Longitudinal Measures of Maternal Vitamin D and Neonatal Body Composition

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Abstract

Background/Objectives—Vitamin D status has been associated with fetal growth and offspring’s bone mass in some observational studies. We characterize the trajectory of total maternal serum 25-hydroxyvitamin D [25(OH)D] concentration by race and examine whether vitamin D status is associated with neonatal anthropometry and body composition as assessed by dual energy X-ray absorptiometry (DXA).

Methods—Three longitudinal pregnancy samples from the Memphis site of the Calcium for Preeclampsia Prevention trial (1992-1995) were used. Racial differences in total 25(OH)D trajectories (n=343 women) were tested using an interaction term between blood draw gestational week and race in linear mixed-effects models. Linear regression and linear mixed-effects models estimated adjusted associations between total 25(OH)D concentration with neonatal anthropometry and body composition (n=252 with DXA), including interactions with infant sex and serum calcium.

Results—Total 25(OH)D concentration increased with gestational age but its trajectory over pregnancy did not differ between African-American and Caucasian women. Deficient maternal vitamin D (25(OH)D concentration <20 ng/ml) was associated with lower neonatal total bone mineral density (β −0.009 g/cm²; 95% CI −0.016, −0.002). Among male newborns, deficiency was also associated with lower lean mass (−217 g; −391, −43) and birthweight (−308 g; −540, −76). Deficient maternal vitamin D was also associated with lower ponderal index (β −2.3 kg/m³; 95% CI −4.0, −0.5) among those in the lowest calcium tertile.
Conclusion—Vitamin D deficiency during pregnancy is associated with lower bone density and smaller size at birth in certain subgroups suggesting its importance in fetal development.

Keywords
Vitamin D; 25-hydroxyvitamin D; Dual energy X-ray absorptiometry; newborn; bone mineral content; bone mineral density; fat mass; lean mass; birthweight; birth length; birth head circumference

INTRODUCTION
Vitamin D has well defined classical functions related to calcium homeostasis and bone development. Profound maternal vitamin D deficiency results in fetal growth delay and rickets. However, consequences of milder vitamin D deficiency during fetal development are less well defined. Vitamin D status has been associated with fetal growth and bone mass of offspring in many but not all observational studies. Conflicting findings might have resulted from differences in study design, quality of studies, limited sample size, and vitamin D status assessment at one time point during pregnancy or at delivery. Additionally, the majority of the studies did not consider the interrelationships between 25 hydroxyvitamin D [25(OH)D] concentration and calcium homeostasis in the context of fetal growth and skeletal development despite the well-known nutrient-responsive hormonal control of the production of 1,25-dihydroxyvitamin D [1,25(OH)₂D] in calcium homeostasis.

Vitamin D status during pregnancy is a modifiable factor and if associated with fetal growth, offers a means to optimize newborn outcomes. We aimed to characterize the trajectory of maternal total serum 25(OH)D concentration, measured on average at three-time points during pregnancy, while exploring racial differences. Subsequently, we examined whether total maternal serum 25(OH)D concentration is associated with anthropometry and body composition among a subgroup of newborns from the Calcium for Preeclampsia Prevention (CPEP) trial.

MATERIALS AND METHODS
Study population
Study subjects came from one center (Memphis, TN) participating in the CPEP trial, a randomized double-blind clinical trial (1992-1995) conducted at five U.S. medical centers to examine whether calcium supplementation in healthy pregnant nulliparous women reduced preeclampsia incidence. Study design details and the main results are published elsewhere. Briefly, women were randomized to calcium or placebo at gestational age 13-21 weeks as determined by ultrasound. At the baseline visit, women also received a daily commercial prenatal supplement (containing 30 mg iron, 100 mg ascorbic acid, 5 mg thiamine, 3 mg pyridoxine, 2 mg riboflavin, 10 mg niacinamide, 1 mg d-calcium pantothenate, 2 μg vitamin B12, 0.4 mg folic acid, 400 IU vitamin A, 400 IU vitamin D₂, and 50 mg elemental calcium; Mission Prenatal, Mission Pharmacal Co., San Antonio, TX) and were instructed not to take antacids, analgesics, or vitamins other than vitamin B6 or iron as prescribed by their

Eur J Clin Nutr. Author manuscript; available in PMC 2018 December 12.
physician. Non-fasting serum samples were collected on average at three-time points during gestation (baseline visit 11-21 weeks before intake of prenatal supplements and study randomization, 26-29 weeks, and close to the delivery time at 36 weeks) and frozen at −70°C for future analyses.

In total, 969 women were randomized at the Memphis site. Of these, 289 were approached to participate in an ancillary study of fetal bone mineralization whereby both the mother and her newborn could receive a dual energy X-ray absorptiometry (DXA) scan. Thirteen women refused to have their infants participate, DXA scans were not performed on an additional 8 infants (2 deaths, technical problems and unavailability of the DXA machine 6 infants), and 12 infants had their scans delayed beyond the first week of life resulting in 256 infants (89%) receiving DXA scans within the first week after birth. Of the total 256 infants with DXA scans, maternal serum samples were available on 252 mothers (220 African-Americans and 32 Caucasians). To better examine racial differences, we additionally measured all available serum samples from 91 Caucasian women without DXA scans at the Memphis site resulting in 123 Caucasian and 220 African-American women. In total, 983 serum samples (n=16 women with 1 sample, n=65 with 2 samples, n=212 with 3 samples, n=49 with 4 samples, and n=1 with 5 samples) were sent for measurement. This study was exempt from Institutional Review Board but approved by the National Institutes of Health’s Office of Human Subjects Research given the use of existing de-identified samples.

### Laboratory Measurements

Total serum 25(OH)D concentration is currently considered the best biomarker of vitamin D status. Both vitamin D isomers (25(OH)D$_2$ and 25(OH)D$_3$) were measured in stored serum using liquid chromatography mass spectrometry (LC-MS/MS, Trip Quad LC Mass) from AB SCIEX (Framingham, MA) as per the National Institute of Standards and Technology, with interassay coefficients of variation (CVs) of 8.2% for 25(OH)D$_2$ and 5.9% for 25(OH)D$_3$. Total 25(OH)D concentration was calculated as the sum of 25(OH)D$_2$ and 25(OH)D$_3$ concentrations averaged at all time points during pregnancy. Vitamin deficiency was defined based on the Endocrine Society guidelines as total 25(OH)D concentration <20 ng/ml. We also examined the Endocrine Society definition of vitamin D status based on total 25(OH)D concentration <20 ng/ml as deficient, 20-29 ng/ml as insufficient, and >29 ng/ml as sufficient.

In addition to total 25(OH)D concentration, albumin and serum calcium were measured using an automated clinical chemistry platform at all time points during pregnancy. Calcium (mg/dl) was corrected based on the serum albumin level as: [0.8 × (4 − participant’s albumin g/dl)] + serum Ca level mg/dl.

### DXA and Anthropometric Assessment

DXA scans were conducted on the newborn’s whole body and lumber spine (L1-L4) with whole-body scanner operated in a single-beam mode (Hologic QDR 1000/W Densitometer; Hologic Inc., Bedford, MA). Each infant was swaddled in a cotton blanket during scanning and placed on a pediatric platform. Scanning of the infants occurred without sedation or
restraint and infants were directly observed by a research team member. If movement artifact was noted, scans were repeated. Scans were examined by the software created in conjunction with the manufacturer (Version V5.64P for the whole body and V4.57Q for the lumbar spine). The CV for the determination of BMC, skeletal area, and BMD was less than 0.31% based on quality-control scans conducted on a manufacturer-supplied anthropometric spine phantom. For infants with DXA scans, weight, length, and head circumference were measured by the same team. For infants without DXA scans, birthweight, length, and head circumference were extracted from the newborn’s medical record. Ponderal index (PI) was calculated as \((\text{birthweight (kg)/crown-heel length (m)}^3)\).

**Covariates**

At enrollment, women self-reported their age, race/ethnicity, smoking status, education, insurance, and marital status. Body mass index (BMI) was calculated from weight measured during the screening visit before 22 weeks’ gestation and self-reported height. Maternal dietary intake was measured using two 24-h dietary recalls (296 women had 2 recalls, 45 had 1 recall, and 2 were missing dietary recall), at randomization and at 32-33 weeks’ gestation with the help of a certified dietician or research nurse. Total dietary intake of calorie, calcium, magnesium, and phosphorus were calculated using an extensive nutrient database at Tufts University and were averaged across the two-time point measurements.

**Statistical Methods**

We first examined racial differences in maternal characteristics using proportions and means as appropriate. To examine the predictors of total 25(OH)D concentration, log transformed for normality, and whether its trajectory differs by race across pregnancy, we used mixed models with a random intercept and tested for the significance of an interaction term between blood draw gestational week and race in a crude and an adjusted model. The adjusted model included corrected serum calcium, blood draw season based on vernal equinox, BMI, caloric intake, and magnesium and phosphorus intake. In the subsequent aim, we examined maternal and newborn characteristics by maternal vitamin D deficiency status. When examining the associations between total 25(OH)D concentration and neonatal body composition with DXA scans and anthropometric outcomes (for all sample irrespective of DXA scans), we used linear regression models with total 25(OH)D concentration averaged across the pregnancy measurement time points and examined as a binary variable (25(OH)D concentration <20 ng/ml). We report the \(\beta\)-coefficients and 95% CIs from the crude and the adjusted models. Models were adjusted for maternal smoking status, race, BMI, caloric intake, corrected serum calcium levels, and infant sex. In these models, we also assessed the significance of the interaction between vitamin D deficiency and each of infant sex, race, and serum calcium tertile. The interaction term with race was dropped due to non-significance for all outcomes. The interaction term between vitamin D deficiency status and serum calcium tertiles was significant for PI only (p-value<0.05) while the interaction terms between deficiency status and infant sex were significant for lean mass and birthweight (p-value<0.05). We report the results stratified by calcium tertile for PI and by sex for lean mass and birthweight. Using linear mixed-effects models, we subsequently examined all total 25(OH)D measurements across pregnancy by evaluating how the 25(OH)D trajectory...
(individual slopes) is associated with the examined newborn outcomes adjusting for the same above variables. All analyses were conducted using SAS 9.4 and R 3.1.

RESULTS

Baseline characteristics and serum 25(OH)D concentration differed by race (Table 1). White women were more likely to be married, be smokers, and have higher total 25(OH)D and calcium compared to black women. Differences in total 25(OH)D concentration remained even after accounting for the multiple measures over pregnancy (Table 2). In adjusted analyses, white women had a higher concentration of log total 25(OH)D throughout pregnancy ($\beta$ 0.31 ng/ml; 95% CI 0.19, 0.44) compared to black women. Independent of race, maternal total 25(OH)D concentration increased throughout pregnancy. Increases in serum total 25(OH)D concentration did not differ by race (non-significant interactions). Serum calcium, seasonality (spring and summer compared with winter), and phosphorus intake were also associated with increased maternal total 25(OH)D concentration while BMI and caloric intake were negatively associated with total 25(OH)D.

Table 3 displays the characteristics of the mothers and their infants by vitamin D deficiency$^{24}$ averaged across pregnancy among newborns with DXA measures ($n=252$) and among all newborns irrespective of DXA measures’ availability ($n=343$). Among infants with DXA measures ($n=252$), 25% ($n=63$) of women were vitamin D deficient (25(OH)D concentration <20 ng/ml). Alternatively, based on the IOM definition,$^{25}$ only 5 (1.5%) women had deficient vitamin D status (25(OH)D concentration <12 ng/ml). As such, we used the endocrine society deficiency definition which also corresponds with the insufficient IOM definition.$^{25}$ Deficient mothers were more likely to be black, have a higher BMI, and lower total 25(OH)D concentration. Newborns of deficient mothers had lower total BMC, BMD, fat mass, lean mass, and birthweight compared to newborns of non-deficient mothers.

When examining the association between deficient vs. non-deficient vitamin D status and newborn body composition and anthropometric outcomes in the unadjusted models, vitamin D deficiency was significantly associated with lower total BMC ($\beta$ −4.5 g; 95% CI −8.9, −0.1), total BMD (−0.010 g/cm$^2$; −0.017, −0.003), fat mass (−54 g; −108, −0.6), lean mass (−122 g; −241, −2), and birthweight (−188 g; −349, −28) (Table 4). After adjustment, only total BMD ($\beta$ −0.009 g/cm$^2$; 95% CI −0.016, −0.002) remained significantly associated with maternal vitamin D deficiency while lean mass (−217 g; −391, −43) and birthweight (−308 g; −540, −76) were significantly negatively associated among males only after stratifying by sex. PI was significantly negatively associated with maternal vitamin D deficiency only among those in the lowest serum calcium tertile ($\beta$ −2.3 g; 95% CI −4.0, −0.5). Only the Endocrine Society’s deficiency cutoff (25(OH)D concentration <20 ng/ml)$^{24}$ was associated with outcomes while there were no significant differences for 20-29 ng/ml 25(OH)D concentration with outcomes as compared with >29 ng/ml (data not shown). Longitudinal changes in maternal 25(OH)D concentration (per SD increase in total 25(OH)D over pregnancy) were not associated with neonatal body composition and anthropometry (data not shown).
DISCUSSION

In this study, total maternal 25(OH)D concentration increased with gestation and its trajectory did not differ between African-American and Caucasian women despite having different overall concentrations. That is, while Caucasian women perpetually had higher total 25(OH)D concentration throughout pregnancy than African-American women, the concentration increased in a similar manner regardless of race. We also report that maternal vitamin D deficiency (serum 25(OH)D concentration <20 ng/ml) was associated with lower total neonatal BMD. Further, sex-specific differences were observed, with maternal vitamin D deficiency associated with lower birthweight and lean mass among males. Maternal vitamin D deficiency was also associated with lower PI among infants whose mothers were in the lowest calcium tertile.

Investigations examining the association between maternal vitamin D status and fetal or neonatal bone have produced mixed findings. Four clinical trials examining the effects of maternal vitamin D supplementation on neonatal bone health reported mainly null findings. The trials however, differed in their study design and vitamin D dosage. One small trial did not randomize the study participants (n=64) while a more recent trial among Brazilian adolescent women used a low dosage of vitamin D supplementation (200 IU/d) limiting the supplementation to the last trimester. The MAVIDOS trial reported an overall null effect with a supplementation dose of 1000 IU/d before 17 weeks’ gestation, but in a pre-specified secondary analysis, an interaction was reported between treatment effect and birth season with infants born in the winter to supplemented mothers having a higher BMC, bone area, BMD, and body fat. In a trial conducted in India, vitamin D supplementation (60,000 units 4 or 8 weekly starting at gestational age <20 weeks) did not result in improved bone health or body composition among 12-16 months old infants. The majority of the women (88%) in this trial had vitamin D deficiency (<20 ng/ml), with severe deficiency (<10 ng/ml) reported among 46%. Findings from observational studies have been conflicting, with some reporting positive associations between vitamin D status in pregnancy and certain newborn bone indices and others reporting no association. Worth noting is that among these four observational studies, 25(OH)D concentration was measured at one time point either at delivery or during the third trimester with only one study measuring 25(OH)D concentration during the 1st trimester and at 2 days postpartum. In our adjusted analyses, we only show an association between vitamin D deficiency status and total BMD (β=−0.009 g/cm²; 95% CI −0.016, −0.002) when averaging across all the 25(OH)D measurements during pregnancy. This difference in BMD, was small and only observable at extremes (deficiency).

Adequate vitamin D status during pregnancy may function through ensuring appropriate maternal responses to the calcium needs of the fetus. However, some investigators have reported that maternal calcium absorption during pregnancy is independent of vitamin D stores. Potentially, the placenta may play a modulatory role in vitamin D metabolism. Several observational studies and trials examining the impact of vitamin D supplementation in women at high risk of vitamin D deficiency, show that improving maternal vitamin D concentration results in infants with higher serum calcium concentrations at delivery or within the first week of life compared to infants of mothers who received placebo or took no
In our study, serum calcium was a significant predictor of total 25(OH)D concentration. We also reported a significant negative association between vitamin D deficiency and PI at the lowest serum calcium tertile. Such an interaction has been reported between maternal vitamin D deficiency and fetal femur and humerus z-scores at maternal calcium intake <1050mg. Previously, our study observed that randomization to calcium during pregnancy had a positive impact on neonatal BMC only if mothers had the lowest quintile of dietary calcium intake.

Although the most widely appreciated role of vitamin D is related to calcium homeostasis and bone development, evidence also suggests that vitamin D might influence fetal growth and neonatal mass. Our findings are consistent with the observation of fetal growth restriction in the presence of maternal vitamin D deficiency noted at mid-gestation. Pooled analysis of randomized controlled trials was also suggestive of a protective effect of maternal supplementation on birthweight (mean difference: 108 g; 95% CI 60-155). Similarly, a meta-analysis of observational studies reported a positive association between vitamin D (25(OH)D >15 ng/ml) and birthweight (130.9 g; 95% CI 75.1-186.7). While the exact mechanism is unknown, authors speculate that vitamin D receptors and 1,25(OH)_2D regulate secretion of placental lactogen and other hormones that impact maternal transplacental glucose and fatty acid transport increasing neonatal mass and fat accretion.

Human placental trophoblasts both hydroxylate 25(OH)D into 1,25(OH)_2D and respond to the hormone’s biological actions. In our study, while the overall unadjusted association with birthweight among mothers with deficient vitamin D (−188 g; −349, −28) is similar to what has been reported, we noted an interaction term with sex and this association became significant only among male infants (−308 g; −540, −76). The lower birthweight among vitamin D deficient mothers is mainly attributed to lean mass among males (−217 g; −391, −43). Although to our knowledge, such an interaction has not been previously reported, the sex-specific rates of fetal growth suggest male fetuses may be more vulnerable to insufficiencies in pregnancy.

Strengths of our study include a racially diverse relatively large sample size. We also measured serum 25(OH)D concentration and calcium across several time points allowing us to better capture vitamin D status during pregnancy especially during the period of most rapid fetal growth. The DXA scans occurred at a very narrow range of ages before the extremely rapid newborn postnatal growth. Additionally, an experienced investigator reviewed the DXA scans for quality.

In conclusion, deficient vitamin D status during pregnancy was associated with lower neonatal BMD, with male infants also having lower lean mass and birthweight. Future studies should explore the potential sex-specific modifying effect of newborn outcomes in association with maternal vitamin D status.

Acknowledgments

Financial support: Supported by the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The CPEP trial was originally supported by contracts (N01-HD-1-3121, -3122, -3123, -3124, -3125, and -3126; N01-HD-3154; and N01-HD-5-3246) with the National Institute of Child Health and Human Development, with co-funding from the National Heart, Lung, and Blood Institute.
Institute. Additional biomarker assays including for vitamin D was supported by contract (HHSN275201300023I-HHSN2750002) with the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

Abbreviations

| Abbreviation | Definition                      |
|--------------|--------------------------------|
| BMC          | bone mineral content           |
| BMD          | bone mineral density           |
| BMI          | body mass index                |
| CPEP         | Calcium for Preeclampsia Prevention trial |
| CV           | coefficient of variation       |
| DXA          | Dual energy X-ray densitometry  |
| IOM          | Institute of Medicine          |
| PI           | ponderal index                 |
| 25(OH)D-25   | hydroxyvitamin D               |
| 1,25(OH)_2D-1,25 | dihydroxyvitamin D       |

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### Table 1
Characteristics of study participants by race in the CPEP Study

|                     | White N=123 | Black N=220 | p-value |
|---------------------|-------------|-------------|---------|
| Married n (%)       | 49 (39.8)   | 17 (7.7)    | <0.001  |
| Less than high school n (%) | 58 (47.2) | 120 (54.6) | 0.19    |
| Private insurance n (%) | 8 (6.5)   | 9 (4.1)     | 0.32    |
| Smoker n (%)        | 37 (30.1)   | 5 (2.3)     | <0.001  |
| Body mass index (kg/m²) n (%) |          |            | 0.11    |
| Underweight/normal  | 79 (64.8)   | 124 (56.4)  |         |
| Overweight          | 27 (22.1)   | 47 (21.4)   |         |
| Obese               | 16 (13.1)   | 49 (22.3)   |         |
| Randomized to calcium n (%) | 58 (47.2) | 106 (48.2) | 0.86    |
| Vitamin D deficiency n (%) | 6 (4.9)   | 62 (28.2)   | <0.001  |
| Total 25(OH)D (ng/ml) | 33.8 (8.3) | 25.2 (8.2)  | <0.001  |
| 25(OH)D₂           | 1.5 (1.6)   | 1.4 (1.1)   | 0.45    |
| 25(OH)D₃           | 32.3 (8.2)  | 23.8 (8.0)  | <0.001  |
| Corrected serum calcium (mg/dl) | 9.8 (0.3) | 10.0 (0.3)  | <0.001  |
| Caloric intake (kcal) | 2578 (777) | 2632 (905)  | 0.57    |
| Calcium             | 1172 (693)  | 929 (531)   | <0.001  |
| Magnesium           | 269 (100)   | 243 (114)   | 0.04    |
| Phosphorus          | 1577 (590)  | 1489 (601)  | 0.20    |

All figures are mean (SD) unless otherwise indicated.

Caloric intake, calcium, magnesium, and phosphorus measured from 24 h dietary recalls.

Data missing on body mass index n=1, caloric intake n=2, calcium n=2, magnesium n=2, phosphorus n=2.

Vitamin D deficiency defined based on the Endocrine Society guidelines as <20 ng/ml.

Longitudinal measures of total 25(OH)D were averaged across each pregnancy.
Table 2
Predictors of total maternal 25(OH)D in the CPEP Study

| Predictor                                | Crude Model $\beta$ (95% CI) | Adjusted Model $\beta$ (95% CI) |
|-----------------------------------------|------------------------------|---------------------------------|
| Log total 25(OH)D                       |                              |                                 |
| White versus Black                      | 0.34 (0.21, 0.47)            | 0.31 (0.19, 0.44)               |
| Gestational age at blood draw (per week)| 0.0074 (0.0050, 0.0098)      | 0.0054 (0.0030, 0.0078)         |
| Gestational age at blood draw × race    | −0.0008 (−0.0049, 0.0033)    | −0.0004 (−0.0044, 0.0036)       |
| Corrected serum calcium (mg/dl)         |                              | 0.085 (0.024, 0.150)            |
| Season of blood draw                    |                              |                                 |
| Fall versus winter                      | 0.029 (−0.024, 0.081)        |                                 |
| Spring versus winter                    | 0.074 (0.024, 0.120)         |                                 |
| Summer versus winter                    | 0.22 (0.16, 0.27)            |                                 |
| Body mass index (kg/m$^2$)              | −0.0096 (−0.0150, −0.0044)   |                                 |
| Caloric intake (kcal)                   | −0.00007 (−0.00014, −3.24 × 10$^{-6}$) |                                 |
| Magnesium                               | −0.0002 (−0.0007, 0.0004)    |                                 |
| Phosphorus                              | 0.00015 (0.00004, 0.00027)   |                                 |

$\beta$s and 95% CIs from mixed models with a random intercept. For the crude model N=983; for the adjusted model N=978 (2 observations missing caloric intake and 3 missing body mass index).

Bolded figures indicate statistical significance.

Caloric intake, magnesium, and phosphorus measured from 24 h dietary recalls.

Season of blood draw: Spring (March 20-June 20), Summer (June 21-September 21), Fall (September 22-December 20), Winter (December 21-March 19).
Table 3
Maternal and newborn characteristics of infants by maternal vitamin D deficiency status in the CPEP Study

|                              | Deficient N=63 | Non-deficient N=189 | Total N=252 | p-value  |
|------------------------------|---------------|---------------------|-------------|----------|
| Mothers                      |               |                     |             |          |
| Age (years)                  | 19.5 (3.4)    | 19.6 (3.6)          | 19.6 (3.6)  | 0.8      |
| Black n (%)                  | 62 (98.4)     | 158 (83.6)          | 220 (87.3)  | 0.002    |
| Married n (%)                | 6 (9.5)       | 24 (12.7)           | 30 (11.9)   | 0.5      |
| Less than high school n (%)  | 32 (50.8)     | 108 (57.1)          | 140 (55.6)  | 0.4      |
| No private insurance n (%)   | 61 (96.8)     | 180 (95.2)          | 241 (95.6)  | 0.6      |
| Current smoker n (%)         | 2 (3.2)       | 15 (7.9)            | 17 (6.8)    | 0.2      |
| Body mass index (kg/m2)      | 27.8 (8.8)    | 25.5 (6.4)          | 26.1 (7.1)  | 0.027    |
| Caloric intake (kcal)        | 2539 (860)    | 2638 (901)          | 2613 (890)  | 0.4      |
| Randomized to calcium n (%)  | 36 (57.1)     | 88 (46.6)           | 124 (49.2)  | 0.2      |
| Total 25(OH)D (ng/ml)        | 15.8 (3.0)    | 30.0 (7.0)          | 26.5 (8.8)  | <0.001   |
| Corrected serum calcium (mg/dl) | 9.9 (0.26)   | 10.0 (0.25)         | 10.0 (0.26) | 0.014    |
| Newborns                     |               |                     |             |          |
| With DXA scans N=63          |               |                     |             |          |
| Male n (%)                   | 33 (52.4)     | 101 (53.4)          | 134 (53.2)  | 0.9      |
| Gestational age (weeks)      | 39.1 (2.7)    | 39.4 (1.8)          | 39.3 (2.1)  | 0.3      |
| Age at DXA scan (days)       | 1.5 (1.1)     | 1.8 (1.6)           | 1.7 (1.5)   | 0.08     |
| Total BMC (g)                | 59.8 (15.9)   | 64.3 (15.0)         | 63.1 (15.3) | 0.044    |
| Total BMD (g/cm²)            | 0.206 (0.026) | 0.216 (0.024)       | 0.214 (0.025) | 0.005 |
| Lumbar BMC (g)               | 1.7 (0.45)    | 1.8 (0.45)          | 1.8 (0.45)  | 0.09     |
| Lumbar BMD (g/cm²)           | 0.23 (0.040)  | 0.23 (0.033)        | 0.23 (0.035) | 0.2     |
| Fat mass (g)                 | 439 (184)     | 494 (188)           | 480 (188)   | 0.048    |
| Lean mass (g)                | 2545 (440)    | 2666 (408)          | 2636 (419)  | 0.046    |
| Fat mass (%)                 | 13.9 (3.7)    | 14.9 (3.7)          | 14.6 (3.7)  | 0.063    |
| Birth weight (g)             | 2929 (595)    | 3117 (548)          | 3070 (565)  | 0.021    |
| All infants irrespective of DXA scans N=68 |       |                     |             |          |
| Birth weight (g)             | 2989 (585)    | 3177 (587)          | 3140 (591)  | 0.018    |
| Length (cm)                  | 49.4 (2.8)    | 49.9 (2.8)          | 49.8 (2.8)  | 0.2      |
| Ponderal index (kg/m²)       | 24.6 (2.7)    | 25.5 (3.0)          | 25.3 (3.0)  | 0.020    |
| Head circumference (cm)      | 33.4 (2.0)    | 33.6 (1.7)          | 33.5 (1.8)  | 0.3      |

Abbreviations: BMC: bone mineral content; BMD: bone mineral density.
All figures are mean (SD) unless otherwise indicated.
Longitudinal measures of total 25(OH)D were averaged across each pregnancy. Vitamin D deficiency defined based on the Endocrine Society guidelines as <20 ng/ml.
Data missing on: 9 infants for lumbar BMC and BMD; 32 infants for length; 32 infants for ponderal index; 30 infants for head circumference. Missing data for anthropometric measurements are from babies who did not have DXA measurements.
Table 4
Associations between maternal 25(OH)D status (deficient vs. non-deficient) and newborn body composition in the CPEP Study

|                          | Unadjusted β (95% CI) | Adjusted β (95% CI) |
|--------------------------|-----------------------|---------------------|
| With DXA scans N=252    |                       |                      |
| Total BMC (g)            | −4.5 (−8.9, −0.1)     | −3.8 (−8.2, 0.7)    |
| Total BMD (g/cm²)        | −0.010 (−0.017, −0.003) | −0.009 (−0.016, −0.002) |
| Lumbar BMC (g)           | −0.11 (−0.24, 0.02)   | −0.063 (−0.190, 0.065) |
| Lumbar BMD (g/cm²)       | −0.007 (−0.018, 0.003) | −0.0023 (−0.0120, 0.0078) |
| Fat mass (g)             | −54 (−108, −0.6)      | −49 (−103, 4)       |
| Lean mass (g)            | −122 (−241, −2)       | Male N=134: −217 (−391, −43) Female N=118: 61.3 (−107, 229) |
| % fat mass               | −1.00 (−2.05, 0.05)   | −0.94 (−1.98, 0.11) |
| Birth weight (g)         | −188 (−349, −28)      | Male n=134: −308 (−540, −76) Female n=118: 26 (−205, 257) |
| All infants irrespective of DXA scans N=343 | | |
| Birth weight (g)         | −188 (−345, −32.1)    | Male N=172: −322 (−551, −92.2) Female N=168: −7.7 (−236, 221) |
| Length (cm) N=311        | −0.49 (−1.27, 0.28)   | Male N=152: −1.22 (−2.46, 0.02) Female N=156: 0.16 (−0.87, 1.19) |
| Ponderal index (kg/m³)   | −0.96 (−1.78, −0.15)  | Serum calcium tertile =1 N=102: −2.3 (−4.0, −0.5) Serum calcium tertile =2 N=101: 0.22 (−1.05, 1.48) Serum calcium tertile =3 N=105: −0.62 (−2.20, 0.97) |
| Head circumference (cm)  | −0.24 (−0.72, 0.25)   | −0.02 (−0.53, 0.49) |

Abbreviations: BMC: bone mineral content; BMD: bone mineral density.

Vitamin D deficiency defined based on the Endocrine Society guidelines as <20 ng/ml.

Bolded figures indicate statistical significance.

Adjusted for maternal ethnicity/race (White vs. Black), age (continuous), body mass index (continuous), smoking status (yes vs. no), caloric intake (continuous), corrected serum calcium (continuous), and newborn sex (male vs. female). For the adjusted model: with DXA scans, data missing on 1 caloric intake; without DXA scans, data missing on 2 caloric intake, data missing on 1 BMI.

Significant interaction (p<0.01) reported for lean mass, birth weight, and length between 25(OH)D deficiency status and sex; data are presented stratified by sex. Significant interaction reported for ponderal index between 25(OH)D deficiency status and calcium tertiles; data are presented stratified by calcium tertile.

Serum calcium tertile 1 (mean=9.64 mg/dl, SD=0.14, range: 9.19 to 9.80), tertile 2 (mean=9.91 mg/dl, SD=0.06, range 9.81 to 10.0), tertile 3 (mean=10.2 mg/dl, SD=0.15, range 10.0 to 10.7).

aData missing on 9 infants for lumbar BMC and BMD.

bFor infants with DXA scans, weight was measured at the same time as the DXA scan. For infants without DXA scans, birth weight was extracted from medical records.