

Observational Study of Bone Accretion During Successful Weight Loss in Obese Adolescents

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Objective: To assess bone mineral content (BMC) among obese adolescents who lose weight during a critical period for bone accretion.

Methods and Procedures: Whole body, lumbar spine, lower, and upper limb BMC were measured in 62 obese adolescents who completed an intensive 12-month weight loss trial. BMC was adjusted for height (z-scores) using data from a reference group of 66 adolescents (who were 18% overweight).

Results: At baseline, the BMC of the obese group was higher than the reference group. During the 12-month weight loss program, unadjusted BMC increased among the obese adolescents, despite successful weight loss. After adjustment for height, whole body BMC did not change significantly from baseline to 12 months (mean \pm s.d.: 1.08 ± 0.67 to 1.06 ± 0.67 , $P = 0.7$). Region-specific BMC-for-height however decreased for the lower (1.07 ± 0.57 to 0.95 ± 0.59 , $P < 0.001$) and upper (1.29 ± 0.56 to 1.18 ± 0.57 , $P = 0.01$) limbs, but lumbar spine BMC-for-height increased (0.14 ± 1.06 to 0.40 ± 0.94 , $P < 0.001$). These changes were largely and independently explained by changes in lean and fat mass.

Discussion: This study confirms that obese adolescents have high BMC for height and suggests that, unlike adults, their BMC continues to increase during weight loss and remains higher than the BMC of a reference group. After adjustment for growth-related changes, lower and upper limb BMC appears to decrease, while lumbar spine BMC appears to increase. These results suggest that to optimize the health benefits of weight loss among obese adolescents, their bone health should be better understood and addressed.

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INTRODUCTION

Obesity and osteoporosis are major and potentially preventable public health problems. The prevalence of obesity continues to increase in the US pediatric and adult populations (1), and the aging of the population is expected to result in increasing osteoporotic fractures (2). The growing pediatric obesity epidemic raises important clinical and public health questions about the effects on lifelong bone health of early onset obesity and its treatment. Although osteoporotic fractures mainly cause morbidity and mortality among the elderly, peak bone mass, achieved shortly after puberty, is the key determinant of lifetime osteoporotic fracture risk (3). Several risk factors for pediatric obesity, such as a sedentary lifestyle (4), high consumption of soda (5), and low consumption of dairy products (6), also are risk factors for poor bone accrual (7–9), thus raising concerns about short-term and long-term bone health in obese adolescents.

In adults, obesity is associated with increased bone mineral density (BMD) as measured by dual-energy X-ray absorptiometry (DXA) (10), and with decreased risk of hip fracture in postmenopausal women (11). Furthermore, voluntary weight loss in adults is associated with a decrease in BMD (12), partially preventable with calcium supplements or exercise (13–15). In children and adolescents, however, the association of obesity with bone mineral content (BMC), BMD, or fracture risk is less clear. Some studies have suggested an increased risk for fracture in overweight compared to non-overweight children and adolescents (16,17), while another study did not confirm these findings (18). Initial studies suggested that overweight children and adolescents had insufficient bone mass relative to body weight (19). We reported that, in overweight children, bone mass was high relative to height (20) and lean body mass (21). Furthermore, recent findings

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from a large cohort study suggest that fat mass may be positively associated with BMC in children and with changes in BMC over time among prepubertal children, independent of changes in height and lean mass (22).

Despite the technical difficulties in measuring and interpreting measures of bone health in obese children, it is important to identify determinants of bone health in this population in order to understand the impact of childhood obesity on peak bone mass and lifetime risk of fracture. Furthermore, as obesity treatment during adolescence becomes more frequent, and as data on bone health during weight management in adolescents are limited (23), it is important to understand the impact of voluntary weight loss on bone health during this critical period. Considering that 90% of peak bone mass is acquired by age of 18 and that 25% is acquired during the 2-year period surrounding peak height velocity in adolescence (7), a decrease in BMD, as has been observed in adults (12–14), or a suboptimal increase in BMC during weight loss, may have important consequences on long-term bone health and fracture risk. The aim of this study was to assess changes in BMC in obese adolescents during an intensive weight loss program (24), compared with cross-sectional reference data, for the whole body and three regions: a mostly cortical weight-bearing site (lower limb), a mostly cortical non-weight-bearing site (upper limb), and a site that contains both cortical and trabecular bone (lumbar spine).

METHODS AND PROCEDURES

This is an observational study of bone accretion in obese adolescents taking part in a randomized controlled trial of weight loss (24). A detailed description of the trial methods and results has been provided elsewhere (24). Boys and postmenarcheal girls aged 9–17 years were eligible if their BMI (weight/height²) was between 32 and 44 kg/m² and if they had no significant physical or psychiatric condition. The study was aimed at testing the effectiveness of sibutramine in conjunction with a comprehensive, family-based, behavioral weight control program. All participants were included in a comprehensive weight loss program that included 13-weekly sessions, followed by 9 bi-weekly group sessions, and 3-monthly group sessions, for a total of 25 group sessions over 12 months. Parents met separately from the adolescents on the same schedule. The subjects were instructed to consume a 1,200–1,500 kcal/day balanced diet and prescribed an eventual goal of walking (or engaging in similar aerobic activities) for 120 min or more per week. During the first 6 months, half of the participants were randomized to escalating doses of sibutramine up to 15 mg/day and the other half to a matching placebo. Dosage was decreased or medication interrupted if significant increases in blood pressure occurred. For the second 6-month period, all subjects received the active drug in an open-label trial.

Anthropometry and bone parameters were measured at a single time point in a separate sample of 66 reference boys and postmenarcheal girls ages 9–18 years, who were part of a larger study (25) between October 1997 and November 1999. These reference subjects were recruited from general pediatric clinics and the surrounding community through advertisement and were excluded for chronic medical conditions or medications that could affect growth, pubertal development, nutritional status, or dietary intake. Obesity was not an exclusion criterion.

Body weight was measured to the nearest 0.1 kg using a digital electronic scale (Seca, Munich, Germany), and stature to the nearest 0.1 cm using a stadiometer (Holtain, Crymych, UK). Measurements were obtained at baseline, 6 months, and 12 months in the weight loss

trial subjects and once in the reference subjects. Weight, height, and BMI were converted to age- and sex-specific *z*-scores based on the Centers for Disease Control and Prevention reference growth charts (26).

Lumbar spine (L1-L4) BMC (g) and bone area (BA, cm²), as well as whole body BMC were measured by DXA (QDR2000, Hologic, Bedford, MA) with a fan beam in the array mode. Using standard line placement, BMCs of the two lower limbs and the two upper limbs were measured separately. Measures of fat mass (kg) and lean mass (kg) were also generated from the whole body DXA scans. Lean mass does not include bone mass in these analyses. All subjects were measured on the same machine using standard positioning techniques. Measurements were obtained between May 1999 and July 2002 for the obese study subjects on the same schedule as those for weight, described above. Quality control scans were performed daily using a simulated L1-L4 spine of hydroxyapatite encased in resin. In our institution, the *in vitro* coefficient of variation was <0.6% and *in vivo* in adults <1%. The study was approved by the Institutional Review Boards of the University of Pennsylvania School of Medicine and The Children's Hospital of Philadelphia.

Statistical analyses were performed using Stata 8.0 (Stata Corporation, College Station, TX). Two-sided tests of hypotheses were used and a *P* < 0.05 was considered statistically significant. Descriptive analyses were conducted that included constructing graphical displays of the data and calculation of mean and s.d., or frequencies as appropriate. Subjects in the weight loss trial who completed the 12-month assessment were compared to those who did not complete it with respect to baseline variables using the *t*-test, rank-sum test, or chi-square test as appropriate. Baseline characteristics of the obese subjects in the weight loss trial who completed the 12-month assessment were compared in a similar way to the characteristics of the reference group.

Longitudinal analyses were restricted to study subjects who completed the 12-month assessment. Analyses of subjects with incomplete data in weight loss trials is controversial (27), because subjects who do not complete the study are often those subjects who are less successful in their weight loss. This makes accurate estimation of the average weight changes and a comparison of the two treatment arms difficult, especially if completion rates differ between the two treatment arms. However, the aim of the present study was not to compare two obesity treatment arms, but to describe observed changes in bone parameters and their relationship with observed changes in weight. As a result, the potential bias due to non-completion may not be as serious because there is no reason to expect that the relationship between bone changes and weight changes will differ according to whether or not the subject completed the study. Therefore, restriction to completers is a reasonable approach in this case. Data analyses of the obese subjects in the weight loss trial at baseline, 6 months, and 12 months were performed using repeated measures ANOVA. To test for interaction by study group assignment (sibutramine vs. placebo in the first 6 months, in the second 6 months all subjects received sibutramine), an interaction term of group assignment by time was used.

In children and adolescents, BMC, BA, lean mass and fat mass change markedly and at variable rates with growth (28). The relationship between BMC and BA is not linear and has a non-zero intercept, rendering BMD (calculated as BMC divided by BA) an inappropriate method for adjusting BMC for differences in BA (29). Rather, the preferred method for evaluating bone status in children is to analyze BMC relative to a measure of bone size or body size (28–30). Because bones in the total body are not uniform in shape, height is used as an overall indicator of skeletal size. Moreover, we have shown previously that whole body BMC adjusted for stature, using sex-specific log-linear regression models, is the best indicator of bone strength as determined by three-dimensional quantitative computed tomography (31). For the current analysis, whole body, upper limb, lower limb, and lumbar spine BMC were transformed, as described below, in sex- and height-specific *z*-scores (s.d.) for height using data from 66 reference subjects (25). In order to integrate lean mass and fat mass into multivariate models, these variables were similarly transformed in lean mass-for-height and fat mass-for-height *z*-scores. Although these transformations are not conventional in obesity research, we felt that it was important to use the same approach to adjustment for body size

for all variables included in the same multivariate model. Lumbar spine BMCs were also transformed in sex- and BA-specific *z*-scores using data from the same 66 reference subjects. Because lumbar vertebrae are fairly uniform in shape, BA can also be used to adjust for bone size (29). The adjusted analyses for lumbar spine were however performed using BMC-for-height, in order to be consistent between variables introduced in the multiple regression models.

In our analyses, the reference subjects are not directly compared with the obese study subject group, as would be the case in a case-control study, but rather used to derive normalized bone data, as if often done, e.g., for BMI-for-age. Therefore, it is not critical that the two groups be matched for age or height, as long as the range of the variable used to normalize the data (in this case height and lumbar spine area) is similar between the two groups. First, natural log transformations of BMC and height or BA were used to improve the fit of models. Then, the assumptions of the regression models (linearity, normality of residuals, and constant variance) were assessed graphically and using the following tests: the Shapiro–Wilk test of normality of residuals, and the Cook–Weisberg test for heteroscedasticity. Finally, whole body, lower limb, upper limb and lumbar spine BMC of the study subjects were transformed into *z*-scores relative to height using the sex-specific prediction equations, while lumbar spine BMC was also transformed into *z*-scores relative to BA using the sex-specific prediction equations using the method described by Altman (32). *z*-Score values >0 represent values higher than the mean of the reference group, while an increase in *z*-scores over time represents an increase in bone status relative to the reference group. Adjusted analyses of the BMC *z*-scores of the obese subjects in the weight loss trial at baseline, 6 months, and 12 months were performed using ANOVA for repeated measurements. In this type of analysis for repeated measurements, each individual is compared to him/herself over time; therefore, no adjustment for constant individual potential confounding variables, such as race or socioeconomic status, is necessary. Time-dependent confounding variables, such as height, are adjusted in the *z*-score transformation described above, but, in order to assess if the observed changes in BMC could be explained by changes in lean mass and fat mass, lean mass-for-height and fat mass-for-height *z*-scores were added to the time variable as time-dependent variables in an ANCOVA for repeated measurements.

RESULTS

Among the 89 obese adolescents enrolled and measured at baseline, 82 were randomized in the weight loss trial, and 62 (69.7% of enrolled subjects, 75.6% of randomized subjects) completed the 12-month assessment. The characteristics of the subjects who completed the study did not differ at baseline from the characteristics of the subjects who did not. As compared to the reference group of 66 adolescents, the 62 adolescents who completed the 12-month assessment were older and taller and, by design, had a higher weight, BMI, weight *z*-score and BMI *z*-score, but had the same sex and race distribution (Table 1). Furthermore, the race distribution within sex-specific tertile of obese subject heights was not significantly different from the race distribution of the reference group in the corresponding height range. The height-for-age *z*-score was slightly higher in the obese adolescents of the weight loss trial, but this difference was not statistically significant.

As reported previously (24), among the 62 obese subjects who completed the weight loss trial, body weight, BMI, and fat mass decreased significantly over the 12 months of the study, while height and lean mass increased (Table 2). Height-for-age *z*-score decreased slightly. The whole body, lower limb, upper limb, and lumbar spine BMCs increased significantly over the

Table 1 Comparison of baseline characteristics (mean \pm s.d. or proportion) between the obese study subjects in the weight loss trial who completed the 12-month assessment and the reference group

	Obese study subjects (<i>n</i> = 62)	Reference group (<i>n</i> = 66)	<i>P</i> value
Age (year)	14.5 \pm 1.1	13.3 \pm 2.7	0.001
Sex (% female)	66.1	53.0	0.13
Black race (%)	37.1	37.9	0.3
Weight (kg)	100.0 \pm 15.3	52.1 \pm 18.1	<0.001
Height (cm)	164.4 \pm 8.2	155.6 \pm 13.6	<0.001
BMI (kg/m ²)	36.8 \pm 3.7	21.1 \pm 5.4	<0.001
Weight-for-age <i>z</i> -score (s.d.)	2.54 \pm 0.42	0.42 \pm 1.18	<0.001
Height-for-age <i>z</i> -score (s.d.)	0.37 \pm 1.02	0.24 \pm 1.24	0.5
BMI-for-age <i>z</i> -score (s.d.)	2.40 \pm 0.19	0.34 \pm 1.16	<0.001
Overweight (%)	100.0	18.2	<0.001

12-month interval. There was no interaction of group assignment by time on any of the bone variables (all *P* > 0.2), confirming the lack of effect of sibutramine on bone health. Therefore all further bone data analyses were performed using the pooled sample of study subjects regardless of group assignment.

At baseline, mean whole body, lower limb, and upper limb BMC-for-height *z*-scores were >0 (Table 2), corresponding to mean between the 86th and the 90th percentiles, and suggesting that these obese adolescents had higher BMC-for-height than the reference group. The whole body BMC-for-height *z*-score did not change significantly during the study. However, lower limb and upper limb BMC-for-height *z*-scores decreased slightly (Figure 1), suggesting a decrease in BMC status relative to height. At the end of the study, BMC-for-height *z*-scores remained elevated (>zero) with mean values between the 83rd and the 88th percentiles. Mean lumbar spine BMC-for-height and BMC-for-area *z*-score were also >0 at baseline. In contrast to lower and upper limbs, lumbar spine BMC-for-height and BMC-for-area *z*-score increased significantly during the study, suggesting an increase in lumbar BMC relative to height and bone size.

The changes in lower limb and upper limb BMC-for-height *z*-scores were independently explained (residual association with time *P* = 0.7 and *P* = 0.2, respectively) by lean mass-for-height *z*-scores (*P* = 0.002 and *P* = 0.02, respectively) and fat mass-for-height *z*-scores (*P* < 0.001 and *P* < 0.001, respectively). The changes in lumbar spine BMC-for-height were only partially explained (residual association with time *P* = 0.003) by lean mass-for-height *z*-scores (*P* = 0.05) and fat mass-for-height *z*-scores (*P* = 0.02).

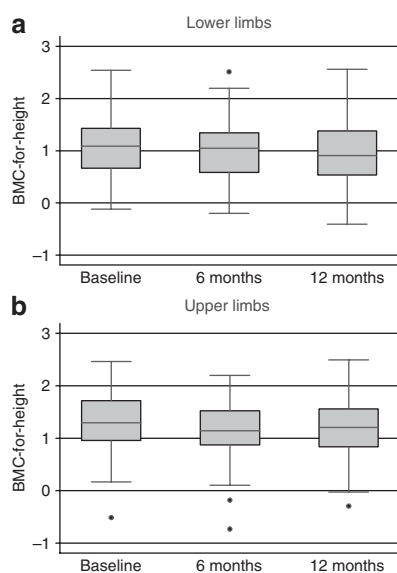
DISCUSSION

This study confirms previous findings that obese adolescents have elevated BMC for their height (20–22). During successful

Table 2 Changes in anthropometric and bone variables in 62 subjects who completed a 12-month comprehensive weight loss program with sibutramine or placebo

	Baseline mean \pm s.d.	6 Months mean \pm s.d.	12 Months mean \pm s.d.	P value ^a
Weight (kg)	100.0 \pm 15.3	94.8 \pm 16.4	94.5 \pm 19.5	<0.001
Fat mass (kg)	50.4 \pm 10.8	44.6 \pm 11.4	42.0 \pm 12.9	<0.001
Lean mass (kg)	47.0 \pm 8.2	46.8 \pm 7.9	48.3 \pm 8.1	0.002
Height (cm)	164.4 \pm 8.2	165.6 \pm 7.8	166.7 \pm 7.7	<0.001
BMI (kg/m ²)	36.8 \pm 3.7	34.4 \pm 4.4	33.9 \pm 6.2	<0.001
Weight-for-age z-score (s.d.)	2.54 \pm 0.42	2.27 \pm 0.54	2.15 \pm 0.67	<0.001
Height-for-age z-score (s.d.)	0.37 \pm 1.02	0.31 \pm 0.99	0.31 \pm 1.00	0.05
BMI-for-age z-score (s.d.)	2.40 \pm 0.19	2.20 \pm 0.30	2.08 \pm 0.43	<0.001
Whole body BMC (g)	2,422 \pm 478	2,469 \pm 451	2,527 \pm 446	<0.001
Lower limbs BMC (g)	997 \pm 190	1,008 \pm 186	1,029 \pm 187	<0.001
Upper limbs BMC (g)	333 \pm 71	331 \pm 71	344 \pm 72	0.02
Lumbar spine BMC (g)	52.2 \pm 14.3	54.6 \pm 14.0	57.5 \pm 13.3	<0.001
Whole body BMC-for-height z-score (s.d.)	1.08 \pm 0.67	1.06 \pm 0.65	1.06 \pm 0.67	0.7
Lower limbs BMC-for-height z-score (s.d.)	1.07 \pm 0.57	0.99 \pm 0.56	0.95 \pm 0.59	<0.001
Upper limbs BMC-for-height z-score (s.d.)	1.29 \pm 0.56	1.16 \pm 0.56	1.18 \pm 0.57	0.01
Lumbar spine BMC-for-height z-score (s.d.)	0.14 \pm 1.06	0.26 \pm 0.98	0.40 \pm 0.94	<0.001
Lumbar spine BMC-for-area z-score (s.d.)	0.58 \pm 1.17	0.81 \pm 1.11	0.85 \pm 1.02	0.006
Fat mass-for-height z-score (s.d.)	2.04 \pm 0.45	1.81 \pm 0.50	1.66 \pm 0.58	<0.001
Lean mass-for-height z-score (s.d.)	1.44 \pm 1.07	1.22 \pm 1.05	1.34 \pm 1.17	0.02

BMC, bone mineral content.

^aANOVA for repeated measurements.**Figure 1** Changes in limb bone mineral content (BMC) z-scores during weight loss in 62 obese adolescents: (a) lower limb BMC-for-height z-scores, (b) upper limb BMC-for-height z-scores.

weight loss, the BMC of these adolescents continued to increase. Although during successful weight loss, whole body and lumbar spine BMC increased relative to bone size or height, this study suggests that lower limb and upper limb BMC decreased relative to height, but remained above average, compared to

a reference group. The reason for these regional differences is unclear. The changes in BMC observed in this study were largely explained by changes in lean mass and fat mass during the successful weight loss trial.

Although earlier studies suggested that there was insufficient bone mass for body weight in obese adolescents (19), more recent studies suggest that bone mass is high relative to height (20,21). The results of this study confirm these recent findings, with mean BMC z-scores >0 for the whole body, lower limb, upper limb, and lumbar spine (Table 2). This is important and reassuring, as many of the determinants of obesity also are determinants of poor bone health during adolescence (4–9). These findings also mean that in order to understand the increased risk for fracture in obese compared to non-obese adolescents, factors other than low BMC need to be explored, such as increased impact during falls because of the excessive weight or decreased coordination and impaired reactions related to a sedentary lifestyle (16,17,33).

This study is unique because it reports longitudinal changes in BMC, by region, in obese adolescents during a successful weight loss program. The BMC of the adolescents in this study continued to increase during the time of weight loss. During adolescence, rapid gains in total body BMC occur following peak height velocity, with as much as 25% of peak bone mass acquired during the 2 years surrounding the growth spurt (7). Significant gains in trabecular and cortical BMD occur with advancing sexual maturation and skeletal maturation (34,35).

Obese children tend to be tall for their age and advanced in sexual and skeletal development although not different in adult height. The observed differences in BMC between the obese and healthy weight groups may only reflect the effect of this advanced sexual development. Measures of sexual and skeletal maturation were not available and their contribution could not be ascertained. Furthermore, in the longitudinal data, the observed increase in BMC may reflect normal growth during adolescence. Although reference data for gain in BMC are not available, our data were analyzed after adjustment for height or bone size to account for bone size. After accounting for height and bone size status, our findings demonstrate longitudinal changes in whole body and lumbar spine BMC that are in proportion or better than changes in height or bone size during linear growth. Furthermore, and as expected, these changes were largely and independently explained by changes in lean and fat mass. Despite these reassuring results for whole body and lumbar spine BMC, the results of our study suggest regional differences in the longitudinal changes in BMC during a period of successful weight loss. The BMC-for-height z-scores of the lower and upper limbs tended to decrease over time, but remained, on average, above the values of the reference group. This is a concern, as most of the increased risk for fractures observed in obese adolescents is due to limb fractures (16,17), and in the long-term, wrist fracture is a frequent complication of osteoporosis in the elderly (3).

The reasons for these regional differences in longitudinal changes in BMC during weight loss are unknown. These findings could be due to an artifact of the DXA technology in assessing spine and limb BMC in obese individuals during weight loss (36). Changes in mechanical load, as well as changes in circulating hormonal and inflammatory factors during weight loss may explain some of the changes reported in this study. Unfortunately, these were not measured. The changes in lower and upper limb BMC-for-height were entirely explained by changes in lean- and fat mass-for-height during this weight loss program. The contribution of lean mass was expected, because of the close relationship between muscle mass and BMC, but the independent association with fat mass is more difficult to explain. One could speculate that this association reflects changes in biological factors produced by fat cells or by the mechanical loading of bone due to the fat mass. In contrast to the limbs, the increase in lumbar spine BMC-for-height over time was not completely explained by changes in lean or fat mass and may be due to other elements of the weight loss program, such as an increase in physical activity, which was not measured in the present study.

This study had several limitations. The main limitation is the use of DXA to assess changes in bone measurements among obese adolescents. This technique provides limited information on bone geometry, does not differentiate trabecular from cortical bone, and is subject to projection error when subjects lose weight and their bones become closer to the table as the soft tissues surrounding the bone declines (37). The data collected in the reference group were cross-sectional and the use of cross-sectional data to interpret

longitudinal data is problematic, even though this approach is widely used. Unfortunately, no reference data exist for changes in BMC over time among adolescents. Most of the data of the reference group were collected before the data of the obese study subjects group. However, all data for reference and study subjects were collected within a 5-year period, which should limit the impact of potential secular trends. Furthermore, the lack of assessment of sexual and skeletal developments, calcium intake, and physical activity in this study may have introduced biases. As inflammatory and hormonal factors were not measured, the mechanisms underlying the observed results cannot be investigated in this sample. This study also had unique strengths. The subjects in this study had significant weight loss during the 12-month intervention, in contrast to another study that investigated the same question (23). The data were adjusted for height and bone size and analyzed separately by regions.

In conclusion, this study shows that obese adolescents have high BMC for their height and that, unlike what has been shown in adults (12–14), BMC continues to increase during successful weight loss. The increase in BMC during weight loss is similar to or faster than changes in height or bone size for the whole body and lumbar spine, but slower for the lower and upper limbs, and can be largely explained by changes in lean mass and fat mass. The implications of these findings on the short- and long-term risk for fracture is unknown but our results suggest that further research should be conducted to assess region-specific changes in BMC, dimensions, and strength with weight loss during adolescence, a critical period for long-term bone health.

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DISCLOSURE

The authors declared no conflict of interest.

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REFERENCES

1. Ogden CL, Carroll MD, Curtin LR *et al*. Prevalence of overweight and obesity in the United States, 1999–2004. *JAMA* 2006;295:1549–1555.
2. Schneider EL, Guralnik JM. The aging of America. Impact on health care costs. *JAMA* 1990;263:2335–2340.
3. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. *JAMA* 2001;285:785–795.
4. Robinson TN. Reducing children's television viewing to prevent obesity: a randomized controlled trial. *JAMA* 1999;282:1561–1567.

5. James J, Thomas P, Cavan D, Kerr D. Preventing childhood obesity by reducing consumption of carbonated drinks: cluster randomised controlled trial. *BMJ* 2004;328:1237.
6. Carruth BR, Skinner JD. The role of dietary calcium and other nutrients in moderating body fat in preschool children. *Int J Obes Relat Metab Disord* 2001;25:559–566.
7. Bailey DA, McKay HA, Mirwald RL, Crocker PR, Faulkner RA. A six-year longitudinal study of the relationship of physical activity to bone mineral accrual in growing children: the university of Saskatchewan bone mineral accrual study. *J Bone Miner Res* 1999;14:1672–1679.
8. Stear SJ, Prentice A, Jones SC, Cole TJ. Effect of a calcium and exercise intervention on the bone mineral status of 16–18-y-old adolescent girls. *Am J Clin Nutr* 2003;77:985–992.
9. McGartland C, Robson PJ, Murray L *et al*. Carbonated soft drink consumption and bone mineral density in adolescence: the Northern Ireland Young Hearts project. *J Bone Miner Res* 2003;18:1563–1569.
10. Albala C, Yanez M, Devoto E *et al*. Obesity as a protective factor for postmenopausal osteoporosis. *Int J Obes Relat Metab Disord* 1996;20:1027–1032.
11. Folsom AR, Kushi LH, Anderson KE *et al*. Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. *Arch Intern Med* 2000;160:2117–2128.
12. Van Loan MD, Johnson HL, Barbieri TF. Effect of weight loss on bone mineral content and bone mineral density in obese women. *Am J Clin Nutr* 1998;67:734–738.
13. Shapses SA, Von Thun NL, Heymsfield SB *et al*. Bone turnover and density in obese premenopausal women during moderate weight loss and calcium supplementation. *J Bone Miner Res* 2001;16:1329–1336.
14. Ryan AS, Nicklas BJ, Dennis KE. Aerobic exercise maintains regional bone mineral density during weight loss in postmenopausal women. *J Appl Physiol* 1998;84:1305–1310.
15. Riedt CS, Schlüssel Y, von Thun N *et al*. Premenopausal overweight women do not lose bone during moderate weight loss with adequate or higher calcium intake. *Am J Clin Nutr* 2007;85:972–980.
16. Goulding A, Jones IE, Taylor RW, Williams SM, Manning PJ. Bone mineral density and body composition in boys with distal forearm fractures: a dual-energy x-ray absorptiometry study. *J Pediatr* 2001;139:509–515.
17. Goulding A, Jones IE, Taylor RW, Manning PJ, Williams SM. More broken bones: a 4-year double cohort study of young girls with and without distal forearm fractures. *J Bone Miner Res* 2000;15:2011–2018.
18. Ma D, Jones G. Television, computer, and video viewing; physical activity; and upper limb fracture risk in children: a population-based case control study. *J Bone Miner Res* 2003;18:1970–1977.
19. Goulding A, Taylor RW, Jones IE *et al*. Overweight and obese children have low bone mass and area for their weight. *Int J Obes Relat Metab Disord* 2000;24:627–632.
20. Leonard MB, Shults J, Wilson BA, Tershakovec AM, Zemel BS. Obesity during childhood and adolescence augments bone mass and bone dimensions. *Am J Clin Nutr* 2004;80:514–523.
21. Petit MA, Beck TJ, Shults J *et al*. Proximal femur bone geometry is appropriately adapted to lean mass in overweight children and adolescents. *Bone* 2005;36:568–576.
22. Clark EM, Ness AR, Tobias JH. Adipose tissue stimulates bone growth in prepubertal children. *J Clin Endocrinol Metab* 2006;91:2534–2541.
23. Rourke KM, Brehm BJ, Cassell C, Sethuraman G. Effect of weight change on bone mass in female adolescents. *J Am Diet Assoc* 2003;103:369–372.
24. Berkowitz RI, Wadden TA, Tershakovec AM, Cronquist JL. Behavior therapy and sibutramine for the treatment of adolescent obesity: a randomized controlled trial. *JAMA* 2003;289:1805–1812.
25. Leonard MB, Feldman HI, Shults J *et al*. Long-term, high-dose glucocorticoids and bone mineral content in childhood glucocorticoid-sensitive nephrotic syndrome. *N Engl J Med* 2004;351:868–875.
26. Kuczmarski RJ, Ogden CL, Grummer-Strawn LM *et al*. CDC growth charts: United States. *Adv Data* 2000:1–27.
27. Ware JH. Interpreting incomplete data in studies of diet and weight loss. *N Engl J Med* 2003;348:2136–2137.
28. Heaney RP. Bone mineral content, not bone mineral density, is the correct bone measure for growth studies. *Am J Clin Nutr* 2003;78:350–351; author reply 351–352.
29. Prentice A, Parsons TJ, Cole TJ. Uncritical use of bone mineral density in absorptiometry may lead to size-related artifacts in the identification of bone mineral determinants. *Am J Clin Nutr* 1994;60:837–842.
30. Molgaard C, Thomsen BL, Prentice A, Cole TJ, Michaelsen KF. Whole body bone mineral content in healthy children and adolescents. *Arch Dis Child* 1997;76:9–15.
31. Leonard MB, Shults J, Elliott DM, Stallings VA, Zemel BS. Interpretation of whole body dual energy X-ray absorptiometry measures in children: comparison with peripheral quantitative computed tomography. *Bone* 2004;34:1044–1052.
32. Altman DG. Construction of age-related reference centiles using absolute residuals. *Stat Med* 1993;12:917–924.
33. Goulding A, Jones IE, Taylor RW, Piggot JM, Taylor D. Dynamic and static tests of balance and postural sway in boys: effects of previous wrist bone fractures and high adiposity. *Gait Posture* 2003;17:136–141.
34. Gilsanz V, Kovanlikaya A, Costin G *et al*. Differential effect of gender on the sizes of the bones in the axial and appendicular skeletons. *J Clin Endocrinol Metab* 1997;82:1603–1607.
35. McKay HA, Bailey DA, Mirwald RL, Davison KS, Faulkner RA. Peak bone mineral accrual and age at menarche in adolescent girls: a 6-year longitudinal study. *J Pediatr* 1998;133:682–687.
36. Brownbill RA, Ilich JZ. Measuring body composition in overweight individuals by dual energy x-ray absorptiometry. *BMC Med Imaging* 2005;5:1.
37. Leonard MB, Zemel BS. Current concepts in pediatric bone disease. *Pediatr Clin North Am* 2002;49:143–173.