

Original Article

## Gender Differences in the Heritability of Musculoskeletal and Body Composition Parameters in Mother-Daughter and Mother-Son Pairs

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### Abstract

Bone mass and body composition traits are genetically programmed, but the timing and gender and site specificities of their heritability are unclear. Mother-child correlations of bone mineral density (BMD) and bone mineral content, lean mass, and fat mass were studied in 169 premenopausal mothers and their 239 children. Heritability estimates of lean mass, fat mass, BMD, and area were derived for each gender and pubertal stage. There were significant correlations for most densitometry-derived variables at the spine, hip, femoral neck (FN), and total body ( $r = 0.192$ – $0.388$ ) in mother-postmenarcheal daughter pairs, for bone areas at all sites in early puberty ( $r = 0.229$ – $0.508$ ) and for volumetric-derived density at FN and spine ( $r = 0.238$ – $0.368$ ) in mother-son pairs. Fat mass correlations were significant in both genders after puberty ( $r = 0.299$ – $0.324$ ) and lean mass in postmenarcheal girls only ( $r = 0.299$ ). Heritability estimates varied between 21% and 37% for mother-daughter and 18% and 35% for mother-son pairs for density-derived variables and between 26% and 40% for body composition variables. Maternal inheritance of bone traits is expressed in early-pubertal boys for several skeletal site traits but consistently involves most site traits in girls and boys by late puberty. Body composition inheritance is more variable.

**Key Words:** Adolescence; body composition; bone mass; gender differences; heritability.

### Introduction

Osteoporosis, a worldwide public health problem, is a multifactorial disease with genetic, environmental, and lifestyle

influences. Bone mass is a strong determinant of bone strength, and peak bone mass, half of which is accrued before puberty, is a major determinant of osteoporotic fractures in elderly life. Bone mass is in large part determined by genetic factors (1–3), and the impact of environmental influences may be most relevant during intrauterine or early postnatal life (4). Studies suggest that heritability of bone mass traits in parental-offspring pairs is apparent by adolescence or early adulthood (5–11), with few studies demonstrating expression of familial resemblance before pubertal development in mother-offspring pairs (5,7,8). Studies varied in terms of skeletal sites investigated and age of offspring that ranged from prepubertal (5,7) to early adolescence (8,10) and into adulthood (6,11).

Received 03/15/12; Revised 04/22/12; Accepted 04/23/12.

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While studies on heritability of body composition traits in adults are few (12), similar studies in children are even more scarce (7). Sexual dimorphism in body composition, present since birth, becomes more striking during pubertal years due to the diverging effects of gonadal hormones on fat and lean masses. Hence, the resultant variation in body composition, which is exhibited as greater skeletal and lean masses in males vs more fat mass in females (13–15). Bone mass heritability may be related, at least in part to heritability of lean mass (12,16). We thus hypothesized that gender differences may exist in the heritability of bone mass traits. In addition, because of the substantial impact of puberty on bone mass and body composition, it becomes critical to study the impact of familial resemblance on these traits in large cohorts to allow detailed analyses of parents-offspring at various stages of development and in both genders. We are aware of only 1 study evaluating heritability estimates for both bone mass and body composition traits in mother-offspring pairs that included both genders, at multiple skeletal sites, but only in early puberty (7).

In this study, we investigated maternal heritability of bone size (area), body composition variables, and skeletal mass parameters in a cohort of boys and girls across pubertal stages, to explore possible gender differences, define the timing of familial resemblance, and determine skeletal site specificity of such resemblance, if any.

## Materials and Methods

The study results are the outcome of post hoc analyses implemented on baseline data obtained at study entry in a large vitamin D trial conducted in school children and their mothers (17).

### Subjects

The original trial cohort consisted of 326 healthy children with an age range of 10–17 yr recruited from 4 schools in Greater Beirut area, to ensure balanced geographical and socioeconomical representation. The wide age range was chosen because it captures all pubertal stages because adolescence is a critical time for peak bone mass accrual. Subjects were enrolled in the trial if they were considered healthy, based on careful physical examination and absence of any condition or drug intake known to affect bone metabolism. All children had normal serum calcium, phosphorus, and alkaline phosphatase levels for age. The study was approved by the institutional review board, and informed consent was obtained from all subjects and their parents. For the purpose of the present study, we analyzed the data of 239 children and their 169 premenopausal mothers who had no history of any disorder and were on no medication that may affect bone metabolism.

### Data Collection

All children underwent a complete physical examination that included height, weight, and Tanner stage assessment (17). Pubertal stage was assessed according to Tanner's

criteria (18). Areal bone mineral density (BMD) and bone mineral content (BMC) at the lumbar spine (LS) (L1–L4), femur (total hip and femoral neck [FN]), total body, lean mass, and fat mass were measured with a Hologic 4500 A densitometer (software version 11.2:3; Hologic, Bedford, MA). Because inclusion of the head in the calculation of total body BMD may lower the predictive value of some parameters for this variable, total body measurements excluding the head were used (19). Z-scores were calculated from our study population's characteristics and were derived using the gender- and pubertal stage-specific mean and standard deviation (SD) for the variable of interest. Volumetric bone mineral apparent density (BMAD) for the spine and FN was calculated as described by Katzman et al (20).

### Statistical Analyses

All variables of interest were summarized using means and SDs, if normally distributed, and medians, if the data were not normally distributed. Gender differences were assessed using the independent *t*-test. Pearson or Spearman correlation coefficients were used to evaluate the relationship between mother and child bone mass and body composition variables, as dictated by normality of distribution. Analysis was stratified by pubertal stages within each gender and was adjusted for the presence of possible correlation in the data where 1 mother had more than 1 child enrolled in the study (sibling effect) because data from siblings are not totally independent. This adjustment was done using robust estimates of standard errors that allow siblings' data to be correlated within a cluster (the mother). Heritability estimates by maternal descent,  $\frac{1}{2} h^2$  (%), were estimated for bone mass and body composition variables. The heritability estimate defines the proportion of variance in offspring traits that is explained by mothers' traits. This was done as described previously (5,12), using the slope of the regression ( $\beta$  coefficient) between the residuals of the multiple regression of bone parameter Z-score of the children on the body mass index (BMI), daily calcium intake, exercise, and sun exposure of the children and the residuals of a similar regression on the mother's data except for sun exposure due to unavailability of such data on the mothers. Adjustment for BMI, calcium intake, sun exposure, and exercise was implemented to dissect the inherent impact of heritability of bone mass trait expression independently of these known predictors of bone mass. We used the Statistical Package for Social Science (SPSS version 18; SPSS Inc., Chicago, IL) and STATA (STATA version 10; StataCorp LP, College Station, TX) for data analyses. Significance was set at  $p < 0.05$  and was not adjusted for multiple analyses.

## Results

### Characteristics of Mothers and Children

There were 169 mothers (mean age:  $40.5 \pm 5.2$  yr) and 239 children, 126 boys (53%) and 113 girls (47%) with similar mean ages (boys:  $12.8 \pm 1.8$  yr; girls:  $13.2 \pm 2.2$  yr). Boys differed significantly from girls in having greater total hip

area, BMC and BMD, FN area, subtotal lean mass, sun exposure, and physical activity. In contrast, girls had significantly greater spine BMD, BMAD and BMC, and subtotal body % fat (Table 1). When broken down by pubertal stage, there were 72 early-pubertal (Tanner Genitalia stages 1 or 2) vs 54 late-pubertal boys (Tanner Genitalia stages 3, 4, or 5) and 22 premenarcheal vs 91 postmenarcheal girls. Table 2 shows the anthropometric skeletal parameters and body composition characteristics of children by gender and pubertal stage. Mean volume-adjusted BMD, that is BMAD, was comparable in boys and girls with the mean value in mothers at the FN (Table 1). The BMAD was achieved by early puberty in boys at the FN and by late puberty in the spine in both genders (Table 2).

### Mother-Child Skeletal Parameters Correlations

#### Mother-Daughter Relationships

Table 3 summarizes the analyses after adjusting for the inclusion of siblings. Whereas significant positive correlations existed in mother-postmenarcheal daughter pairs at spine (BMD, BMC, BMAD, and area), total hip (BMD, BMC, and area), FN (BMC and area) and total body (BMC and area) ( $r = 0.192$ – $0.388$ ), FN BMAD, and total hip bone

area were the only sites with significant correlations in mother-premenarcheal daughter pairs ( $r = 0.440$  and  $0.398$ , respectively).

#### Mother-Son Relationships

Adjusted analyses revealed significant correlations in bone area at the spine, total hip, FN and total body, and in hip BMC for mother-early-pubertal son pairs ( $r = 0.229$ – $0.508$ ). In contrast, significant correlations existed for hip and FN BMD in postpubertal boys ( $r = 0.313$  and  $0.329$ , respectively) and for spine and FN BMAD ( $r = 0.238$ – $0.368$ ) (Table 3).

#### Mother-Child Body Composition Correlations

There were no significant correlations in body composition parameters between mother-child pairs in early-pubertal stages in either gender. In contrast, significant correlations existed in fat mass parameters of mothers and late pubertal sons ( $r = 0.324$  for fat mass;  $0.307$  for % fat mass) and postmenarcheal daughters ( $r = 0.299$  for fat mass;  $0.301$  for % fat mass) (Table 3). There was also a significant correlation in lean mass in mother-postmenarcheal daughter pairs ( $r = 0.299$ ).

**Table 1**  
Baseline Characteristics of Mothers and Their Children (Mean  $\pm$  SD or Median [Range])

| Characteristics                        | Boys, N = 126 (53%) | Girls, N = 113 (47%) | <i>p</i> Value* | Mothers, N = 169    |
|--|---------------------|----------------------|-----------------|---------------------|
| Age (yr)                               | 12.8 $\pm$ 1.8      | 13.2 $\pm$ 2.2       | NS              | 40.0 (30.0–55.0)    |
| Height (cm)                            | 153.4 $\pm$ 12.4    | 153.0 $\pm$ 10.3     | NS              | 158.0 (145.0–175.0) |
| Weight (kg)                            | 50.7 $\pm$ 15.7     | 48.0 $\pm$ 11.8      | NS              | 63.0 (41.0–131.0)   |
| BMI (kg/m <sup>2</sup> )               | 20.2 (14.7–31.4)    | 20.2 $\pm$ 3.6       | NS              | 25.0 (17.7–42.8)    |
| Calcium intake (mg/d)                  | 745.9 (21.4–1738.6) | 674.6 (42.9–2159.1)  | NS              | 495.4 $\pm$ 242.6   |
| Physical activity (hours of sport/wk)  | 5.0 (0.0–26.0)      | 2.0 (0.0–24.0)       | <0.001          | 1.5 (0.0–14.0)      |
| Sun exposure (h/wk)                    | 8.5 (1.25–24.67)    | 7.0 (0.6–29.0)       | 0.03            | —                   |
| L1–L4 spine area (cm <sup>2</sup> )    | 49 $\pm$ 7          | 49 $\pm$ 7           | NS              | 57 (47–80)          |
| L1–L4 spine BMC (g)                    | 34.4 $\pm$ 10.5     | 39.5 $\pm$ 12.4      | 0.001           | 54.4 (36.3–84.0)    |
| L1–L4 spine BMD (g/cm <sup>2</sup> )   | 0.665 (0.468–0.999) | 0.789 $\pm$ 0.158    | <0.001          | 0.976 (0.749–1.260) |
| L1–L4 BMAD (g/cm <sup>3</sup> )        | 0.097 $\pm$ 0.014   | 0.112 $\pm$ 0.018    | <0.001          | 0.129 $\pm$ 0.013   |
| Total hip area (cm <sup>2</sup> )      | 32 $\pm$ 6          | 29 $\pm$ 4           | 0.001           | 32 $\pm$ 0          |
| Total hip BMC (g)                      | 24.6 (12.3–47.4)    | 23.2 $\pm$ 5.7       | 0.001           | 28.1 (18.8–42.7)    |
| Total hip BMD (g/cm <sup>2</sup> )     | 0.818 (0.514–1.146) | 0.783 $\pm$ 0.129    | 0.012           | 0.877 $\pm$ 0.109   |
| Femoral neck area (cm <sup>2</sup> )   | 4.8 $\pm$ 0.5       | 4.6 $\pm$ 0.5        | 0.001           | 4.9 $\pm$ 0.4       |
| Femoral neck BMC (g)                   | 4.0 (1.8–5.5)       | 3.3 $\pm$ 0.7        | <0.001          | 3.6 (2.6–5.2)       |
| Femoral neck BMD (g/cm <sup>2</sup> )  | 0.767 $\pm$ 0.107   | 0.720 $\pm$ 0.119    | 0.002           | 0.766 $\pm$ 0.096   |
| Femoral neck BMAD (g/cm <sup>3</sup> ) | 0.167 $\pm$ 0.022   | 0.158 $\pm$ 0.026    | NS              | 0.159 $\pm$ 0.025   |
| Subtotal body area (cm <sup>2</sup> )  | 1366 $\pm$ 305      | 1363 $\pm$ 265       | NS              | 1622 (1346–2065)    |
| Subtotal body BMC (g)                  | 1071 (361–2101)     | 1150 $\pm$ 334       | NS              | 1520 (1111–2158)    |
| Subtotal body BMD (g/cm <sup>2</sup> ) | 0.805 (0.631–1.110) | 0.828 $\pm$ 0.095    | NS              | 0.929 $\pm$ 0.061   |
| Subtotal body lean mass (g)            | 32128 (17644–64112) | 30016 $\pm$ 621      | <0.001          | 38224 $\pm$ 5732    |
| Subtotal body fat mass (g)             | 9931 (3254–34768)   | 13244 $\pm$ 6140     | NS              | 19923 (8090–61558)  |
| Subtotal body % fat                    | 23.1 (9.8–44.4)     | 28.6 $\pm$ 6.9       | <0.001          | 34.4 $\pm$ 6.0      |

Abbr: BMAD, bone mineral apparent density; BMC, bone mineral content; BMD, bone mineral density; BMI, body mass index; NS, not significant; SD, standard deviation.

\**p* Value comparing variables in boys and girls.

**Table 2**  
Children's Baseline Characteristics by Gender and Pubertal Stage (Mean  $\pm$  SD or Median [Range])

| Characteristics                        | Boys (N = 126)         |                       | p Value | Girls (N = 113)      |                       | p Value |
|--|------------------------|-----------------------|---------|----------------------|-----------------------|---------|
|  | Early puberty (N = 72) | Late puberty (N = 54) |         | Premenarche (N = 22) | Postmenarche (N = 91) |         |
| Age (yr)                               | 11.8 $\pm$ 1.3         | 13.9 $\pm$ 1.8        | <0.001  | 10.7 $\pm$ 0.9       | 13.8 $\pm$ 1.9        | <0.001  |
| Height (cm)                            | 146.9 $\pm$ 8.9        | 162 $\pm$ 11.1        | <0.001  | 140.3 $\pm$ 7.8      | 156 $\pm$ 8.4         | <0.001  |
| Weight (kg)                            | 45 $\pm$ 12.9          | 58.3 $\pm$ 16         | <0.001  | 36.7 $\pm$ 8.5       | 50.7 $\pm$ 10.8       | <0.001  |
| BMI (kg/m <sup>2</sup> )               | 20.6 $\pm$ 4.1         | 21.8 $\pm$ 4.3        | 0.089   | 18.4 $\pm$ 3.2       | 20.6 $\pm$ 3.6        | 0.011   |
| Calcium intake (mg/d)                  | 714.21 (21.4–1437.0)   | 772.0 (274.9–1738.6)  | NS      | 726.0 (42.9–2159.0)  | 673.4 (153.3–2067.0)  | NS      |
| Physical activity (h/wk)               | 5.0 (0.0–24.0)         | 5.0 (0.0–26.0)        | NS      | 2.0 (0.0–20.0)       | 3.0 (0.0–24.0)        | NS      |
| Sun exposure (h/wk)                    | 8.5 (1.25–23.0)        | 8.5 (1.67–24.7)       | NS      | 6.5 (0.6–11.0)       | 7.0 (1.0–29.0)        | NS      |
| L1–L4 spine BMD (g/cm <sup>2</sup> )   | 0.629 $\pm$ 0.077      | 0.762 $\pm$ 0.125     | <0.001  | 0.604 $\pm$ 0.094    | 0.835 $\pm$ 0.136     | <0.001  |
| L1–L4 spine BMC (g)                    | 28.7 $\pm$ 4.9         | 42.1 $\pm$ 11.1       | <0.001  | 15.7 (11.1–24.5)     | 42.8 $\pm$ 11.2       | <0.001  |
| L1–L4 spine area (cm <sup>2</sup> )    | 46 $\pm$ 5             | 55 $\pm$ 7            | <0.001  | 43 $\pm$ 5           | 51 $\pm$ 6            | <0.001  |
| L1–L4 BMAD (g/cm <sup>3</sup> )        | 0.093 $\pm$ 0.012      | 0.103 $\pm$ 0.014     | <0.001  | 0.092 $\pm$ 0.013    | 0.117 $\pm$ 0.016     | <0.001  |
| Total hip area (cm <sup>2</sup> )      | 28 $\pm$ 5             | 36 $\pm$ 5            | <0.001  | 26 $\pm$ 4           | 30 $\pm$ 3            | <0.001  |
| Total hip BMC (g)                      | 22.1 $\pm$ 5.1         | 32.1 $\pm$ 8.3        | <0.001  | 16.6 $\pm$ 4.4       | 24.8 $\pm$ 4.8        | <0.001  |
| Total hip BMD (g/cm <sup>2</sup> )     | 0.776 $\pm$ 0.098      | 0.891 $\pm$ 0.135     | <0.001  | 0.641 $\pm$ 0.096    | 0.818 $\pm$ 0.111     | <0.001  |
| Femoral neck area (cm <sup>2</sup> )   | 4.6 $\pm$ 0.4          | 5.1 $\pm$ 0.5         | <0.001  | 4.2 $\pm$ 0.5        | 4.7 $\pm$ 0.4         | <0.001  |
| Femoral neck BMC (g)                   | 3.3 $\pm$ 0.6          | 4.2 $\pm$ 0.8         | <0.001  | 2.5 $\pm$ 0.6        | 3.5 $\pm$ 0.6         | <0.001  |
| Femoral neck BMD (g/cm <sup>2</sup> )  | 0.732 $\pm$ 0.088      | 0.809 (0.604–1.004)   | <0.001  | 0.604 $\pm$ 0.088    | 0.748 $\pm$ 0.108     | <0.001  |
| Femoral neck BMAD (g/cm <sup>3</sup> ) | 0.162 $\pm$ 0.021      | 0.156 $\pm$ 0.023     | NS      | 0.145 $\pm$ 0.020    | 0.161 $\pm$ 0.027     | 0.01    |
| Subtotal body area (cm <sup>2</sup> )  | 1215 $\pm$ 227         | 1572 $\pm$ 279        | <0.001  | 1043 $\pm$ 203       | 1440 $\pm$ 217        | <0.001  |
| Subtotal body BMC (g)                  | 941.2 $\pm$ 250        | 1426 $\pm$ 393        | <0.001  | 751 $\pm$ 202        | 1246 $\pm$ 284        | <0.001  |
| Subtotal body BMD (g/cm <sup>2</sup> ) | 0.777 $\pm$ 0.065      | 0.891 $\pm$ 0.104     | <0.001  | 0.710 $\pm$ 0.056    | 0.856 $\pm$ 0.079     | <0.001  |
| Subtotal body lean mass (g)            | 29045 $\pm$ 5909       | 40233 $\pm$ 10040     | <0.001  | 23125 $\pm$ 4556     | 31682 $\pm$ 5372      | <0.001  |
| Subtotal body fat mass (g)             | 8443 (3254–34768)      | 12446 $\pm$ 6788      | NS      | 7867 (3602–23667)    | 14067 $\pm$ 6028      | 0.003   |
| Subtotal body % fat                    | 25.3 $\pm$ 8.9         | 21.8 $\pm$ 7.8        | 0.026   | 27.6 $\pm$ 8.4       | 28.9 $\pm$ 6.5        | NS      |

*Abbr:* BMAD, bone mineral apparent density; BMC, bone mineral content; BMD, bone mineral density; BMI, body mass index; SD, standard deviation; NS, not significant.

**Table 3**Pearson or Spearman Correlation Coefficients and *p* Values Between Mothers and Children for BMD, BMC, Area, and Body Composition, by Gender and Pubertal Stage, Adjusted for Sibling Effect

| Parameters                | Boys (N = 126)            |                             | Girls (N = 113)         |                          |
|---------------------------|---------------------------|-----------------------------|-------------------------|--------------------------|
|                           | Early puberty<br>(n = 72) | Midlate puberty<br>(n = 54) | Premenarcho<br>(n = 22) | Postmenarcho<br>(n = 91) |
| <b>Lumbar spine</b>       |                           |                             |                         |                          |
| BMD (g/cm <sup>2</sup> )  | —                         | —                           | —                       | 0.281*                   |
| BMC (g)                   | —                         | —                           | —                       | 0.300**                  |
| Area (cm <sup>2</sup> )   | 0.409**                   | —                           | —                       | 0.286**                  |
| BMAD (g/cm <sup>3</sup> ) | —                         | 0.238*                      | —                       | 0.249*                   |
| <b>Total hip</b>          |                           |                             |                         |                          |
| BMD (g/cm <sup>2</sup> )  | —                         | 0.313*                      | —                       | 0.192*                   |
| BMC (g)                   | 0.243*                    | —                           | —                       | 0.282**                  |
| Area (cm <sup>2</sup> )   | 0.508**                   | 0.306                       | 0.398 <sup>a</sup>      | 0.388**                  |
| <b>Femoral neck</b>       |                           |                             |                         |                          |
| BMD (g/cm <sup>2</sup> )  | —                         | 0.329** <sup>a</sup>        | —                       | —                        |
| BMC (g)                   | —                         | —                           | —                       | 0.202*                   |
| Area (cm <sup>2</sup> )   | 0.229*                    | —                           | —                       | 0.308**                  |
| BMAD (g/cm <sup>3</sup> ) | —                         | 0.368**                     | 0.440*                  | —                        |
| <b>Total body</b>         |                           |                             |                         |                          |
| BMD (g/cm <sup>2</sup> )  | —                         | —                           | —                       | 0.184                    |
| BMC (g)                   | —                         | —                           | —                       | 0.300**                  |
| Area (cm <sup>2</sup> )   | 0.237*                    | —                           | —                       | 0.326**                  |
| <b>Body composition</b>   |                           |                             |                         |                          |
| Lean mass (g)             | —                         | —                           | —                       | 0.299**                  |
| Fat mass (g)              | —                         | 0.324* <sup>a</sup>         | —                       | 0.299** <sup>a</sup>     |
| % Fat mass                | —                         | 0.307*                      | —                       | 0.301**                  |

Abbr: BMAD, bone mineral apparent density; BMC, bone mineral content; BMD, bone mineral density.

*p* Value only reported if <0.1; \**p* < 0.05; \*\**p* < 0.01.

<sup>a</sup>Spearman correlation (R).

### Heritability Estimates

Table 4 summarizes the heritability estimates by maternal descent,  $\frac{1}{2} h^2$  (%), of lean mass and fat mass Z-scores, and of BMD, BMAD, and area Z-scores adjusted for BMI, daily calcium intake, exercise, and sun exposure at different sites, and by gender and pubertal stage. In early-pubertal boys, heritability estimates were significant for total hip area and BMD and for area at spine and total body (estimate range: 20–35%), whereas in late puberty, significant heritability estimates were noted in area at total hip, spine, and total body (estimate range: 18–29%) and almost significant in FN bone mass (20%; *p* = 0.052). In contrast, none of the heritability estimates were significant in premenarcheal girls, whereas in postmenarcheal girls, heritability estimates for bone mass and area were significant at all sites (total hip, FN, spine, and total body; estimate range: 21–37%). In addition, heritability estimates for spine BMAD were significant in early-pubertal boys (22%) and in postmenarcheal girls (28%), whereas that for FN BMAD was significant in late-pubertal

boys only (26%). Heritability estimates for lean and fat masses were significant in early-pubertal boys and postmenarcheal girls (estimate range: 26–40%).

### Discussion

Our study reveals gender differences in maternal transmission of bone mass and body composition traits that are most consistently expressed after puberty. In boys, maternal bone size inheritance is expressed mainly in early puberty and is consolidated at the hip and spine in postpuberty. In girls, bone mass correlations and heritability estimates of bone mass and area were significant only in postmenarche. As for body composition variables, early but not late pubertal boys showed significant heritability estimates with their mothers, whereas these were significant only in postmenarcheal and not premenarcheal girls. The latter is possibly due to a diverging effect of differentially increasing sex steroids (androgens in boys and estrogens in girls) by late puberty.

**Table 4**  
 Mother-Child Heritability Estimates,  $\frac{1}{2} h^2$  (%)<sup>a</sup>, by Gender and Pubertal Stage, Based on the Z-score for the Parameters of Interest

| Z-scores                    | Boys                      |                             | Girls                   |                          |
|-----------------------------|---------------------------|-----------------------------|-------------------------|--------------------------|
|                             | Early puberty<br>(n = 68) | Midlate puberty<br>(n = 53) | Premenarcho<br>(n = 21) | Postmenarcho<br>(n = 86) |
| Z-score of bone mass        |                           |                             |                         |                          |
| Total hip                   | 30*                       | 19                          | —                       | 25**                     |
| Femoral neck                | —                         | 20                          | —                       | 21*                      |
| Lumbar spine                | —                         | —                           | —                       | 34**                     |
| Total body                  | —                         | —                           | —                       | 24*                      |
| Z-score of BMAD             |                           |                             |                         |                          |
| Femoral neck                | —                         | 26*                         | —                       | 20                       |
| Lumbar spine                | 22*                       | —                           | —                       | 28*                      |
| Z-score of bone area        |                           |                             |                         |                          |
| Total hip                   | 33**                      | 29**                        | —                       | 34**                     |
| Femoral neck                | —                         | —                           | —                       | 31**                     |
| Lumbar spine                | 35**                      | 26*                         | —                       | 29**                     |
| Total body                  | 20*                       | 18*                         | —                       | 37**                     |
| Z-score of body composition |                           |                             |                         |                          |
| Lean mass                   | 26**                      | —                           | —                       | 26*                      |
| Fat mass                    | 36**                      | 24                          | —                       | 40**                     |

Note: Calculated Z-scores were derived using the gender- and pubertal stage-specific mean and standard deviation for the variable of interest.

Abbr: BMAD, bone mineral apparent density.

\* $p < 0.05$ ; \*\* $p < 0.01$ .

<sup>a</sup>Heritability is the proportion of variance in offspring Z-score that is explained by mothers' Z-score. This was done using the slope of the regression ( $\beta$  coefficient) between the residuals of the multiple regression of bone parameter Z-score of the children on the body mass index, daily calcium intake, physical activity, and sun exposure of the children and the residuals of a similar regression on the mother's data except for sun exposure due to unavailable data.  $p$  Value only reported if  $< 0.1$ .

Maternal bone mass heritability was mostly studied in prepubertal or adolescent children, almost exclusively in girls (5–8,10). Ferrari et al studied 138 prepubertal girls (mean age: 8 yr) and their mothers and reported that 18–37% of bone traits (BMC, area, areal density, and size-adjusted density) at LS, FN, and midfemoral diaphysis were directly determined by maternal descent (5). Runyan et al evaluated 72 adolescent girls, mean age 12.8 yr, Tanner stages 2 and 3, and their mothers and found significant correlations at the LS BMD ( $r = 0.52$ ) and trochanter ( $r = 0.39$ ) but not total hip or FN, as well as significant correlations in their height ( $r = 0.45$ ) and weight ( $r = 0.27$ ) (8). Kuroda et al (10) described strong familial resemblance for lumbar BMD-SD (Z-score) in prepubertal girls and their premenopausal mothers ( $r = 0.281$ ) and in 338 postmenarcheal girls and their mothers ( $r = 0.301$ ;  $R^2 = 0.073$ ;  $p < 0.001$ ) that was independent from their age at menarche, height, weight, or exercise intensity. Tylavsky et al (6) evaluated 84 premenopausal mothers and their college-age daughters and found significant correlations in their mid- and distal radial BMC ( $r = 0.37$ – $0.47$ ) and BMD ( $r = 0.32$ – $0.34$ ). In our study,

the significant correlations noted in BMD, BMC, and area at most skeletal sites in postmenarcheal girls, and the consistent and significant heritability estimates at several skeletal sites, are similar to what was described previously (5–8,10). The lack of significant findings in premenarcheal girls is possibly due to their small sample size ( $n = 22$ ). It is important to stress, however, that the findings were present, despite adjustments for BMI and important confounders such as calcium intake, exercise, or sun exposure.

Maternal bone size heritability as assessed by the derived heritability estimates for bone area was present in both genders in late puberty, except for FN area in boys, and was significant for bone area in early-pubertal boys at hip, spine, and total body. It has indeed been shown that bone structure is in large part due to genetic factors and is established during growth, most probably before puberty (21–24). A recent study evaluating different parameters of bone structure (tibia cross-sectional area) and mass by computed tomography (CT) in young girls demonstrated such traits to be established before puberty, with additional increments thereafter (22). The same group also demonstrated early postnatal familial

resemblance in anthropometric parameters and bone mass traits in girls, to consolidate thereafter (24). The differences in the timing of bone size heritability between our study and the last 2 studies may be due to differences in study designs, methods to assess heritability, the actual traits studied, the adjustments made, and sample size considerations.

To our knowledge, this study is the first to investigate heritability of body composition during puberty in mother-daughter and mother-son pairs, across different pubertal stages. The correlations of fat traits between mothers and their pubertal sons and daughters are in sharp contrast to adult studies that did not find significant fat mass heritability from parents to their adult sons or daughters (12), which may be explained by the more powerful effects of environmental or hormonal factors over genetic influences during adulthood. The fat mass correlations in our cohort may be due to the shared family environment. On the other hand, the lack of lean mass correlations in mother-son (but not mother-daughter pairs) may be due to the differential effects of gonadal hormones, namely testosterone and estrogen on body composition parameters (13,14). Sex-specific genetic effects have been shown to influence heritability of lean mass, %fat mass, and fat distribution in a cohort of 2506 young adults from a Dutch genetic isolate (25). Cheng et al (26) had established tracking of bone mass and body composition traits before menarche sets in a longitudinal cohort of 396 girls, ages 10–13 yr, followed for 7 yr. Although the correlation coefficients obtained for the previously mentioned traits between mothers and their 18-yr-old daughters were somewhat comparable with those noted in our study, the tempo of onset of such correlations in the various pubertal stages was not evaluated. Tracking of bone mass traits has been described in prepuberty (22) and as early as the first year of postnatal life (24). The cumulative evidence from available studies demonstrating the tracking of phenotypic traits in cohorts followed longitudinally reflects the substantial impact of genes on the phenotype of interest early during growth and development (5,7,22–25).

This study provides new insights into the heritability of skeletal and body composition traits and the important effects of puberty as a critical time to express genetic potential, and thus familial resemblance, and in determining site specificity by gender. The strength of this study is that it investigates heritability at multiple sites, in both genders, and before and after puberty simultaneously, within the same study. It also shows significant correlations in body composition traits for mother-child pairs, but more importantly, it is the only study demonstrating significant correlations in hip traits between mothers and their sons and the heritability of bone size in mother-son pairs in general. Additionally, it highlights the site specificity of skeletal and body composition parameters in each gender: fat mass and hip bone mass traits in boys vs all bone mass traits and lean and fat masses in girls.

Our study is limited by the small sample size of premenarcheal girls that might have precluded detection of significant correlations as previously reported by other investigators (5,7,8,10). Other limitations to our study are its cross-

sectional nature, thus its inability to track trait heritability longitudinally; the unavailability of parameters reflecting bone strength such as captured with CT technology; and the lack of paternal heritability estimates of the same traits. It, however, bridges some knowledge gaps as detailed previously.

In conclusion, maternal bone mass heritability is expressed before puberty in boys and after menarche in girls, and whereas it includes all skeletal sites in postmenarcheal girls, it is restricted to the hip site in boys. The expression of body composition inheritance is more variable.

## Acknowledgments

This study was supported by an educational grant from the Nestle Foundation and a grant from Merck KGaA.

We thank the administrators, school nurses, parents, and students from the American Community School, the International College, the Amlieh School, and the Ashbal Al Sahel School for making the study possible.

Conflict of interest: MN, ZM, RE, LA, and JM have nothing to disclose. GEHF received an unrestricted educational grant from Novartis pharmaceuticals for investigator-initiated study protocols.

Authors' contributions: All authors participated in the writing of the manuscript and have seen and approved the final version. MN reviewed the literature, participated in data collection, analysis, and manuscript write-up. LA and ZM participated in statistical analysis. RE participated in literature review and data analysis. JM did data collection. GEHF was the lead investigator who designed the study, secured its funding, oversaw all aspects of protocol implementation, data entry, analyses, and oversaw manuscript write-up and finalization.

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