Body Mass Index Trajectories From Birth to Midlife and Vertebral Dimensions in Midlife: the Northern Finland Birth Cohort 1966 Study

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ABSTRACT

Vertebral fracture risk is higher among individuals with small vertebral dimensions. Obesity is a global health problem and may also contribute to bone size and fracture risk. In this work we report the association between life course body mass index (BMI) and vertebral cross-sectional area (CSA) in midlife. The Northern Finland Birth Cohort 1966 study with its 46-year follow-up provided the material for this study. A subsample of 780 individuals had attended lumbar magnetic resonance imaging (MRI) at the age of 46 years, and had records of objectively measured BMI from the ages of 0, 7, 15, 31, and 46 years. Of these, MRI-derived data on vertebral size was available for 682 individuals. We identified latent lifelong BMI trajectories by performing latent class growth modeling (LCGM) on the BMI data, and then used sex-stratified linear regression models to compare the identified trajectory groups in terms of midlife vertebral CSA. Gestational age, education years, adult height, lifelong physical activity, lifelong smoking history, and adulthood diet were assessed as potential confounders. Three distinct trajectory groups ("stable slim," "stable average," and "early onset overweight") were identified among both sexes. Comparisons to the stable slim trajectory revealed that vertebral CSA was significantly ($p < 0.001$) larger among the stable average and early onset overweight trajectories (69.8 and 118.6 mm^2 larger among men, 57.7 and 106.1 mm^2 larger among women, respectively). We conclude that lifelong BMI has a positive association with midlife vertebral size among both sexes. Future studies should characterize the mediating factors of this association. © 2018 American Society for Bone and Mineral Research

KEY WORDS: ANALYSIS/QUANTITATION OF BONE–OTHER; EPIDEMIOLOGY–GENERAL POPULATION STUDIES; PRACTICE/POLICY-RELATED ISSUES–FRACTURE PREVENTION; RADIOLOGY; STATISTICAL METHODS

Introduction

Vertebral fractures are a common manifestation of osteoporosis.[1–4] Considering that small vertebral size increases the risk of sustaining a vertebral fracture,[5,6] further understanding of the lifestyle determinants of vertebral size is likely to improve fracture prevention. Approaches investigating the entire life course are especially needed.[7] This is particularly important among aging populations in which the number of osteoporotic individuals is rapidly increasing.[2]

It is clear that overweight (corresponding to adult body mass index [BMI] 25.0 to 29.9 kg/m^2) and obesity (BMI $\geq$30 kg/m^2) constitute a globally substantial health problem.[8–10]

Interestingly, despite its abundant adverse health effects, excess weight has been considered a protective factor against bone deterioration, mainly due to the claimed role of adipose tissue as an energy reserve.[10] In line with these considerations, a recent meta-analysis detected an inverse association between BMI and vertebral fracture risk.[11] Excess weight has also been associated with increased bone mass and size in childhood and adolescence.[12,13] However, there seems to be no current consensus on the relationship, because neutral or even negative influences of excess weight on bone health and fracture risk have been suggested.[14]

Vertebral size is positively associated with both height and weight.[5] This may be explained, at least in part, by (i) the

conjoint development of the body and the skeleton during growth,[15] and (ii) increased biomechanical loading, caused by large body size, inducing vertebral enlargement.[6,16] Despite this knowledge, very little data exist on the longitudinal associations between body size and vertebral size. In our earlier study, we were able to show the association between high BMI at various time points in early life and large vertebral size in midlife.[17] However, not only the early years, but the entire life course should be studied in this regard.[7,18,19]

In the present study, we aimed to study the association between lifelong BMI and midlife vertebral size in a lumbar magnetic resonance imaging (MRI)-scanned subsample of a Finnish birth cohort. First, we investigated the life course BMI data of the study population, and conducted a trajectory analysis of their BMI development from birth to midlife (0 to 46 years). Then, we used linear regression to analyze the association between BMI trajectory and vertebral size, which was measured from lumbar MRI scans at the age of 46 years.

Subjects and Methods

Study population

The Northern Finland Birth Cohort 1966 (NFBC1966) is a prospective, population-based birth cohort study with an initial coverage of 96% of births in Northern Finland (ie, in the provinces of Oulu and Lapland) between January 1, 1966, and December 31, 1966 (n = 12,231 children).[20] Data collection was initiated antenatally, and the population has been closely followed ever since. Major follow-ups, including postal questionnaires and/or clinical examinations have been arranged at the ages of 14, 31, and 46 year. In the 14-year, 31-year, and 46-year follow-ups (in 1980, 1997 to 1998, and 2012 to 2014, respectively), a total of 11,010, 6033, and 5861 NFBC1966 participants attended the data collections, respectively. At the age of 46 years, respondents living in the Oulu area were further invited to attend a lumbar MR scan (n = 1988), and the final number of scanned individuals was 1540.

The sample of the present study was constituted by those NFBC1966 participants who (i) had undergone lumbar MRI at the age of 46 years, and (ii) had sufficient records of anthropometric measurements from their life course (n = 780 individuals). Of these, data on vertebral size were available for 682 individuals. Figure 1 is a flowchart showing the progression of the study with a detailed list of exclusions. Importantly, individuals with vertebral pathologies were excluded from the sample, and the use of bone-affecting medications (including osteoporosis medication and calcium supplements) was not reported among the sample.

Life course anthropometry

Height and weight were directly measured by healthcare staff and recorded to an accuracy of 0.1 to 1 cm/10 g at the maternity hospital, child health clinics, and school healthcare; during other healthcare visits; and at the 31-year and 46-year follow-up examinations organized by the NFBC1966 project. BMI values (kg/m^2) were calculated as weight (kg)/height (m) squared.[21]

Because of the individual nature of the healthcare visits, a distinct set of measurements was available for each subject. We therefore decided to investigate the following time points: (i) birth, (ii) childhood (age 7 ± 1 years), (iii) late puberty (age 15 ± 1 years), (iv) early adulthood (31-year clinical examination), and (v) midlife (46-year clinical examination). These time points were
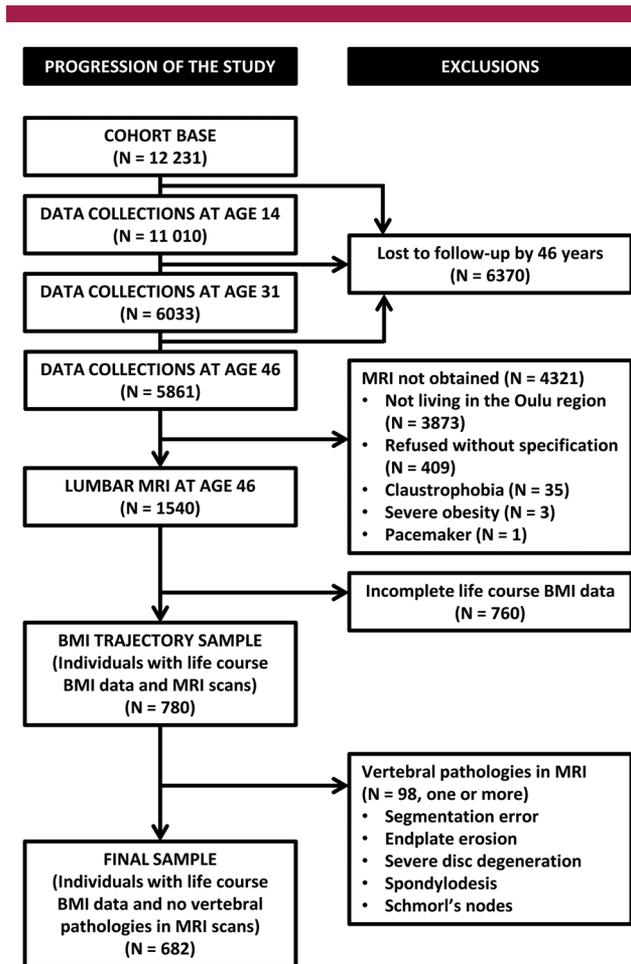

Fig. 1. Flow chart of the study. MRI = magnetic resonance imaging; BMI = body mass index.

chosen because they are relatively evenly scattered across the life course (0–46 years), including the main periods of growth.[22,23]

The crude BMI values were converted to BMI Z-scores. The Z-score is an age- and sex-specific standardized value that is calculated against the population mean and standard deviation of each time point.[24] This is a commonly applied procedure in BMI research[25,26] because it enhances the comparability of BMI values between time points. We used the recommendations of the World Health Organization (WHO) for discriminating between underweight, normal weight, and overweight/obesity.[21,25] To ensure that the BMI trends in our population were truthful, we chose not to exclude underweight or overweight/obese individuals from the sample.

Lumbar MRI

Equipment

We obtained lumbar MR scans using 1.5-T imaging equipment (Signa HDxt; General Electric, Milwaukee, WI, USA). T2-weighted fast-recovery fast spin-echo images were obtained in sagittal plane (repetition time/effective echo time 3500/112 ms, 4 averages, field-of-view 280 × 280 mm, acquisition matrix 448 × 224, slice thickness 3 mm, interslice gap 1 mm) and transverse plane (repetition time/effective echo time

3600/118 ms, 4 averages, field-of-view 180×180 mm, acquisition matrix 256×224, slice thickness 4 mm, interslice gap 1 mm).

Vertebral dimensions

One blinded researcher (PO) measured the corpus of the fourth lumbar vertebra (L_4) using NeaView Radiology Software version 2.31 (Neagen Oy, Oulu, Finland). The following eight dimensions were measured from the MR scans of each individual: (i) maximum width, (ii) minimum width, (iii) cranial depth, (iv) midaxial depth, (v) caudal depth, (vi) anterior height, (vii) posterior height, and (viii) minimum height. An illustration of the measurements is provided in Fig. 2. Vertebral heights were measured from the midsagittal slice, and vertebral widths and depths from the axial slices. The measurements were recorded to an accuracy of 0.1 mm.

An estimate of vertebral size was obtained by calculating the axial cross-sectional area (CSA, mm^2) of L_4 using the validated ellipsoid formula[27,28]: $CSA = \pi * a/2 * b/2$, where $a =$ mean of width measurements (i and ii) and $b =$ mean of depth measurements (iii–v). Vertebral height was calculated as the mean of the anterior, posterior, and minimum height measurements (vi–viii).

We investigated L_4 because it is more stable than L_5[29] and represents the other lumbar vertebrae accurately.[30,31] CSA was chosen because of its direct association with vertebral weight-bearing capacity[32] and fracture risk.[5] The CSA of L_4 has also been a common outcome in similar studies.[17,30,33–35] We have previously shown that vertebral dimensions can be accurately measured using MRI.[36] We have also shown that the intrarater reliability of our vertebral measurements is high and the measurement errors are low.[30]

Confounders

We chose potential confounder candidates for evaluation according to the suggestions of the literature: gestational age,[15] education years,[37] adult height,[5,17] lifelong physical activity,[30,35] lifelong smoking history,[38] and adulthood diet.[39] Gestational age (in weeks) was recorded at the maternity hospital. Socioeconomic status was evaluated via education years (<9 years, 9–12 years, >12 years) by asking the questions (i) "What is your basic education?" (Less than 9 years of elementary school,

elementary school, matriculation examination) and (ii) "What is your vocational education?" (None, occupational course, vocational school, vocational college, polytechnic, university, other, unfinished course). Adult height was measured by a trained study nurse at the 46-year follow-up examination. Physical activity was self-reported at the ages of 14 years, 31 years, and 46 years. At each time point, the subjects were asked how often they participated in sports during their leisure time. At the age of 14 years, the response alternatives were as follows: daily, every other day, twice/week, once/week, every other week, once/month, generally not at all. At the ages of 31 and 46 years, the response alternatives were: daily, 4 to 6 times/week, 2 to 3 times/week, once/week, 2 to 3 times/month, once/month, or less often. As described in our earlier publication,[30] we applied latent class analysis to the data and created a lifelong physical activity cluster variable (active, moderately active, inactive), which we used in the present analyses. Life course smoking (nonsmoker, former smoker, current smoker) was determined in the 46-year postal questionnaire by the questions (i) "Have you ever smoked cigarettes?" (yes/no) and (ii) "Do you currently smoke?" (yes/no). Adulthood diet was self-reported in the 46-year questionnaire by responding to the question "Do you follow a specific diet?" (Vegetarian, lactose-free, gluten-free, food allergy, diabetes, cholesterol-lowering, weight-loss, low-salt). Because of the small number of respondents, the responses were categorized as follows: no specific diet, vegetarian diet, weight-loss diet, other diets.

Statistical analysis

BMI trajectory modeling

We used SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and the PROC TRAJ latent class growth modeling (LCGM) macro[40] to study the latent BMI trajectory groups in our BMI Z-score data.[41] LCGM is a semi-parametric statistical modeling technique that aims to reveal latent subgroups which follow a similar pattern of change (ie, trajectory) over time.[42] Because natural growth differs between the sexes[43] and we have previously observed this in the NFBC1966 population,[17] we modeled men and women separately.

For the PROC TRAJ procedure, we used the censored normal (CNORM) model and tested one to six trajectory groups with linear and quadratic slopes. As recommended,[41] nonsignificant
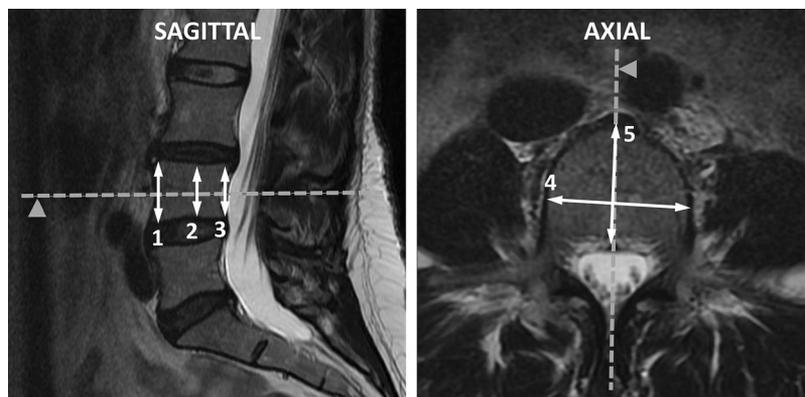

Fig. 2. Annotated MR scans illustrating the measurement process. 1 = anterior height; 2 = minimum height; 3 = posterior height; 4 = minimum and maximum widths; 5 = superior, inferior, and midaxial depths. Dashed lines indicate corresponding planes.

quadratic terms were removed from the models. The best model was chosen according to (i) fit statistics (Bayesian Information Criterion [BIC], in which lower absolute values indicate a better fit), (ii) posterior probabilities (in which group averages of >0.7 are considered acceptable), (iii) sufficient group sizes, and (iv) the clinical significance of the models.[41,42] Once the best model was found, each individual was assigned to the trajectory group with the highest posterior membership probability.[41,42] Because the necessary BMI data was available for all the modeled subjects, PROC TRAJ did not have to deal with missing data.

LCGM was conducted in a subsample; ie, the NFBC1966 members with both lumbar MRI data and sufficient life course BMI data available. We chose this approach as it enabled us to directly assess the meaningfulness of the trajectory models in relation to the MRI parameters. The validity of this approach was investigated by studying the representativeness of the LCGM subsample.

Association between BMI trajectory and vertebral size

We used SPSS version 24 (IBM Corp., Armonk, NY, USA) to conduct linear regression analyses that investigated the association between BMI trajectory and vertebral CSA. The

continuous outcome, vertebral CSA, was normally distributed among both sexes. Other assumptions of linear regression were also tested and met. We used the categorical BMI trajectory variable, which we created at the LCGM stage, as the primary explanatory variable in the regression models; we compared the trajectory groups, and chose the slimmest trajectory group as the reference group.

We evaluated the effect of the covariate candidates on the regression models. Gestational age and adult height were assessed in their continuous form, whereas education years, physical activity, smoking, and diet were assessed as categorical variables according to the categorizations presented above. We excluded nonsignificant covariate candidates that had little influence on the models from the final adjusted analyses. We did not assess weight because of its significant collinearity with BMI. We ran both crude and adjusted regression analyses, and gathered beta estimates (β) with their 95% confidence intervals (CIs).

Representativeness of the sample

We evaluated the representativeness of the LCGM sample by comparing it to the rest of the NFBC1966 population. We used the chi square test for categorical variables and Student's independent-samples t test for continuous variables.

Table 1. General Characteristics of the BMI Trajectory Sample and the Rest of the NFBC1966 Population

	Men			Women		
Characteristic	Sample	Excluded	p	Sample	Excluded	p
Sex distribution, n (%)	362 (46.4)	5870 (51.6)	**<0.01**[a]	418 (53.6)	5515 (48.4)	**<0.01**[a]
Gestational age (weeks), mean ± SD	40.0 ± 1.9	39.8 ± 2.3	**0.05**[b]	40.2 ± 1.8	39.9 ± 2.3	**<0.01**[b]
Education (years), n (%)						
>12	76 (21.7)	609 (22.6)		111 (27.0)	1006 (31.1)	
9–12	261 (74.6)	1961 (72.7)		289 (70.3)	2116 (65.3)	
<9	13 (3.7)	129 (4.8)	0.60[a]	11 (2.7)	116 (3.6)	0.12[a]
Anthropometry at age 46 years, mean ± SD						
Height (cm)	177.8 ± 6.0	178.7 ± 6.2	**0.02**[b]	164.6 ± 5.7	165.0 ± 6.0	0.15[b]
Weight (kg)	85.3 ± 12.5	87.1 ± 14.6	**0.02**[b]	70.3 ± 13.7	71.4 ± 14.8	0.14[b]
BMI (kg/m^2)	27.0 ± 3.7	27.2 ± 4.2	0.26[b]	25.9 ± 4.9	26.2 ± 5.2	0.33[b]
Lifelong physical activity, n (%)						
Active	86 (27.0)	539 (25.5)		90 (22.7)	586 (21.6)	
Moderate	136 (42.8)	920 (43.6)		187 (47.1)	1336 (49.2)	
Inactive	96 (30.2)	652 (30.9)	0.85[a]	120 (30.2)	794 (29.2)	0.74[a]
Lifelong smoking, n (%)						
Nonsmoker	175 (51.2)	1174 (43.9)		242 (59.5)	1822 (56.9)	
Former	117 (34.2)	800 (29.9)		100 (24.6)	753 (23.5)	
Current	50 (14.6)	700 (26.2)	**<0.01**[a]	65 (16.0)	628 (19.6)	0.22[a]
Adulthood diet, n (%)						
No specific diet	189 (72.1)	1299 (70.8)		197 (64.2)	1372 (61.3)	
Vegetarian	3 (1.1)	25 (1.4)		7 (2.3)	46 (2.1)	
Weight loss	3 (1.1)	45 (2.5)		12 (3.9)	87 (3.9)	
Other	67 (25.6)	466 (25.4)	0.60[a]	91 (29.6)	732 (32.7)	0.75[a]
MRI at age 46 years, mean ± SD						
Age at MRI (years)	46.8 ± 0.4	46.8 ± 0.5	0.81[b]	46.7 ± 0.4	46.8 ± 0.4	0.20[b]
CSA of L$_4$ (mm^2)	1318.5 ± 175.8	1328.8 ± 165.1	0.50[b]	1048.2 ± 128.9	1061.6 ± 132.8	0.16[b]
Height of L$_4$ (mm)	28.0 ± 1.5	28.2 ± 1.5	0.10[b]	26.6 ± 1.4	26.6 ± 1.5	0.66[b]

Values are general characteristics of the BMI trajectory sample ("Sample" column) and the rest of the NFBC1966 population ("excluded" column). Values of n vary due to missing data. Bold values are significant.

BMI = body mass index; MRI = magnetic resonance imaging; CSA = cross-sectional area.

[a]Chi square test.

[b]Student's independent-samples t test.

Generally, values of $p < 0.05$ were considered statistically significant.

Ethical considerations

The data were accessed and analyzed in an encrypted format with anonymous identification codes. Informed consent was collected from the study population. The study protocol followed the Declaration of Helsinki and was approved by the Ethics Committee of the Northern Ostrobothnia Hospital District.

Results

Study sample

A total of 780 individuals (362 men and 418 women) had undergone lumbar MRI at the mean age of 46.8 years and had the necessary life course BMI data (ie, all time points between 0 and 46 years) available for trajectory modeling. The general characteristics of the LCGM sample and the comparisons to the rest of the cohort are presented in Table 1. Generally, the present sample did not differ from the rest of the cohort in most parameters. We detected minor, statistically significant differences in sex distribution, gestational age, male height and weight, and the percentage of male nonsmokers between the sample and those who were excluded.

BMI trajectories

The LCGM resulted in three distinct life course trajectories for BMI among both sexes. The three-trajectory models had substantially lower absolute BIC values (BIC $=-2403.10$ and -2705.51 for men and women, respectively) than the corresponding one-trajectory (BIC $=-2574.61$ and -2972.13 for men and women, respectively) and the two-trajectory models (BIC $=-2430.68$ and -2762.45 for men and women, respectively). The three-trajectory models also had high average posterior probabilities and sufficient group sizes (Table 2). The four-trajectory, five-trajectory, and six-trajectory models were unacceptable mainly because of small group sizes and poor distinction between individuals (data not shown). The general characteristics of the identified trajectory groups are presented

in Table 2, with the Z-score-based illustrations of the trajectories in Fig. 3 and Fig. 4.

Based on the Z-scores and crude BMIs, the trajectory groups of both sexes were named as follows: "stable slim" (group 1), "stable average" (group 2), and "early onset overweight" (group 3). Notably, the stable slim group was the only one to remain within the normal BMI range[21] throughout the life course. The stable average group exceeded the adult overweight cutoff (BMI $\geq 25 \text{ kg/m}^2$) at the age of 31 years, and the early onset overweight group already exceeded the overweight cutoff for children (Z-score $> +1$) at the first time point after birth (Fig. 3, Fig. 4, Table 2).

Association between BMI trajectory and vertebral size

Data on lifelong BMI trajectory and vertebral size were available for 682 individuals (306 men and 376 women). Crude and adjusted linear regression models were used to compare the trajectory groups in terms of vertebral CSA. Of the covariate candidates (gestational age, education years, adult height, physical activity, smoking, diet), only adult height remained significant in the models (data not shown) and was therefore used as a covariate in the final adjusted analyses.

The results of the linear regression models are shown in Table 3. Among both sexes, the trajectories that indicated a higher BMI (ie, stable average and early onset overweight) were associated with a significantly larger vertebral CSA than the stable slim trajectory ($p < 0.001$). According to the adjusted β coefficients, the difference between the slim and overweight/obese trajectories was as high as 118.6 mm^2 (9.4%) among men and 106.1 mm^2 (10.4%) among women.

Discussion

This population-based birth cohort study with its 46-year follow-up investigated the association between the BMI trajectory across the life course and vertebral size in midlife. Three BMI trajectory groups were identified among both sexes: "stable slim," "stable average," and "early onset overweight." Comparisons with the slimmest trajectory showed that vertebral CSA in

Table 2. Characteristics of the BMI Trajectory Groups ($n = 780$)

	Men ($n = 362$)			Women ($n = 418$)		
	Group 1	Group 2	Group 3	Group 1	Group 2	Group 3
Group size, n (%)	111 (30.7)	217 (59.9)	34 (9.4)	239 (57.2)	145 (34.7)	34 (8.1)
Average posterior probability[a]	0.84	0.87	0.92	0.89	0.85	0.90
Crude BMI (kg/m^2), mean (minimum–maximum)						
At birth	12.8 (9.2–15.8)	14.1 (11.1–18.6)	14.1 (9.7–17.2)	13.4 (9.7–17.8)	14.3 (11.4–16.7)	14.0 (11.5–16.9)
At age 7 years	14.5 (12.4–16.9)	15.9 (13.4–19.2)	17.3 (14.2–21.5)	14.9 (12.1–18.3)	16.6 (13.6–20.8)	17.8 (13.8–21.7)
At age 15 years	17.7 (14.0–21.4)	19.9 (15.9–26.5)	23.3 (19.0–32.8)	18.9 (14.0–25.1)	21.6 (16.9–27.9)	24.8 (20.0–31.8)
At age 31 years	22.3 (15.3–27.5)	25.3 (20.7–31.2)	31.3 (28.1–37.2)	21.7 (16.1–27.9)	25.3 (21.1–32.0)	34.4 (25.8–44.0)
At age 46 years	23.9 (16.2–29.8)	27.5 (21.7–35.2)	33.9 (29.0–43.2)	23.4 (17.3–36.3)	28.4 (21.2–37.1)	37.1 (28.9–50.9)

BMI = body mass index.
[a]Average probability of belonging to the respective group.
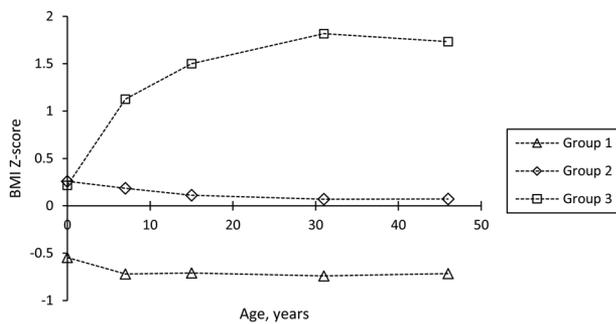
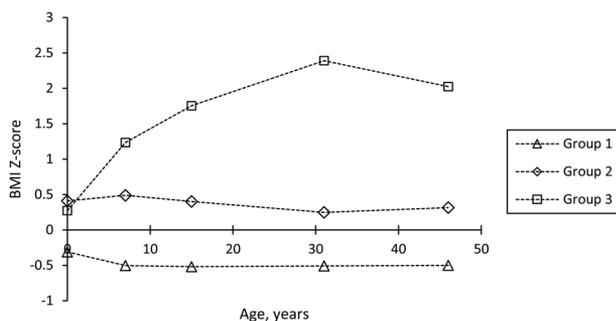**Fig. 3.** BMI Z-score trajectories among men ($n = 362$).

Fig. 4. BMI Z-score trajectories among women ($n = 418$).

midlife was significantly larger among the average and overweight/obese groups ($\sim$6% and $\sim$10% larger CSA, respectively).

Several studies have estimated BMI trajectories across various periods of the life course.[44–47] Generally, three to four distinct trajectory groups have been identified among the study populations: one trajectory indicating normal weight, one indicating severe overweight/obesity, and one or two trajectories scattered in between. The present LCGM results thus comply with previous reports. In comparison, the follow-up period of our study was exceptionally long, extending over five decades (0–46 years) and covering the entire life course of the population

while maintaining a relatively large sample size ($n = 780$). Moreover, our BMI data were based on direct height and weight measurements that were objectively conducted by healthcare staff. As we made the decision to improve the accuracy of our BMI modeling by excluding those who did not have all the necessary BMI data, the models did not have to deal with missing data. Those who did not undergo MR scans were not included in the trajectory analysis because we wanted to assess the meaningfulness of the trajectory models directly in relation to the MRI parameters. This choice was made in accordance with the primary aim of the present study (association between lifelong BMI and MRI-derived vertebral size) and was justified by the high representativeness of the LCGM sample.

Our linear regression models demonstrated a significant positive association between lifelong BMI and vertebral CSA in midlife. The findings give grounds for three principal remarks. First, the association between body size and vertebral size is statistically significant among both sexes, and the effect sizes of men and women were of similar magnitude. This is congruent with previous studies investigating the association between early growth and vertebral size.[17,48] Interestingly, the difference was already apparent between the slim and average trajectories. Second, the present effect sizes regarding BMI seem markedly more prominent than those for other lifestyle factors such as lifelong physical activity. For example, in the present work, we found a striking $\sim$10% difference in the vertebral CSA of the slim and overweight/obese groups, whereas our earlier publication[30] studying the association between lifelong physical activity (14–46 years) and CSA among the same population observed only a $\sim$3% difference between active and inactive women. CSA substantially affects the weight-bearing capacity of a vertebra,[32] indicating that a 10% difference is a considerable finding. Third, the associations between the BMI trajectory and vertebral CSA remained significant despite the wide range of potential covariates that we assessed in the models (gestational age, education years, adult height, lifelong physical activity, lifelong smoking, adulthood diet). Even adjustment for adult height, which is a strong correlate of skeletal size[49] and an indicator of chronic malnutrition during growth,[50] did not attenuate the associations. Importantly, the stable slim and stable average groups included certain individuals whose BMIs fell below the cutoffs for underweight[25] but their height/skeletal (under)development did not explain the association between BMI trajectory and vertebral CSA. Correspondingly, being tall and thus having large skeletal size did not seem to

Table 3. Vertebral CSA Among the Trajectory Groups and Results From Linear Regression Models Comparing the Trajectory Groups in Terms of Midlife Vertebral CSA ($n = 682$)

Trajectory group	CSA (mm²)		
	Mean ± SD	Crude β (95% CI)[a]	Adjusted β (95% CI)[a]
Men ($n = 306$)			
Group 1 (stable slim) ($n = 97$)	1259.3 ± 158.2	Reference	Reference
Group 2 (stable average) ($n = 180$)	1345.4 ± 178.1	86.0 (43.5–128.5)	69.8 (31.9–107.8)
Group 3 (early onset overweight) ($n = 29$)	1360.3 ± 171.6	101.0 (29.6–172.4)	118.6 (54.3–182.9)
Women ($n = 376$)			
Group 1 (stable slim) ($n = 212$)	1021.5 ± 126.0	Reference	Reference
Group 2 (stable average) ($n = 136$)	1075.0 ± 125.7	53.5 (26.5–80.5)	57.7 (34.4–81.0)
Group 3 (early onset overweight) ($n = 28$)	1120.1 ± 114.6	98.6 (49.1–148.1)	106.1 (63.9–148.2)

CSA = cross-sectional area; SD = standard deviation; β = beta coefficient; CI = confidence interval.
[a]Beta coefficients from crude and height-adjusted linear regression models.

mediate the association. However, we do acknowledge the fact that a limited set of adjustments can never be fully exhaustive. In particular, our study lacked detailed data on lifelong nutrition.

Speculative explanations can be offered for the positive association between lifelong BMI and midlife vertebral size. From the traditional biomechanical perspective, long-term exposure to skeletal loading due to increased body weight may cause the weight-bearing skeleton, including lumbar vertebrae, to enlarge in size.[6,16] This may happen not only during growth but also in later life.[6] If this is the case, the present findings would underline the positive aspects of excess weight on bone health. However, we emphasize that the negative health effects of obesity are of course substantial.[8] Interestingly, recent research has suggested that obesity associates with altered intestinal microbiome,[51] which may in turn regulate bone mass and density.[52] Research on germ-free mice showed bone mass and density to be regulated by intestinal microbiome via inflammatory mechanisms in the bone, including altered osteoclast activity.[53] However, the intestinal microbiome also affects the absorption and further processing of nutrients,[52] implying that the resultant effect of the intestinal microbiome on bone remains obscure and requires further study.

The strengths of our study are numerous. We were able to include several time points representing the entire life course of the population in our trajectory analysis while maintaining a large sample size. Importantly, all measurements were objectively measured by healthcare professionals. Our follow-up of nearly 50 years was exceptionally long. As a birth cohort population, the individuals were coeval, which minimized the confounding effect of age. Our trajectory analysis identified three distinct trajectory groups with acceptable fit statistics; although group sizes were uneven, and the overweight/obese groups in particular were small, this was in line with findings from previous studies on BMI trajectories. We investigated only those with available MR scans, and this choice was justified by the high representativeness of the sample. Because the NFBC1966 population has been closely followed, we had access to various potential confounders that we were able to assess in the regression models. Moreover, we were able to use MR scans to measure each individual's vertebral dimensions, and we recorded several dimensions per vertebra in order to enhance the accuracy of vertebral size estimation. We could not find earlier studies investigating the association between lifelong BMI trajectories and vertebral size.

Our study has several limitations. First, the MR imaging was performed only once, at the age of 46 years; we were therefore only able to study lifelong BMI in relation to vertebral size in midlife. Because we had no longitudinal MRI data on the participants' lumbar spine, we were limited to studying associations instead of actual changes in vertebral size. Second, we had no data on the bone mineral density or other material or microarchitectural parameters of vertebral bone, which are also linked to vertebral fracture risk. Obesity is likely to affect not only bone size but also these parameters simultaneously. Our study also lacked data on serum levels of calcium, vitamin D, and other bone metabolism markers. Although we were able to exclude individuals with vertebral pathologies on their MRI scans, we did not have data on the presence/history of fractures at other skeletal sites. Third, the analysis of representativeness revealed minor differences between the sample and the rest of the NFBC1966 population in some background variables. However, these differences were small, and among most variables, no differences were detected. The sample is thus a good representation of the general middle-aged Northern Finnish population.

We conclude that lifelong BMI has a positive association with midlife vertebral size. Lifelong overweight/obesity seems to predict a ~10% larger vertebral CSA in midlife than lifelong normal weight. The findings were similar among both sexes. Considering that low BMI increases the risk of vertebral fracture,[11] our findings suggest that vertebral size may, in part, mediate this effect. Future studies should aim to confirm the association between lifelong BMI and vertebral size using longitudinal data on vertebral size, and provide insights into the mediating factors of this association.

Disclosures

Acknowledgments

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