

## COMMENT &amp; RESPONSE

**Ascorbic Acid Supplements and Kidney Stone Risk**

**To the Editor** In their Research Letter, Thomas et al<sup>1</sup> report an increased risk of first-episode renal stone in Swedish men who took ascorbic acid supplements (but no other supplements). This risk is almost certainly overestimated. Cases were identified according to code N20 of the *International Statistical Classification of Diseases*: calculus of kidney or ureter in the absence of hydroureter ([www.cdc.gov/nchs/data/dvs/2006-Vol-I.pdf](http://www.cdc.gov/nchs/data/dvs/2006-Vol-I.pdf)). Contrary to what the authors claim, the symptoms of renal colic are often nonspecific, especially in the absence of hydroureter<sup>2,3</sup>, and for this reason, nonspecific abdominal or flank pain frequently prompts an investigation for renal stone.<sup>2,3</sup> As many as 40% of renal stones identified by means of imaging studies are asymptomatic<sup>4</sup>—not surprisingly, since the prevalence of renal stone in asymptomatic men is 10%.<sup>5</sup> The fact that physicians and the general public are repeatedly warned that ascorbic acid supplements cause renal stones (even though the evidence is inconclusive) predictably lowers the threshold for testing for them. Thus, all other things being equal, takers of high-dose ascorbic acid supplements are much more likely than nontakers to be investigated for renal stone, artificially increasing the number of code N20 cases linked to vitamin C. These factors, combined with the authors' sole reliance on registry entries for case identification, strongly expose their study to the important epidemiological error of "confounding by indication."

L. John Hoffer, MD, PhD

**Author Affiliation:** Lady Davis Institute for Medical Research, Jewish General Hospital, McGill University, Montreal, Quebec, Canada.

**Corresponding Author:** L. John Hoffer, MD, PhD, Lady Davis Institute for Medical Research, McGill University and Jewish General Hospital, 3755 Cote Sainte Catherine, Montreal, QC H3T 1E2, Canada ([hoffer@mcgill.ca](mailto:hoffer@mcgill.ca)).

**Conflict of Interest Disclosures:** None reported.

1. Thomas LDK, Elinder CG, Tiselius HG, Wolk A, Akesson A. Ascorbic acid supplements and kidney stone incidence among men: a prospective study. *JAMA Intern Med.* 2013;173(5):386-388.
2. Ahmad NA, Ather MH, Rees J. Incidental diagnosis of diseases on un-enhanced helical computed tomography performed for ureteric colic. *BMC Urol.* 2003;3:2.
3. Rucker CM, Menias CO, Bhalla S. Mimics of renal colic: alternative diagnoses at unenhanced helical CT. *Radiographics.* 2004;24(suppl 1):S11-S33.
4. Bansal AD, Hui J, Goldfarb DS. Asymptomatic nephrolithiasis detected by ultrasound. *Clin J Am Soc Nephrol.* 2009;4(3):680-684.
5. Boyce CJ, Pickhardt PJ, Lawrence EM, Kim DH, Bruce RJ. Prevalence of urolithiasis in asymptomatic adults: objective determination using low dose noncontrast computerized tomography. *J Urol.* 2010;183(3):1017-1021.

**In Reply** Dr Hoffer reasons that the investigation of nonspecific abdominal or flank pain may result in the diagnosis of nonsymptomatic kidney stones and that such diagnoses are more likely among ascorbic acid supplement users, leading to an overestimation of the risk. We believe it is highly improbable that those presenting with such symptoms would be more likely to be examined with respect to stone disease if they have

a history of ascorbic acid supplement use. First, for this to be the case, the patient would have to provide information on their supplement use either after being asked by their physician or without having been prompted to do so. Second, the physician would have to consider use of ascorbic acid supplements, by the patient, sufficient to warrant the prioritization of diagnostic tests for kidney stones over those of other potential causes.

The results of previous studies investigating the role of vitamin C in kidney stone formation have proved contradictory.<sup>1-3</sup> Recommendations based on the available evidence have concluded that doses below 4 g/d pose no increased risk even among those with recurrent stones.<sup>4,5</sup> Because of this, a high intake of vitamin C has not generally been considered as an important risk factor, either within the medical community or among the general public. It is therefore highly unlikely that someone presenting with nonspecific abdominal or flank pain would volunteer information on their supplement use or be asked for such information by their physician in order to aid diagnosis. This is certainly highly improbable within Sweden.

It is also important to note that renal stones represent by far the most common cause of flank pain in patients undergoing computed tomographic scans for suspected renal colic.<sup>6</sup> In Sweden it is not common practice to carry out imaging for renal stones in those with nonspecific abdominal or flank pain.

We do not, therefore, believe that differential diagnosis of renal stones between ascorbic acid supplement use groups represents a likely cause of bias within our study. Our findings of a significant dose response also support this conclusion.

Hans-Göran Tiselius, MD

Agneta Åkesson, PhD

Laura D. K. Thomas, MSc

**Author Affiliations:** Department of Clinical Science, Intervention, and Technology, CLINTEC, Karolinska Institutet, Stockholm, Sweden (Tiselius); Institute of Environmental Medicine, Division of Nutritional Epidemiology, Karolinska Institutet (Åkesson, Thomas).

**Corresponding Author:** Agneta Åkesson, PhD, Institute of Environmental Medicine, Division of Nutritional Epidemiology, Karolinska Institutet, PO Box 210, 171 77 Stockholm, Sweden ([Agneta.Akesson@ki.se](mailto:Agneta.Akesson@ki.se)).

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1. Traxer O, Huet B, Poindexter J, Pak CY, Pearle MS. Effect of ascorbic acid consumption on urinary stone risk factors. *J Urol.* 2003;170(2, pt 1):397-401.
2. Taylor EN, Stampfer MJ, Curhan GC. Dietary factors and the risk of incident kidney stones in men: new insights after 14 years of follow-up. *J Am Soc Nephrol.* 2004;15(12):3225-3232.
3. Curhan GC, Willett WC, Speizer FE, Stampfer MJ. Twenty-four-hour urine chemistries and the risk of kidney stones among women and men. *Kidney Int.* 2001;59(6):2290-2298.
4. Tiselius HG; Advisory Board of European Urolithiasis Research and EAU Health Care Office Working Party for Lithiasis. Possibilities for preventing recurrent calcium stone formation: principles for the metabolic evaluation of patients with calcium stone disease. *BJU Int.* 2001;88(2):158-168.
5. Tiselius HGAP, Buck C, Gallucci M, Knoll T, Sarica K, Türk C. *Guidelines on Urolithiasis: 2009 Edition.* Arnhem, the Netherlands: European Association of Urology; 2009.
6. Katz DS, Scheer M, Lumerman JH, Mellinger BC, Stillman CA, Lane MJ. Alternative or additional diagnoses on unenhanced helical computed tomography for suspected renal colic: experience with 1000 consecutive examinations. *Urology.* 2000;56(1):53-57.