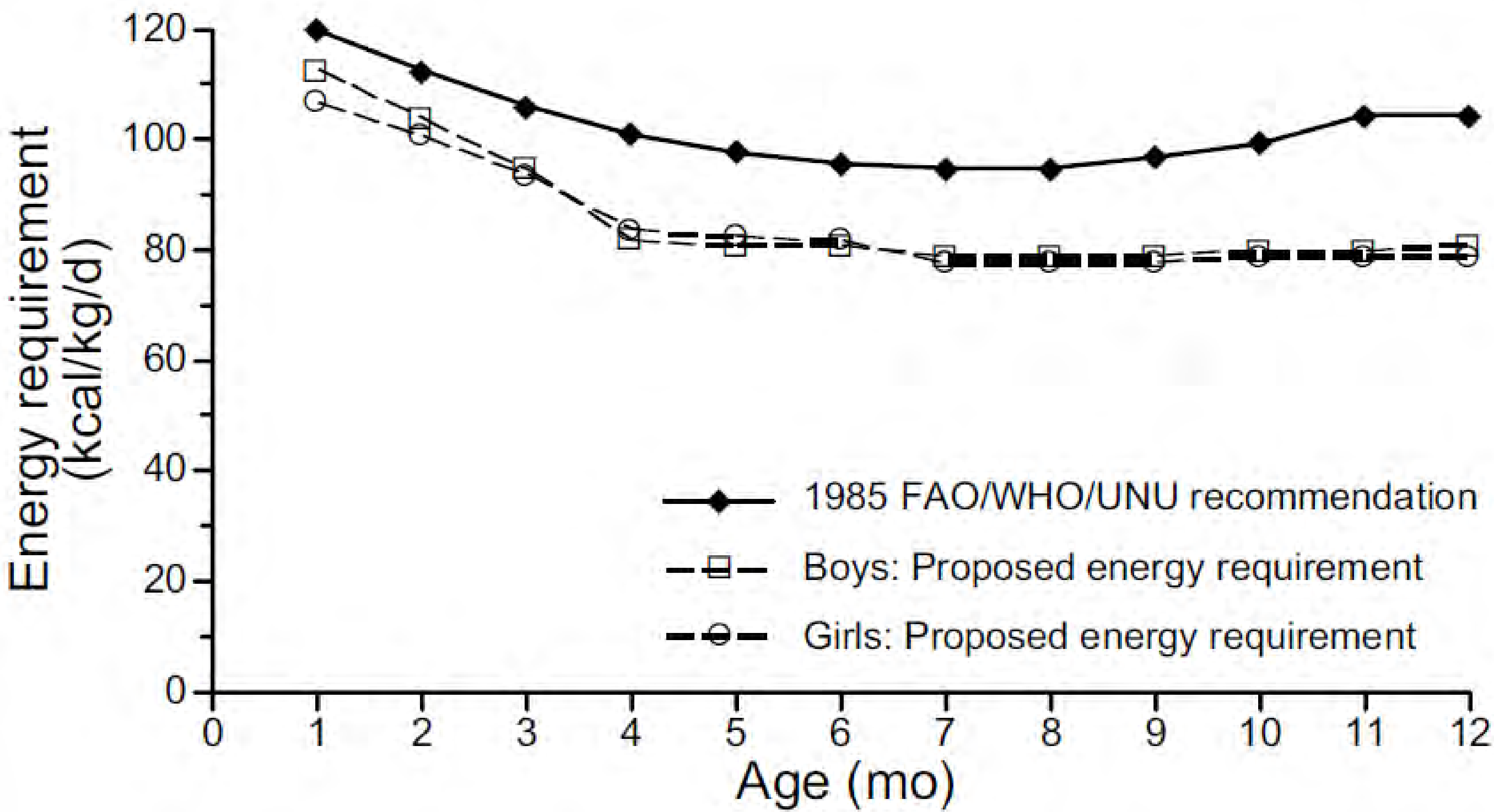
mean energy intake at 4 months old
in formula-fed infants

Ong et al, *Pediatrics* 2006

Human energy requirements

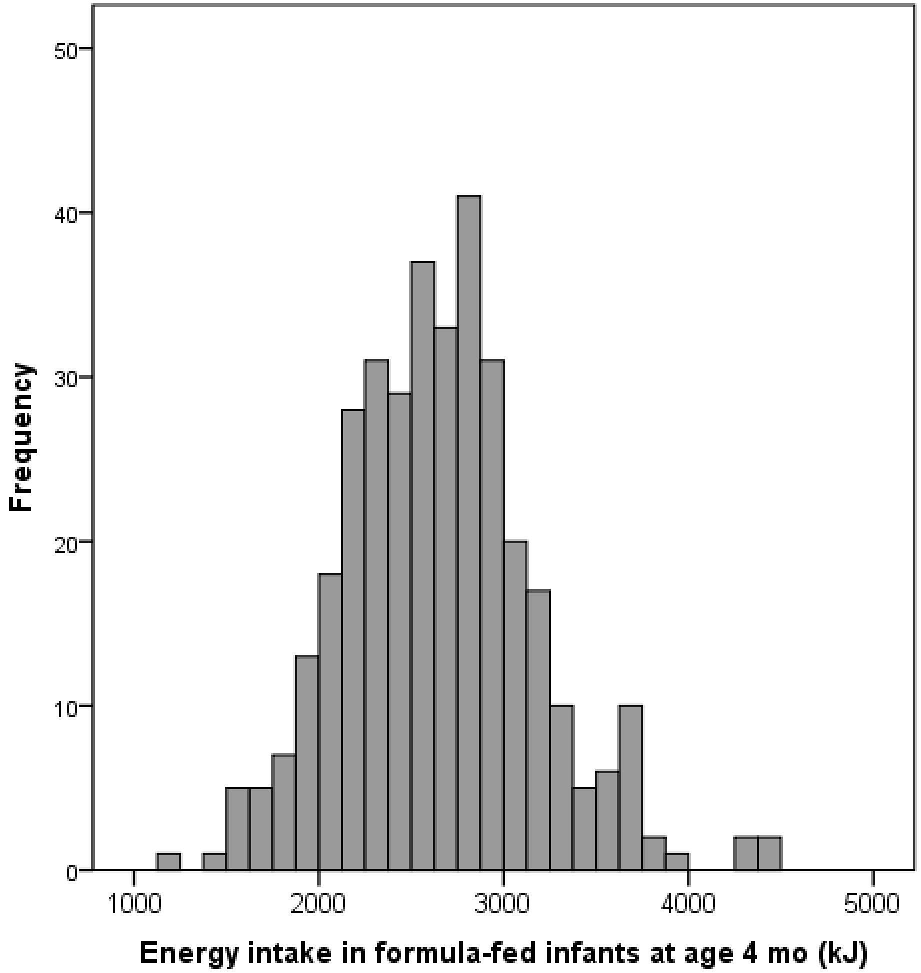
Report of a Joint FAO/WHO/UNU Expert Consultation

Rome, 17–24 October 2001



FAO/WHO/UNU Report 2005

Wide variation in energy intake in formula-fed infants



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Ong et al, *Pediatrics* 2006

The Baby Milk Trial

Baby Milk Study

PROGRAMME for Healthy Growth and Nutrition

UK CLINICAL RESEARCH COLLABORATION igniting our potential

MRC Medical Research Council

UNIVERSITY OF CAMBRIDGE Institute of Public Health

UEA University of East Anglia

CEDAR Centre for Diet and Activity Research
A UKCRC Public Health Research Centre of Excellence

Child: care, health and development
Original Article
doi:10.1111/j.1365-2214.2011.01283.x

Developing a programme for healthy growth and nutrition during infancy: understanding user perspectives

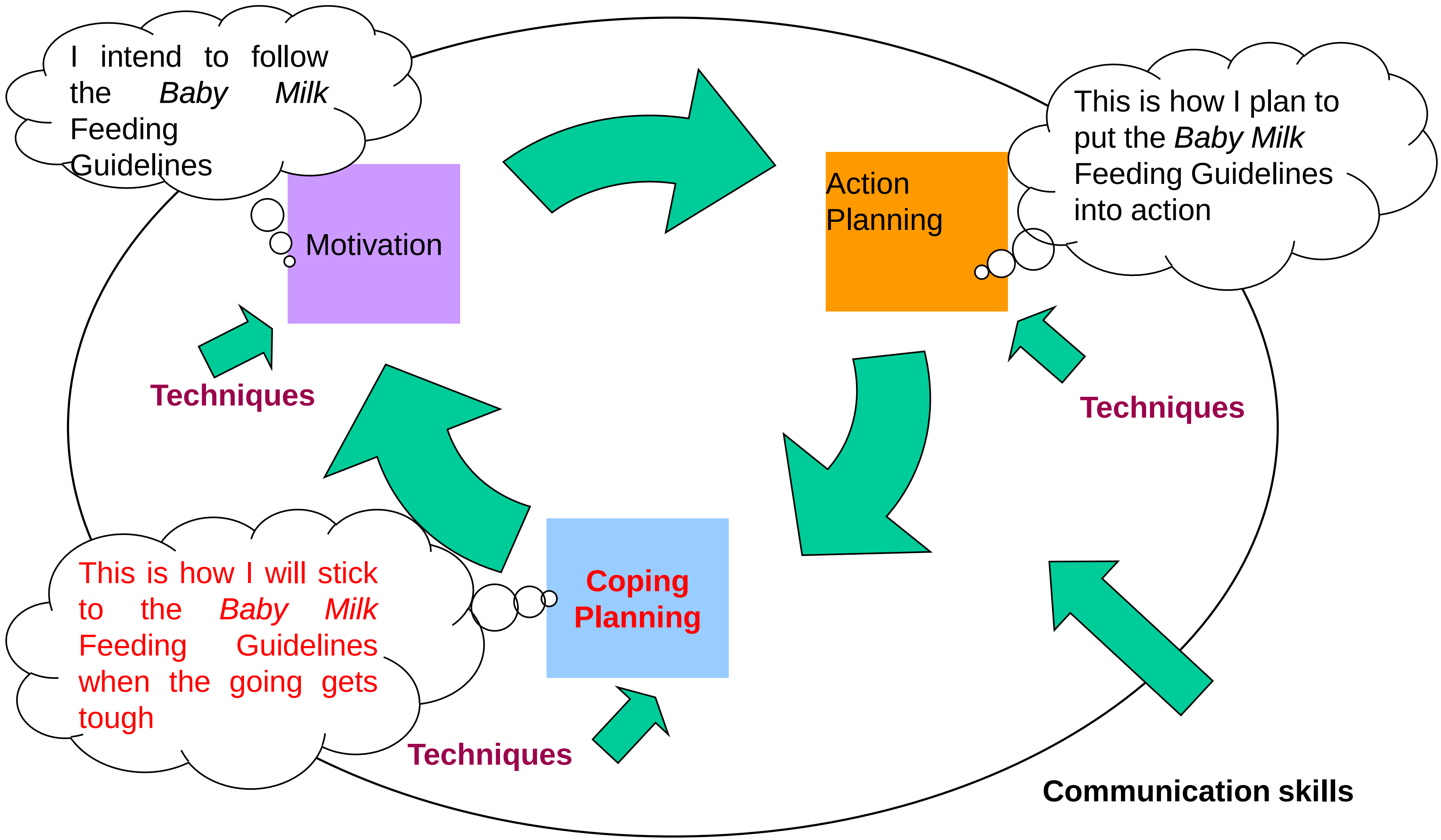
R. Lakshman,*† J. R. Landsbaugh,*† A. Schiff,*† S. Cohn,‡ S. Griffin*† and K. K. Ong*†§

- Systematic reviews
- Interviews & Focus groups with mothers and healthcare providers

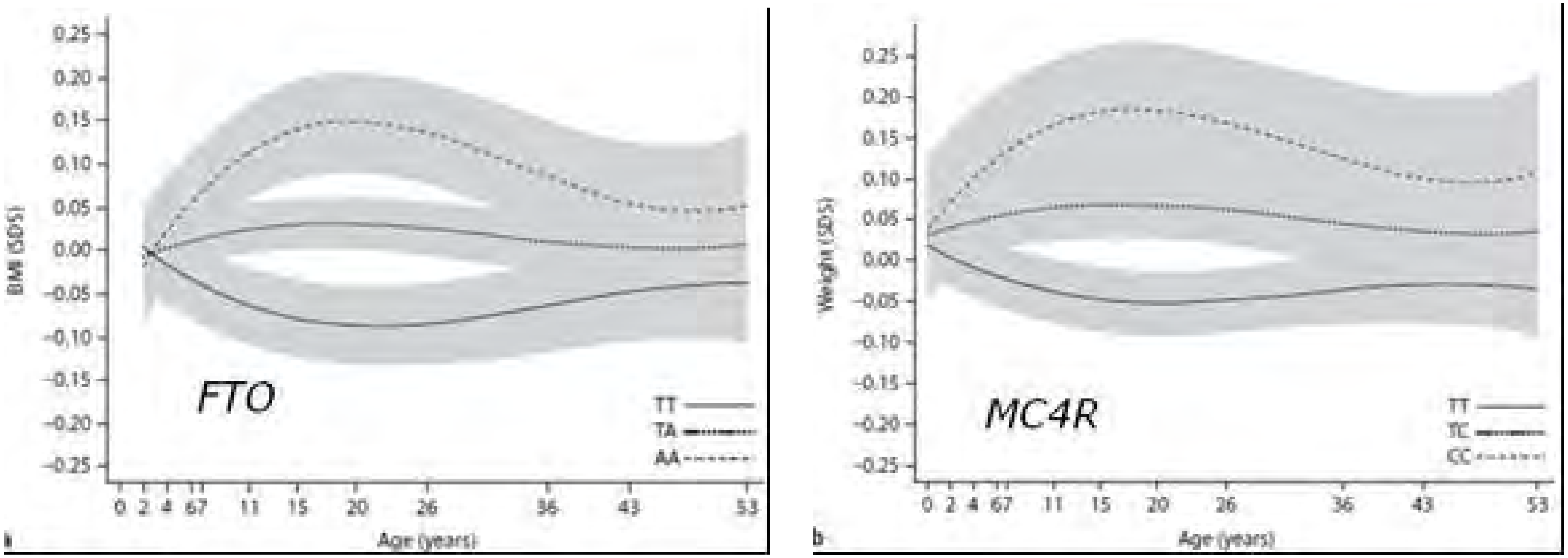
- *'I had no advice on bottle feeding and he was crying so much that I was feeding him every ten minutes…..'*

- *'He drank for six and a half hours and he was swallowing for six and a half hours. He would drink about two and a half bottles. …..sometimes he'd have nine bottles a day.'*

A theory-based intervention (Socio-cognitive theory)



Longitudinal associations with FTO and MC4R



1946 British Birth Cohort Study

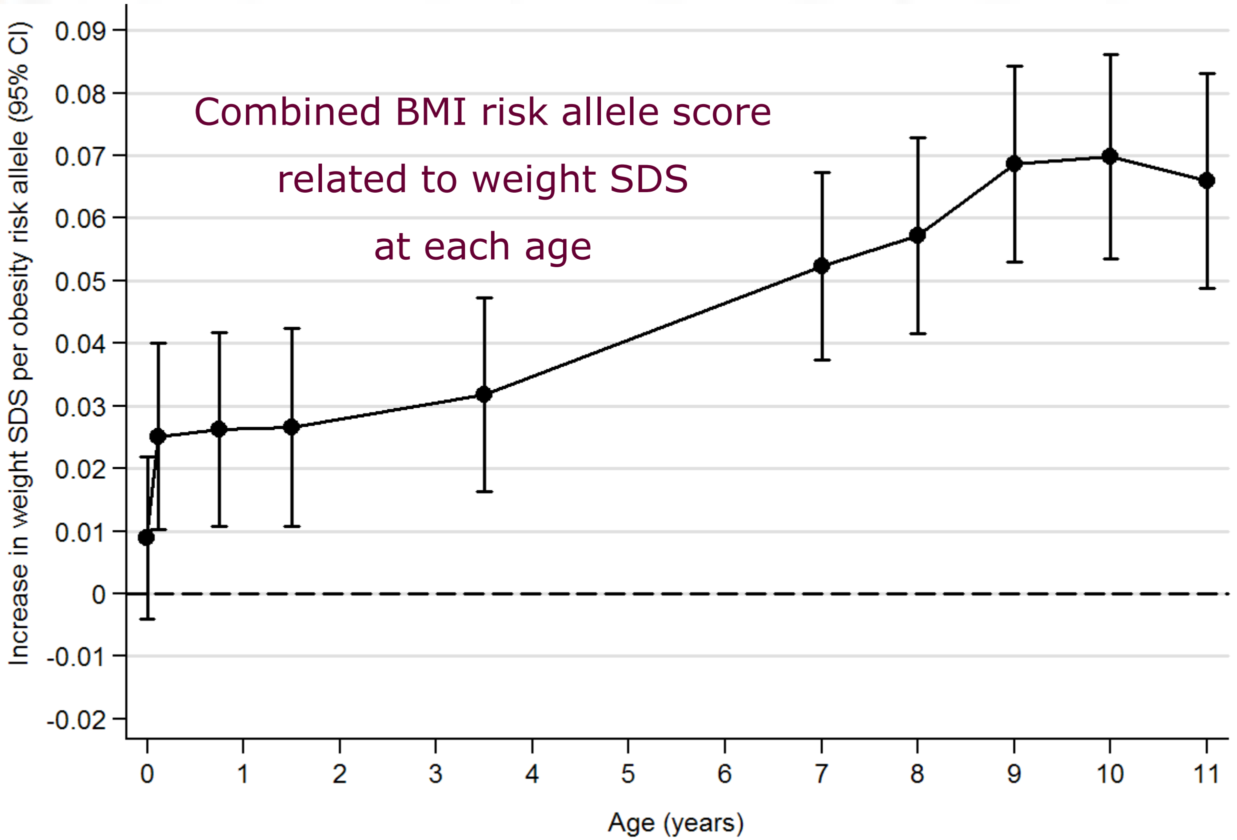
Hardy et al. *Human Molecular Genetics* 2010

OPEN ACCESS Freely available online

PLoS MEDICINE

Genetic Markers of Adult Obesity Risk Are Associated with Greater Early Infancy Weight Gain and Growth

Cathy E. Elks[1,2], Ruth J. F. Loos[1,2], Stephen J. Sharp[1,2], Claudia Langenberg[1,2], Susan M. Ring[3], Nicholas J. Timpson[4], Andrew R. Ness[5], George Davey Smith[4], David B. Dunger[6], Nicholas J. Wareham[1,2], Ken K. Ong[1,2,6*]



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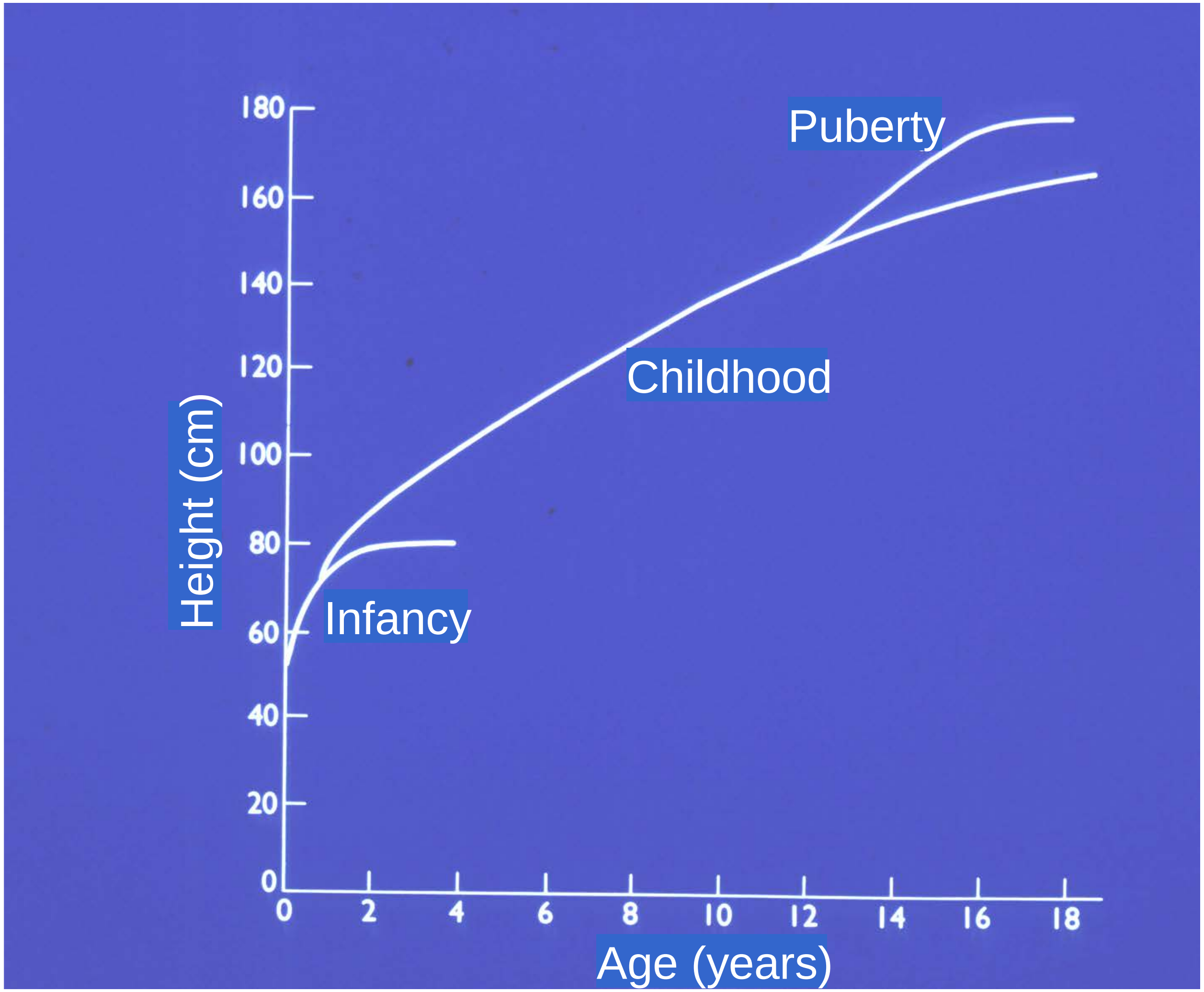
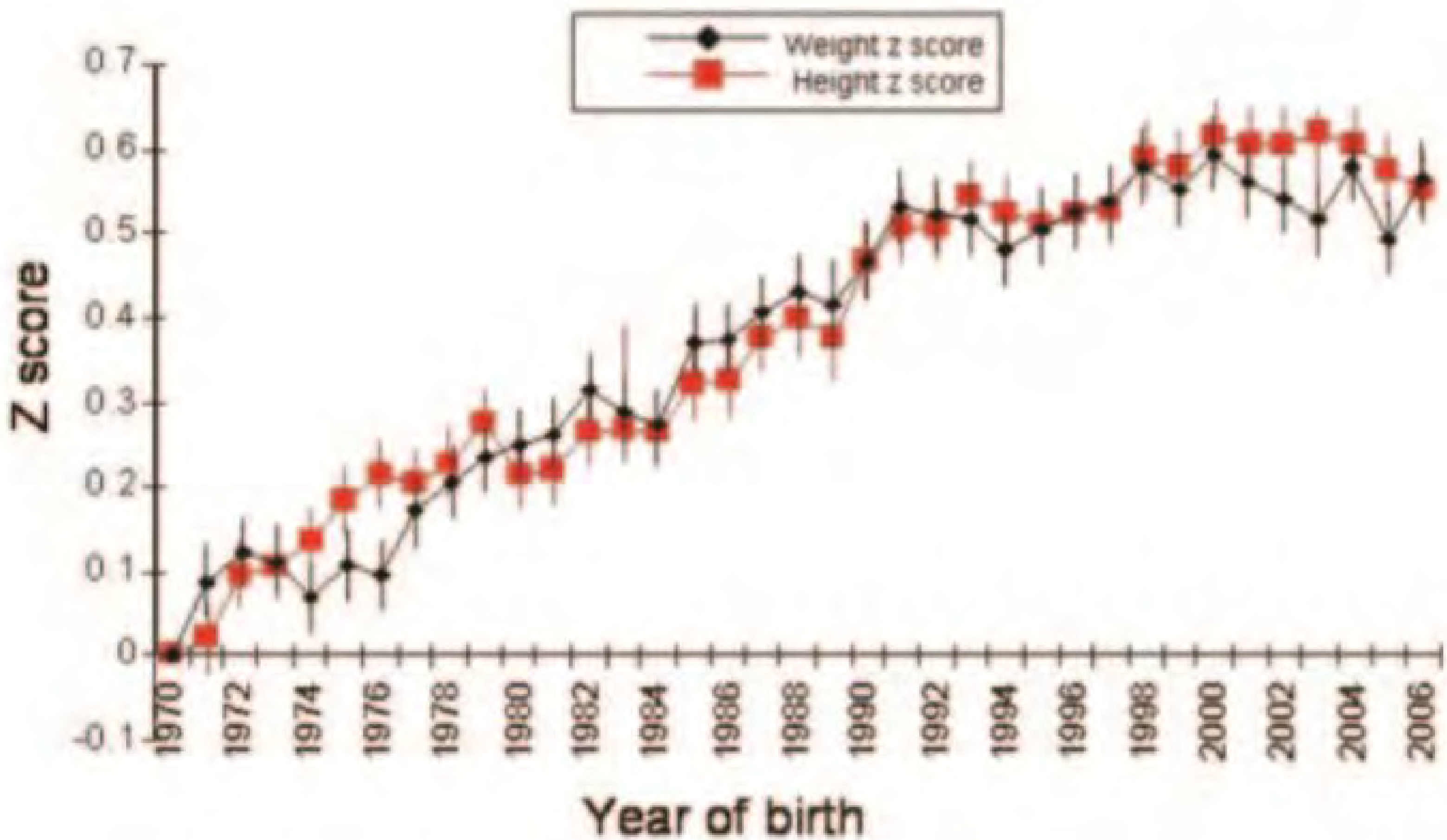
Elks et al, *PLoS Medicine* 2010

Karlberg Model of human growth



Secular trends in both height and weight in 5-6y
1970 to 2006, North East Scotland



Sarah Smith et al, *Arch Dis Child* 2013

‘Co-heritability’ of infant appetite & weight gain

<u>Gemini cohort study (n=4,804 twins)</u>

- Significant shared genetic influences on:
    - Infant weight
    - Appetite
    - Satiety responsiveness
    - Slowness in eating

“Approximately one-third of the genetic effects on appetite also influenced weight”

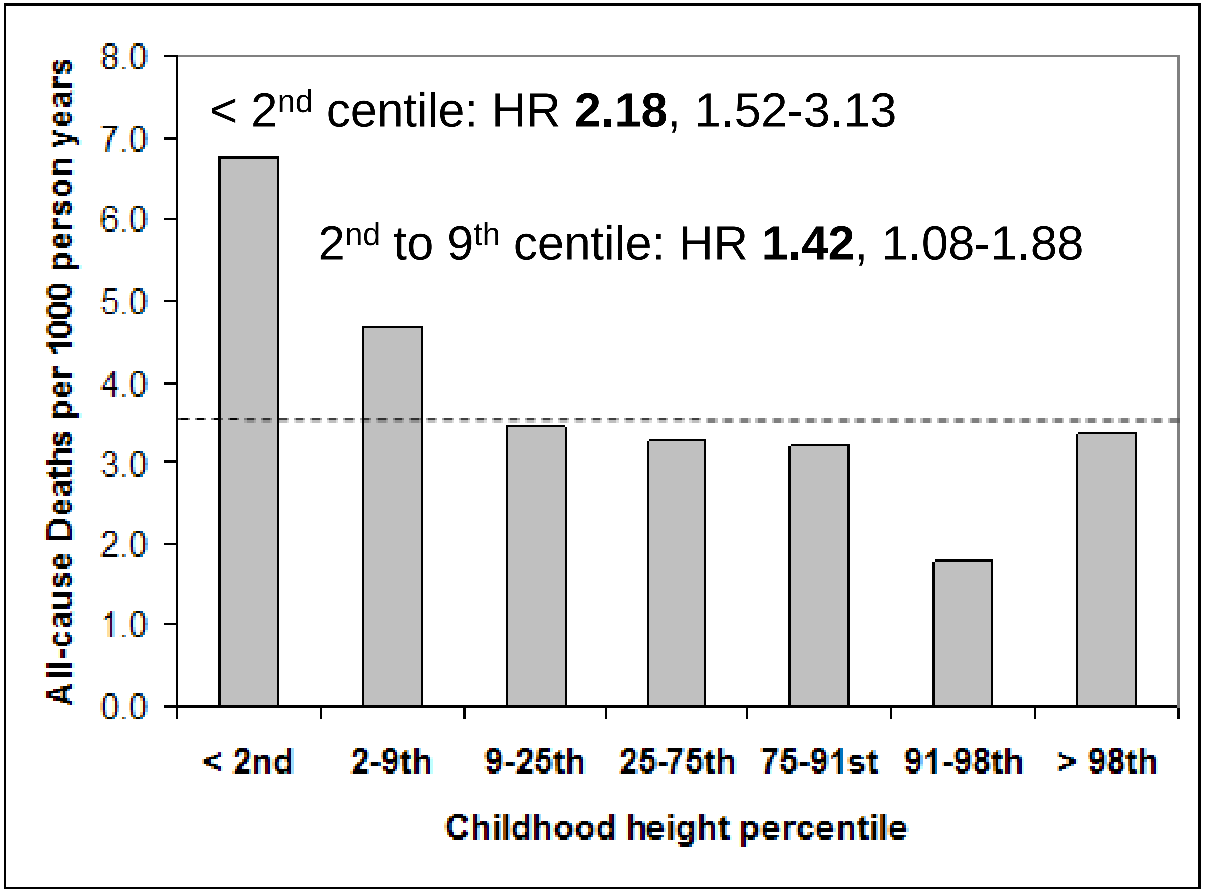
Llewellyn et al, *Am J Clin Nutr* 2012

Baby Milk Trial: Potential adverse effects

- Irritable hungry infants (and discontented parents)
- Underweight / growth faltering

- Increased susceptibility to infection / illness
- Possible long-term adverse sequelae?
    - Cognition
    - Height (stunting)
    - *Long-term mortality…*

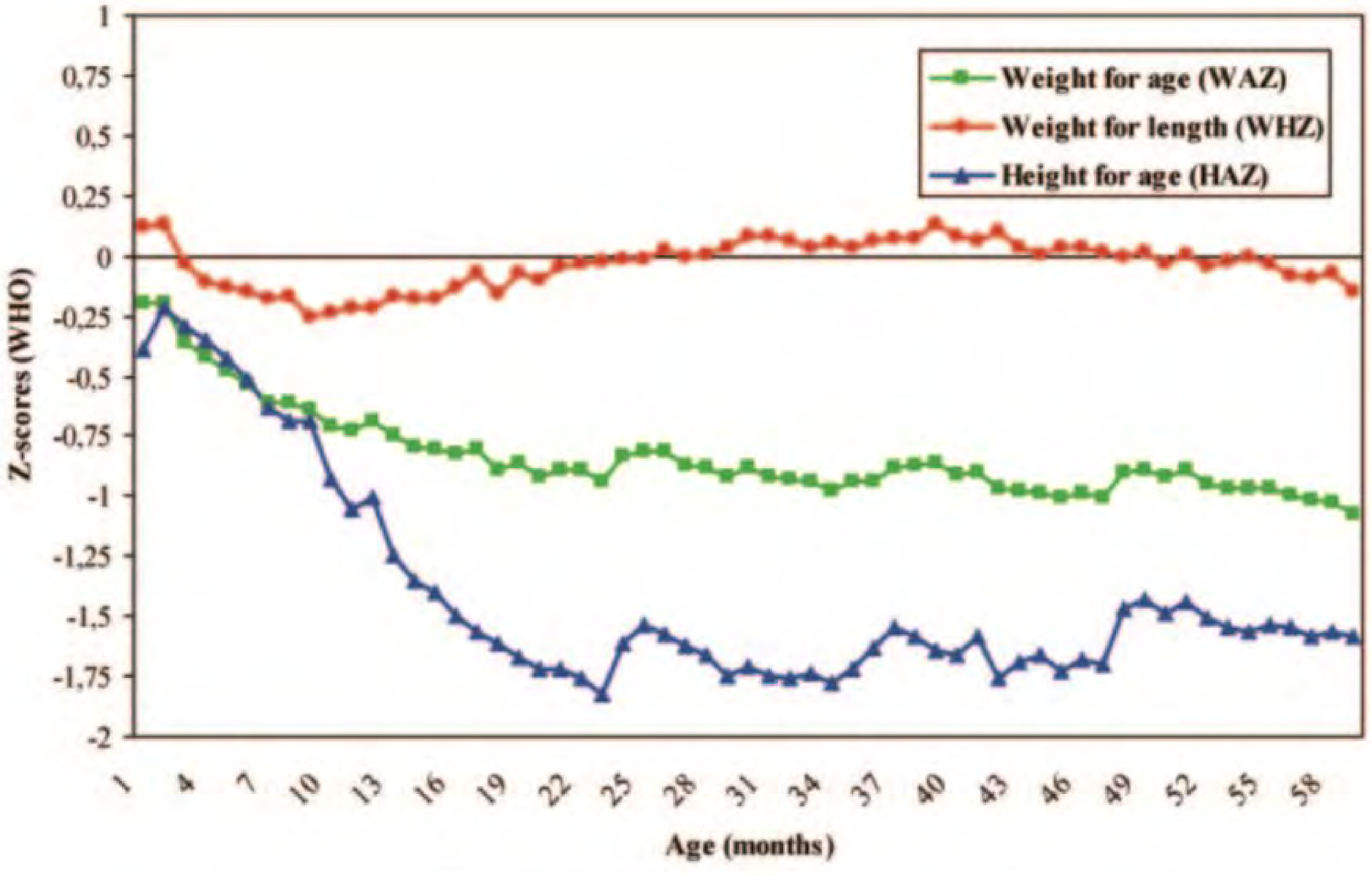
Mortality between 36-64 years by height at age 6 years against the current WHO 2007 growth reference



British 1946
Birth Cohort Study

Ong et al. *J Clin Endocrinol Metab* 2013

Early Growth Faltering in Low & Middle income settings



Victora et al. *Pediatrics* 2010

Summary – Infant weight gain & obesity

1. No exclusive window (greatest variation in the first 1-2 years)
2. Continuum with higher weight gain (esp. high if > +1.33 SDS)
3. Mechanisms include insulin resistance and early puberty
4. Modifiable factors: Infant nutrition (<u>including</u> breast-feeding)

Formula milk composition and infant weight gain

- Lower protein (1.77 vs. 2.9 g/100 kcal) → Lower Wt gain and BMI (Koletzko AJCN 2009)
- Low protein formula (Nestle) → Lower Wt gain (unpublished)
- Low calorie formula (Singhal) → Lower Wt gain (pilot, unpublished)

Summary – Infant weight gain & obesity

1. No exclusive window (greatest variation in the first 1-2 years)
2. Continuum with higher weight gain (esp. high if > +1.33 SDS)
3. Mechanisms include insulin resistance and early puberty
4. Modifiable factors: Infant nutrition (<u>including</u> breast-feeding)
5. Genetic susceptibility to rapid weight gain and obesity: needs to be acknowledged
6. Context (setting) is crucial

Thank You – the Baby Milk Study team

CEDAR support

Rebecca Strafford	Research Manager, CEDAR
Annie Schiff	Study Co-ordinator, CEDAR
Alvaro Ullrich	Data Manager, CEDAR
Intervention Facilitators	Paediatric Research Nurses, University of Cambridge

MRC Epidemiology Unit support

James Sylvester	Research Manager, MRC
Measurement Team	Research Assistants, MRC

Investigators

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Simon Griffin	**Assistant Director, MRC**
Wendy Hardeman	Senior Research Associate, IPH
Simon Cohn	Senior Lecturer, IPH
Marc Suhrcke	Prof Health Economics, UEA
Ed Wilson	Lecturer Health Economics, UEA

Collaborators

David Vickers	Medical Director, CCS NHS Trust
Alison Lennox	Principal Investigator Scientist, MRC HNR

Funders & Institutions

Medical Research Council

UK Clinical Research Collaboration

Centre for Diet and Activity Research
A UKCRC Public Health Research Centre of Excellence

National Research Prevention Initiative

University of Cambridge Institute of Public Health

Baby Milk Study

Programme for Healthy Growth and Nutrition

University of East Anglia




Maternal Beliefs and Behaviors about Infant Feeding

Margaret E. Bentley, PhD

Carla Smith Chamblee Distinguished Professor of Global Nutrition

Associate Dean for Global Health

Gillings School of Global Public Health

University of North Carolina, Chapel Hill

Amanda Thompson, PhD

Assistant Professor, Anthropology Department

Heather Wasser, PhD, RD, IBCLC

Project Director, Center for Women's Health Research

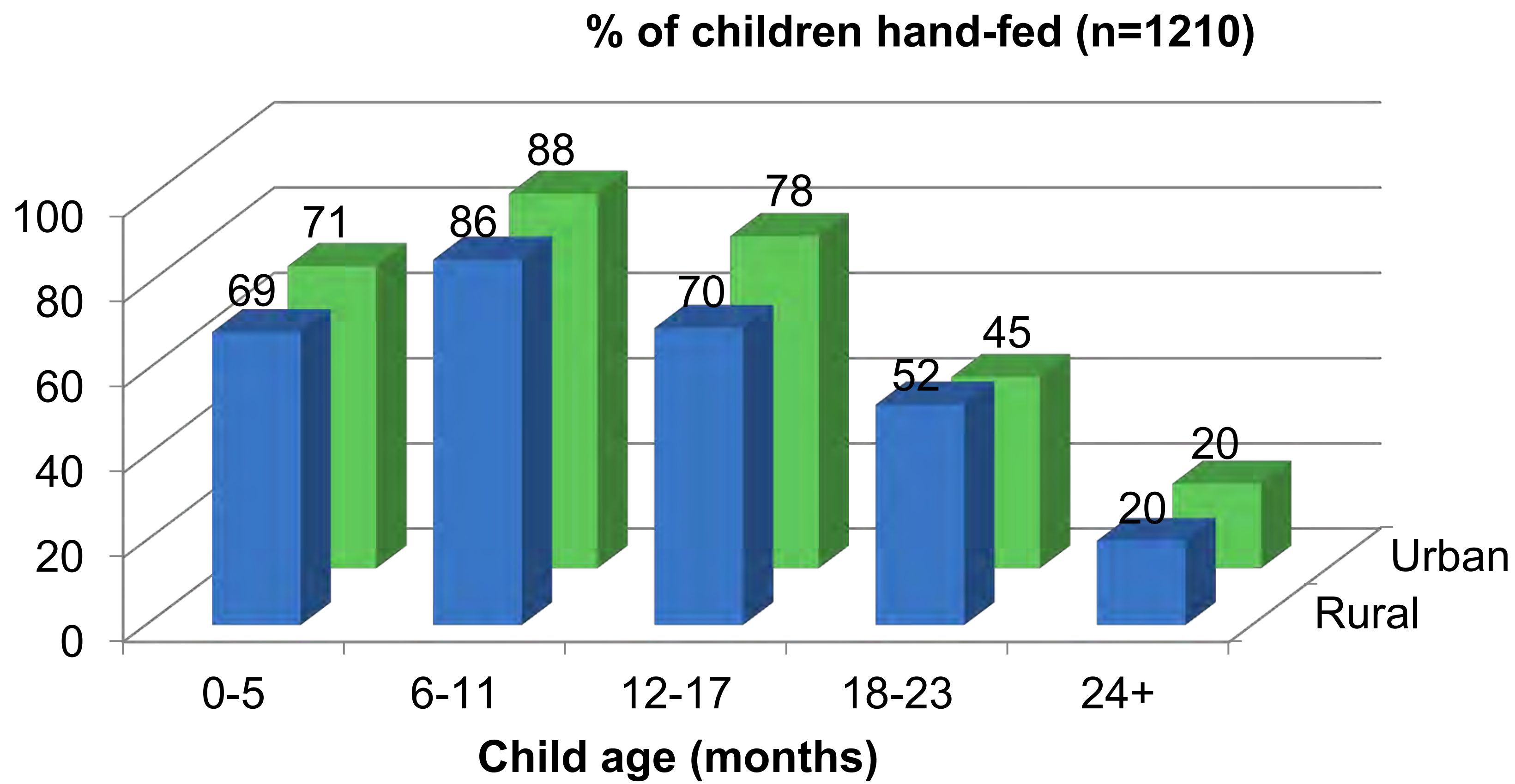
UNC GILLINGS SCHOOL OF GLOBAL PUBLIC HEALTH

Overview

- Why are maternal beliefs important?
- How do we measure them?
- What are the research gaps?
- What are the implications for intervention?

Why are maternal beliefs important?
Hand-feeding among the Yoruba

Hand-feeding normative across urban and rural settings



Hand and force feeding take less time

- Structured observation datasheet developed to code during repeated 12-hr observations:
  - Method of feeding (hand, force, or spoon)
  - Length of feeding

MODE OF FEEDING	*n*	MINUTES *Mean (SD)*
Hand	267	2.60 (2.05)
Force	284	2.72 (1.34)
Spoon	93	6.05 (3.26)

Beliefs may underlie feeding behaviors, *but*… a linear view is much too simplistic

Political (Local, state and national laws and policies)

Community (Relationships among organizations, institutions and networks)

Organizational (Policies and practices of employers, health care facilities)

Interpersonal (Beliefs and behaviors of family, friends, coworkers)

Beliefs → Behaviors → Infant dietary intake → Infant growth

Across disciplines, beliefs are key components of theoretical frameworks

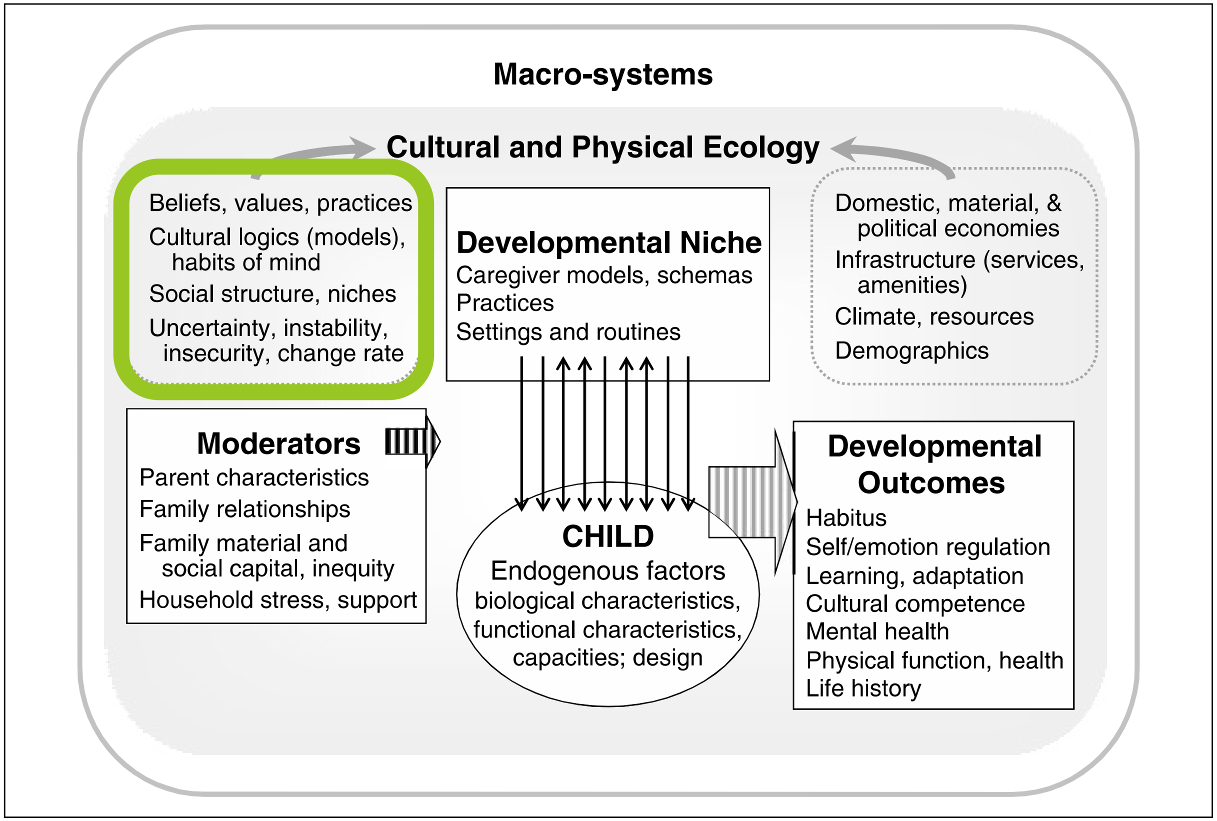
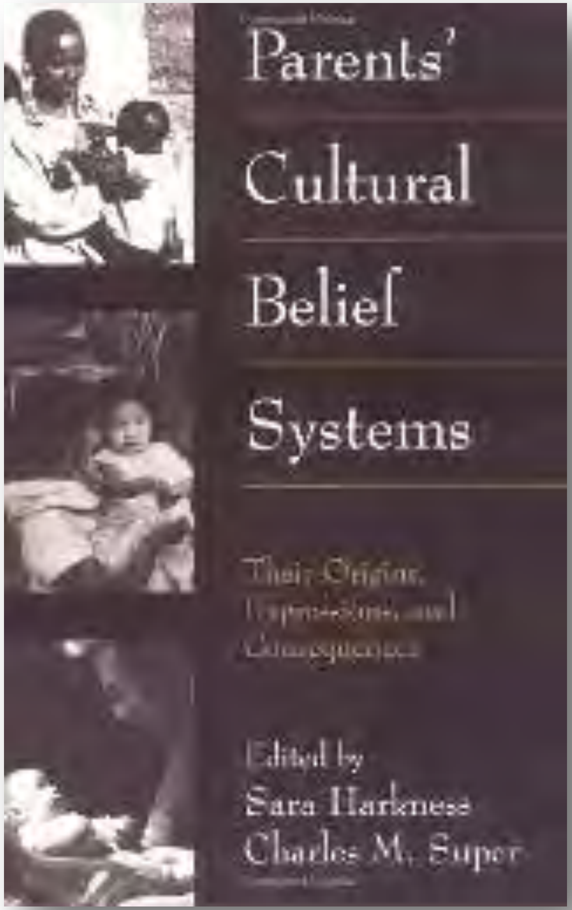


Figure 4. Diagram of a biocultural model that highlights elements and pathways of embodiment in child development
Source: Described in Worthman (2003, 2009).
Note: The large arrow from the child/microniche complex to developmental outcomes indicates the combined ongoing impact of dynamics in that complex on individual outcomes across the life course.

Worthman, 2010, J Cross Cultural Psychology

Seminal publications that have influenced the field



Ethnographic work in Baltimore

Breastfeeding Promotion among WIC Moms

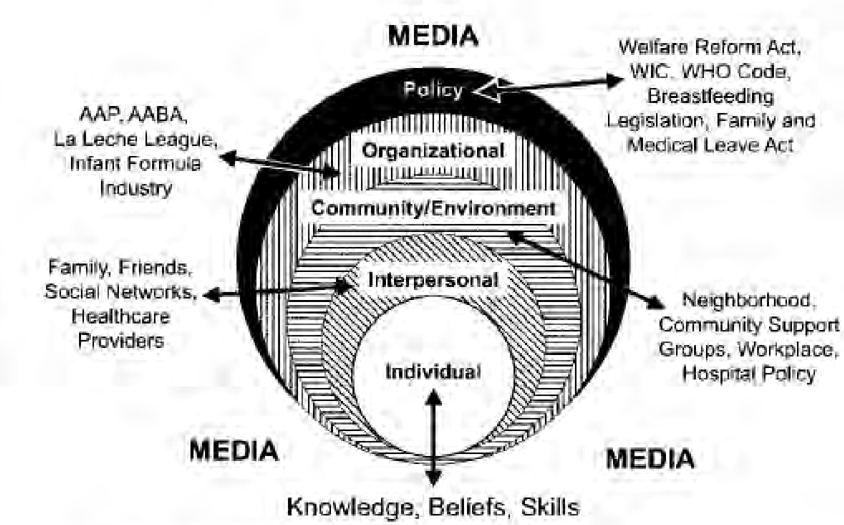
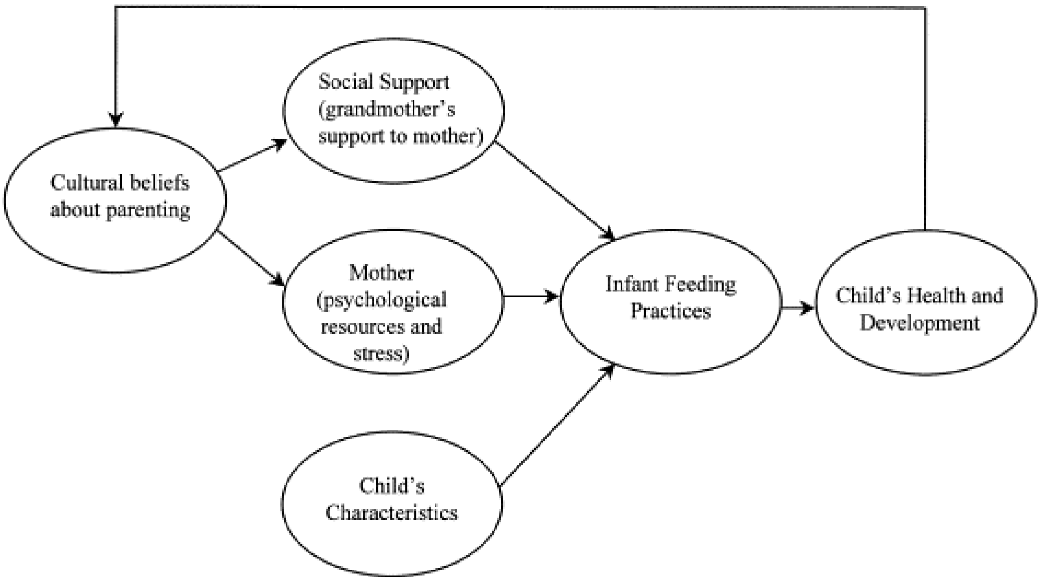


FIGURE 2 Social Ecological Framework.

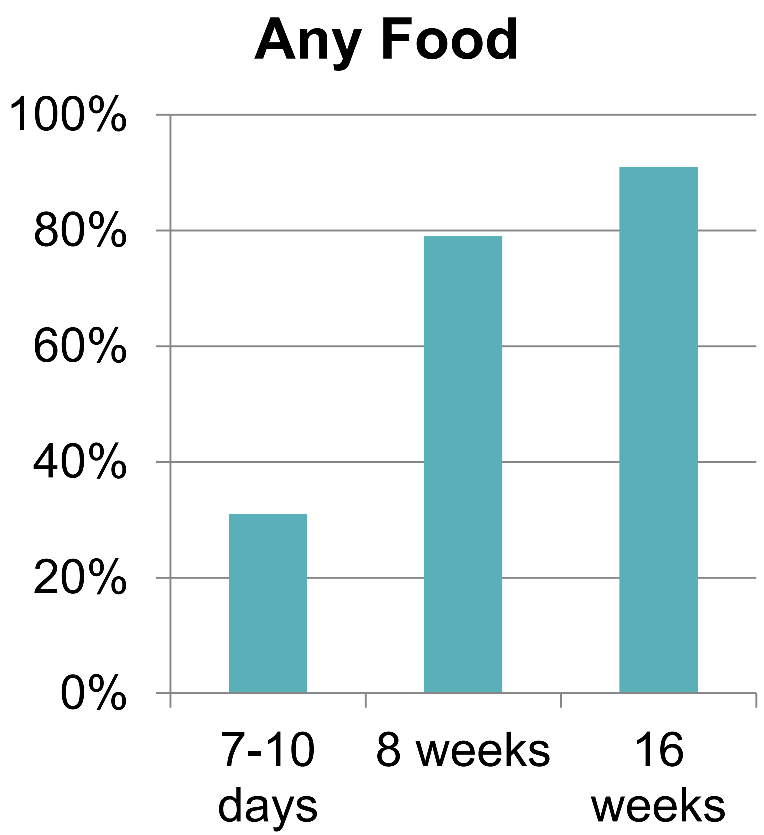
Bentley et al., 2003, *J Nutr*

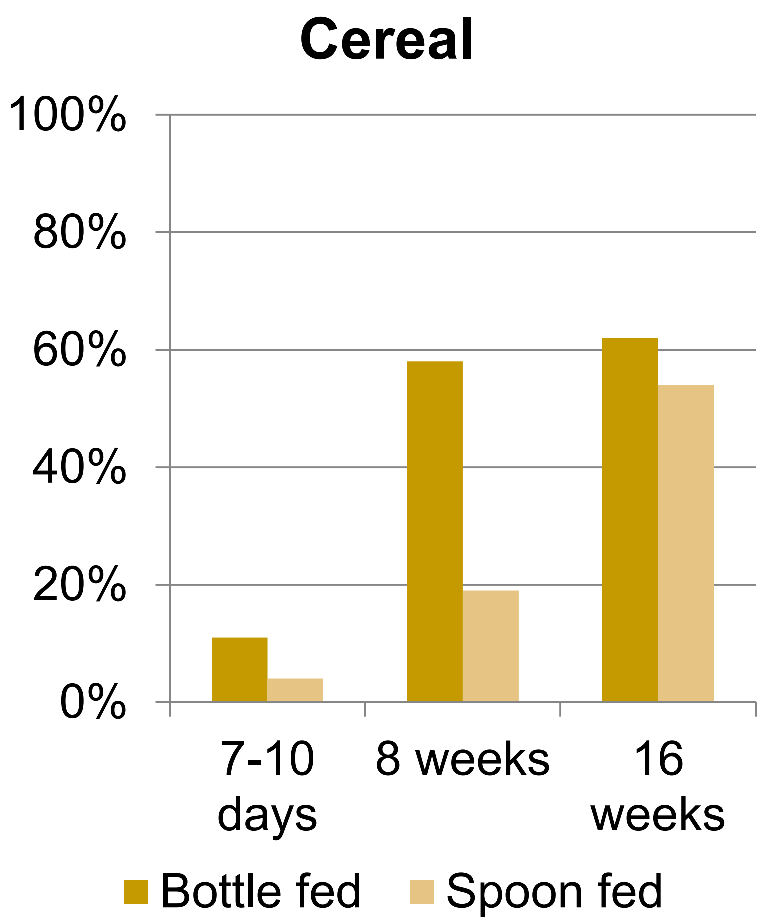
Three Generation Study



Bentley et al., 1999, *J Hum Lact*

Very early introduction of 'any' complementary food and cereal in the bottle





Bronner et al., 1999, *J Am Diet Assoc.*

Giving cereal will help "fill up" a hungry child and help him/her sleep through the night

"Some babies, they tend to eat what they're supposed to eat. Then some babies are greedy. So you've got to feed that baby. If you don't that baby gonna holler, holler, holler."

- Mother of two biological children and two foster children

"I told Sarina I was gonna put him on cereal now, but she's scared. Maybe I'll sneak it in there, you know [laughter]. When I make the bottles, I make two bottles with cereal in it…I started at 5 weeks. She says, 'no, he's too fat, he don't need anything in it…and when I gave him cereal one night, she said, 'Ma, he slept all night', and I said, 'Oh, he did?'" [laughter]

- Grandmother

Bentley M et al. (1999). Infant feeding practices of low-income, African-American, adolescent mothers: an ecological, multigenerational perspective. *Soc Sci Med,* 49(8), 1085-100.

Identifying and intervening on early life risk factors for obesity

The Infant Care Project

mothers & others

5 R01 HD042219 (PI: Margaret E. Bentley) 2003-2007

National Institute of Child Health and Development

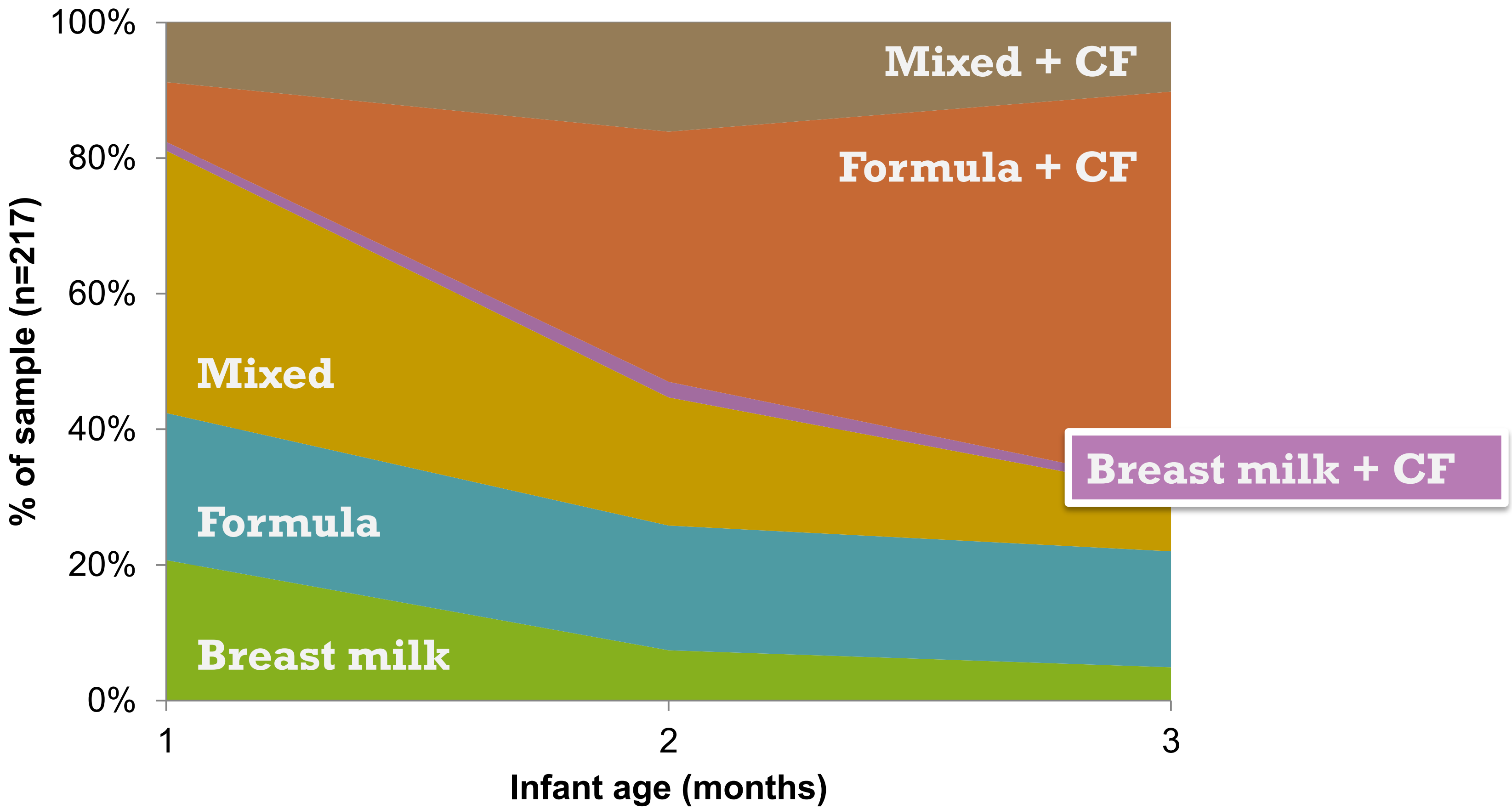
The Infant Care Project

- In-depth interviews with 20 mothers of infants 3-18 months
- Prospective study of 217 first-time, African-American mother-infant pairs
  - Recruited from WIC clinics in central North Carolina
  - Followed from 3 to 18 months postpartum with in-home visits

Why are Maternal Beliefs Important?

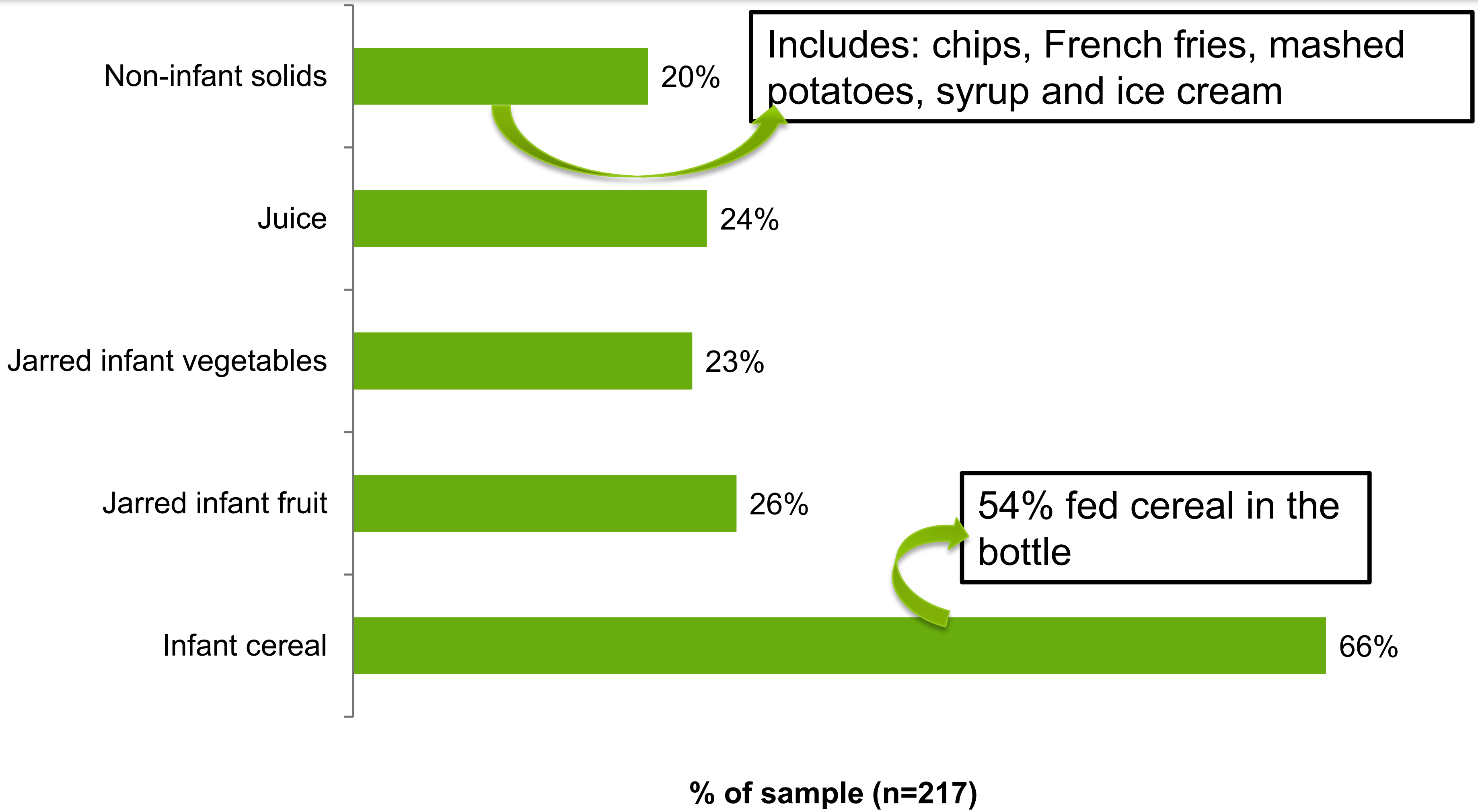
Early Complementary Feeding and Diet Quality

Early infant feeding patterns



Wasser et al. Infants perceived as "fussy" are more likely to receive complementary foods before 4 months *Pediatrics* 2011;127:229–237

Types of complementary foods given at 3 months



Thompson and Bentley, *Soc Sci & Med*, 2013

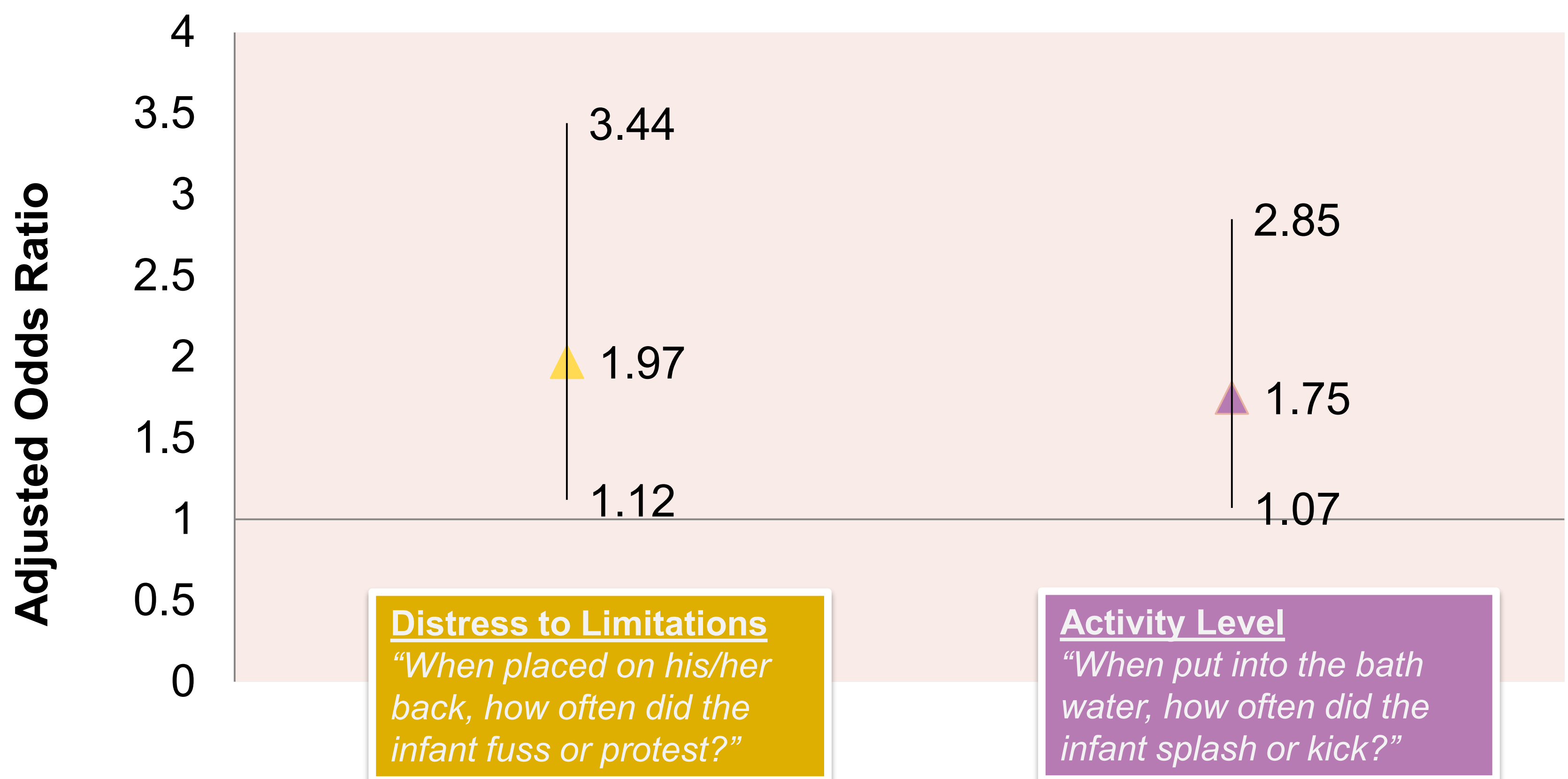
Similar beliefs underlie early cereal

"Well, at first I was giving her regular milk in it. But she drank the bottle about two a [night]…around three she'd want another one. So, my mom told me to start putting a little cereal in and make her full so she won't be asking for some more so much."

- Mother of 7-10 month old

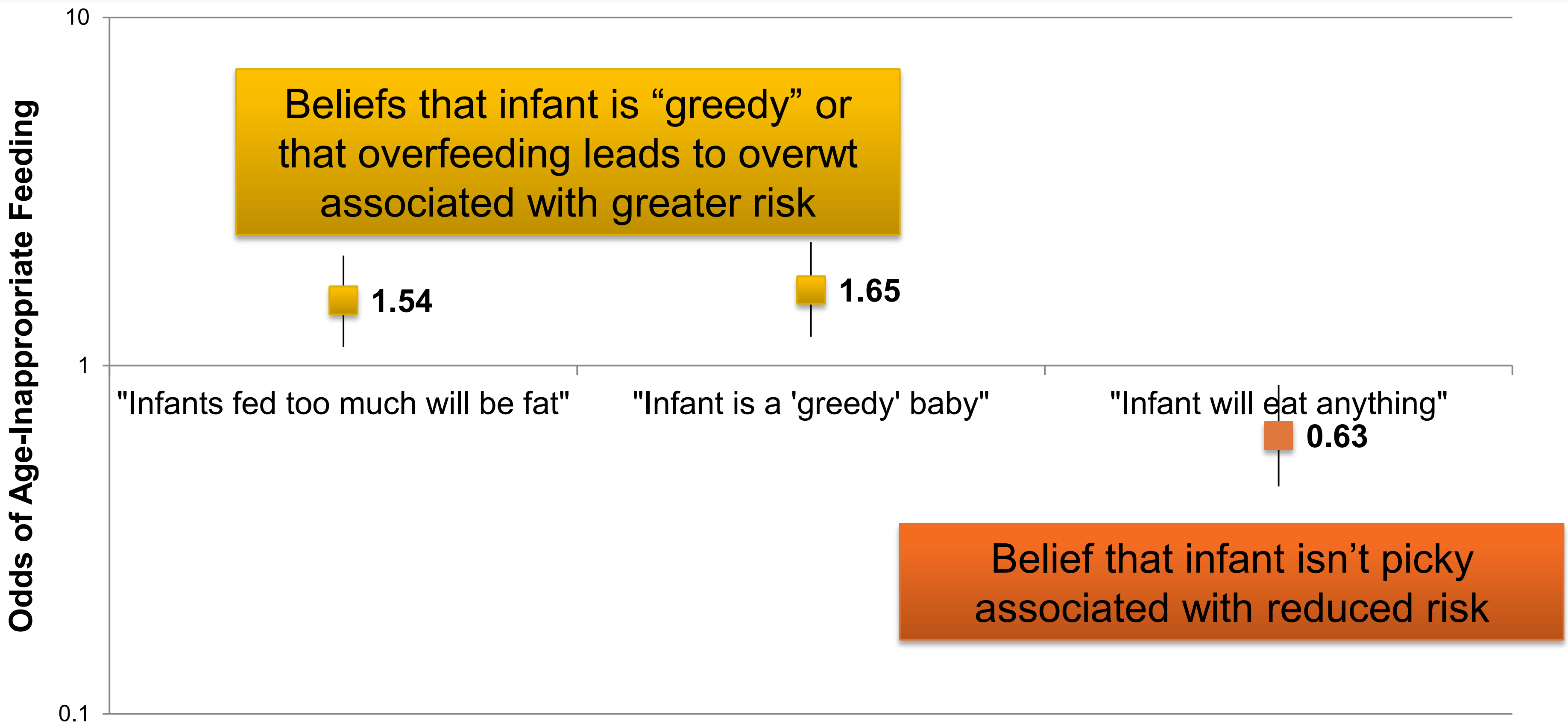
The Infant Care Project

Infants perceived as “fussy” more likely to be given CF before four months



Wasser et al., *Pediatrics* 2011

Maternal beliefs about infant size and diet associated with age-inappropriate feeding



OR from logistic models controlling for maternal age, infant age, infant sex and repeated measures across infants. Beliefs represent maternal agreement or strong agreement with the statement.

Thompson and Bentley, *Soc Sci & Med*, 2013

Why are Maternal Beliefs Important?

Maternal Feeding Styles and Infant Diet

Feeding styles incorporate beliefs and behaviors

- Attitudes and behaviors that characterize parental approaches to maintaining or modifying children's eating behavior
- Reflect the degree to which parents are demanding or responsive or indulgent during feeding
- Numerous ways to measure in older children (CFQ, CFSQ)
- But important predictors of the intake of infants as well

IFSQ: Measurement and validation

- IFSQ includes:
  - items for assessing maternal beliefs
  - items for assessing reported milk and solid feeding behaviors of infants and young children
- Items developed based on formative research and constructs validated by CFA
- 5 feeding styles measured across 13 sub-constructs
  - sub-constructs based on relevant themes
    - *Ex: diet quantity vs. diet quality*
  - good fit consistent across samples for majority of sub-constructs
  - sub-constructs capture different feeding style domains

Thompson et al., 2009, *Appetite*

Definitions of feeding styles

Laissez-faire	parent has no limits regarding food (quality or quantity), and little or no interaction with child during feeding
Pressuring/ controlling	parent feeds child to soothe or because of concern that child is undereating
Restrictive/ controlling	parent limits child to healthy foods and limits quantities of all foods
Responsive	parent is attentive to child's cues while setting appropriate limits; encourages exploration in a positive environment
Indulgent	parent does not set limits on the quantity or quality of food consumed

Thompson et al., 2009, *Appetite*

Feeding styles associated with infant feeding practices

- Higher **pressuring** feeding style scores
  - greater infant energy intake (β 32.84, p=.02)
  - reduced odds of breastfeeding (OR =0.45, 95% CI:0.27-0.74)
  - higher risk of inappropriate feeding (OR =1.30, 95% CI:1.04-1.63)

- Higher **restrictive** feeding style scores
  - lower energy intake (β -36.31, p=0.03)
  - higher odds of breastfeeding (OR=2.99, 95% CI:1.70-5.37)
  - lower risk of inappropriate feeding (OR=0.69, 95% CI:0.52-0.91)

Effect of 1-unit increase in feeding style score on daily energy intake or odds of breastfeeding/inappropriate feeding controlling for maternal age, education and marital status.

Thompson et al, 2013, *Obesity*

The Infant Care Project

Longitudinal analysis shows that feeding styles are associated with infant size

Feeding Style$_t$ - - → Infant WAZ$_{t+1}$

Restrictive (diet quality) → ↑ WAZ
Pressuring (finish) → ↓ WAZ

Effect of 1-unit increase in feeding style score on WAZ, controlling for sex, age at measurement, infant activity level and birthweight; Results significant at $p<.05$

Thompson et al, 2013, *Obesity*

And also…feeding styles are responsive to infant size

Feeding Style$_t$ - - → Infant WAZ$_{t+1}$

Restrictive (diet quality) → ↑ WAZ
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Effect of 1-unit increase in feeding style score on WAZ, controlling for sex, age at measurement, infant activity level and birthweight; Results significant at $p<.05$

Infant WAZ$_t$ - - → Feeding Style $_{t+1}$

↑WAZ → ↓Restrictive (diet quality)
↑ WAZ → ↓Pressuring (finish)

Effect of 1-unit increase in infant WAZ on feeding style score at the next visit, controlling for infant age, sex, birth weight, breastfeeding and subject as a random effect.

Thompson et al, 2013, *Obesity*

Why are Maternal Beliefs Important?

Maternal Perception of Infant Growth and Size

Maternal perception of infant underweight could lead to overfeeding or poor diet choices

"Well…. try to find food, maybe increasing it, giving them more snacks. Or like, not necessarily like junk snacks but feed them even more times a day. Like, my friend, [her] doctor was saying that her child might be a little bit underweight so to put more water in their juice so that way they'll get more calories from food instead of the liquid."

- Mother, 17-month-old girl

The Infant Care Project

Maternal perception of infant overweight doesn't necessarily lead to healthier infant feeding practices

"I don't know how a baby would be overweight, I mean I guess if the mother just fed them too much, but I have definitely, they used to tell me he was overweight, but to me he wasn't overweight because he wasn't like, he wasn't where he didn't do everything that a normal child does, or where it was just impairing or anything like that, and look at him now and he eats just as much, he eats good now but he's just so active that it doesn't, so I didn't listen, I kept feeding him"

- Mother of 12-month-old boy

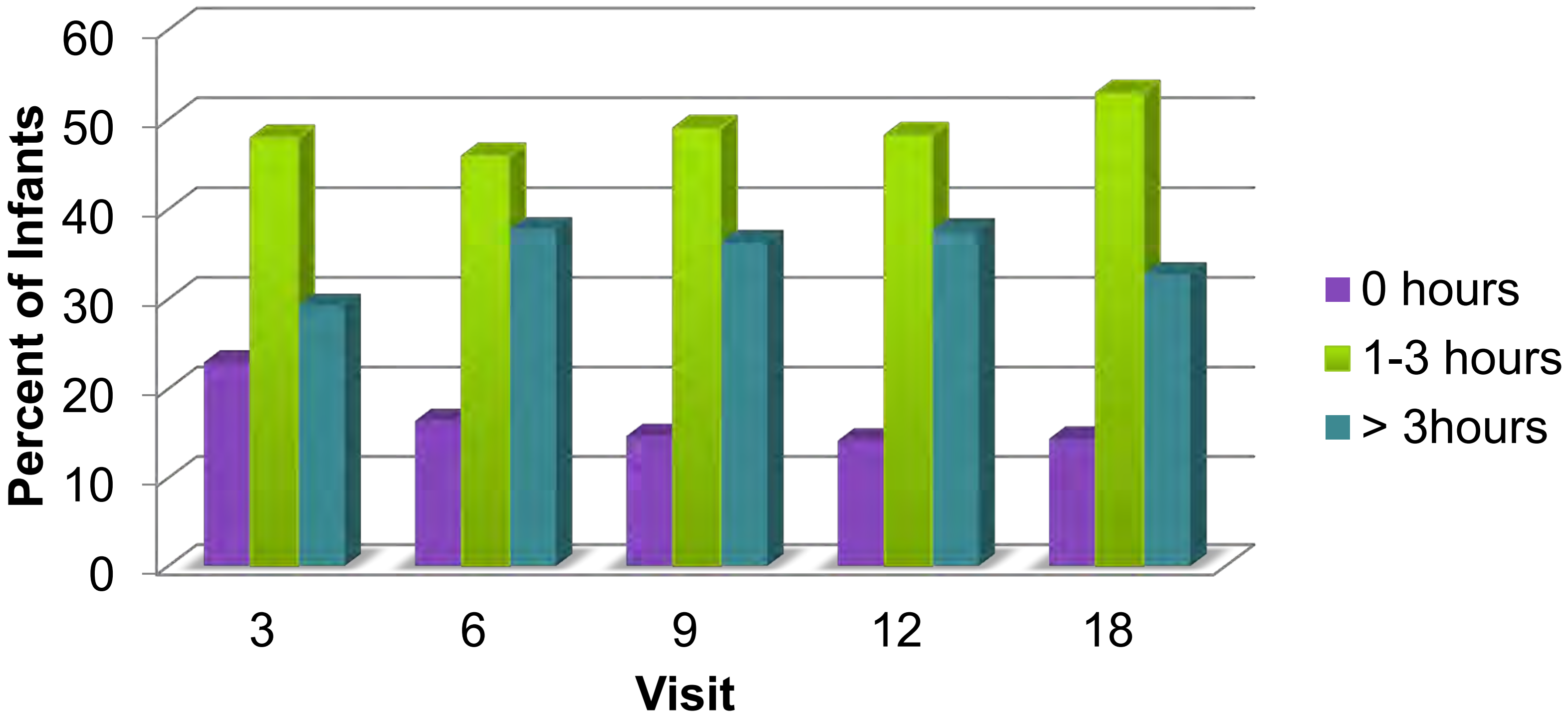
The Infant Care Project

Why are Maternal Beliefs Important?

Infant Television Exposure and Responsivity

Infant television exposure

On average, how many hours does your infant spend in front of the TV (when it is on) on a typical weekday/weekend?”



[a] Proportion of infants in each of the television exposure groups at each visit.

* Significantly different from 3-month baseline visit (p<0.05) in mixed logistic model testing for effect of visit controlling for repeated measures across subjects

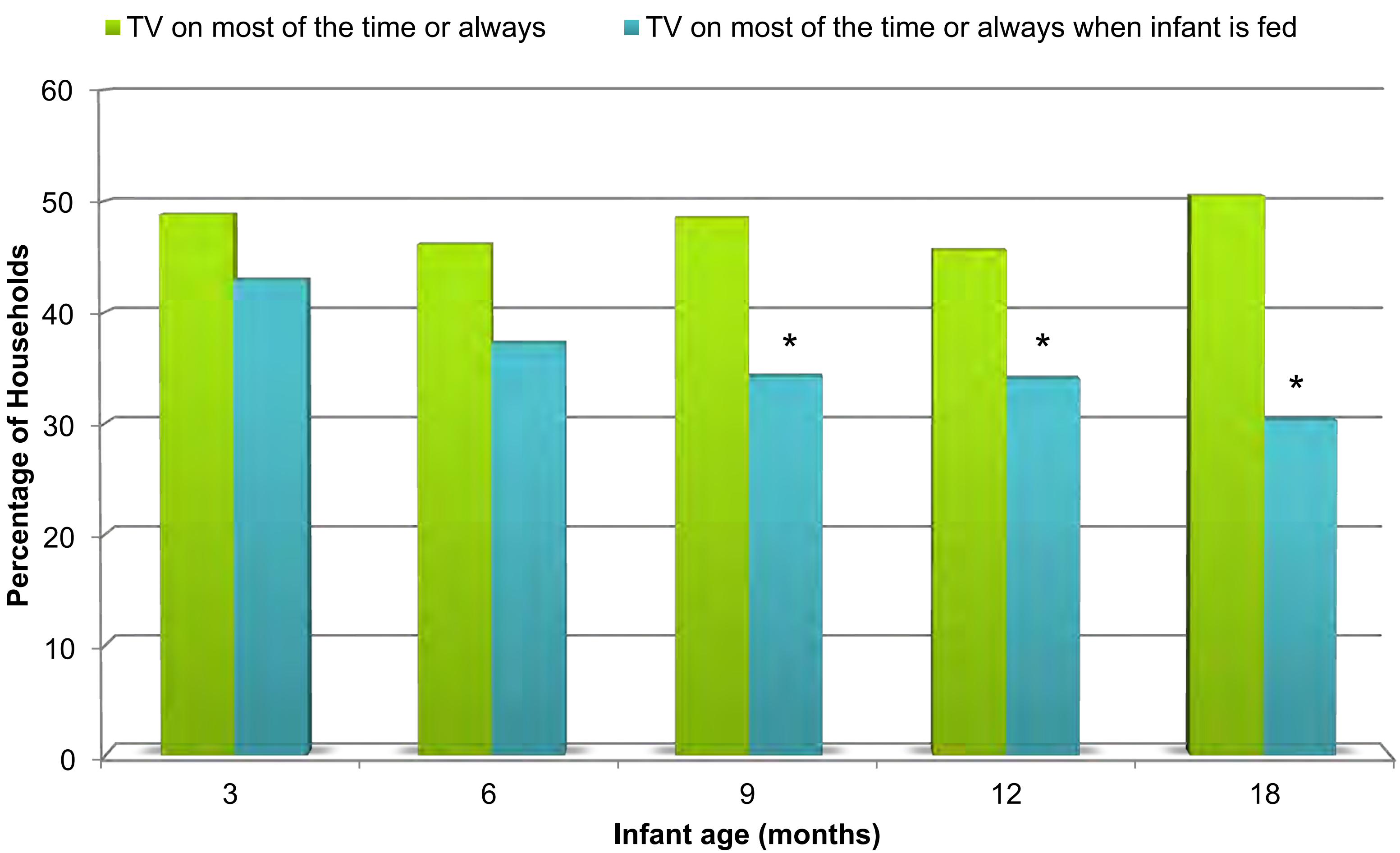
Thompson et al, 2013, *Pediatrics*

Maternal beliefs about television for infants

- Over 90% of mothers of 3-month-olds think that they enjoy being in front of the TV

- Relatively few mothers agree that toddlers should be allowed to eat in front of the TV:
  - if they want to (20-24%)
  - to stop them from crying or being fussy (5-9%)
  - to get them to eat (4-13%)
  - to keep them happy (7-12%)

Rates of feeding in front of the television are much higher



* Significantly different from 3-month baseline measure

Thompson et al, 2013, *Pediatrics*

Television a barrier to maternal responsivity during mealtimes?

“Most of the time I’m watching Oprah, and, you know, most of the time, they’re just eating, they don’t even have this TV up here on cartoons too much. So usually I’m the one that’s looking at TV when we’re eating.”

- Mother of 11-14 month-old

Measurement Challenges and Research Gaps

Measurement challenges

- Infant feeding practices are complex and nuanced
  - Change across infancy
  - Differ across ethnicities/samples
- Maternal beliefs and behaviors both matter, but don’t necessarily coincide
- Complexity requires multiple methods (survey, observational, qualitative)
  - Observational data time intensive to collect and code
  - Qualitative data needed for interpretation

General guide for conducting formative research for design of IYCF interventions

Ann. N.Y. Acad. Sci. ISSN 0077-8923

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Issue: *Integration of Nutrition and Early Childhood Development Interventions*

Formative research methods for designing culturally appropriate, integrated child nutrition and development interventions: an overview

Margaret E. Bentley,[1,2] Susan L. Johnson,[3] Heather Wasser,[4] Hilary Creed-Kanashiro,[5] Monal Shroff,[6] Sylvia Fernandez Rao,[7] and Melissa Cunningham[1]

[1]Department of Nutrition, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina. [2]Carolina Population Center, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina. [3]Children's Eating Laboratory, Department of Pediatrics, Section of Nutrition, University of Colorado Anschutz Medical Campus, Aurora, Colorado. [4]Center for Women's Health Research, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina. [5]Instituto de Investigacion Nutricional, Lima, Peru. [6]Michigan Public Health Institute, Okemos, Michigan. [7]National Institute of Nutrition, Andhra Pradesh, India

Address for correspondence: Margaret E. Bentley, Ph.D., Carolina Population Center, University of North Carolina at Chapel Hill, University Square, 123 West Franklin St., Chapel Hill, NC 27516-3997. pbentley@unc.edu

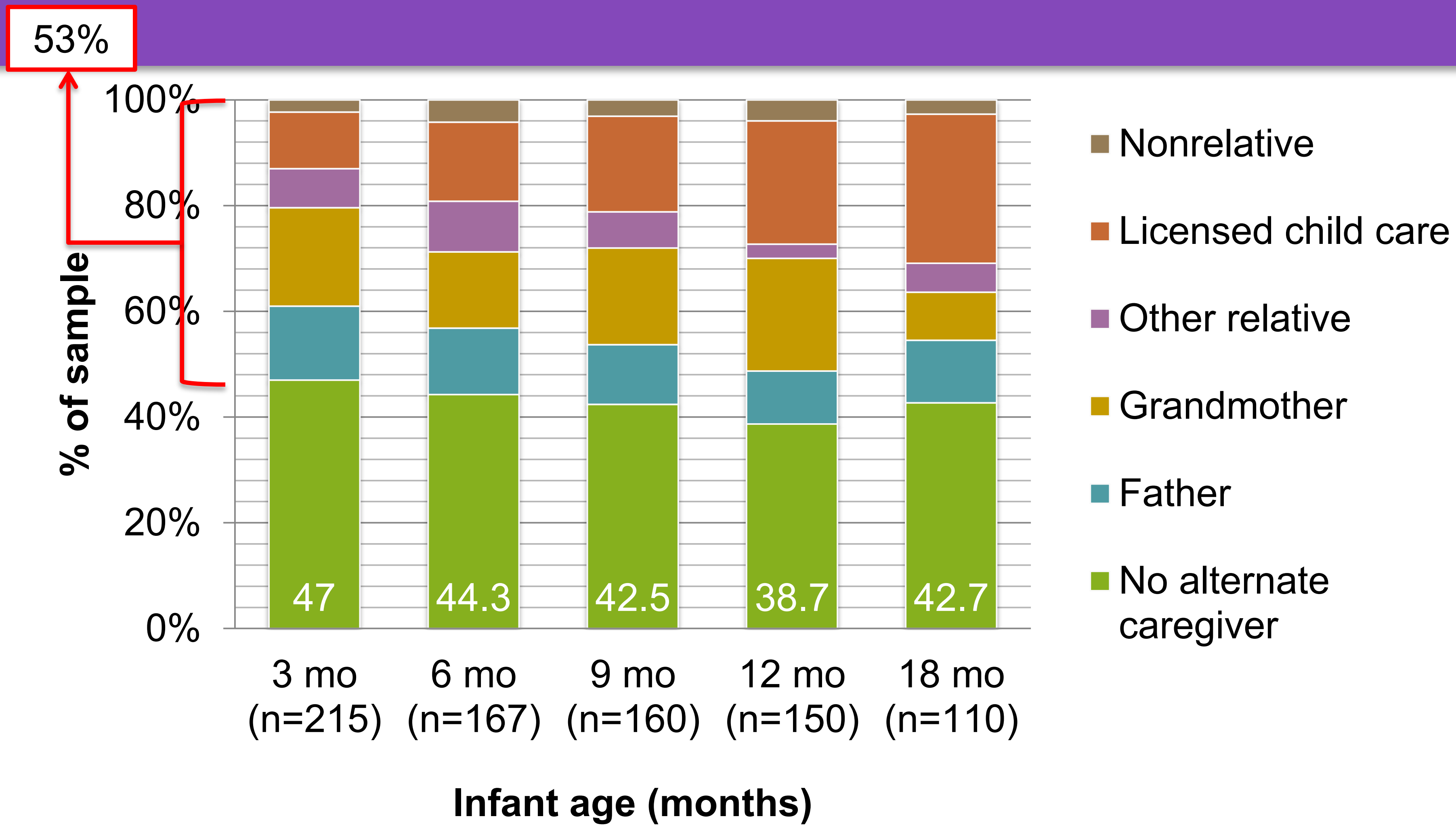
Research gaps

- How do beliefs differ by maternal and household characteristics?
  - Maternal SES
  - Maternal weight status
  - Household characteristics

- Are there limitations to measuring only *maternal* perception?

The Infant Care Project

Prevalent use of 'alternate caregivers'
(feed infant ½ or more of his/her daily meals)



Wasser et al. Who's feeding baby? Non-maternal involvement in feeding and its association with intakes of obesity-related foods among infants and toddlers. *Appetite 71:7-15.*

mothers & others

Implications for RCTs:

Mothers and Others: Family-based Obesity Prevention for Infants and Toddlers (1R01HD073237-01)

‘Mothers and Others’ sample

- Inclusion criteria:
  - African-American women < 27 weeks gestation
  - English-speaking
- Exclusion criteria:
  - Delivery < 36 weeks gestation
  - Hospital stay ≥ 7 days
  - Medical condition that significantly affects feeding or growth

Conceptual framework

Modifiable Risk Factors (Mediators)	Health Behaviors (Secondary Outcomes)	Infant Growth (Primary Outcomes)

Maternal characteristics

Positive BF attitude

High parenting and
BF self-efficacy

Responsive feeding style

High accuracy in perceiving
infant weight status

Diminished perception of infant
fussiness

"Other" characteristics

Positive BF attitude

Responsive feeding style

High accuracy in perceiving
infant weight status

Diminished perception of infant
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EBF until 6 mo.

Continued BF to 12 mo.

Delayed CF until 6 mo.

High quality transitional diet

Age-appropriate infant sleep

Minimal TV/media exposure

Lower mean weight-for-length z-score (WLZ) at 18 months

Smaller change in mean WLZ between 0-18 months

Lower likelihood of overweight (WLZ ≥ 95th %ile) at 18 months

mothers
& others

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mothers & others

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mothers & others

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mothers & others

Who's Feeding Baby?

http://www.aetv.com/modern-dads/about/

Summary

- Maternal beliefs are embedded in complex cultural and biological systems
- Maternal beliefs help us understand *why* certain behaviors exist – this understanding is critical to the design of interventions
- The use of mixed methods is ideal, qualitative research is essential
- More research is needed to understand how beliefs differ by maternal (and non-maternal) characteristics

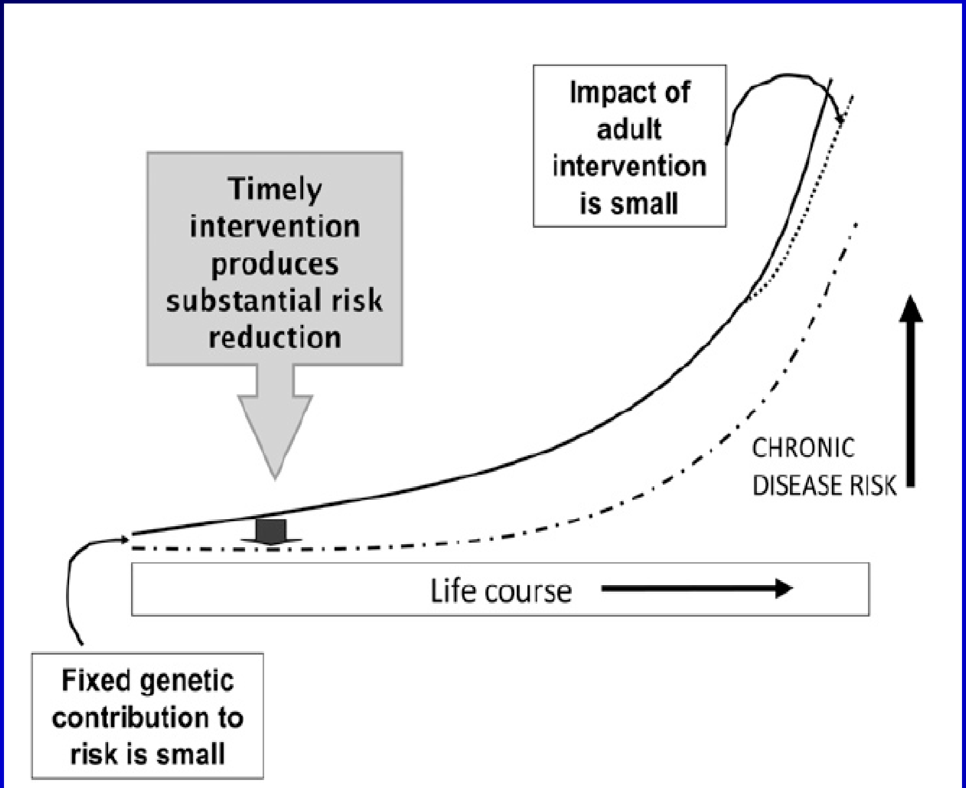
Lessons Learned in Clinical Trials Designed For Primary Prevention of Obesity among Children Ages 0-3 Years

Ian M. Paul, MD, MSc

Departments of Pediatrics & Public Health Sciences

Penn State College of Medicine & Children's Hospital

Rationale for Infancy-Based Intervention



Hanson M and Gluckman P, Am J Clin Nutr 2011; 94: 1754S-8S

- Metabolic plasticity
  - programming via epigenetic mechanisms?
- Behavioral plasticity
  - many obesogenic behaviors have origins during infancy

(Debatable) Targets on an Individual Level

- Early feeding mode (breastfeeding vs. formula)
- Age at complementary food introduction
- Diet quality and quantity (solids and liquids)
- Parent feeding practices (attention to cues, feeding style)
- Sedentary behaviors and physical activity
- Sleep hygiene and duration
- Parent regulation of distress
- Growth education; setting expectations for growth
- Parent modeling of behavior and diet

Obesity prevention is hard!

SLIMTIME → INSIGHT Lessons Learned

- SLeeping and Intake Methods Taught to Infants and Mothers Early in Life (SLIMTIME) Study (R56DK72996)
  - Pilot study conducted 2006-2008
- The Intervention Nurses Start Infants Growing on Healthy Trajectories (INSIGHT) Study (R01DK088244) & SIBSIGHT (R01DK099364)
  - Ongoing trials informed by pilot experience

How to proceed in an intervention trial?

- What? - Conceptual framework
- Where? - Delivery location and provider
- Who? - Patient population
- When? - Timing
- How much? - Dose, Data Collection
- How long? - Duration

SLIMTIME Study

- RCT with birth cohort intending to breastfeed
- Two home nurse visits – 2-3 weeks, 4-6 months after birth plus clinical research center visit at 1 year

	Introduction of Solids	Control
Soothe/Sleep	N = 42 2 interventions	N = 39 1 intervention
Control	N = 38 1 intervention	N = 41 0 interventions

Paul IM et al. Obesity, 2011

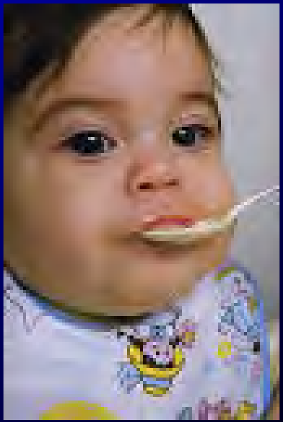
SIMTIME Inclusion/Exclusion Criteria

- 1) Full or near-term singleton
- 2) No significant morbidities
- 3) Primiparous mother intending to breastfeed without major morbidities
- 4) Pediatric primary care at University-affiliated clinic
- 5) English speaking mother

SLIMTIME Interventions

- "<u>Soothe/Sleep</u>" (2-3 weeks)
  - Crying ≠ Hunger; discriminate hunger vs. other distress
  - Soothing strategy: 5 S's (Swaddling, Side/Stomach, Shushing, Swinging, Sucking)
  - Day/night differences

- "<u>Introduction of Solids</u>"
  - delay introduction, hunger/satiety cues (2-3 wks)
  - repeated exposure to vegetables (~4-6 mos)



Results - Demographics

- 110/160 (69%) completed the 1 year follow-up
- Infants completing study
  - 51% female
  - Mean birth weight – 3.33 kg (45th percentile for GA)
- Mothers completing study
  - Mean age – 27.1 years
  - 91% White, 90% married
  - 65% completed college

SLIMTIME Primary Outcome: Weight-for-Length at age 1 year (N=110)

- “Soothe/Sleep” breastfeeding infants slept more, had fewer nocturnal and total daytime feeds
- “Introduction of Solids” infants – later intro & were more likely to accept novel healthy foods at age 1 year

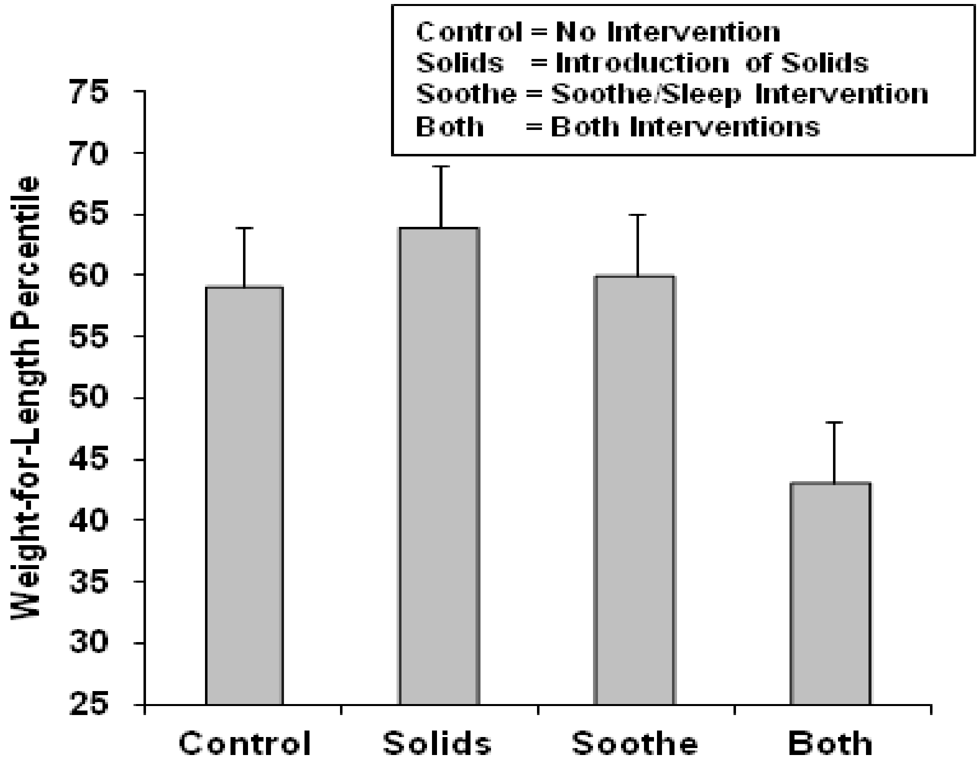


Figure 1 Study group weight-for-length percentiles at 1 year (both interventions group vs. other three groups; $P = 0.009$).

Lesson Learned – What? Conceptual Framework

- SLIMTIME contained messages related to responsive parenting, but lacked a focused conceptual framework to guide our interventions.

- INSIGHT is "stealth" in terms of obesity prevention focus and been developed around the framework of responsive parenting in multiple domains/states of arousal: Sleep, Drowsiness, Fussiness, Alert and Calm (Eating, Active/Social Play).

Early Insight: Helping parents raise healthy babies in the first 4 months

Fussy

- Newborns cry up to 3 ½ hours per day, decreasing around 2 months
- Hunger is only one of many reasons why babies cry
- A crying baby may not be hungry
- Try the 5 S's to calm your baby

Sleeping

- 1 to 4 month olds sleep 11 to 18 hours per day
- Babies sleep for a few minutes to a few hours at a time
- White noise may help your baby sleep
- Give your baby a chance to go back to sleep on own after waking at night

Active Social Play

- Babies can lift their heads, look at and reach for new things
- Around 2 months of age, practice tummy time with your baby 2-3 times daily, 10-15 minutes at a time

Your Baby is Unique!

- Learn to read your baby's signals
- Try different soothing strategies
- Use different routines for the day and night

Alert & Calm

Drowsy

- Drowsy babies rub their eyes, yawn, or get a little fussy
- Put your baby to bed between 7 and 8 pm
- Begin to use a bedtime routine
- Put your baby to bed drowsy but still awake

Feeding

- Your baby only needs breastmilk and/or formula
- 1 to 2 month olds eat 2-3 oz. every 2-3 hours (8-12 feedings daily)
- 2 to 4 month olds eat 2-4 oz. every 2-4 hours (6-12 feedings daily)
- How much your baby eats may differ, meal to meal and day to day
- Learn your baby's hunger and fullness signs

IRB #34493

Lesson Learned – Where?
Delivery Location and Provider

- Home-based interventions went well, participants very much liked their visiting nurses. Visits were relatively long, ~60 minutes duration, but few no-shows.

- Video observations of nurses taught us consequence of close research nurse – parent relationship …   "I'm not supposed to tell you this, but …"

Lesson Learned – Who? Patient Population

- Chose first time mothers for SLIMTIME
  - More open to new parenting advice given lack of parenting experience
  - Don’t have bad parenting habits to break, which may have been effective in short-term but destructive over the longer-term
- Continued this with INSIGHT
- Opportunity with SIBSIGHT

Lesson Learned – Who? Patient Population

- SLIMTIME has convenience sample from our maternity ward in Hershey, but had high drop-out rate 50/160 (31%)

- Attempts to minimize attrition in INSIGHT
  - 9/16 (56%) mothers <20 years of age dropped out compared with 41/144 (26%) 20 or older (*p*=.02)
  - 7/50 (14%) drop outs occurred prior to the first home visit

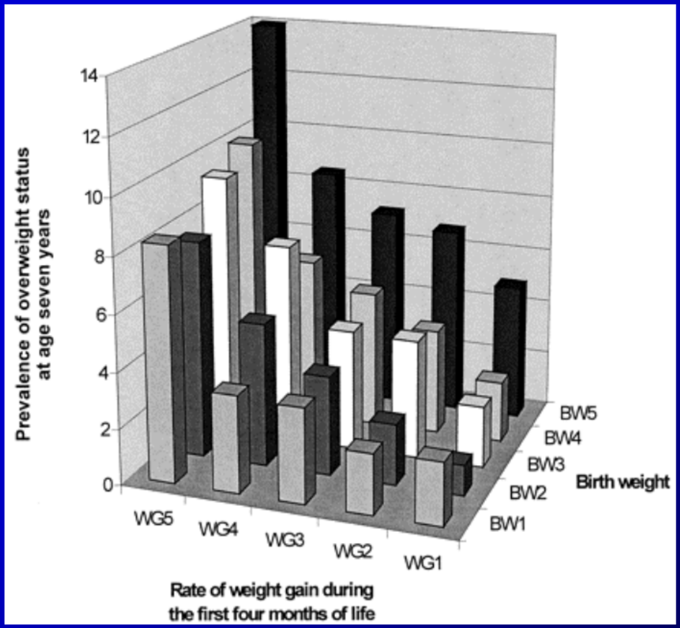
Lesson Learned – Who? Patient Population

- Only 9/160 (6%) were born <37 weeks gestation
  - changed this for INSIGHT so must be 37 weeks gestation or more

- SLIMTIME - randomization stratified newborns by maternal pre-pregnancy BMI category
  - at end of study, pre-pregnancy BMI was not associated with birth weight or any subsequent weight for study infants.

Lesson Learned – When? Timing of Intervention

- Rapid infant weight gain in first weeks → months associated with later obesity. SLIMTIME's first intervention visit was at 2-3 weeks after birth, which allowed time for:
  - Regain of initial weight loss
  - Settle into some sort of a routine
  - Parent questions emerge – what now?
- <u>Negative</u> - Lots of lactation support
  - first INSIGHT visit at 3-4 weeks



Stettler N et al., Pediatrics, 2002.
National Collaborative Perinatal Project (n=19,397)

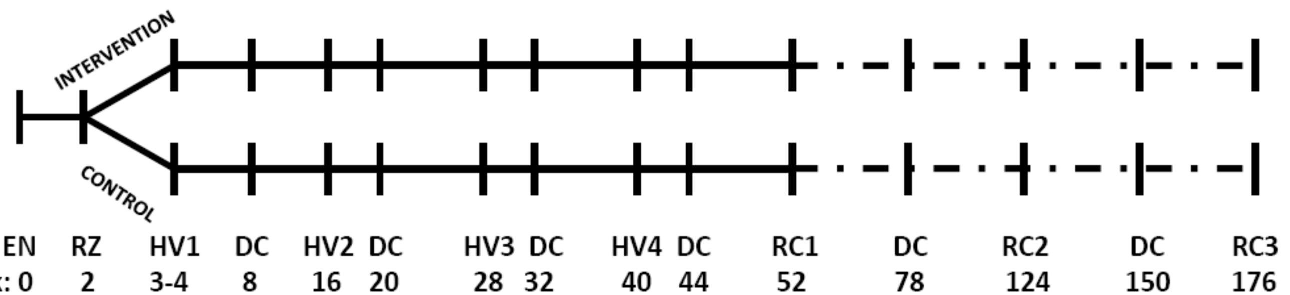
Lesson Learned – When? Timing of Intervention

- SLIMTME 2nd home visit was supposed to be between 4-6 months at the time parents indicated they were ready to introduce solid foods.
  - Variable timing of weight measurements (some visits <4 months, some >6 months) made some analyses more challenging
  - Delay in intervention and variable delivery

Lesson Learned – When? and How much? Timing of Intervention and "Dose"

- INSIGHT 2nd visit fixed for all participants at 16 weeks; additional visits added for developmentally appropriate interventions
- Also, fully developed control intervention – in SLIMTIME, ¼ of sample got very little benefit

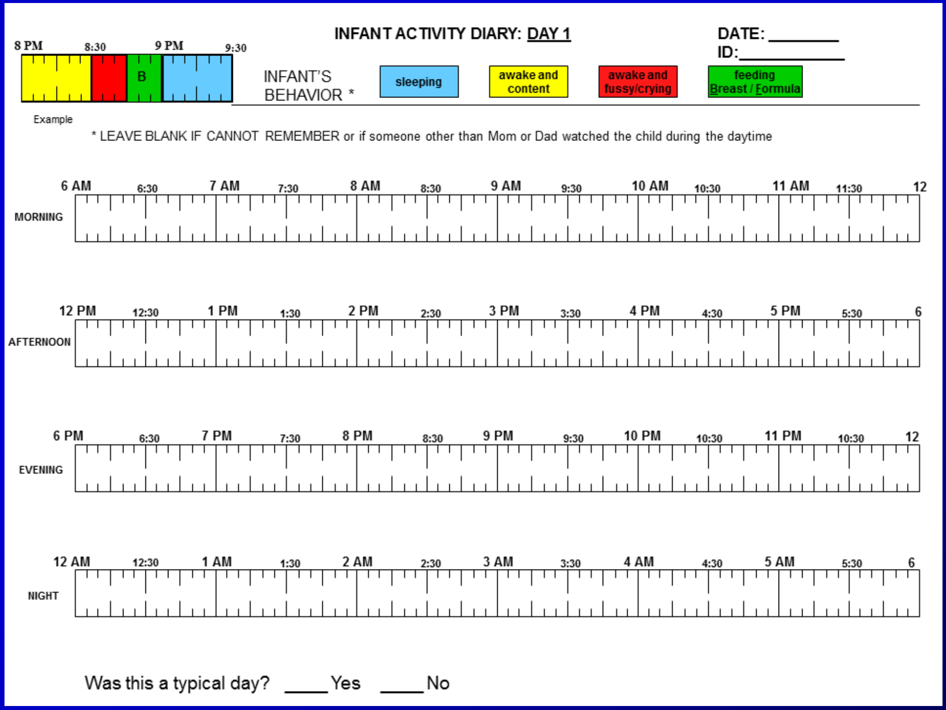
Figure 2. INSIGHT Study Visit Schedule



Legend: EN – Enrollment, RZ – Randomization, HV – Home Visit, DC – Data Collection only, RC – Research Center Visit

Lesson Learned – How Much? Data Collection

- Diary Cards used in SLIMTIME for real-time data collection on maternal responses to fussiness
  - Poorly received, unsure of data quality, difficult entry
  - Large participant burden
- Switched to smartphone application for INSIGHT
  - Also poorly received by participants


INFANT ACTIVITY DIARY: DAY 1

DATE: ________
ID: ___________

8 PM 8:30 9 PM 9:30
B
Example

INFANT'S BEHAVIOR *
sleeping
awake and content
awake and fussy/crying
feeding Breast / Formula

* LEAVE BLANK IF CANNOT REMEMBER or if someone other than Mom or Dad watched the child during the daytime

MORNING
6 AM 6:30 7 AM 7:30 8 AM 8:30 9 AM 9:30 10 AM 10:30 11 AM 11:30 12

AFTERNOON
12 PM 12:30 1 PM 1:30 2 PM 2:30 3 PM 3:30 4 PM 4:30 5 PM 5:30 6

EVENING
6 PM 6:30 7 PM 7:30 8 PM 8:30 9 PM 9:30 10 PM 10:30 11 PM 10:30 12

NIGHT
12 AM 12:30 1 AM 1:30 2 AM 2:30 3 AM 3:30 4 AM 4:30 5 AM 5:30 6

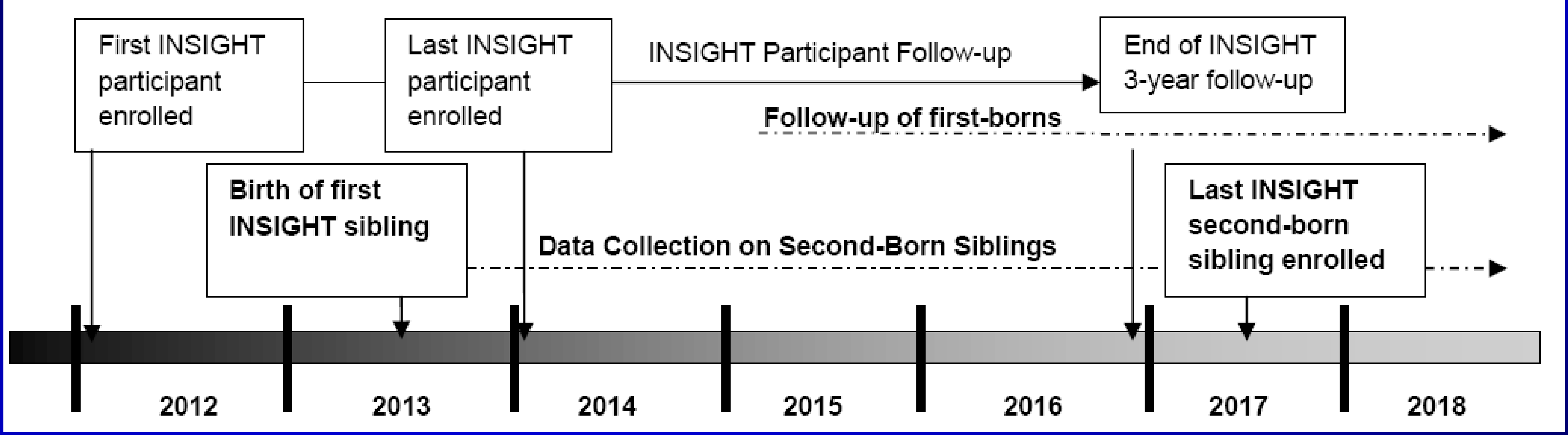
Was this a typical day? ____ Yes ____ No

Lesson Learned – How much? and How long? Dose and Duration

- SLIMTIME – 2 intervention visits with final data collection at 1 year
  - Probably not enough of a dose or duration for sustained effect
  - Need developmentally appropriate interventions given our obesogenic environment
  - Need for following children longitudinally

“Can’t Wait 30 years …”

-- LL Birch, PhD on October 31, 2013



EarlyInsight
for new parents

- Special thanks for our generous funding from NIDDK:
  - R56DK72996 → SLIMTIME
  - R01DK088244 → INSIGHT
  - R01DK099364 → SIBSIGHT
- and to our great team:
  - Jennifer Savage-Williams, Stephanie Anzman-Frasca, Lindsey Brubaker, Michele Marini, numerous graduate students
  - Jessica Beiler, Jennifer Stokes, Amy Shelly, Pat Carper, Gabrielle Murray, Nicole Verdiglione, Susan Rzucidlo

Evaluating the evidence base to support the inclusion of infants and children from birth to 24 months of age in the Dietary Guidelines for Americans- "The B-24 Project"

Daniel J. Raiten

Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

DGA: WHAT ARE THEY?

- The Dietary Guidelines for Americans (DGA) are legislatively mandated Federal guidance on healthy eating, and have traditionally focused on Americans ages 2 and above.

- The DGA are issued jointly every five years by HHS and USDA, and are developed through the use of a discretionary Federal advisory committee.

- **Specific recommendations for infants and toddlers have not been addressed since the 1985 edition, although some general guidance was included in the 1990 DGA.**

continued

DGA: WHAT ARE THEY?

- A systematic literature review process, introduced during the development of the 2005 DGA, was fully implemented for the 2010 DGA, to ensure that present and future Federal policy recommendations are evidence-based and developed using a rigorous, transparent process.
- This systematic review was guided by the Nutrition Evidence Library (NEL) team within the USDA Center for Nutrition Policy and Promotion (CNPP).

B-24

GOALS AND OBJECTIVES

- **Review and evaluate the evidence and identify priority topics** that could be the focus of systematic reviews re:
  - **Diets** of infants and toddlers ages birth to 24 months including,
  - factors affecting caregivers (mothers and others) choice and implementation of health feeding practices

- **Use the deliberations to identify a research agenda** to address critical gaps in our understanding of the role of diet/nutrition in the health and development of infants/children 0-2 years.

- **Discuss relevance of systematic reviews to nutrition**

- **Triage**: Identification of critical issues that fall outside DGA purview for triage to other agencies/organizations (AND, AAP, WHO etc.)

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B-24 STRUCTURE

THE B-24 TEAM

Core Federal Steering Committee

- Richard Olson, ODPHP/DHHS
- Robert Post, CNPP/USDA
- Joanne Spahn/Julie Obbagy, Donna Blum-Kemelor, EALD, CNPP-NEL/USDA
- Van Hubbard, DNRC/NIH

Workshop Planning Committee (WPC)

- Ronald Kleinman, Chair

Working Groups

0-6 months	Susan Baker
6-12 months	Frank Greer
12-24 months	Stephanie Atkinson
	Leann Birch
Caregivers	Kathleen Rasmussen
	Emily Oken

NICHD

- Alan Guttmacher
- Yvonne Maddox
- Gilman Grave

Secretariat

- Dan Raiten
- Kripa Raghavan, Project Manager
- Fayrouz Ashour
- Alexandra Porter
- Tamika Gillum

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ROLE OF THE B-24 WG

- This is NOT guidelines development: WG and the overarching goal of this project is **not** to develop dietary guidelines nor will they perform systematic reviews

- **Identify the key topics and questions** that will eventually be the focus of NEL systematic reviews.

- **Inform the NEL:** With the application of the topic nomination and refinement process, the WG will support the efforts of the USDA Nutrition Evidence Library (NEL) to conduct systematic reviews that will support efforts to develop guidance for infants and children birth to 24 m

- Develop a targeted RESEARCH AGENDA

- Identify topics that might be addressed by other agencies/organizations (AND/AAP/WHO): (PRE-B project)

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WG PROCESS

- WG were organized around 3 sub-themes or focal points:
  - Epidemiology/population based data (exposure and relevant health outcomes),
  - Biology to support specific dietary needs/patterns,
  - Environmental factors (social/behavioral) affecting and affected by diet/nutrition.
- Additional expertise was identified and invited by each WG to provide content specific presentations to the B-24 Prime meeting
- WG held a series of conference calls and email exchanges to develop their respective lists of priority topics
- Topics have been entered in the NEL sponsored "survey monkey"
- Cross-cutting and over-lapping issues were identified andmade the focus of specific presentations and WG sessions during B-24 Prime.

B-24: EFFORTS TO DATE

- WG constituted: 0-6 m, 6-12 m, 12-24 m and caregivers (moms/others)
- "All Hands" meeting of all WG, WPC and FSC held Oct 15-16, 2012
- WG held series of conference calls to develop lists of topics, questions, data resource needs and research priorities
- "B-24 Prime": meeting of all WG, WPC, FSC and speakers invited by WG to address issues specific to each group as well as several "cross-cutting issues including:
  - Relationships between diet and development of the human gut microbiome
  - Development of taste preferences: ontogeny and health implications
  - Role of early dietary exposure in development of NCD "DOHAD"
  - Current knowledge and theories about development of eating behavior/preferences
  - Factors involved in development and prevention of food allergies

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B-24 UPDATE

OVERVIEW OF RESULTS

DATA NEEDS AND RESEARCH AREAS

- **Human Milk composition: need for** up-to-date analyses of human milk across populations including
  - Nutrients
  - Bioactive components of human milk
- **Update of nutrient specification for infant formulas:** driven by new information about human milk composition
- **Factors affecting the ontogeny of the gut miocrobiome:** its impact on nutrition and role in human health and development
- **Expanded knowledge with regard to the dietary patterns of infants >6 m** including
  - Optimal duration of exclusive breastfeeding (is the 6 month "line in the sand" justified?)
  - Duration of breastfeeding (is there benefit of extended breastfeeding in the US?)
  - Timing and composition of complementary foods
  - Timing of introduction of allergens (earlier better?)
- **Role of maternal nutrition and health on successful lactation initiation and performance:**
  - Dietary factors influencing human milk composition
  - Impact of body composition on breastfeeding initiation, duration
- **Social/behavioral context influencing infant feeding choice**

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TOPICS HIGHLIGHTED: WG 1 (0-6 M)

- Duration of Exclusive Breast feeding;
- **Relationship between huiman milk composition and infant health outcomes;**
- Delivery mechanism for human milk;
- Necessity of micronutrient supplements for breastfed infants (iron, zinc, vitamin D, fluoride);
- Maternal diet and allergy risk;
- Introduction of complementary and transitional foods into the diets of infants/toddlers at high risk for allergic disease;
- Infant formula: which type formula(s) are comparable to human milk in terms of health outcomes in healthy infants;
- **Health outcomes in formula vs. breastfed infants;**
- **Type (e.g., suckled, fresh, stored, banked) of human milk consumed;**
- **Factors influencing infant appetite;**
- Factors influencing the ontogeny of the Infant Microbiome and related health outcomes.

TOPICS HIGHLIGHTED: WG 2 (6-12 M)

- The impact of differences in protein intake in infants in the first 12 months of life including:
  - Total amount and source (human milk vs protein sources in infant formula) of protein consumed;
  - The timing and duration of exposure to various protein sources during the first year of life;
- **The role of beverages (including fruit juices and sugar-sweetened beverages) in complementary feeding between 6 and 12 months;**
- Can fluid cow's milk be introduced before 12 months of age?
- Micronutrients of concern: iron, zinc, vitamin D, LCPUFA's, fluoride, and B12;
- Appropriate complementary food choices for human milk, formula or mixed fed infants from a macro- and micro-nutrient standpoint;
- **Early dietary influences on food and flavor preferences, especially for nutrient dense foods (fruits, vegetables, meat, diary, etc). What are the evidence-based strategies to enhance acceptance of nutrient dense foods like fruits and vegetables?**
- **Development of taste preferences for salt and sweet in infants and the impact on dietary intake and long-term health outcomes.**
- **The role, timing and value of snacking (i.e. food consumed between meals);**
- **Method(s) of Complementary Feeding;**
- **Physical activity in prevention of childhood obesity;**
- Impact of the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) food package on infant and young child diets

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TOPICS HIGHLIGHTED: WG 3 (12-24 M)

- **What are the specific energy needs of infants and children 12-24 to promote optimal growth, health and physical development?**
- **What is the optimal type and amount of physical activity to promote health of infants and toddlers 12-24 months of age?**
- Micronutrients and other dietary constituents which may be under/over consumed by infants/toddlers 12-24 months of age;
- **Impact of different approaches to weaning off the breast or bottle on infant/toddler health;**
- **Implication of consumption of different types of post-weaning beverages in infant/toddler growth, development and health;**
- Implications of sleep patterns for infant/toddler nutrition, growth and health;
- **"Micro-environmental" effects on the transition to the adult diet. How do inborn responses to basic tastes, learning and experience with food and eating, and exposure to caregiver practices influence the transition to the adult diet during the period of 12-24 months of age?**
- **Factors affecting exposure to and impact of media (e.g., TV, PDAs etc) in infants/toddlers;**
- **Impact of food insecurity on infant/toddler health and development;**
- Specific food safety concerns for this population, such as exposure to lead and mercury and potential choking risks associated with food (texture, shape, etc.);
- General food preparation, handling and storage issues related to this population

TOPICS HIGHLIGHTED: WG 4 (CAREGIVERS)

- What maternal factors (other than dietary intake and/or nutritional status) affect lactation initiation and success?
- What predicts maternal feeding choices:
  - to feed human milk at the breast or with a bottle? and
  - to feed on demand or on schedule?
- **What are the relationships of maternal feeding practices and styles to infant growth and physical development, overweight/obesity, and eating behaviors?**
- What are the benefit or harm of maternal fish consumption during lactation?
- **What is the relationship between lactating mothers' energy balance (energy intake, energy expenditure and postpartum weight loss) on breast milk volume and composition, infant growth and body composition?**
- **Maternal and caregiver predictors of infant dietary quality (i.e., what do we know about maternal and caregiver adherence to dietary guidelines for infants and how can we increase the number of infants and toddlers who would benefit, especially low-income/high risk?).**
- What are the effects of dietary patterns (e.g., vegan/vegetarian) on breast milk composition?

TOPICS HIGHLIGHTED: WG 4 (CAREGIVERS)

- What is the influence of maternal dietary intake on human milk composition?
- What are infant/children 0-24 months being fed and what are they consuming in non-parental child care settings?
- Effects of maternal alcohol consumption during lactation on milk production, composition, and infant outcomes.
- Effects of maternal caffeine consumption during lactation on milk production, composition, and infant outcomes.
- **How can we assist women across the BMI spectrum to reach national goals for breastfeeding duration?**
- Effects of maternal probiotic consumption on human milk composition or infant outcomes.

B-24 UPDATE TIMELINES AND NEXT STEPS

B-24
TIMELINE/ACTIVITIES/PRODUCTS

- **Final product** delivered to the partner agencies containing:
  - Executive Summary of the B-24 Process
  - WG reports with topic briefs with research agendas
  - Coverage of cross-cutting issues
  - Manuscripts from presentations at B-24 Prime

- **Publication of the final report:** the material above have been submitted to the American Journal of Clinical Nutrition for publication.

CURRENT ACTIVITIES

American Journal of Clinical Nutrition: manuscripts submitted and under review. The report includes:

- Invited speaker manuscripts
- Executive Summary drafted to incldue:
  - Project history
  - Process
  - Summaries of WG reports including
    - Topics with a referenced justification
    - Questions for which there is sufficient evidence to support systematic reviews
    - Data/Research Priorities x topic

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INVITED MANUSCRIPTS

B-24 Executive Summary (including the WG Summaries); D Raiten/K. Raghavan
NEL Methodology: J. Spann/J Obbagy/D Blum-Kemelor
The marriage of nutrigenomics with the microbiome: infant-associated bifidobacteria and milk (D. Mills)
Ontogeny of taste preferences: Basic biology and implications for health (J. Mennella)
Infant formula and infant nutrition: bioactive components of human milk and implications for composition of infant formulas
(B. Lonnerdal)
Protein needs early in life and long term health (K. Michaelson and F. Greer)

Learning to eat: Birth to 2 years (L. Birch)
Physical activity in infancy: Developmental aspects, measurement, and importance
(J. Worobey)
Impact of maternal diet on human milk composition and neurological development of infants (S. Innis)
WIC infant and toddler feeding practices study (WIC ITFPS-2) (G. Harrison and J. Hirschman)
Data needs for B-24 and beyond: National Health and Nutrition Examination Survey (NHANES) data relevant for nutrition surveillance of infants and young children
(N Ahluwalia et al.)

B-24 TIMELINE FOR FUTURE ACTIVITIES

Phase I (2012-2013)

Develop key topics and questions to serve as a basis for future DGA for B-24 population (B-24 Project)

Phase II (2014-2017)

Conduct systematic reviews using existing and new data

Phase III (2018)

Develop unified dietary guidelines for B-24 for use by the DGA Advisory Committee 2020

Phase IV (2020)

Publish DGAC for Americans including B-24 population

THE FUTURE OF B-24: NEXT STEPS

- 2013-2015- interim period to:
  - Allow the NEL to further refine questions and plans for systematic reviews.
  - Allow for completion of the 2015 Dietary Guidelines for the population ages 2 years and older.
  - Allow researchers time to identify high priority topics for rapid publications, particularly if they have on-going projects relevant to the priority research needs for the 0-24 month age group. This would expand the research base to inform future systematic reviews and guidance development.
- Phase II: expected to begin in early 2015, and will include
  - Conduct of systematic reviews by the NEL utilizing existing and new data identified with the support of an expert Federal scientific panel.
  - These systematic reviews and data analyses will be derived from the topic briefs developed during Phase I, taking into consideration evolution in the science and policy needs.
- Phase III: the development of unified dietary guidance for the B-24 population,
  - The goal of releasing the guidance in 2018 for consideration by the experts convened to develop the 2020 DGA in early 2018.
  - Federal agencies would be able to utilize the final policy document for their programs, once it has been approved by USDA and HHS, and is publically available.
  - Phase IV: the policy document will be provided to the 2020 DGAC for its their use in incorporating the B-24 population into the 2020 DGAC Report. The process will be transparent, and public input will be collected and considered throughout this phase of the process.

GreenLight: A Randomized Trial Addressing Health Literacy and Communication to Prevent Pediatric Obesity

Greenlight
First steps to growing healthy

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Associate Professor, Internal Medicine & Pediatrics
Director, Vanderbilt Center for Health Services Research
Chief, Internal Medicine/Pediatrics Section

Co-PIs: Eliana Perrin MD MPH (UNC), Lee Sanders MD MPH (Stanford), Shonna Yin MD MSc (NYU), Alan Delamater PhD

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NYU School of Medicine NYU LANGONE MEDICAL CENTER
STANFORD SCHOOL OF MEDICINE
Stanford University Medical Center

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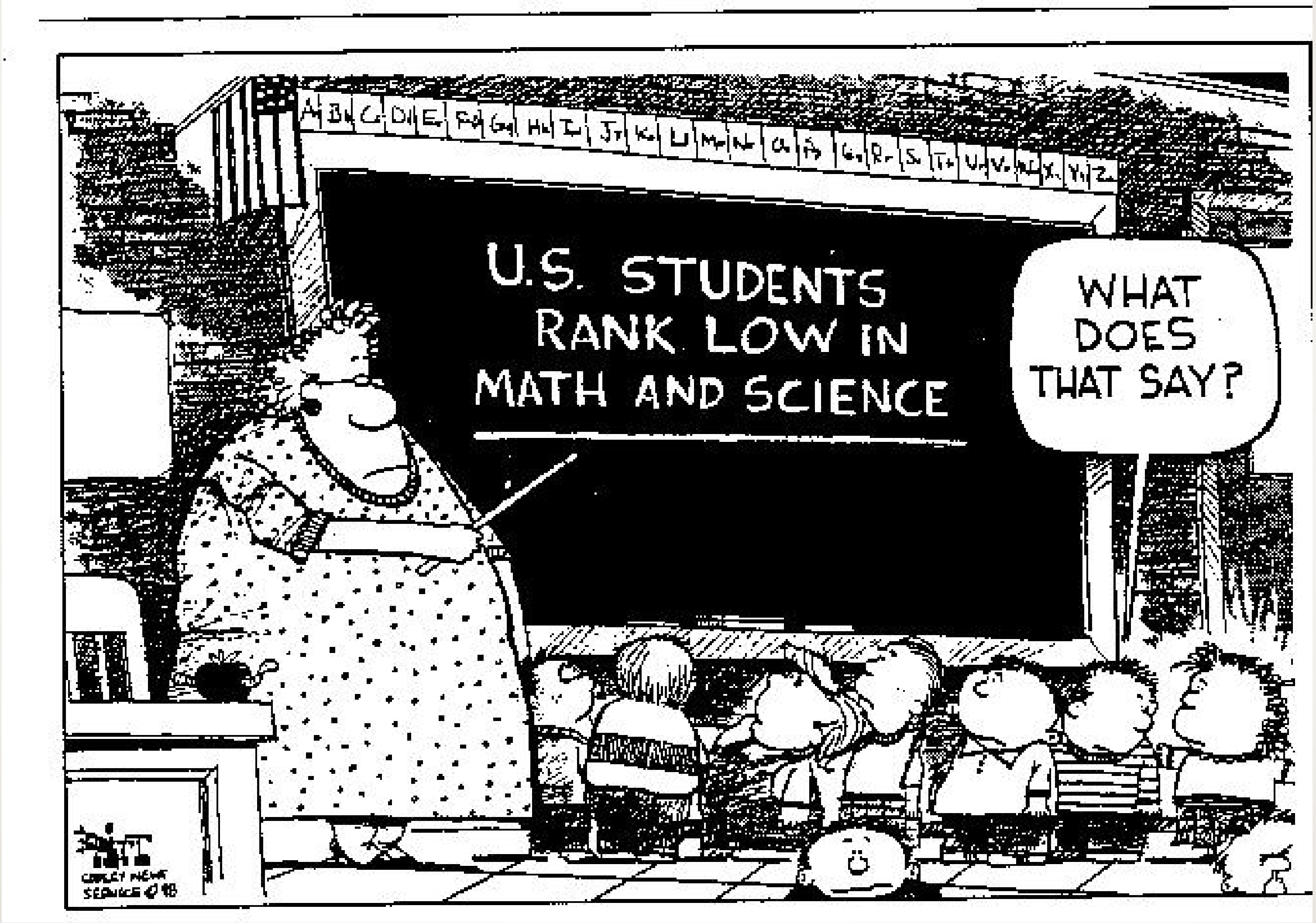
Childhood Obesity

- 1 in 4 preschoolers in the US are overweight/obese
- Overweight in infancy associated with increased risk for overweight in adulthood
- Weight gain in first few months of life associated with increased CV risks in adulthood
- “Obesogenic” behaviors start early in infancy and are very common!

Concern about Literacy and Numeracy Skills



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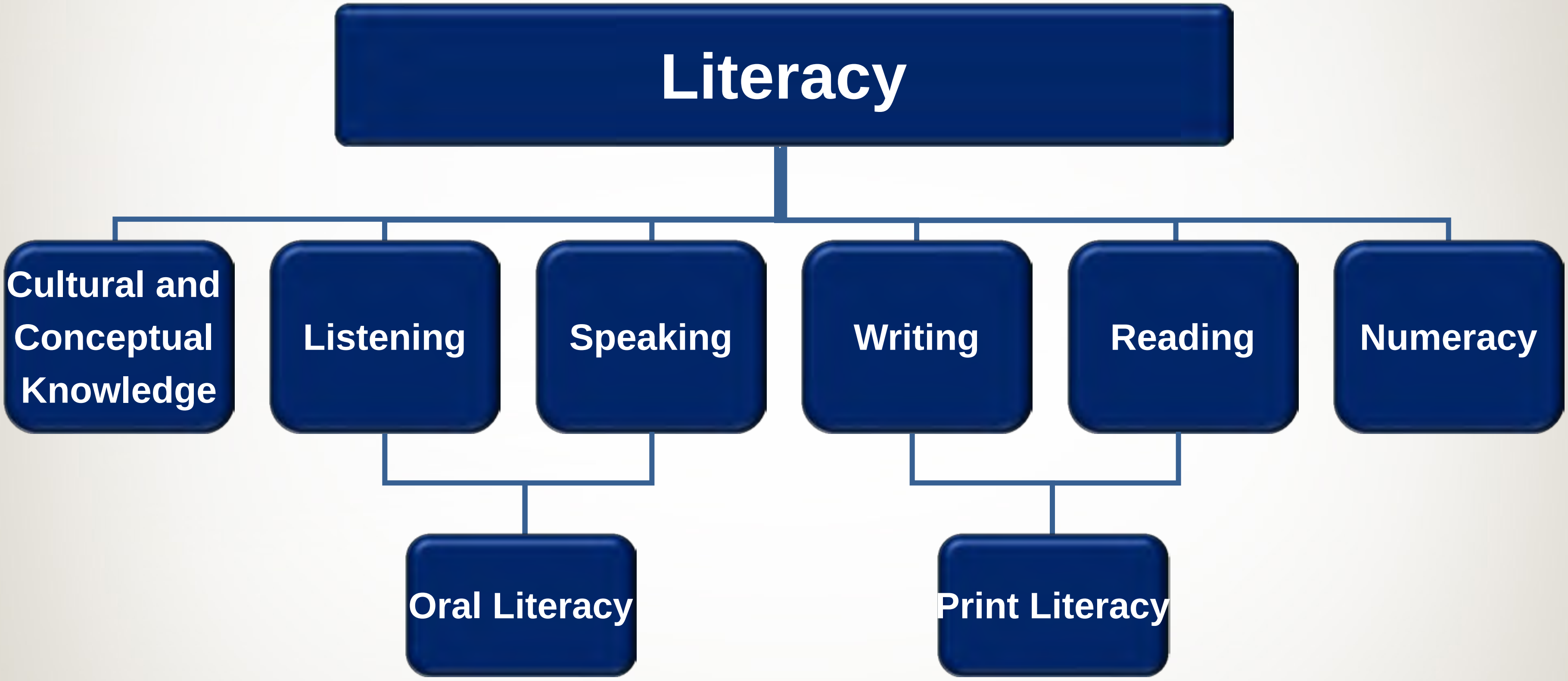
Components of Literacy



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IOM, Health Literacy, 2004

Who has poor literacy/numeracy in the U.S?

- NALS (1992) and NAAL (2003)
  - Over 90 million Americans have low or marginal literacy and numeracy skills.
  - Average American reads at 8th-9th grade level
  - Quantitative skills are often worse

Literacy/Numeracy & Pediatric Obesity Prevention

- Literacy skills needed:
  - Knowledge of disease prevention
  - Understanding of educational materials
  - Performance of child care tasks
  - Interaction with medical system (appointments, etc)

- Numeracy skills needed:
  - Understanding of risk and probability
  - Understanding weight status
  - Understanding nutrition information
  - Understanding food labels, formula mixing
  - Understanding portion size
  - Understanding exercise and “screen” time

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Health Literacy and Childhood Obesity

- Low health literacy associated with obesity in children (Huizinga 2006, Yin 2008)
- Low health literacy and obesity related knowledge/behaviors
  - Poorer maternal breastfeeding knowledge and feeding practices (Kaufman 2001, Fredrickson 2005, Kumar 2010)
  - Poorer understanding of mixing formula, and WIC guidelines (Kumar 2010, Yin 2011)
  - Difficulty understanding BMI Charts (Oettinger 2008, Kumar 2010, Yin 2011)
  - Difficulty understanding and using food labels (Rothman 2006; Kyvelos 2008)
  - Difficulty understanding portion sizes (Rothman 2006)

Resident Clinics to Address Obesity

- Pediatric resident clinics provide care for 1/5 of the socioeconomically disadvantaged families in the nation
- This includes many families with limited literacy and English proficiency who have higher rates of obesity
- Pediatricians often feel ill prepared to address childhood obesity management or prevention
- Pediatric residents are our future pediatricians

Greenlight Study

- NIH (NICHD) Funded R01
- Design: Cluster Randomized Trial of Literacy Sensitive Obesity Prevention intervention vs Active Control (Injury Prevention)
- Setting: 4 academic primary care resident clinics (Vanderbilt, NYU, UNC, and U Miami)
- Participants:
  - Over 400 pediatric residents at the 4 sites
  - 865 English and Spanish speaking families with children enrolled at 2 months of age and followed until 2 years of age
  - Children with weight/length z score >3% (WHO Criteria) without significant chronic health issues or FTT or history of prematurity (<35 weeks)

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Intervention Design

- Intervention
  - Training of residents in effective health communication
  - Provision of Greenlight Toolkit to use at well child visits (2,4,6,9,12, 15/18, 24 months)
- Active Control
  - Training of residents in injury prevention
  - Use of AAP Training in Injury Prevention Program (TIPPs) to use at well child visits (2,4,6,9,12, 15/18, 24 months)

Resident Training in Effective Health Communication

- Lectures, pre-clinic conference, role-playing
- Use effective health communication principles
  – Use plain language. Avoid jargon
  – Limit advice to 1-3 key concepts
  – Use "teach back" technique to confirm understanding
  – Address culture, language and family issues
  – Perform shared goal setting
- Perform in-room observations ("certifications")

Greenlight Toolkit Materials

- 1-2 Booklets per Well Child Visit
  - 1 CORE booklet focused on key behaviors
  - 1-3 SUPPLEMENTAL booklets *(Provider Chooses)*
  - Booklets are 2-6 pages and end with goal setting
- Designed to be used interactively during the visit
- Available in English and Spanish

EARLY CHILDHOOD

Obesity Prevention Counseling Schedule

AGE	CORE TOPICS	SUPPLEMENTAL TOPICS
2 months	Recognizing Satiety Cues Breastfeeding Promotion Child Physical Activity Promotion (Tummy time / TV)	Breastfeeding Tips Formula Feeding Tips Family Physical Activity Family Nutrition
4 months	Recognizing Satiety Cues Giving Liquids (Liquid Choices / Portion Size) Introducing Solid Foods (Wait to Start Solids / Portion Size)	Breastfeeding Tips Child Physical Activity Promotion (Tummy time / TV) Family Physical Activity Family Nutrition
6 months	Giving Liquids (Liquid Choices / Portion Sizes) Giving Solid Foods (Food Choices / Portion Size) Child Physical Activity Promotion (Age-appropriate activities / TV)	Breastfeeding Tips Nutrition Label Reading – 100% Juice vs. Juice Drinks Family Physical Activity Family Nutrition
9 months	Giving Liquids (Liquid Choices / Portion Size) Switching to the Sippy Cup Giving Solid Foods (Food Choices / Portion Size)	Child Physical Activity Promotion (Age-appropriate activities / TV) Child Growth Family Physical Activity Family Nutrition
12 months	Giving Liquids (Liquid Choices / Portion Size) Giving Solid Foods (Food Choices / Portion Size) Child Physical Activity Promotion (Age-appropriate activities / TV)	Nutrition Label Reading Switching to the Sippy Cup Family Physical Activity Family Nutrition
15-18 months	Giving Liquids (Liquid Choices / Portion Size) Giving Solid Foods (Food Choices / Portion Size) Child Physical Activity Promotion (Age-appropriate activities / TV)	Nutrition Label Reading Child Growth Family Physical Activity Family Nutrition

Toolkit Design

- **Cover Page of each CORE booklet has 3 core messages**
- **Language is**
  - Direct
  - Easy-to-understand
  - 4^{th}-6^{th} grade reading level
  - Positive tone

Toolkit Components

- **Traffic light color theme**
  - **Green**
    - Good for your baby!
    - Give your baby
  - **Yellow**
    - Not so good
    - Try not to give
  - **Red**
    - Not good for your baby
    - Try not to give!

Use of Traffic Lights

- **Traffic light icon**
  - **IMPORTANT message!**
  - Distills / simplifies the main message of the page into a few sentences

Tips for starting solid foods

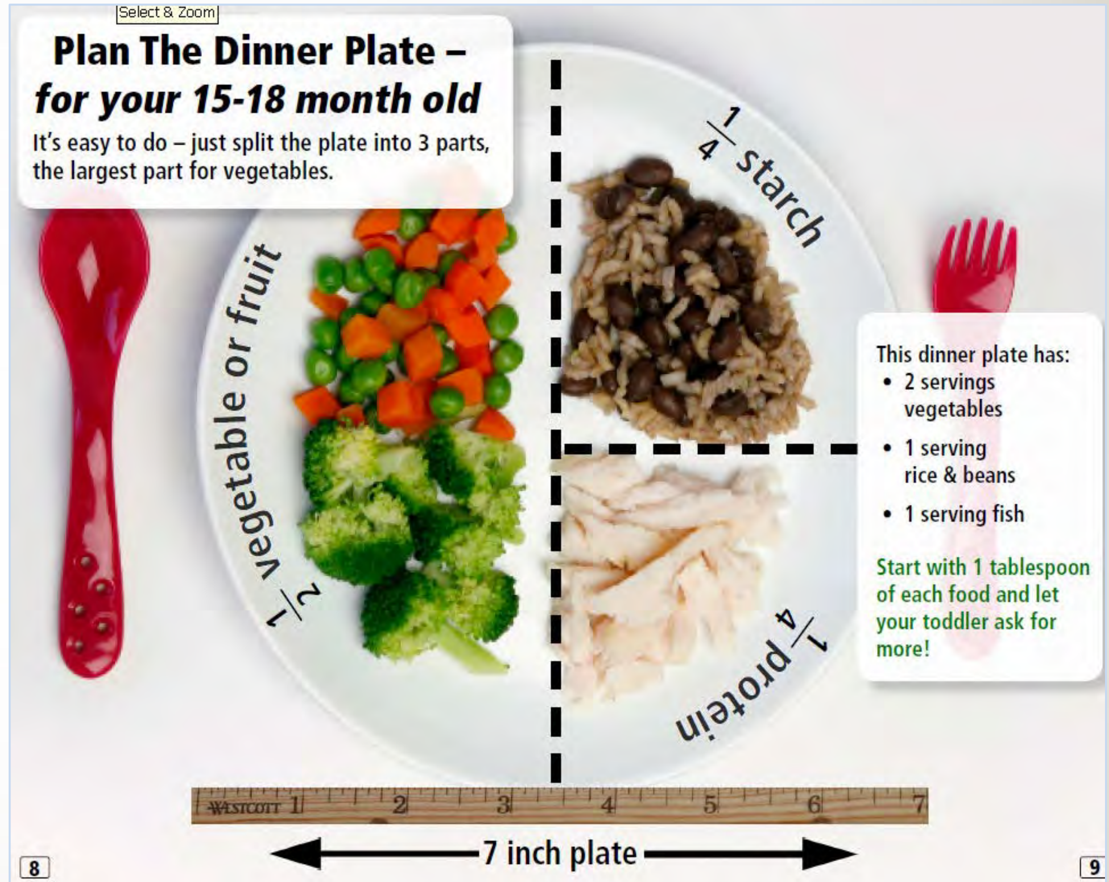
How do I start solid food?

- Make a liquid mixture of a little rice cereal with formula or breast milk.
- Put a little bit on a baby spoon and see if she can swallow it.
- She may spit the food out make a face. Be patient. Try again another day.
- As the baby gets used to eating this mixture, you can begin to make it a little thicker.
- In a few weeks you can try another pureed food like a vegetable or fruit.

Start slowly!
Breast milk or formula is still the most important food for your baby.

10

Sample Materials: 15 months



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15 Month Materials

Do not give your toddler drinks with added sugar.

Drinks with a lot of sugar can make children gain too much weight. Drinks with sugar are bad for your toddler's teeth.

When children start to drink juice or sugary drinks as toddlers, they grow up wanting <u>only</u> sugary things to drink.

TIP: If your toddler is already drinking juice and sugary drinks – you can help her learn to drink water instead. Add water to juice, a little more each day until she is mostly getting water. Then give her all water.

Breakfast

2% Milk – 6 ounces

Egg – 1 egg, cut up
Toast – ¼ cup, small bite-sized pieces
Banana – ¼ cup, cut up

Lunch

2% Milk – 6 ounces

Soup with:
- Carrots and peas – ¼ cup
- Potatoes – ¼ cup
- Chicken – ¼ cup

Feeding Your Toddler

Your toddler enjoys eating with the whole family now. She likes to eat what everyone else is eating – cooked just right for toddlers!

<u>How often</u> should I feed my toddler?

Toddlers should have 3 meals and 2 snacks each day – family mealtimes are best!

<u>How much</u> of each food should I give my toddler?

A serving size for a toddler is 2 to 4 tablespoons of each food (up to a ¼ cup) – about the size of your child's fist.

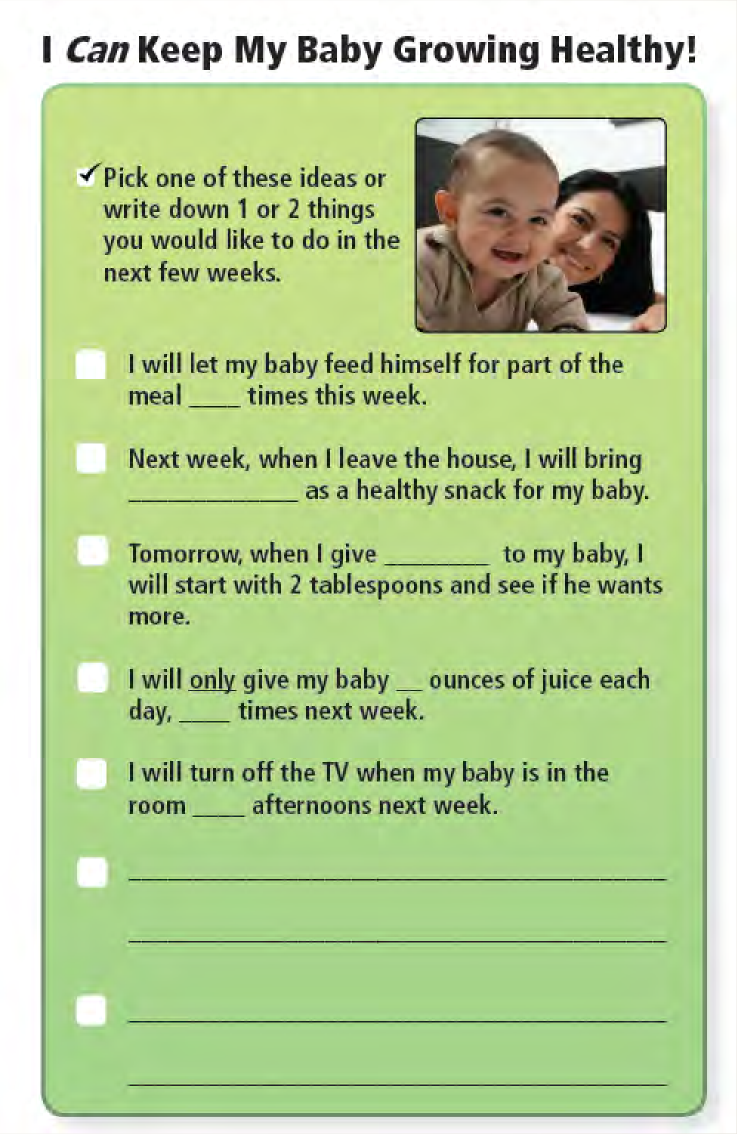
Start with 1 tablespoon and let your toddler ask for more if she is hungry!

1 serving = ¼ cup = size of your child's fist

Cultural Adaptation for Spanish Version

Goal Setting with the Toolkit

- **Last page of each CORE booklet**
  - Parent-centered
  - Do-able; “baby step”
  - Make goal with specific time frame
  - Can choose from examples or can WRITE ONE DOWN



I *Can* Keep My Baby Growing Healthy!

✓ Pick one of these ideas or write down 1 or 2 things you would like to do in the next few weeks.

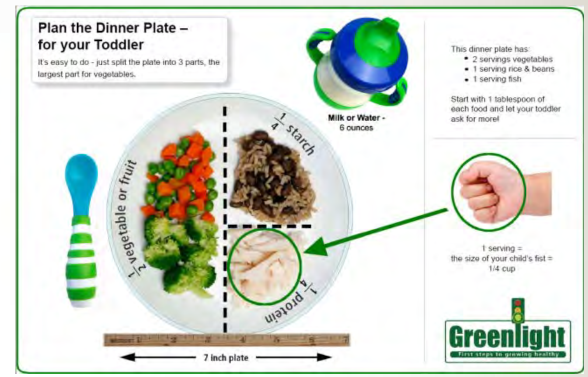
- ☐ I will let my baby feed himself for part of the meal ____ times this week.
- ☐ Next week, when I leave the house, I will bring ____________ as a healthy snack for my baby.
- ☐ Tomorrow, when I give _______ to my baby, I will start with 2 tablespoons and see if he wants more.
- ☐ I will only give my baby __ ounces of juice each day, ____ times next week.
- ☐ I will turn off the TV when my baby is in the room ____ afternoons next week.
- ☐ ______________________________________
  ____
- ☐ ______________________________________
  ____

Greenlight Toolkit Tangible Tools

2 months: onesie

9 months: sippy cup

12 months: portion size cups



15 months: placemat

Study Measures

- Baseline Measures
  - Resident age, gender, year of training
  - Family demographics, socioeconomic factors, literacy/numeracy, self-efficacy, food insufficiency, depression, acculturation
  - Child weight/length, feeding and physical activity behaviors, birth weight
- Outcome Measures
  - Overweight (BMI>85th percentile by CDC) at 2 years of age
  - BMI z-score at 2 years of age, WHO weight/length z scores
  - Child eating and PA related beliefs and behaviors
  - IFSQ (12 months)
  - Socioemotional Development (ASQ-SE) (12 months)
  - Parent satisfaction, self-efficacy
  - Parent perception of resident health communication
  - Use of services (clinic visits, ED, immunization rates)
  - Child/Parent injury prevention beliefs/behaviors
  - Resident knowledge and satisfaction

Preliminary Results

- Recruited 865 families
  - To date over 400 have completed 2 year follow-up
- Recruited and "certified" over 400 pediatric residents

Baseline Demographics

DATA REMOVED:
Manuscript currently in press or under review

Obesogenic Behaviors are Common

DATA REMOVED:
Manuscript currently in press or under review

Behaviors at 2 months

DATA REMOVED:
Manuscript currently in press or under review

Racial/Ethnic Differences

DATA REMOVED:
Manuscript currently in press or under review

Complex Relationship with Acculturation

DATA REMOVED:
Manuscript currently in press or under review

Literacy and Behaviors

DATA REMOVED:
Manuscript currently in press or under review

Challenges

Challenge	Approach
Prevention of contamination at the health care provider level	Cluster randomized trial
Hawthorne effects	Attention Control with similar level of engagement in "control" arm
Inclusion of smaller children	Changed from <10^{th} percentile to < 3^{rd} percentile (from CDC to WHO criteria)
Development of toolkit materials for Spanish	Cognitive interviews and multiple advisors to develop materials with broad generalizability
Engagement of Residents (intervention fidelity)	Identified Clinic Champions; Encouraged use of Toolkit for ALL patients; Developed "certification" checklist

Challenges II

Challenge	Approach
Assessment of intervention fidelity	Assess via post-visit surveys of residents and families and count of materials; select audiotaping
Measurement of parental/child behaviors	Developed our own measurement of behaviors. Adapted some items from IFSQ
Measurement for Spanish speaking patients	Had to translate/validate several measures in Spanish that were not available
Robust measurement of primary outcome	Training of clinic staff in length and weight measurement.
Analytic Challenges	N=4. Will perform adjusted analyses for site differences. Use of WHO or CDC weight/length z scores for children < 2 years.

Next Steps

- Completion of intervention anticipated by Fall 2014.
- Competitive renewal for long-term follow-up of families (until age 5)
- Adaptation of intervention for other settings that allow for more frequent contact with families
- Development of mobile/informatics interventions for additional customization

QUESTIONS

Social Cognitive Development & Food

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Department of Psychology
University of Wisconsin - Madison
October 31, 2013

Food Selection

Omnivore's dilemma: So many options… What should I eat?

Capacities

- Innate taste biases (+ sugar; - bitter)
- Detect and consume familiar flavors

(Aldridge et al., 2009, Mennella et al., 2001; Steiner, 1979; Rosenstein & Oster, 1988)

Difficulties

- Infants have difficulty classifying foods (from visual information).

- Infants and toddlers put inedible, dangerous, and disgusting things in their mouths.

- Poisoning in children < 2 years.

(Cashdan, 1994; Rozin et al., 1986; Shutts et al., 2009a)

One Solution

Social Learning

- Social influences on how much children eat:
  Lumeng & Hillman, 2007; Greenhalgh et al., 2009
- Social influences on what children like:
  Birch, 1980; Birch et al., 1980
- Specific influences on preferences and choice:
  Duncker, 1938; Frazier et al., 2012; Hendy & Raudenbush, 2000; Shutts et al., 2010

Social Learning

- Interested in other people from birth.
- Imitate other people's actions (facial gestures, object-directed actions).
- Change their own behaviors in response to others people's emotions.

(e.g., Johnson et al., 1991; Meltzoff & Moore, 1977; Mumme & Fernald, 2003; Sorce et al., 1985)

Social Influences: Infants & Food

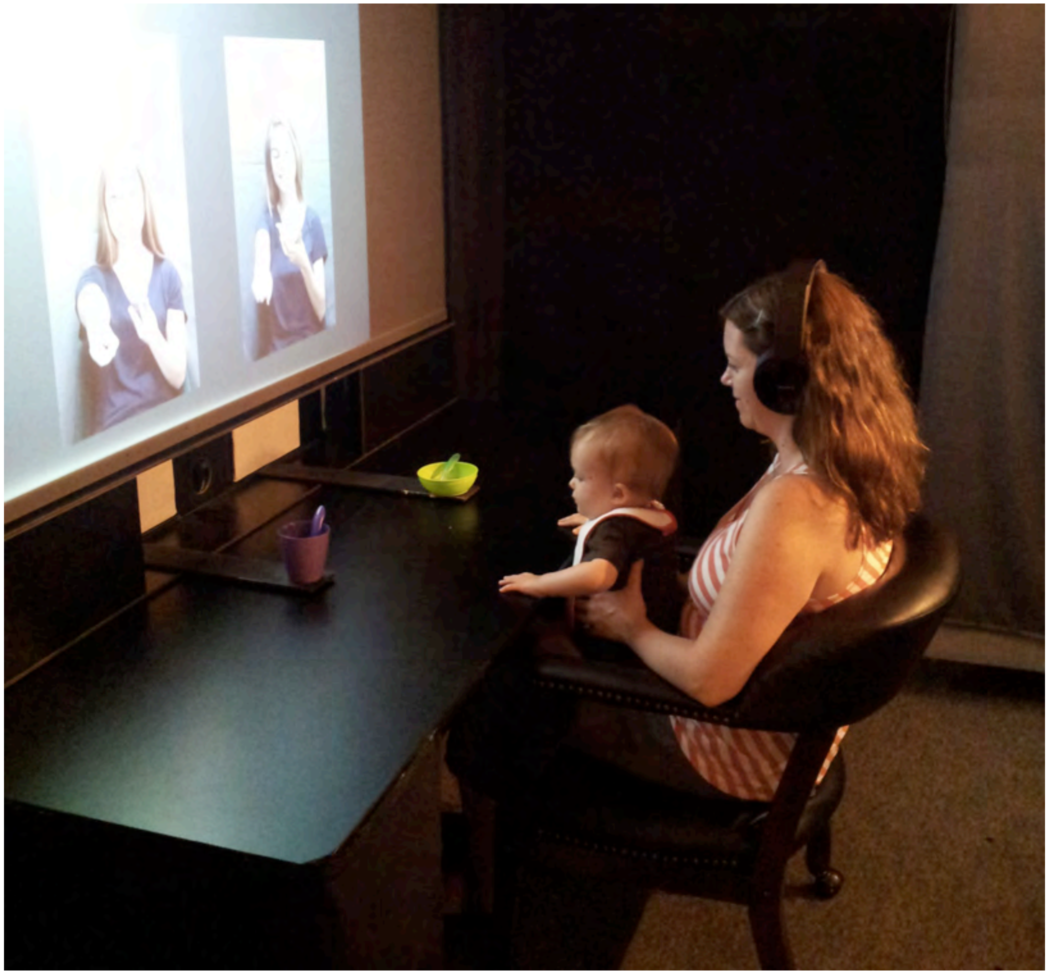
- **Question**: Are infants sensitive to social characteristics of people who endorse different foods?

- **Participants**: 12-month-old infants from monolingual English-speaking homes.

- **Social characteristic**: The language spoken by people modeling different foods.

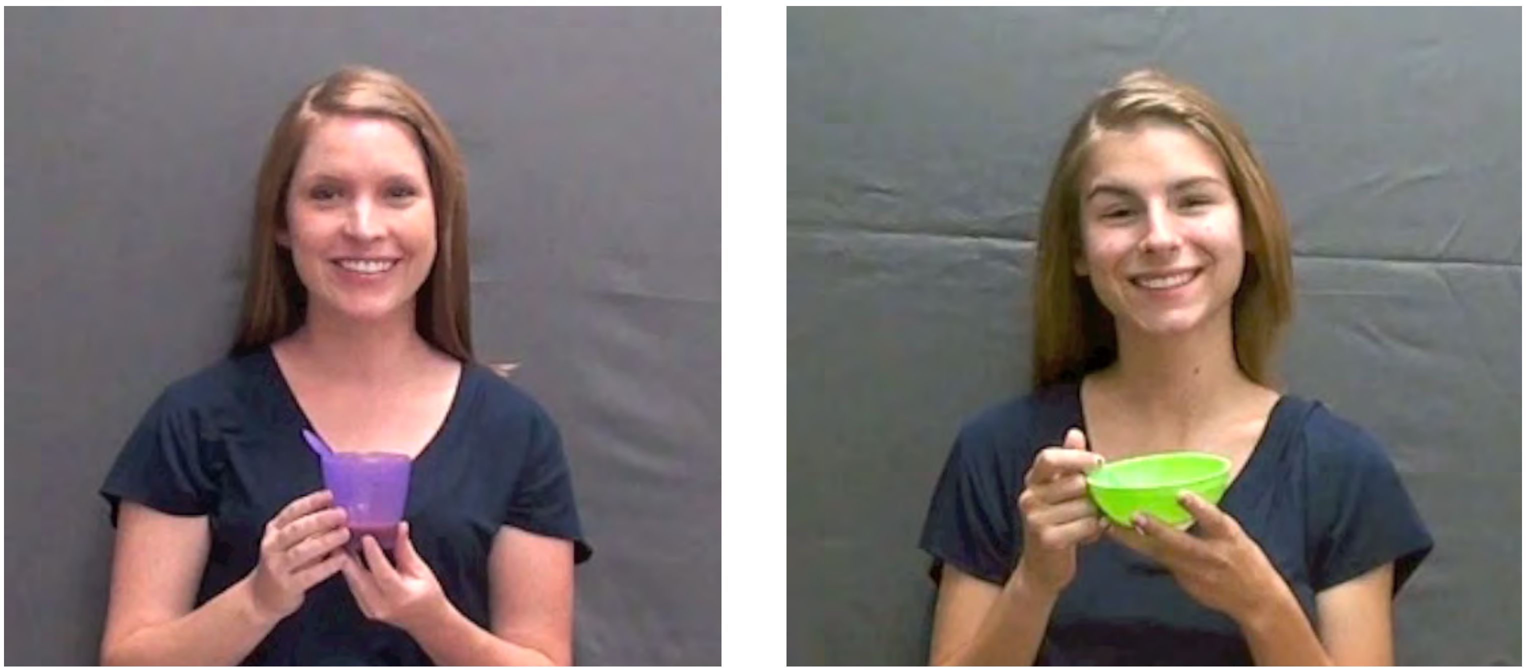
(Shutts et al., 2009; Shutts et al., in preparation)

Social Influences: Infants & Food



(Shutts et al., 2009; Shutts et al., in preparation)

Social Influences: Infants & Food



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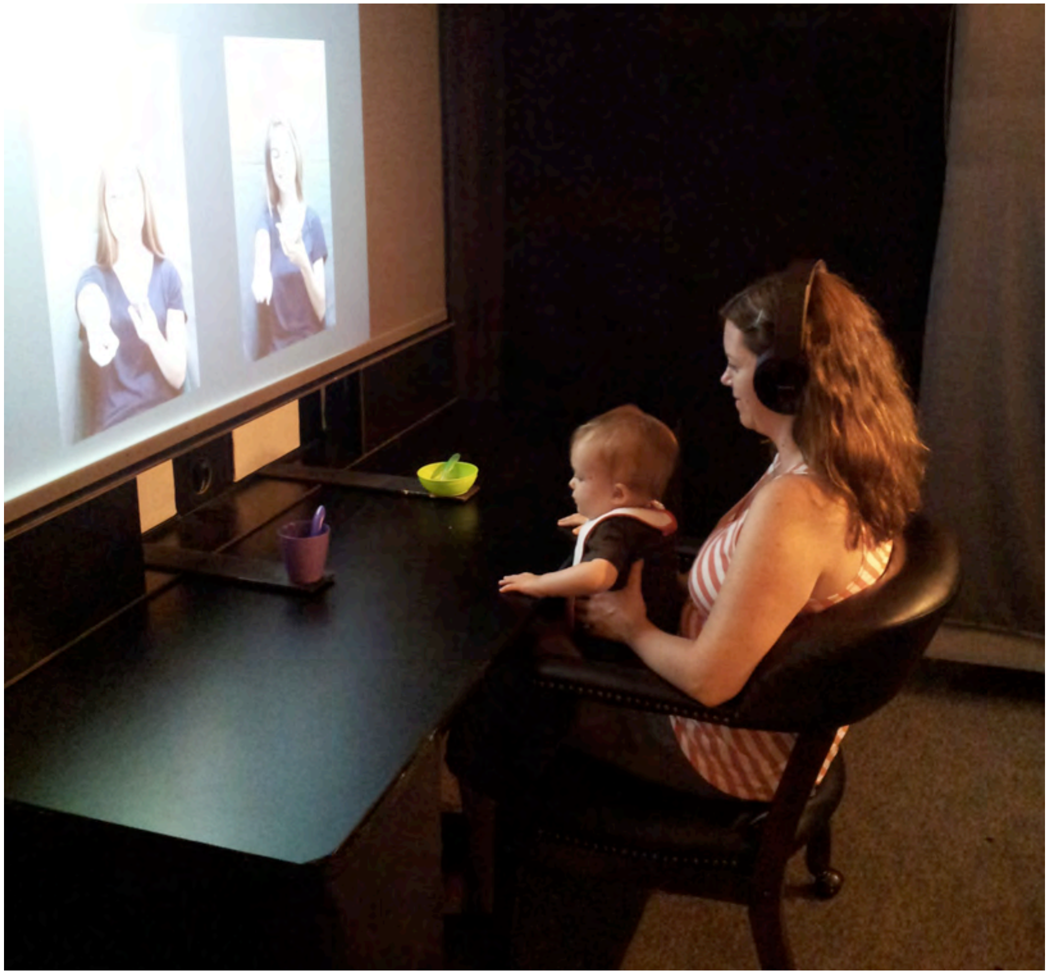
Social Influences: Infants & Food



(Shutts et al., 2009; Shutts et al., in preparation)

Social Influences: Infants & Food

- **Key finding**: Infants were significantly more likely to reach for the food that was previously endorsed by the English speaker ($p < .05$).

- **Conclusion**: Infants show selectivity when foods are presented in a context with social information.

(Shutts et al., 2009; Shutts et al., in preparation)

Further Questions

- What other kinds of social information might influence infants' food choices? (e.g., other social categories? emotions?)
- What other kinds of food behaviors in infancy are affected by social information?
- Is there anything special about social influences in the food domain?

Implications

- Effects of television and advertising

Implications

- Infants notice, learn about, and are affected by the behaviors of those around them.

Thank you!

- To you, for listening
- To my collaborator, Katie Kinzler
- NICHD R01R01HD070890

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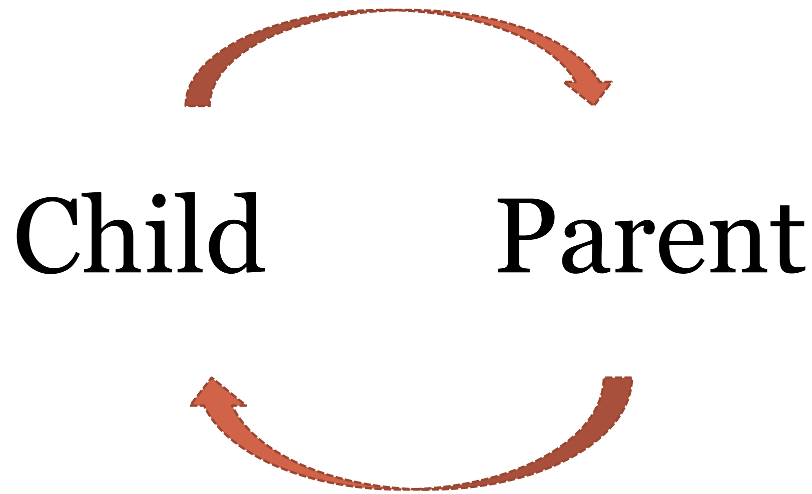
Infant Temperament, Parenting and the Development of Regulation

CYNTHIA STIFTER
THE PENNSYLVANIA STATE UNIVERSITY

Journal of Pediatrics 2004 Editorial
Zeller & Daniels

"More systematic inquiry into whether specific family/parent characteristics, child-rearing practices, and parent beliefs contribute to the development of obesity in childhood and how these factors may interrelate with child characteristics is needed. "

Bi-directional Influences in Development



Temperament

- Constitutional differences in **reactivity** and **self- regulation** with constitutional seen as the relatively enduring biological makeup of the organism influenced over time by heredity, maturation and experience
  - **Reactivity**
    - The individual's reactions to changes in the environment as reflected in somatic, endocrine and autonomic nervous systems
  - **Self-Regulation**
    - The processes that function to modulate reactivity such as through attentional and behavioral patterns of approach and withdrawal

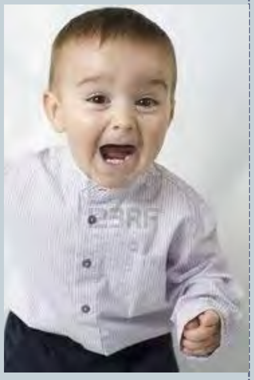
Rothbart & Derryberry, 1981

Principles of Temperament

- Temperament is relatively stable
- Temperament develops
  - Reactivity develops early in the first year of life
  - Self-regulation comes on-line at the end of the first year with rapid development thereafter through preschool
- Temperament is modifiable through experience

Temperament Types

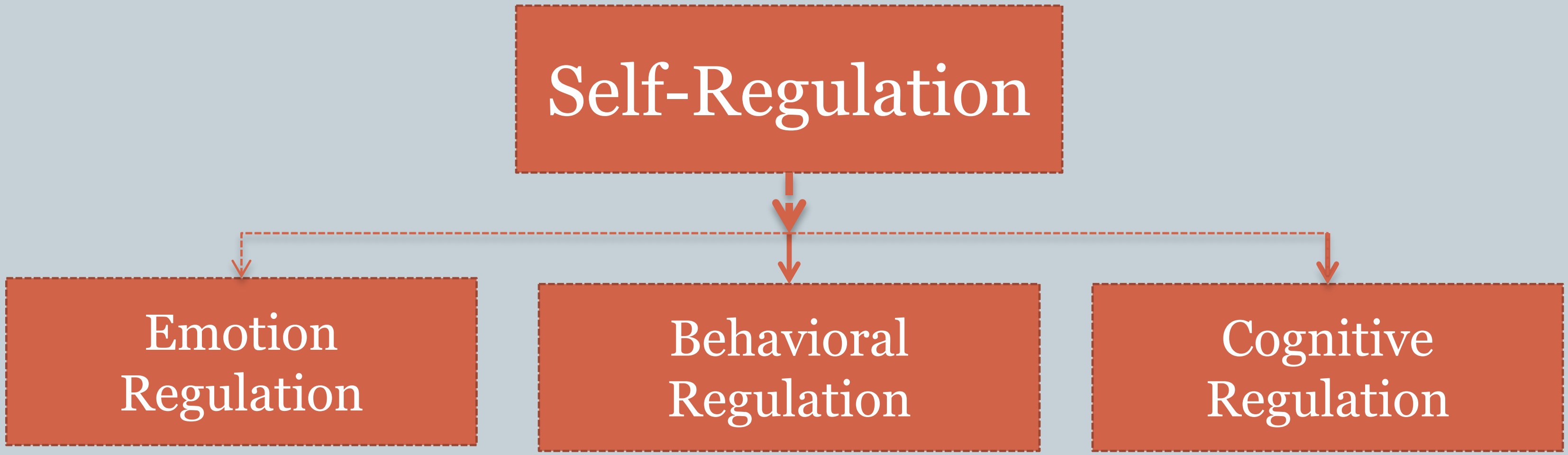
Exuberant (surgent, uninhibited, fearless)	Inhibited (behaviorally inhibited, fearful)
Approach to Novelty	Avoidance of novelty
High Intensity Pleasure	Fearful
High Active	Slow to warm up
Impulsive	Socially withdrawn
Easily Frustrated	



The Development of Self-Regulation

What is Self-regulation?

- Self-regulation refers to the capacity to alter one's behaviors in accordance to some standards, ideals or goals either stemming from internal or external expectations



Development of Self-Regulation

- Neurophysiological Modulation (Birth – 2-3 months)
  - Regulate arousal
- Sensorimotor Modulation (3 to 9 months+)
  - Change ongoing behavior in response to environmental stimuli
- Control (9-12 to 18 months)
  - Awareness of social demands; initiate, maintain and cease activities
- Self-control (24 months+)
  - Control behavior without monitoring (wait, behave according to expectations)
- Self-regulation (36 months+)
  - Flexibility of control (Stop a pleasurable task for a not so pleasurable task)

Kopp, 1989

Parenting and the Development of Self-Regulation

TEMPERAMENT MATTERS

Parent Attention Strategies

- Attention-focusing
  - Foundation of good self-regulation
- Attention re-direction
  - Use at low levels of distress
  - Contingent to child behavior
  - Inhibited
    - If on-task – poorer executive function
- Attention-grabbing
  - Exuberant
    - especially when involved in a pleasurable activity - better emotion regulation

Parental Responsiveness

- Mutually responsive orientation/Shared positive affect
  - Better EF performance
  - Exuberant –
    - Better self-regulation
- Attachment
  - Better EF performance
  - Exuberant –
    - secure – better self-regulation

Parent Discipline/Control

- Gentle discipline
  - Better self-regulation
  - Inhibited
    - positive effect
  - Exuberant
    - no effect
- Harsh discipline
  - Negative effect on later self-regulation
- Control
  - Mixed findings
    - Positive control – good self-regulation
    - Negative control – poor self-regulation
  - Exuberant – with warmth – positive effect

What Do We Know So Far

THE EFFECT OF TEMPERAMENTAL REACTIVITY, SELF-REGULATION, PARENTING AND THEIR INTERACTION ON

INFANT AND CHILD WEIGHT OUTCOMES

Research on Emotional Reactivity and Infant/Child Weight Outcomes

Infants/Toddlers

- Difficultness (Carey, 1985, Niegel et al., 2007; Pryor et al., 2011;)
- Negative Emotionality (Stifter et al., 2011)
  - Distress to Limitations (Agras et al., 2004; Darlington & Wright, 2006; Slining et al., 2009; Wells et al., 1997; Wright et al., 2011)
- Surgency (Burton et al., 2011)

Child Weight/BMI

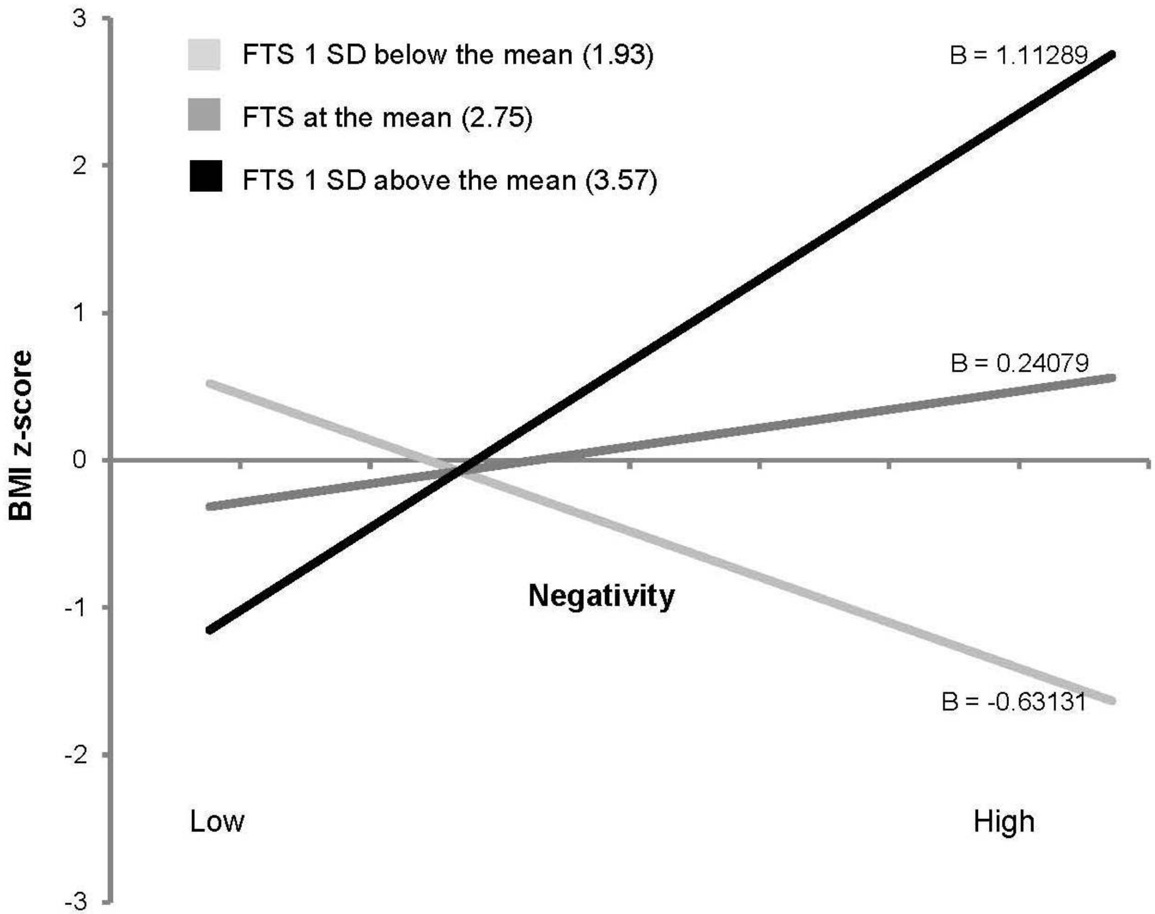
- Difficultness (Carey et al., 1988)
- Negative Emotionality (Hughes et al., 2008; Pulkki-Raback et al, 2005)
- Reward Sensitivity (Nederkoorn et al, 2006)
- Novelty Seeking (Hwang et al, 2006)

Research on Self-Regulation and Infant/Child Weight Outcomes

- Emotion Regulation
  - Inability to regulate frustration →
    - child and early adolescent BMI (Graziano et al., 2010, 2013)
- Behavioral Regulation
  - Difficulty delaying gratification →
    - greater change in child BMI (Francis & Susman, 2009)
    - more overweight (Seeyave et al., 2009)
  - Low inhibitory control →
    - greater change in child BMI (Anzman & Birch, 2009)
- Cognitive Regulation
  - Attention/persistence →
    - greater weight change for boys (Faith & Hitner, 2010)
  - Executive function →
    - Obese boys performed poorly (Cserjesi et al., 2007)

Research on Temperament, Parenting and Infant/Child Weight Outcomes

- Infant negative emotionality X low maternal self-efficacy
  → greater weight gain from 1 to 3 years (Anzman-Frasca et al., 2013)
- Infant difficult temperament X insensitive parenting
  → higher weight in school age children (Wu, et al., 2011)
- Youth difficult temperament X low maternal warmth
  → more likely to be obese (Zeller et al., 2008)
- Girls low inhibitory control X perceived food restriction
  → greater weight gain (Anzman & Birch, 2009)
- Infant/toddler negative emotionality X food to soothe
  → higher weight (Stifter et al., 2011)



Stifter, Birch, Anzman-Frasca & Voegtline, 2011

Potential Mediating/Moderating Parent Behaviors

- Formula feeding
- Insensitivity to infant feeding cues
- Introduction of solids
- Instrumental feeding
  - Using food to soothe
  - Using food to control behavior
- Feeding obesogenic foods
- Restrictive feeding
- TV exposure
- Sleep restriction
- Physical activity restriction

Measuring Temperament

Parent Ratings of Temperament

- Advantages
  - Ease of administration
  - Low cost – time and money
  - Provide a fuller, more ecologically-valid description
  - May capture infrequent behaviors
- Disadvantages
  - Parent ratings are subjective and influenced by other characteristics including parent personality
  - Different interpretation of questions
  - Different experiences with children for comparison purposes

Infant/Early Childhood Behavior Questionnaires (Rothbart)

- Reduce parental bias
  - Asks specific questions about behavior in specific contexts
  - Responses are about frequency of behavior vs. general disposition (e.g., My child is easily angered)

<u>During the past week, when being dressed or undressed during the last week, how often did the baby:</u>

1 2 3 4 5 6 7 X . . . . (39) squirm and/or try to roll away?
1 2 3 4 5 6 7 X . . . . (40) smile or laugh?
1 2 3 4 5 6 7 X . . . . (41) coo or vocalize?

<u>When approached by an unfamiliar person in a public place (for example a grocery store) how often did your child</u>

1 2 3 4 5 6 7 X . . . . (4) remain calm?
1 2 3 4 5 6 7 X . . . . (5) pull back and avoid the person?
1 2 3 4 5 6 7 X . . . . (6) cling to a parent?

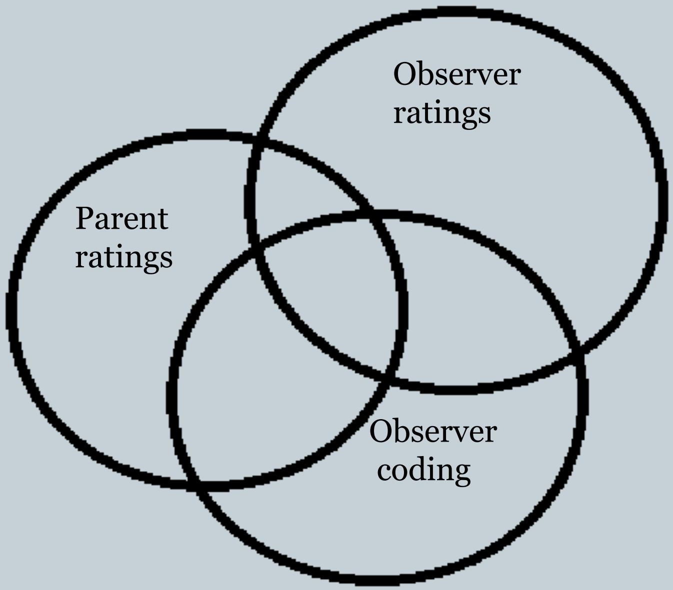
Observational Measures

- Laboratory/Home Observations
  - Tasks designed to elicit temperamental reactivity
    - Anger/distress to limitations – arm restraint, toy removal
    - Fear – stranger interaction, risk room
    - Positive affect – free play
    - Activity level – observer ratings, actigraphs
  - Tasks designed to measure regulation
    - Emotion regulation – self-soothing responses to emotional reactivity tasks, disappointment
    - Behavioral regulation – delay of gratification, go/no go
    - Cognitive regulation – attention shifting, executive function

Observational Measures

- Lab-TAB (Goldsmith)
  - Standardized observational measures of temperament
- Infant Behavior Record/Observation of Child Temperament (Bayley, Stifter)
  - Ratings by observers of child's behavior across lab or home visits
- Infant cry diary
  - 24 hour/3-5 day diaries of infant state including crying, fussing, awake, feeding, sleeping

Components of Variance



Implications for Prevention of Childhood Obesity

Conclusions	Recommendations
➢ Children affect their own development through their temperament	➢ Educating parents about the role of temperament in their child's development
➢ The ability to regulate reactivity emerges in infancy and becomes more mature during the preschool years	➢ Childhood obesity prevention should start as early as possible
➢ Parents are central to the development of self-regulation in their children	➢ Parents should be the target of obesity intervention
➢ Positive self-regulation development most likely results when the parents adjusts their behavior in accordance with their children's temperament	➢ Direct or "stealth" obesity programs that focus on self-regulation. Parents are interested in how to get their children to follow rules and standards

Thank you

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- Penn State Social Science Research Institute

Early Life Systems and Contexts to Support Families in Obesity Prevention

Elsie M. Taveras, M.D., M.P.H

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MassGeneral Hospital *for* Children℠

Overview

- Prevalence, consequences of, and disparities in childhood obesity
  - Trends among low income preschool age children
- Established early life risk factors and potential levers of influence
- Early life systems and contexts to support obesity prevention

Childhood obesity is prevalent and spares no age group (NHANES 2009-2010)

- 9.7% of infants and toddlers <2 years have a high weight-for-recumbent length (WFL >95th based on CDC charts); 8.6% based on World Health Organization >97.7th cutpoint
- 12.1% of children 2 – 5 years are obese (BMI ≥ 95th)
  - Highest prevalence among **non-Hispanic black boys** (20.5%) and **non-Hispanic black girls** (17%)
- 18.2% of children age 6 – 19 years are obese
  - Highest prevalence among **Mexican-American boys** (25.6%) and **non-Hispanic black girls** (26.1%)

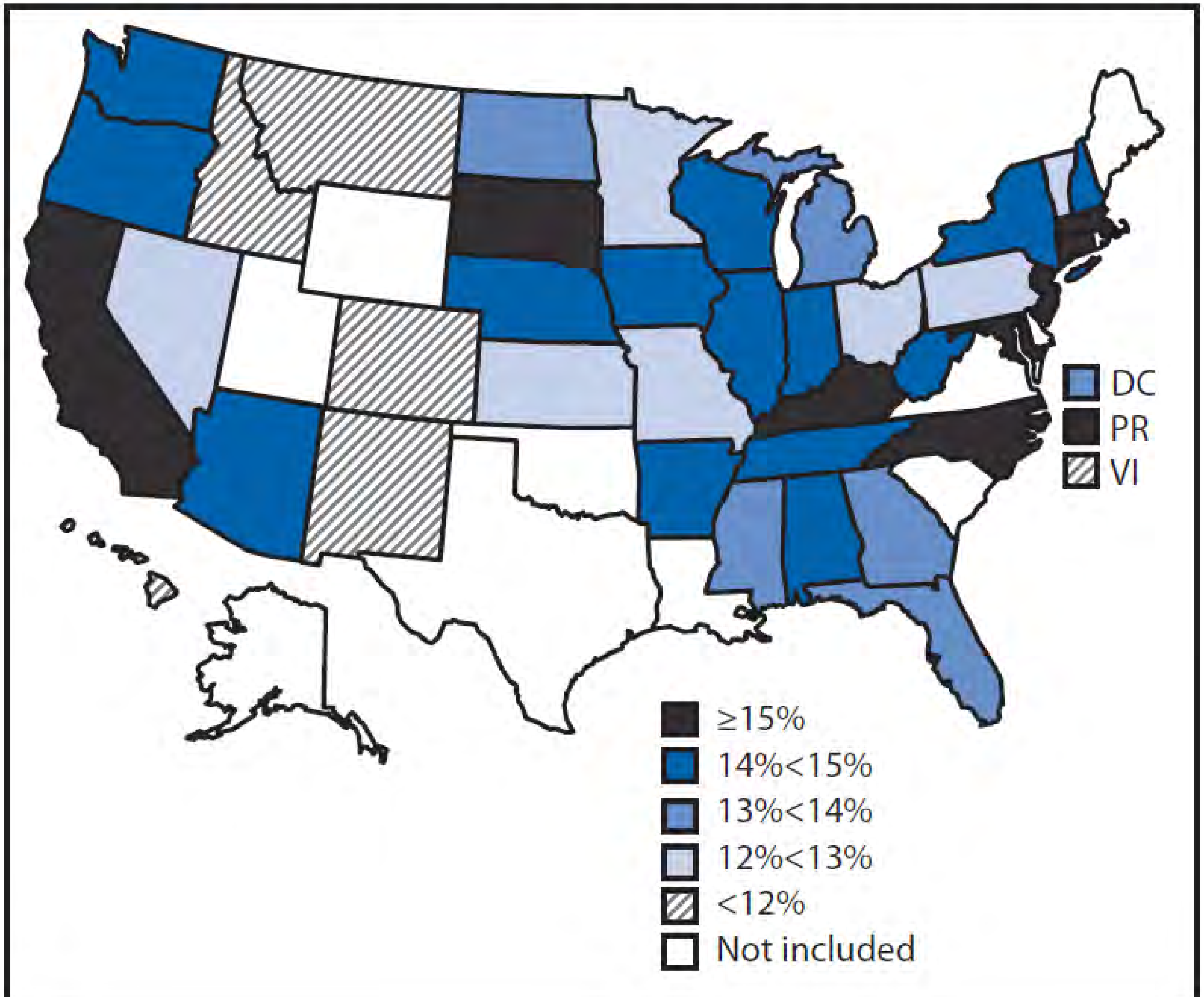
Childhood obesity disproportionately affects racial/ethnic minorities

- Overall, 9.7% of infants and toddlers are obese
  - 8.4% non-Hispanic white, 8.7% non-Hispanic black, **14.8% Hispanic**
- Overall, 12.1% of children 2 – 5 years are obese
  - 9.2% non-Hispanic white, **18.9% non-Hispanic black**, 16.2% Hispanic
- Overall, 18.2% of children age 6 – 19 years are obese
  - 15.2% non-Hispanic white, **25.7% non-Hispanic black**, 22.9% Hispanic

Racial/ethnic differences emerge early in life and persist throughout childhood

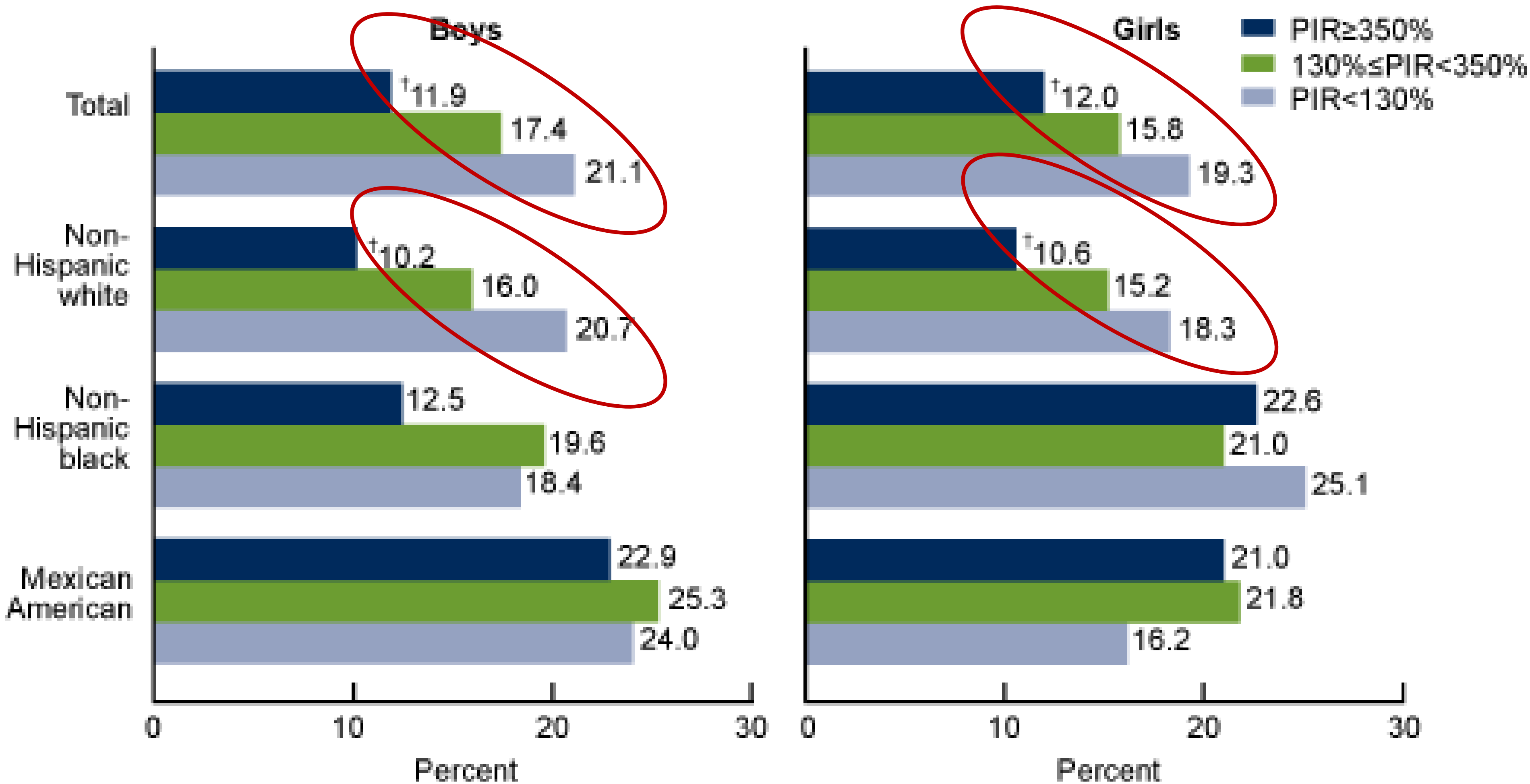
Prevalence of childhood obesity high among low-income preschoolers (PedNSS)

FIGURE 2. Prevalence of obesity among low-income, preschool-aged children — Pediatric Nutrition Surveillance System, United States, 2011



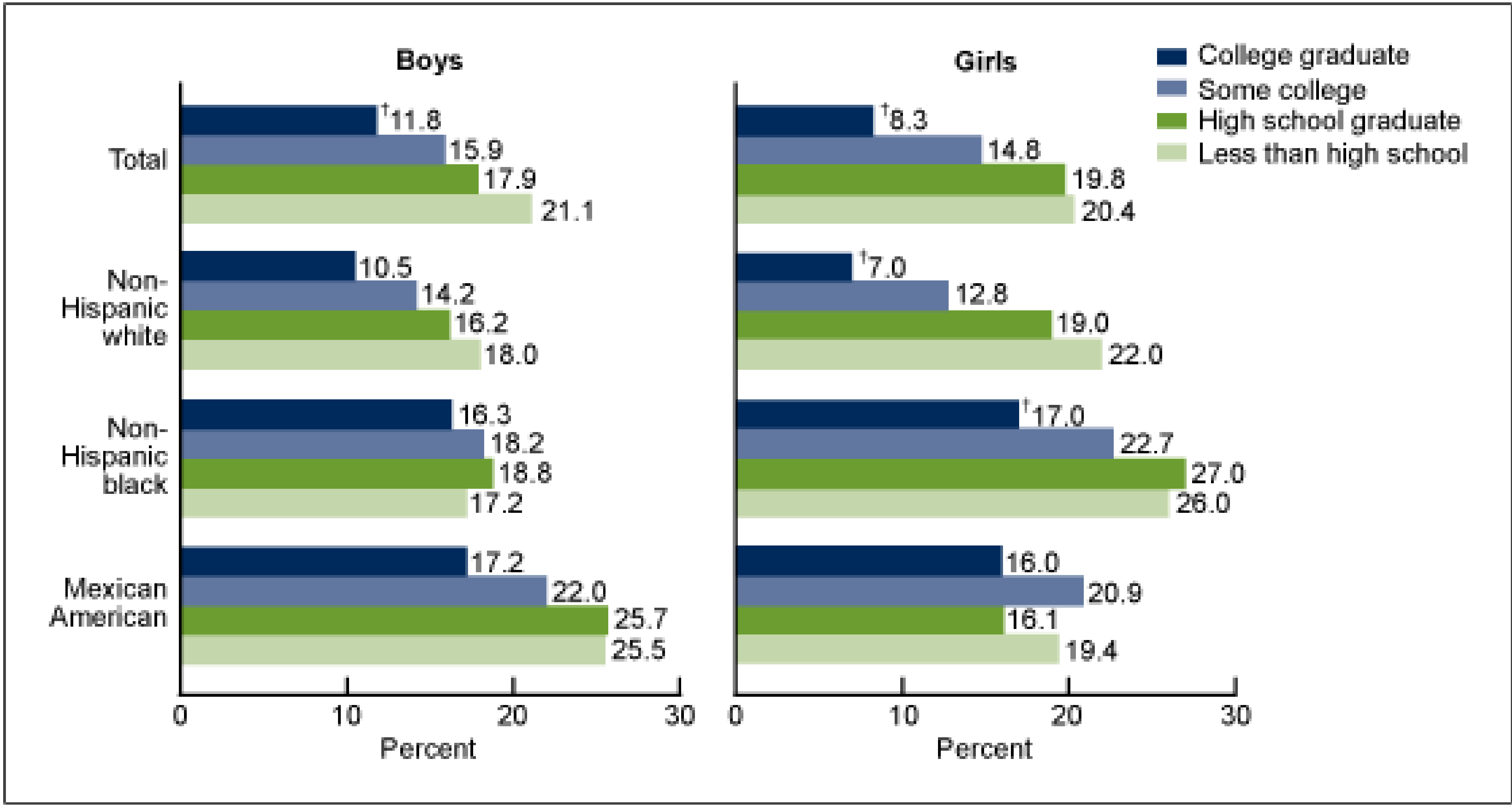
- State-based public health surveillance system monitors nutritional status of low-income, birth to 4 year olds;
- Data of 2-4 years old children in 2011: 14.4% obese (12.1% NHANES 2-5 y/o);
- 10 states had obesity prevalence ≥ 15%;
- Highest prevalence Puerto Rico (17.9%)

Complicated socioeconomic story.....



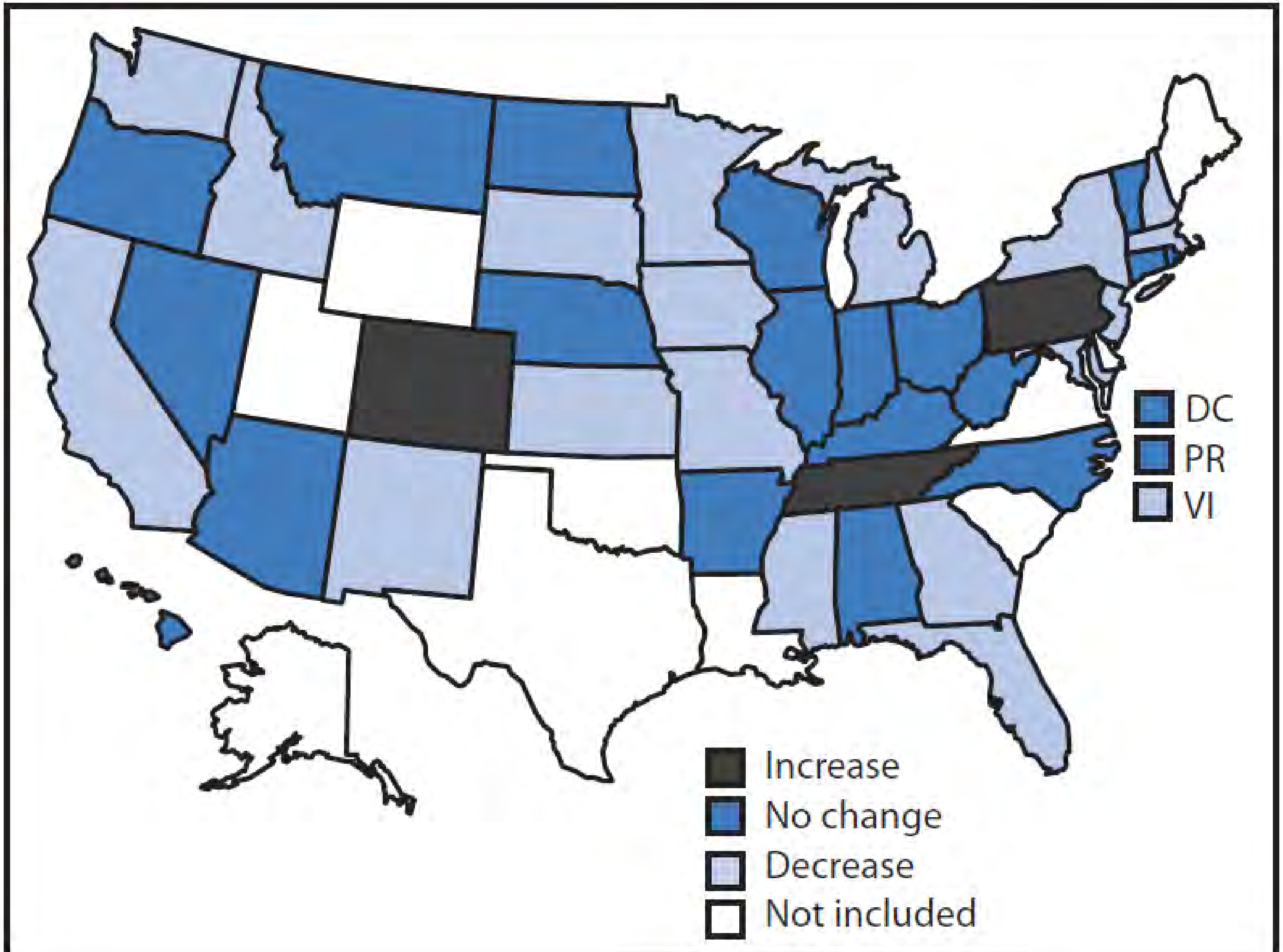
- Among non-Hispanic white children and adolescents, the prevalence of obesity increases as income decreases

Complicated socioeconomic story…..



- Inverse relationship between obesity prevalence and education of household head

Decreases in obesity among low-income preschoolers, 2008-2011



- 19 states/ territories experienced a decrease

Reasons?

- Updates in Women, Infants, and Children
- New nutrition and physical activity standards for early child care programs
- Increased support for breastfeeding mothers

Signs of progress but not yet closing disparities gaps

- Despite signs of progress, socioeconomic, geographic, and racial and ethnic disparities in obesity rates are persisting in many places
  - Mississippi reported a significant drop in overweight and obesity only among White students.
  - In NYC, obesity decreases were smaller among populations at higher risk for obesity, including Black or Hispanic children and students in high-poverty schools

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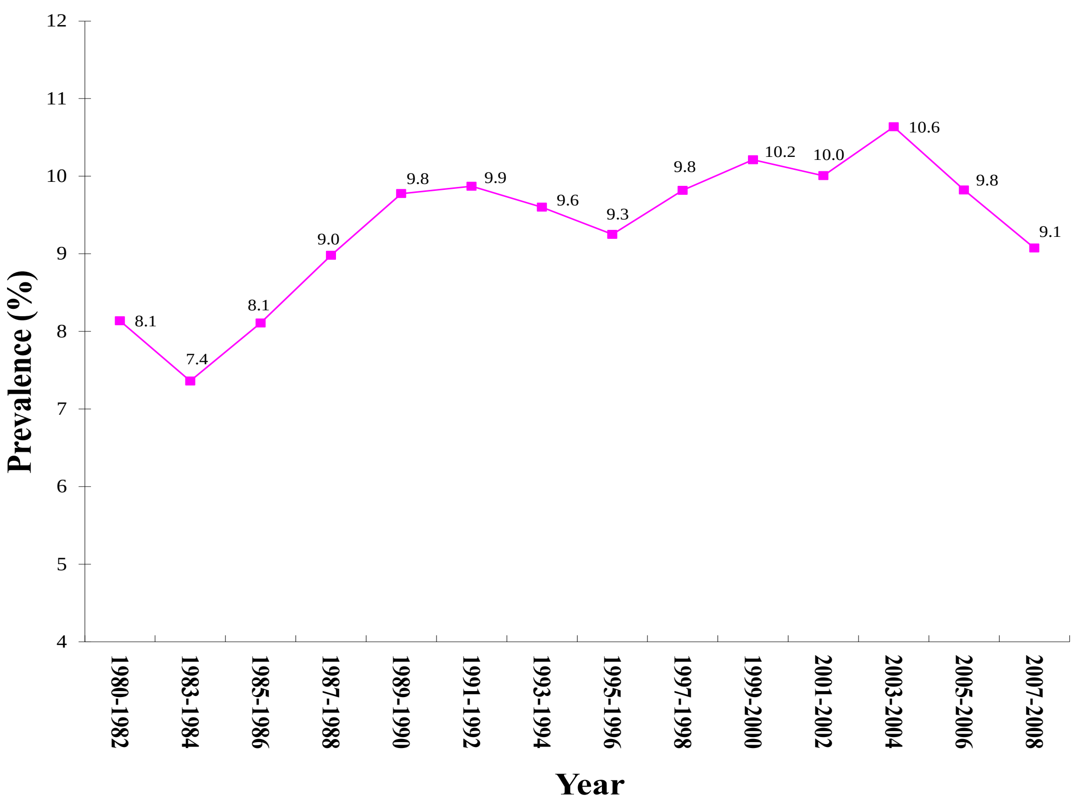
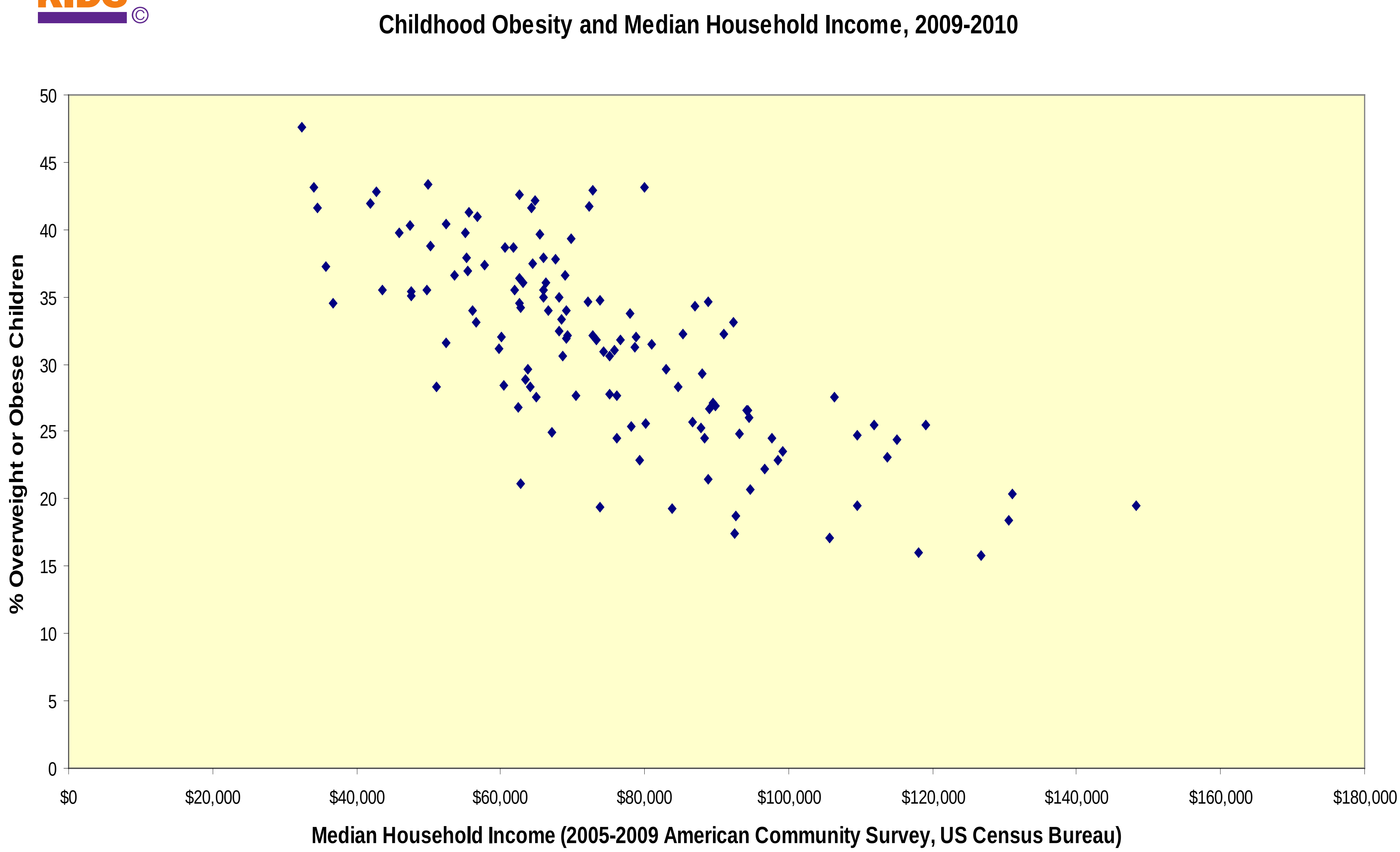
Decreasing Prevalence of Obesity Among Young Children in Massachusetts From 2004 to 2008

Xiaozhong Wen, Matthew W. Gillman, Sheryl L. Rifas-Shiman, Bettylou Sherry, Ken Kleinman and Elsie M. Taveras



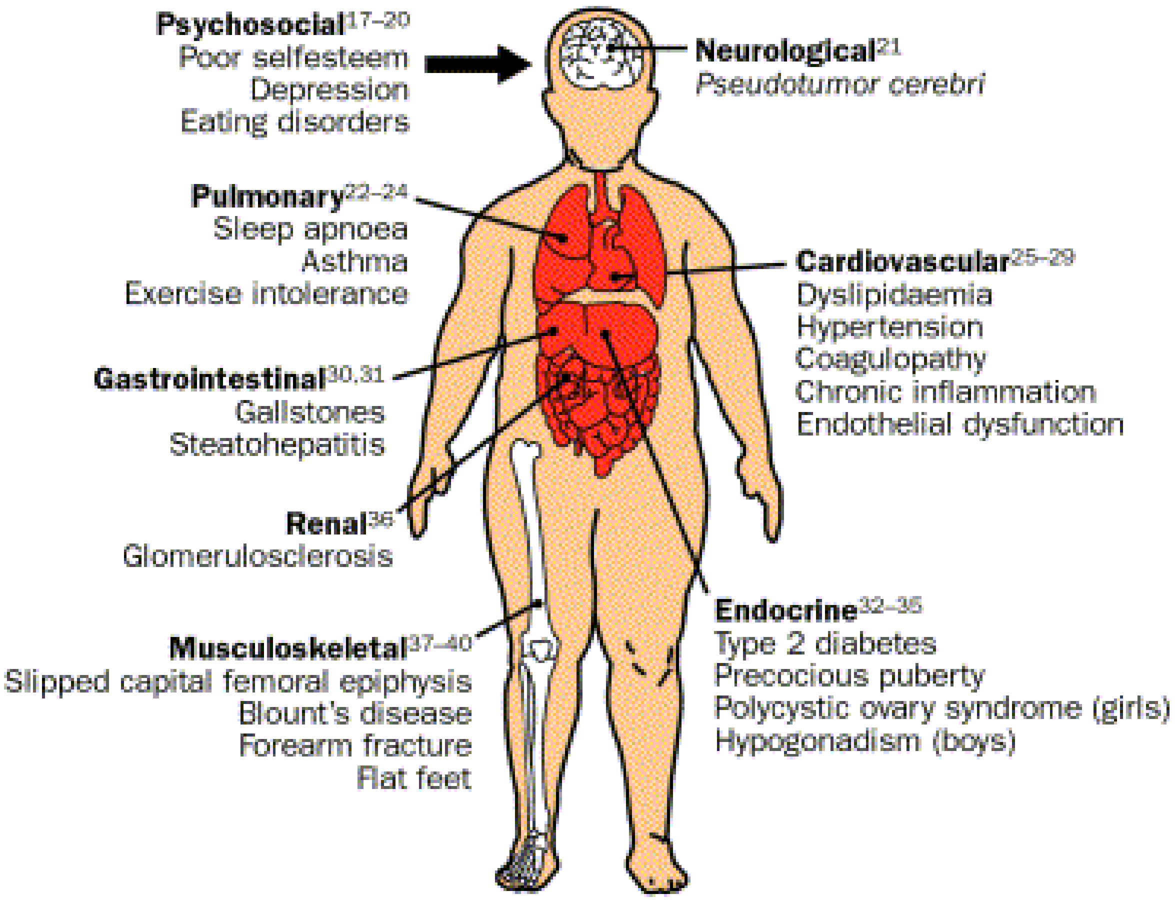
- Among children 0-6 years in MA, the prevalence of obesity substantially decreased during 2004–2008.
- Decrease was smaller among children insured by Medicaid than children insured by non-Medicaid health plans

Childhood Obesity is Not Randomly Distributed Among our Communities



Childhood obesity is of consequence

- Childhood obesity is associated with both short- and long-term adverse outcomes and may presage reduced life expectancy

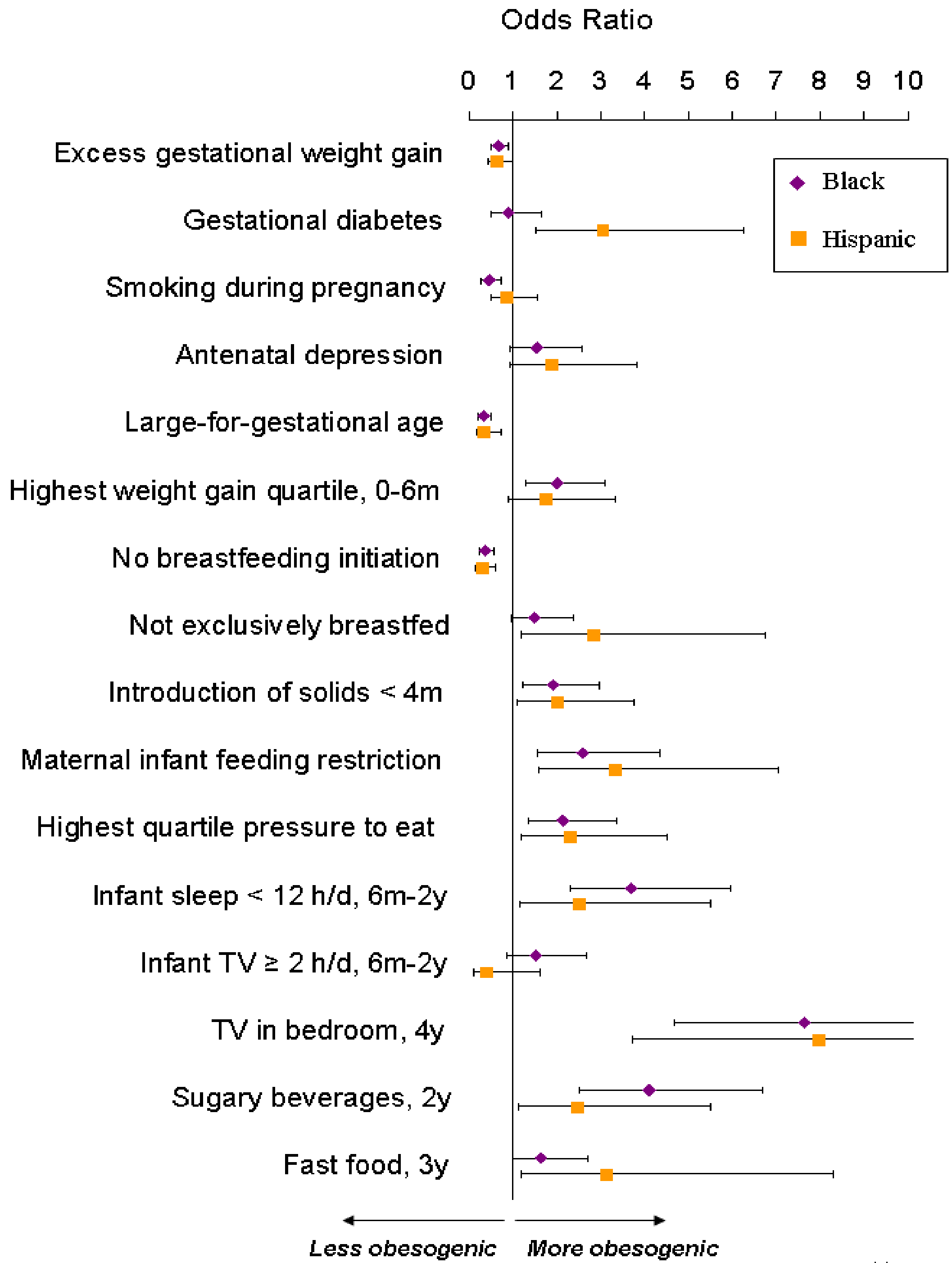


Summary of Evidence & Recent Trends

- Childhood obesity is highly prevalent, spares no age group, and is of consequence;
- Obesity disproportionately affects racial/ethnic minorities;
- Among non-Hispanic white children, obesity prevalence increases as household income and education of head of household decreases – inconsistent association among non-white children;
- Progress has been made in obesity reductions among low-income preschool age children;
- Not yet closing the gap in disparities with evidence to suggest that the highest risk children have not benefited equally from national obesity prevention efforts.

Selected Determinants of Childhood Obesity

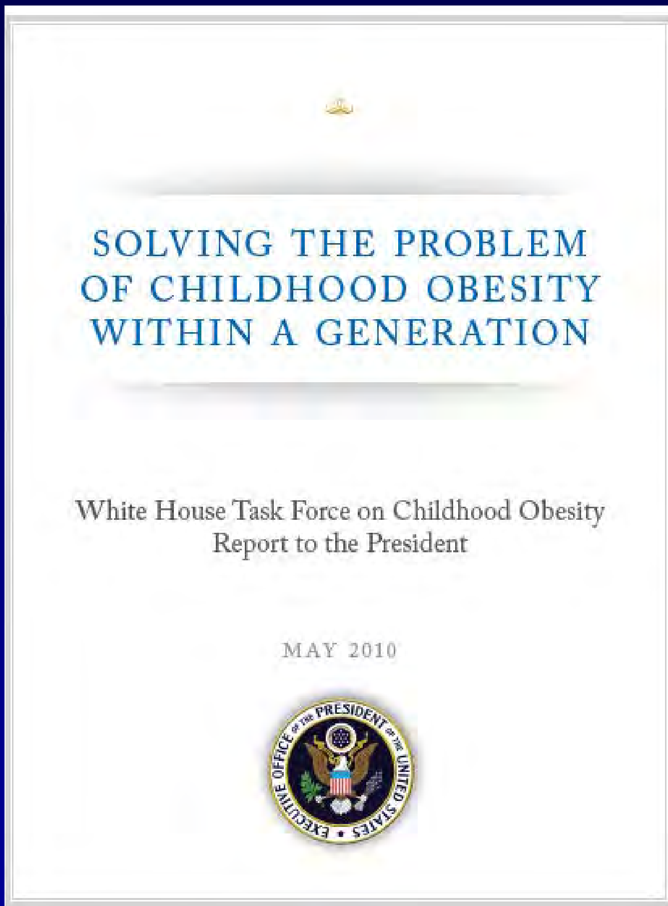
- Gestational weight gain (Oken, et al. 2006) and GDM
- Maternal smoking during pregnancy (Oken et al. 2006)
- Rapid infant weight gain (Taveras et al. 2009)
- Breastfeeding (Gillman et al. 2001, Taveras et al. 2005)
- Sleep duration and quality (Taveras et al. 2008)
- Television viewing (Taveras et al. 2007) & TV sets in bedrooms
- Food supply & marketing environments
- Responsiveness to infant hunger and satiety cues (Hodges and Fisher, 2008)
- Parental feeding practices, eating in the absence of hunger (Taveras, 2006, Fisher and Birch, 1998 & 2009)
- Portion sizes (Fisher et al. 2008)
- Fast food intake (Taveras et al. 2006)
- Sugar-sweetened beverages
- Physical activity
- Socio-cultural, recreation, & transport environments



- Racial/ethnic differences exist in many early life risk factors for childhood obesity

Taveras, et al. *Pediatrics; 2010*

White House Task Force Report on Childhood Obesity, May 2010

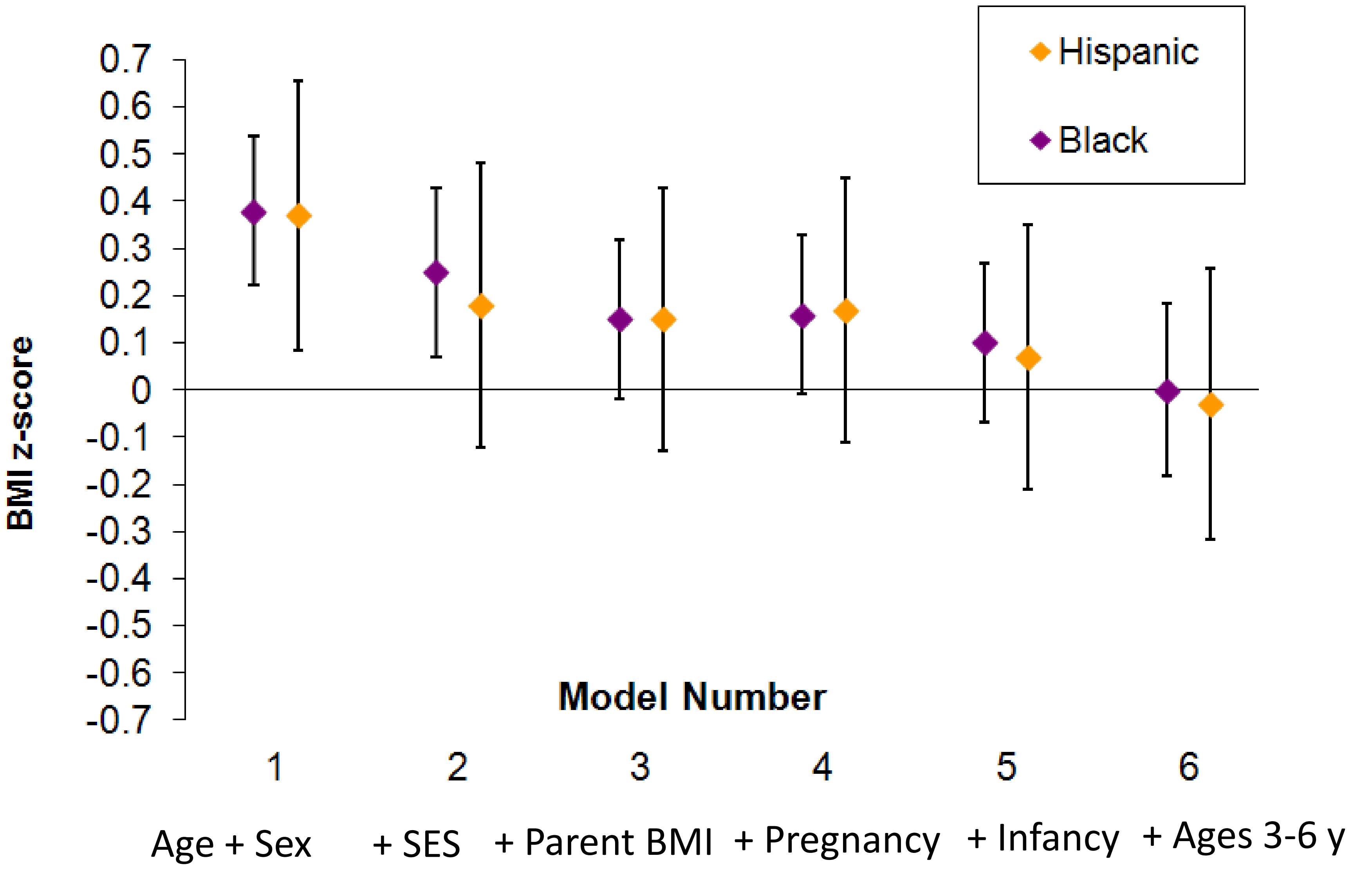


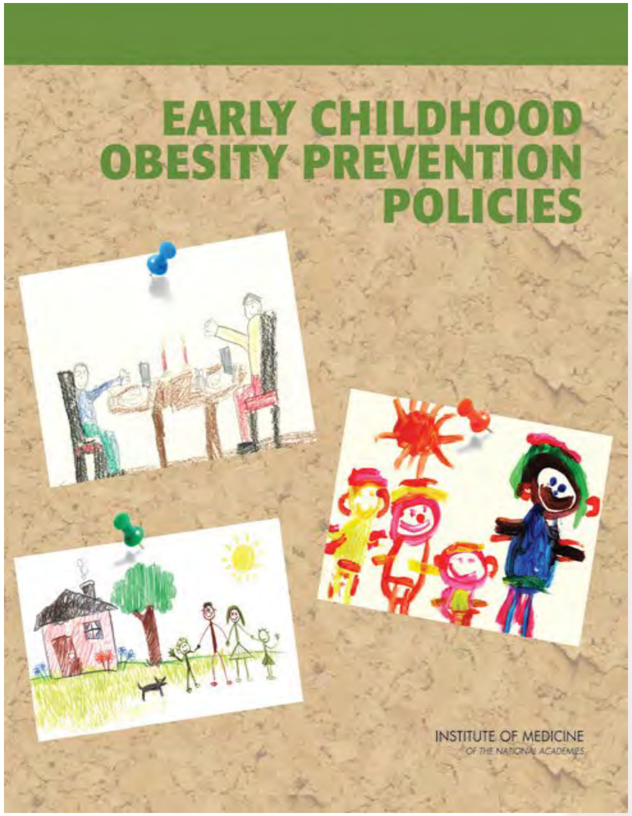
"Racial and ethnic differences in obesity may be partly explained by differences in risk factors during the prenatal period and early life."

Original Investigation

Reducing Racial/Ethnic Disparities in Childhood Obesity

The Role of Early Life Risk Factors





Early Childhood Obesity Prevention Policies

Supported by the Robert Wood Johnson Foundation

The report is available for free download at: http://iom.edu/obesityyoungchildren.

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Advising the nation / Improving health

Why focus on early childhood?

- Early childhood lends itself to effective preventive interventions, with opportunities each year to alter the lifetime weight gain trajectory of a new birth cohort.
- Infancy and the preschool years are periods of sensitivity to environmental influences, maximum societal care and protection, multiple settings for intervention, and, changeability.
- Sustained changes in obesogenic behaviors require altering the environments that facilitate healthful choices, especially among young children, who have little individual control over their social ecology.

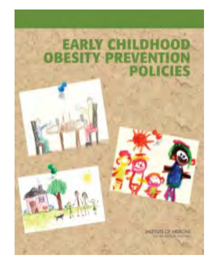
IOM Targets for Pregnancy & Existing Systems

Pregnancy:

- Good pre-, post-, and inter-conception care
- Enter pregnancy at a healthy weight;
- Gestational weight gain based on IOM recommendations;
- Appropriate management of GDM;
- No smoking;
- Prepare to breastfeed

Systems, Policies, & Contexts:

- Healthcare system: Obstetrics, Hospitals, and Women's Health
- Public health system:
  - Women, Infants, and Children Program and Supplemental Nutrition Assistance Program
  - Maternal, Infant, Early Childhood Home Visitation Program
- Community:
  - Safe, walkable environments
- Family systems:
  - Fatherhood Initiatives
- Individual & Home



Leveraging Early Life Systems:
What would an effective system look like?

- OB provider trained in IOM/ACOG GWG policies;
- OB uses electronic records to track GWG & GDM;
- Referred to WIC for nutrition counseling;
- Provided a referral to OutdoorRx;
- Population health manager enrolls family in Text4Baby, Fatherhood support, Home Visiting;
- Local supermarket has healthy food endcaps;
- Local community policies support safety, walkability, access to Farmer's markets and water, and active transportation;
- Community health center offers group support classes and parenting preparation;
- Mother delivers in a Baby Friendly hospital;
- EHR automatically links family units after delivery

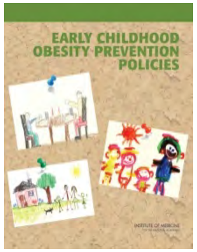
IOM Targets for Infancy & Existing Systems

Infancy:

- Prolonged breastfeeding;
- Responsive feeding;
- Appropriate timing of introduction of complementary foods;
- High quality sleep;
- Avoid accelerated crossing of growth percentiles;
- Allow ability to develop motor skills;
- Avoid exposure to food marketing

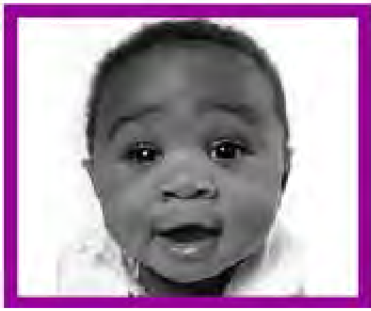
Systems, Policies, & Contexts:

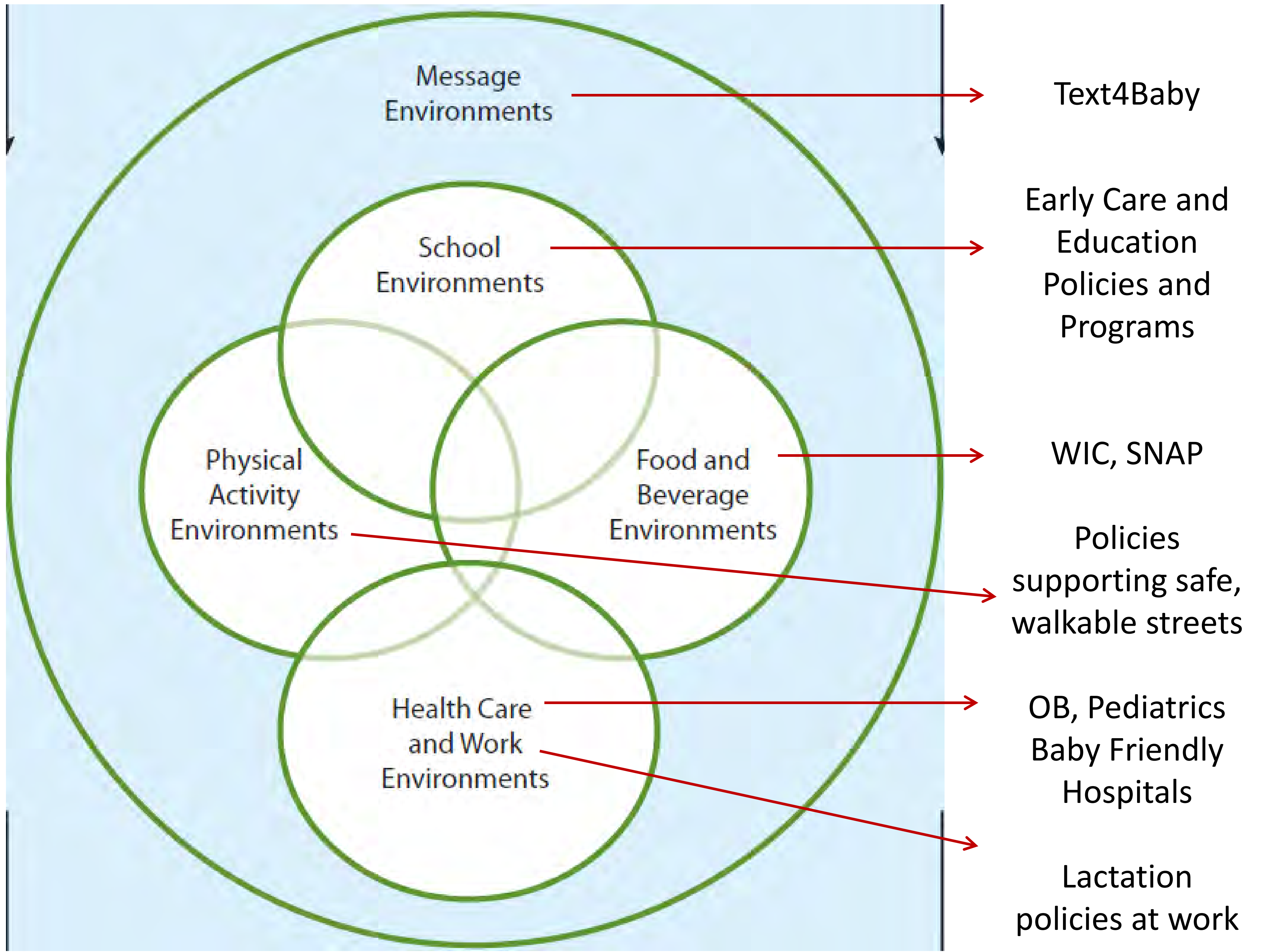
- Healthcare system: Pediatrics
- Public health system:
  - WIC
  - Home Visitation Program
- Early Care & Education
  - Nutrition, physical activity, screen, and sleep policies
- Worksite:
  - Lactation policies
- Family systems:
  - Fatherhood Initiatives
- Individual & Home



Postpartum & Infancy

- Mother re-connected with primary care for inter-conception care and screening;
- Lactation support offered in hospital, Pediatric primary care, and community;
- Pediatrician trained to use WHO growth charts and knows red flags for accelerated weight gain;
- Referred to WIC; Home Visiting Program;
- Early care and education provider has policies in place that support healthy feeding, activity, screen time, and sleep behaviors




Message Environments
Text4Baby
School Environments
Early Care and Education Policies and Programs
Physical Activity Environments
Food and Beverage Environments
WIC, SNAP
Policies supporting safe, walkable streets
Health Care and Work Environments
OB, Pediatrics Baby Friendly Hospitals
Lactation policies at work

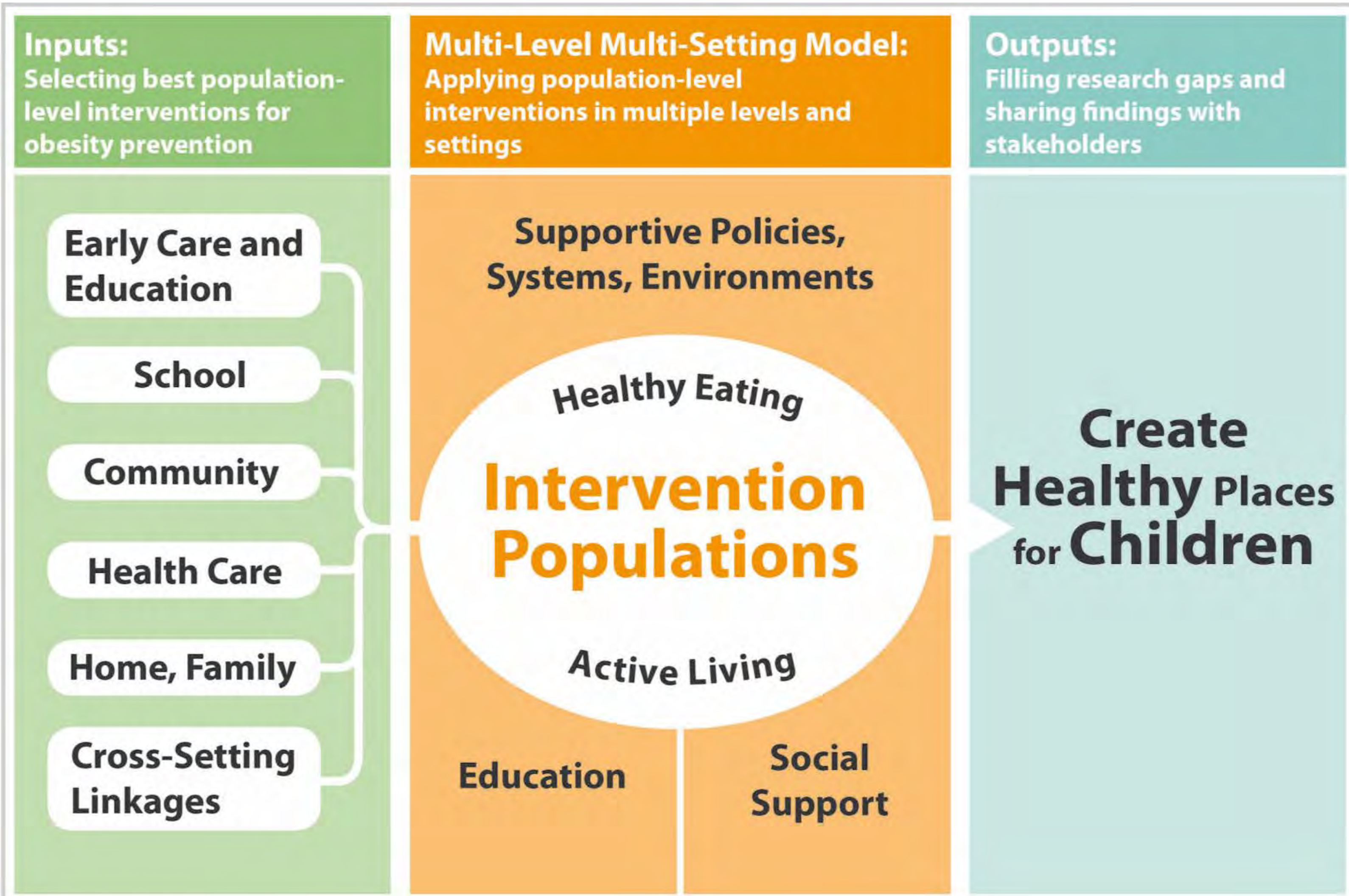
Few existing systems-level interventions under age 2 but several opportunities.....

- Several ongoing trials but few that are multi-sector or multi-level;
- Home Visiting: Research agenda from the Home Visiting Research Network of Johns Hopkins (http://www.hvrn.org/)
- WIC: IOM Report – Planning a WIC Research Agenda, (http://www.iom.edu/Reports/2010/Planning-a-WIC-Research-Agenda.aspx)
  - RFA from the USDA Center for Collaborative Research on WIC Nutrition Education Innovations: letters of intent due Dec 16 (https://www.bcm.edu/research/centers/childrens-nutrition-research-center/wiccenter/home)
- Home and Family Based Approaches for the Prevention or Management of Overweight or Obesity in Early Childhood (R01): http://grants.nih.gov/grants/guide/pa-files/PA-13-153.html

Summary

- Search for modifiable targets of interventions in early life
- Examine early origins of racial/ethnic and socioeconomic differences
- Leverage existing early life systems to deliver preventive interventions based on the best available evidence
- Pay close attention to equity in national obesity prevention efforts

Multi-sector, population-level strategies hold the most promise for obesity prevention



Foltz JL, et al. 2012.
Annu. Rev. Nutr. 32:391–415

Physical Activity & Sedentary Behavior in Infants and Toddlers

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General Outline of Talk:

- What is currently known about physical activity and sedentary behavior during the first 24 months of life?
- How does motor behavior emerge over 24 months?
- Physical activity exposures to consider during this age span
- Critical research questions

What is Currently Known About Physical Activity During the First 24 Months of Life?

- We currently know very little about physical activity (PA) in infants and nothing about the intensity of their activity.

- We do know a little more about PA in toddlers (1-2 years) once they begin to walk but I do not trust the data and conclusions reported on the intensity and time spent in sedentary, light, moderate, and vigorous activity.
- So, what do we know?

What is Currently Known About Physical Activity During the First 24 Months of Life?

1. It appears from several studies that there are no gender differences in PA during this age span (Cossette, Malcuit, & Pomerleau, 1991; Hauck, 2012; Hnatiuk, Rogers, et al, 2012)

2. Most recorded activity in infants occurs in short intermittent bursts (Cardon G, et al, 2011) requiring objective measurement.

Hauck (2012) measured physical activity monthly in 27 infants beginning at one month of age through six months of age employing accelerometers on the right ankle and wrist.

Average activity counts per minute recorded monthly included:

	Mo 1	Mo 2	Mo 3	Mo 4	Mo 5	Mo 6
A	59 (31)	85 (35)	95 (29)	96 (39)	114 (49)	124 (46)
W	71 (48)	113 (78)	124 (70)	114 (85)	120 (54)	128 (69)

Hauck (2012) – more active infants had significantly lower peak weight velocity over 6 months.

Hnatiuk et al (2012) reported an interesting study on 19 month old toddlers:

1. 4 days of PA monitoring are needed to derive a reliable (.70) estimate of PA. No mention of sedentary level.
2. Mid morning (8-10) and mid afternoon (4-5)were more active periods while early morning and after 5 pm were least active.

Tennefors ,et al (2003) found an inverse relationship between PA and total body fat suggesting that infants with a higher percent body fat displayed lower levels of PA.

Wells & Ritz, (2001) report that higher PA levels in infants were associated with lower skinfold thickness.

With the dearth of information available on infants and toddlers, it is difficult to determine the amount, intensity, or type of PA needed to promote their health.

During the first 24 months of age, sedentary behavior is primarily associated with screen time & infant positioning device use.

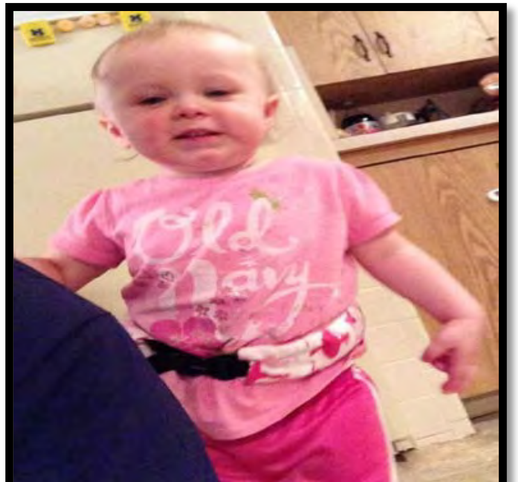
Infants are already exposed to watching television and DVDs and screen time increases dramatically with age.

Caregivers place their infants in infant positioning devices which frequently constrain leg movements.

Hauck (2012) reported that mothers with less formal education used these devices more frequently.

Studies by Van Cauwenberghe, et al(2011) and Hauck(2012) support the view that infants and toddlers can wear accelerometers with parents reporting little problem with their use. They also suggest the use of activity counts/minute as the measure of activity.

Hauck's (2012) protocol included the following procedure:



How Do Motor Behaviors Emerge Over the First 24 Months?

Primitive reflexes, spontaneous movements, gross motor behaviors.

Walking at 11-14.5 mo and running 6-7 months later.

Dynamic Systems Principles- Humans are thermodynamic systems (Thelen, Corbetta, & Spencer, 1996).

Attractors-preferred patterns of movement behavior based on the status of your various subsystems—walking

Control parameters or facilitators-internal or external

How Do Motor Behaviors Emerge Over the First 24 Months?

Some evidence exists that overweight or obesity during infancy is associated with delays in motor behavior (Benjamin-Neelon et al, 2011; Slining et al, 2010).

High levels of subcutaneous fat appear to be related to delayed motor development (Slining et al, 2010) in infants.

In the Hauck (2012) longitudinal study, she reported that infants who displayed more physical activity in their legs and arms acquired motor behaviors significantly earlier.

Amount of time an infant is exposed to tummy time (prone positioning) appears to be related to the age of onset of prone specific motor milestones but not other motor milestones (Kuo et al, 2008).

No data are available to suggest an appropriate dose of tummy time—IOM suggests daily supervised tummy time.

Physical Activity Exposures to Consider During this Age Span

General Strategies

1. PA interventions must be combined with other successful public health strategies (maternal weight, infant sleep, infant feeding practices, smoking) to reduce rapid weight gain during infancy.
2 PA interventions must be developed to involve parents at home and other child care professionals during the day.
3. No potential risks have been reported with increasing PA during the first 24 months of life.

Physical Activity Exposures to Consider

4. Interventions that involve regular home visits are more successful in keeping parents motivated & to answer questions
5. Parents will be much less motivated to intervene without a diagnosis of a health concern (Angulo-Barroso, et al, 2010).

<u>Specific PA Exposures</u>

1. Newborn stepping - beginning by 2-4 weeks of age (Ulrich & Hauck, In Press).

Physical Activity Exposures to Consider

2. Supervised Tummy Time (Kuo, et al, 2008) beginning once the infant can clear her face from the surface. Usually by the second month. Gradually increase daily time with a goal of a minimum of 60 minutes distributed throughout the day

3.Bouncing infant on your thighs to help strengthen their legs. This can begin by 3 months of age.

4. Conjugate Reinforced Kicking beginning by 4 months & continuing until the infant gets bored (Rovee & Rovee, 1969)

Physical Activity Exposures to Consider

Bouncing

Kicking Device

Physical Activity Exposures to Consider

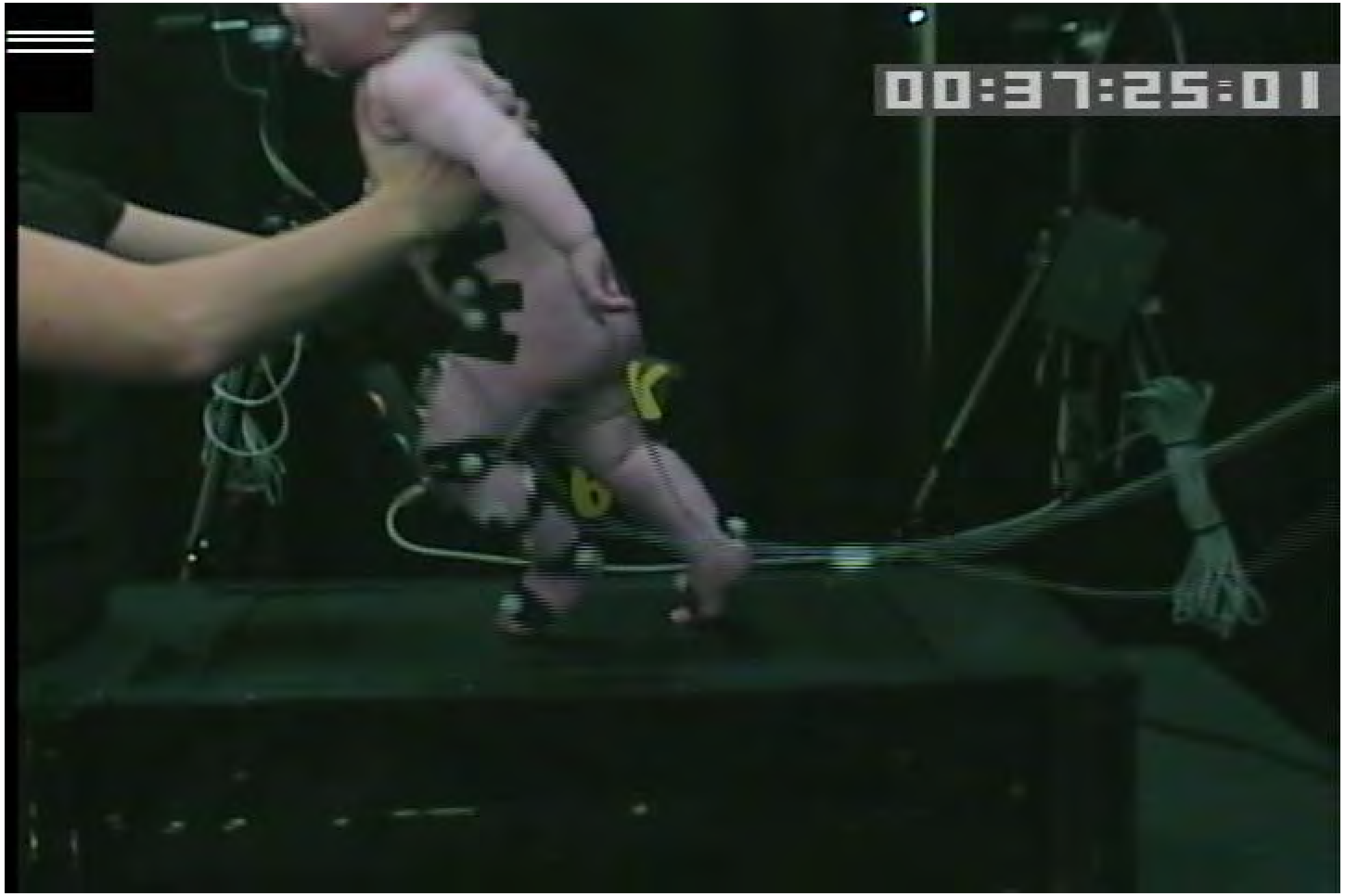
Spontaneous Kicking vs Conjugate Reinforced Kicking

Physical Activity Exposures to Consider

5. Treadmill Stepping beginning at 4-5 months (Thelen & Ulrich, 1991; Ulrich, Ulrich, et al, 2001; Ulrich, Lloyd, et al, 2008).

Thelen and B. Ulrich (1991) demonstrated that infants as young as 2 months can take steps when supported on a slow moving treadmill (less than ½ mile per hour). Their longitudinal study demonstrated that without training, all infants were stepping well by 4 and 5 months.

Example infant stepping at 6 months



General Results of Our Treadmill Studies

1. No injuries or negative effects on physical growth (Angulo-Barroso et al 2010; Ulrich, Ulrich, et al, 2001; Ulrich, Lloyd, et al, 2008).
2. Parents implement training with good fidelity in their homes & like the structure.
3. Treadmill trained infants acquire most locomotor behaviors significantly earlier than the control group (Ulrich, Ulrich, et al, 2001; Ulrich, Lloyd, et al, 2008).

4. Treadmill trained infants became more physically active over the intervention period compared to the control group and this lasted up to 6 months post training (Angulo-Barroso, et al 2008; 2010).

Critical Research Questions

1. What is the appropriate protocol for measuring PA in infants and toddlers?

2. What is the typical level of PA observed in infants and toddlers ? Does it differ across racial and ethnic groups?

3. Does increased physical activity mediate the rate of weight gain and fat gain in infants and toddlers and does it influence patterns of sleep?

Critical Research Questions

4. What dose of physical activity is needed daily to achieve health benefits?

5. Need to include infants with a disability known to be at higher risk of early obesity in our research.

6. Must go beyond correlation studies.

Conclusion

Research clearly recognizes the critical contribution of early life exposures to a child’s health and development (Monasta et al, 2010; Thelen & Smith, 1996).

Increasing infant ‘s & young children’s daily exposures to physical activity is an important component to any serious early childhood obesity prevention program (Wojcicki & Heyman, 2010)

Questions ?

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