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Mini Abstract

We conducted a prospective study following bone traits from childhood to adulthood.

Our aim was to study if a bone mass scan in childhood can be used to predict bone mass in adulthood. We found that a pediatric bone mass scan has poor ability to predict adult bone mass.

Abstract

Purpose: As the correlation of bone mass from childhood to adulthood is unclear, we conducted a long-term prospective observational study to determine if a pediatric bone mass scan could predict adult bone mass.

Methods: We measured cortical bone mineral content (BMC; g), bone mineral density (BMD; g/cm^2) and bone width (cm) in the distal forearm by single photon absorptiometry in 120 boys and 94 girls with a mean age of 10 years (range 3–17) and mean 28 years (range 25–29) later. We calculated individual and age specific bone mass Z-scores, using the control cohort included at baseline as reference and evaluated correlations between the two measurements with Pearson's correlation coefficient. Individual Z-scores were also stratified in quartiles to register movements between quartiles from growth to adulthood.

Results: BMD Z-scores in childhood and adulthood correlated in both boys ($r=0.35$; $p<0.0001$) and girls ($r=0.50$, $p<0.0001$) and in both children ≥10 years at baseline (boys $r=0.43$ and girls $r=0.58$, both $p<0.0001$) and in children <10 years at baseline (boys $r=0.26$ and girls $r=0.40$, both $p<0.05$).

Of the children in the lowest quartile of BMD, 58% had left the lowest quartile in adulthood. A pediatric bone scan with a value in the lowest quartile had a sensitivity of 48% (95% CI 27%, 69%) and a specificity of 76% (95% CI 66%, 84%) to identify individuals who would remain in the lowest quartile also in adulthood

Conclusions: Childhood forearm BMD explained 12% of the variance in adult BMD in men and 25% in women. A pediatric distal forearm BMD scan has poor ability to predict adult bone mass.

Introduction

Bone loss is a physiological process related to aging[1-2] that results in low bone mineral density (BMD) and possibly osteoporosis [2]. There are no prospective studies that have followed bone mass from young adulthood into the ages when osteoporosis becomes a problem of magnitude. However calculations have inferred that 50% of the variance in BMD at age 65 could be predicted by peak bone mass[3-4] it has also been shown that individuals with high bone mass at age 30 are likely to have high bone mass also at age 70[5].

This has led to speculations inferring that a reduction of age-related bone loss[2] or optimizing of peak bone mass[1,4]could possibly reduce the prevalence of osteoporosis. For intervention strategies in adulthood it thus seem feasible to target not only the population at large[6], but also high-risk individuals.

In contrast, the level of bone mass tracking from childhood to adulthood is unclear. There are some reports that infer a childhood excess[7-8] or deficit[9-10] in BMD to remain in adulthood and the few prospective studies that have addressed this question infer a partial tracking of BMD during growth[11-14] But, as these the studies have all been shorter than a decade and terminated before the age of 17, and since peak bone mass is reached later [15], it seems unlikely that peak bone mass was actually captured in any of these.

We therefore set up a prospective long-term study to answer the following questions: (i) Does bone mass track from childhood to adulthood? (ii) Is tracking more evident in older than younger children and is there a gender discrepancy? (iii) What proportion of individual remains in the lowest quartile of bone mass in both childhood and adulthood and what is the sensitivity and specificity of a pediatric bone scan to predict low bone mass also in adulthood? (iv) Is movement from one BMD quartile in childhood to another in adulthood due to different accrual of bone mineral or gain in bone size?

Materials

Distal forearm bone mineral content (BMC; g), bone mineral density (BMD; g/cm^2), and bone width (cm) were measured by single-photon absorptiometry (SPA) in 120 boys with a mean age of 9.9 years (range 3–17) and 94 girls with a mean age of 10.7 years (range 4–17). The children were included from three published cohort studies between the years 1979-1981: 48 boys and 28 girls with a previous fracture[16], 31 boys and 25 girls with premature birth[17] and 41 boys and 43 girls from a healthy control cohort within same ages[16-18]. All participants were Caucasians, without any disease or medication known to affect bone metabolism. No follow-up measurements were originally planned but several decades later we designed the present study and conducted follow-up measurements by inviting all participants originally included. 214 of the original 296 participants were re-measured with the same SPA apparatus, a mean 28 years (range 25–29) later, then at a mean age of 37 years (range 28–44). Among the non-participants, 5 men and 2 women had died, 13 men and 9 women had relocated, 19 men and 15 women could not be located, 9 men and 8 women declined further participation, and 2 men were unable to attend due to illness. This corresponds to an overall participation rate of 72%, equally distributed in both genders. Seventy-four of the original 90 individuals (82%) were re-measured in the fracture cohort, 56/75 (75%) in the premature birth cohort and 84/131 (64%) in the control cohort. Age, height, weight and body mass index (BMI), gender distribution and lifestyle factors were similar in the three cohorts, as well as in those individuals who attended the follow-up exam and those who did not (data not shown).

Bone traits were measured in the distal forearm 6 cm proximal to the ulnar styloid on both occasions. The scanning technique has previously been described in detail[2, 16]. We scanned both arms and used the mean value except for in individuals with a history of upper extremity fracture (11 on the right side and 17 on the left side), where we used only the result from the non-fractured arm. The coefficient of variation (CV) was 2% with a standardized phantom and 4% after repeated measurements in 14 subjects after repositioning. The long-term drift, evaluated by a standardized phantom was 0.1% per year at baseline and follow-up measurements (95% CI –0.2, 0.4) [2]. Because of the non significant drift there were no corrections of data. One technician performed all baseline measurements, another all follow-up measurements and one of the authors analyzed all plots. Body weight and height were measured with standard equipment. Lifestyle factors, diseases, and medications were evaluated by questionnaires at both baseline[16-17] and follow-up[6].

Statistical evaluation

The study was approved by the Ethics Committee of Lund University. We used SPSS® version 20.0 for statistical calculations. Group differences were evaluated by chi-square test, Student´s t-test or ANCOVA with adjustment for age, height and weight. As there were no existing reference data at baseline individual and age specific Z-scores (the number of standard deviation above or below the age predicted mean) were gender specifically derived by linear regression at baseline and follow-up, respectively, using the baseline control cohort as reference population. Tracking (i.e. correlation) of the Z-scores between baseline (age 4-16) and follow-up (age 28-44) was evaluated by Pearson's correlation coefficient, partial correlation was used to adjust for height and weight. We also stratified the Z-scores of each bone trait in quartiles and (i) examined the proportion of individuals that left their original quartile during the study period, (ii) estimated the sensitivity of a pediatric bone scan with a result in the lowest quartile to predict an adult result in the same quartile, and (iii) the specificity for a scan outside the lowest quartile to predict an adult result outside the lowest quartile. Data are presented as numbers (n), means ± standard deviations (SD), means with 95% confidence intervals (95% CI) or as proportions (%).

Results

Children aged 3–17 years at baseline (all; n=214)

Anthropometry, bone traits, and lifestyle data are presented in table 1. There were correlations between Z-scores in childhood and adulthood for BMC (r=0.56, p<0.001), BMD (r=0.42, p<0.0001), and bone width (r=0.58, p<0.001), evident also in gender specific analyses (table 2). Adjustment for differences in height and weight at baseline did not change the results (data not shown). Correlations between Z-scores were also found in sub-group analyses of children with a history of fracture (BMC r=0.51, BMD r=0.32, and bone width r=0.64, all p< 0.01), children with premature birth (BMC r=0.65, BMD r=0.48 and bone width r=0.56, all p<0.0001), and children from the former control cohort (BMC r=0.53, BMD r=0.44 and bone width r=0.55, all p<0.0001)

The sensitivity and specificity of a childhood measurement in the lowest quartile of Z-scores to predict an adult value in the same quartile of Z-scores are further shown in table 3. The low correlations, (table 2) and low sensitivity (table 3) indicate that a large proportion of participants moved from one quartile of Z-scores to another (figures 2–4). The proportion of participants who left the lowest quartile of Z-scores (for higher quartiles) during growth was 58% for BMD (figure 2), 47% for BMC (figure 1) and 53% for bone width (figure 3).

As expected, there were some correlation between Z-scores of the accrued amount of mineral (BMC) and gain in bone size, (r=0.43, p<0.001), although 93/211 (44%) of the participants had a proportionally higher accrual of BMC Z-scores than gain in bone size Z-scores (points above the dotted line in figure 4) and 118/211 (56%) a proportionally higher gain in bone size Z-scores than accrual of BMC Z-scores (points below the dotted line in figure 4). This heterogeneity was more evident in those who left the lowest quartile of BMD Z-scores during the study period (n=31), as we in this group found a higher accrual of bone mineral (BMC) (ΔZ-score 0.54; 95% CI 0.19, 0.89) and a trend for a lower gain in bone size (ΔZ-score –0.31, 95% CI –0.65, 0.02) (figure 5). In contrast, those who left the highest quartile of BMD Z-scores during the study period (n=26) had a lower accrual of bone mineral (BMC) (ΔZ-score –1.10; 95% CI –1.44, –0.76) but also a trend for a higher gain in bone size (ΔZ-score 0.24, 95% CI –0.08, 0.56) (figure 5).

Children 10 years or older at baseline (n=110)

In children ≥10 years at baseline we found Z-score correlations between bone traits in childhood and adulthood, for BMC ($r=0.64$, $p<0.001$), BMD ($r=0.51$, $p<0.0001$) and bone width ($r=0.64$, $p<0.0001$), evident also in gender specific analyses (table 2). Adjustment for differences in height and weight at baseline did not change the results (data not shown). The sensitivity and specificity (as described above) of a bone mass measurement in children aged ≥10 years to predict the adult values are further shown in table 4. Due to the small sample size we did not estimate gender-specific sensitivity and specificity.

Children below age 10 at baseline (n=104)

In children <10 years at baseline we also found Z-score correlations between bone traits in childhood and adulthood, for BMC ($r=0.47$, $p<0.001$), BMD ($r=0.31$, $p<0.05$) and bone width ($r=0.50$, $p<0.001$), evident also in gender specific analyses (table 2). Adjustment for differences in height and weight at baseline did not change the results (data not shown). The sensitivity and specificity (As described above) of a bone mass measurement in children <10 years to predict the adult values are shown in table 4. Due to the small sample size we did not estimate gender-specific sensitivity and specificity.

Discussion

This study shows that a pediatric BMD scan has a poor ability to predict adult BMD, and that childhood BMD was only able to explain 12% of the variance in adult BMD for men and 25% for women. The sensitivity of a pediatric BMD scan in the lowest quartile to predict an adult result in the same quartile was also low. The variance for BMC was 23% in men and 41% in women. The higher correlation for BMC than BMD is supported by previous reports[11-12, 19]. This could reflect that BMC although associated with skeletal size, only estimates the amount of mineral while BMD reflects two separate estimates, the amount of bone mineral and areal bone size. This hypothesis is supported by the greater change in bone size in those who changed quartile of BMD during growth (figure 5). It must however be emphasized that there were children in our study with BMD below –2.5 SD who ended with a higher than average BMD in adulthood (figure 2).

There are prospective studies that have followed bone mass in the short term perspective during growth[11-14, 19-22]. The only longitudinal study with distal forearm SPA data by Magarey et al.[19] utilized measurements every second year during a 6 year period in 108 children aged 11 years at baseline. They reported that up to 88% of the variance in bone mass at age 17 years could be explained by the bone mass at age 11 years and that 80–90% of those in the top or bottom quintile at baseline remained in the same quintile 6 years later[19]. Kalkwarf et al. followed 1 554 children aged 6–16 at baseline for 3 years with dual energy X-ray absorptiometry (DXA) for total body, spine, hip and radius and reported that 58%–76% of the variance in bone mass at follow-up was explained by baseline values and that 72%–87% of children with a bone mass below –1.5 SD had a value lower than –1.0 SD at follow-up[22]. Another longitudinal (8.5 year follow-up) study in 125 pre-pubertal girls by Ferrari et al. reported that a pediatric BMC scan explained 29%–66% of the variance in their post-pubertal BMC [11], Foley et al. reported that a pre-pubertal scan explained 24%–79% of the variance in post-pubertal bone mass in 183 children followed from age 8 to 16 years[14], Budek et al. inferred that 25%–66% of the BMC at age 17 years could be explained by the level of BMC at age 11 years[23] while Fujita et al., when following 225 children from age 9–12 years for a 6 year period, inferred that 42% of the variance in BMD in older boys and 58% in older girls could be explained by the baseline BMD[24]. It is however unlikely that peak bone mass was captured in any of these studies as they all ended before termination of growth and peak bone mass, usually regarded to occur around age 20 in the hip[15] and after age 30 in the distal radius[1]. The long observation period in our study however covers this period and probably also explains our lower correlations [20, 21].

The inclusion of pre-, peri-, and post-pubertal children could influence our inferences since bone properties change rapidly at puberty[1]. As girls in the study experienced menarche at a mean age of 12.7 years (range 10–18) and boys are known to reach puberty approximately 1.5 year later [25] we stratified children below and above age 10 years. We hence predominantly include children before they reach the fast pre-pubertal growth spurt[25] in the strata of children <10 years. This enables us to confirm our hypothesis of higher tracking in older than younger children, probably due to the longer remaining growth period in young children. The lower correlation in boys than girls of the same chronological age probably reflect the later onset of puberty in boys and their longer remaining growth period.[19, 22]

About 44% of the participants in our study had a more pronounced accrual of bone mineral than expected (markers positioned above the dotted line in figure 4) and 56% a more pronounced gain in bone width (markers positioned below the dotted line in figure 5). If the accrual of bone mineral (BMC) and the gain in bone size had been proportional, BMD would remain the same, as BMD is an estimate that combines the amount of bone mineral (BMC) and the bone size. We found however low correlation between BMD in childhood and adulthood and that a large proportion of participants also changed BMD quartile during growth. Actually, we could identify individuals who had a childhood BMD Z-score of –2.7 and an adult Z-score of 1.5 (marked with (a) in figure 2). The different accrual of bone mineral and gain in bone size during growth is supported by our data, in which individuals who improved from the lowest quartiles of BMD had a higher accrual of bone mineral (BMC) but also a trend for a smaller gain in bone size (Figure 5). In contrast, those deteriorating from the highest quartile of BMD had a smaller accrual of bone mineral but also a trend of greater gain in bone size (Figure 5). The heterogeneity of bone mineral accrual and gain in bone size could also explain why a pediatric bone mass scan could explain 31% of the variance in adult BMC (which only evaluates the amount of mineral) but only 18% of the variance in adult BMD (which in addition to the amount of both mineral also reflects bone size).

Study strengths are the prospective study design, the long follow-up spanning the period of peak bone mass, measurements by the same scanner at the same skeletal site and continuous validation of the apparatus by a phantom during the entire study. The fact that all measurements at each occasion were performed by one technician and all graphical analyses by one author is also advantageous. An attendance rate of 72% after 28 years is superior to previous prospective studies[11, 13-14, 19, 22, 26-27], and the fact that dropout analyses revealed similar anthropometrics, bone trait, and lifestyle factors in participants and non-participants further strengthens

the quality of the data. Limitations include few individuals in the sub-groups resulting in a risk of a type II error, forcing us to refrain from gender-specific evaluations in separate age strata. SPA was the only available scanning technique in year 1979 but it would have been advantageous to use modern scanning techniques as well as evaluation of other anatomical regions, especially the hip and spine, commonly used for clinical evaluation of osteoporosis. [28] As growth occurred and ended during the study period, this could hypothetically influence the location of the position of measurement and influence the acquired absolute bone mass value. To take this into account we used Z-scores and estimated tracking between Z-scores instead of absolute values. A registration of pubertal maturity to stratify the children by true pubertal status would have been preferred as well as individual registration of menopause which would have given reasonable estimates of individuals at risk of post-menopausal bone loss. As the oldest women in our cohort was 44 years, the mean age of menopause in Scandinavia is 51 (95% CI 45–55) years[29], and bone loss in the cortical region of the distal forearm is initiated after age 40 years[30], there is a low risk of any significant age-related bone loss in our data Finally it would have been advantageous to have serial measurements to pinpoint the exact time for peak bone mass.

The association between childhood and adult BMD was in our study low. The data further implied that a childhood BMD scan is of limited use for prediction of adult BMD, at least in healthy children. Further long term longitudinal studies preferably with modern measuring techniques (DXA and pQCT) and sites (spine and hip) as well as inclusion of children with BMD below – 2.5 SD are advocated before any definite clinical inferences can be drawn regarding the use of childhood BMD measurements.

We conclude that the correlation of distal forearm bone mass from childhood to adulthood is low, and that a pediatric bone mass scan has poor ability to predict adult BMD. This seems attributable mainly to heterogeneity of bone mineral accrual and gain in bone size during growth.

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Table 1 Age, anthropometry, body mass index (BMI; kg/m^2), distal forearm bone mineral content (BMC; g), bone mineral density (BMD; g/cm^2) and bone width (cm) in 120 boys and 94 girls with a mean age of 10.3 years (range 3–17) at baseline and mean 28 years (range 25–29) later at a mean age of 37 years (range 28–44). Data are shown as unadjusted means ± standard deviation (SD), as proportions (%) or as numbers (n).

	Cases			
	Baseline	Follow-up	Baseline	Follow-up
	Women		**Men**	
	n=94		n=120	
Age (year)	10.7±3.9	37.4±4.1	9.9±4.0	36.6±4.0
Height (cm)	142.4±20.3	166.7±6.4	140,3±23.5	179.4±7.6
Weight (kg)	37.0±13.9	72.7±15.9	35.7±17.4	86.3±14.3
BMI (kg/m^2)	17.4±2.5	26.1±5.3	17.2±3.0	26.8±4.0
BMC (g/cm)	0.47±0.2	0.72±0.1	0.47±0.2	1.03±0.1
BMD (g/cm^2)	0.42±0.1	0.54±0.1	0.42±0.1	0.67±0.1
Bone width (cm)	2.1±0.31	2.65±0.24	2.17±0.4	3.09±0.23
Age at menarche (years)	12.7±1.3	12.7±1.3	–	–
Smokers* (%)	–	35.1	–	33.1
Alcohol** (%)	–	3.2	–	12.5
Chronic disease *** (n)	–	1	–	2
Food intolerance (n)	–	4	–	2

*Proportion of individuals with a smoke history of at least 5 years
**Proportion of risk consumers of alcoholic beverages as defined by the National Board of Health and Welfare in Sweden (>9 units of alcohol/week for women and >14 units for men)
*** Number of individuals with chronic disease with medication (men – hypertension and Mb Crohn, a type of inflammatory bowel disease (IBD), resulting in swelling and dysfunction of the intestinal tract.; women – hypothyroidism).

Table 2 Correlations between baseline and follow-up Z-scores of distal forearm bone mineral content (BMC; g), bone mineral density (BMD; g/cm^2) and bone width (cm) measured by single photon absorptiometry (SPA) in 214 children with a mean age of 10.3 years (range 3–17) at baseline and mean 28 years (range 25–29) later at a mean age of 37 years (range 28–44). Data are reported as the Pearson's correlation coefficient (r) with the number of individuals in the analyses within brackets. *p<0.05, **p<0.01, all other analyses were significant at a level of p< 0.0001.

	Bone mineral content (BMC)			**Bone mineral density (BMD)**			**Bone width**		
	All Children	Girls	Boys	All Children	Girls	Boys	All Children	Girls	Boys
Children 3–17 years at baseline	0.56 (n=214)	0.64 (n=94)	0.48 (n=120)	0.42 (n=214)	0.50 (n=94)	0.35 (n=120)	0.58 (n=214)	0.65 (n=94)	0.51 (n=120)
Children ≥10 years at baseline	0.64 (n=110)	0.73 (n=51)	0.52 (n=59)	0.51 (n=110)	0.58 (n=51)	0.43 (n=59)	0.64 (n=110)	0.73 (n=51)	0.55 (n=59)
Children <10 years at baseline	0.47 (n=104)	0.52 (n=43)	0.44 (n=61)	0.31* (n=104)	0.40** (n=43)	0.26* (n=61)	0.50 (n=104)	0.52 (n=43)	0.50 (n=61)

Table 3 Sensitivity* and specificity** of a pediatric bone mass scan to predict adult bone mass. Bone mineral content (BMC; g), bone mineral density (BMD; g/cm^2) and bone width (cm) were measured by single photon absorptiometry (SPA) in the distal forearm in 214 children with mean age of 10.3 years (range 3–17) at baseline and mean 28 years (range 25–29) later at a mean age of 37 years (range 28–44). BMC, BMD and bone width Z-scores in childhood and adulthood were calculated for each individual using all 214 individuals as controls. The individuals were stratified in quartiles based on Z-scores at baseline and follow-up. Data are shown as means with 95% confidence intervals (95% CI) within brackets.

	Bone mineral content (BMC)			**Bone mineral density (BMD)**			**Bone width**		
	All Children	Girls	Boys	All Children	Girls	Boys	All Children	Girls	Boys
Sensitivity(%)	52 (38, 66)	48 (27, 69)	55 (36, 74)	48 (27, 69)	65 (43, 84)	38 (21, 57)	50 (36, 65)	55 (32, 76)	46 (28, 66)
Specificity(%)	75 (69, 81)	76 (66, 84)	75 (66, 83)	76 (66, 84)	89 (79, 95)	79 (69, 87)	83 (77, 89)	85 (74, 92)	82 (73, 89)

*Sensitivity(%): The probability of a pediatric bone scan in the lowest quartile to predict an adult result in the same quartile.
**Specificity (%): The probability of a pediatric bone mass scan in the three highest quartiles to predict an adult result outside the lowest quartile.

Table 4 Sensitivity* and specificity ** of a pediatric bone mass scan to predict adult bone mass. Bone mineral content (BMC; g), bone mineral density (BMD; g/cm^2) and bone width (cm) were measured by single photon absorptiometry (SPA) in distal forearm in 214 children with mean age 10.3 years (range 3–17) at baseline and mean 28 years (range 25–29) later at a mean age of 37 years (range 28–44) years. BMC, BMD and bone width Z-scores in childhood and adulthood were calculated for each individual using all 214 individuals as controls. The children were stratified by age < 10 years or ≥10 years, and there after by quartile of baseline and follow-up Z-score. Due to the sample size, no gender-specific analyses were done. Data are presented as means with 95% confidence intervals (95% CI) within brackets.

	Bone mineral content (BMC)		**Bone mineral density (BMD)**		**Bone width**	
	Children <10 years at baseline	Children ≥10 years at baseline	Children <10 years at baseline	Children ≥10 years at baseline	Children <10 years at baseline	Children ≥10 years at baseline
	n=104	n=110	n=104	n=110	n=104	n=110
Sensitivity(%)	52 (31, 72)	50 (30, 71)	40 (21, 66)	46 (27, 67)	35 (15, 59)	60 (41, 77)
Specificity(%)	85 (75, 92)	84 (75, 91)	81 (71, 89)	83 (73, 91)	88 (79, 94)	78 (21, 57)

*Sensitivity(%): The probability of a pediatric bone scan in the lowest quartile to predict an adult result in the same quartile.
**Specificity (%): The probability of a pediatric bone mass scan in the three highest quartiles to predict adult result outside the lowest quartile.

Figure legends

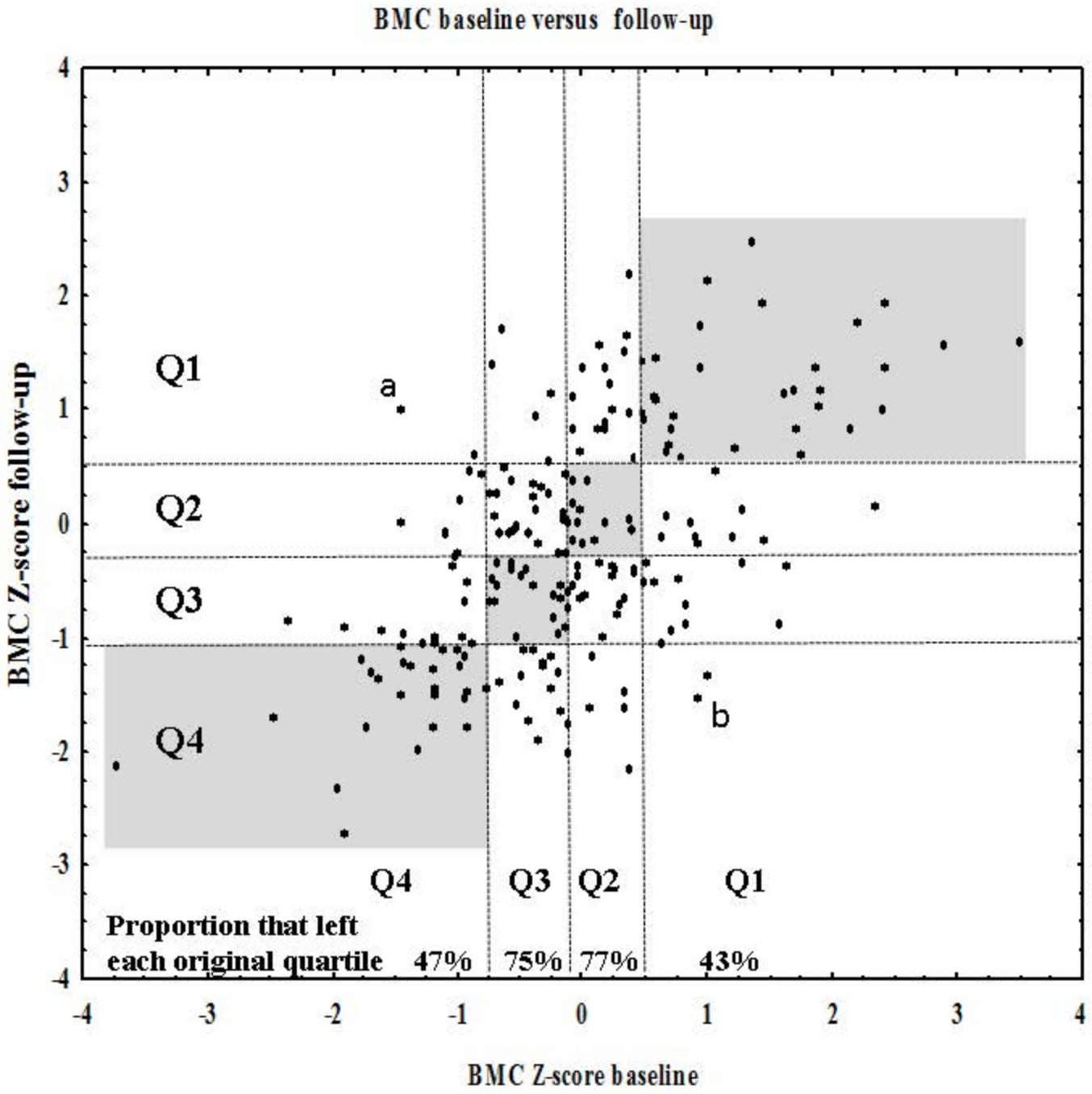
Figure 1 Z-scores for bone mineral content (BMC) in childhood and adulthood in each participant. Data points within the shadowed squares represent individuals that remained in their baseline quartile of BMC at follow-up. Among the participants we found individuals who moved from the lowest quartile of BMC at baseline to the highest at follow-up (a) and others who moved from the highest to the lowest quartiles of BMC (b).

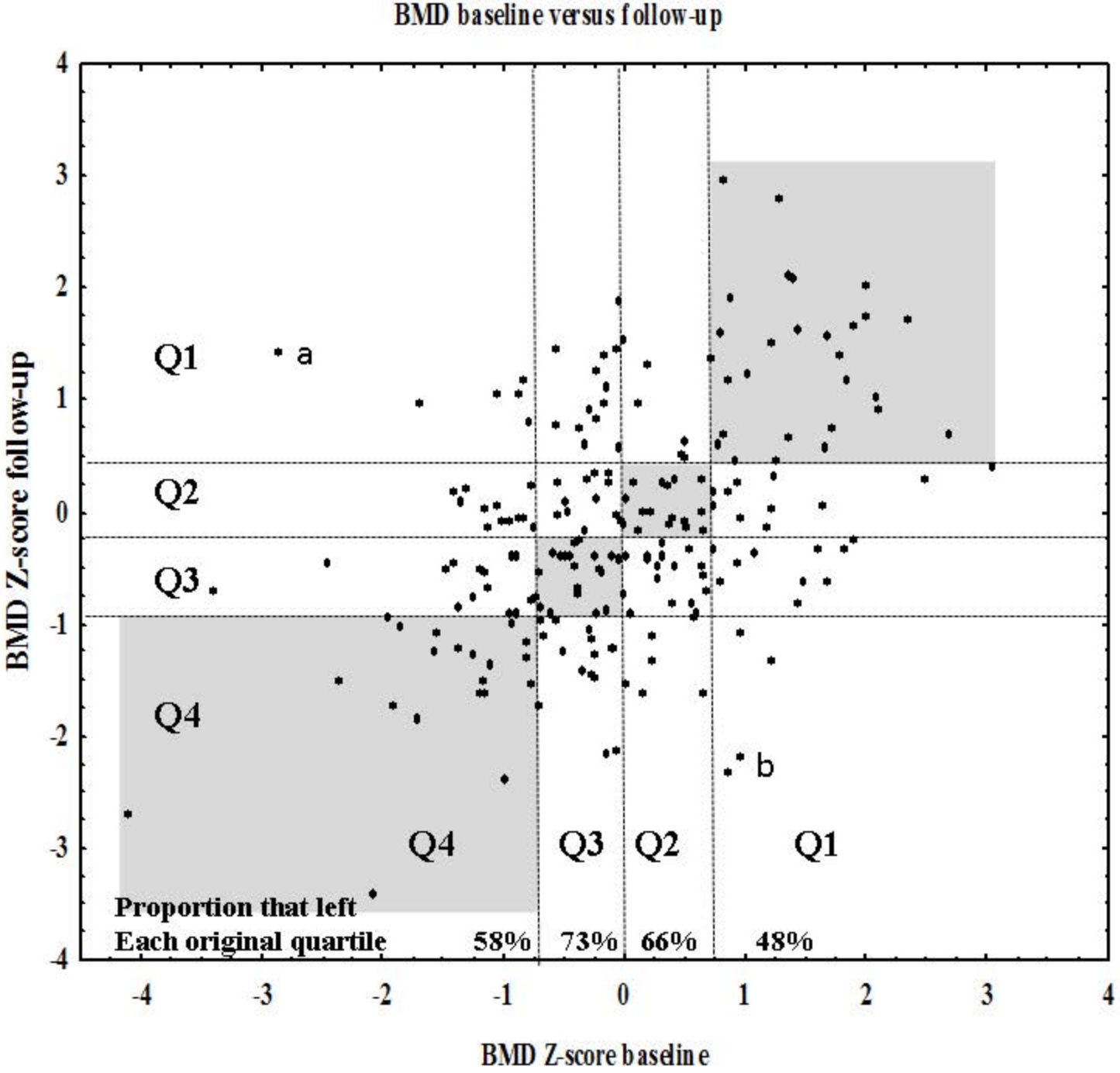
Figure 2 Z-scores for bone mineral density (BMD) in childhood and adulthood in each participant. Data points within the shadowed squares represent individuals that remained in their baseline quartile of BMD at follow-up. Among the participants we found individuals who moved from the lowest quartile of BMD at baseline to the highest at follow-up (a) and others who moved from the highest to the lowest quartiles of BMD (b).).

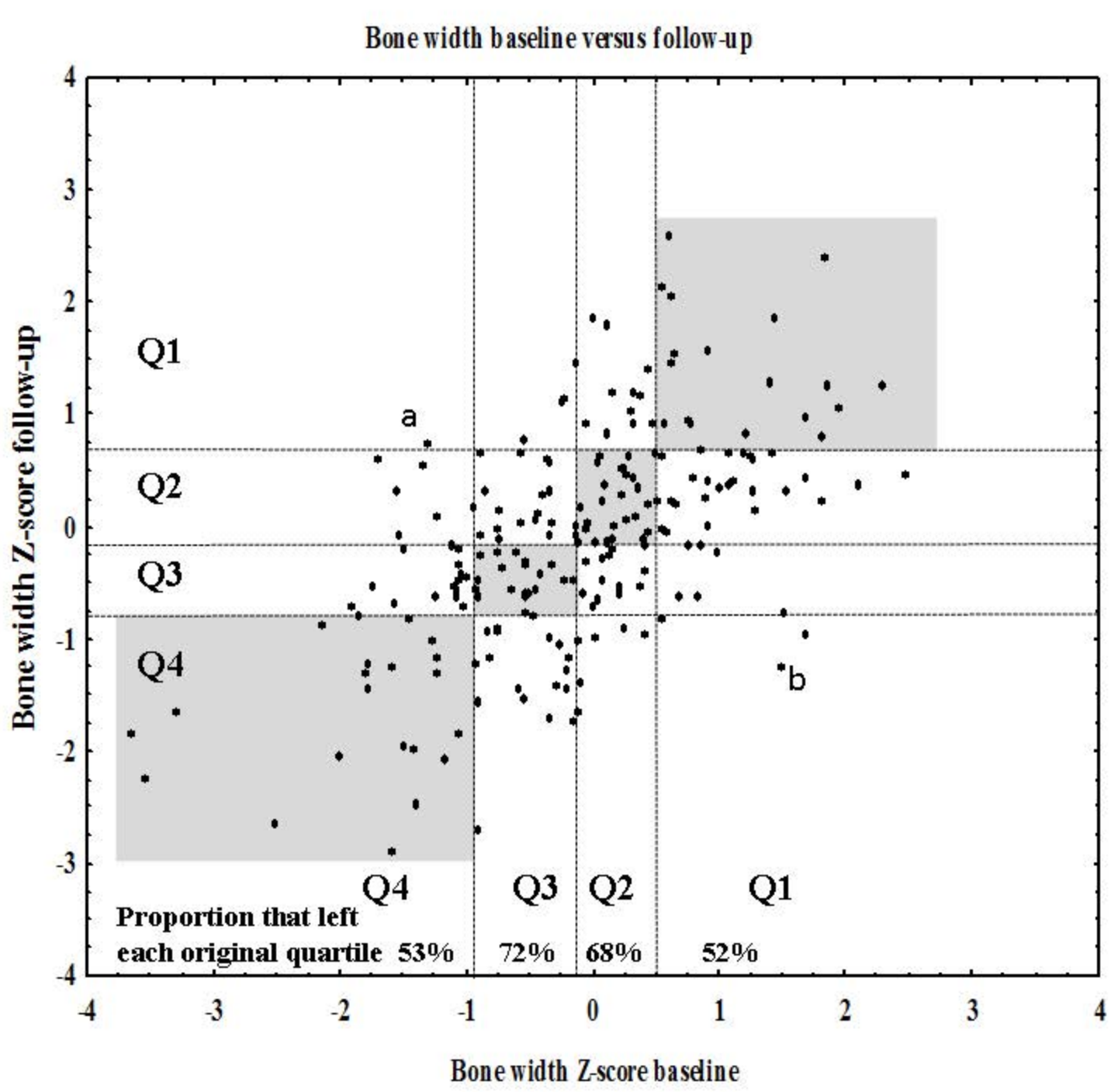
Figure 3 Z-scores for bone width in childhood and adulthood in each participant. Data points within the shadowed squares represent individuals that remained in their baseline quartile of bone width at follow-up. Among the participants we found individuals who moved from the lowest quartile of bone width at baseline to the highest at follow-up (a) and others who moved from the highest to the lowest quartiles of bone width (b).

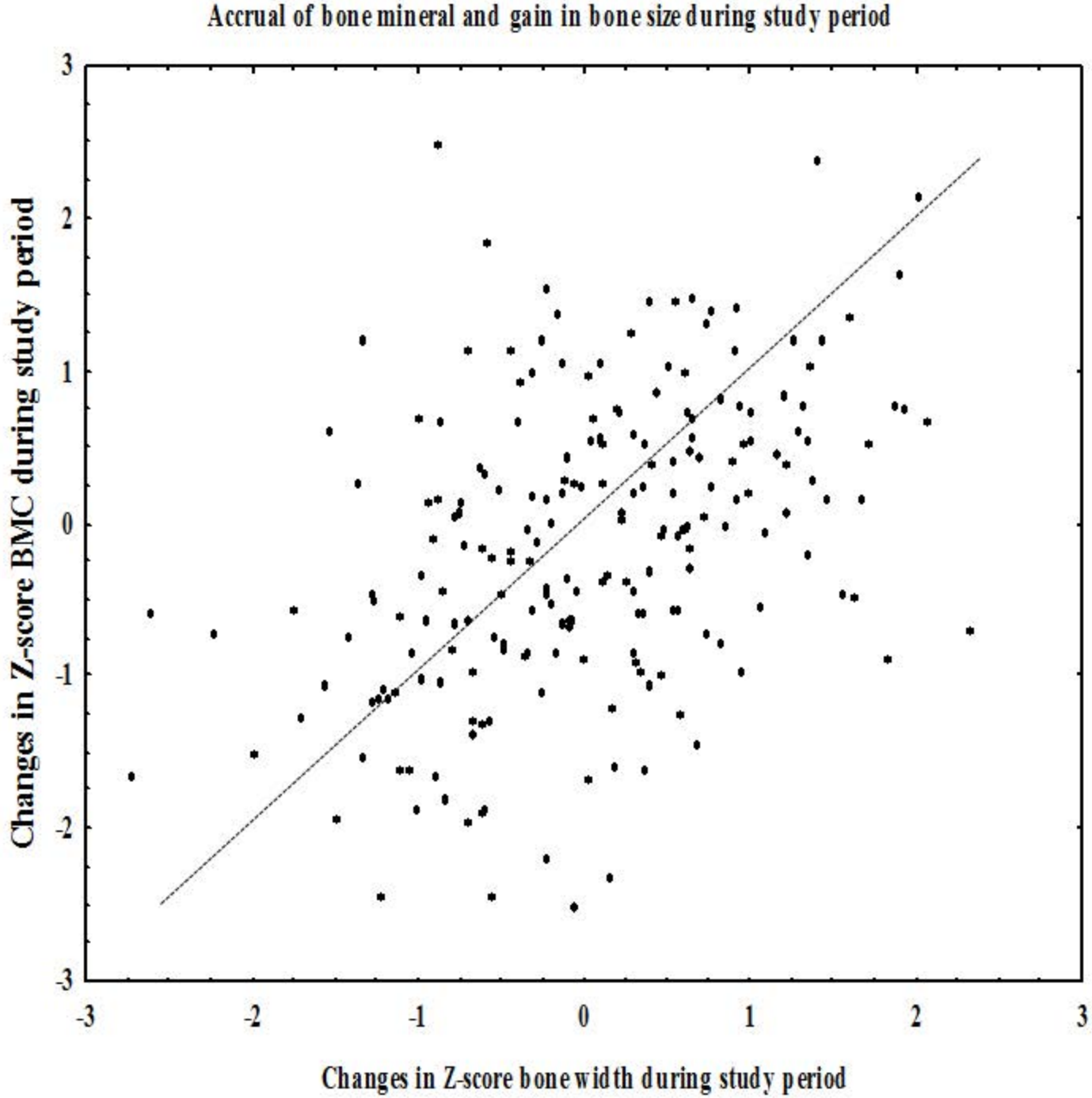
Figure 4 Individual bone growth (delta Z-score of bone width) and bone mineral accrual (delta Z-score of bone mineral content; BMC). 93/211 (44%) of the participants had a proportional larger accrual of BMC than gain in bone size (markers above the dotted line) and 118/211 (56%) a proportional higher gain in bone size than accrual of BMC (marker below the dotted line).

Figure 5 Changes in Z-score in participants who left the lowest quartile of BMD during the study period (n=31) and those who left the highest quartile (n=26). Those who left the lowest quartile of BMD had a significantly higher accrual of bone mineral and a trend for a lower gain in bone size. Those who left the highest quartile of BMD had a significantly lower accrual of bone mineral and a trend for a larger gain in bone size. Data are presented as means with 95% confidence intervals (95% CI).


BMC baseline versus follow-up
BMC Z-score follow-up
BMC Z-score baseline
Q1
Q2
Q3
Q4
a
b
Q4
Q3
Q2
Q1
Proportion that left
each original quartile
47%
75%
77%
43%
4
3
2
1
0
-1
-2
-3
-4
-4
-3
-2
-1
0
1
2
3
4


BMD baseline versus follow-up
BMD Z-score follow-up
BMD Z-score baseline
Q1
Q2
Q3
Q4
a
b
Q4
Q3
Q2
Q1
Proportion that left
Each original quartile
58%
73%
66%
48%
4
3
2
1
0
-1
-2
-3
-4


Bone width baseline versus follow-up
Bone width Z-score follow-up
Bone width Z-score baseline
Q1
Q2
Q3
Q4
a
b
Q4
Q3
Q2
Q1
Proportion that left
each original quartile
53%
72%
68%
52%
4
3
2
1
0
-1
-2
-3
-4


Accrual of bone mineral and gain in bone size during study period
Changes in Z-score BMC during study period
Changes in Z-score bone width during study period
3
2
1
0
-1
-2
-3
-3
-2
-1
0
1
2
3

Mean accrual of bone mineral and mean gain in bone size in those participants who left the lowest or highest quartile during the follow-up