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## INVITED COMMENTARY

# Vitamin and Mineral Supplement Use in Relation to All-Cause Mortality in the Iowa Women's Health Study

The beneficial influence of a proper diet on our health has been known since ancient times. Our diet provides a number of compounds that are essential for our health. Although a healthy diet provides a sufficient amount of vitamins and minerals, many individuals regularly take vitamin and mineral supplements hoping to further improve their health and prevent diseases. More than one-third of adults in high-income countries regularly take these supplements.<sup>1</sup>

Many studies have been conducted to verify the assumed beneficial effects of vitamin and mineral supplements. Although the results of epidemiologic observational studies almost uniformly have been positive, the results of individual randomized clinical trials undertaken to corroborate this hypothesis have remained largely inconclusive. Only through the systematic review of several randomized clinical trials have we gained the power and the precision to detect clinical harms and benefits.

In this issue of the *Archives*, Mursu and colleagues<sup>2</sup> report the results of the Iowa Women's Health Study. The authors assessed the use of vitamin and mineral supplements in relation to all-cause mortality in older women. The use of multivitamins, vitamin B<sub>6</sub>, folic acid, magnesium, zinc, iron, and copper was individually statistically associated with increased risk of all-cause mortality when compared to nonuse.<sup>2</sup> After adjustment for multiplicity, only multivitamins and copper retained the

significant association. The use of calcium and vitamin D was associated with a decreased risk of all-cause mortality when compared to nonuse before and after adjustment for multiplicity.<sup>2</sup> The Iowa Women's Health Study is observational; therefore, confounding by indication and by other such factors cannot be excluded. However, the study is large, well designed, and well conducted.

Mursu and colleagues add to the growing evidence demonstrating that certain antioxidant supplements, such as vitamin E, vitamin A, and beta-carotene, can be harmful.<sup>3-5</sup> Their results also concur with the findings of recent observational studies.<sup>6,7</sup> The belief that antioxidant supplements are beneficial seems likely to have resulted from a collective error. Perhaps oxidative stress is one of the keys to extension of our life span.<sup>8</sup>

The findings by Mursu and colleagues that calcium and vitamin D were associated with better survival also are interesting. Their results regarding calcium seem to contrast with those of a recent meta-analysis<sup>9</sup> of randomized trials that observed that calcium supplementation is associated with an increased risk of myocardial infarction and those of an observational study<sup>10</sup> that reported a 24% increase in coronary heart disease in Finnish postmenopausal women using calcium supplements. High intake of calcium also has been associated with an increased risk of prostate cancer.<sup>11</sup> Is taking only calcium supplements perhaps not a good idea? An intervention review published

in the Cochrane Database of Systematic Reviews<sup>12</sup> found evidence that vitamin D<sub>3</sub> decreases mortality in predominantly elderly women who mainly live in institutions and receive dependent care. Thus, the observational data by Mursu and colleagues regarding vitamin D are in accord with our results based on systematic review and meta-analyses of randomized clinical trials.

Dietary supplementation has shifted from preventing deficiency to trying to promote wellness and prevent diseases. Consumers believe that vitamin and mineral supplements are safe and use them without the supervision of their physicians. Until recently, the available data regarding the adverse effects of dietary supplements has been limited and grossly underreported.<sup>13,14</sup> We think the paradigm “the more the better” is wrong. One should consider the likely U-shaped relationship between micronutrient status and health. We believe that for all micronutrients, risks are associated with insufficient and too-large intake. Low levels of intake increase the risk of deficiency. High levels of intake increase the risk of toxic effects and disease. Therefore, we believe that politicians and regulatory authorities should wake up to their responsibility to allow only safe products on the market.

We cannot recommend the use of vitamin and mineral supplements as a preventive measure, at least not in a well-nourished population. Those supplements do not replace or add to the benefits of eating fruits and vegetables and may cause unwanted health consequences.<sup>3</sup> Consumption of a varied, healthful diet seems to be a prudent preventive strategy. Older women (and perhaps men) may benefit from intake of vitamin D<sub>3</sub> supplements, especially if they have insufficient vitamin D supply from the sun and from their diet. The issue of whether to use calcium supplements may require further study.

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## EDITOR'S NOTE

# Vitamin Supplements

## More Cost Than Value

**V**itamin and dietary supplement use has increased steadily in the United States, with a whopping 85% of women in the Iowa Women's Health Study reporting supplement use. The 1994 Dietary Supplement Health and Education Act helped to foster the growth of this industry by creating a new regu-

latory framework, which puts the onus on the US Food and Drug Administration (FDA) to show that supplements are unsafe before it can take action. Manufacturers are not required to disclose to the FDA or to consumers the evidence they have regarding their products' safety, nor must they empirically back up claims of pur-