

Potassium, magnesium, and fruit and vegetable intakes are associated with greater bone mineral density in elderly men and women¹⁻³

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ABSTRACT

Background: Osteoporosis and related fractures will be growing public health problems as the population ages. It is therefore of great importance to identify modifiable risk factors.

Objective: We investigated associations between dietary components contributing to an alkaline environment (dietary potassium, magnesium, and fruit and vegetables) and bone mineral density (BMD) in elderly subjects.

Design: Dietary intake measures were associated with both cross-sectional (baseline) and 4-y longitudinal change in BMD among surviving members of the original cohort of the Framingham Heart Study. Dietary and supplement intakes were assessed by food-frequency questionnaire, and BMD was measured at 3 hip sites and 1 forearm site.

Results: Greater potassium intake was significantly associated with greater BMD at all 4 sites for men and at 3 sites for women ($P < 0.05$). Magnesium intake was associated with greater BMD at one hip site for both men and women and in the forearm for men. Fruit and vegetable intake was associated with BMD at 3 sites for men and 2 for women. Greater intakes of potassium and magnesium were also each associated with less decline in BMD at 2 hip sites, and greater fruit and vegetable intake was associated with less decline at 1 hip site, in men. There were no significant associations between baseline diet and subsequent bone loss in women.

Conclusion: These results support the hypothesis that alkaline-producing dietary components, specifically, potassium, magnesium, and fruit and vegetables, contribute to maintenance of BMD. *Am J Clin Nutr* 1999;69:727-36.

KEY WORDS Bone mineral density, dietary intake, magnesium, potassium, fruit, vegetables, elderly, osteoporosis, food-frequency questionnaire

INTRODUCTION

Osteoporosis and related fractures are major public health problems that are growing in importance as the population ages (1). It has been estimated that the lifetime risk of fracture exceeds 40% for women and 13% for men (2). In the elderly, hip fractures are associated with mortality in up to 20% of cases, with costly long-term nursing home care required for most survivors (3). Reported risk factors for osteoporosis include low

physical activity (4), smoking (5, 6), alcoholism (7), and lack of estrogen in postmenopausal women (8). High body weight and moderate alcohol use appear to protect against osteoporosis (9, 10), although weight gain and alcohol consumption are not recommended as interventions because of other potential health risks associated with them.

Nutritional factors are of particular importance to bone health because they are modifiable. It is generally agreed that calcium and vitamin D are important nutrients for bone health, and supplements containing these nutrients are prescribed widely (11, 12). Much less is known about the effect of other nutrients on bone, although effects have been hypothesized for protein, phosphorus, vitamin C, and vitamin K (13). In 1968 Wachman and Bernstein (14) hypothesized that bone mineral functions as a buffer base and that lifetime buffering of the acid load from the ingestion of mixed diets leads to gradual and accumulated bone loss. They suggested that "The therapy of osteoporosis may lie in its prevention...it might be worthwhile to consider decreasing the rate of bone attrition by the use of a diet favouring 'alkaline ash.' This type of diet would emphasize the ingestion of fruits, vegetables, vegetable protein, and moderate amounts of milk." Two nutrients that may have such buffering effects are potassium and magnesium, which are found in a variety of whole, unrefined foods, including fruit and vegetables (15, 16). Diets high in fruit and vegetables produce a more alkaline urine by contributing a variety of compounds that accept hydrogen ions during their metabolism (14, 16).

Although there is both theoretical and some clinical evidence of an association, relatively few studies have examined the effects of either potassium or magnesium intake on bone. Low

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potassium intake has been shown to increase rates of calcium excretion (17). A 2-y controlled trial of magnesium supplementation in osteoporotic women resulted in slower bone loss and fewer fractures in supplemented women than in unsupplemented women (18). Only a few population-based studies have reported associations between dietary intake of potassium, magnesium, or fruit and vegetables and bone status in women (19–22) or elderly men (23). The few studies that examined the associations of both of these minerals with bone saw similar patterns with each (20, 23). In this study, we investigate both cross-sectional and longitudinal relations between potassium, magnesium, and fruit and vegetable intakes and bone mineral density (BMD) in elderly men and women in the Framingham Heart Study. To our knowledge, this is the first study to relate usual intake of these nutrients and foods to BMD and to change in BMD over time in older men.

SUBJECTS AND METHODS

Subjects

The Framingham Heart Study is a longitudinal cohort study that was initiated in 1948 to examine risk factors for heart disease. The original subjects were selected to constitute a two-thirds random sample of the households in Framingham, MA. At baseline, 5209 men and women were examined. Subjects have returned biennially to complete a battery of questionnaires, examinations, and other testing (24). At the 20th examination (1988–1989), more than half of the original cohort had died, leaving 1402 surviving subjects. Of these remaining subjects, measurements of BMD were available for 1164 (448 men and 716 women). Most of the subjects for whom no BMD measures were available were homebound and unable to have bone density assessments in the clinic. Of those with available bone measures, 345 men and 562 women also had completed food-frequency questionnaires (FFQs). These subjects (aged 69–97 y at the time of the first bone measurement) were included in the cross-sectional analyses. Bone density measures were repeated during the 22nd examination (1992–1993) on 229 of the men and 399 of the women; these subjects were included in the analyses of baseline diet and change in BMD. Our study was approved by the Institutional Review Board responsible for protecting the rights of human subjects at Boston University Medical Center and at the Hebrew Rehabilitation Center for the Aged. Written, informed consent was obtained from all subjects.

Comparison of subjects with and without complete baseline data on bone and dietary intake revealed no significant differences in sex, education level, smoking status, or body mass index (BMI; in kg/m²). Subjects with complete data were younger (\bar{x} : 75.2 y compared with 79.1 y; $P = 0.0001$) and more physically active [physical activity score of 33.5 compared with 31.3 (see “Measurement of confounders” section); $P = 0.0001$] than those without bone measures or complete FFQs. Subjects with complete data for analysis of change in BMD tended to be younger and female, with somewhat greater baseline BMDs; for example, trochanter BMD among women with complete data was greater than among women without follow-up measures (0.63 compared with 0.59 g/cm²; $P = 0.002$).

BMD measurements

The Framingham Osteoporosis Study began with bone measurements of participants at the 20th examination. At this exami-

nation, BMD measures of the trochanter, femoral neck, and Ward's area were taken by dual-photon absorptiometry (DPA). DPA measurements were made with a dual-photon scanner (Lunar Radiation Corp, Madison, WI). The CVs for repeated measurements over 2 y in young, healthy individuals with this method were 2.65% for the femoral neck, 2.8% for the trochanter, and 4.16% for Ward's area (25). At the 22nd examination, BMDs were measured in the femoral neck by dual-energy X-ray absorptiometry (DXA). These had a precision (CV) of 2%, similar to the range of 1.8–1.9% reported by others (26, 27). To correct for measurement differences between the 2 machines (DPA and DXA), we used equations derived by scanning a group of subjects with both machines (28).

At both the 20th and the 22nd examination, BMD was also measured in the forearm (shaft of the radius) by using an SP2 single-photon absorptiometer (Lunar Radiation Corp). In all cases, the right arm was measured unless there was a history of previous fracture. The precision was 2% at the radius, similar to other published reports (29). Further details of these measurements were published previously (25). In the few cases in which different sides were measured at different times, subjects were deleted from analyses of change in BMD ($n = 17$ for hip and 16 for radius).

Dietary intake

Usual dietary intake for the previous year was assessed at the 20th examination with a semiquantitative 126-item FFQ (30, 31). Questionnaires were mailed to the subjects and subjects were asked to bring the completed questionnaires to the examination. Questionnaires on which energy intakes <2.51 or >16.74 MJ (600 or 4000 kcal)/d were reported or with >12 food items left blank were considered invalid and excluded from further analysis. Information about use of vitamin and mineral supplements and specific type of breakfast cereal most frequently consumed was used to estimate total micronutrient intakes. Reported intake frequency of individual fruit and vegetable items was summed to obtain the average number of fruit and vegetables consumed per day for each person.

This FFQ has been validated for many nutrients and in several populations against multiple diet records and blood measures (30–33). Correlations between estimates from the questionnaire and multiple diet records have been reported to be 0.64–0.73 for potassium intake (30, 32–34) and 0.67–0.71 for magnesium intake (30). There is some evidence that this FFQ underestimates energy intake (35) and that it may overestimate intake of fruit and vegetables (36). However, our own comparison of fruit and vegetable intakes with plasma folate and homocysteine concentrations with this questionnaire in this population supports the validity of this variable (37).

Measurement of confounders

Factors reported to affect BMD include body weight or BMI, physical activity (38), alcohol use (10), smoking (6), estrogen use by women (8), dietary intake of calcium and vitamin D, and use of calcium or vitamin D supplements (12, 39). BMI was calculated from measurements of height at the first examination (1948–1950)—before height may have been lost as a result of osteoporosis—and weight measured at the 20th examination. Physical activity was measured at the 20th examination with the Framingham physical activity index, which asked about the number of hours spent in heavy, moderate, light, or sedentary activity and the number of hours spent sleeping during a typical day. Each compo-



ment of these 24-h summaries was then multiplied by an appropriate weighting factor based on estimated associated energy expenditure and summed to arrive at a physical activity score (40). The maximum score possible was 63.2 (note that this score would be unrealistic to obtain because it reflects high-intensity activity for 24 h).

On the questionnaire administered at the 20th examination, subjects were also asked to quantify their weekly intake of liquor, wine, and beer. From this information, total grams of alcohol consumed per week was estimated. Based on 13.2 g alcohol per drink, a variable was created by which subjects were classified as nondrinkers, moderate drinkers (based on the current recommendations for moderate intake: up to 1 drink/d for women and 2 drinks/d for men), or heavy drinkers (if intakes were greater than these cutoffs). Subjects were also classified as current smokers, former smokers, or nonsmokers on the basis of questionnaire responses. Dietary calcium and vitamin D intakes were assessed from the food-based section of the FFQ. Use of calcium or vitamin D supplements, as recorded on the supplement section of the FFQ, were coded as dummy (yes or no) variables. For women, estrogen users were defined as those currently receiving estrogen therapy, with continuous use for ≥ 2 y, compared with those who had never received estrogen or were past users, on the basis of evidence that past use does not sustain bone benefits (8).

Because previous research showed that there are seasonal changes in BMD in New England, we also created a categorical variable for time of BMD measurement (12, 41). July, August, and September were coded as summer; October, November, and December as fall; January, February, and March as winter; and April, May, and June as spring.

Statistical analyses

All statistical analyses were performed with SAS (version 6.12; SAS Institute Inc, Cary, NC) on a VAX mainframe computer (Digital Equipment Corp, Maynard, MA). For cross-sectional analyses, measures of BMD at the femur and the radius were regressed on total potassium, magnesium, and fruit and vegetable intakes separately for men and women, with adjustment for potential confounders in the general linear models procedure. These potential confounders included age, BMI, physical activity score, smoking status, alcohol use, calcium supplement use, vitamin D supplement use, season of bone measurement, total energy intake, dietary calcium intake, dietary vitamin D intake, and, for women, current estrogen use. This list differed slightly for fruit and vegetable models, in which we included servings per day from other food groups (milk, other dairy, breads and cereals, and meat, poultry, and fish) in place of dietary calcium and vitamin D. Because most nutrients correlate with energy intake, adjustment for this variable allows an assessment of the independent effect contributed by the nutrient. It also allows for differences in intake that may have been due to body size or activity levels and corrects for some of the measurement error inherent in the FFQ (34).

To better understand the potential collinearity between energy intake, potassium intake, and magnesium intake, we examined simple and partial (adjusted for age and BMI) correlations among these 3 variables. Because these analyses showed evidence of high collinearity between potassium intake and magnesium intake, it was not possible to assess the independent effects of potassium and magnesium on BMD in the same model. We therefore created a score by summing the standardized z scores (to adjust for the different scales of the 2 variables) of potassium and magnesium intake and restandardizing the score. The mod-

els described above were rerun, and potassium and magnesium intake variables were replaced with this combined score. We also tested potassium-by-magnesium and calcium-by-magnesium interactions.

Change in BMD was defined as BMD at the 22nd examination minus BMD at the 20th examination. These change measures were regressed on potassium intake, on magnesium intake, on the potassium plus magnesium z score, and on fruit and vegetable intake for men and women separately, with all the potential confounders used in the cross-sectional analyses described above, plus the corresponding baseline measure of BMD at the 20th examination. This baseline BMD measure was included because of the likelihood that change in BMD may be related to initial BMD. Several models were evaluated, parallel to those described above for the cross-sectional analysis. For visual presentation, and to assess the form of the relation, we also created quartile groups for the combined z score and present adjusted means for changes in bone measures by intake quartile. Statistical differences ($P < 0.05$) across quartile groups were tested in the general linear model procedure in SAS, adjusted for the set of confounders described above, with t test comparisons of least-squares means.

To understand the composition of diets associated with high potassium or magnesium intakes, the contribution of each of the food items on the FFQ to total potassium and magnesium intakes was determined and ranked. Intake of magnesium and potassium from supplements recorded on the FFQ was included in the ranking.

RESULTS

Descriptive statistics

Mean values (\pm SDs) for BMD measures and for all continuous independent variables and potential confounders used in these analyses are presented in **Table 1**. For categorical variables, percentages in each category are presented. The average age for both men and women was 75 y. The average BMIs were 27.2 for men and 26.3 for women. Proportionally more women than men were current smokers, although more men were past smokers. About 17% of women and 20% of men reported consuming more than the currently recommended maximum of 1 drink/d for women and 2 drinks/d for men. Only 8.7% of men used calcium supplements, compared with 23% of women. More men and women used vitamin D supplements than calcium supplements. Only 5% of women were taking estrogen at the time of measurement.

Average reported energy intakes, as calculated from the FFQs, were low for both women and men [6.91 and 7.80 MJ (1653 and 1865 kcal), respectively]. Average magnesium intakes just exceeded the 1989 recommended dietary allowance (RDA) (42), but fell below the recently released RDA of 320 mg/d (43) for women and were far below the new RDA of 420 mg/d for men. There is no RDA for potassium, but intakes reported here are consistent with other data for US urban white adults (44). Intakes of magnesium and potassium were mainly from dietary sources. About 2% of total magnesium consumed by the population came from supplements (1.98% from multivitamins and 0.18% from magnesium supplements); only 0.04% of potassium intake was from nutrient supplements.

Average reported calcium intakes were also just below the 1989 RDA—and well below the recently released adequate intake of 1200 mg/d (43). Mean vitamin D intakes were just above the 1989 RDA, but were much lower than the new ade-



TABLE 1
Basic description of the study population¹

| | Men | Women |
|--|--------------------------------|----------------------|
| Descriptive variables | | |
| Age (y) | 75.1 ± 4.89 [345] ² | 75.3 ± 4.83 [562] |
| BMI (kg/m ²) | 27.2 ± 4.45 [345] | 26.3 ± 5.57 [562] |
| Physical activity score | 33.9 ± 6.40 [339] | 33.2 ± 5.04 [551] |
| Smoking status (%) | | |
| Past smoker | 56.8 [345] | 40.6 [562] |
| Current smoker | 9.3 [345] | 11.7 [562] |
| Alcohol use (%) | | |
| Moderate | 44.9 [345] | 34.5 [562] |
| Heavy | 20.3 [345] | 17.1 [562] |
| Calcium supplement use (%) | 8.7 [345] | 23.0 [562] |
| Vitamin D supplement use (%) | 22.6 [345] | 29.7 [562] |
| Current estrogen use (%) | — | 5.0 [560] |
| Season of BMD measurement (%) | | |
| Winter | 22.8 [330] | 30.0 [536] |
| Spring | 28.2 [330] | 28.5 [536] |
| Summer | 23.3 [330] | 19.0 [536] |
| Fall | 19.7 [330] | 22.4 [536] |
| Dietary variables | | |
| Energy intake (MJ) | 7.80 ± 2.60 [345] | 6.91 ± 2.31 [562] |
| Potassium intake (mg) | 2988 ± 1011 [345] | 2930 ± 995 [562] |
| Magnesium intake (mg) | 299.7 ± 110.2 [345] | 287.7 ± 105.8 [562] |
| Calcium intake (mg) | 739.8 ± 378.2 [345] | 709.2 ± 333.0 [562] |
| Vitamin D intake (IU) | 232.9 ± 164.8 [345] | 212.5 ± 139.9 [562] |
| Fruit and vegetable intake (serving/d) | 4.66 ± 2.39 [345] | 5.30 ± 2.65 [562] |
| Baseline BMD (g/cm ²) | | |
| Femoral neck | 0.878 ± 0.146 [330] | 0.720 ± 0.114 [536] |
| Trochanter | 0.847 ± 0.151 [322] | 0.625 ± 0.127 [532] |
| Ward's area | 0.686 ± 0.173 [330] | 0.559 ± 0.126 [536] |
| Radius | 0.719 ± 0.085 [342] | 0.510 ± 0.094 [558] |
| 4-y change in BMD (g/cm ²) | | |
| Femoral neck | -0.013 ± 0.064 [229] | -0.025 ± 0.054 [399] |
| Trochanter | 0.003 ± 0.086 [221] | -0.020 ± 0.062 [395] |
| Ward's area | -0.003 ± 0.069 [229] | -0.026 ± 0.063 [399] |
| Radius | -0.026 ± 0.043 [228] | -0.024 ± 0.044 [424] |

¹BMD, bone mineral density. Physical activity score, past or current smoker, moderate or heavy alcohol use, calcium or vitamin D supplement use, estrogen use, and season of BMD measurement defined in the Methods.

² $\bar{x} \pm SD$; total *n* in brackets.

quate intake value of 10–15 μg (400–600 IU)/d for older individuals. In addition, this variable was highly skewed, with higher intakes achieved through supplementation in a subset of subjects. Average reported fruit and vegetable intakes were 4.7 fruit or vegetables or both/d for men and 5.3/d for women, which is somewhat higher than the 3.1–3.4 servings/d reported in national surveys (45).

Average BMDs ranged from 0.69 g/cm² for Ward's area to 0.88 g/cm² for the femoral neck in men and from 0.51 g/cm² for the radius to 0.72 g/cm² for the femoral neck in women. Over the 4 y of observation, average loss of BMD ranged from ≈0 for the trochanter and Ward's area in men to 0.026 ± 0.06 g/cm² for Ward's area in women.

Cross-sectional associations between potassium, magnesium, and fruit and vegetable intakes and bone measures

Simple correlations between dietary potassium and dietary magnesium were 0.85 and 0.88 for men and women, respectively, suggesting high collinearity. Adjustment for age, BMI, and energy intake did not change these correlations. Because of this high collinearity, models containing both potassium and magnesium

tended to not show independent effects of either after the other was controlled for, although each appeared to be important on its own. None of the nutrient interactions was significant in any of these models tested. In **Tables 2** and **3**, therefore, the results are presented of only the regression of adjusted BMD measures on 1) potassium, 2) magnesium, 3) the potassium plus magnesium *z* score variable, and 4) fruit and vegetable intake, for men and women, respectively.

In men (Table 2), the association between potassium and BMD was significant for all 4 bone sites, with slopes ranging from 0.022 to 0.04 g/cm², or ≤5.8% of average BMD for every 1000 mg K. For magnesium intake, results were significant for the radius and the trochanter and approached significance for the remaining 2 hip sites. Differences in BMD associated with each 100-mg difference in magnesium intake ranged from 0.023 to 0.027 g/cm². These represent differences of ≤3.8% of average BMD. The combined *z* score, summing potassium and magnesium intakes, was significant for all 4 bone sites. Fruit and vegetable intake was significant for all sites except the trochanter. For the femoral neck, the slope of 0.0086 represents a 1% greater BMD for each fruit or vegetable consumed per day.

TABLE 2

Cross-sectional difference in bone mineral density (BMD) per unit difference in potassium, magnesium, or fruit and vegetable intake in men¹

| Dietary variable | BMD | | | |
|--|-------------------------|---------------------|--------------------|---------------------|
| | Femoral neck | Trochanter | Ward's area | Radius |
| | <i>g/cm²</i> | | | |
| Potassium (/1000 mg) | 0.032 ² | 0.030 ² | 0.040 ² | 0.022 ³ |
| Magnesium (/100 mg) | 0.023 ⁴ | 0.027 ² | 0.026 ⁴ | 0.023 ³ |
| Potassium plus magnesium z score (/SD) | 0.034 ² | 0.035 ² | 0.040 ² | 0.028 ³ |
| Fruit and vegetables (/serving) | 0.0086 ² | 0.0068 ⁴ | 0.011 ² | 0.0043 ² |

¹ Adjusted for age, BMI, physical activity score, smoking status, alcohol use, calcium supplement use, vitamin D supplement use, season of BMD measurement, energy intake, dietary calcium intake, and dietary vitamin D intake. For fruit and vegetable models, servings per day from food groups (milk, other dairy, bread and cereal, and meat, poultry, and fish) were used in place of dietary calcium and vitamin D intakes.

² $P < 0.05$.

³ $P < 0.01$.

⁴ $P < 0.1$.

In women (Table 3), potassium intake was significantly associated with BMD at 3 sites, with a difference in bone per 1000 mg K of 5.4% of average BMD for the trochanter, 3.4% for Ward's area, and 3.1% for the radius. Magnesium intake was significantly associated with BMD at the trochanter and approached significance at Ward's area when all potential confounders were adjusted for. For each 100-mg difference in magnesium intake, there were differences in average BMD of 3.2% and 2.9% for the trochanter and Ward's area, respectively. The combined z score was also significantly associated with the trochanter and Ward's area and approached significance for the other 2 sites. Finally, fruit and vegetable intake was associated with BMD at the radius, the trochanter, and Ward's area.

Adjusted mean BMDs by quartile of the potassium plus magnesium z score are presented in **Figures 1** and **2** for men and women, respectively. For all bone measures and for both sexes, BMDs were lowest in those with the lowest intakes of these combined nutrients. For men, there was a clear dose-response relation with higher BMDs corresponding with higher intake quartiles. For all sites except the femoral neck, BMD was significantly greater in men in the highest quartile than in at least one other quartile of potassium plus magnesium intake. Separate figures for potassium and magnesium (not shown) revealed similar patterns, with somewhat stronger differences across groups seen for potassium than for magnesium.

For women, the group in the lowest intake quartile had significantly lower BMDs than at least one other quartile group for all hip sites; however, there were no significant differences in radius

BMD across potassium plus magnesium intake quartiles. Again, separate figures for potassium and magnesium (not shown) followed similar trends. Because women in the lowest intake quartile consistently had the lowest BMD, whereas BMD in the upper 3 quartiles did not tend to increase linearly, we also examined the dichotomous difference for magnesium intake by using the cutoff of two-thirds of the current RDA (43). This analysis (not shown) reconfirmed that women with low magnesium intakes had significantly lower BMD at the femoral neck, trochanter, and Ward's sites than did women with intakes above the cutoff ($P < 0.05$).

Effect of baseline potassium, magnesium, and fruit and vegetable intakes on subsequent 4-y change in BMD

Results for the relation between baseline dietary potassium, magnesium, and fruit and vegetable intakes and subsequent 4-y change in BMD are presented for men and women in **Tables 4** and **5**, respectively. In men, greater baseline potassium intake was significantly associated with lower subsequent 4-y loss of BMD at the femoral neck and trochanter. Magnesium intake was significantly associated with subsequent change in BMD at the femoral neck and trochanter, and approached significance at Ward's area. The combined potassium plus magnesium z score appeared to be the strongest predictor of change in BMD. It was significant for the femoral neck, trochanter, and Ward's area. Fruit and vegetable intake approached significance at the trochanter and was significant at Ward's area.

TABLE 3

Cross-sectional difference in bone mineral density (BMD) per unit difference in potassium, magnesium, or fruit and vegetable intake in women¹

| Dietary variable | BMD | | | |
|--|-------------------------|---------------------|---------------------|---------------------|
| | Femoral neck | Trochanter | Ward's area | Radius |
| | <i>g/cm²</i> | | | |
| Potassium (/1000 mg) | 0.012 | 0.034 ² | 0.019 ³ | 0.016 ³ |
| Magnesium (/100 mg) | 0.012 | 0.020 ³ | 0.016 ⁴ | 0.006 |
| Potassium plus magnesium z score (/SD) | 0.014 ⁴ | 0.032 ² | 0.021 ³ | 0.013 ⁴ |
| Fruit and vegetables (/serving) | 0.0024 | 0.0056 ³ | 0.0038 ⁴ | 0.0049 ² |

¹ Adjusted for age, BMI, physical activity score, smoking status, alcohol use, calcium supplement use, vitamin D supplement use, estrogen use, season of BMD measurement, energy intake, dietary calcium intake, and dietary vitamin D intake. For fruit and vegetable models, servings per day from food groups (milk, other dairy, bread and cereal, and meat, poultry, and fish) were used in place of dietary calcium and vitamin D intakes.

² $P < 0.01$.

³ $P < 0.05$.

⁴ $P < 0.1$.



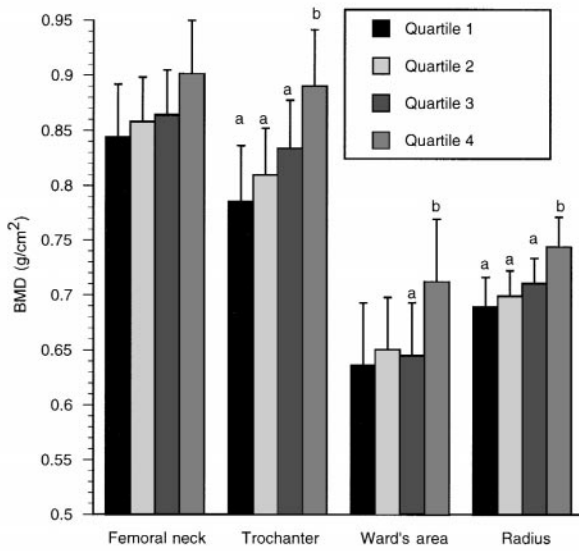


FIGURE 1. Mean (\pm SD) bone mineral density (BMD) at 4 sites by potassium plus magnesium z score quartiles in men. Quartiles 1–4 are listed from left to right. Bars with different letters are significantly different, $P < 0.05$.

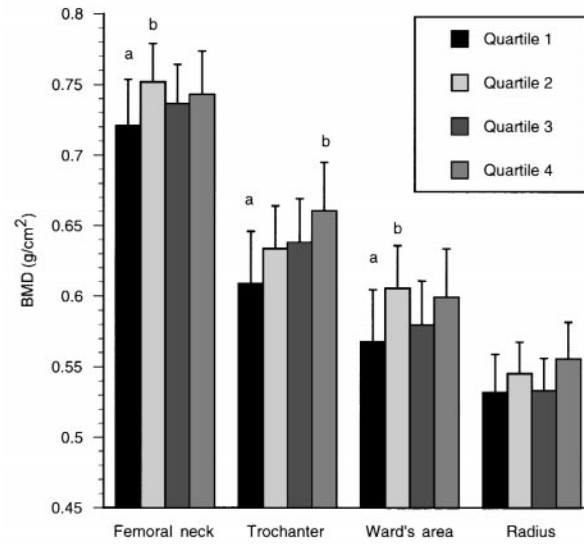


FIGURE 2. Mean (\pm SD) bone mineral density (BMD) at 4 sites by potassium plus magnesium z score quartiles in women. Quartiles 1–4 are listed from left to right. Bars with different letters are significantly different, $P < 0.05$.

Results for change in BMD in women are presented in Table 5. In contrast with both the men and with the cross-sectional results in women, there was no association between baseline diet and longitudinal change in BMD in women.

Mean changes in BMD over the 4-y observation period are presented by combined potassium plus magnesium intake quartiles for men in Figure 3. Separate potassium and magnesium figures (not shown) revealed similar patterns, with significant differences across quartiles for the femoral neck, trochanter, and Ward's area, but not for the radius. For each of these, being in the lowest intake quartile was associated with a significantly greater loss of BMD over the 4 y of observation. Mean differences between the lowest and highest quartile ranged from 0.032 to 0.042 g/cm^2 across the 3 hip sites, representing a difference in BMD loss of 4.0–4.8% of average baseline bone. For women, there were no significant differences in BMD changes across intake quartiles (not shown).

Dietary sources of potassium and magnesium

The major food sources of potassium and magnesium are listed in Table 6. Both nutrients are found in a wide range of whole foods including fruit and vegetables, whole grains, and milk. Top sources of potassium in this population included potatoes, milk, orange juice, and bananas. Overall, fruit and vegetables contributed more than half of the total potassium consumed. Magnesium is found in a wide variety of foods, but particularly in those close to their natural, unrefined state. Important sources of magnesium in this population included whole-grain bread, milk, breakfast cereal, bananas, and orange juice. Thus, although not identical in ranking, there were strong similarities in food sources for potassium and magnesium. It is noteworthy that important sources of calcium and vitamin D also overlapped with these. Intakes of these 2 nutrients were adjusted for in the analyses discussed above.

TABLE 4

Longitudinal change in bone mineral density (BMD) per unit difference in potassium, magnesium, or fruit and vegetable intake in men¹

| Dietary variable | 4-y change in BMD | | | |
|--|--------------------|---------------------|---------------------|--------|
| | Femoral neck | Trochanter | Ward's area | Radius |
| | g/cm^2 | | | |
| Potassium (/1000 mg) | 0.018 ² | 0.026 ³ | 0.015 ⁴ | 0.004 |
| Magnesium (/100 mg) | 0.018 ³ | 0.022 ³ | 0.013 ⁴ | 0.004 |
| Potassium plus magnesium z score (/SD) | 0.023 ³ | 0.030 ³ | 0.018 ² | 0.005 |
| Fruit and vegetables (/serving) | 0.0022 | 0.0049 ⁴ | 0.0053 ² | 0.0011 |

¹ Adjusted for baseline BMD, age, BMI, physical activity score, smoking status, alcohol use, calcium supplement use, vitamin D supplement use, season of BMD measurement, energy intake, dietary calcium intake, and dietary vitamin D intake. For fruit and vegetable models, servings per day from food groups (milk, other dairy, bread and cereal, and meat, poultry, and fish) were used in place of dietary calcium and vitamin D intakes.

² $P < 0.05$.

³ $P < 0.01$.

⁴ $P < 0.1$.

TABLE 5

Longitudinal change in bone mineral density (BMD) per unit difference in potassium, magnesium, or fruit and vegetable intake in women¹

| Dietary variable | 4-y change in BMD | | | |
|--|-------------------|------------|-------------|--------|
| | Femoral neck | Trochanter | Ward's area | Radius |
| Potassium (/1000 mg) | -0.001 | 0.002 | -0.002 | -0.002 |
| Magnesium (/100 mg) | 0.002 | -0.000 | 0.001 | 0.003 |
| Potassium plus magnesium z score (/SD) | 0.000 | 0.001 | -0.000 | 0.001 |
| Fruit and vegetables (/serving) | 0.0005 | -0.0008 | -0.0005 | 0.000 |

¹Adjusted for baseline BMD, age, BMI, physical activity score, smoking status, alcohol use, calcium supplement use, vitamin D supplement use, estrogen use, season of BMD measurement, energy intake, dietary calcium intake, and dietary vitamin D intake. For fruit and vegetable models, servings per day from food groups (milk, other dairy, bread and cereal, and meat, poultry, and fish) were used in place of dietary calcium and vitamin D intakes. There were no significant associations between baseline diet and longitudinal change in BMD.

DISCUSSION

We showed that there are significant and important associations between intakes of potassium and magnesium and BMD. In men, significant cross-sectional associations were seen at all BMD measurement sites, but were most consistently observed for the radius. In women, cross-sectional associations between potassium and magnesium intakes and BMD were strongest at the trochanter. The strong correlation between potassium and magnesium intakes, driven by the heavy overlap in dietary sources of these nutrients, made it impossible to separate the effects of these 2 nutrients on BMD. A combined z score proved to be the most consistently significant variable associated with BMD cross-sectionally for both men and women, although it usually did not perform much more strongly than either one of the individual nutrients. Even after we controlled for total energy intake, which itself is correlated with each of the mineral intakes, the associations appeared to be consistent. It is likely that the diets reported at baseline represented long-standing dietary patterns for most subjects. The cross-sectional BMD measures also represented the subjects' accumulated lifetime status. Together, these associations suggest that long-term diets high in potassium or magnesium or both may protect BMD.

In analyses of 4-y change in BMD, significant results were seen only in men. Baseline potassium and magnesium intakes, both separately and combined, were predictive of subsequent 4-y bone loss in men, but not women, at all 3 hip sites. These longitudinal associations represent more time-delimited associations and suggest that a current diet high in these nutrients may protect against bone loss in elderly men. The lack of predictive association between these nutrients and longitudinal change in BMD in women, despite a strong cross-sectional association, was not expected and is difficult to explain. It is possible that the protective effect of magnesium and potassium over years of exposure was seen in the cross-sectional analyses, but that hormonal factors or other unmeasured interactions in the metabolic environment of these postmenopausal women at the time of measurement overwhelmed the short-term effects of these nutrients. Estrogen deficiency has been hypothesized to cause loss of tissue magnesium (46). Further investigation of these differences is needed.

There are theoretical reasons to expect associations between bone and each of these nutrients, but there is only limited empirical evidence. Metabolic balance studies have shown that potassium administration promotes renal calcium retention, whereas low potassium intake increases daily and fasting urinary calcium excretion rates (17). Dietary potassium may influence bone

resorption through these effects on calcium balance. A study of 18 postmenopausal women showed improved calcium balance, increased serum osteocalcin concentrations, and decreased urinary hydroxyproline excretion when the women were given enough potassium bicarbonate to neutralize endogenous acid loads from normal diets (47). The authors concluded that this buffering protects the skeleton.

Two studies reported cross-sectional associations between potassium intake and BMD in free-living adult populations (20, 21). Potassium intake, as measured both by an FFQ and by the average of 4 wk of diet records, was significantly associated with total-body BMD in 213 Swedish women aged 28–74 y (21). A study of 994 premenopausal Scottish women aged 45–49 y also found nearly significant (*P* < 0.10) associations between potassium intake and BMD at the lumbar spine, femoral neck, and trochanter (20). We have seen no longitudinal reports of potassium and change in BMD and no studies of this association in men. Our results strongly support a cross-sectional association between

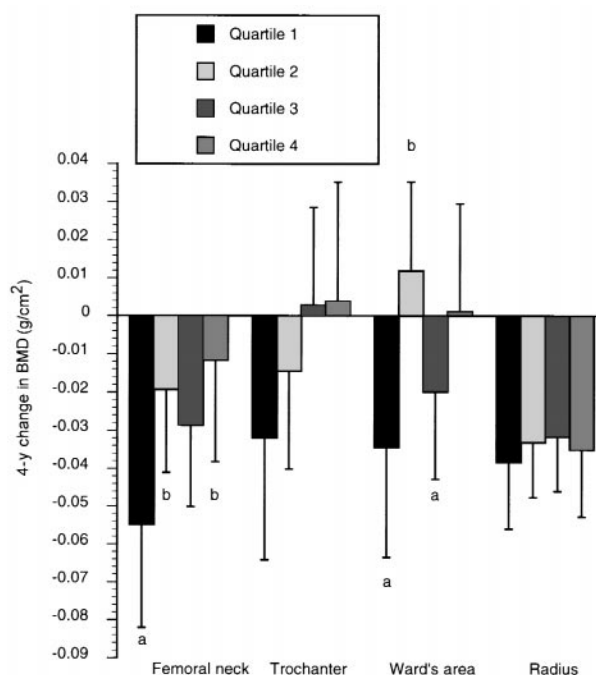


FIGURE 3. Mean (±SD) change in bone mineral density (BMD) at 4 sites by potassium plus magnesium z score quartiles in men. Quartiles 1–4 are listed from left to right. Bars with different letters are significantly different, *P* < 0.05.

TABLE 6Top 20 food sources of potassium and magnesium in the study population¹

| Rank | Potassium | | Magnesium | |
|------|--------------------------|--|------------------|--|
| | Food source | Contribution to total intake ² % | Food source | Contribution to total intake ² % |
| 1 | Potatoes | 8.76 ± 6.92 | Dark bread | 6.37 ± 8.01 |
| 2 | Skim milk | 7.35 ± 9.40 | Skim milk | 6.06 ± 7.80 |
| 3 | Orange juice | 6.54 ± 6.05 | Cold cereal | 5.51 ± 8.18 |
| 4 | Bananas | 6.17 ± 6.27 | Bananas | 4.83 ± 5.08 |
| 5 | Coffee | 4.62 ± 5.89 | Coffee | 4.53 ± 5.74 |
| 6 | Tomatoes | 2.86 ± 3.11 | Orange juice | 3.65 ± 3.67 |
| 7 | Meat, main dish | 2.75 ± 3.13 | Cooked oatmeal | 2.56 ± 4.54 |
| 8 | Whole milk | 2.65 ± 6.23 | Whole milk | 2.47 ± 5.87 |
| 9 | English muffin or bagels | 2.29 ± 3.73 | Fish | 2.16 ± 2.44 |
| 10 | Cold cereal | 1.91 ± 2.84 | Meat, main dish | 2.10 ± 2.49 |
| 11 | Chicken, no skin | 1.81 ± 1.74 | Spinach, cooked | 2.08 ± 2.81 |
| 12 | Tomato sauce | 1.73 ± 2.06 | Multivitamins | 1.98 ± 7.43 |
| 13 | Orange | 1.59 ± 2.66 | Chicken, no skin | 1.97 ± 1.96 |
| 14 | Apple or pear, fresh | 1.48 ± 2.14 | Peanut butter | 1.92 ± 3.09 |
| 15 | Broccoli | 1.34 ± 1.69 | White bread | 1.91 ± 2.82 |
| 16 | Cantaloupe | 1.29 ± 2.07 | Nuts | 1.66 ± 4.14 |
| 17 | Dark bread | 1.26 ± 1.77 | Beer | 1.58 ± 5.61 |
| 18 | Hamburger | 1.22 ± 1.32 | Pasta | 1.55 ± 1.77 |
| 19 | Tea | 1.20 ± 2.15 | Tomatoes | 1.51 ± 1.81 |
| 20 | Carrots, cooked | 1.20 ± 1.16 | Bean or lentils | 1.46 ± 1.90 |

¹ $\bar{x} \pm SD$. Total percentage potassium contribution of the foods listed: 60.02%; total percentage magnesium contribution of the foods listed: 57.86%.

² Average percentage contribution to total intake of all subjects in the study.


potassium intake and bone in both elderly men and women, and a protective effect against further bone loss in elderly men.

The role of magnesium in bone metabolism has been reviewed (46, 48). Magnesium contributes macroelement quantities to bone ash and is essential for appropriate calcium metabolism, affecting calcium balance (46, 49). Cancellous bone in osteoporotic women has been shown to have a low magnesium content, which is associated with crystals that are more "perfect" and brittle than those seen in magnesium-replete bone (50, 51). Despite the experimental and circumstantial evidence supporting the role of magnesium in maintaining bone health and preventing osteoporosis, few studies have evaluated this relation in humans. Trabecular but not cortical bone was improved with peroral magnesium in a small group of postmenopausal osteoporotic women (18). In another study, the effects of magnesium given to postmenopausal women could not be separated from the effects of the simultaneous administration of estrogen (52).

A few population studies have shown low magnesium intake, serum concentrations, or both in osteoporotic postmenopausal women (19, 53). A recent cross-sectional study of premenopausal women showed a significant association between magnesium intake and BMD at the lumbar spine (20). An earlier study found a significant positive association with forearm bone mineral content in premenopausal but not postmenopausal women (22). Additionally, one longitudinal study reported a significant positive association between magnesium intake and change in total-body BMD in 66 premenopausal women who were taking calcium supplements and were followed for 1 y (54). Our findings of a significant cross-sectional association between magnesium intake and hip, but not radius, BMD among postmenopausal women are consistent with these reports.

The only longitudinal study of change in bone status of post-

menopausal women we could locate included just 33 subjects, with measurement of bone mineral content at the radius and ulna only (55). As in our study, the authors did not observe a significant predictive effect of magnesium intake on 4-y change in BMD in these postmenopausal women, although they did detect a protective association between magnesium intake and bone loss at the humerus in 9 premenopausal women.

Our results for fruit and vegetable intakes were also interesting, with significant protective cross-sectional associations in both men and women and suggestive protective longitudinal effects in men. Fruit and vegetables are important sources of potassium and magnesium and this finding supports their potential role in the prevention of osteoporosis. We found only one other study that looked at this association. New et al (20) found significant associations between past reported fruit intake and BMD at the spine and trochanter in premenopausal women. Although the evidence remains limited, our findings support the hypothesis put forth by Wachman and Bernstein (14) in 1968 that a diet emphasizing the "ingestion of fruits, vegetables, vegetable protein, and moderate amounts of milk," all good sources of potassium and magnesium, may be protective of bone. Further investigation of the suggestion that these nutrients serve to buffer the acid load of the diet and thereby reduce bone loss is warranted. 

REFERENCES

1. Riggs BL, Melton LJ III. Involutional osteoporosis. *N Engl J Med* 1986;314:1676–86.
2. Kanis J, WHO Study Group. Assessment of fracture risk and its applications to screening for postmenopausal osteoporosis: synopsis of a WHO report. *Osteoporos Int* 1994;4:368–81.
3. Cummings SR, Kelsey JL, Nevitt MC, O'Dowd KJ. Epidemiology

- of osteoporosis and osteoporotic fractures. *Epidemiol Rev* 1985;7:178–208.
4. Nelson ME, Fiatarone MA, Morganti CM, Trice I, Greenburg RA, Evans WJ. Effects of high-intensity strength training on multiple factors for osteoporotic fractures: a randomized controlled trial. *JAMA* 1994;272:1909–14.
 5. Seeman E, Melton LJ III, O'Fallon WM, Riggs BL. Risk factors for spinal osteoporosis in men. *Am J Med* 1983;75:977–83.
 6. Kiel DP, Zhang Y, Hannan MT, Anderson JJ, Baron JA, Felson DT. The effect of smoking at different life stages on bone mineral density in elderly men and women. *Osteoporos Int* 1996;6:240–8.
 7. Scharfira D. Alcohol abuse and osteoporosis. *Semin Arthritis Rheum* 1990;19:371–6.
 8. Felson DT, Zhang Y, Hannan MT, Kiel DP, Wilson PWF, Anderson JJ. The effect of postmenopausal estrogen therapy on bone density in elderly women. *N Engl J Med* 1993;329:1141–6.
 9. Felson DT, Zhang Y, Hannan MT, Anderson JJ. Effects of weight and body mass index on bone mineral density in men and women: the Framingham Study. *J Bone Miner Res* 1993;8:567–73.
 10. Felson DT, Zhang Y, Hannan MT, Kiel DP. Alcohol intake and bone mineral density in elderly men and women. *Am J Epidemiol* 1995;142:485–92.
 11. Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. *N Engl J Med* 1990;323:878–83.
 12. Dawson-Hughes B, Dallal GE, Krall E, Harris S, Sokoll LJ, Falconer G. Effect of vitamin D supplementation on wintertime and overall bone loss in healthy postmenopausal women. *Ann Intern Med* 1991;115:505–12.
 13. Heaney RP. Nutritional factors in osteoporosis. *Annu Rev Nutr* 1993;13:287–316.
 14. Wachman A, Bernstein DS. Diet and osteoporosis. *Lancet* 1968;1:958–9.
 15. Chan JCM. Nutrition and acid-base metabolism. *Fed Proc* 1981;40:2423–8.
 16. Remer T, Manz F. Potential renal acid load of foods and its influence on urine pH. *J Am Diet Assoc* 1995;95:791–7.
 17. Lemann J Jr, Pleuss JA, Gray RW. Potassium causes calcium retention in healthy adults. *J Nutr* 1993;123:1623–6.
 18. Stendig-Lindberg G, Tepper R, Leichter I. Trabecular bone density in a two year controlled trial of peroral magnesium in osteoporosis. *Magnes Res* 1993;6:155–63.
 19. Tranquilli AL, Lucino E, Garzetti GG, Romanini C. Calcium, phosphorus, and magnesium intakes correlate with bone mineral content in postmenopausal women. *Gynecol Endocrinol* 1994;8:55–8.
 20. New SA, Bolton-Smith C, Grubb DA, Reid DM. Nutritional influences on bone mineral density: a cross-sectional study in premenopausal women. *Am J Clin Nutr* 1997;65:1831–9.
 21. Michaëlsson K, Holmberg L, Maumin H, Wolk A, Bergstrom R, Ljunghall S. Diet, bone mass and osteocalcin: a cross-sectional study. *Calcif Tissue Int* 1995;57:86–93.
 22. Angus RM, Sambrook PN, Pocock NA, Eisman JA. Dietary intake and bone mineral density. *Bone Miner* 1988;4:265–77.
 23. Yano K, Heilbrun LK, Wasnich RD, Hankin JH, Vogel JM. The relationship between diet and bone mineral content of multiple skeletal sites in elderly Japanese-American men and women living in Hawaii. *Am J Clin Nutr* 1985;42:877–88.
 24. Dawber TR, Meadors GF, Moore FEJ. Epidemiological approaches to heart disease: the Framingham Study. *Am J Public Health* 1951;41:279–86.
 25. Hannan MT, Felson DT, Anderson JJ. Bone mineral density in elderly men and women: results from the Framingham Osteoporosis Study. *J Bone Miner Res* 1992;7:547–53.
 26. Mazess RB, Barden HS, Ettinger M, et al. Spine and femur density using dual-photon absorptiometry in US white women. *Bone Miner* 1987;2:211–9.
 27. Nilas L, Christiansen C. Rates of bone loss in normal women: evidence of accelerated trabecular bone loss after the menopausal. *Eur J Clin Nutr* 1988;18:529–34.
 28. Kiel DP, Mercier CA, Dawson-Hughes B, Cali C, Hannan MT, Anderson JJ. The effects of analytic software and scan analysis technique on the comparison of dual X-ray absorptiometry with dual photon absorptiometry of the hip in the elderly. *J Bone Miner Res* 1995;10:1130–6.
 29. Greenspan SL, Maitland LA, Myers ER, Krasnow MB, Kido TH. Femoral bone loss progresses with age: a longitudinal study in women over age 65. *J Bone Miner Res* 1994;9:1959–65.
 30. Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. *Am J Epidemiol* 1992;135:1114–26.
 31. Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol* 1985;122:51–65.
 32. Ascherio A, Stampfer MJ, Colditz GA, Rimm EB, Litin L, Willett WC. Correlation of vitamin A and E intake with plasma concentrations of carotenoids and tocopherols among American men and women. *J Nutr* 1992;122:1792–801.
 33. Jacques PF, Sulsky SI, Sadowski JA, Philips JC, Rush D, Willett WC. Comparison of micronutrient intake measured by a dietary questionnaire and biochemical indicators of micronutrient status. *Am J Clin Nutr* 1993;57:182–9.
 34. Willett WC, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. *Am J Epidemiol* 1986;124:17–27.
 35. Sawaya AL, Tucker K, Tsay R, et al. Evaluation of four methods for determining energy intake in young and older women: comparison with doubly labeled water measurements of total energy expenditure. *Am J Clin Nutr* 1996;63:491–9.
 36. Feskanih D, Rimm E, Giovannucci EL, et al. Reproducibility and validity of food intake measurements from a semiquantitative questionnaire. *J Am Diet Assoc* 1993;93:790–6.
 37. Tucker KL, Selhub J, Wilson PWF, Rosenberg IH. Dietary intake pattern relates to plasma folate and homocysteine concentration in the Framingham Heart Study. *J Nutr* 1996;126:3025–31.
 38. Greendale GA, Barrett-Connor E, Edelstein S, Ingles S, Haile R. Lifetime leisure exercise and osteoporosis: the Rancho Bernardo Study. *Am J Epidemiol* 1995;141:951–9.
 39. Dawson-Hughes B. Calcium supplementation and bone loss: a review of controlled clinical trials. *Am J Clin Nutr* 1991;54(suppl):274S–80S.
 40. Kannel WB, Sorlie PD. Some health benefits of physical activity: the Framingham Study. *Arch Intern Med* 1979;139:857–61.
 41. Krall EA, Sahyoun N, Tannenbaum S, Dallal GE, Dawson-Hughes B. Effect of vitamin D intake on seasonal variations in parathyroid hormone secretion in postmenopausal women. *N Engl J Med* 1989;321:1777–83.
 42. National Research Council. Recommended dietary allowances. 10th ed. Washington, DC: National Academy Press, 1989.
 43. Standing Committee of the Scientific Evaluation of Dietary Reference Intake. Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride. Washington, DC: Institute of Medicine, National Academy of Science, 1997.
 44. Khaw KT, Barrett-Connor E. Dietary potassium and stroke-associated mortality: a 12-year prospective study. *N Engl J Med* 1987;316:235–40.
 45. Byers T. Dietary trends in the United States. Relevance to cancer prevention. *Cancer* 1993;72:1015–8.
 46. Seelig MS. Interrelationship of magnesium and estrogen in cardiovascular and bone disorders, eclampsia, migraine and premenstrual syndrome. *J Am Coll Nutr* 1993;12:442–58.
 47. Sebastian A, Harris ST, Ottaway JH, Todd KM, Morris RC Jr. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *N Engl J Med* 1994;330:1776–81.

48. Sojka JE, Weaver CM. Magnesium supplementation and osteoporosis. *Nutr Rev* 1995;53:71-4.
49. Kenney MA, McCoy H, Williams L. Effects of magnesium deficiency on strength, mass and composition of rat femur. *Calcif Tissue Int* 1994;54:44-9.
50. Manicourt DH, Orloff S, Brauman J, Schoutens A. Bone mineral content of the radius: correlations with physicochemical determinations in iliac crest trabecular bone of normal and osteoporotic subjects. *Metabolism* 1981;30:57-62.
51. Cohen L, Kitzes R. Infrared spectroscopy and magnesium content of bone mineral in osteoporotic women. *Isr J Med Sci* 1981;17:1123-5.
52. Abraham G, Grewal H. A total dietary program emphasizing magnesium instead of calcium: effect on mineral density of cancellous bone in postmenopausal women on hormone therapy. *J Reprod Med* 1990;35:503-7.
53. Reginster JY, Strause L, Deroisy R, Lecart MP, Saltman P, Franchimont P. Preliminary report of decreased serum magnesium in postmenopausal osteoporosis. *Magnesium* 1989;8:106-9.
54. Houtkooper LB, Ritenbaugh C, Aickin M, et al. Nutrients, body composition and exercise are related to change in bone mineral density in premenopausal women. *J Nutr* 1995;125:1229-37.
55. Freudenheim JL, Johnson NE, Smith EL. Relationships between usual nutrient intake and bone-mineral content of women 35-65 years of age: longitudinal and cross-sectional analysis. *Am J Clin Nutr* 1986;44:863-76.

