Osteoporos Int (2001) 12:199–206

Osteoporosis International

Original Article

Bone Mineral Density During Reduction, Maintenance and Regain of Body Weight in Premenopausal, Obese Women

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Abstract. Weight loss may lead to bone loss but little is known about changes in bone mass during regain of reduced weight. We studied changes in bone mineral density (BMD) and bone mineral content (BMC) during voluntary weight reduction and partial regain. The study consisted of three phases: a 3 month weight reduction with very-low-energy diet (VLED), a 9 month randomized, controlled walking intervention period with two training groups (target energy expenditure 4.2 or 8.4 MJ/week) and a 24-month follow-up. The participants were premenopausal women with a mean body mass index of 34.0 (SD 3.6) kg/m^2. Seventy-four of 85 subjects completed the whole study. Total body, lumbar spine, proximal femur and dominant radius BMD and BMC were measured with dual-energy X-ray absorptiometry (DXA). The mean weight loss during VLED was 13.2 (3.4) kg, accompanied by unchanged total body BMC and decreased lumbar, trochanteric and radial BMD ($p < 0.05$). During months 3–36, an average of 62% of the weight loss was regained, total body BMC decreased and trochanteric BMD increased ($p < 0.05$). At the end of the study, total body BMC and lumbar and femoral neck BMD were lower than initially ($p < 0.05$). Weight change throughout the study correlated significantly with the change in radial ($r = 0.54$), total body ($r = 0.39$) and trochanteric ($r = 0.37$) BMD. Exercise-group assignment had no effect on BMD at weight-bearing sites. In conclusion, the observed changes in BMD and BMC during weight reduction and its partial regain were clinically small and partly reversible. More studies are needed to clarify whether the observed weight changes in BMD and BMC are real or are artifacts arising from assumptions, inaccuracies and technical limitations of DXA.

Keywords: Body composition; Obesity; Osteoporosis; Physical activity; Weight cycling

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Introduction

Body weight, and especially the fat-free body mass, is one of the major determinants of bone mass [1]. Consequently, compared with normal-weight individuals, people with obesity have higher bone mineral content (BMC) and bone mineral density (BMD) both in weight-bearing (e.g., femur) and in non-weight-bearing (e.g., radius) bone sites [2,3]. Because of all the negative physiologic and psychosocial consequences associated with an excessive amount of body fat, obese people frequently try to lose weight. Although reduction of overweight reduces the risk for several chronic diseases, it may lead to bone loss [2].

Several studies have indicated that reduction of overweight (mean weight loss from 3 to 22 kg) is followed by small (1–6%) losses in total body BMC [4–6], and even more frequently by reduced BMD [4,6–11]. However, the results are not consistent, because a few other studies have not found any significant changes in total body BMC [11–13] or BMD [12,13] following weight reduction.

Although a majority of studies suggest that total BMC and/or BMD decrease during substantial weight reduction, much less is known about the changes in different

bone sites. It has been reported that after weight reduction BMD is maintained in the spine but reduced in the femoral neck region [10,13]. In contrast, some groups found reduced spinal BMD and maintained femoral neck or hip BMD [8,14] after voluntary weight loss. Results on changes in the greater trochanter BMD are also conflicting [10,13].

After weight reduction, very few subjects are able to maintain their new, lowered body weight [15]. Compston et al. [4] measured BMD during an almost total weight regain (mean reduction 15.6 kg in 2 months, followed by weight regain of 12.7 kg during 12 months) in 8 women. They found that total body BMD returned to the same and BMC to almost the same level as before weight reduction. In contrast, Avenell et al. [14] suggested that BMD in the spine was not reversed by weight regain.

Given the apparent lack of conclusive data on the relationship between changes in body overweight and bone mineral status, the aim of the present study was to shed light on site-specific changes in bone mass during substantial weight reduction and subsequent partial or total weight regain. The present study describes changes in total body, lumbar spine, femoral neck, trochanteric region and distal radius BMD and BMC during weight loss, maintenance and regain, and compares these changes in premenopausal obese women with different outcomes in body weight (total, partial or no weight regain).

Subjects and Methods

Study Design

The duration of the study was 3 years and it consisted of three phases. First, all subjects participated in a 3 month weight reduction phase. After weight reduction, the subjects were randomized into three groups: a control group with no increase in habitual exercise, and two exercise groups with walking training targeted to expend either 4200 kJ (1000 kcal) or 8400 kJ (2000 kcal) weekly. The exercise intervention has been described in detail previously [16].The main objective of the exercise group allocation was to test the effects of an exercise-based maintenance program on weight, rather than on bone. The duration of the supervised phase after randomization, with or without an exercise training program, was 9 months. This phase was followed by two yearly measurements. The total study duration was 36 months. In the present report, the entire 33 month period after weight reduction was treated as a single post-weight-reduction follow-up phase.

Subjects

Eligibility criteria were body mass index 30–46 kg/m^2 and age 30–45 years. Women had to be clinically healthy and premenopausal. Only volunteers with a stable weight (± 3 kg for at least 3 months before the study) were included. The women were not on any medication, excluding hormonal contraceptives. None of the subjects was physically active (leisure-time physical exercise $\leqslant 2$ times/week), pregnant or lactating, nor did any of them smoke. Eighty-five women were accepted, 82 subjects (drop-out rate 4%) completed the weight reduction phase, and 74 subjects (drop-out rate 13%) were measured at the end of the entire study. The present report shows results of only those whose body composition and bones were measured at 0, 3, 12 and 36 months (n = 74). The study was approved by the ethics committee of the UKK Institute for Health Promotion Research. Written informed consent was obtained from the participants.

Weight Reduction Phase

The 3 month weight reduction program consisted of three parts: week 1, low-energy diet based on a meal-exchange system; weeks 2 to 9, very-low-energy diet (VLED, Nutrilett, Nycomed-Pharma, Oslo, Norway); and weeks 10–12, low-energy diet. The subjects met weekly in small groups (5–12 participants), overseen by a nutritionist. The meeting topics included instructions for low-energy and very-low-energy diets, general knowledge on diet and weight maintenance, and basics of relapse prevention techniques. All subjects were weighed before each meeting.

Anthropometry and Body Composition

Body weight was measured after an overnight fast, with a high-precision scale (F150S-D2, Sartorius, Goettingen, Germany), with the subjects wearing only their underwear. The subjects' body density was measured by underwater weighing, after full exhalation [17]. Body composition was calculated from the body density by a two-component model in which the body was divided into fat and fat-free compartments with assumed densities of 0.9 and 1.1 g/cm^3, respectively [18]. Waist circumference was measured midway between the lowest rib and the iliac crest. Hip circumference was measured at the tip of the greater trochanter. The mean of three readings was used.

Bone Densitometry

The areal BMD (g/cm^2) and BMC (g) were measured at lumbar spine (L2–L4), femoral neck, trochanteric region and dominant distal radius using dual-energy X-ray absorptiometry (DXA, Norland XR-26; Norland, Fort Atkinson, WI; software version 2.2.2). Also the total body scan was done by Norland XR-26, from which the total body BMD and BMC were calculated using the new total body composition scan software (version 2.5.2). Bone projectional areas (BA, cm^2) within the

given regions of interest were measured, too. All scans and analyses were carried out according to our established procedures [19,20]. The in vivo day-to-day precision (coefficient of variation, CV%) was better than 1% for proximal femur and lumbar spine and better than 2% for distal radius [20]. The corresponding CV% for total body BMC is 1.5% (repeated measurements of 18 subjects, unpublished data). The scanner was calibrated daily, and its performance was monitored with our quality assurance protocol [21]. No sign of scanner drift was observed during the study period.

Statistical Analyses

The main outcome measures were changes in BMD from the beginning to the end of the study (months 0 to 36). Secondary outcomes were changes in BMD during weight reduction (months 0 to 3) and during the follow-up phase (months 3 to 36). Moreover, the respective results for BMC and BA were reported and analyzed. The effect of exercise-group allocation, time (0, 3 or 36 months) or group-by-time interaction was tested by analysis of variance (ANOVA) with repeated measurements. To test the time-effect among all subjects ANOVA with repeated measurements without the group factor was used. Post-hoc multiple comparisons of differences were done by Sidak's method.

The relationship between changes in bone measurements and changes in weight was assessed by dividing the subjects retrospectively into five groups by quintiles of weight change (months 0 to 36). Between-group differences in changes of BMD, BMC and BA were analyzed by one-way ANOVA, including the test for linear trend. In addition, Pearson's product–moment correlation coefficients were calculated for changes (months 0 to 36) in weight, fat free mass and circumferences, against the respective changes in BMD and total body BMC. The results are presented as mean, standard deviation (SD) and 95% confidence interval (CI) for the mean. $p < 0.05$ was chosen as the level of statistical significance. All statistical analyses were done by the SPSS statistical software package, version 8.0 (SPSS, Chicago, IL).

Results

Characteristics of the subjects before weight reduction are shown in Table 1. Mean body mass index (BMI) was 34.0 (SD 3.6) kg/m^2 and mean age 40 (SD 4.0) years. All eligible subjects had a BMI of at least 30 kg/m^2 in the screening assessment. Waist circumference of all subjects was at least 88 cm. Eight to 13 persons took contraceptive hormones during various phases of the study. About one-third of them took both estrogen and progestagens orally and the rest had intrauterine devices releasing levonorgestrel. No major change in menstrual status was observed during the study.

Table 1. Anthropometric and bone measurements in 74 premenopausal women before the study

	Mean (SD)	Range
Weight (kg)	92.0 (9.8)	75.2–125.6
Fat-free mass (kg)	51.3 (4.2)	43.9–61.9
Waist (cm)	102 (9)	88–121
Hip (cm)	113 (10)	94–143
Total body BMD (g/cm^2)	1.11 (0.07)	0.98–1.25
Spine BMD (g/cm^2)	1.13 (0.12)	0.89–1.43
Femoral neck BMD (g/cm^2)	0.99 (0.10)	0.77–1.22
Trochanter BMD (g/cm^2)	1.06 (0.10)	0.84–1.29
Distal radius BMD (g/cm^2)	0.43 (0.05)	0.31–0.54
Total body BMC (g)	2951 (262)	2332–3543
Spine BMC (g)	51.8 (7.8)	34.8–70.2
Femoral neck BMC (g)	7.4 (2.4)	3.2–14.5
Trochanter BMC (g)	27.5 (3.7)	18.1–37.2
Distal radius BMC (g)	2.0 (0.3)	1.4–2.6
Total body BA (cm^2)	2664 (172)	2149–3068
Spine BA (cm^2)	45.6 (3.6)	37.3–54.5
Femoral neck BA (cm^2)	7.5 (2.3)	3.6–14.7
Trochanter BA (cm^2)	25.8 (2.2)	19.4–32.9
Distal radius BA (cm^2)	4.6 (0.3)	3.9–5.2

BMD, areal bone mineral density; BMC, bone mineral content; BA, projectional bone area.

A total of 14.3% of initial body weight was lost during the 3 months' weight reduction period (Table 2). The corresponding mean reductions in the fat-free mass, waist circumference and hip circumference were 8.6%, 11.8% and 8.0%. Hence, the subjects apparently lost more fat than fat-free mass, and more abdominal than peripheral fat. Femoral neck BMD was unchanged during weight reduction. In contrast, BMD of total body, and of the spine, trochanter and distal radius decreased statistically significantly ($p < 0.05$). Moreover, the calculated BMC of spine, femoral neck and trochanter, and BA of total body, femoral neck and trochanter decreased significantly ($p < 0.005$).

During the 33 month follow-up, an average of 62% of the reduced weight was regained. The regains of the fat-free mass, waist circumference and hip circumference were 22%, 42% and 88% of the losses during weight reduction. These results indicate that more fat than fat-free mass, and more peripheral than abdominal fat was regained. The changes in BMD were minor during the follow-up. However, trochanter BMD increased slightly, but statistically significantly ($p < 0.05$).

The mean body weight was 5% lower at the end of the study than before weight reduction. Eighteen (25%) of the subjects regained all the weight lost during weight reduction. The final mean fat-free mass and waist circumference were 7%, and hip circumference 1% smaller than before weight reduction. The final BMD of total body, spine and femoral neck, BMC of total body, and BA of distal radius were statistically significantly ($p < 0.05$) lower than before weight reduction. In contrast, the BA of trochanter increased ($p < 0.05$) during the study period.

Table 2. Changes (mean, SD, 95% confidence interval (CI) for the mean) in anthropometric bone measurements during weight reduction, after weight reduction and during the entire study

	Change during weight reduction (months 0–3)		Change after weight reduction (months 3–36)		Change during the entire study (months 0–36)	
	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI
Weight (kg)	–13.2 (3.3)*	–14.2 to –12.2	8.3 (6.1)*	6.6 to 10.0	–4.9 kg (7.1)*	–6.9 to –2.9[a]
Fat-free mass (kg)	–4.3 (2.7)*	–5.1 to –3.5	1.1 (2.5)*	–1.8 to –0.3	–3.3 (2.9)*	–4.1 to –2.4
Waist (cm)	–12 (4)*	–13 to –11	5 (6)*	4 to 7	–7 (8)*	–9 to –4
Hip (cm)	–9 (3)*	–10 to –8	8 (5)*	6 to 9	–1 (5)	–3 to 0
Total body BMD (g/cm^2)	–0.01 (0.03)*	–0.02 to –0.005	–0.004 (0.04)	–0.01 to 0.007	–0.02 (0.04)*	–0.03 to –0.005
Spine BMD (g/cm^2)	–0.02 (0.04)*	–0.03 to –0.006	0.003 (0.03)	–0.006 to 0.01	–0.01 (0.04)*	–0.03 to –0.005
Femoral neck BMD (g/cm^2)	–0.005 (0.03)	–0.01 to 0.003	–0.004 (0.03)	–0.01 to 0.004	–0.009 (0.03)*	–0.02 to –0.0003
Trochanter BMD (g/cm^2)	–0.01 (0.02)*	–0.02 to –0.008	0.01 (0.03)*	0.002 to 0.02	–0.003 (0.03)	–0.01 to 0.006
Distal radius BMD (g/cm^2)	–0005 (0.02)*	–0.009 to – 0.0004	0.001 (0.02)	–0.005 to 0.007	–0.004 (0.02)	–0.01 to 0.003[b]
Total body BMC (g)	6 (129)	–30 to 43	–46 (115)*	–79 to -13	–39 (136)*	–78 to –0
Spine BMC (g)	–1.02 (2.22)*	–1.65 to –0.38	0.78 (2.48)*	0.07 to 1.49	–0.24 (2.31)	–0.90 to 0.42
Femoral neck BMC (g)	–0.47 (1.00)*	–0.75 to –0.18	0.24 (1.08)	–0.08 to 0.55	–0.22 (1.20)	–0.57 to 0.12
Trochanter BMC (g)	–0.72 (1.14)*	–1.05 to –0.40	1.15 (1.67)*	0.68 to 1.16	0.43 (1.58)	–0.02 to 0.88
Distal radius BMC (g)	–0.02 (0.08)	–0.04 to 0.007	–0.02 (0.11)	–0.06 to 0.009	–0.04 (0.12)	–0.08 to 0.004
Total body BA (cm^2)	39 (108)*	8 to 70	–31 (108)	–61 to 0.4	9 (122)	–27 to 43
Spine BA (cm^2)	–0.20 (1.39)	–0.60 to 0.20	0.59 (1.80)*	0.07 to 1.10	0.39 (1.44)	–0.03 to 0.80
Femoral neck BA (cm^2)	–0.43 (0.96)*	–0.70 to –0.15	0.27 (1.07)	–0.03 to 0.58	–0.15 (1.18)	–0.49 to 0.18
Trochanter BA (cm^2)	–0.33 (0.77)*	–0.55 to –0.11	0.82 (1.16)*	0.49 to 1.16	0.50 (1.02)*	0.20 to 0.78
Distal radius BA (cm^2)	0.01 (0.13)	–0.02 to 0.05	–0.07 (0.15)*	–0.11 to –0.02	–0.05 (0.13)*	–0.09 to –0.02

BMD, areal bone mineral density; BMC, bone mineral content; BA, projectional bone area.
* Change significantly ($p < 0.05$) different from zero (ANOVA, Sidak's post-hoc contrasts).
[a]Time-by-exercise group interaction ($p = 0.06$).
[b]Time-by exercise group interaction ($p = 0.01$).

The exercise group-by-time interaction terms for fat-free mass, waist and hip circumferences, total body BMD, spine BMD, femoral neck BMD and trochanter BMD were not statistically significant (p = 0.39–0.97), implying that the exercise group allocation did not affect the above results. In contrast, the interaction term was statistically significant for weight ($p = 0.05$) and radius BMD ($p = 0.01$). The post-hoc comparisons at 36 months, with adjustment for initial body weight, showed that the exercise group assigned to the lower (4200 MJ/week) energy consumption had smaller post-weight-reduction regains in body weight (–3.9 kg, 95% CI –7.8 to –0.0 kg, $p = 0.05$) and radius BMD (–0.02 g/cm^2, 95% CI –0.03 to –0.003 g/cm^2, $p = 0.01$) compared with the controls. The corresponding differences between the two exercise groups, or between the control and the exercise group assigned to the higher (8400 KJ/week) energy consumption level, were not statistically significant.

To test whether weight change explained the between-group differences in change of radius BMD, we did a repeated measures analysis of covariance (ANCOVA) with radius BMD (at 0, 3 and 36 months) as the dependent variable, exercise group allocation as the grouping factor, and weight (at 0, 3 and 36 months) as the time-dependent covariate. In this analysis, the group-by-time interaction was no longer statistically significant ($p = 0.11$). A similar repeated measures ANCOVA was not done with other bone sites, because they did not show an association with the exercise group.

Quintiles of weight change (months 0 to 36) were −11.4 kg (20th percentile), −4.5 kg (40th percentile), −2.1 kg (60th percentile) and 0.9 kg (80th percentile). The changes in trochanter and radius BMD appeared to be most strongly associated with the quintiles of weight change, that is, the change (difference between the 0 and 36 month results) in BMD was the most negative (decrease) for the lowest quintile, and the least negative, or even positive (increase), for the highest or two highest quintiles (Fig. 1). The linear trend of BMD change across the levels of weight change was statistically significant ($p < 0.01$) and positive for total body, trochanter and radius (Fig. 1b, e, f). The strong association for weight change versus change in radius

Table 3. Pearson correlation for changes (0 to 36 months) in body weight, composition or fat distribution, against the respective changes in BMC and BMD, in 74 premenopausal obese women during weight loss and regain

	Weight	Fat-free mass	Waist circumference	Hip circumference
Total body BMC	–0.02	0.05	–0.05	–0.05
Total body BMD	0.39*	0.34*	0.36*	0.39*
Spine BMD	0.14	0.10	0.15	0.06
Femoral neck BMD	0.19	0.19	0.12	0.17
Trochanter BMD	0.37*	0.22	0.42*	0.43*
Distal radius BMD	0.54*	0.35*	0.48*	0.44*

*$p < 0.01$.

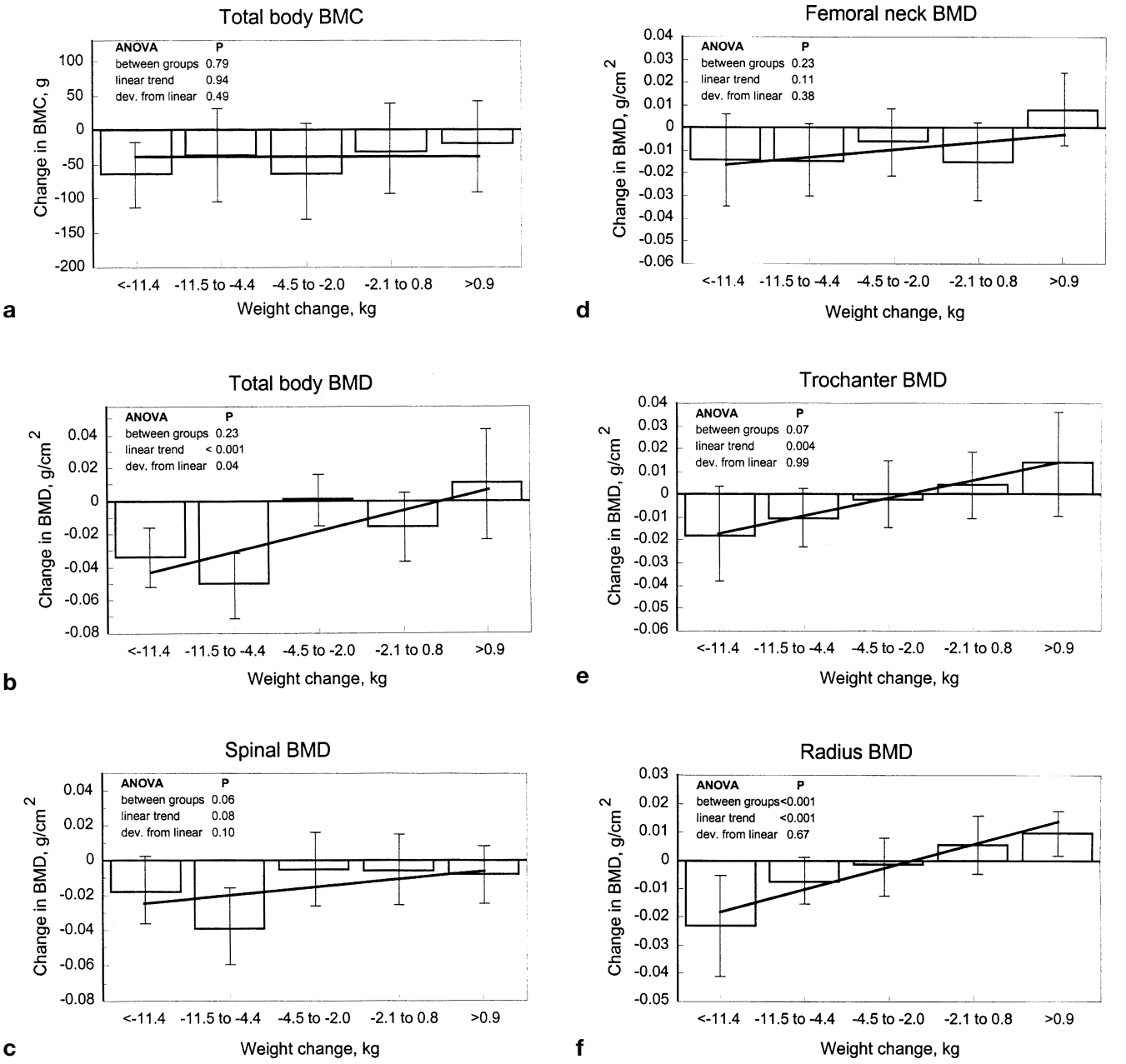

Fig. 1. Change in total body BMC (**a**), total body BMD (**b**), lumbar spine BMD (**c**), femoral neck BMD (**d**), trochanter BMD (**e**) and distal radius BMD (**f**) in premenopausal women grouped by quintiles of weight change over the entire study period (36 months). The mean changes (and their 95% confidence intervals) in BMC or BMD are shown by *vertical bars*. The linear regression between the weight change quintiles and the change in BMC or BMD is shown by the *thick line*. The results of the analysis of variance, including the test for linear trend, are shown in the *upper left* corner of each figure.

BMD, in particular, was also seen when the correlation coefficients (change in weight, fat-free mass or circumferences throughout months 0 to 36, against the respective changes in BMD or total body BMC) were compared (Table 3). Only the changes in radius showed statistically significant ($p < 0.001$) differences between the five classes (quintiles) of weight change (Fig. 1f).

Discussion

This is the first study to show that long-term changes in BMD in a non-weight-bearing bone site (distal radius) are related to changes in excess weight at least as evidently as changes in BMD in weight-bearing sites. Another unique aspect of the present study was that the follow-up period after weight reduction was much longer

than in previous studies. We regard this important, because of the lack of conclusive data on the extent of bone regain following weight regain. Because of the long duration of our study, an untreated, obese control group was not included in the study design. We felt that it would have been unethical to restrict any voluntary attempts of obese people to reduce weight during such a long period.

During weight reduction, we observed a decrease in total body BMD, without a corresponding change in total body BMC. Similar results were reported by Van Loan et al. [11], while other studies have found that changes in total body BMD were reflected by corresponding changes in BMC [6,12,13]. Reasons for these discrepancies are not known. The small, but statistically significant decrease in radius BMD was of special interest. In an earlier study, Svendsen et al. [7], in contrast to our study, did not find any changes in forearm BMD, during an 8 kg weight reduction.

Two-thirds of the subjects were allocated to a walking-training intervention for 9 months after the weight reduction phase. The exercise group with a moderate training program (target energy expenditure 4.2 MJ/week) showed the smallest regain in radius BMD. At first, this finding was surprising, because earlier studies have shown that even moderate-intensity exercise during weight reduction prevents bone loss in weight-bearing sites [10,22]. However, our exercise group with the 4.2 MJ/week target also showed the best weight maintenance. When body weight at the different time-points was used as a covariate in the statistical analysis, the association between exercise group and BMD changes disappeared. This finding suggests that the between-group difference in weight change was the main explanation for the between-group difference in BMD change. Therefore, because walking training apparently had no independent effect on BMD in the present study, we felt that it was appropriate to pool the entire data for analysis.

Our main interest was the changes in BMD during the entire study period. The changes in site-specific and total body BMD in our quintile analysis indicated that a total regain in body weight was accompanied by a similar regain of BMD. Spinal BMD appeared to be the only exception, because it usually decreased even in those subjects who eventually gained more weight than they lost. Hence, the results regarding spine are similar to those reported by Avenell et al. [14]. Our earlier study [23] suggested that not only lumbar BMD, but also radius BMD was negatively affected by weight cycling. However, the cross-sectional study design does not allow comparison with the present prospective study. Compston et al. [4], whose subjects gained most of the weight loss, has earlier reported an almost complete regain in total body BMD.

In the present study the similar directions in changes in weight and BMD during both weight loss and regain may be interpreted in two different ways. First, one might assume that the changes identified by DXA are real, that is, BMD actually decreased during weight reduction, and increased during weight regain. Support for actual BMD loss comes from earlier studies showing increased bone resorption, observed by biochemical markers following weight reduction [9,22,24].

Several factors may explain changes in BMD during weight changes. A simple reason would be decreased mechanical loading due to lighter body weight [8]. However, this would not explain the positive associations between the non-weight-bearing radius BMD and weight, as seen so clearly in the present study. In this light, our results rather support the view that changes in BMD are caused by humoral factors [24]. One theory is that changes in energy balance are associated with changes in sex-hormone-binding globulin that alter the bioavailability of estrogen in target tissues [25].

Another potential explanation of decreased BMD during weight reduction is malnutrition, especially a lack of dietary calcium [8]. We do not find this a plausible explanation in our study, because all subjects used a VLED formula with supplemental vitamins and minerals. Indeed, the mean calcium intake during weight reduction was 910 mg (calculated from food records; unpublished results). Many other authors also share the view that low calcium intake is an unlikely explanation for decreased BMD during weight reduction [4,6,13,14,22]. Nevertheless, an interesting question is whether calcium supplementation could attenuate BMD losses in subjects with initially low (<800 mg/day) calcium intake [9].

The second interpretation for the association seen between body weight and BMD is that the DXA results are entirely or partly an artifact, rather than an indication of true changes in bone tissue. Based on chemical indicators of bone resorption [22], and on BMD measurements after increasing tissue thickness artificially by adding lard [4,5,26], some authors argue against an artifact or any other considerable error. In contrast, Van Loan et al. [11] underscore their finding of decreased BMD, but unchanged BMC. Although changes BMD and BMC in our study were usually positively associated, the contradictory response of total body BMD and BMC was also seen in our study.

Since BMD, by arithmetic definition, is equal to BMC divided by BA, a decreased BMD and unchanged BMC would be an indication of increased bone area (e.g., changes in total body BMC and BA during weight reduction in the present study). Indeed, the many of the changes in BA were significant and, in all instances, positively correlated with respective changes in BMC (results not shown). A change in BA should, however, not be considered likely, given the 3 year duration of the present follow-up and the typical rate of age-related expansion of long bone shafts (approximately 0.3% per year in femur) [27]. It is thus more likely that the bone edge detection by DXA is affected by the thickness, composition and distribution of the surrounding soft tissues [28]. The pixels along the actual bone edge may, depending on the soft tissue composition and the proportion of bone mineral present in the given pixel area, be considered either as bone or soft tissue pixel,

and this partial volume effect might result in changes in BA and BMC as well. The possibility that the changed soft tissue distribution may have altered the bone alignment and thus BA cannot be ruled out either. In addition, the inherent, systematic inaccuracy of DXA arising from the violation of the two-component assumption (i.e., the regions of interest should comprise bone and a homogeneous soft tissue only) may well play a role in the simultaneous changes in body composition and BMD [29]. Hence, it appears that something is wrong in the DXA-derived results, but unfortunately our data are not able to identify the specific cause, and which outcome (BMD or BMC) is more biased.

Body composition results vary by DXA system and software version [30]. Therefore, one may speculate that the somewhat inconsistent results on BMD changes after weight reduction could depend of the device and software. In the pertinent studies we have referred to [4–9,10–14,22], three different systems and a total of 10 software versions were used. We could not identify any logical association between the outcome (BMD vs. weight change) and system or software.

In summary, we measured BMD in several bone sites, and total body BMD and BMC, during a rapid and substantial weight reduction, and a 33-month follow-up. During the follow-up, about 25% of the subjects regained at least all the weight lost during the weight reduction period. The DXA measurements showed decreases in BMD at several bone sites, including distal radius, during weight reduction, and a recovery in BMD during weight regain. Only spine BMD appeared to remain incompletely recovered, even in subjects with total weight regain. However, all the observed changes in BMD were small and reversible, and most likely without any clinical relevance. We argue that voluntary weight reduction and cycling apparently do not compromise health in obese premenopausal women. Nevertheless, it should be kept in mind that DXA results do not elucidate whether rapid bone loss and regain are associated with undesirable changes in bone micro-architecture and structure [25]. More studies are also needed to clarify whether the observed changes in bone are real or artifacts arising from assumptions and technical limitations of DXA.

Acknowledgements. Supported by grants from the Ministry of Education, the Yrjö Jahnsson Foundation and the Juho Vainio Foundation.

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Received for publication 20 April 2000
Accepted in revised form 20 September 2000