**Title:** Postmenopausal women with osteoporosis consume high amounts of vegetables but insufficient dairy products and calcium to benefit from their virtues: the CoLaus/OsteoLaus cohort.

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# Postmenopausal women with osteoporosis consume high amounts of vegetables but insufficient dairy products and calcium to benefit from their virtues. The Colaus/Osteolaus cohort

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**Conflict of interest**

Audrey Lanyan, Pedro Marques-Vida, Elena Gonzalez Rodriguez, Didier Hans and Olivier Lamy declare that they have no conflict of interest

**Mini Abstract**

We evaluated the associations between nutrients, dietary patterns or compliance to dietary guidelines and bone health among postmenopausal women from the CoLaus/OsteoLaus cohort. Postmenopausal women with osteoporosis consume a high amount of vegetables but insufficient amount of dairy products and calcium to benefit from their adherence to dietary guidelines.

**Abstract**

**Purpose:** Diet plays a significant role in the prevention of osteoporosis (OP). We evaluated the associations between nutrients, dietary patterns or compliance (expressed in odds of meeting) to dietary Swiss guidelines and bone health (T-score <-2.5 SD, TBS < 1230) among postmenopausal women.

**Methods:** 1215 women (64.3±7.5 years) from the CoLaus/OsteoLaus cohort (Lausanne, Switzerland) had their dietary intake assessed using a validated food frequency questionnaire. Bone mineral density (BMD), trabecular bone score (TBS) and vertebral fractures were evaluated with DXA. OP risk factors, calcium supplements (≥500 mg) and prevalent major OP fractures were assessed by questionnaire.

**Results:** 180/1195 women had OP according to BMD, 87/1185 a low TBS, and 141/1215 prevalent major OP fractures. In multivariate analysis (adjusted for total energy intake, age, antiosteoporotic treatment, educational level, BMI, sedentary status and diabetes), OP women consumed more vegetable proteins (21.3±0.4 vs 19.6±0.2 g/d), more fibers (18.2±0.5 vs 16.5±0.2 g/d), less animal proteins (40.0±1.1 vs 42.8±0.4 g/d), less calcium (928±30 vs 1010±12 mg/d) and less dairy products (175±12 vs 215±5 g/d), all p≤0.02. According to guidelines, OP women had a tendency to higher compliance for vegetables (OR (95% CI): 1.50 (0.99-2.26)), and a lower compliance for dairy (OR (95% CI): 0.44 (0.22-0.86)) than those without OP. Women taking calcium supplements consumed significantly higher amounts of dairy products. No association was found between TBS values or prevalent OP fractures and any dietary components.

**Conclusion:** Postmenopausal women with OP consume a high amount of vegetables but insufficient amount of dairy products and calcium. TBS does not seem to be influenced by diet.

**Keywords:** osteoporosis, postmenopausal women, vegetables, calcium supplements (≥500 mg/d), dairy products

## Introduction

Osteoporosis is a widespread bone disorder characterized by both a loss of bone mineral density (BMD) and an alteration of bone micro-architecture leading to an increased fracture risk. Worldwide, one out of two women, and one out of five men aged over 50 will be affected by an osteoporotic fracture (1,2). In Switzerland, due to population ageing and the increase in life expectancy, the osteoporotic fracture rate among elderly women is expected to double by 2050 (3). In the EU, health expenditures related to osteoporosis amounted to 37 billion € in 2010, and this value is expected to increase by 25% in 2025 (4). Due to these public health and economic challenges, global, inexpensive and easily implemented preventive measures against osteoporosis are particularly needed.

A healthy lifestyle, and especially diet, plays a significant role in the prevention of chronic diseases, such as osteoporosis (5). Nevertheless, the impact of food intake on bone health is difficult to study, as diet is a combination of different foods and not of individual nutrients. Indeed, diet might be better assessed by dietary patterns, which take into consideration this diversity (6). A healthy dietary pattern with high intakes of fruit and vegetables may lead to less bone resorption and a poor dietary pattern rich in processed foods is associated with a decrease in BMD (6). A review of 49 studies worldwide has identified healthy diets as those « that emphasized the intake of fruits, vegetables, whole grains, poultry and fish, nuts and legumes, and low-fat dairy products and de-emphasized the intake of soft drinks, fried foods, meat and processed products, sweets and desserts, and refined grains » (7). High quality nutritional diets are associated with a high BMD and a low fracture risk in older women (8,9). This stresses the potential for food to have a preventive and maybe therapeutic impact.

BMD is the hallmark for the diagnosis of osteoporosis. Yet, BMD provides an incomplete evaluation of bone health status. For example, nearly half of patients who present a fragility fracture have either normal or osteopenic (between -1 and -2.5 SD) BMD values (10,11). The Trabecular Bone Score (TBS) provides additional information on bone structure not covered by the BMD (12). TBS consists of a re-analysis of dual-energy X-ray absorptiometry (DXA) images obtained during BMD measurement. A low TBS corresponds to a porous, poorly connected micro-architecture, whereas a high TBS corresponds to a dense, well-connected micro-architectural bone setting (12). TBS improves the prediction of fracture risk, especially in patients with secondary osteoporosis (13). Yet, to our best knowledge, no study has ever analysed the association between dietary intake and the TBS. As TBS is an independent risk factor for predicting osteoporotic fracture, it is possible to hypothesize that a high quality nutritional diet is associated with a high TBS.

Hence, our study aimed to investigate the association of food habits (through single nutrient intake, dietary pattern and compliance to dietary guidelines) of postmenopausal women in the OsteoLaus cohort and BMD, osteoporotic fracture prevalence and TBS values. Our hypothesis was that women with poor bone health (lower BMD, lower TBS or higher osteoporotic fracture prevalence) would have a lower dietary pattern quality, particularly a lower intake of calcium and protein. This is the first study to investigate in detail the relationship between eating habits and TBS.

## PARTICIPANTS AND METHODS

*Participants*

The participants of our study belong to the OsteoLaus cohort. OsteoLaus is a substudy of the CoLaus study, an ongoing prospective study aiming to assess the determinants of cardiovascular and psychiatric diseases using a population-based sample drawn from the city of Lausanne, Switzerland (14). The latter was initiated in 2003, including 6733 men and women aged 35 to 75 years.

The goal of OsteoLaus is to obtain more precise fracture risk models and to evaluate the link between cardiovascular diseases and osteoporosis (15). Between September 2009 and September 2012, all women aged between 50 and 80 years from the CoLaus study were invited to participate in OsteoLaus. Of the initial 1704 women invited, 1500 (88%) accepted, 1475 were included and 1215 were retained for our study; 98.4% were Caucasian. Participants were excluded if they: 1) had no data for dietary intake; 2) reported a total energy intake <500 or >3500 calories/day; or 3) had missing data for covariates. Calcium supplements were considered only if they contained at least 500 mg of calcium.

*Bone mineral density, TBS and fractures*

Each participant had: 1) a questionnaire on potential risk factors for fracture/osteoporosis, on conditions affecting bone metabolism, and on prevalent fractures; 2) a spine (L1 to L4) and femur DXA scan using the Discovery A System (Hologic, USA); 3) a blind central processing of TBS (TBS iNsight v2.1, Medimaps, Pessac, France) based on a previously acquired anteroposterior spine DXA scan; and 4) a vertebral fracture assessment (VFA) by two experimented clinicians using a semi-quantitative approach (16). Vertebral fractures were classified as grade 1, 2 or 3, according to the severity of the fracture.

Osteoporosis was defined as a T-score ≤ -2.5 SD on lumbar spine, femoral neck or total hip. Major osteoporotic fractures included at least one fracture of the vertebrae (clinical or radiologic from grade 2/3 on

VFA), hip, pelvis, humerus and radius, occurring spontaneously or after falling from the patient's own height. Low TBS values were defined as < 1.23 (17).

*Dietary intake*

Dietary intake was assessed in CoLaus using a validated, self-administered, semi-quantitative food frequency questionnaire (FFQ) which also included portion size (18). For each item, consumption frequencies ranging from "less than once during the last 4 weeks" to "2 or more times per day" were provided, and participants indicated the average serving size (smaller, equal or bigger) compared to a reference size.

Reported frequencies were transformed into daily consumption frequencies as follows: "never these last 4 weeks"=0; "once/month"=1/28; "2–3/month"=2.5/28; "1–2/week"=1.5/7; "3–4 times/week"=3.5/7; "once/day"=1 and "2+/day"=2.5. The consumption frequency of one food category was obtained by summing up all individual consumption frequencies of foods related to that category. For example, daily fruit consumption was obtained by summing up the daily consumptions of fresh fruits (5 items) and fruit juices (fresh and processed without added sugar). For each food, daily frequencies and multiplied by the average serving size to obtain the amount of the food consumed per day; this amount was used to compute the contribution of the selected food to total energy, macro- and micronutrient intake, using the French CIQUAL food composition table.

The quality of dietary intake was assessed using three different approaches. The first approach assessed dietary quality via three dietary scores. The first dietary score (hereby designated as "Mediterranean score 1") was derived from Trichopoulou *et al*. (19); the score ranges between zero and eight. The second Mediterranean dietary score (hereby designated as "Mediterranean score 2") is adapted to the Swiss population and was computed according to Vormund *et al*. (20). Contrary to the score from Trichopoulou *et al*., dairy products are considered as beneficial; the score ranges between zero and nine. The alternative healthy eating index (AHEI) was adapted from McCullough et al. (21); it does not include dairy products. In our study, the amount of trans fatty acids could not be assessed, and we considered all participants taking multivitamins as taking them for a duration ≥5 years. Thus, the modified AHEI score ranged between 2.5 and 77.5 instead of 2.5 and 87.5 for the original one (21). For all three scores, higher values represented a healthier diet.

The second approach assessed dietary quality *via* dietary patterns, assessed using consumption frequencies as reported previously (22). Briefly, three "naïve" dietary patterns were obtained: "Meat & chips", with high loadings for all types of meat and French fries; "Fruits & vegetables", with high loadings for most fruits and vegetables; and "Fatty & sugary", with high loadings for sugar, sweets, and fatty foods.

The third approach assessed the compliance to the Swiss Society of Nutrition for fruits, vegetables, meat, fish and dairy products (23) The guidelines are a) ≥2 fruit portions/day; b) ≥3 vegetable portions/day; c) ≤5 meat portions/week; d) ≥1 fish portion/week and e) ≥3 dairy products portions/day. As the FFQ queried about fresh and fried fish, two categories were considered: one including and one excluding fried fish, as several studies have shown that fried fish or fried foods are associated with an increased risk of cardiovascular events (24). Participants were further dichotomized if they complied with at least three guidelines or not; two categories of compliance were created, depending on the type of fish consumed (including or excluding fried fish).

*Covariates*

Participants were queried regarding their medical treatment, physical activity and socio-economic status. Educational level was self-reported using a questionnaire and categorized into mandatory, apprenticeship, high school and university. Smoking status was self-reported and categorized into never, former (irrespective of the time since quitting) and current (irrespective of the amount of tobacco smoked). Physical activity was assessed using a physical activity frequency questionnaire (PAFQ) validated in the population of Geneva, Switzerland (25). Sedentary status was considered if the participant spent less than 10% of daily time in activities ≥4 times the basal metabolic rate (26, 27).

Body weight and height were measured with participants barefoot and in light indoor clothes. Body weight was measured in kilograms to the nearest 100 g using a Seca® scale (Hamburg, Germany). Height was measured to the nearest 5 mm using a Seca® (Hamburg, Germany) height gauge. Body mass index (BMI) was categorized into normal+low (<25 $kg/m^2$), overweight (25-29.99 $kg/m^2$) and obese (≥30 $kg/m^2$).

Blood was drawn in the morning after overnight fasting. Biological assays were performed by the CHUV Clinical Laboratory on fresh blood samples within 2 hours of blood collection. Glucose levels were assessed using glucose hexokinase, with maximum inter and intra-batch CVs of 1.6% and 0.8%, respectively. Diabetes was considered for a fasting plasma glucose level ≥7.0 mmol/l or the presence of antidiabetic treatment. Although several measurements are recommended to diagnose diabetes, this would be impractical to perform in an epidemiological setting.

*Statistical analysis*

Statistical analysis was performed using the Stata version 15.0 for windows (Stata Corp, College Station, Texas, USA). Descriptive results were expressed as number of participants (percentage) for categorical variables or as average ± standard deviation for continuous variables. Bivariate comparisons between groups were performed using chi-square or Fisher's exact test for categorical variables and Student's t-test, analysis of variance or Kruskal-Wallis test for continuous variables. Associations between bone and dietary markers were assessed using Spearman correlation. Multivariable analysis was performed using logistic regression for categorical variables and analysis of variance for continuous variables. Multivariable models were adjusted for total energy intake (continuous), age (continuous), BMI (continuous), educational level (mandatory/apprenticeship/high school/university), antiosteoporotic treatment (yes/no), sedentary status (yes/no) or diabetes (yes/no). Results were expressed as multivariable-adjusted odds ratio (OR) and 95% confidence interval (95% CI) for the logistic models and as multivariable-adjusted average ± standard error for analysis of variance. Statistical significance was assessed for a two-sided test with $p<0.05$.

*Ethical statement*

The CoLaus and OsteoLaus studies were approved by the Institutional Ethics Committee of the University of Lausanne, which afterwards became the Ethics Commission of Canton Vaud (http://www.cer-vd.ch). The studies were performed in agreement with the Helsinki Declaration and its former amendments, and in accordance with the applicable Swiss legislation. All participants gave their written informed consent before entering the study.

## RESULTS

*Characteristics of participants*

From the initial 1475 women, 260 (17.6%) were excluded. The reasons for exclusion are provided in **Figure 1** and the characteristics of the included and excluded participants are provided in **Supplemental Table 1**. Excluded participants were older, had a higher BMI, a lower educational level, and presented more frequently with diabetes. The baseline characteristics of the women included in the analysis according to presence or absence of osteoporosis (BMD criteria) are summarized in **Table 1**. Women with osteoporosis were older, had a lower BMI and a lower prevalence of diabetes.

*Osteoporosis and dietary markers*

The levels of dietary markers according to presence or absence of osteoporosis are summarized in **Table 2**. On multivariate analysis, women with osteoporosis had a higher consumption of vegetable protein, fibre, polysaccharides and iron, and a lower consumption of animal protein, calcium, saturated fatty acids and dairy than women without osteoporosis. They scored higher in the AHEI and had a lower compliance to the dairy guideline than women without osteoporosis.

*Trabecular bone score and dietary markers*

Out of the 1185 with TBS values, 87 (7.3%) had a low TBS. The baseline characteristics of the women with or without low TBS are summarized in **Supplemental table 2**. Women with low TBS were older and had a lower BMI. The levels of dietary markers according to a normal or a low TBS are summarized in **Table 3**. On bivariate analysis, women with low TBS had a lower consumption of processed meat and of fish, which disappeared on multivariate analysis. The amount of macronutrients or micronutrients consumed, the prevalence of patterns or compliance with guidelines were the same in both groups.

*Major osteoporotic fractures and dietary markers*

Out of the 1215 participants, 141 (11.6%) had at least one prevalent major osteoporotic fracture. The levels of dietary markers according to presence or absence of prevalent major osteoporotic fracture are summarized in **Supplemental table 3**. On multivariate analysis, women with prevalent major osteoporotic fracture had a higher consumption of fruits than women without. The pattern "fat and sugar" was less prevalent in women with osteoporotic fracture. The amount of macronutrients or micronutrients consumed, and the compliance with guidelines were the same in both groups.

*Calcium supplements*

Out of the 1215 participants, 531(43.7%) were taking calcium supplements ($\geq$ 500 mg/d). The **Supplemental table 4** describes specific dietary habits and medical conditions among participants taking or not supplements. On bivariate analysis, women taking calcium supplements had higher intakes of calcium and dairy, which disappeared on multivariate analysis, but they had a higher compliance to dairy products with multivariate-adjusted OR at 1.72 (95% CI 1.12-2.64, p=0.015). Among women with osteoporosis, 103/180 (57%) were taking calcium supplements; and among women with low TBS 43/87 (61%).

*Post-hoc analysis*

We carried out complementary analyses by considering the medians of calcium, dairy products and vegetables consumption. Among women who consumed more calcium, respectively more dairy products than the median, those who consumed more vegetables tended to have osteoporosis more often than those who consumed less vegetables than the median (11.0% vs 9.5%, ns; respectively 11.0% vs 9.8%, ns).

## DISCUSSION

Our results indicate that women with osteoporosis (as defined by BMD) consume higher amounts of vegetables, more vegetable proteins and fiber while consuming lower amounts of dairy products, animal proteins and calcium than women without osteoporosis. No association was found between dietary markers and TBS.

*Osteoporosis and dietary markers*

Women with osteoporosis (as defined by BMD) consumed higher amounts of vegetables than women without these conditions, and had a trend to adhere more often to the fruits and vegetables dietary pattern with multivariate-adjusted OR at 1.50 (95% CI 0.99-2.26, p=0.056). Those findings do not replicate those of a Chinese study, were vegetable intake was independently associated with a higher BMD and a lower prevalence of osteoporosis (22). In a Scottish study conducted among more than 3000 post-menopausal women, a high intake of fruits and vegetables was associated with a decreased bone resorption (6). Moreover, it is assumed that an alkaline environment, provided by potassium-rich foods such as fruits and vegetables, benefits BMD (28). However, the effect of dietary fiber on BMD in clinical trials in postmenopausal women is inconsistent. In the Framingham Offspring Study, higher dietary total fiber and fruit fiber was protective against bone loss at the femoral neck in men but not in women (29). It is possible that the benefits of vegetables intake could be reduced by a high fiber intake, or an insufficient intake of dairy and/or calcium, or animal protein. Indeed, we found that women with osteoporosis consumed more dietary fiber than women without osteoporosis. In human, dietary fiber has been shown to reduce calcium absorption in some studies (30, 31), and to increase calcium absorption in other (32, 33, 34). Nevertheless, in the post-hoc analyses, Holloway et al. demonstrated that positive responders had significantly lower lumbar spine BMD than non-responders (33). We carried out complementary analyses by considering the medians of calcium and vegetables consumed. Among women who consumed more calcium than the median, those who consumed more vegetables tended to have osteoporosis more often than those who consumed less than the median (11.0% vs 9.5%, ns). In our study, women with osteoporosis consumed less dairy products than women without osteoporosis. Several studies suggest that the benefits of a diet rich in vegetables regarding BMD are only achieved if combined with an adequate consumption of dairy products and protein. A Korean study showed that, in postmenopausal women, the “dairy & fruit” dietary pattern was the most efficient in decreasing the risk of osteoporosis (35). A Swedish prospective study following over 5000 women for 22 years showed that a dietary pattern including fermented milk, fruits and vegetables provided the highest protection against fracture (36). Finally, an Australian prospective study concluded that a dietary pattern characterized by a high intake of fruits, vegetables and dairy products was positively associated with

BMD (37). In our study, considering the medians of vegetables and dairy consumption, among women who consumed more dairy products than the median, those who consumed more vegetables tended to have osteoporosis more often than those who consumed less than the median (11.0% vs 9.8%, ns). We analyzed whether OsteoLaus women who consume less dairy products take more calcium supplements. The results showed that women taking calcium supplements (≥500 mg/d) consumed higher amounts of dairy products (**Supplemental Table 4**), and had a higher compliance to dairy products with multivariate-adjusted OR at 1.72 (95% CI 1.12-2.64, p=0.015). We therefore have several indirect arguments suggesting that women in the Osteolaus cohort do not consume enough calcium and/or dairy products to have the benefit of vegetables on the BMD. This hypothesis must be confirmed in other larger cohorts.

The total amount of protein was the same in women with or without osteoporosis. However, the benefit of protein on BMD may be reduced in women with osteoporosis since they had a lower calcium intake and/or a higher vegetable/animal protein ratio than women without osteoporosis. A recent systematic review and meta-analysis from the National Osteoporosis Foundation found no significant interaction between protein and calcium (38). However, studies were highly heterogeneous. Dairy protein but not plant protein was associated with bone strength of the radius and tibia in older men in the MrOS study (39). As ours, the Swiss cross-sectional GERICO study (conducted among 65 year old women with clinical characteristics similar to our sample) found that the non-osteoporotic participants had lower vegetable/animal protein ratio and higher dairy protein intake, emphasizing the idea that animal protein could protect against osteoporosis (40, 41). Still, contradictory statements are found in the literature regarding the association between animal protein consumption and osteoporosis. It can be hypothesized that women in the Osteolaus cohort with osteoporosis do not consume enough protein from dairy products. The ongoing follow-up of the OsteoLaus cohort will hopefully enable a better assessment of the associations between type of protein intake and incidence of osteoporosis.

Phosphorus is essential for bone mineralization, and may explain some of our results. Phosphorus intake was not assessed in our study. It is found mainly in meat and dairy products, but very little in vegetables. Its absorption also varies according to calcium intake (42). Several randomized controlled trials have shown positive relations between dairy intake and BMD. A recent study from New Zealand demonstrated that a nutrient pattern high in phosphorus and calcium was positively associated with lumbar spine and femoral neck BMD in postmenopausal women (43). Thus, indirectly, women without osteoporosis seem to have a higher intake of phosphorus, dairy products and calcium that could improve the benefit of phosphorus on bone health.

We found that women with osteoporosis had a higher consumption of polysaccharides and iron, and a lower consumption of saturated fatty acids than women without osteoporosis. The P-value of iron consumption was very close to 0.05 and the small difference in iron quantity (10.0 mg/d versus 9.7 mg/d) has probably no clinical relevance. The higher amount of polysaccharides reflects a higher consumption of vegetables, and the lower amount of saturated fatty acids reflects a lower consumption of animal foods. There was no between groups difference for the dietary Mediterranean scores. Women with osteoporosis scored higher in the AHEI, an adapted Mediterranean score not including dairy products.

The influence of vitamin D cannot be assessed, mainly because serum 25-hydroxyvitamin D was not measured. The amount of vitamin D from the diet was the same in both groups. However, digestive absorption varies depending on the source of vitamin D and supplements have a major influence. Calcium supplements - that contain 400 or 800 IU of vitamin D - were taken by 103/180 (57%) women with and 428/1015 (42%) without osteoporosis (**Supplementary Table 4**). In the multivariate analysis, there was no between groups difference for calcium supplements (p = 0.454). It is therefore unlikely that vitamin D can explain the observed differences.

*Trabecular bone score and dietary markers*

No association was found between dietary markers and the TBS in multivariate analysis. This stresses the fact that TBS and BMD are two independent and distinctive measures (12, 44). Evidence shows on one hand that efficacious therapies for osteoporosis influence more BMD than TBS values and on the other hand that the impact on the TBS is also influenced by the type of therapeutic agent (12). In our study, several hypotheses can be put forward to explain this absence of association. First, the effect of diet on TBS might be too small to be detected with our sample size. Second, only a small number of women in our cohort had a low TBS, so the sample may be too small to detect a difference. Third, there is indeed no difference in the diet of women with a low TBS compared to those with a partially altered or normal TBS.

The influence of diet on bone microarchitecture was assessed in other studies. In a cross-sectional study including 746 Caucasian women, animal and dairy protein intakes were associated with bone strength (finite element analysis), and microstructure at the radius and the tibia measured by high-resolution peripheral quantitative computed tomography (HRpQCT) (40). In the Geneva Retirees Cohort, fermented dairy products consumption was associated with attenuated loss of radius total volumetric BMD and of cortical volumetric BMD, area, and thickness (41). Milk consumption was associated with lower decrease of areal BMD and of failure load at the radius (41). The relationship between diet quality and HRpQCT and pQCT was evaluated in

350 older adults in United Kingdom (45). Diets rich in fruits, vegetables, oily fish and whole grain cereals in early old age were associated with greater bone size but not volumetric BMD or microarchitecture in later life in women (45). However, the measurement methods as well as the bone sites evaluated differed from our study. This could explain the differences observed. To our knowledge, it is the first study that analyses the link between TBS and diet among post-menopausal women. One Japanese cross sectional study has compared the milk intake habits to the TBS in elderly men (46). The study concluded that greater milk intake was associated with higher TBS. However, as more than 30 studies published by Sato Y. have been withdrawn due to the recognition of scientific misconduct, it is not possible to know whether this conclusion is valid.

*Major osteoporotic fractures and dietary markers*

Two associations were found between the diets of the participants with major osteoporotic fractures compared to those without: a higher fruit consumption and a less prevalent pattern "fat and sugar" in women with osteoporotic fracture. The inverse link between the "sugar and fat" pattern and the fracture is contrary to the conclusions of the literature and experts. These associations may be fortuitous, and they are no longer significant after Bonferroni's correction for multiple analyses (0.05/7 = 0.007). Hence, our findings should be considered with caution, and need to be replicated in other settings. Since fractures are often related to falls, it is probably more difficult to identify eating habits that affect favourably BMD, muscle mass and balance.

**Strengths and limitations**

Our study has several limitations. Firstly, its cross-sectional setting does not allow drawing inferences regarding the impact of diet on the development of osteoporosis. The ongoing follow-up of the Osteolaus cohort will provide important information regarding the causal associations in the near future. Secondly, the included participants were younger, more likely to have a higher educational background and less likely to have diabetes than the excluded. Hence, it is possible that our findings do not apply to the whole population of postmenopausal women. Thirdly, dietary intake was assessed for the last four weeks, and might not represent the average yearly consumption. Still, there is no validated FFQ assessing one-year dietary intake, and it is likely that FFQs covering longer periods would be more prone to recall bias. Fourthly, the osteoporotic women of our study had a lower BMI than the non-osteoporotic. We created four BMI sub-division groups and realized the underweighted participants (<18.5 kg/$m^2$) only represented 5.6 % of the osteoporotic and 1.3% of the non osteoporotic women. To take into account that the osteoporotic group has a lower BMI and may have a lower total energy intake, the multivariable models were adjusted for BMI and total energy intake. Fifthly, women with already diagnosed osteoporosis may potentially be a biased sample. Those who have preferred a specific nutritional approach (e.g., more vegetable-based foods, less dairy products) to drug treatment may be over-represented. However, this was a first densitometric exam for most women; and the eating habits were the same for women with or without osteoporotic fractures. Sixthly, serum 25-hydroxyvitamin D was not measured. In Switzerland, more than 90% of supplements with at least 500 mg of calcium contain 400 or 800 IU of vitamin D. So we can assume that people taking these supplements could have higher serum 25-hydroxyvitamin D, and that this could have a benefit on bone health. Finally, unaccounted confounders in this analysis may have masked the benefits or risks of different types of diets. Despite these weaknesses, the study has strengths, including the homogeneity of a Caucasian population, and the large sample of the OsteoLaus cohort that provides adequate statistical power. All nutritional assessment was based on standardized tools that had been previously tested and validated in the French-speaking population of Switzerland.

**Conclusion**

In a sample of postmenopausal women living in Lausanne, women with osteoporosis as defined by BMD consumed a high amount of vegetables and a too low amount of dairy products and calcium compared to non-osteoporotic women. The benefit of vegetables on BMD seems to decrease when calcium and dairy intakes are insufficient. Trabecular bone score does not seem to be associated with dietary intake. Further studies on the association between dietary habits and TBS should be determined and verified on larger groups.

## Authors' Roles

Study design: AL, PMV, and OL. Study conduct: PMV and OL. Data collection: AL. Data analysis: PMV. Data interpretation: AL, PMV and OL. Drafting manuscript: AL. Revising manuscript content: PMV, EGR, DH, and OL. Approving final version of manuscript: AL, PMV, EGR, DH, and OL. PMV takes responsibility for the integrity of the data analysis.

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## FIGURE AND TABLES LEGENDS

**Figure 1**:

Flowchart of the study highlighting the inclusion and exclusion criteria

**Table 1**:

Characteristics of the participants with and without osteoporosis (based on bone mineral density T-score definition).

**Table 2:**

Bivariate and multivariable analysis of the dietary markers among participants with and without osteoporosis (based on bone mineral density T-score definition).

**Table 3**:

Bivariate and multivariable analysis of the dietary markers among participants with and without low TBS.

**Table 1**

| | No osteoporosis | Osteoporosis | P-value |
|---|---|---|---|
| Sample size | 1015 | 180 | |
| Age (years) | 64.0 ± 7.6 | 65.7 ± 6.6 | 0.005 |
| Education | | | 0.668 |
| University | 140 (13.8) | 28 (15.6) | |
| High school | 276 (27.2) | 45 (25) | |
| Apprenticeship | 420 (41.4) | 70 (38.9) | |
| Mandatory | 179 (17.6) | 37 (20.6) | |
| Body mass index (kg/m$^2$) | 26.1 ± 4.4 | 23.6 ± 3.9 | <0.001 |
| Body mass index categories | | | <0.001 |
| Underweight | 13 (1.3) | 10 (5.6) | |
| Normal | 432 (42.6) | 114 (63.3) | |
| Overweight | 385 (37.9) | 42 (23.3) | |
| Obese | 185 (18.2) | 14 (7.8) | |
| Smoking status | | | 0.484 |
| Never | 469 (46.2) | 86 (47.8) | |
| Former | 381 (37.5) | 60 (33.3) | |
| Current | 165 (16.3) | 34 (18.9) | |
| Sedentary | 665 (65.5) | 114 (63.3) | 0.571 |
| Diabetes | 68 (6.7) | 4 (2.2) | 0.017 § |

Results are expressed as number of participants (percentage) for categorical variables or as average ± standard deviation for continuous variables. Between group comparisons using chi-square or Fisher's exact test (§) for categorical variables or student's t-test for continuous variables.

**Table 2**

| | Bivariate | | | Multivariable | | |
|---|---|---|---|---|---|---|
| | **No OP** | **OP** | **P-value** | **No OP** | **OP** | **P-value** |
| N | 1015 | 180 | | 1015 | 180 | |
| **Macronutrients** | | | | | | |
| Total protein | 62.3 ± 22.8 | 61.9 ± 20.1 | 0.758 | 62.4 ± 0.4 | 61.3 ± 1.0 | 0.323 |
| Vegetal protein | 19.5 ± 8.6 | 21.5 ± 8.8 | **0.004** | 19.6 ± 0.2 | 21.3 ± 0.4 | **<0.001** |
| Animal protein | 42.7 ± 18.7 | 40.4 ± 16.0 | **0.049** | 42.8 ± 0.4 | 40.0 ± 1.1 | **0.020** |
| Carbohydrates | 195.4 ± 79.5 | 205.7 ± 78.9 | 0.098 | 195.9 ± 1.2 | 202.8 ± 3 | 0.036 |
| Disaccharides | 103.6 ± 52.1 | 106.2 ± 49.9 | 0.220 | 104.1 ± 1.2 | 103.7 ± 3 | 0.917 |
| Polysaccharides | 91.3 ± 47.5 | 99.2 ± 49.9 | 0.028 | 91.4 ± 1.1 | 98.8 ± 2.6 | **0.010** |
| Total fat | 62.6 ± 24.8 | 62.3 ± 22.1 | 0.607 | 62.8 ± 0.4 | 60.8 ± 1.0 | 0.070 |
| SFA | 22.8 ± 10.4 | 22.3 ± 9.0 | 0.969 | 23.0 ± 0.2 | 21.6 ± 0.5 | **0.012** |
| MUFA | 25.3 ± 10.8 | 25.3 ± 9.8 | 0.556 | 25.4 ± 0.2 | 24.6 ± 0.5 | 0.179 |
| PUFA | 8.7 ± 4.0 | 9.0 ± 4.1 | 0.380 | 8.8 ± 0.1 | 8.8 ± 0.2 | 0.765 |
| Fiber | 16.4 ± 8.5 | 18.4 ± 8.7 | **<0.001** | 16.5 ± 0.2 | 18.2 ± 0.5 | **0.002** |
| **Micronutrients** | | | | | | |
| Cholesterol (mg/d) | 264 ± 122 | 258 ± 122 | 0.578 | 265 ± 3 | 255 ± 7 | 0.197 |
| Calcium (mg/d) | 1006 ± 507 | 954 ± 420 | 0.634 | 1010 ± 12 | 928 ± 30 | **0.012** |
| Iron (mg/d) | 9.6 ± 3.4 | 10.1 ± 3.5 | 0.100 | 9.7 ± 0.1 | 10.0 ± 0.1 | **0.044** |
| Vitamin D | 2.5 ± 1.8 | 2.3 ± 1.6 | 0.480 | 2.5 ± 0.1 | 2.2 ± 0.1 | 0.094 |
| **Foods (g/day)** | | | | | | |
| Dairy | 213 ± 178 | 188 ± 151 | 0.098 | 215 ± 5 | 175 ± 12 | **0.003** |
| Red meat | 36 ± 32 | 34 ± 31 | 0.378 | 36 ± 1 | 35 ± 2 | 0.772 |
| Processed meats | 10 ± 12 | 9 ± 12 | 0.130 | 10 ± 1 | 9 ± 1 | 0.869 |
| Wholegrain | 51 ± 55 | 61 ± 60 | **0.030** | 52 ± 2 | 58 ± 4 | 0.157 |
| Fruits [a] | 290 ± 256 | 316 ± 233 | **0.036** | 290 ± 7 | 315 ± 18 | 0.215 |
| Fruits [b] | 330 ± 280 | 359 ± 255 | **0.037** | 331 ± 8 | 354 ± 20 | 0.284 |
| Fruits [c] | 385 ± 304 | 416 ± 288 | 0.038 | 387 ± 9 | 409 ± 21 | 0.340 |
| Vegetables | 169 ± 109 | 182 ± 116 | 0.132 | 168 ± 3 | 184 ± 8 | 0.070 |
| Fish [d] | 29 ± 25 | 30 ± 24 | 0.570 | 29 ± 1 | 30 ± 2 | 0.604 |
| Fish [e] | 36 ± 28 | 37 ± 27 | 0.258 | 36 ± 1 | 37 ± 2 | 0.435 |
| **Dietary scores** | | | | | | |
| Mediterranean [f] | 3.9 ± 1.4 | 4.2 ± 1.6 | **0.010** | 3.9 ± 0.1 | 4.2 ± 0.1 | 0.056 |
| Mediterranean [g] | 4.7 ± 2.0 | 4.9 ± 1.9 | 0.196 | 4.7 ± 0.1 | 4.8 ± 0.1 | 0.366 |
| AHEI | 33 ± 10 | 35 ± 10 | **0.010** | 33 ± 1 | 35 ± 1 | **0.021** |
| **Dietary scores** | | | | | | |
| Meat & chips | -0.40 ± 1.05 | -0.45 ± 1.08 | 0.331 | -0.41 ± 0.03 | -0.39 ± 0.08 | 0.794 |
| Fruits & vegetables | 0.40 ± 1.53 | 0.64 ± 1.47 | **0.015** | 0.41 ± 0.04 | 0.56 ± 0.10 | 0.185 |
| Fat & sugar | -0.10 ± 1.38 | -0.02 ± 1.36 | 0.351 | -0.09 ± 0.03 | -0.11 ± 0.08 | 0.791 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Guidelines** | | | | | | |
| Fruits ≥2/d | 519 (51.1) | 109 (60.6) | **0.020** | 1 (ref.) | 1.37 (0.96-1.96) | 0.088 |
| Vegetables ≥3/d | 81 (8.0) | 22 (12.2) | 0.062 | 1 (ref.) | 1.59 (0.92-2.76) | 0.099 |
| Meat ≤5/week | 725 (71.4) | 125 (69.4) | 0.588 | 1 (ref.) | 0.83 (0.56-1.22) | 0.337 |
| Fish ≥1/week [a] | 676 (66.6) | 122 (67.8) | 0.757 | 1 (ref.) | 1.01 (0.70-1.46) | 0.954 |
| Fish ≥1/week [b] | 460 (45.3) | 88 (48.9) | 0.376 | 1 (ref.) | 1.10 (0.78-1.54) | 0.602 |
| Dairy ≥3/d | 107 (10.5) | 12 (6.7) | 0.110 | 1 (ref.) | 0.44 (0.22-0.86) | **0.017** |
| At least three [a] | 323 (31.8) | 70 (38.9) | 0.063 | 1 (ref.) | 1.24 (0.86-1.77) | 0.249 |
| At least three [b] | 252 (24.8) | 58 (32.2) | **0.037** | 1 (ref.) | 1.29 (0.88-1.88) | 0.195 |
| **Dietary patterns §** | | | | | | |
| Mediterranean [c] | 145 (14.3) | 35 (19.4) | 0.075 | 1 (ref.) | 1.51 (0.97-2.35) | 0.067 |
| Mediterranean [d] | 199 (19.6) | 37 (20.6) | 0.768 | 1 (ref.) | 1.06 (0.68-1.65) | 0.810 |
| AHEI | 229 (22.9) | 57 (32.2) | **0.008** | 1 (ref.) | 1.73 (1.17-2.56) | **0.006** |
| **Dietary patterns §** | | | | | | |
| Meat & chips | 245 (25.2) | 42 (23.9) | 0.710 | 1 (ref.) | 1.02 (0.67-1.55) | 0.936 |
| Fruits & vegetables | 231 (23.7) | 57 (32.4) | **0.015** | 1 (ref.) | 1.50 (0.99-2.26) | 0.054 |
| Fat & sugar | 242 (24.9) | 48 (27.3) | 0.500 | 1 (ref.) | 1.06 (0.67-1.68) | 0.794 |

[a], fresh fruit only; [b], fresh fruit + fresh juice; [c], any fruit and fruit juice; [d], fish, excluding fried; [e], any fish; [f], according to Trichopoulou et al.; [g], according to Vormund et al. §, highest quartile.

OP, osteoporosis; AHEI, alternative healthy eating index; MUFA, monounsaturated fatty acids; PUFA; polyunsaturated fatty acids; SFA; saturated fatty acids.

Results are expressed as number of participants (percentage) for categorical variables and as average ± standard deviation for continuous variables. Between group comparisons using chi-square for categorical variables and Kruskal-Wallis test for continuous variables. Multivariable analysis was performed using logistic regression for categorical variables and analysis of variance for continuous variables. Multivariable models were adjusted for total energy intake (continuous), age (continuous), body mass index (continuous), educational level (mandatory/apprenticeship/high school/university); sedentary status (yes/no), diabetes (yes/no) and antiosteoporotic treatment (yes/no). Results were expressed as multivariable-adjusted odds ratio (95% confidence interval) for the logistic models and as multivariable-adjusted average ± standard error for analysis of variance.

**Table 3**

| | Bivariate | | | Multivariable | | |
|---|---|---|---|---|---|---|
| | **Normal** | **Low TBS** | **P-value** | **Normal TBS** | **Low TBS** | **P-value** |
| N | 1098 | 87 | | 1098 | 87 | |
| **Macronutrients** | | | | | | |
| Total protein | 62.4 ± 22.6 | 58.1 ± 20.2 | 0.127 | 62.2 ± 0.4 | 60.5 ± 1.3 | 0.214 |
| Vegetal protein | 19.8 ± 8.7 | 19.4 ± 7.9 | 0.971 | 19.8 ± 0.2 | 19.9 ± 0.6 | 0.803 |
| Animal protein | 42.5 ± 18.4 | 38.7 ± 16.7 | 0.050 | 42.4 ± 0.4 | 40.5 ± 1.5 | 0.237 |
| Carbohydrates | 196.2 ± 79.5 | 197.6 ± 80.3 | 0.738 | 195.9 ± 1.1 | 201.6 ± 4.1 | 0.186 |
| Disaccharides | 103.4 ± 51.0 | 108.3 ± 61.2 | 0.607 | 103.3 ± 1.1 | 109.5 ± 4.1 | 0.149 |
| Polysaccharides | 92.3 ± 48.1 | 89.0 ± 44.4 | 0.626 | 92.1 ± 1.0 | 91.7 ± 3.6 | 0.917 |
| Total fat | 62.7 ± 24.4 | 59.4 ± 22.4 | 0.344 | 62.5 ± 0.4 | 61.5 ± 1.4 | 0.525 |
| SFA | 22.8 ± 10.2 | 21.4 ± 9.7 | 0.249 | 22.8 ± 0.2 | 22.1 ± 0.7 | 0.375 |
| MUFA | 25.3 ± 10.7 | 24.0 ± 9.8 | 0.364 | 25.3 ± 0.2 | 25.0 ± 0.8 | 0.727 |
| PUFA | 8.8 ± 4.1 | 8.3 ± 3.5 | 0.501 | 8.8 ± 0.1 | 8.6 ± 0.3 | 0.594 |
| Fiber | 16.7 ± 8.7 | 17.2 ± 8.7 | 0.447 | 16.7 ± 0.2 | 17.5 ± 0.7 | 0.250 |
| **Micronutrients** | | | | | | |
| Cholesterol (mg/d) | 263 ± 122 | 253 ± 124 | 0.286 | 263 ± 3 | 263 ± 10 | 0.940 |
| Calcium (mg/d) | 1000 ± 498 | 963 ± 460 | 0.602 | 998 ± 12 | 982 ± 42 | 0.715 |
| Iron (mg/d) | 9.7 ± 3.4 | 9.4 ± 3.2 | 0.603 | 9.7 ± 0.1 | 9.7 ± 0.2 | 0.924 |
| Vitamin D | 2.5 ± 1.8 | 2.1 ± 1.4 | 0.059 | 2.5 ± 0.1 | 2.1 ± 0.2 | 0.078 |
| **Foods (g/day)** | | | | | | |
| Dairy | 209 ± 174 | 203 ± 170 | 0.577 | 209 ± 5 | 202 ± 17 | 0.691 |
| Red meat | 36 ± 32 | 31 ± 32 | 0.074 | 36 ± 1 | 34 ± 3 | 0.576 |
| Processed meats | 10 ± 12 | 9 ± 14 | **0.045** | 10 ± 1 | 10 ± 1 | 0.873 |
| Wholegrain | 53 ± 56 | 48 ± 53 | 0.251 | 54 ± 2 | 47 ± 6 | 0.258 |
| Fruits [a] | 291 ± 249 | 337 ± 313 | 0.362 | 291 ± 7 | 344 ± 25 | 0.041 |
| Fruits [b] | 331 ± 273 | 377 ± 329 | 0.424 | 331 ± 8 | 382 ± 27 | 0.071 |
| Fruits [c] | 387 ± 299 | 424 ± 345 | 0.576 | 387 ± 8 | 432 ± 30 | 0.144 |
| Vegetables | 170 ± 109 | 168 ± 119 | 0.396 | 170 ± 3 | 175 ± 11 | 0.624 |
| Fish [d] | 30 ± 25 | 25 ± 23 | **0.035** | 29 ± 1 | 26 ± 3 | 0.232 |
| Fish [e] | 36 ± 28 | 31 ± 25 | 0.064 | 36 ± 1 | 32 ± 3 | 0.270 |
| **Dietary scores** | | | | | | |
| Mediterranean [f] | 4.0 ± 1.5 | 4.1 ± 1.4 | 0.479 | 4.0 ± 0.1 | 4.1 ± 0.2 | 0.353 |
| Mediterranean [g] | 4.7 ± 2.0 | 4.5 ± 1.9 | 0.401 | 4.7 ± 0.1 | 4.7 ± 0.2 | 0.869 |
| AHEI | 34 ± 10 | 33 ± 10 | 0.899 | 34 ± 1 | 34 ± 1 | 0.738 |
| **Dietary patterns** | | | | | | |
| Meat & chips | -0.42 ± 1.05 | -0.41 ± 1.12 | 0.706 | -0.43 ± 0.03 | -0.28 ± 0.11 | 0.204 |
| Fruits & vegetables | 0.44 ± 1.54 | 0.38 ± 1.51 | 0.929 | 0.43 ± 0.04 | 0.44 ± 0.15 | 0.976 |
| Fat & sugar | -0.11 ± 1.37 | -0.07 ± 1.45 | 0.695 | -0.11 ± 0.03 | -0.06 ± 0.11 | 0.664 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Guidelines** | | | | | | |
| Fruits ≥2/d | 571 (52) | 50 (57.5) | 0.326 | 1 (ref.) | 1.25 (0.78-2.00) | 0.354 |
| Vegetables ≥3/d | 92 (8.4) | 10 (11.5) | 0.319 | 1 (ref.) | 1.50 (0.72-3.11) | 0.275 |
| Meat ≤5/week | 778 (70.9) | 66 (75.9) | 0.321 | 1 (ref.) | 1.09 (0.64-1.86) | 0.763 |
| Fish ≥1/week [e] | 743 (67.7) | 52 (59.8) | 0.131 | 1 (ref.) | 0.80 (0.50-1.27) | 0.339 |
| Fish ≥1/week [d] | 507 (46.2) | 35 (40.2) | 0.284 | 1 (ref.) | 0.85 (0.54-1.34) | 0.481 |
| Dairy ≥3/d | 109 (9.9) | 8 (9.2) | 0.826 | 1 (ref.) | 0.84 (0.38-1.88) | 0.675 |
| At least three [e] | 358 (32.6) | 33 (37.9) | 0.309 | 1 (ref.) | 1.25 (0.78-2.01) | 0.354 |
| At least three [d] | 280 (25.5) | 25 (28.7) | 0.506 | 1 (ref.) | 1.18 (0.71-1.96) | 0.530 |
| **Dietary scores §** | | | | | | |
| Mediterranean [f] | 162 (14.8) | 14 (16.1) | 0.736 | 1 (ref.) | 1.24 (0.67-2.29) | 0.498 |
| Mediterranean [g] | 217 (19.8) | 15 (17.2) | 0.568 | 1 (ref.) | 1.06 (0.58-1.97) | 0.844 |
| AHEI | 263 (24.4) | 20 (23.5) | 0.865 | 1 (ref.) | 1.10 (0.63-1.90) | 0.744 |
| **Dietary patterns §** | | | | | | |
| Meat & chips | 259 (24.6) | 24 (29.3) | 0.341 | 1 (ref.) | 1.64 (0.96-2.79) | 0.070 |
| Fruits & vegetables | 266 (25.2) | 20 (24.4) | 0.869 | 1 (ref.) | 1.03 (0.58-1.84) | 0.908 |
| Fat & sugar | 260 (24.6) | 23 (28.1) | 0.492 | 1 (ref.) | 1.32 (0.72-2.40) | 0.368 |

[a], fresh fruit only; [b], fresh fruit + fresh juice; [c], any fruit and fruit juice; [d], fish, excluding fried; [e], any fish; [f], according to Trichopoulou et al.; [g], according to Vormund et al. §, highest quartile.

TBS, trabecular bone score; AHEI, alternative healthy eating index; MUFA, monounsaturated fatty acids; PUFA; polyunsaturated fatty acids; SFA; saturated fatty acids.

Results are expressed as number of participants (percentage) for categorical variables and as average ± standard deviation for continuous variables. Between group comparisons using chi-square for categorical variables and Kruskal-Wallis test for continuous variables. Multivariable analysis was performed using logistic regression for categorical variables and analysis of variance for continuous variables. Multivariable models were adjusted for total energy intake (continuous), age (continuous), body mass index (continuous), educational level (mandatory/apprenticeship/high school/university); sedentary status (yes/no), diabetes (yes/no) and antiosteoporotic treatment (yes/no). Results were expressed as multivariable-adjusted odds ratio (95% confidence interval) for the logistic models and as multivariable-adjusted average ± standard error for analysis of variance.

## SUPPLEMENTAL FILES

**Supplemental table 1**: clinical characteristics of included and excluded participants.

| | Included | Excluded | P-value |
|---|---|---|---|
| Sample size | 1215 | 260 | |
| Age (years) | 64.3 ± 7.5 | 65.5 ± 7.9 | 0.017 |
| Educational level | | | <0.001 |
| University | 171 (14.1) | 26 (10.3) | |
| High school | 327 (26.9) | 55 (21.8) | |
| Apprenticeship | 496 (40.8) | 88 (34.9) | |
| Mandatory | 221 (18.2) | 83 (32.9) | |
| Family history of osteoporosis | 205 (16.9) | 35 (13.9) | 0.244 |
| Smoking status | | | 0.056 |
| Never | 565 (46.5) | 110 (46.8) | |
| Former | 451 (37.1) | 73 (31.1) | |
| Current | 199 (16.4) | 52 (22.1) | |
| Body mass index ($kg/m^2$) | 25.7 ± 4.4 | 26.8 ± 4.9 | <0.001 |
| Body mass index categories | | | 0.006 |
| Normal | 576 (47.4) | 102 (39.2) | |
| Overweight | 434 (35.7) | 94 (36.2) | |
| Obese | 205 (16.9) | 64 (24.6) | |
| Sedentary status | 793 (65.3) | 30 (69.8) | 0.542 |
| Diabetes | 72 (6.0) | 37 (14.7) | <0.001 |
| Antiosteoporotic treatment | 113 (9.3) | 28 (10.8) | 0.465 |

Results are expressed as number of participants (percentage) for categorical variables or as average ± standard deviation for continuous variables. Statistical analysis by chi-square for categorical variables and student's t-test for continuous variables.

**Supplemental table 2**: Characteristics of the participants with and without low trabecular bone score.

| | Normal TBS | Low TBS | P-value |
|---|---|---|---|
| Sample size | 1098 | 87 | |
| Age (years) | 64.1 ± 7.4 | 68.3 ± 7.0 | <0.001 |
| Education | | | 0.387 |
| University | 157 (14.3) | 9 (10.3) | |
| High school | 299 (27.2) | 19 (21.8) | |
| Apprenticeship | 445 (40.5) | 40 (46.0) | |
| Mandatory | 197 (17.9) | 19 (21.8) | |
| Body mass index (kg/m$^2$) | 25.8 ± 4.4 | 24.6 ± 4.1 | 0.011 |
| Body mass index categories | | | 0.064 § |
| Underweight | 18 (1.6) | 3 (3.5) | |
| Normal | 491 (44.7) | 47 (54.0) | |
| Overweight | 397 (36.2) | 29 (33.3) | |
| Obese | 192 (17.5) | 8 (9.2) | |
| Smoking status | | | 0.370 |
| Never | 510 (46.5) | 43 (49.4) | |
| Former | 417 (38.0) | 27 (31.0) | |
| Current | 171 (15.6) | 17 (19.5) | |
| Sedentary | 719 (65.5) | 53 (60.9) | 0.390 |
| Diabetes | 67 (6.1) | 4 (4.6) | 0.814 § |

TBS: Trabecular bone Score.

Results are expressed as number of participants (percentage) for categorical variables or as average ± standard deviation for continuous variables. Between group comparisons using chi-square or Fisher's exact test (§) for categorical variables or student's t-test for continuous variables.

**Supplemental table 3**: Bivariate and multivariable analysis of the dietary markers among participants with and without major osteoporotic fracture.

| | Bivariate | | | Multivariable | | |
|---|---|---|---|---|---|---|
| | **No MOF** | **MOF** | **P-value** | **No MOF** | **MOF** | **P-value** |
| N | 1074 | 141 | | 1074 | 141 | |
| **Macronutrients** | | | | | | |
| Total protein | 61.9 ± 22.4 | 63.2 ± 22.4 | 0.416 | 62 ± 0.4 | 62.4 ± 1.0 | 0.716 |
| Vegetal protein | 19.8 ± 8.8 | 19.8 ± 7.5 | 0.440 | 19.8 ± 0.2 | 19.5 ± 0.4 | 0.451 |
| Animal protein | 42.1 ± 18.3 | 43.4 ± 18.8 | 0.361 | 42.2 ± 0.4 | 43.0 ± 1.2 | 0.550 |
| Carbohydrates | 196.0 ± 80.6 | 199.3 ± 68.9 | 0.237 | 196.5 ± 1.2 | 195.6 ± 3.3 | 0.808 |
| Disaccharides | 103.0 ± 52.1 | 110.0 ± 48.0 | **0.022** | 103.3 ± 1.2 | 107.7 ± 3.2 | 0.205 |
| Polysaccharides | 92.6 ± 48.6 | 88.5 ± 41.1 | 0.689 | 92.8 ± 1.0 | 87.3 ± 2.8 | 0.072 |
| Total fat | 62.2 ± 24.2 | 63.9 ± 25.2 | 0.360 | 62.3 ± 0.4 | 62.7 ± 1.1 | 0.777 |
| SFA | 22.6 ± 10.1 | 23.8 ± 11.1 | 0.176 | 22.6 ± 0.2 | 23.3 ± 0.6 | 0.262 |
| MUFA | 25.2 ± 10.6 | 25.3 ± 10.8 | 0.786 | 25.3 ± 0.2 | 24.9 ± 0.6 | 0.563 |
| PUFA | 8.8 ± 4.0 | 8.8 ± 4.1 | 0.914 | 8.8 ± 0.1 | 8.6 ± 0.3 | 0.445 |
| Fiber | 16.6 ± 8.7 | 17.2 ± 7.8 | 0.159 | 16.7 ± 0.2 | 16.8 ± 0.6 | 0.793 |
| **Micronutrients** | | | | | | |
| Cholesterol (mg/d) | 263 ± 120 | 265 ± 132 | 0.898 | 263 ± 3 | 260 ± 8 | 0.713 |
| Calcium (mg/d) | 991 ± 496 | 1032 ± 476 | 0.203 | 995 ± 12 | 1008 ± 33 | 0.694 |
| Iron (mg/d) | 9.6 ± 3.4 | 10.0 ± 3.3 | 0.198 | 9.7 ± 0.1 | 9.8 ± 0.2 | 0.332 |
| Vitamin D | 2.4 ± 1.7 | 2.6 ± 2.3 | 0.376 | 2.4 ± 0.1 | 2.5 ± 0.1 | 0.709 |
| **Foods (g/day)** | | | | | | |
| Dairy | 207 ± 174 | 219 ± 168 | 0.279 | 208 ± 5 | 212 ± 14 | 0.824 |
| Red meat | 36 ± 32 | 35 ± 30 | 0.573 | 36 ± 1 | 35 ± 3 | 0.698 |
| Processed meats | 9 ± 12 | 10 ± 15 | 0.396 | 9 ± 0 | 10 ± 1 | 0.544 |
| Wholegrain | 52 ± 56 | 54 ± 55 | 0.571 | 53 ± 2 | 53 ± 5 | 0.957 |
| Fruits [a] | 290 ± 251 | 325 ± 264 | 0.076 | 291 ± 7 | 318 ± 20 | 0.194 |
| Fruits [b] | 329 ± 275 | 373 ± 290 | 0.061 | 330 ± 8 | 363 ± 22 | 0.152 |
| Fruits [c] | 382 ± 300 | 447 ± 310 | **0.004** | 383 ± 8 | 437 ± 23 | **0.030** |
| Vegetables | 172 ± 111 | 161 ± 108 | 0.147 | 172 ± 3 | 160 ± 9 | 0.220 |
| Fish [d] | 29 ± 24 | 30 ± 30 | 0.978 | 29 ± 1 | 30 ± 2 | 0.932 |
| Fish [e] | 36 ± 27 | 37 ± 36 | 0.791 | 36 ± 1 | 36 ± 2 | 0.816 |
| **Dietary scores** | | | | | | |
| Mediterranean [f] | 4.0 ± 1.5 | 3.9 ± 1.4 | 0.422 | 4.0 ± 0.1 | 3.8 ± 0.1 | 0.295 |
| Mediterranean [g] | 4.7 ± 1.9 | 4.7 ± 2.1 | 1.000 | 4.7 ± 0.1 | 4.6 ± 0.1 | 0.655 |
| AHEI | 34 ± 10 | 34 ± 10 | 0.640 | 34 ± 0.3 | 34 ± 0.8 | 0.916 |
| **Dietary patterns** | | | | | | |
| Meat & chips | -0.42 ± 1.02 | -0.37 ± 1.27 | 0.488 | -0.42 ± 0.03 | -0.36 ± 0.09 | 0.520 |
| Fruits & vegetables | 0.43 ± 1.50 | 0.45 ± 1.75 | 0.814 | 0.44 ± 0.04 | 0.39 ± 0.11 | 0.674 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Fat & sugar | -0.10 ± 1.39 | -0.14 ± 1.22 | 0.903 | -0.09 ± 0.03 | -0.20 ± 0.09 | 0.253 |
| **Guidelines** | | | | | | |
| Fruits ≥2/d | 552 (51.4) | 85 (60.3) | 0.047 | 1 (ref.) | 1.31 (0.89-1.92) | 0.168 |
| Vegetables ≥3/d | 92 (8.6) | 13 (9.2) | 0.795 | 1 (ref.) | 1.03 (0.54-1.96) | 0.924 |
| Meat ≤5/week | 761 (70.9) | 104 (73.8) | 0.474 | 1 (ref.) | 1.16 (0.76-1.77) | 0.499 |
| Fish ≥1/week [e] | 718 (66.9) | 96 (68.1) | 0.770 | 1 (ref.) | 1.01 (0.68-1.49) | 0.969 |
| Fish ≥1/week [d] | 498 (46.4) | 58 (41.1) | 0.241 | 1 (ref.) | 0.76 (0.52-1.11) | 0.152 |
| Dairy ≥3/d | 103 (9.6) | 16 (11.4) | 0.509 | 1 (ref.) | 1.04 (0.57-1.91) | 0.887 |
| At least three [e] | 349 (32.5) | 51 (36.2) | 0.383 | 1 (ref.) | 1.04 (0.71-1.54) | 0.834 |
| At least three [d] | 273 (25.4) | 40 (28.4) | 0.451 | 1 (ref.) | 1.05 (0.69-1.59) | 0.815 |
| **Dietary scores §** | | | | | | |
| Mediterranean [f] | 163 (15.2) | 20 (14.2) | 0.757 | 1 (ref.) | 0.94 (0.56-1.57) | 0.804 |
| Mediterranean [g] | 207 (19.3) | 31 (22.0) | 0.446 | 1 (ref.) | 1.27 (0.83-1.94) | 0.271 |
| AHEI | 251 (23.8) | 39 (28.5) | 0.225 | 1 (ref.) | 1.27 (0.83-1.94) | 0.271 |
| **Dietary patterns §** | | | | | | |
| Meat & chips | 258 (25) | 33 (24.8) | 0.967 | 1 (ref.) | 1.00 (0.64-1.57) | 0.997 |
| Fruits & vegetables | 258 (25) | 33 (24.8) | 0.967 | 1 (ref.) | 0.86 (0.54-1.38) | 0.527 |
| Fat & sugar | 265 (25.7) | 26 (19.6) | 0.126 | 1 (ref.) | 0.55 (0.32-0.93) | **0.027** |

[a], fresh fruit only; [b], fresh fruit + fresh juice; [c], any fruit and fruit juice; [d], fish, excluding fried; [e], any fish; [f], according to Trichopoulou et al.; [g], according to Vormund et al. §, highest quartile.

MOF, major osteoporotic fracture; AHEI, alternative healthy eating index; MUFA, monounsaturated fatty acids; PUFA; polyunsaturated fatty acids; SFA; saturated fatty acids.

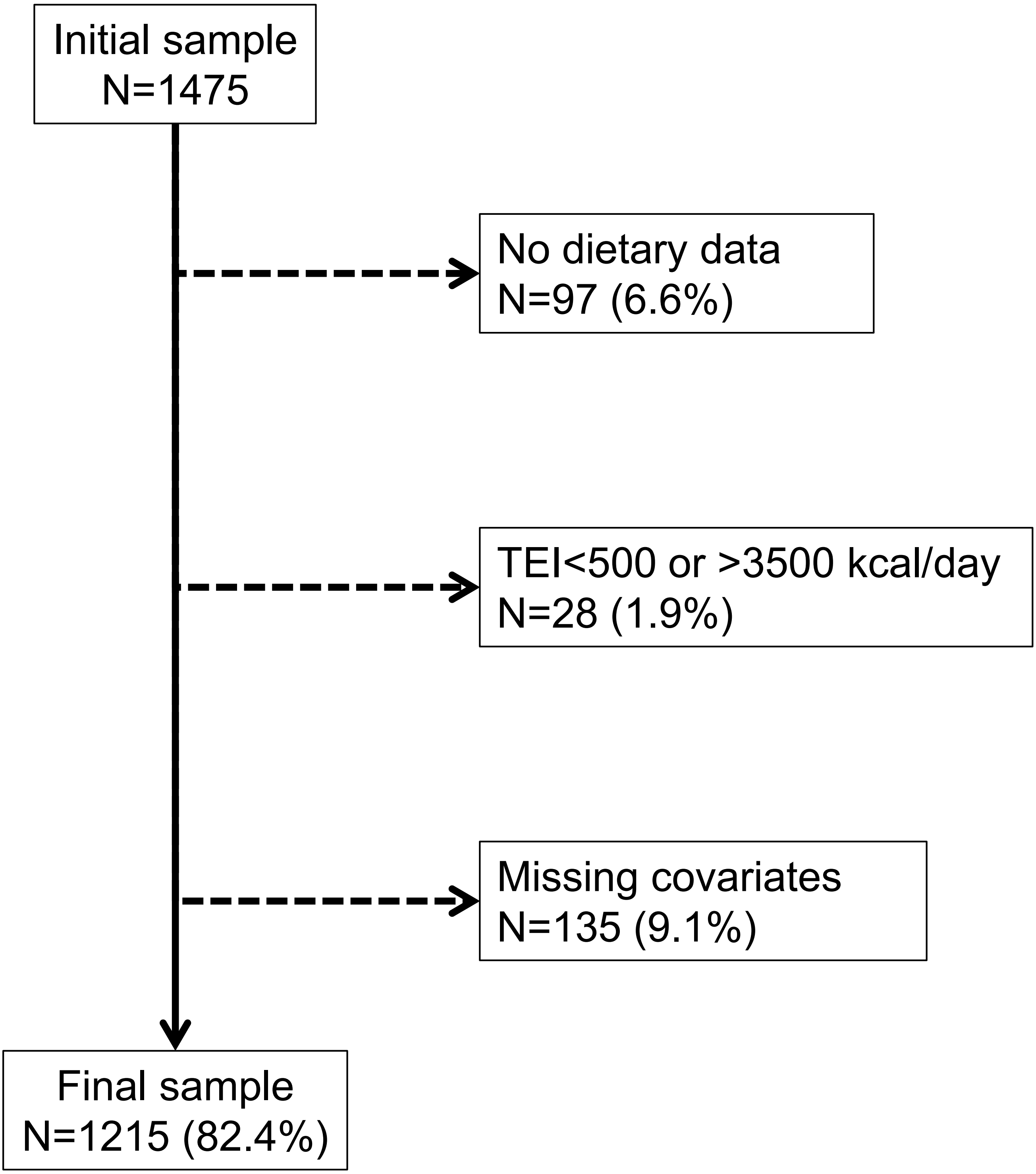
Results are expressed as number of participants (percentage) for categorical variables and as average ± standard deviation for continuous variables. Between group comparisons using chi-square for categorical variables and Kruskal-Wallis test for continuous variables. Multivariable analysis was performed using logistic regression for categorical variables and analysis of variance for continuous variables. Multivariable models were adjusted for total energy intake (continuous), age (continuous), body mass index (continuous), educational level (mandatory/apprenticeship/high school/university); sedentary status (yes/no), diabetes (yes/no) and antiosteoporotic treatment (yes/no). Results were expressed as multivariable-adjusted odds ratio (95% confidence interval) for the logistic models and as multivariable-adjusted average ± standard error for analysis of variance.

**Supplemental table 4**: Analysis of specific dietary habits and medical conditions among participants with or without calcium supplements (≥ 500mg/d).

| | **No supplements** | **Supplements** | **P-value** |
|---|---|---|---|
| N | 684 | 531 | |
| Dietary calcium (mg/day) | | | |
| Bivariate | 968 ± 495 | 1032 ± 490 | 0.008 |
| Multivariable | 984 ± 15 | 1011 ± 17 | 0.257 |
| Dairy (g/day) | | | |
| Bivariate | 199.9 ± 177.2 | 220.1 ± 168.5 | 0.006 |
| Multivariable | 203.7 ± 6.3 | 215.2 ± 7.2 | 0.243 |
| Dairy ≥ 3/day (%) | | | |
| Bivariate | 50 (7.3) | 69 (13.0) | 0.001 |
| Multivariable | 1 (ref.) | 1.72 (1.12 - 2.64) | 0.013 |
| Osteoporosis | | | |
| Bivariate | 77 (11.4) | 103 (19.8) | <0.001 |
| Multivariable | 1 (ref.) | 1.15 (0.80 - 1.67) | 0.454 |
| Low TBS | | | |
| Bivariate | 34 (5.1) | 53 (10.2) | 0.001 |
| Multivariable | 1 (ref.) | 1.61 (0.99 - 2.62) | 0.055 |
| Prevalent major fracture | | | |
| Bivariate | 52 (7.6) | 89 (16.7) | <0.001 |
| Multivariable | 1 (ref.) | 1.79 (1.21 - 2.67) | 0.004 |
| Prevalent grade 2-3 fractures | | | |
| Bivariate | 102 (14.9) | 124 (23.3) | <0.001 |
| Multivariable | 1 (ref.) | 1.32 (0.96 - 1.82) | 0.090 |

TBS: trabecular bone score.

Results are expressed as number of participants (percentage) for categorical variables and as average ± standard deviation for continuous variables. Between group comparisons using chi-square for categorical variables and Kruskal-Wallis test for continuous variables. Multivariable analysis was performed using logistic regression for categorical variables and analysis of variance for continuous variables. Multivariable models were adjusted for total energy intake (continuous), age (continuous), body mass index categories (continuous), educational level (mandatory/ apprenticeship/high school/university); sedentary status (yes/no), diabetes (yes/no) and antiosteoporotic treatment (yes/no). Results were expressed as multivariable-adjusted odds ratio (95% confidence interval) for the logistic models and as multivariable-adjusted average ± standard error for analysis of variance.


Initial sample
N=1475
No dietary data
N=97 (6.6%)
TEI<500 or >3500 kcal/day
N=28 (1.9%)
Missing covariates
N=135 (9.1%)
Final sample
N=1215 (82.4%)