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Comparison of Weight-for-Length or Body Mass Index During the First 2 Years of Life With Cardiometabolic Risk in Early Adolescence

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Key points

Question: Is weight-for-length (WFL) or body mass index (BMI) in children below 2 years a better predictor of future health outcomes?

Findings: In this prospective study based in two birth cohorts, being ever overweight (vs. never overweight) during 6–24 months provided adjusted estimates for early adolescent cardio-metabolic outcomes (fat-mass index, insulin resistance, metabolic risk score) that did not differ greatly across WFL and BMI cut-points.

Meaning: Choice of WFL vs. BMI to define overweight in the first 2 years of life does not greatly affect the associations with cardio-metabolic outcomes at early adolescence.

Abstract

Importance: The American Academy of Pediatrics currently recommends weight-for-length (WFL) for assessment of weight status in children <2 years, but body mass index (BMI) for children above 2 years. Yet the clinical implications of using WFL vs BMI in children <2 years as a predictor of future health outcomes remains understudied.

Objective: To compare associations of overweight based on WFL vs BMI in children <2 years with cardio-metabolic outcomes in early adolescence.

Design: Prospective study of two birth cohorts in United States (Project Viva) and Belarus (Promotion of Breastfeeding Intervention Trial, PROBIT)

Main exposure: Overweight by Centers for Disease Control and Prevention (CDC) WFL≥95th percentile, World Health Organization (WHO) WFL ≥97.7th percentile or WHO BMI ≥97.7th percentile at 6, 12, 18 or 24 months

Main outcomes and measures: Fat-mass index, insulin resistance, metabolic risk score, obesity (primary outcomes); height and body mass index z-scores, sum of skinfolds, waist circumference, systolic blood pressure (secondary outcomes) in early adolescence

Results: Our analysis included 919 (50.1% male, 65.1% white ethnicity) children from Project Viva and 12747 (48.7% male, 100% white ethnicity) from PROBIT. During 6–24 months, 22.4%, 17.4% and 17.5% of children in Project Viva, and 29.1%, 24.1% and 24.5% of children in PROBIT, were overweight at any of the four timepoints using CDC WFL, WHO WFL and WHO BMI cut-points, respectively. After adjusting for maternal and child characteristics, being ever overweight (vs. never overweight) during 6–24 months of age was associated with higher likelihood of adverse cardio-metabolic risk markers in early adolescence, yet associations did not differ greatly across WFL and BMI cut-points in either cohort [e.g. for fat-mass index (in kg/m^2) Project Viva – CDC WFL: β 0.9 (95% CI 0.5,1.4); WHO WFL: 1.1 (0.6,1.6); WHO BMI: 1.4 (0.9,1.9); PROBIT – CDC WFL: 0.5 (0.4,0.6); WHO WFL: 0.6 (0.5,0.7); WHO BMI: 0.6 (0.5,0.6)]. Neither growth metric in infancy was superior over the others, based on F-statistics. Findings were similar for insulin resistance, metabolic risk score, obesity and secondary outcomes.

Conclusions: Choice of WFL vs. BMI to define overweight in the first 2 years of life does not greatly affect the associations with cardio-metabolic outcomes in early adolescence.

Introduction

Physical growth of children is a well-recognized indicator of subsequent health and wellness.[1,2] The American Academy of Pediatrics and Centers for Disease Control and Prevention (CDC) currently recommend using weight-for-length (WFL) for assessment of overweight in children below 2 years of age;[3] it is also a predominant standard used internationally.[4] WFL percentile curves do not, however, reflect the age-dependent variation of weight or length with age. The World Health Organization (WHO) has provided body mass index (BMI)-for-age curves for children 0–5 years, which overcomes this limitation.[5]

As both CDC[6] and WHO[5] charts are available, clinicians and researchers now have a choice of growth charts and anthropometric measures to use. It is therefore important to understand how they compare in predicting later clinical outcomes, as clinicians might prefer to use the metric that more strongly predicts later health. Yet few studies have compared these anthropometric measures in terms of their associations with direct measures of adiposity and cardio-metabolic risk later in life. Rifas-Shiman *et al*. previously showed that WFL and BMI cut-points for overweight in the first 2 years of life provided similar estimates of obesity risk at 5 years.[7] Roy *et al*. observed that high BMI at ages 2–6 months was more strongly associated with obesity at 2 years than high WFL.[8] To our knowledge, no studies have compared being overweight by WFL or BMI percentiles in the first 2 years of life with respect to later adiposity or other cardio-metabolic risk markers other than BMI, such as insulin resistance or metabolic risk score.

To address these gaps, we used data from two longitudinal cohorts [Project Viva[9] and the Promotion of Breastfeeding Intervention Trial (PROBIT)[10]] to compare associations between being overweight by CDC WFL, WHO WFL or WHO BMI cut-points in the first 2 years of life and cardio-metabolic outcomes in early adolescence. Analyzing data in two different populations with different confounding structures enables us to assess the robustness

of the observed associations. We hypothesized that being overweight in the first 2 years by any of the three cut-points would provide similar estimates of association.

Methods

Study populations

i. *Project Viva:* Project Viva is an ongoing prospective cohort study of pre- and perinatal influences on maternal, fetal and child health, as detailed elsewhere.[9] Mothers provided written informed consent at enrollment and follow-up visits, and children provided verbal assent at the early adolescent visit. The Institutional Review Board of Harvard Pilgrim Health Care approved the project in line with ethical standards established by the Declaration of Helsinki.

During research examinations in infancy (median 6.3 months; range 4.9–10.6 months), trained research assistants measured weight and length using standardized protocols.[11,12] We also obtained additional data on weight and length from medical records, where pediatric clinics recorded these measures at each well-child visit during infancy and early childhood (<2 years). As described previously,[13] clinicians used the paper and pencil technique for measuring recumbent length for infants 0-2 years at pediatric clinics. We applied a correction algorithm to account for the systematic overestimation of lengths resulting from this technique.[13] Of 2128 live singleton births, we included 919 (43.2%) children who had a measure of weight and length at 6, 12, 18 or 24 months (within ±2 months at each timepoint) and at least one outcome measure at the early adolescent visit (median 12.9 years) (**eFigure 1**).

ii. *PROBIT:* PROBIT is a cluster-randomized trial of breastfeeding promotion intervention in the Republic of Belarus. The design of PROBIT has been published previously.[14] The initial PROBIT trial and subsequent follow-ups were approved by the Belarussian Ministry of Health and received ethical approval from the McGill University Health

Centre Research Ethics Board, the Institutional Review Board at Harvard Pilgrim Health Care, and the Avon Longitudinal Study of Parents and Children (ALSPAC) Law and Ethics Committee. A parent or legal guardian provided written informed consent in Russian at enrollment and at the follow-up visits, and all children provided written assent at the 11.5-year visit.

Polyclinic pediatricians measured infant weight and length (with a length board) at follow-up visits at 1, 2, 3, 6, 9 and 12 months; home visits were made when polyclinic visits were missed.[14] We also obtained additional data from polyclinic charts, where the study pediatricians recorded length/height and weight data at each well-child visit between 12 months and 6.5 years [10] We had no information on the method of length measurement in the data extracted from the charts, but we have no reason to think that the pediatricians changed their method of length measurement until upright height measurement replaced supine length. Of 17,046 healthy, singleton, term live births, we studied 12,747 (74.8%) children who had a measure of weight and length at 6, 12, 18 or 24 months (within ±2 months at each timepoint) and at least one outcome measure at the early adolescent visit (median 11.5 years) (**eFigure 1**).

Exposure: Infant and child overweight status

In both cohorts, we used length and weight measurements at 6, 12, 18, and 24 months (within ±2 months at each time point) to derive sex-specific CDC WFL, WHO WFL, and age- and sex-specific WHO BMI percentiles. The main exposures were being overweight at any of the four time points ("ever overweight") between 6 and 24 months using each of three cut-points: CDC WFL ≥95th percentile, WHO WFL or BMI ≥97.7th percentile. In secondary analyses, we examined overweight status at each individual time point between 6 and 24 months. We also categorized children according to number of time points overweight between 6 and 24 months (range 0–4) for each of the three cut-points. As few children were

overweight at all four time points, we combined those children with those who were overweight at any three time points.

Outcomes: Early adolescent body composition and cardio-metabolic risk markers

At 12.9 years (range 11.9–16.6 years) in Project Viva, and 11.5 years (10.2–14.5 years) in PROBIT, we obtained the following measures of body composition and cardio-metabolic risk markers:

i. *Body composition:* As detailed previously, trained research assistants (in Project Viva[15,16]) and pediatricians (in PROBIT[10,17,18]) measured child's weight, standing height, waist circumference (WC), subscapular (SS) and triceps (TR) skinfolds, and foot-to-foot bio-impedance fat mass. In both cohorts, we calculated BMI, derived age- and sex-specific height and BMI z-scores using CDC reference data,[6] and defined obesity as BMI $\geq 95^{th}$ percentile (vs BMI $< 95^{th}$ percentile) in accordance with current guidelines of the American Academy of Pediatrics.[19] We calculated the sum of the SS and TR skinfolds and fat mass index (FMI=fat mass/height^2).

ii. *Cardio-metabolic risk markers:* Trained research assistants (in Project Viva) and pediatricians (in PROBIT) measured the child's systolic blood pressure (SBP) using calibrated automated oscillometric monitors, as detailed previously.[12,20] We calculated age-, sex- and height-specific SBP z-scores according to the 2017 American Academy of Pediatrics BP reference for adolescents.[21] In both cohorts, we collected blood specimens after a minimum 8-hour fast[22,23] and measured glucose and insulin as detailed previously,[18,20,24] calculated insulin resistance using the homeostasis model assessment (HOMA-IR) and transformed the HOMA-IR values using natural logarithms to normalize the distribution. Furthermore, we measured high-density lipoprotein cholesterol (HDL-C) and triglycerides in Project Viva, and apolipoprotein A1 (Apo A1) in PROBIT, according to standard protocols.[20,24] We calculated cohort-specific metabolic risk z-scores using the

following variables: in Project Viva,[24] the average of within-cohort age- and sex-specific WC, SBP, triglycerides (log transformed), HDL cholesterol (inverted), and HOMA-IR (log transformed); in PROBIT,[25] the average of age- and sex-specific WC, SBP, Apo A1, fasting insulin and glucose. This cluster of factors comprising the metabolic risk score were first formalized by the World Health Organization[26] and the National Cholesterol Education Program Adult Treatment Panel III.[27] Previous studies by Morrison *et al*.[28,29] demonstrated that children with high metabolic risk score have an increased risk of developing type 2 diabetes, cardiovascular disease and metabolic syndrome adulthood, suggesting its importance in children. In PROBIT, cardio-metabolic risk markers were measured using frozen dried bloodspots. Neither triglycerides nor HDL-cholesterol could be validly measured from those samples, and Apo-A1 was therefore used as a surrogate for dyslipidemia as previously defined by Bachorik *et al*.[30]

Statistical analysis

We assessed for agreement between overweight by CDC WFL, WHO WFL and WHO BMI cut-points using kappa statistics. We used multivariable linear (for continuous outcomes) and logistic regression (for obesity) to examine associations between being ever overweight (vs. never overweight) in the first 2 years and cardio-metabolic outcomes in early adolescence, adjusting for the following covariates in each cohort: Project Viva – maternal age (<20, 20-34 or ≥35 years), marital status (married/co-habitating or not married), educational attainment (non-university vs university educated), pre-pregnancy BMI, total gestational weight gain, smoking history (never, smoked prior to pregnancy or smoked during pregnancy), glucose tolerance status (normoglycemia, isolated hyperglycemia, impaired glucose tolerance or GDM), gestational hypertensive disorders (normal blood pressure, gestational hypertension, chronic hypertension and pre-eclampsia), gestational age at delivery and child race/ethnicity (white, black, Hispanic, Asian or others), sex (male or female), birth-

weight-for-gestational-age z-scores, breastfeeding status at 6 months (formula only, weaned, mixed feeding or breastmilk only) and age at outcome measurement; PROBIT – maternal age (<20, 20-34 or ≥35 years), maternal BMI at 6.5 years (as a proxy for BMI before pregnancy), educational attainment (did not complete or completed university), marital status (registered/unregistered marriage or unmarried), smoking during pregnancy (yes or no), and child gestational age at delivery, sex (male or female), birth-weight-for-gestational-age z-scores and age at outcome measurement.

We also assessed associations of overweight at each "time point" (6, 12, 18, and 24 months), or the number of time points with overweight, with adiposity and cardio-metabolic risk in early adolescence in both cohorts. For all analyses of PROBIT data, we accounted for clustered measurements within hospitals/polyclinics by including a random effect term for hospital/polyclinic but did not adjust for intervention vs. control arms, as earlier analyses showed no differences in early adolescent cardio-metabolic outcomes between these two study arms.[18,20]

To compare CDC WFL, WHO WFL and WHO BMI as predictors of adiposity and cardio-metabolic outcomes, we used the overall F-statistic from linear models predicting each of these outcomes[31] which reflect the predictive values of the models. At each timepoint within each cohort, the models for CDC WFL, WHO WFL and WHO BMI contain the same number of covariates. Hence, models with larger F-statistics are more strongly predictive of outcomes than models containing a different growth metric. We have also set a value of 5% greater difference between largest and second-largest F-statistic values to indicate a "meaningful" advantage for the model with the larger value, as described previously by Kleinman *et al*.[31] In our study, the use of language around prediction connotes a temporal relationship, that the exposure (i.e., overweight by CDC or WHO growth metrics during 6–24 months) precedes the subsequent outcome and does not refer to "prediction modeling". We

analysed all data using Stata version 15 (StataCorp, Texas, USA), conducted all statistical analyses as 2-sided and defined statistical significance at an α-level of 0.05.

Results

Table 1 describes the characteristics of participating children from both cohorts. Over the period spanning 6 to 24 months, 22.4%, 17.4% and 17.5% of children in Project Viva, and 29.1%, 24.1% and 24.5% of children in PROBIT were ever overweight using CDC WFL, WHO WFL, and WHO BMI cut-points, respectively. In both cohorts, overweight children had a higher birthweight-for-gestational age z-score and were more likely to have mothers who smoked during pregnancy. In early adolescence, children in Project Viva generally had higher adiposity than children in PROBIT (**Table 2**).

We observed strong intra-class correlations between CDC and WHO z-scores, and agreements between overweight by CDC WFL, WHO WFL and WHO BMI cut-points in both cohorts (**eTable 1**). In Project Viva, we observed no differences in overweight prevalence between included and excluded children. Those included in the study however, were more likely to have mothers who were older (≥35 years), university-educated and to have breastfed at 6 months but less likely to have smoked during pregnancy than those who were excluded. In PROBIT, the differences in characteristics and overweight prevalence between included and excluded children were small overall (**eTable 2**).

In both cohorts, we found that ever overweight (vs. never overweight) at any of the four time points in the first 2 years was associated with higher FMI (**Figure 1A**), BMI z-score, sum of SS and TR skinfolds, and WC (**eTable 3**) in early adolescence. Significant associations with higher HOMA-IR and metabolic risk z-score were observed only in PROBIT (**Figures 1B-C**), perhaps because of the relatively small number of Project Viva children with fasting blood samples and thus limited power in this population. No associations with HDL-C or triglycerides were evident. Ever overweight at 6-24 months

yielded unadjusted (**eTable 3**) and adjusted estimates for early adolescent FMI, HOMA-IR and, metabolic risk z-score and odds of obesity (**Figures 1A-D**) that did not differ greatly across WFL and BMI cut-points. In Project Viva, the adjusted estimates (in kg/m^2) and F-statistics for FMI were – CDC WFL: β 0.9 (95% CI 0.5,1.4), F-statistic = 17.1; WHO WFL: 1.1 (0.6,1.6), F-statistic = 17.3; WHO BMI: 1.4 (0.9,1.9), F-statistic = 17.8. No interactions were observed between ethnicity and overweight status for any outcomes in Project Viva (all $p_{int} > 0.05$). In PROBIT, the adjusted estimates for FMI were similar in direction but of lower magnitude – CDC WFL: 0.5 (0.4,0.6), F-statistic= 88.7; WHO WFL: 0.6 (0.5,0.7), F-statistic = 88.3; WHO BMI: 0.6 (0.5,0.6), F-statistic = 87.1. In comparing the F-statistics, we observed that none of the metrics was superior (>=5% larger) to the others. Similar findings were observed for other outcomes (**eTable 3**).

In both cohorts, we observed adjusted estimates of association with adolescent FMI (**Figure 1A**), BMI z-score, sum of SS and TR skinfolds, WC (**eTables 4–7**), HOMA-IR (**Figure 1B**), metabolic risk z-score (**Figure 1C**) and odds of obesity (**Figure 1D**) in early adolescence that were generally higher with increasing age (from 6 to 24 months) at overweight. No associations with HDL-C or triglycerides were observed, nor did we see any interactions in Project Viva between ethnicity and overweight status for all outcomes ($p_{int} > 0.05$). Choice of WFL or BMI to define overweight at each time point between 6 and 24 months did not greatly affect the unadjusted (**eTables 4-7**) or adjusted estimates of associations with FMI, HOMA-IR, metabolic risk z-score and odds of obesity (**Figures 1A-D**). In comparing the F-statistics, neither growth metric was superior to the others. Similar findings were observed for other outcomes (**eTables 4–7**).

In PROBIT, each additional time point from 6 to 24 months at which the child was overweight was associated with increasing FMI (**Figure 2A**), BMI z-score, sum of SS and TR skinfolds, WC (**eTable 8**), HOMA-IR (**Figure 2B**), metabolic risk z-score (**Figure 2C**)

and odds of obesity (**Figure 2D**) in early adolescence. For example, the adjusted FMI estimate for overweight at two vs. zero time points during 6–24 months was 0.7 kg/m^2 (95% CI 0.6,0.9) using WHO BMI, while for overweight at 3–4 time points, the adjusted estimate was 1.4 kg/m^2 (1.1,1.7). In Project Viva, each additional time point that the child was overweight during 6–24 months was associated with increasing FMI (**Figures 2A**) in early adolescence, while point estimates for HOMA-IR and metabolic risk z-score (**Figures 2B-C**) were stronger in children who were overweight at two (vs. zero) time points. For both cohorts, estimates using CDC or WHO cut-points were similar (**eTable 8**).

Discussion

We found that ever being overweight in the first two years was a predictor of higher fat-free mass and adiposity in early adolescence. Consistent with previous findings,[32] the CDC WFL cut-point classified more children as overweight than the WHO WFL or BMI cutpoints. This is not surprising, given that the CDC charts used a lower percentile cut-point than WHO charts for classifying overweight.[5,6] More importantly, the estimates of association with fat mass index, insulin resistance and metabolic risk score in early adolescence did not differ greatly among the three cut-points.

Our findings suggest that choice of WFL or BMI in children below 2 years does not greatly affect the ability to predict future adiposity and cardio-metabolic outcomes. Earlier studies[8,33] have identified high concordance between WFL and BMI after 6 months of age, indicating that either metric may be a reasonable measure in later infancy for assessing risk of later health outcomes. BMI may be preferable to WFL for other reasons, however. Within-subject BMI measurements have greater consistency over time than within-subject WFL measurements,[8] suggesting greater stability of BMI vs WFL. Existing guidelines already suggest use of BMI for growth and obesity screening after age 2.[3] Applying the same metric for children below 2 years would therefore streamline clinical practice. Thus if BMI replaced

WFL for assessment of weight status in children below 2 years, it could improve monitoring of longitudinal growth patterns from infancy to adulthood without the need to transition between differing growth metrics after 2 years.

To date, few studies have examined the meaning of BMI calculated from recumbent length, or the consequences of high BMI during infancy and early childhood. Because of these unanswered questions, BMI is not currently recommended for clinical use in children below 2 years.[3] Recent studies, however, have indicated that BMI may be a suitable proxy of adiposity in older infants[34-36] that also provides information about future obesity[37-39] and cardio-metabolic risk[40-42] in later childhood. We have also demonstrated that high BMI in the first 2 years is predictive of adiposity and metabolic risk in early adolescence, with estimates that are comparable to those for high WFL. We do acknowledge, however, that our findings would benefit from replication in other population cohorts from different settings. Furthermore, associations with outcomes other than adiposity or cardio-metabolic risk might differ.

The strength of the associations observed was smaller for children in PROBIT than for those in Project Viva. We speculate that this difference is because children in PROBIT were larger in size during infancy than those in Project Viva (as indicated by the higher overweight prevalence in PROBIT infants than in Project Viva), while adolescent adiposity was higher in Project Viva than in PROBIT. It is likely that these growth metrics contribute a smaller explained variance for cardio-metabolic risk markers such as insulin resistance and metabolic risk score (as indicated by the small effect sizes in both cohorts) than true adiposity-related outcomes such as FMI.

Our findings address important evidence gaps. First, we have shown that both CDC and WHO cut-points for infant or early childhood overweight provided similar adjusted estimates and model predictive values for cardio-metabolic outcomes in early adolescence.

This suggests that if pediatricians were to switch from using CDC WFL ≥95th percentile to WHO WFL or BMI ≥97.7th percentile in the first 2 years, the ability to predict future cardio-metabolic outcomes would not be greatly affected. Second, we have shown that growth percentiles in children below 2 years that are indicative of potential health problems (i.e., high WFL or BMI) are associated with direct measures of adiposity and cardio-metabolic risk later in life. Third, we have provided evidence on the clinical implications of using WFL or BMI percentiles in children below 2 years as predictors of future health outcomes beyond childhood. Previous studies[7,8] were only limited to associations with risk of obesity, and to follow-up in childhood, rather than adolescence.

BMI is a widely recommended metric for obesity screening in children.[43-45] Children who were screened and underwent intensive behavioral interventions that encompassed nutritional counselling (e.g., providing information about healthy eating, reading food labels, encouraging the use of stimulus control) and physical activity, had improvements in weight status for up to 12 months with minimal harm from screening.[45] Evidence favoring early life screening and subsequent interventions in children below 6 years remains scarce, however.[46] Existing obesity prevention studies in early childhood have shown only modest benefits, and few have examined its impact on later cardio-metabolic health.[47] Further research is needed to develop and test preventive interventions, especially for children who are diagnosed as overweight/obese during early life.

Strengths of our study include its relatively large sample size of over thirteen thousand children from two prospective cohorts, multiple measures of growth in early life, and a wide range of cardio-metabolic outcomes in early adolescence obtained by highly-trained research staff using standardized protocols. In addition, our study benefits from the variability in designs and populations in two very different populations. The robustness and similarity of the findings in both cohorts, despite differing confounding structures (degree of

income inequality, health care systems) and different obesity prevalence, suggests that bias due to uncontrolled (residual) confounding is an unlikely explanation for the observed associations.

Our study is not without limitations, however. First, we used both research-standard and routinely collected anthropometric measurements from well child visits across the first 2 years of life, which may be subject to differences in agreement.[48] A recent study,[33] however, identified high agreement between these two data sources when using WFL or BMI to classify overweight status in children below 2 years. Second, the value of length-based indices such as WFL or BMI could be affected by inaccurate length assessments due to measurement difficulties in infants and toddlers, especially considering that length is squared when calculating BMI. Third, we made no attempts to standardize the measurement of length in infancy across hospital or polyclinic sites in PROBIT, as differences in length gain were not among the study's major hypotheses during the first year of follow-up.[14] As we were unable to assess the reliability of infant length measurements in PROBIT, the associations of WFL or BMI with early adolescent outcomes could have been attenuated by measurement error. Fourth, our study findings may not be generalizable to other ethnic groups and populations, since many of our participants were white (both cohorts) or university-educated (in Project Viva). Fifth, some children were not followed up in both cohorts. In Project Viva, differences between children who were or were not followed up may limit the generalizability of our findings. In PROBIT, however, differences in characteristics between subjects followed up or not were small overall and therefore unlikely to have biased our findings. Sixth, the use of foot-to-foot bio-impedance methods in our study may underestimate adiposity compared with other methods, such as the 4-compartment model. Comparisons between the different methods, however, have reported the validity of bio-impedance to accurately rank individuals[15,49] and groups.[50] Seventh, we investigated multiple

cardio-metabolic outcomes, therefore increasing the risk of false-positive results. We chose not to adjust for multiple comparisons. Instead, the "significance" of our findings is based on the consistency of the associations observed across related outcomes.[51] Lastly, our study did not address underweight status in the first 2 years using WFL or BMI, nor its associations with subsequent outcomes. Rather, our study focused on later cardio-metabolic sequalae, which are much more strongly associated with overweight than with underweight.[52]

In conclusion, we found that choice of WFL vs. BMI to define overweight in infancy and early childhood does not greatly affect associations with adiposity and cardio-metabolic outcomes in early adolescence. Although our findings would benefit from replication in other population cohorts, they have important implications for investigators seeking to use BMI as a growth metric for epidemiologic research, and for clinicians monitoring the weight status of children below 2 years of age.

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References

1. Cole TJ. The secular trend in human physical growth: a biological view. *Econ Hum Biol.* Jun 2003;1(2):161-168.

2. Black MM, Walker SP, Fernald LCH, et al. Early childhood development coming of age: science through the life course. *Lancet.* Jan 7 2017;389(10064):77-90.

3. Grummer-Strawn LM, Reinold C, Krebs NF. Use of World Health Organization and CDC growth charts for children aged 0-59 months in the United States. *MMWR Recomm Rep.* Sep 10 2010;59(RR-9):1-15.

4. de Onis M, Onyango A, Borghi E, Siyam A, Blossner M, Lutter C. Worldwide implementation of the WHO Child Growth Standards. *Public Health Nutr.* Sep 2012;15(9):1603-1610.

5. World Health Organization. WHO child growth standards: length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age. *Methods and development. WHO (nonserial publication). Geneva: WHO.* 2006.

6. Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, et al. CDC growth charts: United States. *Adv Data.* Jun 8 2000(314):1-27.

7. Rifas-Shiman SL, Gillman MW, Oken E, Kleinman K, Taveras EM. Similarity of the CDC and WHO weight-for-length growth charts in predicting risk of obesity at age 5 years. *Obesity (Silver Spring).* Jun 2012;20(6):1261-1265.

8. Roy SM, Spivack JG, Faith MS, et al. Infant BMI or Weight-for-Length and Obesity Risk in Early Childhood. *Pediatrics.* May 2016;137(5).(pii):peds.2015-3492.

9. Oken E, Baccarelli AA, Gold DR, et al. Cohort profile: project viva. *Int J Epidemiol.* Feb 2015;44(1):37-48.

10. Patel R, Oken E, Bogdanovich N, et al. Cohort profile: The promotion of breastfeeding intervention trial (PROBIT). *Int J Epidemiol.* Jun 2014;43(3):679-690.

11. Perng W, Hajj H, Belfort MB, et al. Birth Size, Early Life Weight Gain, and Midchildhood Cardiometabolic Health. *J Pediatr.* Jun 2016;173:122-130.e1.(doi).

12. Perng W, Rifas-Shiman SL, Kramer MS, et al. Early Weight Gain, Linear Growth, and Mid-Childhood Blood Pressure: A Prospective Study in Project Viva. *Hypertension.* Feb 2016;67(2):301-308.

13. Rifas-Shiman SL, Rich-Edwards JW, Scanlon KS, Kleinman KP, Gillman MW. Misdiagnosis of overweight and underweight children younger than 2 years of age due to length measurement bias. *MedGenMed.* Nov 29 2005;7(4):56.

14. Kramer MS, Chalmers B, Hodnett ED, et al. Promotion of Breastfeeding Intervention Trial (PROBIT): a randomized trial in the Republic of Belarus. *JAMA.* Jan 24-31 2001;285(4):413-420.

15. Boeke CE, Oken E, Kleinman KP, Rifas-Shiman SL, Taveras EM, Gillman MW. Correlations among adiposity measures in school-aged children. *BMC Pediatr.* Jun 24 2013;13:99.

16. Li LJ, Rifas-Shiman SL, Aris IM, et al. Associations of maternal and cord blood adipokines with offspring adiposity in Project Viva: is there an interaction with child age? *Int J Obes.* Oct 13 2017;13(10):256.

17. Kramer MS, Zhang X, Bin Aris I, et al. Methodological challenges in studying the causal determinants of child growth. *Int J Epidemiol.* Dec 1 2016;45(6):2030-2037.

18. Martin RM, Patel R, Kramer MS, et al. Effects of promoting longer-term and exclusive breastfeeding on adiposity and insulin-like growth factor-I at age 11.5 years: a randomized trial. *JAMA.* Mar 13 2013;309(10):1005-1013.

19. Barlow SE. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. *Pediatrics.* Dec 2007;120(Suppl 4):S164-192. .
20. Martin RM, Patel R, Kramer MS, et al. Effects of promoting longer-term and exclusive breastfeeding on cardiometabolic risk factors at age 11.5 years: a cluster-randomized, controlled trial. *Circulation.* Jan 21 2014;129(3):321-329.
21. Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. *Pediatrics.* Sep 2017;140(3).(pii):peds.2017-1904. .
22. Perng W, Rifas-Shiman SL, Hivert MF, Chavarro JE, Oken E. Branched Chain Amino Acids, Androgen Hormones, and Metabolic Risk Across Early Adolescence: A Prospective Study in Project Viva. *Obesity (Silver Spring).* May 2018;26(5):916-926.
23. Guthrie LB, Oken E, Sterne JA, et al. Ongoing monitoring of data clustering in multicenter studies. *BMC Med Res Methodol.* Mar 13 2012;12:29.
24. Haugaard LK, Baker JL, Perng W, et al. Growth in Total Height and Its Components and Cardiometabolic Health in Childhood. *PLoS One.* Sep 22 2016;11(9):e0163564.
25. Oken E, Tilling K, Rifas-Shiman S, et al. Early Growth and Dysmetabolism at 11.5 years: A Cohort Analysis of the PROBIT Study. *The FASEB Journal.* 2015;29(1 Supplement):906.914.
26. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med.* Jul 1998;15(7):539-553. .
27. National Cholesterol Education Program Adult Treatment Panel III. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. *Circulation.* 2002;106:3143-3421.
28. Morrison JA, Friedman LA, Gray-McGuire C. Metabolic syndrome in childhood predicts adult cardiovascular disease 25 years later: the Princeton Lipid Research Clinics Follow-up Study. *Pediatrics.* Aug 2007;120(2):340-345. .
29. Morrison JA, Friedman LA, Wang P, Glueck CJ. Metabolic syndrome in childhood predicts adult metabolic syndrome and type 2 diabetes mellitus 25 to 30 years later. *J Pediatr.* Feb 2008;152(2):201-206. .
30. Bachorik PS, Lovejoy KL, Carroll MD, Johnson CL. Apolipoprotein B and AI distributions in the United States, 1988-1991: results of the National Health and Nutrition Examination Survey III (NHANES III). *Clin Chem.* Dec 1997;43(12):2364-2378.
31. Kleinman KP, Oken E, Radesky JS, Rich-Edwards JW, Peterson KE, Gillman MW. How should gestational weight gain be assessed? A comparison of existing methods and a novel method, area under the weight gain curve. *Int J Epidemiol.* Dec 2007;36(6):1275-1282.
32. Mei Z, Ogden CL, Flegal KM, Grummer-Strawn LM. Comparison of the prevalence of shortness, underweight, and overweight among US children aged 0 to 59 months by using the CDC 2000 and the WHO 2006 growth charts. *J Pediatr.* Nov 2008;153(5):622-628.
33. Furlong KR, Anderson LN, Kang H, et al. BMI-for-Age and Weight-for-Length in Children 0 to 2 Years. *Pediatrics.* Jul 2016;138(1).(pii):peds.2015-3809.
34. Perng W, Ringham BM, Glueck DH, et al. An observational cohort study of weight- and length-derived anthropometric indicators with body composition at birth and 5 mo: the Healthy Start study. *Am J Clin Nutr.* Aug 2017;106(2):559-567.

35. Johnson W, Choh AC, Lee M, Towne B, Czerwinski SA, Demerath EW. Characterization of the infant BMI peak: sex differences, birth year cohort effects, association with concurrent adiposity, and heritability. *Am J Hum Biol.* May-Jun 2013;25(3):378-388.
36. Bell KA, Wagner CL, Perng W, Feldman HA, Shypailo RJ, Belfort MB. Validity of Body Mass Index as a Measure of Adiposity in Infancy. *The Journal of Pediatrics.* 2018.
37. Slining MM, Herring AH, Popkin BM, Mayer-Davis EJ, Adair LS. Infant BMI trajectories are associated with young adult body composition. *J Dev Orig Health Dis.* Feb 2013;4(1):56-68.
38. Silverwood RJ, De Stavola BL, Cole TJ, Leon DA. BMI peak in infancy as a predictor for later BMI in the Uppsala Family Study. *Int J Obes (Lond).* Aug 2009;33(8):929-937.
39. Roy SM, Chesi A, Mentch F, et al. Body mass index (BMI) trajectories in infancy differ by population ancestry and may presage disparities in early childhood obesity. *J Clin Endocrinol Metab.* Apr 2015;100(4):1551-1560.
40. Aris IM, Bernard JY, Chen LW, et al. Infant body mass index peak and early childhood cardio-metabolic risk markers in a multi-ethnic Asian birth cohort. *Int J Epidemiol.* Apr 1 2017;46(2):513-525.
41. Sovio U, Kaakinen M, Tzoulaki I, et al. How do changes in body mass index in infancy and childhood associate with cardiometabolic profile in adulthood? Findings from the Northern Finland Birth Cohort 1966 Study. *Int J Obes (Lond).* Jan 2014;38(1):53-59.
42. Aris IM, Chen LW, Tint MT, et al. Body mass index trajectories in the first two years and subsequent childhood cardio-metabolic outcomes: a prospective multi-ethnic Asian cohort study. *Sci Rep.* Aug 21 2017;7(1):8424.
43. National Heart Lung and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. *Pediatrics.* Dec 2011;128(Suppl 5):S213-256.
44. Committee on Practice and Ambulatory Medicine and Bright Futures Periodicity Schedule Workgroup. 2016 Recommendations for Preventive Pediatric Health Care. *Pediatrics.* 2015;137(1):e20153596.
45. Grossman DC, Bibbins-Domingo K, Curry SJ, et al. Screening for Obesity in Children and Adolescents: US Preventive Services Task Force Recommendation Statement. *JAMA.* Jun 20 2017;317(23):2417-2426.
46. Block JP, Oken E. Practical Considerations for the US Preventive Services Task Force Recommendations on Obesity in Children and Adolescents. *JAMA Intern Med.* Aug 1 2017;177(8):1077-1079.
47. Lanigan J. Prevention of overweight and obesity in early life. *Proc Nutr Soc.* May 29 2018;29:1-10.
48. Weiskopf NG, Weng C. Methods and dimensions of electronic health record data quality assessment: enabling reuse for clinical research. *J Am Med Inform Assoc.* Jan 1 2013;20(1):144-151.
49. Ritchie JD, Miller CK, Smiciklas-Wright H. Tanita foot-to-foot bioelectrical impedance analysis system validated in older adults. *J Am Diet Assoc.* Oct 2005;105(10):1617-1619.
50. Boneva-Asiova Z, Boyanov MA. Body composition analysis by leg-to-leg bioelectrical impedance and dual-energy X-ray absorptiometry in non-obese and obese individuals. *Diabetes Obes Metab.* Nov 2008;10(11):1012-1018.

51. Streiner DL. Best (but oft-forgotten) practices: the multiple problems of multiplicity-whether and how to correct for many statistical tests. *Am J Clin Nutr.* Oct 2015;102(4):721-728. .

52. Kivimaki M, Kuosma E, Ferrie JE, et al. Overweight, obesity, and risk of cardiometabolic multimorbidity: pooled analysis of individual-level data for 120 813 adults from 16 cohort studies from the USA and Europe. *Lancet Public Health.* May 19 2017;2(6):e277-e285.

Figure Legends

Figure 1: Associations of overweight status at 6–24 months (at each timepoint and "ever" overweight) with (**A**) fat mass index, (**B**) HOMA-IR, (**C**) metabolic risk z-score, and (**D**) odds of obesity in early adolescence. Models were adjusted for the following covariates: Project Viva – maternal age, marital status, educational attainment, pre-pregnancy BMI, total gestational weight gain, smoking history, glucose tolerance status, and gestational hypertensive disorders, and child gestational age at delivery, race/ethnicity, sex, birth weight for gestational age z-scores, breastfeeding status and age at outcome measurement; PROBIT – maternal age, BMI at 6.5 years postpartum, educational attainment, marital status, occupation, smoking during pregnancy, gestational age at delivery, child sex, birth weight for gestational age z-scores and age at outcome measurement. Error bars represent 95% confidence intervals.

Figure 2: Associations of number of timepoints overweight between 6 and 24 months with (**A**) fat mass index, (**B**) HOMA-IR, (**C**) metabolic risk z-score, and (**D**) odds of obesity in early adolescence. Models were adjusted for the following covariates: Project Viva – maternal age, marital status, educational attainment, pre-pregnancy BMI, total gestational weight gain, smoking history, glucose tolerance status, and gestational hypertensive disorders, and child gestational age at delivery, race/ethnicity, sex, birth weight for gestational age z-scores, breastfeeding status and age at outcome measurement; PROBIT – maternal age, BMI at 6.5 years postpartum, educational attainment, marital status, occupation, smoking during pregnancy, gestational age at delivery, child sex, birth weight for gestational age z-scores and age at outcome measurement. Error bars represent 95% confidence intervals.

Table 1: Characteristics of study subjects in Project Viva and PROBIT

Project Viva (n=919)	**All**	**Ever overweight by WHO BMI**	**Never overweight by WHO BMI**	**p value**
Maternal				
Age				0.70
<20 years	29 (3.2)	4 (2.5)	25 (3.3)	
20-34 years	610 (66.4)	111 (68.9)	499 (65.8)	
≥ 35 years	280 (30.5)	46 (28.6)	234 (30.9)	
Education level				0.02
Not university educated	261 (28.4)	58 (36.0)	203 (26.8)	
University educated	658 (71.6)	103 (64.0)	555 (73.2)	
Marital status				0.18
Married/co-habituating	851 (92.6)	145 (90.1)	706 (93.1)	
Not married	68 (7.4)	16 (9.9)	52 (6.9)	
Maternal smoking history				0.02
Never smoked	650 (70.7)	105 (65.2)	545 (71.9)	
Smoked prior to pregnancy	184 (20.0)	32 (19.9)	152 (20.1)	
Smoked during pregnancy	85 (9.3)	24 (14.9)	61 (8.1)	
Pre-pregnancy BMI (kg/m^2)	24.8 (5.2)	25.9 (6.0)	24.6 (5.0)	<0.01
Total gestational weight gain (kg)	15.6 (5.3)	16.2 (5.7)	15.4 (5.2)	0.11
Glucose tolerance status				0.04
Normoglycemia	764 (83.1)	142 (88.2)	622 (82.1)	
Isolated hyperglycemia	80 (8.7)	8 (5.0)	72 (9.5)	
Intermediate glucose intolerance	29 (3.2)	1 (0.6)	28 (3.7)	
Gestational diabetes	46 (5.0)	10 (6.2)	36 (4.8)	
Hypertensive disorders of pregnancy				0.73
Normal blood pressure	822 (89.4)	142 (88.2)	680 (89.7)	
Gestational hypertension	63 (6.9)	11 (6.8)	52 (6.9)	
Chronic Hypertension	10 (1.1)	3 (1.9)	7 (0.9)	
Pre-eclampsia	24 (2.6)	5 (3.1)	19 (2.5)	
Child				
Sex				0.10
Male	460 (50.1)	90 (55.9)	370 (48.8)	
Female	459 (49.9)	71 (44.1)	388 (51.2)	
Race/ethnicity				0.04
White	598 (65.1)	98 (60.9)	500 (66.0)	
Black	143 (15.6)	38 (23.6)	105 (13.9)	
Hispanic	39 (4.2)	6 (3.7)	33 (4.4)	
Asian	27 (2.9)	3 (1.9)	24 (3.2)	
Others	112 (12.2)	16 (9.9)	96 (12.7)	
Gestational age at delivery (weeks)	39.6 (1.6)	39.5 (1.7)	39.6 (1.6)	0.42
Birthweight-for-gestational age z-score (SD units)	0.2 (1.0)	0.4 (0.9)	0.2 (1.0)	<0.01
Breastfeeding status at 6 months				<0.01
Formula only	79 (9.1)	13 (8.7)	66 (9.2)	
Weaned	312 (35.9)	70 (47.0)	242 (33.6)	
Mixed feeding	239 (27.5)	41 (27.5)	198 (27.5)	
Breastmilk only	239 (27.5)	25 (16.8)	214 (29.7)	

PROBIT (n=12,747)	**All**	**Ever overweight by WHO BMI**	**Never overweight by WHO BMI**	**p value**
Maternal				
Age				0.20
<20 years	1704 (13.6)	447 (14.6)	1257 (13.3)	
20-34 years	10284 (82.1)	2491 (81.1)	7793 (82.4)	
≥ 35 years	542 (4.3)	134 (4.4)	408 (4.3)	
Education level				0.90
Did not complete university	11047 (86.7)	2718 (87.0)	8329 (86.6)	
Completed university	1700 (13.3)	407 (13.0)	1293 (13.4)	
Marital status				0.19
Registered/unregistered marriage	12280 (96.3)	3027 (96.9)	9253 (96.2)	
Unmarried	467 (3.7)	98 (3.1)	369 (3.8)	
Smoking during pregnancy				0.57
No	12499 (98.1)	3068 (98.2)	9431 (98.0)	
Yes	248 (1.9)	57 (1.8)	191 (2.0)	
BMI at 6.5 years (kg/m^2)	24.5 (4.4)	24.9 (4.3)	24.3 (4.4)	<0.01
Child				
Sex				<0.01
Male	6204 (48.7)	1191 (38.1)	5013 (52.1)	
Female	6543 (51.3)	1934 (61.9)	4609 (47.9)	

Gestational age at delivery (weeks)	39.4 (1.0)	39.4 (1.0)	39.4 (1.0)	0.40
Birthweight-for-gestational age z-score (SD units)	0.4 (1.0)	0.6 (1.0)	0.4 (1.0)	<0.01

Table 2: Prevalence of overweight at 6─24 months and distributions of early adolescent cardio-metabolic outcomes in Project Viva and PROBIT

	Project Viva n=919[a]	**PROBIT n=12,747[a]**
Overweight prevalence at 6–24 months		
Month 6 (range 4-8 months)[b]		
CDC WFL[c] ≥ 95th percentile	134/891 (15.0)	1521/12594 (12.1)
WHO WFL[d] ≥ 97.7th percentile	86/891 (9.7)	998/12594 (7.9)
WHO BMI[e] ≥ 97.7th percentile	75/891 (8.4)	895/12594 (7.1)
Month 12 (range 10-14 months)[b]		
CDC WFL ≥ 95th percentile	64/701 (9.1)	2594/12707 (20.4)
WHO WFL ≥ 97.7th percentile	50/701 (7.1)	2180/12707 (17.2)
WHO BMI ≥ 97.7th percentile	54/701 (7.7)	2171/12707 (17.1)
Month 18 (range 16-20 months)[b]		
CDC WFL ≥ 95th percentile	68/634 (10.7)	424/2965 (14.3)
WHO WFL ≥ 97.7th percentile	63/634 (9.9)	396/2965 (13.4)
WHO BMI ≥ 97.7th percentile	67/634 (10.6)	454/2965 (15.3)
Month 24 (range 22-26 months)[b]		
CDC WFL ≥ 95th percentile	53/563 (9.4)	628/4590 (13.7)
WHO WFL ≥ 97.7th percentile	48/563 (8.5)	567/4590 (12.3)
WHO BMI ≥ 97.7th percentile	44/563 (7.8)	628/4590 (13.7)
Ever overweight[b]		
CDC WFL ≥ 95th percentile	206/919 (22.4)	3715/12747 (29.1)
WHO WFL ≥ 97.7th percentile	160/919 (17.4)	3069/12747 (24.1)
WHO BMI ≥ 97.7th percentile	161/919 (17.5)	3125/12747 (24.5)
Early adolescent outcomes		
Height z-score (SD units)[f]	0.3 (1.0)	0.3 (1.0)
BMI z-score (SD units)[f]	0.4 (1.1)	-0.1 (1.0)
Sum of skinfolds (mm)[f]	28.4 (13.9)	23.1 (11.4)
Fat mass index (kg/m^2)[f]	4.9 (3.5)	3.3 (2.2)
Waist circumference (cm)[f]	73.0 (11.8)	64.8 (8.1)
Systolic BP z-score (SD units)[f]	-0.1 (0.8)	0.4 (0.8)
HOMA-IR[g]	2.6 (2.1)	0.9 (1.2)
HDL-cholesterol (mg/dL)[f]	55.2 (13.6)	NA[h]
Triglycerides (mg/dL)[f]	70.3 (31.1)	NA[h]
Apolipoprotein A1 (g/L)	NA[h]	1.6 (0.4)
Metabolic risk score (SD units)[f]	-0.02 (0.6)	0.01 (0.5)
Obesity[b]	113 (12.3)	632 (5.0)

[a] Sample size is based on those who had a measure of weight and length at 6, 12, 18 or 24 months (within ±2 months at each timepoint) and at least one outcome measure at the early adolescent visit

[b] Numbers represent N (%)

[c] CDC WFL: Center for Disease Control and Prevention weight-for-length

[d] WHO WFL: World Health Organization weight-for-length

[e] WHO BMI: World Health Organization body mass index

[f] Numbers represent mean (SD)

[g] Numbers represent median (interquartile range)

[h] NA: Not applicable