

[Figure]), and medication use for hypercholesterolemia was more than 10 times greater (25.9% vs 1.5%;  $P < .001$ ). Baby boomers were also more likely to have diabetes (15.5% vs 12.0%;  $P = .003$  [Figure]) and take medication for diabetes (11.3% vs 6.2%;  $P < .001$ ). The slight trend toward higher prevalence of cancer in baby boomers vs the previous generation was not significant (10.6% vs 9.5%;  $P = .25$ ). The frequency of emphysema decreased in the baby boomer generation (2.3%) relative to the previous generation (3.5%) ( $P = .03$ ). Baby boomers were also less likely to have had a myocardial infarction (3.6%) compared with the previous generation (5.3%) ( $P = .004$ ).

A logistic regression was conducted to control for changes in demographic characteristics (age, sex, race, and socioeconomic status) of the population between 1988-1994 and 2007-2010. The results indicated, after adjustment, that baby boomers remained more likely than the previous generation to have diabetes (odds ratio [OR], 1.46; 95% CI, 1.16-1.83); hypertension (OR, 1.38; 95% CI, 1.14-1.67); and hypercholesterolemia (OR, 5.94; 95% CI, 4.94-7.14).

**Comment.** Despite their longer life expectancy over previous generations, US baby boomers have higher rates of chronic disease, more disability, and lower self-rated health than members of the previous generation at the same age. On a positive note, baby boomers are less likely to smoke cigarettes and experience lower rates of emphysema and myocardial infarction than the previous generation.

The findings from the present study documenting poorer health status and increased rates of obesity, hypertension, diabetes, and hypercholesterolemia support an increased likelihood for continued rising health care costs and a need for increased numbers of health professionals as baby boomers age.<sup>5,6</sup> Given the link between positive healthy lifestyles and subsequent health in this age group,<sup>7</sup> the present study demonstrates a clear need for policies that expand efforts at prevention and healthy lifestyle promotion in the baby boomer generation.

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## LESS IS MORE

### Ascorbic Acid Supplements and Kidney Stone Incidence Among Men: A Prospective Study

U rinary oxalate is an important determinant of calcium oxalate kidney stone formation.<sup>1</sup> Vitamin C is excreted in urine both in its unmetabolized form and as oxalate; however, there remains considerable uncertainty over the kidney stone risk that may be associated with ascorbic acid supplement use.<sup>2</sup>

We examined whether ascorbic acid supplements (approximately 1000 mg) were associated with kidney stones in a population-based, prospective cohort of men.

*See also Invited Commentary at end of letter and page 355*

**Methods.** The Cohort of Swedish Men (COSM) has been described elsewhere.<sup>3</sup> In brief, 48 850 men, aged 45 to 79 years at baseline, were recruited in 1997 (response rate, 49%). Detailed diet and lifestyle data were collected at baseline using a self-administered questionnaire. Based on validated questions, men reported their use of ascorbic acid (sensitivity=67% and specificity=93%)<sup>4</sup> and of 20 other supplement types. We excluded those with incorrect national registration numbers, implausible energy intake, pre-

baseline cancer diagnosis, and missing supplement use data and those diagnosed as having kidney stones prior to baseline, based on registry (n=1612) and self-reported (n=5898) data, because these men may have changed their diet or supplement use based on medical advice. We also excluded users of supplements other than ascorbic acid as this may be a significant source of confounding (n=12 873). For comparison, we repeated the analysis for multivitamin (only) users.

First incident cases of kidney stones (*International Statistical Classification of Diseases, 10th Revision* code N20) were ascertained from January 1, 1998, to December 31, 2009, using registry data.

We estimated hazard ratios (hereafter, relative risks [RRs]) with Cox proportional hazards regression models using attained age as the timescale. Follow-up was censored at date of kidney stone diagnosis, death, or end of follow-up, whichever occurred first. The Schoenfeld residual test indicated no violation of the proportional hazard assumption.

Dose-response was assessed using the frequency-of-use data, which were available for 91.5% of ascorbic acid users. The linear trend across categories was tested using the median tablet usage within each group as a continuous variable.

Ethical approval was granted by the regional ethical review board in Stockholm, Sweden, and return of the completed questionnaire was considered to imply informed consent.

**Results.** During 11 years of follow-up we ascertained 436 first incident cases of kidney stones. Ascorbic acid use was associated with a statistically significant 2-fold increased risk (**Table**). In contrast, multivitamin use was not associated with kidney stone risk (RR, 0.86 [95% CI, 0.62-1.19]).

Users of only ascorbic acid taking fewer than 7 (median) and 7 or more tablets per week showed increased risks of RR, 1.66 (95% CI, 0.99-2.79) and RR, 2.23 (95% CI, 1.28-3.88), respectively, compared with supplement nonusers in the full multivariate-adjusted model (*P* value for trend = .001).

**Comment.** The strengths of this study include the large population-based prospective cohort design, validated exposure data, and virtually complete follow-up of the study population through linkage to high-quality registers. Furthermore, analysis of kidney stone material collected from 3176 men, treated with extracorporeal shockwave lithotripsy in Stockholm County, found calcium oxalate to be the dominant component in 92.6% (H.-G.T., unpublished data). It could thus be assumed that at least 90% of the kidney stones in our study population were composed primarily of calcium oxalate.<sup>5</sup>

Our results may not be generalizable to women, who typically have a much lower kidney stone risk. Because the risk associated with ascorbic acid may depend both on the dose and on the combination of nutrients with which the ascorbic acid is ingested, our findings should not be translated to dietary vitamin C. Data on the brand of supplement used were not available, and we were not, therefore, able to fully characterize the dose taken. How-

**Table. Characteristics of Study Population and Risk of Kidney Stones in Relation to Use of Ascorbic Acid Only in 23 355 Swedish Men**

	Ascorbic Acid Supplement Use	
	Supplement Nonusers (n = 22 448)	Users of Ascorbic Acid Only (n = 907)
<b>Characteristic<sup>a</sup></b>		
Age, y <sup>b</sup>	58.6 (9.4)	59.4 (9.6)
Postsecondary education, %	15.6	19.4
BMI	26 (3.4)	25 (3.0)
Consumption, g/d, of		
Alcohol	15 (20)	15 (21)
Tea	294 (352)	312 (367)
Coffee	743 (448)	699 (407)
Dietary intake, mg/d <sup>c</sup>		
Calcium	1461 (467)	1451 (445)
Magnesium	457 (64)	463 (62)
Potassium	3946 (656)	3970 (647)
Vitamin B <sub>6</sub>	2.4 (0.4)	2.5 (0.4)
Vitamin C	106 (53)	111 (58)
<b>Cases and Estimation of Risk</b>		
First incident cases, No.	405	31
Person-years	248 884	9995
Rate (per 100 000 person-years) <sup>d</sup>	163	310
Age-adjusted RR	1 [Reference]	1.90 (1.32-2.73)
Multivariate RR (95% CI) <sup>e</sup>	1 [Reference]	1.95 (1.35-2.81)
Multivariate RR (95% CI) <sup>f</sup>	1 [Reference]	1.92 (1.33-2.77)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); RR, relative risk.

<sup>a</sup>Data are given as means (SDs) except where noted.

<sup>b</sup>Age-standardized to entire study cohort.

<sup>c</sup>Adjusted to mean energy intake of the cohort (2600 kcal/d).

<sup>d</sup>Incidence rate difference 147 per 100 000 person-years.

<sup>e</sup>Adjusted for attained age, education level (primary, secondary, postsecondary), BMI (underweight/normal, <25 kg/m<sup>2</sup>; overweight, 25-29 kg/m<sup>2</sup>; obese, ≥30 kg/m<sup>2</sup>), alcohol (quintiles), and dietary intakes of calcium, magnesium, potassium, vitamin B<sub>6</sub>, and vitamin C (quintiles).

<sup>f</sup>Additionally adjusted for consumption of tea (0, <1, 1-3, 4-5, or ≥6 cups/d) and coffee (0, <1, 1-3, 4-5, or ≥6 cups/d). Additional adjustment for smoking status, high blood pressure, and diabetes mellitus did not change the results.

ever, previous studies have demonstrated that ascorbic acid preparations available on the Swedish market typically contain 1000 mg of ascorbic acid per tablet.<sup>6</sup> Supplement users may be more health conscious and therefore more likely to seek medical help; however, given the severe pain associated with kidney stones, this is unlikely to explain our findings. It is also not supported by our null results for multivitamin use. We cannot rule out the possibility of residual confounding.

The rate difference was 147 of 100 000 for first incident cases; however, the recurrent nature of kidney stones implies that the absolute risk increase, for this modifiable risk factor, is potentially higher. Our findings need to be confirmed by other studies but may have important implications for the clinical advice given to kidney stone formers. Currently there are no well-documented benefits of high-dose ascorbic acid supplement use,<sup>7</sup> and, therefore, it seems prudent to advise that high-dose preparations be avoided, particularly by those with a history of kidney stones.

In conclusion, our results indicate that high-dose ascorbic acid supplements—one of the most commonly used vitamin preparations—are associated with a dose-dependent 2-fold increased risk of kidney stone formation among men.

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## INVITED COMMENTARY

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### The Risk of Taking Ascorbic Acid

Vitamin deficiency diseases, such as pellagra, rickets, beriberi, night blindness, and scurvy, used to account for an enormous burden of suffering worldwide. One by one, the underlying dietary deficiencies were defined, and, in the early part of the 20th century, the chemical structures of the missing nutrients were identified. While vitamin deficiency diseases remain endemic in some parts of the world, in most regions they have been eliminated by public health programs and improvements in living conditions. These diseases are rarely seen in most countries, except in individuals at increased risk because of unbalanced diets, malabsorption, abnormal losses (eg, hemodialysis), or uncommon genetic defects.

But more was expected of vitamins, putting them on a roller coaster ride in recent decades. In the 1990s it was widely thought, based on physiologic effects and observational studies, that vitamin supplementation might prevent or treat chronic diseases such as cardiovascular disease and cancer. With time, these hypotheses were put to a strong test with randomized controlled trials. The results were for the most part discouraging, with multiple randomized trials and systematic reviews with meta-analyses ruling out effectiveness. Attention has recently swung to harms, especially at relatively high doses, ones easily obtained from pharmacy and food supplement store counters and the Internet, at the urging of believers and entrepreneurs.

Vitamin C has been on a ride of its own. Until the 1800s, scurvy was the scourge of sea travel, disabling and killing sailors after a few months at sea. Early settlers in the New World also experienced scurvy during the winter months when citrus fruits and vegetables, the main sources of vitamin C, were not available. James Lind, a British medical officer, carried out one of the first controlled trials and showed that scurvy was caused by a dietary deficiency.<sup>1</sup> He allocated 12 sailors who were badly affected by scurvy to receive limes or various other treatments that were touted by experts at the time; within a few days, the 2 sailors treated with limes were well enough to nurse the others or return to work, whereas the other 10 sailors were no better. Lind published these findings in 1753,<sup>1</sup> but dietary prevention of scurvy was not widely practiced until several decades later. The compound responsible for vitamin C activity, ascorbic acid, was identified in the 1930s, well after the disease was being prevented by diet.

But more was expected of vitamin C, too. Linus Pauling, twice Nobel Laureate, came to believe that vitamin C was powerfully effective against the common cold—