

Vitamin K intake and hip fractures in women: a prospective study¹⁻³

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ABSTRACT

Background: Vitamin K mediates the γ -carboxylation of glutamyl residues on several bone proteins, notably osteocalcin. High serum concentrations of undercarboxylated osteocalcin and low serum concentrations of vitamin K are associated with lower bone mineral density and increased risk of hip fracture. However, data are limited on the effects of dietary vitamin K.

Objective: We investigated the hypothesis that high intakes of vitamin K are associated with a lower risk of hip fracture in women.

Design: We conducted a prospective analysis within the Nurses' Health Study cohort. Diet was assessed in 72 327 women aged 38–63 y with a food-frequency questionnaire in 1984 (baseline). During the subsequent 10 y of follow-up, 270 hip fractures resulting from low or moderate trauma were reported.

Results: Women in quintiles 2–5 of vitamin K intake had a significantly lower age-adjusted relative risk (RR: 0.70; 95% CI: 0.53, 0.93) of hip fracture than women in the lowest quintile (<109 $\mu\text{g}/\text{d}$). Risk did not decrease between quintiles 2 and 5 and risk estimates were not altered when other risk factors for osteoporosis, including calcium and vitamin D intakes, were added to the models. Risk of hip fracture was also inversely associated with lettuce consumption (RR: 0.55; 95% CI: 0.40, 0.78) for one or more servings per day compared with one or fewer servings per week), the food that contributed the most to dietary vitamin K intakes.

Conclusions: Low intakes of vitamin K may increase the risk of hip fracture in women. The data support the suggestion for a reassessment of the vitamin K requirements that are based on bone health and blood coagulation. *Am J Clin Nutr* 1999;69:74–9.

KEY WORDS Bone, diet, fractures, hips, osteoporosis, phyloquinone, undercarboxylated osteocalcin, vitamin K, Nurses' Health Study, women

INTRODUCTION

Vitamin K functions as a cofactor for the enzyme that catalyzes the posttranslational conversion of protein-bound glutamyl residues to γ -carboxyglutamyl residues (1). Its classic role in this respect involves the synthesis of several blood coagulation factors (2, 3), and the maintenance of plasma prothrombin concentrations is the basis for the recommended dietary allowance of 1 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ (4). More recently, the identifica-

tion of γ -carboxyglutamyl-containing proteins in bone, notably osteocalcin, has created interest in the role of vitamin K in bone metabolism (5–7). Although most of the osteocalcin synthesized by osteoblasts during bone matrix formation is incorporated into bone because of the high specificity of the γ -carboxyglutamyl residues for the calcium ion of the hydroxyapatite molecule (8), a small amount is released into the circulation. The serum concentration of undercarboxylated osteocalcin may be a more sensitive measure of vitamin K status than the traditional blood coagulation tests (9). High concentrations of circulating undercarboxylated osteocalcin have been associated with low bone mineral density (10, 11) and increased risk of hip fracture (12–14).

In addition to the γ -carboxylation of bone proteins, vitamin K may influence bone metabolism through its effect on urinary calcium excretion (15, 16) or by inhibiting the production of bone resorbing agents such as prostaglandin E_2 (17, 18) and interleukin 6 (19).

Accumulating evidence supports an active role for vitamin K in bone health. Low concentrations of circulating vitamin K have been associated with low bone mineral density (20) and bone fractures (21, 22). Supplementation with vitamin K has been shown to reduce serum concentrations of undercarboxylated osteocalcin (9, 23, 24) and urinary calcium excretion (23, 25) and has been associated with improved bone density (25, 26). Because oral anticoagulants inhibit γ -carboxyglutamyl synthesis, one would expect poorer bone health in patients taking these medications. However, such studies have produced mixed results (27–30), which may be attributed to bias due to lower physical activity levels in cardiac patients taking anticoagulants. A more recent study by Philip et al (31) showed that the bone density of the lumbar spine in patients receiving long-term warfarin therapy was 10% less than that of control subjects.

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Limited data on the vitamin K content of foods has restricted the examination of dietary vitamin K in relation to bone health. With the recent availability of food-composition data on vitamin K, we investigated the association between vitamin K intake and osteoporotic fractures of the hip in women in the Nurses' Health Study. Vitamin K intake in the present study refers exclusively to the intake of phyloquinone (vitamin K₁), which is the predominant form of vitamin K in foods.

SUBJECTS AND METHODS

The Nurses' Health Study is a prospective cohort study that includes 120701 female, registered nurses living in 1 of 11 US states who were 30–55 y of age when they responded to the initial questionnaire that was mailed in 1976. Information on lifestyle, health behaviors, and disease history was obtained at that time and follow-up questionnaires have been mailed every 2 y since then to update data, to collect information on new risk factors of interest, and to identify incident diseases.

Dietary assessment

Dietary intakes were assessed in 1980, 1984, 1986, and 1990 when a semiquantitative food-frequency questionnaire (FFQ) was included with the regular biennial mailing. Each FFQ consisted of a list of foods and a selection of 9 categories ranging from "never or less than once per month" to "six or more times per day" for reporting the frequency of consumption of the standard serving size of each food. Daily nutrient intakes were calculated by multiplying the nutrient content per serving of each food by the reported frequency of consumption and summing over all foods. Participants were also asked to specify the type of fat and brand of oil or margarine that they used in cooking and baking; this information was used to calculate nutrients in the fried and baked food items on the questionnaire. Intakes of multivitamin-mineral preparations and other nutrient supplements were included in total daily intakes. Nutrients that are correlated with total energy intake (vitamin K, calcium, vitamin D, and protein) were adjusted for total energy with regression analysis (32).

The vitamin K contents of the food items on the FFQ were obtained from the US Department of Agriculture, Human Nutrition Research Center on Aging at Tufts University (33, 34). Foods were analyzed for phyloquinone by HPLC (35). In a study of 34 adults, the mean of 3 fasting plasma phyloquinone concentrations was significantly correlated ($r = 0.51$, $P = 0.004$) with the calculated dietary intakes from 3 sets of 4-d weighed diet records (36).

The initial 1980 FFQ, which contained only 60 food items, did not include lettuce, whereas the subsequent expanded questionnaires included both the iceberg and romaine varieties. Because lettuce was the greatest contributor to dietary vitamin K intake in this cohort, we did not use the 1980 dietary data. Data from the 1984 FFQ, which contained 116 food items, became our baseline measure. A few additional foods appeared on subsequent questionnaires, but none of these were important contributors to vitamin K intake. A validation study was performed in 127 men who completed the FFQ and two 1-wk diet records (37, 38). For foods that are good sources of vitamin K, the correlations between daily intakes from the 2 dietary assessment methods were as follows: $r = 0.73$ for lettuce, $r = 0.46$ for broccoli, and $r = 0.25$ for spinach (38). Another study in 27 adults showed a significant correlation ($r = 0.53$, $P = 0.004$) between

vitamin K intake calculated from the FFQ and that from three 4-d diet records; the mean intake from the FFQ was higher than that from the diet records: 192 compared with 121 $\mu\text{g}/\text{d}$ (SL Booth, unpublished observations, 1996).

Identification of fractures

On the 1982 follow-up questionnaire, the women were asked to report all previous hip fractures along with the date of occurrence, the circumstances leading to the fracture, and the exact fracture site. Incident fractures were similarly reported on subsequent questionnaires. Cases in this study included only those fractures of the proximal femur that were due to low or moderate trauma (eg, falling from the height of a chair, tripping, and slipping on ice) and that occurred after the 1984 questionnaire was returned. Fractures due to motor vehicle accidents or high-impact activities (eg, skiing and horseback riding) were excluded from the analysis ($\approx 20\%$). We expected valid self-reported fractures from a population of registered nurses. A validation study in a sample of the population confirmed this expectation when medical records agreed with reported fractures in all 30 cases (39).

Covariate information

Weight was requested on all biennial questionnaires. We calculated current body mass index (BMI; in kg/m^2) from the current weight and from the height reported on the initial 1976 questionnaire. Physical activity was assessed on the 1980 questionnaire when women were asked to estimate the number of hours per weekday and per weekend day that they engaged in vigorous (eg, jogging, heavy housework, and digging in the garden) and moderate (eg, walking, light housework, and yard work) activities. Both BMI and physical activity were categorized into quintiles for analysis. Smoking status (never, past, or current), menopausal status (premenopausal, postmenopausal, or dubious status), and use of estrogen replacement medication by postmenopausal women (never, past, or current) were assessed on all questionnaires.

Study population

Our baseline population included the women ($n = 81\,757$) in the Nurses' Health Study cohort who completed the 1984 FFQ. We then excluded women who reported a hip fracture or a diagnosis of cancer, heart disease, stroke, or osteoporosis before baseline because these conditions could cause a change in usual dietary habits. After these exclusions, 72 327 women remained in the study population.

Statistical analysis

Person-time was accrued for each participant from the return date of their 1984 questionnaire until death, the occurrence of a hip fracture that qualified as a case, or the end of follow-up on June 1, 1994. At each 2-y follow-up period, current BMI, smoking status, menopausal status, and use of estrogen replacement medication were used to allocate person-time to the appropriate category for each variable. For physical activity, the 1980 measure was used to classify person-time for the entire follow-up period.

In the main analyses, women were categorized into quintiles of vitamin K intake in 1984 and this measure was related to the incidence of all subsequent fractures. Women were also classified into categories of lettuce, broccoli, and spinach consumption (the most significant contributors to dietary vitamin K in



this cohort) based on their responses on the 1984 FFQ. Frequency-of-consumption categories were combined as necessary to avoid sparse data cells.

Secondary analyses of vitamin K intakes were performed that incorporated data from the 1986 and 1990 FFQs. In these analyses, the 1984 measure was related to fracture incidence during the first 2-y follow-up period (1984–1986), an average of the 1984 and 1986 measures was related to fracture incidence during the next 2 follow-up periods (1986–1990), and an average vitamin K intake from all 3 questionnaires was related to fracture incidence during the last 2 follow-up periods (1990–1994).

We computed incidence rates for each quintile of vitamin K or category of food consumption by dividing the number of fractures by the person-time within each category. Relative risks were computed by comparing each incidence rate to that in the lowest, or reference, category (40). We used proportional hazards models to adjust simultaneously for potential confounding variables (41). To examine the linear trend over categories of dietary intake, we used the Mantel-Haenszel test with the median intake value assigned to each category.

RESULTS

The food items on the FFQ that contributed the most to dietary vitamin K intakes were iceberg lettuce (29%), broccoli (15%), cooked spinach (12%), cabbage (7%), raw spinach (6%), romaine lettuce (6%), Brussels sprouts (5%), kale and other greens (4%), and oil and vinegar dressing (2%). The vitamin K intake from total oil consumption could not be assessed with our food-based questionnaire. Over the course of the study, only 1–4% of the participants were receiving ≥ 10 μg vitamin K/d from a multivitamin-mineral preparation.

Adjustment for total energy intake did not greatly change the vitamin K values for most women. In 1984, the median vitamin K intake was 169 $\mu\text{g}/\text{d}$ with a range of 41–604 $\mu\text{g}/\text{d}$ (1st–99th percentiles); after adjustment for total energy, the median vitamin K intake was 163 $\mu\text{g}/\text{d}$ with a range of 45–563 $\mu\text{g}/\text{d}$. Energy-adjusted vitamin K values were used in all analyses.

The characteristics of the study population at baseline in 1984, by quintile of vitamin K intake, are presented in **Table 1**. Women in the upper quintiles were older and more likely to be postmenopausal. In addition, calcium and protein intakes increased with increasing concentrations of vitamin K. Because of the large sample size, many of the other characteristics and dietary measures showed significant differences over quintiles of vitamin K, although the actual differences were small and did not appear to be of practical significance.

During 10 y of follow-up (702076 person-years), we identified 270 hip fracture cases in the study population. The median age at the time of the fracture was 62 y. In age-adjusted analyses based on the 1984 baseline measure of diet, women in quintiles 2, 3, 4, and 5 each had a 24–36% reduction in risk of hip fracture compared with the women in quintile 1. However, only the result for quintile 3 was significant. Further multivariate adjustment for BMI, menopausal status, use of estrogen replacement medication, cigarette smoking status, physical activity levels, and daily intakes of calcium, vitamin D, protein, alcohol, and caffeine had little effect on the risk estimates. Although a higher intake of vitamin K was associated with a decreased risk of hip fracture, we did not observe a linear dose-dependent trend ($P = 0.32$). A second-order polynomial model showed a significant improvement in model fit ($P = 0.008$) compared with the linear model.

When data for the women in quintiles 2–5 were combined, the age-adjusted RR of hip fracture was significantly lower (RR: 0.70; 95% CI: 0.53, 0.93) than that of women in quintile 1. Conversely, an increased risk of hip fracture was evident among the women with the lowest vitamin K intakes (quintile 1). The age-adjusted RRs of hip fracture were 1.43 (95% CI: 1.08, 1.89) and 1.55 (95% CI: 1.08, 2.22) in the lowest quintile and decile, respectively. Because this was a post hoc characterization of the data, further studies are needed to confirm the threshold effect observed in this cohort.

In the secondary analysis, in which the 1986 and 1990 dietary data were used to update the vitamin K exposure during follow-up, we observed the same pattern of decreased risk of hip fracture in the upper quintiles of intake. The age-adjusted RR for quintiles

TABLE 1

Characteristics of the women in the study population ($n = 72327$) by quintiles (Q1–Q5) of vitamin K intake at baseline in 1984

	Vitamin K intake ^{1,2}				
	Q1, <109 $\mu\text{g}/\text{d}$ ($n = 14\ 606$)	Q2, 109–145 $\mu\text{g}/\text{d}$ ($n = 14\ 552$)	Q3, 146–183 $\mu\text{g}/\text{d}$ ($n = 14\ 569$)	Q4, 184–242 $\mu\text{g}/\text{d}$ ($n = 14\ 331$)	Q5, >242 $\mu\text{g}/\text{d}$ ($n = 14\ 269$)
Age (y)	49 \pm 7 ³	50 \pm 7	51 \pm 7	51 \pm 7	52 \pm 7
Body mass index (kg/m ²)	25 \pm 5	25 \pm 5	25 \pm 5	25 \pm 5	25 \pm 5
Physical activity (h/wk) ⁴	47 \pm 26	46 \pm 26	46 \pm 26	46 \pm 26	45 \pm 26
Nutrient intake					
Calcium (mg/d) ^{1,2}	805 \pm 412	828 \pm 396	861 \pm 402	899 \pm 424	975 \pm 461
Vitamin D (IU/d) ^{1,2}	283 \pm 245	290 \pm 238	303 \pm 247	313 \pm 251	344 \pm 286
Protein (g/d) ¹	67 \pm 13	69 \pm 12	71 \pm 12	73 \pm 12	77 \pm 14
Alcohol (g/d)	6 \pm 12	6 \pm 11	7 \pm 11	7 \pm 10	7 \pm 10
Caffeine (mg/d)	322 \pm 242	318 \pm 230	320 \pm 232	314 \pm 226	313 \pm 238
Current smoker (%)	28	25	24	22	23
Postmenopausal (%)	42	44	46	50	52
Current user of estrogen replacement medication (%) ⁵	22	23	25	24	24

¹ Adjusted for total energy intake by using regression analysis.

² Includes intake from supplements.

³ $\bar{x} \pm \text{SD}$.

⁴ Includes all moderate and vigorous activities.

⁵ Calculated for the 33791 women who were postmenopausal at baseline.

TABLE 2

Relative risks (RRs) with 95% CIs for risk of hip fracture by quintiles 1–5 (Q1–Q5) of 1984 baseline vitamin K intake in 72 327 women aged 38–63 y who were followed for up to 10 y

Vitamin K intake ¹	Age-adjusted RR (95% CI)	Multivariate RR (95% CI) ²
Q1 (n = 65)	1.00	1.00
Q2 (n = 52)	0.76 (0.53, 1.10)	0.80 (0.55, 1.15)
Q3 (n = 46)	0.64 (0.44, 0.93)	0.67 (0.46, 0.99)
Q4 (n = 52)	0.69 (0.48, 1.00)	0.75 (0.52, 1.09)
Q5 (n = 55)	0.71 (0.50, 1.02)	0.78 (0.54, 1.14)
P for trend ³	0.11	0.32

¹Includes intakes from supplements and was adjusted for total energy intake by using regression analysis.

²Adjusted for age (5-y intervals), follow-up period (2-y intervals), body mass index (quintiles), menopausal status and use of estrogen replacement medication (premenopausal; postmenopausal, never user; postmenopausal, past user; postmenopausal, current user; dubious menopausal status); cigarette smoking (never, past, current), physical activity (<21, 21–35, 36–49, 50–64, >64 h of moderate or vigorous activity/wk), and dietary intakes of calcium, vitamin D, protein, alcohol, and caffeine (quintiles).

³Linear trend over quintiles of vitamin K with the median value per quintile.

2–5 combined was lower than that for quintile 1, but not significantly so (RR: 0.74; 95% CI: 0.54, 1.01).

We further explored the association between vitamin K and the risk of hip fracture in an analysis limited to postmenopausal women. Eighty-nine percent of the hip fractures and 61% of the person-time occurred in these women. The results were almost identical to those in **Table 2** for the entire study population. We then stratified this analysis by use of estrogen replacement medication (**Table 3**). Vitamin K continued to be inversely related to the risk of hip fracture in the postmenopausal women who never used estrogen replacement medication. Although no protection was evident among those who were current estrogen users, the power to assess the association between vitamin K and risk of hip fractures was low and the CI for the RR was wide. For past users of estrogen replacement medication, there was a slight protective effect of vitamin K, although the magnitude was less than that observed for women who never used estrogen replacement medication and was not significant. These results need to be reproduced because they were not an a priori hypothesis.

Both calcium and vitamin D are essential for bone health. Therefore, we examined whether intakes of these nutrients would modify the association between vitamin K and risk of hip fractures. Although the data did not suggest any modification of risk associated with calcium intake, we observed a significant interaction ($P = 0.04$) between vitamin K and vitamin D. Interestingly, women with low vitamin K (<109 $\mu\text{g}/\text{d}$) but high vitamin D (>8.4 $\mu\text{g}/\text{d}$) intakes had a greater risk of hip fracture (RR: 2.17; 95% CI: 1.19, 3.95) than women with low vitamin K and low vitamin D intakes (<4 $\mu\text{g}/\text{d}$). Fracture risk was not reduced in women with high vitamin K ($\geq 109 \mu\text{g}/\text{d}$) and high vitamin D intakes.

Because lettuce (iceberg and romaine), broccoli, and spinach (raw plus cooked) were the greatest contributors to vitamin K intake in this cohort, we examined whether these foods would protect against hip fractures in a manner similar to that observed with vitamin K intake. This did hold true for lettuce. Women who consumed lettuce one or more times per day had a significant 45% lower risk of hip fracture than women who consumed

TABLE 3

Age-adjusted relative risks (RRs) with 95% CIs for risk of hip fracture by quintiles 2–5 (Q2–Q5) compared with quintile 1 (Q1) of vitamin K intake in postmenopausal women stratified by use of estrogen replacement medication

Estrogen replacement medication use	Person-years (thousands)	Number of cases	RR (95% CI)
	Q1/Q2–Q5	Q1/Q2–Q5	
Never	37.9/157.0	31/86	0.65 (0.43, 0.98)
Past	16.4/77.0	15/57	0.78 (0.44, 1.38)
Current	23.1/109.3	8/41	1.01 (0.47, 2.14)

lettuce one or fewer times per week (**Table 4**). We did not observe any associations between risk of hip fractures and broccoli or spinach intake, but this may have been due to the small variation in frequency of consumption of these foods.

DISCUSSION

In this 10-y prospective study of women 38–74 y of age, we observed an inverse association between dietary vitamin K and the risk of hip fracture. The results were similar for lettuce consumption, which provided the greatest contribution to vitamin K intakes in this cohort. Although other studies have not examined this relation directly, our findings are supported by evidence that high intakes of vitamin K can lower serum concentrations of undercarboxylated osteocalcin (9, 23, 24) and the undercarboxylated osteocalcin concentration is positively associated with risk of hip fractures. In recent studies of elderly women, Vergnaud et al (14) reported a significantly elevated odds ratio of 1.9 in women in the highest quartile of the percentage of undercarboxylated osteocalcin after adjustment for bone mineral density and gait speed. Szulc et al (12) found a significantly higher serum concentration of the percentage of undercarboxylated osteocalcin at baseline in the women who subsequently sustained a hip fracture than in those who did not sustain a fracture.

Although the association between vitamin K and risk of hip fractures in our study was inverse, risk of fracture did not decline with higher vitamin K intakes. Rather, there appeared to be a threshold below which the risk of hip fracture increased. Although the threshold in this study was $\approx 109 \mu\text{g}/\text{d}$, which suggests the need for a higher vitamin K requirement than the current recommended dietary allowance of 65 $\mu\text{g}/\text{d}$ for adult women (4), we recognize that our FFQ may have overestimated vitamin K intakes. The median intake of 169 $\mu\text{g}/\text{d}$ in our cohort is much higher than the mean intakes of 59–82 $\mu\text{g}/\text{d}$ calculated for the US

TABLE 4

Age-adjusted relative risks (RRs) with 95% CIs for risk of hip fracture by frequency of lettuce consumption

Lettuce servings ¹	Person-years (thousands)	Number of cases	RR (95% CI)
$\leq 1/\text{wk}$	162.5	65	Reference
2–4/wk	219.2	52	0.65 (0.47, 0.90)
5–6/wk	129.8	46	0.73 (0.52, 1.04)
$\geq 1/\text{d}$	190.6	52	0.55 (0.40, 0.78)
P for trend ²	—	—	0.004

¹Serving size = 1 cup ($\approx 227 \text{ g}$).

²P for trend = 0.004; linear trend over categories of lettuce consumption with the median value per category.


population of adult men and women (42) or the mean intake of 60 $\mu\text{g}/\text{d}$ calculated from 6 wk of food diaries from a group of 202 free-living men and women aged 18–55 y (43). However, it is also possible that the women in our cohort were indeed frequent consumers of green vegetables and other vitamin K-rich foods and that their vitamin K intakes were higher than those observed in other populations. A high vitamin K intake (mean: 156 $\mu\text{g}/\text{d}$) was also observed in another group of healthy postmenopausal women from the New England region (44).

Evidence that vitamin D stimulates the γ -carboxylation of γ -carboxyglutamyl-containing proteins (45), promotes osteocalcin synthesis (46), and decreases undercarboxylated osteocalcin secretion (47) suggests that vitamin D may be a necessary component of the vitamin K-dependent carboxylation process in bone. In a study by Szulc et al (12) of elderly, institutionalized women, serum concentrations of undercarboxylated osteocalcin were negatively correlated with 25-hydroxyvitamin D concentrations and the annual fluctuation in the percentage of undercarboxylated osteocalcin was directly opposite that of 25-hydroxyvitamin D concentrations. In addition, the undercarboxylated osteocalcin concentrations decreased significantly after 1 y of vitamin D and calcium supplementation, particularly in those women with concentrations that were higher than normal reference ranges before supplementation. However, a study by Douglas et al (24) reported that vitamin D and vitamin K supplementation did not reduce further the undercarboxylated osteocalcin concentrations in osteoporotic women that were achieved after 2 wk of treatment with vitamin K alone. In our cohort, we observed a significant interaction between vitamin D and vitamin K intakes as evidenced by the increased risk of hip fracture in women with a low vitamin K but a high vitamin D intake. Theoretically, this finding can be explained by the effects of the 2 vitamins on calcium homeostasis. Vitamin D acts as an inducer of bone resorption and thus higher intakes may result in increased bone turnover and increased urinary calcium excretion. Conversely, results of some studies in animals (16) and humans (15) indicate that vitamin K decreases urinary calcium excretion. Thus, despite high dietary intakes of vitamin D, there may be an increased risk of hip fracture when vitamin K intakes are low.

Our finding that high vitamin K intakes are associated with a decreased risk of hip fracture in postmenopausal women who never used estrogen replacement medication, but not in those who were taking estrogen replacement medication, has not been reported previously. The predominant effect of estrogen on bone is a decrease in resorption (48), and the ensuing benefits for bone density and fracture risk may not be improved by higher vitamin K intakes. However, it is possible that the estrogen receptors on osteoblast cells (49) may have a direct effect on osteocalcin production and vitamin K requirements, although the true function of these receptors is as yet unknown. Both vitamin K and estrogen inhibit the production or function of interleukin 6 (19, 50), a potent bone-resorbing agent.

The magnitude of the effect of vitamin K on bone may be different at various bone sites and therefore the associations between vitamin K intake and other types of osteoporotic fractures need to be investigated. For example, in this same cohort of women, vitamin K appeared unrelated to the incidence of distal forearm fractures. An advantage of this type of prospective cohort study is that the dietary intake of vitamin K was assessed before the fractures occurred. A limitation of the study was that the measure of vitamin K nutrition was based solely on the con-

tent of phyloquinone (vitamin K₁) in foods, although it is still unclear to what extent menaquinones (vitamin K₂) synthesized in the intestine are a source of usable vitamin K (3). In addition, we did not take into account potential differences in the bioavailability of vitamin K, which may be lower from green leafy vegetables than from oil sources, for example.

In conclusion, we found a lower risk of hip fracture in middle-aged and older women with moderate and high intakes of vitamin K than in those with a low intake. Our results support the suggestion that dietary vitamin K requirements should be based on bone health as well as on blood coagulation. 

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