A PROSPECTIVE STUDY OF DIETARY CALCIUM AND OTHER NUTRIENTS AND THE RISK OF SYMPTOMATIC KIDNEY STONES

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Abstract *Background.* A high dietary calcium intake is strongly suspected of increasing the risk of kidney stones. However, a high intake of calcium can reduce the urinary excretion of oxalate, which is thought to lower the risk. The concept that a higher dietary calcium intake increases the risk of kidney stones therefore requires examination.

Methods. We conducted a prospective study of the relation between dietary calcium intake and the risk of symptomatic kidney stones in a cohort of 45,619 men, 40 to 75 years of age, who had no history of kidney stones. Dietary calcium was measured by means of a semiquantitative food-frequency questionnaire in 1986. During four years of follow-up, 505 cases of kidney stones were documented.

Results. After adjustment for age, dietary calcium intake was inversely associated with the risk of kidney stones; the relative risk of kidney stones for men in the highest as compared with the lowest quintile group for calcium intake was 0.56 (95 percent confidence interval, 0.43 to 0.73; P for trend, <0.001). This reduction in risk decreased only slightly (relative risk, 0.66; 95 percent confidence interval, 0.49 to 0.90) after further adjustment for other potential risk factors, including alcohol consumption and dietary intake of animal protein, potassium, and fluid. Intake of animal protein was directly associated with the risk of stone formation (relative risk for men with the highest intake as compared with those with the lowest, 1.33; 95 percent confidence interval, 1.00 to 1.77); potassium intake (relative risk, 0.49; 95 percent confidence interval, 0.35 to 0.68) and fluid intake (relative risk, 0.71; 95 percent confidence interval, 0.52 to 0.97) were inversely related to the risk of kidney stones.

Conclusions. A high dietary calcium intake decreases the risk of symptomatic kidney stones. (N Engl J Med 1993;328:833-8.)

AMONG disorders of the urinary tract, kidney stones are a major cause of morbidity. Approximately 12 percent of the U.S. population will have a kidney stone at some time,[1,2] and the incidence is rising not only in the United States[1,2] but also in Sweden[3] and Japan.[4] Kidney stones cause considerable suffering and have a substantial economic impact. In 1986, more than $2 billion was spent on the treatment of kidney stones, mostly for removal and fragmentation,[5] even before widespread use of extracorporeal shock-wave lithotripsy.[6]

A high dietary calcium intake is strongly suspected of raising the risk that a kidney stone will form. Consequently, patients with calcium-containing stones are often advised to decrease their calcium intake.[7] However, no prospective data demonstrate that lowering calcium intake decreases the risk of kidney stones.

More than 85 percent of stones in men contain calcium; among these, calcium oxalate stones are the most common.[2,8] The hypothesis that a high calcium intake increases the risk of stone formation is based largely on the finding that 20 to 40 percent of patients with recurrent stones have hypercalciuria.[9] The majority of patients with calcium oxalate stones and elevated urinary calcium excretion have idiopathic hypercalciuria; other causes of hypercalciuria, such as hyperparathyroidism or sarcoidosis, are much less common.[8] With similar levels of calcium ingestion, patients with idiopathic hypercalciuria excrete more calcium than normal subjects.[10] Although dietary calcium restriction can decrease urinary calcium excretion in patients with and without idiopathic hypercalciuria,[10,11] little is known about the effect of calcium restriction or other dietary modifications on the rates of recurrence of kidney stones.

In case–control studies, no difference in mean calcium intake was found between patients with kidney stones and control subjects.[12-15] However, these studies failed to control for other risk factors, such as age, urine volume, and the intake of animal protein,[16] sodium,[17] sucrose,[18] and magnesium.[19]

To address further the association between the intake of calcium and other nutrients and the incidence of kidney stones, we examined this relation in a cohort of 45,619 men with no history of kidney stones.

METHODS

Study Population

The Health Professionals Follow-up Study is a longitudinal study of cardiovascular disease and cancer among 51,529 male dentists, optometrists, osteopaths, pharmacists, podiatrists, and veterinarians who were 40 to 75 years of age in 1986. The participants returned a mailed questionnaire in 1986 concerning diet, medical history, and medications. Of the 49,976 men who provided complete information on diet and age, 4357 (8.7 percent) reported a history of kidney stones. These men were excluded from this analysis because of the possibility that they had changed their diet as a consequence of having a kidney stone.

Assessment of Diet

To assess the men's diet we used a semiquantitative food-frequency questionnaire that inquired about the average use of 131 foods and beverages during the previous year. Nutrient intake was computed from the reported frequency of consumption of each specified unit of food or beverage and from published data on the nutrient content of the specified portions.[20] Information was also collected on the amount of supplemental calcium (such as calcium carbonate) ingested, either alone or in multivitamin preparations.

We have previously reported on the reproducibility and validity of this dietary questionnaire in this cohort.[21] Briefly, 127 participants in the Boston area weighed and recorded all foods and bever-

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ages they consumed during two one-week periods six to eight months apart. The mean daily intake of dietary calcium based on the dietary records was 796 mg and that calculated from the questionnaire was 804 mg. The Pearson correlation coefficient for energy-adjusted dietary calcium intake between the dietary records and the questionnaire was 0.53. After adjustment for the week-to-week variation in calcium intake assessed by the two dietary records, the correlation was 0.60. A similar questionnaire has been validated in women.[20,22]

To obtain additional details on the typical pattern of calcium-supplement use, we mailed a questionnaire to a random sample of 100 men who took a supplement, of whom 93 responded. The questionnaire inquired about the specific calcium salt ingested and whether the supplement was taken alone or with particular meals.

Nutrient values were adjusted for total energy intake with use of a regression model, with total caloric intake as the independent variable and absolute nutrient intake as the dependent variable.[22,23] Because total energy intake for a given person tends to be fixed within a very narrow range, changes in nutrient intake must be made primarily by altering the composition of the diet, not the total amount of food consumed. Energy-adjusted values reflect the nutrient composition of the diet independent of the total amount of food consumed. In addition, energy adjustment reduces any variation introduced by underreporting or overreporting of intake on the food-frequency questionnaire, thus improving the accuracy of nutrient measurements.[21,22]

Assessment of Nondietary Factors

In 1986 the men provided information on their state of residence, weight, height, and use of thiazide diuretics. The level of physical activity in metabolic equivalents per week was computed on the basis of the reported frequency and duration of various forms of exercise.

Follow-up and Ascertainment of Cases

We sent follow-up questionnaires in 1988 and in early 1990, asking the men whether a kidney stone had been diagnosed since January 1986. After up to six mailings for each follow-up period,[24] the response rate was 96 percent in 1988 and 93 percent in 1990.

When a kidney stone was reported on a follow-up questionnaire, we mailed the subject a supplementary questionnaire to confirm the report and to ascertain the date of occurrence, symptoms, and any family history of kidney stones. The rate of response to the supplementary questionnaire was 96 percent. The primary end point was a new kidney stone accompanied by pain or hematuria. To confirm the validity of the subjects' reports, we obtained the medical records from a random sample of 60 of the men who had reported having a kidney stone. The records confirmed the diagnosis in 97 percent of the cases; the other 3 percent were bladder stones.

We considered only cases that occurred during the first four years of follow-up — between the return of the 1986 base-line questionnaire and January 31, 1990. After we excluded 97 men for whom the date of occurrence of the kidney stone could not be confirmed or fell outside the study period and 12 men with asymptomatic stones, 45,510 men with no history of kidney stones at base line remained in the study group.

Statistical Analysis

For each participant, person-months of follow-up were counted from the date of return of the 1986 questionnaire to the date of a kidney stone or death or to January 31, 1990, whichever came first. We allocated person-months of follow-up according to exposure status in 1986 (as indicated by the quintile of calcium intake and other variables) and calculated incidence as the number of events divided by the number of person-years of follow-up. Incidence rates were adjusted for age by direct standardization to the whole cohort according to five-year age groups.

The relative risk — the incidence among the men in a particular category of exposure divided by the corresponding rate in the comparison category — was used as the measure of association.[25] Age-adjusted relative risks were calculated after stratification according to five-year age categories.[25] The Mantel extension test was used to evaluate linear trends across categories of calcium intake. In addition, relative risks were adjusted simultaneously for potentially confounding variables by multiple logistic-regression analysis.[26] The variables considered in these models were age (in five-year categories), body-mass index (the weight in kilograms divided by the square of the height in meters; considered in quintile groups), physical-activity level (quartile groups), geographic region (seven categories), specific health profession, use of thiazide diuretics (yes or no), alcohol intake (eight categories), intake of sugared cola (four categories), coffee intake (four categories), and dietary intake of calcium, animal protein, sucrose, magnesium, sodium, phosphorus, potassium, vitamin D, and total fluid (quintile groups). For all relative risks, we calculated 95 percent confidence intervals. All P values are two-tailed.

Results

During 165,090 person-years of follow-up over a four-year period, we documented 505 cases of new symptomatic kidney stones (Table 1). A family history of kidney-stone disease (through first cousins) was reported by 130 of the 505 men (25.7 percent). Pain was the most common presenting symptom (90.5 percent). Of the 221 men who provided information on stone composition, 71.5 percent reported that it contained calcium. The incidence was highest on average among men in the age groups from 40 to 59 years old, declined among men from 60 to 69 years of age, and was markedly lower among men 70 years of age and older (Table 2).

Dietary Calcium Intake

The characteristics of the cohort according to quintile values for energy-adjusted dietary calcium intake are shown in Table 3. The mean daily intake of animal protein, magnesium, vitamin D, phosphorus, potassium, and total fluid increased with increasing dietary calcium intake. The average daily alcohol intake decreased with increasing calcium intake. The mean daily intake of sodium was similar in all quintile groups, as were the percentages of men who took calcium supplements or a thiazide diuretic.

The mean (±SD) daily dietary calcium intake was significantly lower among the men in whom kidney stones later developed than among those who remained free of stones (797±280 vs. 851±307 mg, $P<0.001$). After adjustment for age and energy intake, a higher intake of dietary calcium was strongly associated with a reduced risk of kidney stones (P for trend, <0.001) (Table 4). The relative risk for men in the highest as compared with the lowest quintile group was 0.56 (95 percent confidence interval, 0.43 to 0.73; $P<0.001$).

Adjustment for age, profession, thiazide use, and intake of animal protein, potassium, alcohol, and fluid slightly attenuated the apparent protective effect of dietary calcium, but it remained significant (Table 4). The adjusted relative risk for men in the highest quintile group for dietary calcium intake, as compared with those in the lowest quintile group, was 0.66 (95 percent confidence interval, 0.49 to 0.90), a 34 percent reduction in risk. Further control for geographic region, quartile group for physical-activity level, quin-

Table 1. Characteristics of the 505 Men with Kidney Stones.

CHARACTERISTIC	NO.	PERCENT
Medical conditions		
Inflammatory bowel disease	34	6.7
Hyperthyroidism	6	1.2
Hyperparathyroidism	3	0.6
History of urinary tract infection	43	8.5
Renal tubular acidosis	0	0
Immobilization (>30 days)	7	1.4
Family history of kidney stones	130	25.7
Seen by a physician for symptoms	437	86.5
Symptoms and signs		
Pain	457	90.5
Urgency	148	29.3
Hematuria	207	41.0
Infection	27	5.3
Type of stone reported*		
Calcium	158	71.5
Uric acid	51	23.1
Struvite	11	5.0
Cystine	1	0.5

*This information was available for 221 of the 505 men. The percentages total more than 100 because of rounding.

tile group for body-mass index, and intake of sodium, magnesium, vitamin D, phosphorus, coffee, sucrose, and sugared cola did not alter the results. There was no significant interaction between calcium intake and other variables. In a multivariate analysis including only the 158 men who reported a calcium stone (Table 1), the relative risk for the men with the highest dietary calcium intake as compared with those with the lowest intake (0.64; 95 percent confidence interval, 0.37 to 1.10) was similar to the corresponding relative risk of 0.66 for the whole group.

We also examined the relation of specific foods that are high in calcium content to the risk of kidney stones in order to determine whether a single food was responsible for the observed relation. Skim or low-fat milk and cottage cheese or ricotta cheese had the strongest inverse associations with risk. Men who drank two or more 8-oz (240 ml) glasses of skim milk per day had a relative risk of kidney stones of 0.58 (95 percent confidence interval, 0.42 to 0.79; P for trend, 0.002) as compared with men who drank less than one glass per month. The consumption of two or more half-cup (120 ml) servings of cottage cheese or ricotta cheese per week was associated with a relative risk of 0.70 (95 percent confidence interval, 0.52 to 0.95; P for trend, 0.002) as compared with the consumption of less than one serving per month. Inverse trends were also found for yogurt (P = 0.10) and sherbet (P = 0.15). Nondairy sources of calcium, such as oranges and broccoli, also appeared to be protective (P for trend, 0.03 for both foods).

Calcium from Supplements

We also examined the effect of calcium from supplements and found no significant association between the use of supplements and the risk of kidney stones (data not shown). After we controlled for potential confounders, the relative risk among men who took more than 500 mg of supplemental calcium per day, as compared with the men who took no supplements, was 1.23 (95 percent confidence interval, 0.84 to 1.79; P for trend, 0.29).

Other Factors

Intake of animal protein was directly associated with the risk of kidney stones, whereas potassium intake and fluid intake were inversely related to risk (Table 5). In the multivariate model, the relative risks for the men in the highest as compared with the lowest quintile group were 1.33 for animal-protein intake, 0.49 for potassium intake, and 0.71 for fluid intake. Sodium, magnesium, phosphorus, sucrose, fiber, and sugared cola were not associated with risk when we controlled for potential confounders. Simultaneous adjustment for these nutrients did not materially alter the protective effect of dietary calcium. After we controlled for potential confounders, the relative risk for men taking a thiazide diuretic, as compared with those not taking such a drug, was 0.55 (95 percent confidence interval, 0.36 to 0.83).

DISCUSSION

These prospective data provide no support for the belief that higher consumption of calcium from dietary sources increases the risk of symptomatic kidney stones; in fact, the data suggest that the relation may actually be inverse. In previous case–control studies of diet and kidney stones, the calcium intake in case patients and controls was similar,[12-15] but the patients with kidney stones had higher rates of urinary calcium excretion.[14,15] Because the majority of stones contain calcium[2,8] and because hypercalciuria has been associated with the formation of stones, calcium restriction has been routinely recommended for patients who have kidney stones. However, we are unaware of any data that demonstrate that restriction of calcium intake reduces the recurrence of kidney stones. Indeed, in a prospective study of patients with hypercalciuria, restriction of dietary calcium intake was associated with a 10 percent higher probability of stone forma-

Table 2. Incidence of Kidney Stones among 45,510 Men, According to Five-Year Age Groups.

AGE GROUP (YR)*	NO. OF MEN	NO. OF CASES	PERSON-YEARS†	INCIDENCE (PER 100,000 PERSON-YEARS)
<45	10,114	121	36,871	328
45–49	6,710	92	23,400	377
50–54	6,821	77	24,927	309
55–59	6,768	85	24,479	347
60–64	6,661	66	24,208	273
65–69	5,140	48	18,418	261
≥70	3,296	16	11,788	136

*The ages shown are as of January 1, 1986. The men were prospectively followed from 1986 to 1990.

†Values have been rounded.

Table 3. Characteristics of the Men According to Energy-Adjusted Dietary Calcium Intake.*

Characteristic	Total Group (N = 45,510)	Dietary Calcium†				
		Group 1 (N = 8861)	Group 2 (N = 9029)	Group 3 (N = 9106)	Group 4 (N = 9184)	Group 5 (N = 9330)
Age (yr)	54±10	54	54	54	54	54
Daily intake						
Dietary calcium (mg)	850±307	516	664	783	937	1326
Animal protein (g)	64±17	59	61	63	65	71
Sodium (mg)	3150±1162	3171	3162	3155	3145	3121
Potassium (mg)	3495±736	3165	3308	3425	3582	3964
Sucrose (g)	47±20	49	48	48	47	45
Dietary fiber (g)	23±8	22	22	23	23	23
Magnesium (mg)	378±92	350	362	372	385	418
Vitamin D (IU)	405±325	303	347	384	432	550
Phosphorus (mg)	1348±270	1159	1258	1337	1441	1701
Animal fat (g)	40±12	39	39	40	40	41
Vegetable fat (g)	32±11	35	33	33	32	29
Alcohol (g)	13±17	17	15	14	12	8
Fluid (ml)	1945±790	1789	1859	1915	1985	2167
Body-mass index‡	26±3	26	26	26	26	26
Calcium-supplement use (%)§	24	24	23	23	25	23
Thiazide use (%)	9	10	10	9	9	9

*All values except supplemental calcium intake and thiazide use are means, standardized according to the age distribution of the cohort. Plus–minus values are means ±SD. Nutrient values have been adjusted for energy intake.

†Group 1 had dietary calcium values below the first quintile for the group (lowest intake), group 2 values between the first and second quintiles, group 3 values between the second and third quintiles, group 4 values between the third and fourth quintiles, and group 5 values above the fourth quintile (highest intake).

‡The weight in kilograms divided by the square of the height in meters.

§Calcium from calcium supplements or multivitamin preparations.

tion, as determined on the basis of the urinary excretion of lithogenic factors.[11] In addition, in patients with idiopathic hypercalciuria dietary calcium restriction may lead to negative calcium balance and bone loss.[27]

The apparent protective effect of dietary calcium is intriguing and perhaps counterintuitive. Since 20 to 40 percent of men with recurrent kidney stones have idiopathic hypercalciuria and excrete more calcium with increasing intake, an increased risk of stone formation might have been expected with higher calcium consumption. One possible explanation for these findings involves the role of oxalate, as suggested by indirect experimental evidence.[28-30] Calcium restriction increases the absorption of oxalate in the gastrointestinal tract in normal subjects[11,31,32] and in patients with kidney stones,[29] leading to an increase of 16 percent[33] to 56 percent[29] in urinary oxalate excretion. Among patients with malabsorption, even with a normal calcium intake, binding of calcium by fat in the gastrointestinal tract increases the absorption and urinary excretion of oxalate,[34] suggesting that the inverse relation between dietary calcium and kidney stones may be due to increased binding of oxalate by calcium in the gastrointestinal tract. Urinary oxalate may be more important than urinary calcium for stone formation, because calcium oxalate saturation of urine increases rapidly with small increases in the oxalate concentration.[30] Therefore, calcium restriction could actually be harmful in that it may lead to increased urinary oxalate excretion.[35]

Oxalate is found in many foods, but the content is typically low.[36] Ingestion of foods high in oxalate can lead to hyperoxaluria and to the formation of calcium oxalate stones.[28] Oxalate values are not available for the full range of foods on our questionnaire; thus, total intake could not be calculated. However, our questionnaire included several foods with relatively high oxalate content. When we controlled for potentially confounding variables, the consumption of these foods (chocolate, nuts, tea, and spinach) was not associated with the risk of kidney stones (data not shown).

The association between higher calcium intake and a reduced risk of kidney stones was consistent when we assessed the intake of specific foods that are high in calcium. Thus, it is likely that calcium itself, rather than a single food or food group, accounted for the inverse association.

Calcium supplements did not have the apparent protective effect of dietary calcium, perhaps because

Table 4. Age-Standardized Incidence and Relative Risk of Symptomatic Kidney Stones, According to Dietary Calcium Intake.

Variable*	Dietary Calcium†					Chi (P for Trend)‡
	Group 1 (N = 8861)	Group 2 (N = 9029)	Group 3 (N = 9106)	Group 4 (N = 9184)	Group 5 (N = 9330)	
Dietary calcium intake (mg/day)	<605	605–722	723–848	849–1049	≥1050	—
Incidence/100,000 person-yr	435	310	279	266	243	—
No. of cases	139	102	93	89	82	
Age-adjusted RR	1.0	0.71	0.64	0.61	0.56	−4.37 (<0.001)
95% CI		0.55–0.92	0.50–0.83	0.47–0.80	0.43–0.73	
Multivariate RR	1.0	0.74	0.68	0.68	0.66	−2.38 (0.018)
95% CI		0.57–0.97	0.52–0.90	0.51–0.90	0.49–0.90	

*RR denotes the relative risk as compared with the group with the lowest calcium intake, and CI confidence interval. The multivariate model included age (in five-year age categories), profession, use of thiazide diuretics (yes or no), alcohol (eight categories), and dietary intake of animal protein, potassium, and fluid (quintile groups).

†Group 1 had dietary calcium values below the first quintile for the group (lowest intake), group 2 values between the first and second quintiles, group 3 values between the second and third quintiles, group 4 values between the third and fourth quintiles, and group 5 values above the fourth quintile (highest intake).

‡A chi value of more than 1.96 denotes a P value of less than 0.05. The sign of the chi value indicates the direction of the trend.

Table 5. Age-Standardized Incidence and Relative Risk of Symptomatic Kidney Stones, According to Dietary Consumption of Animal Protein, Potassium Intake, and Fluid Intake.

VARIABLE	DIETARY INTAKE*					CHI (P FOR TREND)†
	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5	
Animal-protein intake (g/day)	≤50	51–58	59–66	67–76	≥77	—
Incidence/100,000 person-yr	293	264	370	271	326	—
No. of cases	98	85	130	86	106	
Age-adjusted RR‡	1.0	0.90	1.26	0.92	1.11	0.80 (0.68)
95% CI		0.68–1.21	0.97–1.64	0.69–1.24	0.85–1.47	
Multivariate RR‡	1.0	0.97	1.41	1.07	1.33	1.99 (0.05)
95% CI		0.73–1.31	1.08–1.85	0.79–1.44	1.00–1.77	
Potassium intake (mg/day)	≤2895	2896–3252	3253–3592	3593–4041	≥4042	—
Incidence/100,000 person-yr	432	365	291	262	184	—
No. of cases	142	116	99	89	59	
Age-adjusted RR‡	1.0	0.83	0.68	0.60	0.43	−6.21 (<0.001)
95% CI		0.65–1.06	0.52–0.87	0.46–0.79	0.32–0.58	
Multivariate RR‡	1.0	0.88	0.74	0.69	0.49	−4.35 (<0.001)
95% CI		0.68–1.14	0.56–0.97	0.52–0.92	0.35–0.68	
Fluid intake (ml/day)	<1275	1275–1669	1670–2049	2050–2537	≥2538	—
Incidence/100,000 person-yr	372	386	307	270	192	—
No. of cases	117	129	101	90	68	
Age-adjusted RR‡	1.0	1.05	0.82	0.72	0.52	−4.87 (<0.001)
95% CI		0.81–1.34	0.63–1.07	0.55–0.95	0.39–0.70	
Multivariate RR‡	1.0	1.16	0.95	0.89	0.71	−2.95 (0.003)
95% CI		0.90–1.49	0.72–1.25	0.67–1.18	0.52–0.97	

*Group 1 had intake values below the first quintile for the group (lowest intake), group 2 values between the first and second quintiles, group 3 values between the second and third quintiles, group 4 values between the third and fourth quintiles, and group 5 values above the fourth quintile (highest intake).

†A chi value of more than 1.96 denotes a P value of less than 0.05. The sign of the chi value indicates the direction of the trend.

‡RR denotes relative risk as compared with the group with the lowest intake, and CI confidence interval. The multivariate model included age (in five-year age categories), profession, use of thiazide diuretics (yes or no), alcohol (eight categories), and dietary intake of calcium, animal protein, potassium, and total fluid (quintile groups).

of the timing of ingestion of the supplements. Calcium given with oral oxalate loads decreases urinary oxalate excretion by 50 percent in patients with ileal disease and in those who have kidney stones and hypercalciuria.[31] The supplements were typically not taken with a meal in our population (51 percent) or were taken only with breakfast (38 percent), when the oxalate content of the meal was likely to be low. Hence, the supplements could provide little or no protection from oxalate absorption. If the supplements are not taken with food, the absorption of calcium may be higher, leading to increased urinary calcium excretion and higher risk.

Dietary intake of animal protein was directly associated with the risk of stone formation, and the intake of potassium and the intake of fluid were inversely related to risk. Animal-protein intake increases the excretion of uric acid[37] and calcium[38] and lowers urinary citrate excretion,[38] all of which predispose a person to the formation of calcium stones. Potassium supplementation reduces calcium excretion in healthy adults, an effect that would decrease the risk of stone formation.[39] The beneficial effect of increased fluid intake and the subsequent dilution of urine is well known.

Biased recall of diet was avoided in this study because the intake data were collected before the diagnosis of kidney stones was made. However, nondietary risk factors for kidney stones could have influenced our results if they were strongly associated with the intake of calcium. We controlled for physical activity, geographic region, and profession, but data on family history were collected only for the men with kidney stones. In an analysis limited to men who reported a family history of kidney stones, there was also an inverse association of risk with calcium intake (data not shown).

Selection bias cannot be completely excluded as an explanation for our results. The men who were most susceptible to the effects of higher calcium intake may have had their first kidney stone before 1986; they would thus have been excluded from the analysis. The exclusion of such men is unlikely to explain our findings, however. A large proportion of first kidney stones occur after 40 years of age. The incidence in this cohort was highest (and was stable) between the ages of 40 and 59. Similarly, Johnson et al. found that 68 percent of men who had kidney stones had their first stone after the age of 39,[2] and Hiatt et al. reported peak incidence among men from 40 to 59 years old.[40] Moreover, if prolonged high calcium intake selected out those most susceptible to stone formation earlier in life, then the relative risk associated with dietary calcium would be expected to decrease with increasing age. We found no change in the effect of calcium with increasing age. Finally, in this cohort, among 4357 men who had a kidney stone before 1986, the same inverse association with calcium intake was found in a retrospective analysis (relative risk for the highest vs. the lowest quintile group, 0.63; 95 percent confidence interval, 0.56 to 0.71).

Although the validity of the dietary questionnaire has been carefully documented,[21] we recognize that calcium intake was not perfectly assessed in this study. Because of the prospective design, any misclassification would be random with respect to case status,

however, and hence would tend to result in an underestimation of the protective effect of calcium.

Our findings are most directly generalizable to men 40 years old and older with no history of kidney stones. Whether these findings apply to women, younger men, or men with a previous kidney stone is not known. We have no reason to believe, however, that the relations we observed would be different in the other groups. These results probably also apply to recurrence among most patients who have calcium oxalate stones, because the physiologic principles are unchanged by the fact that a patient has already had one stone. The protective effect of a high-calcium diet may be mediated through decreased oxalate absorption and excretion or through some other unknown mechanism. However, a prospective study of diet in patients with recurrent kidney stones is necessary to clarify the possible beneficial role of calcium.

Our findings provide no support for the belief that a diet low in calcium reduces the risk of kidney stones. In contrast, they suggest that a higher dietary calcium intake may decrease the incidence of symptomatic kidney stones. The general policy of calcium restriction for patients who have had kidney stones containing calcium should be reexamined.

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