Calcium for prevention of weight gain, cardiovascular disease, and cancer\textsuperscript{1,2}

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Recent randomized trials and meta-analyses have provided important new knowledge about the health aspects of dietary calcium that goes far beyond its role in bone and dental health. The recent reanalysis of the Women’s Health Initiative (WHI) randomized controlled trial (RCT) showed that vitamin D and calcium supplementation significantly reduces the risk of total, breast, and invasive breast cancers by 14–20% over 10 y compared with placebo and reduced the risk of colorectal cancer by 17% in women who were not taking these supplements at baseline (1). These effects have been suggested by observational studies for many years, so it is tempting to recommend that all women should now start taking these supplements. But there are other findings that give grounds for caution. A meta-analysis of RCTs that involved 28,072 participants found that calcium or calcium plus vitamin D supplementation increased the risk of myocardial infarction by 24% (RR = 1.24; 95% CI: 1.07, 1.45) and the composite of myocardial infarction or stroke by 15% (RR = 1.15; 95% CI: 1.03, 1.27) (2). These results were consistent with those of the WHI trial and other RCTs (2). The benefits and risks are summarized as follows: the treatment of 1000 women with calcium plus vitamin D for 5 y would prevent 5 breast cancers and 1 colorectal cancer, and might prevent 1 fracture and 2 deaths, but would cause 4 myocardial infarctions or strokes (1).

Although it is difficult to know for certain whether both nutrients are required to achieve the benefits, it has been shown that the adverse cardiovascular effects are due to the calcium component of the supplement. However, it appears that this adverse effect can be prevented by supplying the calcium in the more complex chemical form found in dairy products (3). Current calcium supplements acutely increase serum calcium concentrations and suppress parathyroid hormone concentrations, and these changes are positively associated with atheroclerosis and incidence of myocardial infarction and mortality. Ingestion of the same amount of calcium from dairy products has a much smaller effect on serum calcium concentrations than do calcium supplements (4), which might explain the absence of adverse vascular effects of dairy calcium in the observational studies reviewed. In this context, it is interesting that intake of high amounts of dairy products, despite high saturated fat contents, seems to protect against cardiovascular disease (5), diabetes, and colonic cancer (6). Therefore, a way to obtain the health benefits of calcium and vitamin D may be to obtain at least 1000 mg calcium from dairy products, which would not pose a problem for most individuals.

Obesity is another important cause of cardiovascular disease, and breast and colonic cancer and several observational studies suggest that dietary calcium may have a direct effect on reducing body fat stores. A recent meta-analysis of RCTs that involved ~600 overweight and obese individuals from 7 trials found that dietary calcium supplementation of ~1000 mg produced a weight loss and fat loss of ~1 kg over 6 mo and had a greater effect in pre- than in postmenopausal women (7). This is consistent with the findings in the RCT performed in 36,282 postmenopausal women as part of the WHI clinical trial (8). Women who received calcium (1000 mg) and vitamin D had a slightly lower weight gain than did those receiving placebo, and after 3 y of follow-up women with daily calcium intakes of <1200 mg at baseline who were randomly assigned to supplements were 11% less likely to experience weight gain.

These modest but potentially important effects on the prevention of weight gain in the public, achieved by dietary supplementation in weight-stable or weight-gaining subjects, could easily be accounted for by the binding of dietary fat by calcium in the intestine, leading to a slight daily loss of fat calories through excretion in the stools, as shown in a meta-analysis of intervention studies (9). However, in this issue of the Journal, Weaver et al (10) report results from a controlled dietary trial in overweight adolescent boys and girls examining the effect of increased calcium intake on energy balance. Healthy girls and boys were enrolled in a summer camp and underwent a 3-wk controlled-feeding period, in which energy intake was controlled through provision of foods. Calcium intake was from either dairy products or dietary supplements and was either 756 or 1400 mg/d. The primary outcomes were fecal fat excretion, energy balance, macronutrient oxidation, and postprandial energy expenditure. At first glance, the results show no effect of either quantity or type of calcium on energy balance or fat excretion, and the authors conclude that there are no grounds for increased calcium intake from either supplements or dairy-rich foods in attempts to influence body fatness in childhood. However, a meta-analysis of similar studies in adults has shown

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First published online October 12, 2011; doi: 10.3945/ajcn.111.024141.
that an increase in dietary calcium intake of 1000 mg increases fecal fat excretion by $\sim 5$ g/d (9).

So why is this study in disagreement with the literature? Perhaps it is not. When the authors pooled the results from the different calcium sources, the change in fecal calcium excretion from the control to the calcium-supplemented diets was positively associated with change in proportion of ingested fat being lost in the stools ($r^2 = 0.70, P < 0.01$) (see the authors’ Figure 1), which suggests that dietary calcium binds fat and can increase fecal excretion. Although the authors do not consider this association to be causal, the result of the meta-analysis does support a causal relation. There is clearly a need for larger, longer-term, controlled dietary calcium intervention studies and updated meta-analyses of these findings if we are to draw more robust conclusions on the effects of calcium on fecal fat excretion.

There is increasing evidence to suggest that insufficient dietary calcium intake produces a calcium-deficient state that is detected by the body, and one effect might be increased hunger. This effect is particularly expressed during energy-restricted diets, where there is growing evidence that insufficient calcium (and vitamin D) intakes are associated with lower adherence to a reduced energy intake, and consequently poorer weight-loss outcome (11, 12). Some studies also suggest that dairy calcium has more pronounced effects than do calcium supplements (13), and one could speculate as to whether the differences between inorganic and organic forms of calcium may exert different hormonal effects, as is the case with the effects of calcium on cardiovascular risk. The potential for a role for calcium in the prevention of obesity and its complications is still promising.

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REFERENCES