



Dairy- and supplement-based calcium intake in adulthood and vertebral dimensions in midlife—the Northern Finland Birth Cohort 1966 Study

P. Oura^{1,2,3} · J. Auvinen^{1,2} · M. Paananen^{1,2} · J.-A. Junno^{1,4} · J. Niinimäki^{1,3} · J. Karppinen^{1,2,5} · M. Nurkkala^{1,2,6}

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Abstract

Summary Among a representative sample of 1064 Northern Finns, we studied the association of dairy- and supplement-based calcium intake in adulthood with vertebral size in midlife. Inadequate calcium intake (< 800 mg/day) from age 31 to 46 predicted small vertebral size and thus decreased spinal resilience among women but not men.

Introduction Small vertebral size predisposes individuals to fractures, which are common among aging populations. Although previous studies have associated calcium (Ca) intake with enhanced bone geometry in the appendicular skeleton, few reports have addressed the axial skeleton or the vertebrae in particular. We aimed to investigate the association of dairy- and supplement-based Ca intake in adulthood with vertebral cross-sectional area (CSA) in midlife.

Methods A sample of 1064 individuals from the Northern Finland Birth Cohort 1966 had undergone lumbar magnetic resonance imaging at the age of 46, and provided self-reported data on diet and Ca intake (dairy consumption and use of Ca supplements) at the ages of 31 and 46. We assessed the association between Ca intake (both continuous and categorized according to local recommended daily intake) and vertebral CSA, using generalized estimating equation and linear regression models with adjustments for body mass index, diet, vitamin D intake, education, leisure-time physical activity, and smoking.

Results Women with inadequate Ca intake (< 800 mg/day) over the follow-up had 3.8% smaller midlife vertebral CSA than women with adequate Ca intake ($p = 0.009$). Ca intake among men showed no association with vertebral CSA.

Conclusions Inadequate Ca intake (< 800 mg/day) from the age of 31 to 46 predicts small vertebral size and thus decreased spinal resilience among middle-aged women. Future studies should confirm these findings and investigate the factors underlying the association of low Ca intake in women but not in men with smaller vertebral size.

Keywords Calcium intake · Cohort study · Diet · Lumbar spine · Magnetic resonance imaging · Vertebra

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✉ P. Oura
petteri.oura@oulu.fi

¹ Medical Research Center Oulu, Oulu University Hospital and University of Oulu, P.O. Box 5000, FI-90014 Oulu, Finland

² Center for Life Course Health Research, Faculty of Medicine, University of Oulu, P.O. Box 5000, FI-90014 Oulu, Finland

³ Research Unit of Medical Imaging, Physics and Technology, Faculty of Medicine, University of Oulu, P.O. Box 5000, FI-90014 Oulu, Finland

⁴ Cancer and Translational Medicine Research Unit, Faculty of Medicine, University of Oulu, P.O. Box 5000, FI-90014 Oulu, Finland

⁵ Finnish Institute of Occupational Health, Aapistie 1, FI-90220 Oulu, Finland

⁶ Department of Sports and Exercise Medicine, Oulu Deaconess Institute, P.O. Box 365, FI-90101 Oulu, Finland

Introduction

Vertebral fractures, one of the most typical complications of osteoporosis, are notoriously common among aging populations [1–3]. Vertebral dimensions have been associated with vertebral fracture risk as individuals with small vertebral size seem to be at an elevated risk of sustaining a morphometrically diagnosed vertebral fracture [4, 5]. While previous research has shown that lifestyle choices in adulthood may influence vertebral size [6–8], the need has arisen to expand current knowledge on the factors affecting one's vertebral size across the life course.

From the nutritional point of view, calcium (Ca) has attracted the most scientific interest in skeletal research, together with vitamin D [9, 10]. Achieving a sufficient Ca intake from diet is essential for skeletal health, not only in childhood and adolescence, when peak bone mass is accumulated [11], but also in later life, when Ca apparently contributes to preventing bone loss and microstructure degradation [12]. Although several studies have associated Ca intake with enhanced bone geometry at various skeletal sites [13–16], contradicting results have also been found [17]. Regarding the lumbar spine, we found only one study that addressed the association between Ca intake and vertebral size [17]: among 111 men aged ≥ 50 years, 2-year consumption of Ca-vitamin-D-fortified milk had no effect on the geometry of L1–L3. Thus, the association between Ca and bone geometry requires further study; studies addressing vertebral geometry should be of particular interest due to the high incidence of vertebral fractures among the elderly [2, 3].

In the present study, we investigated the relationship between self-reported (dairy- and supplement-based) Ca intake at 31 and 46 years and vertebral cross-sectional area (CSA) at 46 years in a large, representative Finnish birth cohort population. We hypothesized that inadequate Ca intake would be associated with small vertebral CSA in midlife.

Methods

Study sample

We used a magnetic resonance imaging (MRI)-scanned subsample of the Northern Finland Birth Cohort 1966 (NFBC1966) as the study population. Figure 1 is a flow chart presenting the progression of the study and the specifications for exclusion. As a prospective population-based birth cohort study, the NFBC1966 included Northern Finnish children whose expected birth date was during the calendar year of 1966 [18]. Initial data collections covered 12,231 children, i.e., 96.3% of births in Northern Finland. Major follow-ups have taken place at 31 and 46 years and have covered the entire cohort. Moreover, those who attended the 46-year

clinical examinations and lived in the Oulu region (radius of 100 km from the city of Oulu) were invited to a lumbar MRI scan at the age of 46. We have previously shown that the MRI sample is representative of the general Northern Finnish population [19]. After all exclusions were completed, the final sample comprised 1064 individuals (Fig. 1). Bone-affecting medications were not reported in the sample.

Vertebral dimensions at age 46 (outcome)

Vertebral dimensions were measured from lumbar MRI scans. As described in our previous publication [7], MRI scans were obtained using a 1.5 T system (Signa HDxt, General Electric, Milwaukee, WI, USA) and a conventional lumbar spine protocol, i.e., T2-weighted fast-recovery fast spin-echo images in sagittal and transverse planes. The sagittal parameters were: repetition time 3500 ms, effective echo time 112 ms, 4 averages, field-of-view 280×280 mm, acquisition matrix 448×224 , slice thickness 3 mm, and interslice gap 1 mm. The transverse parameters were: repetition time 3600, effective echo time 118 ms, 4 averages, field-of-view 180×180 mm, acquisition matrix 256×224 , slice thickness 4 mm, and interslice gap 1 mm.

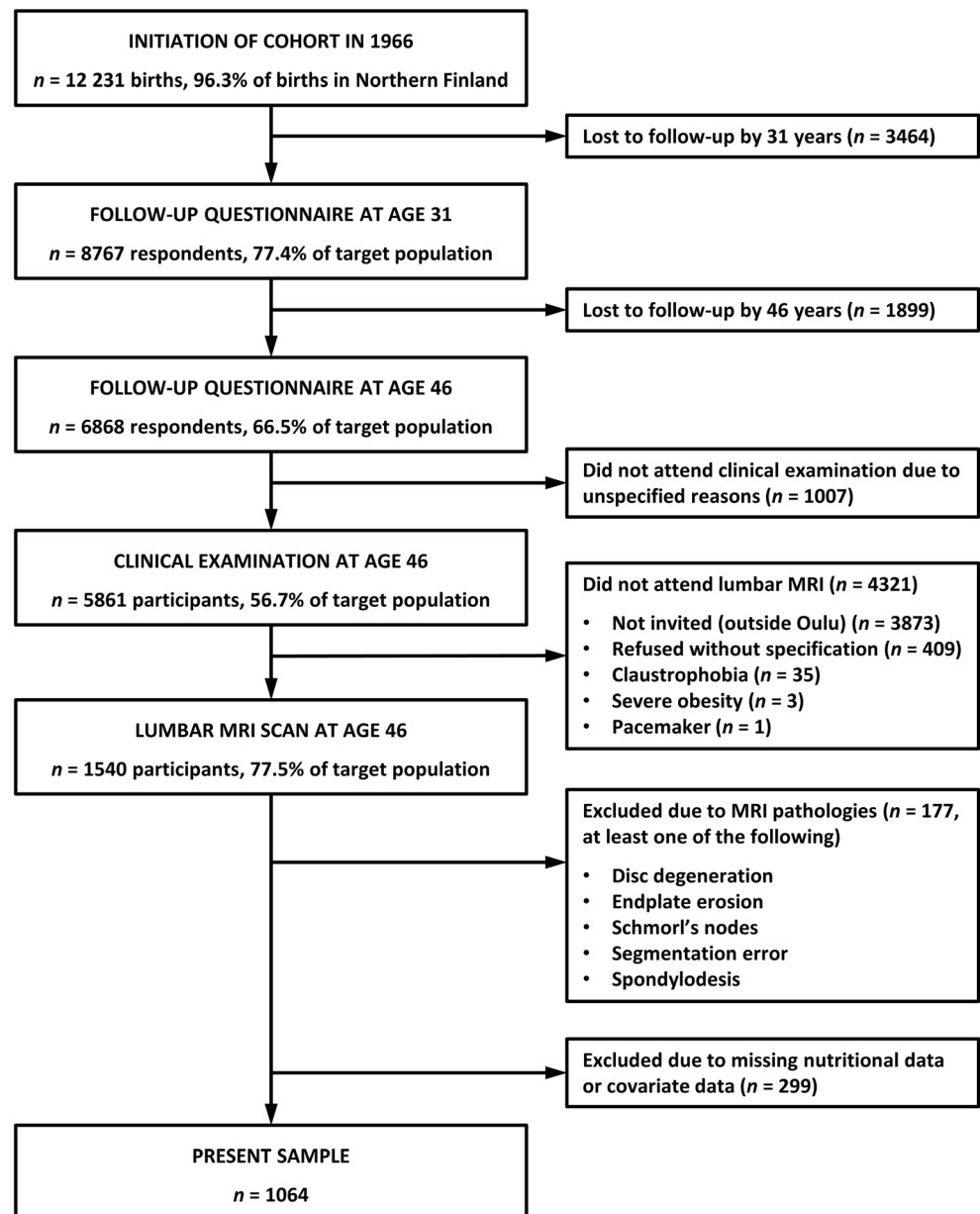
Using NeaView Radiology software version 2.31 (Neagen Oy, Oulu, Finland), one researcher (P.O.) measured two widths (maximum, minimum) and three depths (cranial, caudal, midway) of each applicable L4, as demonstrated in Fig. 2. These dimensions have been previously presented and used in several similar studies [7, 8, 20–24]. Each dimension was documented to an accuracy of 0.1 mm. The CSA of L4 was calculated as $CSA \text{ (mm}^2\text{)} = \pi \times a/2 \times b/2$, where a = mean of width measurements and b = mean of depth measurements. The formula has been validated [25] and used earlier in similar studies [7, 8, 20–22, 24]. We have previously demonstrated that our MRI-derived vertebral measurements are accurate [24]. The intra-rater reliability of our measurement process has been high and measurement errors low [7]. We chose L4 due to its caudal location in the spine and due to higher stability than L5 [26]. L4 has been used in many previous studies [7, 8, 20, 21], and its results seem to be generalizable over other thoracolumbar vertebrae [7, 27].

Calcium intake at age 31 and 46 (exposure)

Calcium intake was approximated on the basis of self-reported dairy consumption and the use of Ca supplements. Dairy consumption in Finland is generally high [28], which provides an ideal setting for studying dairy-based Ca intake [29].

In the questionnaires, dairy consumption was elicited by asking “How many glasses (0.2 L) do you usually drink/eat per day of: (1) milk, (2) sour milk, (3) other dairy products (e.g., yoghurt, other fermented milk products, ice cream)?” and “How many slices of cheese do you eat per day?” The

Fig. 1 Flow chart of the study



31- and 46-year questionnaires were identically formulated with the exception that the 46-year questionnaire elicited cheese consumption separately for low-fat ($\leq 17\%$) and normal fat ($> 17\%$) cheeses. The use of Ca supplements was elicited by asking “Please list all your current medications together with their strength and dosage;” the respondents were instructed to also report vitamins and dietary supplements here.

According to the National Food Composition Database in Finland [30], maintained by the Finnish National Institute for Health and Welfare, 0.2 L of milk, sour milk, yoghurt, and other dairies contain 240 mg of Ca. Correspondingly, an average-sized slice of cheese (8 g [31]) contains 75 mg of Ca [30]. The overall Ca intakes (mg/day) at the ages of 31

and 46 were calculated as these dietary components and Ca supplements. Other sources of Ca (e.g., plant-based “milks” enriched with Ca, nuts, seeds, soya, fish) were not assessed because their consumption was not elicited in enough detail in the food questionnaires, and because they yield relatively little of the daily Ca supply of Finns [32].

According to Finnish [33] and Nordic [34] nutrition recommendations, the recommended daily intake (RDI) of Ca is 800 mg for the general adult population. At both time points, Ca intake was considered “adequate” (≥ 800 $\mu\text{g}/\text{day}$) or “inadequate” (< 800 $\mu\text{g}/\text{day}$). In addition, based on their longitudinal Ca intake in adulthood, we classified the individuals into “adequate” (≥ 800 mg/day at both time points), “ascending” (< 800 mg/day at 31 years, ≥ 800 mg/day at

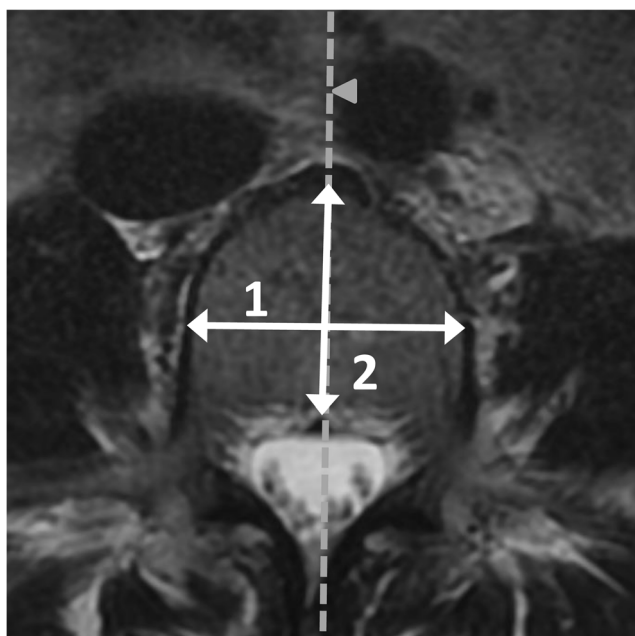


Fig. 2 Annotated MRI scan of L4. 1 = width, 2 = depth. After all axial planes were scanned, we measured the maximum and minimum widths and the cranial, caudal, and midaxial depths

46 years), “descending” (≥ 800 mg/day at 31 years, < 800 mg/day at 46 years), and “inadequate” (< 800 mg/day at both time points) categories, as illustrated in Fig. 3.

Vitamin D intake at age 31 and 46 (confounder)

Vitamin D intake was assessed using food questionnaires and data on vitamin D supplement use from the ages of 31 and 46. At the age of 31, vitamin D intake was approximated on the basis of fish consumption and vitamin D supplements. Due to changes in the Finnish national vitamin D fortification policy between the two follow-ups (i.e., 1998 and 2012) [35], dairy products and bread spreads (i.e., margarines and vegetable oil spreads) were also taken into account as significant sources of vitamin D at the age of 46.

In the 31- and 46-year food questionnaires, we elicited fish consumption by asking “How often do you usually consume

fish or fish dishes? (1) less than once a month or not at all, (2) once or twice a month, (3) once a week, (4) twice a week, (5) almost daily, (6) daily or more often.” The 31- and 46-year questionnaires were identically formulated with the exception that the 46-year questionnaire elicited the consumption of fatty, semi-fatty, and lean fish separately.

According to the National Food Composition Database [30, 31], ten commonly consumed fish in Finland (pike, perch, vendace, Baltic herring, salmon, tuna, rainbow trout, saithe, whitefish, and zander) yield an average of $13.4 \mu\text{g}$ of vitamin D per average-sized portion (140–160 g depending on the species). Thus, eating fish almost every day or more often was approximated as yielding an average vitamin D intake of $13.4 \mu\text{g}/\text{day}$. Correspondingly, eating fish twice a week was estimated to yield an average of $3.8 \mu\text{g}$ of vitamin D per day; once a week yielded $1.9 \mu\text{g}/\text{day}$; and once or twice a month or less often was approximated as yielding $0 \mu\text{g}$ of vitamin D per day.

The consumption of bread spreads was elicited by the following questions at the age of 46:

- 1) “What type of bread spread do you usually use? (choose one category)” with pictures of common Finnish bread spread brands divided into seven categories: vegetable oil spreads with 23–40% fat, vegetable oil spreads with 60–70% fat, mixture of organic butter and vegetable oil with 75% fat, mixture of butter and vegetable oil with 40–80% fat, organic butter, butter, plant-based sterol, and stanol margarines with 32–60% fat.
- 2) “How much spread do you usually put on a slice of bread? (choose one picture)” with actual-sized pictures of bread slices with 3, 5, 9, and 12 g of spread.
- 3) “How many slices of bread do you usually have per day: rye breads, mixed breads and baguettes, white breads and baguettes?”

The average consumption of bread spread per day was calculated for each individual according to the number of bread slices consumed and the amount of bread spread used. Based on the National Food Composition Database [30], the amount of vitamin D was considered to vary depending on spread type as follows: butter and organic butter $0 \mu\text{g}$ of vitamin D per 1 g, vegetable oil spreads and plant-based sterol and stanol margarines $0.2 \mu\text{g}/\text{g}$, and mixtures of butter/organic butter and vegetable oil $0.1 \mu\text{g}/\text{g}$. These data enabled us to calculate the average daily intake of vitamin D from bread spreads for each individual.

The consumption of dairy products and the use of vitamin D supplements were elicited using the same questions as those presented above. According to the National Food Composition Database [30], all dairy products (except for cheese) were approximated as yielding $1 \mu\text{g}$ of vitamin D per 100 mL/100 g.

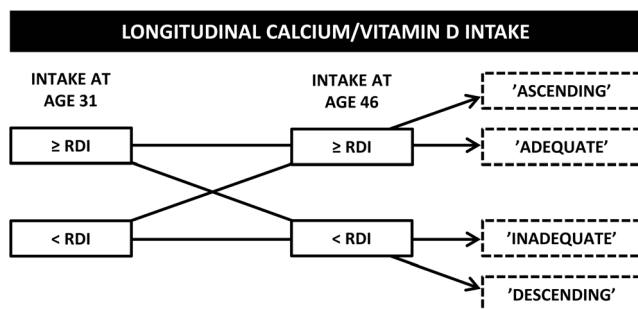


Fig. 3 Classification of individuals into groups on the basis of their Ca/vitamin D intake at ages of 31 and 46. *RDI* recommended daily intake (for Ca, 800 mg/day; for vitamin D, $10 \mu\text{g}/\text{day}$)

Overall vitamin D intake ($\mu\text{g}/\text{day}$) at the ages of 31 and 46 was calculated as the sum of these dietary components and vitamin D supplements. According to Finnish [33] and Nordic [34] nutrition recommendations, the RDI of vitamin D is 10 $\mu\text{g}/\text{day}$ for the general adult population. At both time points, vitamin D intake was considered “adequate” ($\geq 10 \mu\text{g}/\text{day}$) or “inadequate” ($< 10 \mu\text{g}/\text{day}$). In addition, similarly to the longitudinal Ca categorization, individuals were classified into “adequate,” “ascending,” “descending,” and “inadequate” vitamin D intake groups, as illustrated in Fig. 3.

Other confounders

We considered the following variables to be confounding factors: body mass index (BMI), general diet, vitamin D intake, education, leisure-time physical activity, and smoking. At the 46-year clinical examination, the height (cm) and weight (kg) of the participants were systematically measured by a study nurse to an accuracy of 0.1 cm/0.1 kg. BMI was calculated as weight (kg)/height squared (m^2). Lifetime smoking classification (“non-smoker,” “former smoker,” “current smoker”) was based on the responses to the questions “Have you ever smoked cigarettes (yes/no)?” and “Do you currently smoke (yes/no)?” Education years (< 9 years, 9–12 years, > 12 years), indicative of socioeconomic status, were classified according to the responses to the questions “What is your basic education? (1) Less than nine years of elementary school, (2) elementary school, (3) attainment of matriculation examination” and “What is your vocational education? (1) None, (2) occupational course, (3) vocational school, (4) vocational college, (5) polytechnic, (6) university, (7) other, (8) unfinished course.” Leisure-time physical activity (< 1 , 1, 2–3, ≥ 4 times a week) was based on self-reported physical activity during leisure-time in the 46-year questionnaire: (1) daily, (2) 4–6 times a week, (3) 2–3 times a week, (4) once a week, (5) 2–3 times a month, (6) once a month or less often. All these variables have been introduced in our earlier publication [7]. General diet was also self-reported in the 46-year questionnaire (“Do you follow any specific diet: lactose-free, gluten-free, food allergy, diabetic, cholesterol-lowering, weight-loss, vegetarian, low-salt, other diet?”). The diets were not further defined in the questionnaire. Due to the small group sizes, the diets were combined as follows: lactose-free, gluten-free, weight-loss, vegetarian, other diet. As the population was coeval, we did not assess age as a confounder.

Statistical analysis

We administered and analyzed the data using SPSS software version 22 (IBM, Armonk, NY, USA). *p* values of < 0.05 were considered statistically significant. For categorical variables, we presented frequencies with percentages, and for continuous variables, means with standard deviations or medians with

interquartile ranges, depending on the normality of the data. In the analysis of Ca and vertebral CSA, we used crude and multivariable generalized estimating equations (GEE) and linear regression models as specified below. GEE is a regression-based statistical method and is more suitable for processing repeatedly measured and thus correlated data than traditional linear regression [36]. In GEE, we corrected for correlation using the “exchangeable” working correlation matrix. Where appropriate, the assumptions of the models were assured beforehand. Vertebral CSA (mm^2) was the continuous outcome variable in each model. We documented beta coefficients (β) and their 95% confidence intervals (CI) from the models.

We analyzed Ca intake in both categorical and continuous forms. First, the association between Ca intake (adequate versus inadequate at the ages of 31 and 46) and vertebral CSA was analyzed using GEE. In the adjusted models, we used the corresponding 31-year and 46-year categorical vitamin D intake variables as covariates, among other covariates. Then, we analyzed longitudinal Ca intake (adequate, ascending, descending, inadequate) and vertebral CSA, using linear regression. In the adjusted models, we used the corresponding longitudinal vitamin D intake variable as a covariate, among other covariates. Lastly, we used GEE to analyze the association of Ca intake (continuous, mg/day) at the ages of 31 and 46 with vertebral CSA. In the adjusted models, we used the corresponding continuous 31-year and 46-year vitamin D intake variables as covariates, among other covariates. Due to the substantial sex discrepancy in vertebral CSA [26], we stratified all models by sex.

Ethical considerations

The study protocol followed the Declaration of Helsinki and was approved by the Ethics Committee of the Northern Ostrobothnia Hospital District. Participation was voluntary, and participants signed their informed consent at all stages.

Results

Of the 1064 individuals whose data we could evaluate, 56.4% were women and 43.6% were men. Tables 1 and 2 show the background characteristics of the sample. Mean age at lumbar MRI was 46.8 years and mean BMI 26.5 kg/m^2 ; most individuals had attended school for 9 to 12 years, were non-smokers, and did not follow a special diet. Adequate Ca intake ($\geq 800 \text{ mg}/\text{day}$ at both time points) was reported by 58.6% of men and 47.7% women.

The distribution of vertebral CSA across the Ca intake categories, together with between-group comparisons, are shown in Table 3. When Ca intake was analyzed separately at the two time points, no differences were detected between individuals with adequate and inadequate intake. However,

Table 1 General characteristics of the Northern Finland Birth Cohort 1966 subsample ($n = 1064$)

Variable	Men ($n = 464$)	Women ($n = 600$)
Exact age at MRI, years ^a	46.8 (0.4)	46.8 (0.4)
Body mass index at age 46 ^a , kg/m ²	26.8 (3.7)	26.2 (5.0)
Education, years		
< 9 ^b	3.0 (14)	2.0 (12)
9–12 ^b	71.3 (331)	72.3 (434)
> 12 ^b	25.6 (119)	25.7 (154)
Smoking history		
Non-smoker ^b	51.1 (237)	61.5 (369)
Former ^b	33.4 (155)	23.2 (139)
Current ^b	15.5 (72)	15.3 (92)
Leisure-time physical activity at age 46, times/week		
< 1 ^b	26.5 (123)	22.7 (136)
1 ^b	22.2 (103)	19.5 (117)
2–3 ^b	36.4 (169)	41.7 (250)
≥ 4 ^b	14.9 (69)	16.2 (97)
Diet at age 46		
No specific diet ^b	71.3 (331)	65.3 (392)
Lactose-free ^b	9.1 (42)	8.5 (51)
Gluten-free ^b	1.5 (7)	2.8 (17)
Weight-loss ^b	1.9 (9)	5.2 (31)
Vegetarian ^b	1.3 (6)	3.8 (23)
Other ^b	14.9 (69)	14.3 (86)
Dimensions of L4 at age 46		
Cross-sectional area ^a , mm ²	1322.1 (166.6)	1052.6 (130.3)

^a Mean (standard deviation), ^b Percentage (number of individuals). *MRI* magnetic resonance imaging

the longitudinal assessment of Ca intake (from age 31 to 46) revealed that women with inadequate Ca intake had smaller vertebral CSA than those with adequate intake (3.8% difference in vertebral CSA, adjusted $p = 0.009$). No differences were detected among men. Ca intake was also assessed in its continuous form as a predictor of vertebral CSA (Supplementary Table 1); no statistically significant findings were obtained from either sex.

Discussion

Using a general population sample of 1064 middle-aged Northern Finns, this prospective study aimed to determine the association of dairy- and supplement-based Ca intake (from age 31 to 46) with vertebral size (age 46). Among women, inadequate Ca intake was associated with 3.8% smaller midlife vertebral CSA than adequate intake over the follow-up. Among men, Ca intake was not associated with vertebral CSA.

Table 2 Calcium and vitamin D intake among the Northern Finland Birth Cohort 1966 subsample ($n = 1064$)

Variable	Men ($n = 464$)	Women ($n = 600$)
Calcium intake		
At age 31 ^a , mg/day	1170 (780–1511)	945 (690–1241)
< 800 ^b	25.9 (120)	38.5 (231)
≥ 800 ^b	74.1 (344)	61.5 (369)
At age 46 ^a , mg/day	1095 (720–1425)	945 (720–1241)
< 800 ^b	31.0 (144)	34.2 (205)
≥ 800 ^b	69.0 (320)	65.8 (395)
Longitudinal Ca intake ^c from age 31 to 46		
Inadequate ^{b,c}	15.5 (72)	20.3 (122)
Descending ^{b,c}	15.5 (72)	13.8 (83)
Ascending ^{b,c}	10.3 (48)	18.2 (109)
Adequate ^{b,c}	58.6 (272)	47.7 (286)
Vitamin D intake		
At age 31 ^a , µg/day	n/a ^d	n/a ^d
< 10 ^b	97.6 (453)	98.7 (592)
≥ 10 ^b	2.4 (11)	1.3 (8)
At age 46 ^a , µg/day	12.0 (9.0–17.8)	11.0 (8.0–16.8)
< 10 ^b	34.3 (159)	41.0 (246)
≥ 10 ^b	65.7 (305)	59.0 (354)
Longitudinal vitamin D intake from age 31 to 46 ^c		
Inadequate ^{b,c}	33.6 (156)	40.5 (243)
Descending ^{b,c}	0.6 (3)	0.5 (3)
Ascending ^{b,c}	64.0 (297)	58.2 (349)
Adequate ^{b,c}	1.7 (8)	0.8 (5)

^a Median (interquartile range), ^b Percentage (number of individuals), ^c Longitudinal Ca/vitamin D intake categories were defined as follows: inadequate (< RDI at age 31 and 46), descending (≥ RDI at age 31 and < RDI at age 46), ascending (< RDI at age 31 and ≥ RDI at age 46), adequate (≥ RDI at age 31 and 46). ^d Medians and interquartile ranges were not given for vitamin D at age 31 because the data were mostly based on categorical variables. *RDI* recommended daily intake (for Ca, 800 mg/day; for vitamin D, 10 µg/day)

Investigations of Ca and bone morphology in the appendicular skeleton have been carried out previously (e.g., reports of larger femoral cross-sectional area [14–16] and enhanced femoral cortical parameters [13, 17]). However, in these studies, the samples have consisted of mostly women, the results have shown low effect sizes, and the studied doses/cut-offs for Ca intake have varied. Importantly, few reports have addressed the axial skeleton and vertebral morphology. An Australian study [17] of 111 men aged ≥ 50 years showed that the consumption of Ca-vitamin-D-fortified milk had no effect on vertebral geometry in a 2-year follow-up. In our study, neither the cut-off-based comparisons nor the continuous modeling of Ca intake yielded significant results among men. Despite the different study populations and the various methodological differences between the said study and ours,

Table 3 Vertebral cross-sectional area (CSA) across calcium (Ca) intake categories. Coefficients from generalized estimating equation models (Ca intake analyses at separate time points) and linear regression models (longitudinal Ca intake analyses)

	Men (<i>n</i> = 464)		Women (<i>n</i> = 600)					
	Vertebral CSA ^a , mm ²		Adjusted ^b model		Crude model		Adjusted ^b model	
	β^c , mm ²	<i>P</i>	β^c , mm ²	<i>P</i>	β^c , mm ²	<i>P</i>	β^c , mm ²	<i>P</i>
Calcium intake at age 31, mg/day								
<800	1339.4 (179.5)	0.064	33.9 (-3.7; 71.5)	0.077	1041.1 (130.3)	0.269	-12.6 (-35.0; 9.7)	0.248
≥800 (ref.)	1317.0 (161.7)				1059.8 (129.9)			
Calcium intake at age 46, mg/day								
<800	1309.8 (179.8)	0.094	-27.1 (-66.2; 12.0)	0.174	1036.7 (117.8)	0.072	-20.1 (-42.0; 1.8)	0.086
≥800 (ref.)	1327.6 (160.3)				1060.9 (135.8)			
Longitudinal calcium intake from age 31 to age 46 ^d								
Inadequate ^d	1320.0 (193.1)	0.988	1.4 (-45.7; 48.6)	0.953	1018.1 (110.9)	0.004	-39.6 (-69.3; -10.0)	0.009
Descending ^d	1299.6 (166.3)	0.347	-18.6 (-65.2; 28.1)	0.434	1064.9 (110.9)	0.728	8.0 (-25.7; 41.6)	0.643
Ascending ^d	1368.4 (154.4)	0.065	45.5 (-6.5; 97.5)	0.086	1066.9 (137.8)	0.566	9.3 (-20.1; 38.7)	0.535
Adequate ^d (ref.)	1320.3 (160.5)				1058.6 (135.1)			

^a Mean (standard deviation). ^b Adjusted for body mass index, diet, vitamin D intake, education, leisure-time physical activity, and smoking. ^c Beta coefficient (95% confidence interval). ^d Longitudinal Ca intake categories were defined as follows: inadequate (< RDI at age 31 and 46), descending (≥ RDI at age 31 and < RDI at age 46), ascending (< RDI at age 31 and ≥ RDI at age 46), adequate (≥ RDI at age 31 and 46). Statistically significant coefficients have been italicized. *Ref.* reference category, *RDI* recommended daily intake (for Ca, 800 mg/day)

the present findings regarding men are in line with the previous report. As we observed significant results among women, future studies should confirm this sex discrepancy and investigate the potential underlying factors. However, it should be noted that our sample sizes for men were somewhat lower than those for women, particularly in the inadequate Ca intake group, which may explain the lack of statistical significance among men. Another explanation for the detected sex discrepancy may be the potential pregnancy-associated changes in bone metabolism, although in our previous study [37], we observed no association between pregnancy, or even multiple pregnancies, and maternal vertebral CSA or shape.

Among women, our models revealed that inadequate Ca intake from age 31 to 46 was associated with smaller vertebral CSA at age 46. As the cut-off for adequate Ca intake was chosen according to the local Finnish [33] and Nordic [34] nutrition recommendations, our findings underline the benefits of following these recommendations in terms of gaining and maintaining optimal vertebral CSA. Naturally, several other lifestyle factors are also associated with vertebral size [6–8] and should be accounted for in order to optimize one's vertebral size. In the time-point-specific models, we observed no association between Ca intake and vertebral CSA, indicating that Ca intake is likely to affect spinal health over a longer period of time.

Generally, small vertebral size increases susceptibility to morphometric vertebral fractures [4, 5], indicating that studies that aim to reveal lifestyle-related determinants of vertebral size are of high relevance. However, it is not yet known whether this also applies to the more specific, reproducible, and incident fracture predictive morphological fractures that may be without dimensional differences but have cortical disruptions [38]. The incidence of osteoporotic fractures begins to increase after midlife, especially among women [39], justifying our investigation of the 46-year population. Although patients with an osteoporotic fracture apparently have inadequate dietary Ca (and vitamin D) intake [40], recent meta-analyses have questioned the routine use of Ca and vitamin D supplements among older people in terms of reaching higher bone mineral density (BMD) [41] and lower fracture risk [42]. The findings of the present study addressed neither vertebral BMD nor fracture history, but are suggestive of decreased spinal resilience among middle-aged women who have not achieved adequate Ca intake in adulthood.

The main strengths of our study were its large general population sample and longitudinal assessment of Ca intake in adulthood. The study population was representative of the general Northern Finnish population [19], and the 15-year follow-up period, from age 31 to age 46, was rather long. We were also able to control for the potential confounding effect of vitamin D intake on Ca. We obtained data on vertebral geometry from recent MRI scans using a validated approach [24] with high intra-rater reliability and low

measurements errors [7]. We measured several dimensions to maximize measurement accuracy.

Our study also had limitations. With regard to our Ca variables, the approximation of Ca intake was based on dairy consumption and Ca supplements, and was therefore not fully exhaustive, although dairy products are widely used in the Finnish population [28]. As other sources yield relatively little of the daily Ca supply among Finns and more precise evaluation of these sources (e.g., the use of plant-based “milks” enriched with Ca, nuts, seeds, soya) was not achievable, we decided to approximate Ca intake as presented. We also used self-reports to gather nutritional data, which is a potential source of bias, although the test-retest reliability of our questionnaire has shown to be high [43, 44]. For convenience, the questionnaires did not enquire about each food individually but in groups of similar food items, and this may have introduced inaccuracies to our Ca and vitamin D intake estimates. We were unable to take every source of calcium and vitamin D into account when calculating the intake estimates. Instead of self-reported vitamin D intake, the measurement of serum 25-hydroxyvitamin D level would be an interesting target for further studies. The cutoffs for adequate Ca intake were chosen in accordance with local nutrition recommendations and previous literature [33, 34]. We used the general population reference values, as the study population was representative of the general Finnish population. As our nutritional data from childhood and adolescence were scarce, we were unable to provide Ca intake estimates for these time periods, although they may play an important role in the development of vertebral size. However, according to our recent study, vertebral dimensions and CSA undergo changes in adulthood [45], suggesting that later life is also relevant in this regard. In addition to Ca, we acknowledge that a wide range of other relevant nutritional factors may affect vertebral size, e.g., protein and fat intake [10]. Unfortunately, we were unable to provide estimates for protein, fat, or total energy intake due to the structure of the food questionnaires. As for vertebral data, lumbar MRI scans were only obtained in midlife, which prevented us from assessing vertebral size in a longitudinal manner. We also specifically focused on vertebral geometry instead of structural or architectural parameters, which equally influence bone strength [5] and may be more easily affected by Ca. This choice was made due to the lack of studies using vertebral size as outcome. We measured L4 because it was located in the middle of the lumbar MRI scans, with both axial and sagittal slices available. Vertebral geometry and strength seem to follow a stable pattern across the thoracic and lumbar spine [27], indicating that our results regarding L4 should be applicable across the thoracolumbar spine. Future studies should aim to compensate the limitations of our data.

We conclude that inadequate Ca intake (<800 mg/day) in adulthood predicts small vertebral size and thus decreased spinal resilience among middle-aged women. Among men, there

was no association between Ca intake and vertebral size. Future studies should confirm these findings and investigate the potential factors underlying the association of low Ca intake in women but not in men with smaller vertebral size. Moreover, although vertebral dimensions have been previously shown to predict morphometric vertebral fractures, it is not yet known whether this also applies to the more specific, reproducible and incident fracture predictive morphological fractures that may be without dimensional differences but have cortical disruptions.

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Compliance with ethical standards

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

Conflict of interest The financial support received by P. Oura is specified in the Funding section. The remaining authors declare that they have no conflict of interest.

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