Maternal Preconception Body Size and Early Childhood Growth during Prenatal and Postnatal Periods Are Positively Associated with Child-Attained Body Size at Age 6–7 Years: Results from a Follow-up of the PRECONCEPT Trial

Phuong Hong Nguyen,1,2 Melissa F Young,3 Long Quynh Khuong,4 Lan Mai Tran,5 Thai Hong Duong,2,5 Hoang Cong Nguyen,2,5 Reynaldo Martorell,3 and Usha Ramakrishnan3

1International Food Policy Research Institute, Washington, DC, USA; 2Thai Nguyen University of Pharmacy and Medicine, Thai Nguyen, Vietnam; 3Emory University, Atlanta, GA, USA; 4Hanoi University of Public Health, Hanoi, Vietnam; and 5Thai Nguyen National Hospital, Thai Nguyen, Vietnam

ABSTRACT

Background: Growth faltering is associated with adverse consequences during childhood and later life. However, questions remain on the relative importance of preconception maternal nutritional status (PMNS) and child growth during the first 1000 d of life.

Objectives: We examined associations between PMNS, gestational weight gain (GWG), and child growth during the first 1000 d with attained body size at age 6–7 y.

Methods: We used data from a follow-up of a double-blinded randomized controlled trial of preconception micronutrient supplementation in Vietnam (n = 5011 women). The outcomes included offspring height-for-age z score (HAZ), BMI-for-age z score (BMIZ), and prevalence of stunting and overweight/obese at age 6–7 y (n = 1579). We used multivariable linear and Poisson regression models to evaluate the relative contributions of PMNS (height and BMI), GWG, and conditional growth in 4 periods: fetal, 0–6 mo, 6–12 mo, and 12–24 mo.

Results: PMNS was positively associated with child-attained size at 6–7 y. For each 1-SD higher maternal height and BMI, offspring had 0.28-SD and 0.13-SD higher HAZ at 6–7 y, respectively. Higher maternal BMI and GWG were associated with larger child BMIZ (β: 0.29 and 0.10, respectively). Faster linear growth, especially from 6 to 24 mo, had the strongest association with child HAZ at 6–7 y (β: 0.39–0.42), whereas conditional weight measures in all periods were similarly associated with HAZ (β: 0.10–0.15). For BMIZ at 6–7 y, the magnitude of association was larger and increased with child age for conditional weight gain (β: 0.21–0.41) but smaller for conditional length gain. Faster growth in the first 2 y was associated with reduced risk of stunting and thinness but increased risk of overweight/obese at 6–7 y.

Conclusions: Interventions aimed at improving child growth while minimizing the risk of overweight during the school age years should target both women of reproductive age prior to conception through delivery and their offspring during the first 1000 d. The trial was registered at clinicaltrials.gov as NCT01665378. J Nutr 2021;151:1302–1310.

Keywords: conditional growth, gestational weight gain, preconception maternal nutritional status, overweight/obese, stunting, Vietnam

Introduction

The first 1000 d of life that begins from conception to the second birthday is a time of rapid development of a child’s brain and organ systems and has been identified a critical window of opportunity for influencing child growth and long-term consequences (1, 2). Stunting [height-for-age z score (HAZ) ≤−2 SD], a population-level indicator of the adequacy of linear growth during this period, has been associated with poor cognition and educational performance, adult height attainment, reduced productivity and lifelong earnings, increased morbidity and mortality, and intergenerational effects (1–5). Given the importance of early
linear growth, global targets have been set to reduce child stunting by 40% by 2025 (6). However, many nutrition and health interventions during infancy and the second year of life have had modest or null findings (7–9). To address this public health challenge, there have been calls to better understand the complex and multifactorial influences of child growth patterns, especially the contribution of maternal nutrition before and during pregnancy.

There is growing evidence on the critical role of maternal nutrition for child growth and development (3,10–13), but less is known about the relative importance of maternal nutrition before and during pregnancy. We have previously reported that preconception nutrition has a similar and independent influence on birth outcomes compared with maternal nutrition during pregnancy using prospective data from a cohort of Vietnamese women (12). Women with a preconception weight <43 kg or a gestational weight gain <8 kg were around 3 times more likely to give birth to a small for gestational age (SGA) or low birth weight infant. Furthermore, women with preconception height <150 cm or a weight <43 kg were at nearly twice the increased risk of having a stunted child at 2 y (13). However, the long-term influence of maternal preconception nutritional status remains largely unknown.

Child growth during early childhood may set the stage for a lifetime (14–16). Evidence from the Consortium on Health Orientated Research in Transitional Societies (COHORTS) collaboration using data from 5 prospective birth cohort studies found that faster linear growth from birth to age 2 y was associated with reduced risk of adult short stature but not risk of overweight (14). In contrast, faster weight gain during the first 2 y of life was associated with increased risk of overweight in adulthood and elevated blood pressure (14). These studies also showed that child growth patterns during early childhood may influence intergenerational offspring birth outcomes (15). Although COHORTS data provide powerful evidence on the importance of early child growth patterns, these studies were carried out >30 y ago and did not examine the role of maternal nutrition both prior to conception and during pregnancy, nor have reliable measures of growth in utero. Those results may not be generalizable in light of the rapid changes that have occurred in the food and built environment in recent decades characterized by increased reliance on unhealthy ultra-processed foods and sedentary lifestyles. Updated research is needed given the emerging nutrition transition and double burden of malnutrition in low-resource settings.

Understanding the patterns and determinants of child growth from conception through the school-age years is critical for designing effective program and policies that address the growing global health challenge of the double burden of malnutrition (i.e., under- and overnutrition that cluster within households and communities in many low- to middle-income countries) (17,18). This is particularly relevant for Vietnam, a country that is experiencing rapid social and economic change and nutrition transition (19); the prevalence of child (<5 y) stunting has declined (from 40% in early 2000 to 23% in 2017), whereas overweight has increased (from 2.6% to 5.9%) (20). Overweight and obesity are also high among school-age children (at 17% and 8.6%, respectively) (21). Currently, there are limited data from well-designed longitudinal studies that include preconception, pregnancy, and early childhood in low-resource settings to allow for understanding the relative importance of timing across and beyond the first 1000 d. We have the opportunity to use prospectively collected data from the Preconception micronutrient supplementation (PRECONCEPT) study to address these gaps by examining the associations between preconception maternal nutritional status (PMNS), gestational weight gain (GWG), and child growth during the first 1000 d with child malnutrition and attained body size at age 6–7 y.

### Methods

#### Data sources and study population

Children in this study are offspring of women who participated in a double-blind randomized controlled trial (PRECONCEPT; registered at clinicaltrials.gov as NCT01665378), which evaluated the effects of preconception micronutrient supplementation on maternal and child health outcomes (22). Details of the parent study have been published previously (22). Briefly, 5011 women of reproductive age were randomly assigned to receive weekly supplements containing 2800 μg folic acid (FA), 60 mg iron and 2800 μg FA (IFA), or multiple micronutrients (MMs, containing the same amount of IFA and 15 micronutrients as shown in Supplemental Table 1), from baseline until conception, followed by daily prenatal supplements containing 60 mg iron and 400 μg FA until delivery. Women were followed prospectively to identify pregnancies and evaluate birth outcomes; 1813 women conceived between 2012 and 2014, and 1599 had live births (1579 singleton births, 10 twins). Live births were followed at 6 mo and at 1, 2, and 6–7 y (Figure 1) with follow-up rates of 96%, 82%, 94%, and 89%, respectively. We have previously shown that weekly supplementation with MMs or IFA improved linear growth at age 2 y (23), but no impact was found at age 6–7 y (24) compared with FA. The current analysis includes 1402 women who delivered singleton live infants with available data on maternal preconception height/weight and offspring anthropometry data at 6–7 y.

#### Outcome measurements

Child weight and height at 6–7 y were measured by trained and standardized field staff using standard methods (25). Child weight was measured using electronic weighing scales precise to 10 g, and child height was measured with collapsible length boards, which were precise to 1 mm. The average of duplicate measurements of height and weight was then converted into HAZs and BMI-for-age z scores (BMIZs) according to 2006 WHO child growth standards (26). Stunting and thinness were defined as HAZs and BMIZs below −2 z score, respectively. Overweight/obese was defined as BMIZ above 1 z score (27,28).

#### Predictor variables

**Preconception maternal nutritional status and gestational weight gain.**

Maternal prepregnancy weight and height were measured at enrollment (preconception) in community health centers by trained staff using standard procedures (25,29). Prepregnancy BMI was calculated as weight/height² (kg/m²). Maternal underweight was defined as BMI <18.5 and overweight as BMI >25. Gestational weight gain was calculated from maternal weight measured at delivery and prepregnancy weight. Currently in Vietnam, there are no local weight
FIGURE 1  Details of follow-up for the study sample of 1579 singleton livebirths from the first 1000 d to early childhood. All percentages were calculated using the total eligible birth sample (n = 1579).

| In utero            | Did not attend the study visit: 256 (16.2%) | Examined: 1323 (83.8%) | Fetal growth: 1321 (83.7%) |
|---------------------|---------------------------------------------|------------------------|---------------------------|
| At birth            | Drop out of study: 161 (10.2%)               | Examined: 1569 (99.4%) | Length and weight measures: 1389 (88.9%) |
|                     | Did not attend the study visit:              |                        |                           |
| At 6 months         | Death: 7 (0.4%)                               | Examined: 1562 (98.9%) | Length and weight measures: 1510 (95.6%) |
|                     | Did not attend the study visit: 10 (0.6%)    |                        |                           |
| At 12 months        | Death: 7 (0.4%)                               | Examined: 1333 (84.4%) | Length and weight measures: 1293 (81.9%) |
|                     | Migration out of study areas: 9 (0.6%)       |                        |                           |
|                     | Did not attend the study visit: 230 (14.6%)  |                        |                           |
| At 24 months        | Death: 8 (0.5%)                               | Examined: 1536 (97.3%) | Length and weight measures: 1482 (93.9%) |
|                     | Migration out of study areas: 24 (1.5%)      |                        |                           |
|                     | Did not attend the study visit: 11 (0.7%)    |                        |                           |
| At 6-7 years        | Death: 8 (0.5%)                               | Examined: 1441 (91.3%) | Length/height and weight measurements: 1402 (88.8%) |
|                     | Migration out of study areas: 29 (1.8%)      |                        | All variables for the saturated models: 857 (54%) |
|                     | Did not attend the study visit: 85 (5.4%)    |                        |                           |

gain recommendations, and thus we compared gestational weight gain in relation to Institute of Medicine (IOM) recommendations to define those above or below IOM recommendations (30).

**Offspring growth across the first 1000 d.**

Offspring growth during the first 1000 d was measured by ultrasound for fetal growth and child anthropometry at birth, 6 mo, 1 y, and 2 y of age. Fetal measurements including head circumference, abdominal circumference, and femur length were obtained during routine prenatal care visits in the second and third trimesters of pregnancy by trained obstetricians, using standardized ultrasound procedures. Details of the ultrasound examination techniques used are provided elsewhere (31). Duplicate measures obtained from separate scans were then averaged and used to estimate fetal weight using the Hadlock formula (32). Fetal weight and femur length were used in estimating conditional weight gain and linear growth, respectively. Birth weight and birth length was measured within 7 d after birth using standard procedures (25, 29).

Gestational age was estimated based on the date of last menstrual period that was obtained prospectively by village health workers during their biweekly home visits. Child weight and length at 6 mo, 1 y, and 2 y were collected using standard procedures as described above (25).

Potential confounders

Potential confounding variables included maternal age, parity, preconception anemia, child age, sex, preterm status, and household socioeconomic status (SES). Gestational age was calculated as the number of days between the day of delivery and the first day of the last menstrual period, which was obtained prospectively by village health workers during their biweekly home visits. A preterm birth was defined as a birth occurring before 37 completed weeks of pregnancy. Hemoglobin concentrations were measured from capillary blood samples (by finger prick) at preconception using a portable field B-Hemoglobin Analyzer (Radiometer Pacific Pty, Ltd) (34); anemia was defined as a hemoglobin value <12 g/dL (35). Household SES was measured at baseline and was calculated using a principal components analysis of assets and services, including house and land ownership, housing quality, access to services (electricity, gas, water, and sanitation services), and household assets (productive assets, durable goods, animals, and livestock). The first component derived from component scores was used to divide household SES into quartiles (36, 37).

**Statistical analysis**

Normality of the continuous outcome variables was assessed using the Kolmogorov–Smirnov test. Descriptive analyses (means, SDs, percentages) were used to report characteristics of the study population. Multivariable linear regressions with robust standard errors were used to examine associations between PMNS indicators, GWG, and child conditional growth in early childhood with child-attained size at 6–7 y (continuous variables). These models were built in 3 steps: 1) maternal preconception height, BMI, and GWG; 2) child conditional measures; and 3) both maternal and child measures together. All models
adjusted for child (age, sex, and preterm status), maternal (age, parity, and anemia at baseline), and household levels (SES at preconception), as well as treatment group and duration of the preconception intervention. Results for these models were expressed as differences in HAZ and BMIZ associated with a 1–z score change in maternal height, BMI, or child conditional variables. We also conducted sensitivity analysis using full-information maximum likelihood for estimation while accounting for missing data among the controlled variables under the assumption of missing at random and without having to do imputation (38). For the dichotomous indicators of child malnutrition at 6–7 y, we used multivariable Poisson regressions, and results were expressed as incident risk ratios. All data analyses were performed using Stata version 16 (StataCorp). Results were considered significant when \( P < 0.05 \).

**Ethical approval**

The study was approved by the Ethical Committee of the Institute of Social and Medicine Studies in Vietnam and the Emory University Institutional Review Board, Atlanta, Georgia, USA. The trial was registered in at clinicaltrials.gov as NCT01665378. Written informed consent was obtained from all study participants.

**Results**

The final study sample included the singleton live births born to 1402 women with available data on maternal preconception height/weight and offspring anthropometry data at 6–7 y. On average, mothers were 26 y old at the time of enrollment, and >90% had 1 child. More than half of the mothers had completed middle school (54%), and 38% had completed high school or higher. Of the 1402 women included in the study, 30% had height <150 cm, 25.6% were underweight, and 5.7% were overweight/obese (Table 1). More than two-thirds of women had gestational weight gain below the IOM recommendation (30).

Measures of offspring growth and attained size during the first 1000 d through age 6–7 y are also presented in Table 1. Mean birth weight and length were 3.1 kg and 49 cm, respectively. Stunting declined from 11% at birth to 3.6% at 6 mo, followed by an increase to 16.3% at 2 y, and reduced to 9.6% at age 6–7 y. Overweight/obesity declined from 13% at 6 mo to 7% at 6–7 y.

Maternal preconception height and BMI were positively associated with child-attained size at 6–7 y (Table 2). For each 1-SD higher maternal height, offspring had 0.29-SD higher BMIZ at 6–7 y. A 1-SD greater maternal BMI was also associated with 0.12-SD and 0.28-SD greater HAZ and BMIZ at 6–7 y. Moreover, preparations height was positively associated with child HAZ at 6–7 y of age, and these associations remained even after accounting for GWG and child growth in the first 2 y. We also found that linear growth conditionals (particularly from 6 to 24 mo) had the strongest association with HAZ at 6–7 y (effect size: 0.4 SD), whereas weight conditional measures mattered little (effect size: 0.10–0.15 SD). For BMIZ, the opposite is the case, where the association was most pronounced with weight conditional measures, together with preconception maternal BMI.

Several studies, mostly observational and from developed countries, have demonstrated the importance of maternal nutritional status prior to conception for reproductive health outcomes and offspring growth, development, and long-term health (39, 40). Overweight women are especially at increased risk of preeclampsia and delivering preterm, whereas underweight women are at increased risk of delivering SGA infants, who in turn are more likely to experience subsequent growth failure and stunting by age 2 y (11). Possible mechanisms that can explain the association between maternal anthropometry prior to conception and offspring birth weight include shared genes, environment, and epigenetic changes (15). Consistent with a growing body of research, our group has also demonstrated the importance of maternal prepregnancy weight for weight gain during pregnancy as well as birth size (12) and offspring linear growth across the first 1000 d (13). In this article, we extend these findings to growth during the first 6–7 y of age using prospectively collected data that allow us to examine the independent contribution of measures of maternal nutrition status both before and during pregnancy after accounting for growth during the first 1000 d on attained size and BMI as children enter school. We found that higher maternal preconception height was associated with higher child HAZ and reduced risk of stunting at 6–7 y but not risk overweight. In contrast, a 1-SD increase in maternal

**Discussion**

Using prospectively collected data from preconception through age 6–7 y, our findings demonstrate the importance of PMNS, GWG, and early child growth during the first 1000 d on child-attained size and risk of malnutrition among young school-aged children at 6–7 y. Prepregnancy height was positively associated with child HAZ at 6–7 y of age, and these associations remained even after accounting for GWG and child growth in the first 2 y. We also found that linear growth conditionals (particularly from 6 to 24 mo) had the strongest association with HAZ at 6–7 y (effect size: 0.4 SD), whereas weight conditional measures mattered little (effect size: 0.10–0.15 SD). For BMIZ, the opposite is the case, where the association was most pronounced with weight conditional measures, together with preconception maternal BMI.

Additional studies, mostly observational and from developed countries, have demonstrated the importance of maternal nutritional status prior to conception for reproductive health outcomes and offspring growth, development, and long-term health (39, 40). Overweight women are especially at increased risk of preeclampsia and delivering preterm, whereas underweight women are at increased risk of delivering SGA infants, who in turn are more likely to experience subsequent growth failure and stunting by age 2 y (11). Possible mechanisms that can explain the association between maternal anthropometry prior to conception and offspring birth weight include shared genes, environment, and epigenetic changes (15). Consistent with a growing body of research, our group has also demonstrated the importance of maternal prepregnancy weight for weight gain during pregnancy as well as birth size (12) and offspring linear growth across the first 1000 d (13). In this article, we extend these findings to growth during the first 6–7 y of age using prospectively collected data that allow us to examine the independent contribution of measures of maternal nutrition status both before and during pregnancy after accounting for growth during the first 1000 d on attained size and BMI as children enter school. We found that higher maternal preconception height was associated with higher child HAZ and reduced risk of stunting at 6–7 y but not risk overweight. In contrast, a 1-SD increase in maternal

Preconception nutrition and early childhood growth 1305
### TABLE 1  
Comparison of characteristics of the study sample and measures of offspring size and growth during the first 1000 d through 6–7 y in the final analytic sample and those missing data at follow-up

| Characteristic | Study sample*<sup>2</sup>  
| (n = 1402) | Missing data at age 6–7 y  
| (n = 177) |
|---|---|

**Maternal characteristics**

- **Age, y**  
  25.9 ± 4.3  
  25.8 ± 4.2

- **Education, %**
  - Primary school: 7.3  
  - Middle school: 55.3  
  - High school: 25.7  
  - College or higher: 11.6

- **Improved drinking water, %**: 90.8  
- **Improved sanitation facilities, %**: 96.6

- **Prepregnancy weight, kg**: 45.8 ± 5.5  
- **Prepregnancy height, cm**: 152.7 ± 5.0

- **Prepregnancy BMI, kg/m², %**
  - <18.5: 25.5  
  - 18.5 to <25: 68.9  
  - ≥25: 5.7

- **Gestational weight gain, kg, %**
  - Below IOM recommendation: 68.9  
  - Within IOM recommendation: 25.5  
  - Above IOM recommendation: 5.7

**Child characteristics**

- **Female, %**: 49.5  
- **Gestational age, wk**: 39.2 ± 2.0  
- **Exclusive breastfeeding at 3 mo, %**: 59.4  
- **Adequate diet at 12 mo, %**: 75.5  
- **Adequate diet at 24 months, %**: 58.6

**Attained size and growth measures**

- **Second to third trimester of pregnancy**
  - Fetal weight, g: 1.4 ± 0.7  
  - Femur length, cm: 4.9 ± 1.8

- **Birth**
  - Birth weight, g: 3089 ± 444  
  - Birth length, cm: 49.0 ± 3.0

- **Low birth weight, %**: 4.7  
- **SGA, %**: 15.2  
- **Stunting, %**: 11.0  
- **Overweight/obese, %**: 9.2

- **At 6 mo**
  - Weight, kg: 5.2 ± 0.7  
  - Length, cm: 57.4 ± 2.8

- **LAZ**: −0.1 ± 1.0  
- **BMIZ**: −0.1 ± 1.0

- **Stunting, %**: 2.6  
- **Overweight/obese, %**: 12.9

- **At 12 mo**
  - Weight, kg: 8.0 ± 1.0  
  - Length, cm: 68.7 ± 25

- **LAZ**: −0.6 ± 1.0  
- **BMIZ**: −0.1 ± 1.0

- **Stunting, %**: 7.2  
- **Overweight/obese, %**: 11.9

- **At 2 y**
  - Weight, kg: 9.8 ± 1.0  
  - Length, cm: 78.0 ± 2.7

(Continued)
preconception BMI was associated with 1.5 times higher risk of overweight during early childhood. Our findings highlight the need to improve women’s height to prevent stunting in the next generation while addressing the need to ensure healthy weight for women in their reproductive years. The preconception period has been recommended as a period of special opportunity for intervention due to its relevance on life course epidemiology, embryo programming around the time of conception, maternal motivation, and disappointment with interventions starting in pregnancy (40). Although preconceptional interventions have the potential to ensure optimal nutritional status (especially weight and micronutrient status), interventions to improve height will require investments much earlier in the life course (7).

Several studies have examined the importance of GWG for maternal and infant outcomes. Inadequate GWG has been associated with increased risk of giving birth to an SGA infant (12), whereas excessive GWG has been associated with greater postpartum weight retention (41–43) and increased risk of child obesity (44). However, the current recommendations for GWG are based primarily on studies from developed countries. Studies from Asia have shown that 31% of women gained below the IOM recommendations and 37% above the recommended GWG guidelines (45), whereas 70% of women in our study had inadequate GWG, and only 6% gained above the recommendation. Although the current study did not find strong associations between GWG and child nutrition status, further research is needed on both the long-term implications of GWG and appropriateness of IOM recommendations, especially in countries experiencing nutrition transition.

Consistent with a growing body of research that has examined the contribution of child growth during the first 1000 d and thereafter to final attained size, our results show that faster linear growth, particularly during between 6 and 24 mo, was associated with child HAZ at 6–7 y ($\beta$: 0.41–0.42), even after accounting for the strong effects of preconception maternal height and BMI. Similar growth trajectories by 6 mo

| TABLE 1 (Continued) |
|----------------------|
| Characteristic       | Study sample $^2$ (n = 1402) | Missing data at age 6–7 y (n = 177) |
| LAZ                  | $-1.1 \pm 0.9$ | $-1.2 \pm 1.0$ |
| BMIZ                 | $-0.0 \pm 0.8$ | $-0.1 \pm 0.8$ |
| Stunting, %          | 16.3 | 22.9 |
| Overweight/obese, %  | 9.6 | 8.4 |
| At 6–7 y             |
| Weight, kg           | 18.8 ± 3.2 |
| Height, cm           | 113.6 ± 5.3 |
| HAZ $^3$             | $-0.8 \pm 0.9$ |
| BMIZ                 | $-0.7 \pm 1.1$ |
| Stunting, %          | 9.6 |
| Overweight/obese, %  | 8.9 |

$^1$Values are means ± SDs or percentages. BMIZ, BMI-for-age $z$ score; HAZ, height-for-age $z$ score; IOM, Institute of Medicine; LAZ, length-for-age $z$ score; SGA, small for gestational age.

$^2$Values are numbers (percentages).

$^3$Currently in Vietnam, there are no local weight gain recommendations, and thus we compared gestational weight gain in relation to IOM recommendations to define those above or below IOM recommendation.

| TABLE 2 | Association of maternal preconception nutrition status and gestational weight gain with child-attained HAZ and BMIZ at 6–7 y $^1$ |
|----------|-------------------------------------------------------------------------------------------------------------------------------------|
| Outcomes | Model 1 $^2$                                                                                                      | Model 2 $^3$                                                                                   |
|          | Complete case (n = 1271) | FIML $^4$ (n = 1402) | Complete case (n = 857) | FIML (n = 1402) |
|          | $\beta$ (95% CI)         | $\beta$ (95% CI)     | $\beta$ (95% CI)       | $\beta$ (95% CI) |
| HAZ      | Maternal preconception height                                  | 0.29 $^6$ (0.24, 0.34) | 0.28 $^6$ (0.24, 0.33) | 0.07 $^7$ (0.02, 0.12) | 0.09 $^6$ (0.05, 0.13) |
|          | Maternal preconception BMI                                     | 0.12 $^6$ (0.07, 0.17) | 0.13 $^6$ (0.08, 0.18) | 0.06 $^7$ (0.01, 0.11) | 0.07 $^6$ (0.02, 0.11) |
|          | Gestational weight gain                                        | 0.02 $^6$ (–0.03, 0.07) | 0.03 $^6$ (–0.02, 0.08) | –0.02 $^7$ (–0.07, 0.03) | –0.01 $^7$ (–0.06, 0.03) |
| BMIZ     | Maternal preconception height                                  | –0.02 $^6$ (–0.08, 0.04) | –0.02 $^6$ (–0.08, 0.04) | –0.07 $^7$ (–0.14, –0.01) | –0.04 $^7$ (–0.10, 0.01) |
|          | Maternal preconception BMI                                     | 0.28 $^6$ (0.21, 0.34) | 0.29 $^6$ (0.23, 0.35) | 0.16 $^7$ (0.10, 0.23) | 0.17 $^6$ (0.12, 0.23) |
|          | Gestational weight gain                                        | 0.11 $^6$ (0.05, 0.17) | 0.10 $^6$ (0.04, 0.16) | 0.03 $^7$ (–0.04, 0.09) | 0.01 $^7$ (–0.04, 0.07) |

$^1$Values are $\beta$s (95% CIs). BMIZ, BMI-for-age $z$ score; FIML, full-information maximum likelihood with missing values; HAZ, height-for-age $z$ score.

$^2$Model 1 used maternal preconception nutrition status and gestational weight gain as main predictors, adjusted for child age, sex, preterm status, mother age, parity, preconception anemia, household socioeconomic status, treatment group, and duration of the preconception intervention.

$^3$Model 2 included both maternal and child conditional growth variables, adjusted for all covariates as in model 1. Results for the child conditional growth variables are shown in Figure 2.

$^4$Full-information maximum likelihood for estimation while accounting for missing data among the independent variables under the assumption of missing at random and without having to do imputation.

$^5$P < 0.001.

$^6$P < 0.01.

$^7$P < 0.05.
FIGURE 2. Association of maternal preconception nutrition status and early childhood conditional relative weight gain and height gain with attained HAZ and BMIZ at 6–7 y: (A) HAZ 6–7 y and (B) BMIZ 6–7 y. Values are βs (95% CIs). Results from full model include both maternal and child conditional growth variables, adjusted for child age, sex, preterm status, mother age, parity, preconception BMI and anemia, household socioeconomic status, treatment group, and duration of the preconception intervention. BMIZ, BMI-for-age z score; HAZ, height-for-age z score.

Our findings confirm previously reported positive associations between faster weight gain in early life with higher BMI at 6–7 y. This is especially relevant in light of the double burden of malnutrition in many low- to middle-income countries where underweight and stunting remain a persistent problem, but overweight and obesity are on the rise (3, 49). Although underweight and stunting among children are associated with increased risk of infectious disease, poor cognitive development, reduced earning potential, and long-term chronic disease risk (3), overweight and obesity among children are also associated with an increased risk of overweight and obesity and cardiometabolic diseases in later life (50–52). Countries such as Vietnam that have or are experiencing rapid changes in nutrition outcomes (53–57) need critical information on how to optimize targeted interventions that will reduce the burden of undernutrition yet prevent overweight/obesity.

Key strengths of our study include a well-designed longitudinal study that includes preconception, pregnancy, and early childhood in low-resource settings with a high follow-up rate of...
91% at the age of 6 y. The rich data on maternal preconception, gestational weight gain, and fetal growth, as well as multiple assessments of growth at different ages with a standardized methodology, allowed us to examine the relative importance of timing across and beyond the first 1000 d on child growth at school age. Although birth size measurements were collected up to a week, they were obtained for >90% of the births within 24 h of birth, and sensitivity analysis confirmed the robustness of our conclusions. The use of conditional growth analyses had the advantage of reducing the correlations between multiple measurements and allowed us to separate the roles of linear growth from soft tissue gain (fat mass and fat-free mass) (14). Finally, our outcomes measured at age 6–7 y are useful to represent the beginning of the school age years when children are exposed to new and challenging environments.

This study has some limitations—notably, adequacy of data on energy expenditure and changes in diet during the preschool years. The low prevalence of overweight/obesity among children (at 7%) further limited our power to detect significant associations. Our study was restricted to measures of maternal body size to assess maternal nutritional status, and future work should consider inclusion of additional measures of body composition and nutritional biomarkers. Future studies that continue to follow up this cohort have the potential to advance current understanding of the mechanism and patterns of child growth on intellectual development, cardiometabolic risk, and human capital outcomes later in life.

Conclusion
Our results suggest important longstanding effects of preconception nutritional status on child growth. This work has implications for prioritizing women’s nutrition in low-resource settings to optimize child growth. Balanced multidisciplinary programs and policies that combine nutrition education with family planning services as part of preconception care are needed to ensure optimal maternal preconception BMI and GWG in the efforts to prevent and control for the emerging double burden of nutrition.

Acknowledgments
The authors’ contributions were as follows—PHN, RM, and UR: designed research; PHN, THD, and HCN: conducted research; LQK and LMT: analyzed and interpretation of data; PHN, MFY, and UR: wrote the paper; and all authors: provided the critical revision of the manuscript for important intellectual content and have read and approved the final manuscript.

References
1. Martorell R. Improved nutrition in the first 1000 days and adult human capital and health. Am J Hum Biol 2017;29(2):1–24.
2. Victora CG, Adair L, Fall C, Hallal PC, Martorell R, Richter L, Sachdev HS; Maternal and Child Undernutrition Study Group. Maternal and child undernutrition: consequences for adult health and human capital. Lancet 2008;371:340–57.
3. Black RE, Victora CG, Walker SP, Bhutta ZA, Christian P, de Onis M, Ezzati M, Grantham-McGregor S, Katz J, Martorell R, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. Lancet 2013;382:427–51.
4. de Onis M, Branca F. Childhood stunting: a global perspective. Matern Child Nutr 2016;12(Suppl 1):12–26.
5. Ramakrishnan U. Impact of nutrition on the next generation: the INCAP longitudinal study. Food Nutr Bull 2020;41:S50–8.
6. WHO. WHA global nutrition targets 2025: stunting policy brief [Internet]. [Accessed 2020 Aug 10]. Available from: https://www.who.int/nutrition/topics/globaltargets_stunting_policybrief.pdf.
7. Bhutta ZA, Das JK, Rizvi A, Gaffey MF, Walker N, Horton S, Webb P, Larrey A, Black RE; Lancet Nutrition Interventions Review Group, Maternal and Child Nutrition Study Group. Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? Lancet 2013;382:452–77.
8. Christian P, Shaikh S, Shamim AA, Mehra S, Wu L, Mitra M, Ali H, Merrill RD, Choudhury N, Parveen M, et al. Effect of fortified complementary food supplementation on child growth in rural Bangladesh: a cluster-randomized trial. Int J Epidemiol 2015;44:1862–76.
9. Hossain M, Choudhury N, Abd Binte Abdullah K, Mondal P, Jackson AA, Watson J, Ahmed T. Evidence-based approaches to childhood stunting in low and middle income countries: a systematic review. Arch Dis Child 2017;102:903–9.
10. King JC. A summary of pathways or mechanisms linking preconception maternal nutrition with birth outcomes. J Nutr 2016;146:1437S–44S.
11. Ramakrishnan U, Grant F, Goldenberg T, Zongrone A, Martorell R. Effect of women’s nutrition before and during early pregnancy on maternal and infant outcomes: a systematic review. Paediatr Perinat Epidemiol 2012;26(Suppl 1):285–301.
12. Young MF, Nguyen PH, Addo OY, Hao W, Nguyen H, Pham H, Martorell R, Ramakrishnan U. The relative influence of maternal nutritional status before and during pregnancy on birth outcomes in Vietnam. Eur J Obstet Gynecol Reprod Biol 2015;194:223–7.
13. Young MF, Nguyen PH, Gonzalez Casanova I, Addo OY, Tran LM, Nguyen S, Martorell R, Ramakrishnan U. Role of maternal preconception nutrition on offspring growth and risk of stunting across the first 1000 days in Vietnam: a prospective cohort study. PLoS One 2018;13:e0203201.
14. Adair LS, Fall CH, Osmond C, Stein AD, Martorell R, Ramirez-Zea M, Sachdev HS, Dahly DL, Bas J, Norris SA, et al. Associations of linear growth and relative weight gain during early life with adult health and human capital in countries of low and middle income: findings from five birth cohort studies. Lancet 2013;382:525–34.
15. Addo OY, Stein AD, Fall CH, Gigante DP, Guntupalli AM, Horta BL, Kuzawa CW, Lee N, Norris SA, Osmond C, et al. Parental childhood growth and offspring birthweight: pooled analyses from four birth cohorts in low and middle-income countries. Am J Hum Biol 2015;27:99–105.
16. Sutharsan R, O’Callaghan MJ, Williams G, Najman JM, Mamun AA. Rapid growth in early childhood associated with young adult overweight and obesity—evidence from a community based cohort study. J Health Popul Nutr 2015;33:13.
17. Wells JC, Sawaya AL, Wibaek R, Mwamgome M, Poullas MS, Yajnik CS, Demiao A. The double burden of malnutrition: aetiological pathways and consequences for health. Lancet 2020;395:75–88.
18. Popkin BM, Corvalan C, Grummer-Strawn LM. Dynamics of the double burden of malnutrition and the changing nutrition reality. Lancet 2020;395:65–74.
19. Harris J, Nguyen PH, Tran LM, Huyhn PN. Nutrition transition in Vietnam: changing food supply, food prices, household expenditure, diet and nutrition outcomes. Food Security 2020;12:1141–55.
20. Global Nutrition Report. Country nutrition profiles: Viet Nam [Internet]. [Accessed 2020 Aug 10]. Available from: https://globalnutritionreport.org/resources/nutrition-profiles/asia/south-eastern-asia/viet-nam/.
21. Phan HD, Nguyen TNP, Bui PL, Pham TT, Doan TV, Nguyen DT, Van Minh H. Overweight and obesity among Vietnamese school-aged children: national prevalence estimates based on the World Health Organization and International Obesity Task Force definition. PLoS One 2020;15:e0240459.
22. Nguyen PH, Lowe AE, Martorell R, Nguyen H, Pham H, Nguyen S, Harding KB, Neufeld LM, Reinhart GA, Ramakrishnan U. Rationale, design, methodology and sample characteristics for the Vietnam pre-conception micronutrient supplementation trial (PRECONCEPT): a randomized controlled study. BMC Public Health 2012;12:989.
23. Nguyen PH, Gonzalez Casanova I, Young MF, Truong TV, Hoang H, Nguyen H, Nguyen S, DeGirolamo AM, Martorell R, Ramakrishnan U. Preconception micronutrient supplementation with iron and folic acid.
compared with folic acid alone affects linear growth and fine motor development at 2 years of age: a randomized controlled trial in Vietnam. J Nutr 2017;147:1593–601.

24. Nguyen P, Young M, Khuong L, Duong TH, Nguyen HC, Truong TV, DiGirolamo A, Martorell R, Ramakrishnan U. Preconception micronutrient supplementation positively affects child development at 6 years of age: a randomized controlled trial in Vietnam. Curr Dev Nutr 2020;4:876.

25. Cogill B. Anthropometric indicators measurement guide. Washington (DC): Food and Nutrition Technical Assistance Project, Academy for Educational Development; 2003.

26. WHO. The WHO child growth standards [Internet]. [Accessed 2020 Jul 15]. Available from: http://www.who.int/childgrowth/standards/en/.

27. de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. Bull World Health Organ 2007;85:660–7.

28. WHO. BMI-for-age (5–19 years) [Internet]. [Accessed 2020 Jul 15]. Available from: https://www.who.int/childgrowth/standardsforschoolchildren/en/.

29. Lohman T, Roche A, Martorell R. Anthropometric standardization reference manual. Champaign (IL): Human Kinetics; 1988.

30. IOM (Institute of Medicine) and NRC (National Research Council). Weight gain during pregnancy: reexamining the guidelines. Washington (DC): National Academies Press; 2009.

31. Nguyen PH, Addo OY, Young M, Gonzalez-Casanova I, Pham H, Truong TV, Nguyen S, Martorell R, Ramakrishnan U. Patterns of fetal growth based on ultrasound measurement and its relationship with small for gestational age at birth in rural Vietnam. Paediatr Perinat Epidemiol 2016;30:256–66.

32. Hadlock FP, Harrist RB, Sharram RS, Deter RL, Park SK. Estimation of fetal weight with the use of head, body, and femur measurements—a prospective study. Am J Obstet Gynecol 1985;151:333–7.

33. Menezes AMB, Oliveira PD, Wehrmeister FC, Anselmi L, Gonçalves H, Victora CG. Associations between growth from birth to 18 years, intelligence, and schooling in a Brazilian prospective study. Am J Obstet Gynecol 1985;151:333–7.

34. Hemocue. Hemocue Hb301 [Internet]. [Accessed 2020 Jul 15]. Available from: http://www.hemocue.com/international/Products/Hemoglobin-1155.html.

35. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System. Geneva (Switzerland): World Health Organization (WHO/NMH/NHD/NMN/11.1) [Internet]. [Accessed 2020 Jul 15]. Available from: http://www.who.int/vmnis/indicands/haemoglobin.p df.

36. Vyas S, Kumaranyake L. Constructing socio-economic status indices: how to use principal components analysis. Health Policy Plan 2006;21:459–68.

37. Gwatkin D, Rustein S, Johnson K, Suliman E, Wagstaff A, Amouzou A. Socio-economic differences in health, nutrition, and population within developing countries: an overview. Niger J Clin Pract 2007;10:272–82.

38. Arbuckle JL. Full information estimation in the presence of incomplete data. In: Marcoulides GA, Schumacker RE, eds. Advanced structural equation modeling: issues and techniques. Mahwah (NJ): Lawrence Erlbaum; 1996. p. 243–78.

39. Barker M, Dombrowski SU, Colbourn T, Fall CHD, Kriznik NM, Lawrence WT, Norris SA, Ngaiza G, Patel D, Skordis-Worrall J, et al. Intervention strategies to improve nutrition and health behaviours before conception. Lancet 2018;391:1833–64.

40. Stephenson J, Heslehurst N, Hall J, Schoenaker D, Hutchinson J, Cade JE, Poston L, Barrett G, Crozier SR, Barker M, et al. Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. Lancet 2018;391:1830–41.

41. Ha AVV, Zhao Y, Pham NM, Nguyen CL, Nguyen PTH, Chu TK, Tang HK, Binns CW, Lee AH. Postpartum weight retention in relation to gestational weight gain and pre-pregnancy body mass index: a prospective cohort study in Vietnam. Obes Res Clin Pract 2019;13: 143–9.

42. Rong K, Yu K, Han X, Szeto IM, Qin X, Wang J, Ning Y, Wang P, Ma D. Pre-pregnancy BMI, gestational weight gain and postpartum weight retention: a meta-analysis of observational studies. Public Health Nutr 2015;18:2172–82.

43. Nehring I, Schmoll S, Beyerlein A, Hauner H, von Kries R. Gestational weight gain and long-term postpartum weight retention: a meta-analysis. Am J Clin Nutr 2011;94:1225–31.

44. Lai FY, Liu J, Archer E, McDonald SM, Liu J. Maternal weight gain in pregnancy and risk of obesity among offspring: a systematic review. J Obes 2014;2014:524939.

45. Goldstein RF, Abell SK, Ranasinha S, Misso ML, Boyle JA, Harrison CL, Black MH, Li N, Hu G, Corrado F, et al. Gestational weight gain across continents and ethnicity: systematic review and meta-analysis of maternal and infant outcomes in more than one million women. BMC Med 2018;16:153.

46. Giles L, Whitrow M, Davies M, Davies C, Rumbold A, Moore V. Growth trajectories in early childhood, their relationship with antenatal and postnatal factors, and development of obesity by age 9 years: results from an Australian birth cohort study. Int J Obes 2015;39: 1049–56.

47. Dewey KG, Adu-Afarwuah S. Systematic review of the efficacy and effectiveness of complementary feeding interventions in developing countries. Matern Child Nutr 2008;4(Suppl 1):24–85.

48. Imdad A, Yakob MY, Bhutta ZA. Impact of maternal education about complementary feeding and provision of complementary foods on child growth in developing countries. BMC Public Health 2011;11(Suppl 3):523.

49. NCD Risk Factor Collaboration. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. Lancet 2017;390: 2627–42.

50. Singh AS, Mulder C, Twisk JW, van Mechelen W, Chinapaw MJ. Tracking of childhood overweight into adulthood: a systematic review of the literature. Obes Rev 2008;9:474–88.

51. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Int J Obes 2015;39: 1049–56.

52. Munos MK, Stanton CK, Bryce J; Core Group for Improving Coverage Measurement for MNCH. Improving coverage measurement for reproductive, maternal, neonatal and child health: gaps and opportunities. J Glob Health 2017;7:S25.

53. Cuong TQ, Dibley MJ, Bowe S, Hanh TTM, Loan TTH. Obesity in adults: an emerging problem in urban areas of Ho Chi Minh City, Vietnam. Eur J Clin Nutr 2006;61:1673.

54. Nguyen MD, Beresford SAA, Drewnowski A. Trends in overweight by socio-economic status in Vietnam: 1992 to 2002. Public Health Nutr 2007;10:115–21.

55. Khan NC, Khoi HH. Double burden of malnutrition: the Vietnamese perspective. Asia Pac J Clin Nutr 2008;17:116–8.

56. Van Lierop A, Nam NV, Doak C, Hung LQ, Binh TQ, Hoekstra J, De Vlaming J. Socio-economic differences in health, nutrition, and population within Vietnam: changing food supply, food prices, household expenditure, diet and nutrition outcomes [Internet]. [Accessed 2021 Feb 10]. Available from: https://link.springer.com/article/10.1007/s12571-020-01096-x.