Comparing Outcomes in Pediatric Obesity Studies
Two Illustrative Examples

Reneé H. Moore, PhD
Assistant Professor of Biostatistics

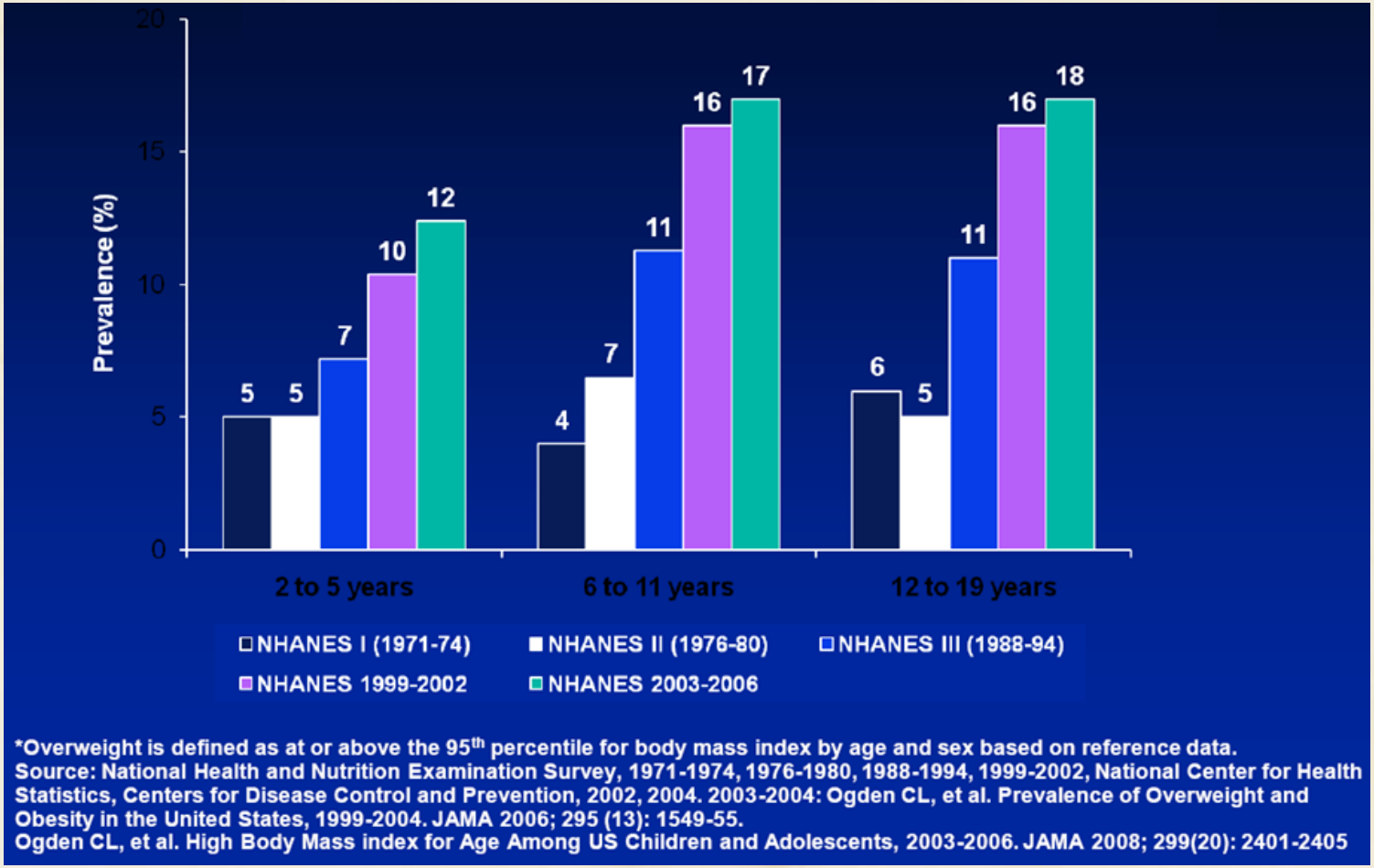
Penn Medicine

CCEB · DBE
Center for Clinical Epidemiology & Biostatistics
Department of Biostatistics & Epidemiology

Outline

- Background
  - Outcomes commonly used to assess changes in weight status in children
  - CDC construction of BMI centile and BMI z-score
- Compare Weight Status Outcomes
  - Adolescent weight loss RCT
  - Prospective longitudinal study of children (3- 14 yrs)
- Summary

Trends in Overweight* Prevalence (%), Children and Adolescents, by Age Group, U.S., 1971 - 2006



*Overweight is defined as at or above the 95th percentile for body mass index by age and sex based on reference data.
Source: National Health and Nutrition Examination Survey, 1971-1974, 1976-1980, 1988-1994, 1999-2002, National Center for Health Statistics, Centers for Disease Control and Prevention, 2002, 2004. 2003-2004: Ogden CL, et al. Prevalence of Overweight and Obesity in the United States, 1999-2004. JAMA 2006; 295 (13): 1549-55.
Ogden CL, et al. High Body Mass index for Age Among US Children and Adolescents, 2003-2006. JAMA 2008; 299(20): 2401-2405

Background: Outcomes

- Both Intervention and Weight Loss Studies require an accurate measure of change in weight status
- Adult studies outcome: change in weight
- Pediatric studies: children are growing
  - No Consensus on best outcome

Weight Status Outcomes

Pediatric studies: children are growing

- No Consensus on best measure
  - Weight
    - % Ideal Weight (ratio of child wgt/ ideal body wgt)
  - BMI = weight (kg)/ height^2 (m^2)
  - BMI percentile
    - age & gender specific
  - BMI z-score
    - age & gender specific

BMI percentile & BMI z-score

- 2000 CDC Growth Charts (Kuczmarski et al 2004)
  - Developed growth curves (height, weight, BMI, etc.) to help clinicians identify children that are underweight or overweight
    - "routine monitoring of growth in infants, children, and adolescents" (Ogden et al. Pediatrics 2002)
  - Great improvement over 1977 National Center for Health Statistics (NCHS) growth charts

BMI percentile & BMI z-score

- 2000 CDC Growth Charts (Kuczmarski et al 2004)
  - Cross-sectional pooled data
    - May not reflect typical age-related patterns of change
    - Data collected prior to obesity epidemic
      - collected in a series of 5 surveys 1963-1994
  - Many of the Age(month) -specific BMI distributions were skewed, so BMI percentiles and z-scores correspond to transformed distributions
    - Different transformations at different ages → may not be best measures of longitudinal change

Question of Interest

- Use two illustrative studies to assess differences in
  - Weight, BMI, BMI centile, and BMI z-score

Does one BMI measurement better capture changes in weight status?

Illustrative Example 1
Adolescent Weight Loss Study

- PI: Robert Berkowitz, MD of CHOP/Penn Medicine
- Double-blinded RCT
- 82 adolescents randomized to behavior therapy (BT) or BT + drug (sibutramine)
- 13 – 17 years old with baseline BMI 32 – 44
- 6 month treatment period

JAMA 2003

Is the mean change in weight status different between the two treatment groups?

Simple Linear Regression*

Outcome	Mean Δ (SE)		P-value	R-Square
	Placebo	Sibutramine		
Δ Weight (lbs)	-8.00 (2.36)	-18.56 (2.17)	0.002	13.1%
Δ BMI	-1.78 (0.41)	-3.38 (0.37)	0.005	11.1%
Δ BMI centile	-0.48 (0.24)	-1.06 (0.22)	0.08	4.8%
Δ BMI z-score	-0.14 (0.03)	-0.24 (0.03)	0.02	7.8%
Percent Δ BMI	*-4.73 (1.10)*	*-8.99 (0.99)*	*0.005*	*10.8%*
Δ Weight adjusted Age, Height & Gender	*-7.18 (2.41)*	*-17.60 (2.27)*	*0.002*	*17.4% adj 12.5%*
Δ BMI adjusted Age & Gender	*-1.82 (0.42)*	*-3.33 (0.39)*	*0.009*	*13.5% adj 8.2%*

* when needed appropriate transformations considered

What makes BMI percentile different?

- Males Summary Statistics

Variable	Mean	Std Dev	25th Pctl	Median	75th Pct
Weight Baseline	228.50	36.87	191.90	229.45	253.60
Δ Weight	-9.86	13.82	-21.60	-7.15	-1.90
BMI Baseline	37.11	2.93	34.72	37.72	39.16
Δ BMI	-2.47	2.24	-3.45	-2.19	-0.92
BMI centile Base	99.40	0.28	99.26	99.52	99.60
Δ BMI centile	-0.36	0.48	-0.38	-0.23	-0.12
BMI z-score Base	2.54	0.15	2.44	2.59	2.65
Δ BMI z-score	-0.15	0.15	-0.20	-0.12	-0.06

Least amount of variability in BMI centile– “ceiling effect”

What makes BMI percentile different?

- Females Summary Statistics

Variable	Mean	Std Dev	25th Pctl	Median	75th Pct
Weight Baseline	226.36	31.19	200.70	227.60	251.00
Δ Weight	-15.55	14.81	-24.60	-14.40	-2.60
BMI Baseline	38.03	4.10	34.32	37.97	41.33
Δ BMI	-2.75	2.51	-4.15	-2.58	-0.81
BMI centile Base	99.05	0.50	98.66	99.25	99.43
Δ BMI centile	-0.99	1.52	-0.98	-0.47	-0.15
BMI z-score Base	2.39	0.20	2.21	2.43	2.53
Δ BMI z-score	-0.22	0.20	-0.27	-0.18	-0.07

Least amount of variability in BMI centile– “ceiling effect”

What makes BMI percentile different?

Variability in Scale of Measures

Baseline Weight	Δ BMI Centile	Δ Weight	Δ BMI z	Δ BMI
185	-0.80	-3.2	-0.13	-0.82
208	-0.80	-8.1	-0.27	-3.89
223	-0.32	-20.2	-0.20	-4.32
183	-0.32	-2.6	-0.10	-1.01
260	-0.30	-3.8	-0.15	-2.29
250	-0.30	-8.8	-0.19	-4.16
268	-0.09	3.4	-0.07	-1.00
263	-0.09	-1.8	-0.10	2.40

Adiposity in Adolescents: Δ in Actual BMI works better than Δ in BMI z score for Longitudinal Studies

Berkey & Colditz 2006 Annals Epi

TABLE 1. Changes in BMI and weight resulting from change of one z unit during 1 year on the Centers for Disease Control and Prevention BMI charts: boys from age 11 to 12 and girls from 15 to 16 years

Girls				
z Score at age 15 years	z Score at age 16 years	Δz	ΔBMI	ΔWeight (lb) (65 inches both years)[a]
+1	+2	+1	+8.9	+53.6
0	+1	+1	+4.5	+27.3
−1	0	+1	+3.0	+17.9
−2	−1	+1	+2.2	+13.3
0[b]	0	0	+0.5	+3.1
+2	+1	−1	−7.3	−43.8
+1	0	−1	−3.4	−20.4
0	−1	−1	−2.0	−11.8
−1	−2	−1	−1.2	−7.5

BMI = body mass index; ΔBMI = change in BMI; Δz = change in z scores.
[a]Assumed heights at 2 ages.
[b]Also shown is z score = 0 at both ages, so Δz is 0.

Adiposity in Adolescents:

Δ in Actual BMI works better than Δ in BMI z score for Longitudinal Studies

Berkey & Colditz 2006 Annals Epi

"Although the CDC never specifically recommended that their z scores be used longitudinally, journal reviewers often insist that Δ z be analyzed, … We propose that using these z scores longitudinally may have unintended consequences."

-For the same reasons, the use of Δ BMI centile "may have unintended consequences".

- Why in our example were significant differences found between groups in BMI z but not BMI centile?... chance?

Power of observed differences

Outcome	BT (Placebo)		Sibutramine		Power
	n	Mean Δ (SD)	n	Mean (SD)	
Δ Weight (lbs)	34	-8.00 (2.36)	40	-18.56 (2.17)	87%
Δ BMI	32	-1.78 (0.41)	39	-3.38 (0.37)	79%
Δ BMI centile	30	-0.48 (0.24)	36	-1.06 (0.22)	41%
Δ BMI z-score	30	-0.14 (0.03)	36	-0.24 (0.03)	56%

Summary of Illustrative Example 1 Weight Loss after intervention

- Which BMI better captures change?
  - No signif differences between treatment groups in BMI centile contradictory to other BMI measures
  - BMI centile had very little variability in this cohort → ceiling effect for showing change
  - BMI centile may not be the best measure to assess change in weight status (consensus)
  - Based on Power Analysis and other work (Berkey& Colditz), BMI z-score also has limitations in assessing change → again obese children with very high BMI z

Will the findings be similar in a longitudinal study looking at

- Growth change
- Normal and Overweight Children

Illustrative Example 2: Infant Growth Study (IGS)

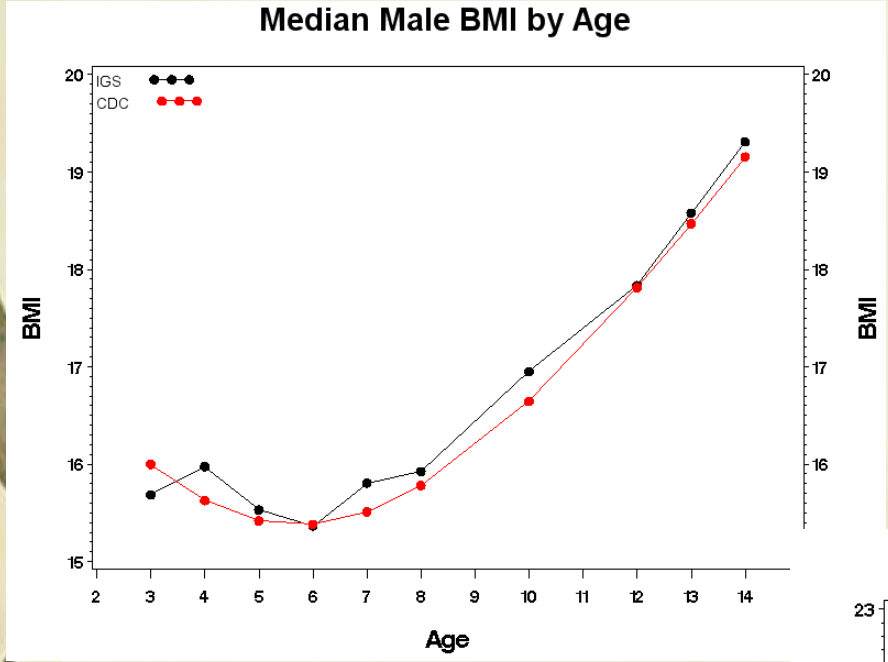
- Current PI: Myles Faith, PhD of Penn/CHOP
- ongoing longitudinal investigation that was designed to assess anthropometric, behavioral and metabolic determinants of growth and development in children with and without maternal risk for obesity
- 82 Caucasian infants designated as low risk (LR) or high risk (HR) for obesity based on mother's pre-pregnancy BMI [*Am J Clin Nutr.* 2005]
- At 3 years: 7% OW (2% LR, 15%HR)
- At 14 years: 35% OW (13% LR, 57% HR)

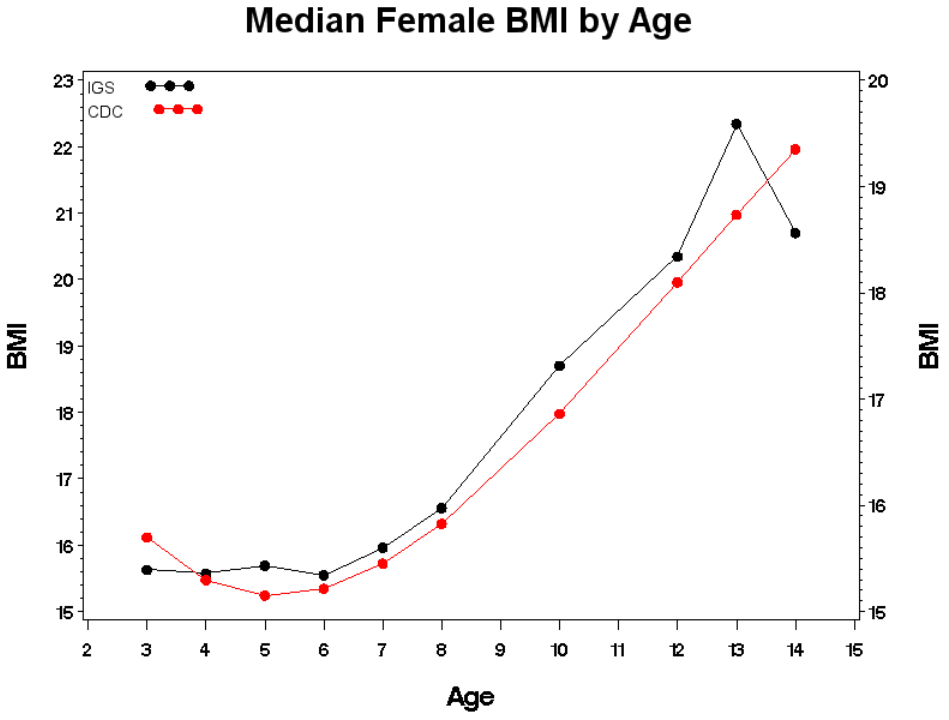
Which outcome better captures change in weight status?

- Are CDC growth curves similar to IGS growth curves?

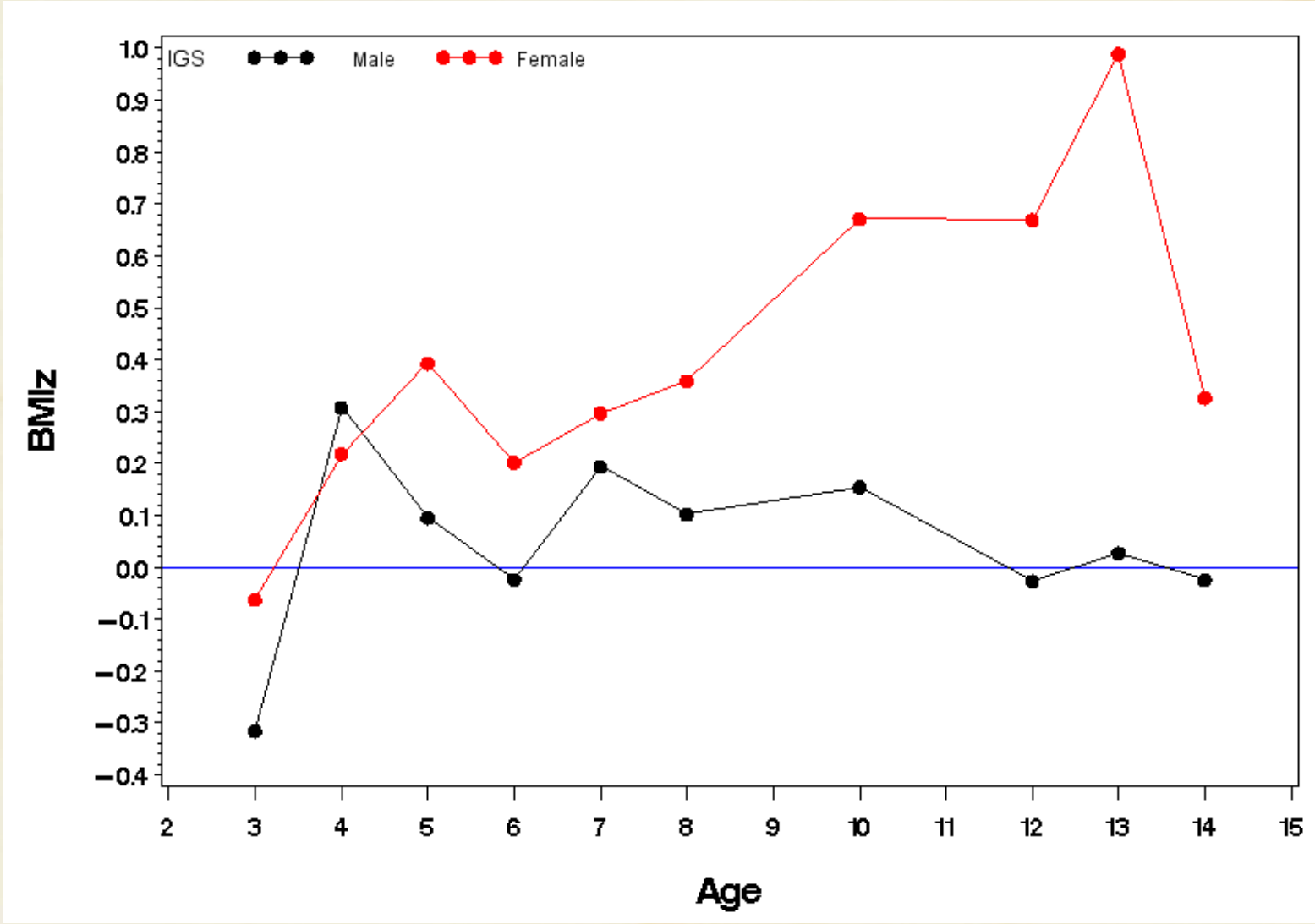
Let’s take a look!

Median BMI: IGS vs CDC





IGS Median BMIz



Δ in Actual BMI works better than Δ in BMI z score for Longitudinal Studies

Berkey & Colditz 2006

GUTS OW children

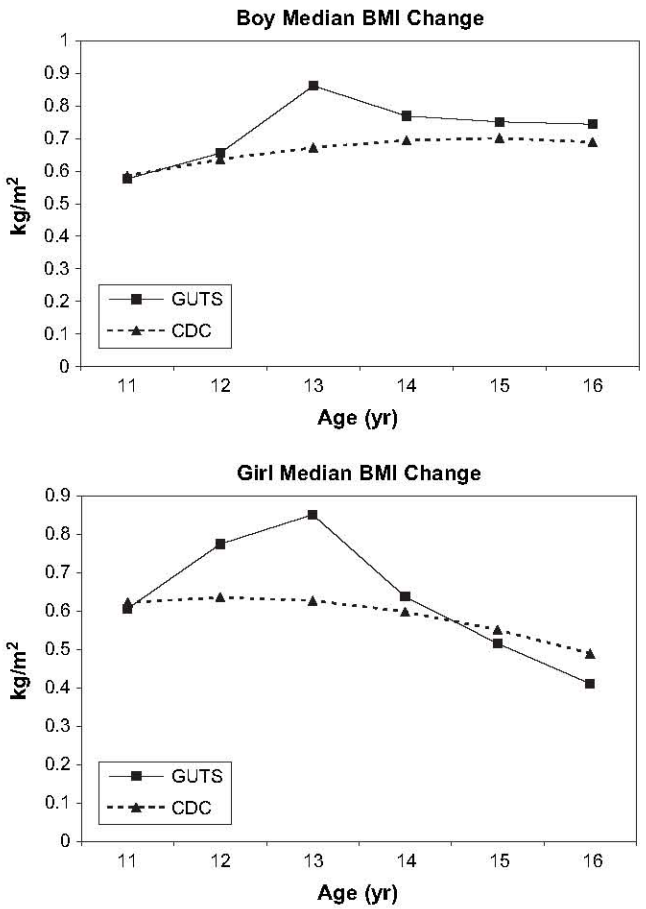


FIGURE 1. Median 1-year body mass index (BMI) changes from a longitudinal study (4290 boys and 5719 girls measured in 1997 and 1998, Growing Up Today Study [GUTS]) and differences between median BMIs 1 year apart on Centers for Disease Control and Prevention charts.

What is the best measure of adiposity change in growing children?

Cole, Faith, et al. 2005 Eur J Clin Nutr

- 135 children aged 29-68 months measured 3x over a 9-month period
- “Variability in BMI z-score and BMI centile depends on baseline adiposity status”
  - Variability in BMI independent of adiposity status
- “BMI centile useful for classifying children’s adiposity but poor at quantifying change”
- “BMI z-score less ideal measure of adiposity change, as its variability gets progressively smaller the fatter the child”

Summary: outcomes in IGS Study

Plots suggest:

- BMI and BMIz may capture different changes
- CDC median growth changes differ from IGS median growth changes

What's the best outcome?

What's the best outcome to assess weight change in growing children?

It's complicated!

- Dependent on adiposity status of children
- Dependent on sex of the children
- Dependent on age (growth stage)
- Dependent on whether summarizing results from weight loss intervention or from prospective growth study

Which outcome should we choose and report?

- Primary Outcome: dependent on aim of the study and characteristics of children included
- But report ALL!
  - Weight, BMI, BMI z-score, BMI centile
  - Only way to compare one study to another study

Two Illustrative Studies

- Limitations
  - Illustrative datasets have small sample size
  - Missing Data
- Strengths
  - Despite small sample size, results consistent with other work in this area
  - Longitudinal aspect of IGS dataset (ages 3 month – 14 years)
  - Datasets contain both BMI measures and adiposity (DXA) measures

My Ongoing Work

- Use Statistical modeling and simulation studies to further examine:
  - Which BMI measure best represents change in weight status?
- Results: help us to better assess the success of weight loss intervention programs in children
- Results: could guide CDC in development of next set of growth curves (BMI centile, z-score)

Acknowledgements

IGS Team

- Myles Faith
- Tanja Kral
- April Kabay
- Robert Berkowitz
- Albert Stunkard
- Nicolas Stettler
- Virginia Stallings

Adolescent Study Team

- Robert Berkowitz
- Thomas Wadden
- Joanna Cronquist
- Chanelle Bishop-Gilyard
- Christine Gehrman
- Natalie Liepinis

CCEB

- Jesse Chittams
- Christopher Coley
- Scarlett Bellamy
- Susan Ellenberg
- Thomas Ten Have

Thank you!

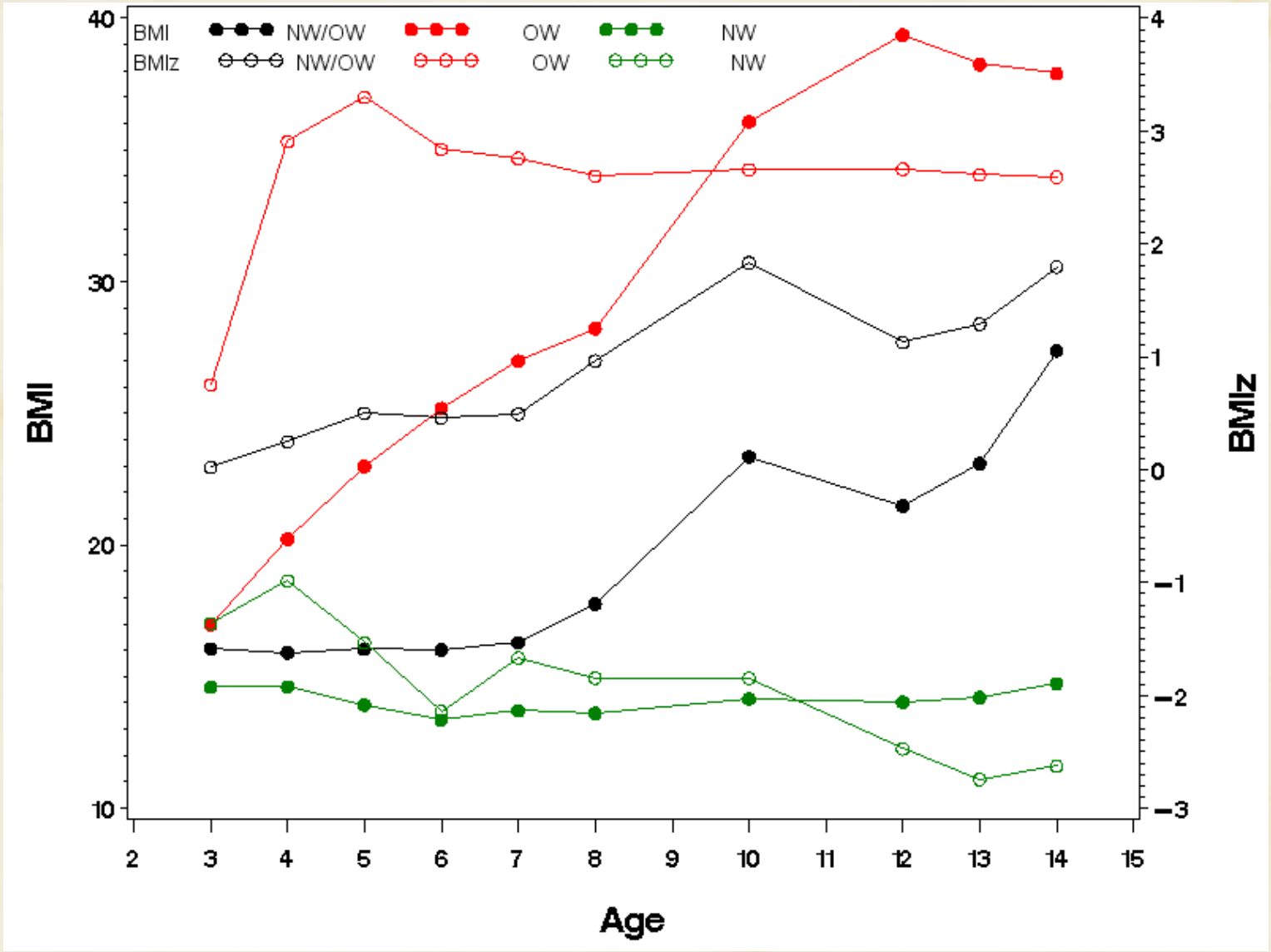
Extra Slides

Background: Measuring Adiposity

- BMI, BMI centile, BMI z-score
  - Just need height and weight (& CDC charts)
  - Overall changes in body composition
  - Proxy? for changes in adiposity
- Measures of Adiposity
  - Total Fat, Total % Fat
  - Fat Free Mass & Fat Mass Indices
  - Skinfold Measurements
  - Need “machinery”
    - Air-displacement plethysmography (ADP- BOD POD)
    - Dual-energy X-ray absorptiometry (DXA)

Buison, Ittenbach, Stallings, Zemel 2006 Amer J of Human Biology

IGS: 3 Children BMI vs. BMI z



	Truth: The Null Hypothesis Correct	Truth: The Alternative Hypothesis is Correct
p-value for the test statistic is < 0.05	Type 1 Error ($\alpha = 0.05$)	Power ($1 - \beta$)
p-value for the test statistic is >= 0.05		Type II Error (β)