Review

Calcium and Weight: Clinical Studies

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Data from six observational studies and three controlled trials in which calcium intake was the independent variable (and either bone mass or blood pressure the original outcome variable) have been reanalyzed to evaluate the effect of calcium intake on body weight and body fat. Analysis reveals a consistent effect of higher calcium intakes, expressed as lower body fat and/or body weight, and reduced weight gain at midlife. Similarly, studies relating nutrient intake to body composition report negative associations between calcium intake and body weight at midlife and between calcium and body fat accumulation during childhood. There is a fairly consistent effect size, with each 300 mg increment in regular calcium intake associated with ~1 kg less body fat in children and 2.5–3.0 kg lower body weight in adults. Taken together these data suggest that increasing calcium intake by the equivalent of two dairy servings per day could reduce the risk of overweight substantially, perhaps by as much as 70 percent.

Key teaching points:

- Increased calcium intake results in reduced body weight, mainly by reducing fat mass.
- Calcium intake variation explains probably less than 10% of inter-individual body weight variation.
- The slope of the relationship of steady state calcium intake and body weight in adults is on the order of −2.5 to −3.0 kg weight for each 300 mg increment in calcium intake.
- Improving the calcium intake of the U.S. population has the potential to effect a substantial reduction in the prevalence of obesity.

INTRODUCTION

In 2000 Zemel *et al*. published a plausible cell biologic basis whereby effectively low calcium intakes could predispose to obesity and, in the same paper, demonstrated, using the NHANES-III database, that, in the U.S. population, the risk of being obese was inversely related to dietary calcium intake [1]. At about the same time Fujita and Palmieri coined the term "calcium paradox disease," which seemed an apt description of such phenomena [2]. (The mechanism is "paradoxical" in that cytosolic calcium levels in key tissues rise as diet calcium falls.) Palmieri *et al.* had earlier observed that parathyroidectomy substantially reduced muscle cell calcium accumulation in muscular dystrophic hamsters, attributing much of the increase in cytosolic calcium to parathyroid hormone (PTH) itself [3]. By contrast, the work of Zemel *et al.* [1] points to the effect's being due to $1,25(OH)_2D$, which generally varies directly with PTH production and could well have been responsible for the effect found by Palmieri. Both PTH production and $1,25(OH)_2D$ levels vary inversely with calcium intake, but so far as is known, Palmieri *et al.* did not follow-up with a calcium feeding study, i.e., suppressing PTH [and $1,25(OH)_2D$] physiologically. Zemel's work, by contrast, showed that, in mice, high calcium diets alone could reduce or block elevation of cytosolic calcium and, correspondingly, its untoward effects.

The work of Zemel *et al*. led a group of us at Creighton's Osteoporosis Research Center to re-examine, using body weight as the dependent variable, the data from several of our study cohorts in which calcium intake had been the independent variable and bone mass, the original dependent variable. The results of this preliminary analysis have been published elsewhere [4]. Briefly we showed that, in third-decade women, body mass index was an inverse function of calcium intake (expressed as the calcium-to-protein diet ratio), that midlife weight gain was also a function of calcium intake and that women over 65 years of age, given 1500 mg of calcium per day

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in a randomized, double-blind, placebo-controlled trial, lost significantly more weight over a nearly four-year treatment period than did placebo-treated control women.

In this paper we extend these analyses, add data from yet another randomized controlled trial and integrate our results with several reports from other investigators which bear on this issue.

Extended Analysis of Prior Studies

In our earlier paper on this topic [4], we described the relationship of baseline calcium intake with body mass index in 348 healthy young women 19 to 26 years of age from two study cohorts and noted both that there was a significant inverse correlation between calcium intake and body mass index (BMI) at entry and that the odds ratio for having a BMI above 26 kg/m^2 was 2.2 for those below the median calcium intake of the cohort, relative to those above the median. In simple bivariate models, estimated calcium intake accounted for ~3% of the variance in BMI in this population. In further analysis of these data, using multiple regression methods, we developed a multivariate model predicting BMI on the basis of energy, calcium and protein intakes. The coefficient of the calcium intake term was -0.003 ($p < 0.001$), which may be evaluated to mean that average BMI was 0.3 kg/m^2 lower for every 100 mg increase in daily calcium intake (or 0.9 kg/m^2 for each increment equivalent to one dairy serving per day).

Since degree of overweight is of as much importance as being overweight itself, we also did a simple chi-squared analysis using BMI cut points of 26 and 30 kg/m^2 and sorted the subjects by calcium intake tertile. The results are shown in Table 1 and demonstrate clearly that the chances of being in one of the overweight classes rose as calcium intake fell from the top to the bottom intake tertile (for χ^2, $p < 0.02$).

As is typical for women of this age, calcium intakes for the entire cohort tended to be low, and an analysis more interesting than comparing tertiles of actual intakes is estimating prevalence of overweight at various intakes, with special reference to intakes recommended for women of this age (1000–1200 mg/day). Holding all other variables in the model constant, we first calculated predicted BMI at 500 and 1100 mg calcium per day. We then used the standard error of the regression estimate from the model as the best estimate of the dispersion of the BMI values around the calcium-specific means. Assuming, for simplicity, a normal distribution for BMI, 16.6% of the women would have been predicted to have a BMI above 26 kg/m^2 at the 500 mg intake, but only 3.6% at the 1100 mg intake. Similarly, using a BMI of 30 kg/m^2 (the current cut off for a designation of "obesity"), 0.99% of these young women would have been predicted to be obese at the 500 mg intake level, whereas only 0.16% would have been obese at the 1100 mg intake. This risk gradient for obesity (~6×) is essentially identical to that found by Zemel *et al.* [1] for the U.S. population in their comparison of body weight for the top and bottom quartiles of calcium intake. The assumption of normality is supported in this dataset, but it may not be applicable to the general population at this age. Nevertheless, the difference in area under the curve above a cutoff point such as 30 kg/m^2, between two distributions with different means, will be much as found here.

Table 1. Distribution of subjects by BMI and calcium intake*

Calcium Intake Tertile	BMI Class			Total
	Normal	Overweight	Obese	
Lowest	84	29	3	116
Middle	98	14	4	116
Highest	102	13	1	116

* Calcium intake expressed as calcium-to-protein diet ratio, chi-squared = 12.24 ($p < 0.02$).

Previously unreported are data from a calcium intervention trial in our unit, in women of the same age as above (19 to 26), given 1500 mg calcium per day or placebo and followed for three years [5]. As is characteristic for this age of body mass consolidation, the group as a whole gained weight; there was no significant difference between the calcium supplemented and control groups. However, body composition was followed serially over the period of observation, using DXA, and there was a clear, significant difference between body fat accumulation, with the calcium supplemented women accumulating body fat at a rate one-half that of the placebo treated controls. Thus the weight gain in the calcium supplemented women consisted primarily in an increase in lean body mass, while the placebo treated women accumulated more body fat. (A more complete description of these observations can be found elsewhere [5]).

Review of the Literature

With the exception of a randomized controlled trial by Zemel *et al.*, described elsewhere [6], there have been very few studies published describing results of trials explicitly testing the effect of calcium intake on body weight. However, there have been a few studies in which the relationship of calcium intake to body weight or body composition has been noted, which provide data bearing on this question.

For example, Zemel *et al.* in their 2000 paper [1] report previously unpublished observations from an intervention trial in African-American hypertensive males, using two servings of yogurt per day for a one-year period of treatment. In addition to the expected (and reported) reduction in blood pressure [7], the investigators observed a 4.9 kg decrease in body fat, relative to controls, which, at that time, had not been anticipated, and which, while statistically significant ($p < 0.01$), was nevertheless not reported in the original communication. (This observation is, thus, similar to the ones described above from

Creighton's Osteoporosis Research Center, inasmuch as it represents an unanticipated outcome from a study with a different design end point.)

More specifically focused on the issue of calcium intake and weight was a recent publication by Carruth and Skinner [8] following body composition change in preschool children from 20 to 70 months of age. They noted, in multiple regression models, a highly significant inverse association of calcium intake and body fat accumulation and a corresponding positive correlation between calcium intake and lean body mass accumulation. (This finding is thus similar to our observation in women 19 to 26 years of age.) Each additional regular serving of a dairy calcium source was associated with 0.9–1.1 kg less body fat and a lower value for percent body fat in the range of 3.5% to 4.5% (depending upon how calculated). In their study, body fat averaged 18% of body weight in males and 21% in females at 70 months of age. Hence a 3.5% to 4.5% lower value translates to 20% less body fat per regular dairy serving.

Lin *et al.* [9], in a secondary analysis of an exercise intervention trial involving 54 normal women 18 to 30 years of age, found significant inverse correlations between calcium intake, adjusted for energy, and change in both body weight and body fat mass over a two-year period of observation. Of special interest is the fact that calcium's negative effect on gain in weight was confined to those subjects below the median energy intake. In other words, calcium did not repeal the law of conservation of mass: if one eats more than one burns, one will store the difference, regardless of calcium intake.

Lovejoy *et al.* [10] in a study of dietary intakes and obesity in midlife noted an inverse correlation ($p < 0.05$) between calcium intake and both BMI and percent body fat in Caucasian, but not African-American women. The paper does not provide the information needed to estimate the size of the calcium effect.

At least two studies have reported effects of weight reduction diets with and without milk. Summerbell *et al.* [11] described results of a randomized controlled trial of three weight reduction regimens, one a standard 800 calorie diet, a second diet also providing 800 calories, but derived solely from dairy foods, and a third, consisting of a 1300 calorie regimen based primarily on dairy foods plus one other food of choice per day. The calcium contents of the three regimens were not described, but can be estimated to be below 500 mg for the conventional regimen and from 1500–2100 mg for the milk-based diets. The results of this interesting trial are shown in Fig. 1. Of those who stayed in the trial to its completion (16 weeks), subjects on the milk-only regimen lost 11.2 kg of weight, while those on the standard 800 calorie diet lost less than 3 kg. The 1300 calorie, milk-plus regimen produced an 8.2 kg weight loss, or about three times as great as observed with the lower calorie, standard regimen. The authors note that the degree of weight loss on the milk-only regimen was as great or greater than had been reported for any drug treatment program. They attributed the greater success of the milk-based regimens to their novelty (with correspondingly better compliance), apparently overlooking the possibility that the higher calcium intake (plus possibly other dairy constituents) may have contributed to the difference.

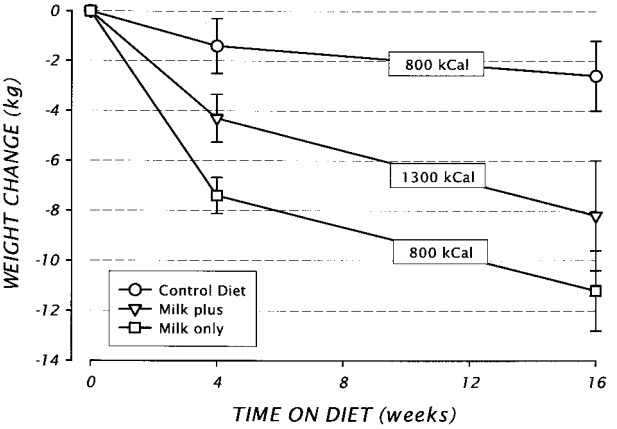

Fig. 1. Plot of the weight change results reported in the paper by Summerbell *et al.* [11]. Error bars are 1 SEM. (Copyright Robert P. Heaney, 2001. Used with permission.)

Garrow *et al.* [12] measured total weight and lean tissue loss in 17 obese women, comparing two diets, one a mixed food, very severely energy-restricted (330 kCal/day) diet, containing 33 g protein, and the other consisting solely of milk, providing 780 kCal and 46 g protein. Weight loss was not significantly different for the two regimens, but the milk diet resulted in substantially less lean tissue loss (and, by difference, greater fat mass loss). The small sample size and the protein intake differences each make it difficult to draw conclusions about what role milk calcium may have played. Nevertheless, the similar weight loss despite a substantial difference in energy intake is concordant with the corresponding differences in the study by Summerbell *et al.* [11]. Both studies suggest that a high milk intake increases the effectiveness of a weight reduction program.

Comment

Body weight regulation is a manifestly multifactorial matter. The data summarized in this brief review show a consistency of findings that establishes calcium intake as one of the several factors involved. As reported elsewhere, the studies analyzed by Davies *et al.* [4] found that about 3% of the variability in BMI could be attributed to calcium intake differences. This is a small enough contribution to explain why calcium's effect might not have been recognized heretofore. Because none of the studies reanalyzed by Davies was designed with weight as an outcome variable, it is likely that the estimated 3% figure understates the real contribution of calcium intake variation, and Zemel's estimate (personal communication) is closer to 10%. Whatever the actual contribution, it seems doubtful that calcium can account for much more than a small fraction of interindividual variability in weight.

A related, but distinct question deals with the size of the calcium *effect* (rather than the size of the calcium *contribution*).

Table 2. Estimates of calcium effect size*

Study	Cohort	Effect Variable				
		Body Fat (kg)	Body Fat (%BW)	Δ Body Fat (yr^{-1})	Wt (kg)	Δ Wt ($kg*yr^{-1}$)
[4]	Young women				−2.5	
[4]	Middle-aged women					−0.11
[4]	Elderly women					−0.16
[1]	Adult women†				−3	
[7]	African-American male hypertensives	−4.9		−15%		
[8]	Children	−1.0	−20%			
[11]	Young women			−1.2 kg		−1.3
[5]	Young women			−1.1%		

* For a steady state intake difference of 300 mg Ca/day.

† Calculated for a 1200 mg difference between top and bottom quartiles of calcium intake, a reduction in the upper tail area from 25% to 4.2%, and an estimated population standard deviation for weight that is ~18% of the mean.

In other words, how much does the population mean (i.e., for weight, BMI or percent body fat) differ for different calcium intakes? Table 2 assembles estimates of effect size derived from those of the studies reviewed in this report which contain sufficient information to allow one to make the needed calculations. The effect variable necessarily differs from study to study, as measured. Nevertheless, not only are the results directionally congruent, but the sizes of the effects in the various studies are of the same general magnitude. Thus, for both middle-aged and older women, a calcium intake difference of 300 mg (~1 dairy serving) is associated with decreased weight gain (or greater weight loss) in the range of 0.11–0.16 kg/year. In cross-sectional studies of adults, the same intake difference is associated with from 2.5 to 3 kg less body weight and, in the hypertensives at one year, a difference of 4.9 kg body fat. The longitudinal changes show the greatest dispersion, which is not surprising, since each is a rate, calculated over varying time periods, and the time course of the change in fat after a change in calcium intake is not known.

Even small shifts in the mean of a population, assuming constant dispersion, are widely recognized as important for any number of variables (such as blood pressure or, in this case, body weight). That importance is illustrated by the difference in predicted prevalence of overweight or obesity in the young women described above. A drop in mean BMI of 1.8 kg/m^2 (a downward shift of the mean by only 8%), which the data predict for an intake difference of 600 mg calcium, reduces predicted prevalence of overweight in that age group by nearly 70%.

Most of the other recognized factors in weight control (appetite, exercise, self-image, heredity, food availability, social setting and so on) have been notoriously difficult to alter effectively. Hence calcium intake, which can be easily and effectively altered at a population level and which has important beneficial effects on many other body systems, seems a useful stratagem to deploy as a part of an overall approach to the growing problem of obesity in North America.

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