Effects of Calcium Supplementation on Body Weight and Adiposity in Overweight and Obese Adults

A Randomized Trial

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Background: Some data suggest that increasing calcium intake may help prevent weight gain.

Objective: To test the hypothesis that calcium supplementation can prevent weight gain in persons who are overweight or obese.

Design: Randomized, placebo-controlled trial. Randomization was computer-generated, and allocation was assigned by pharmacy personnel who prepared intervention and placebo capsules. Participants, providers, and those who assessed outcomes were blinded to study group assignment.

Setting: Single research center.

Participants: 340 overweight (body mass index [BMI], 25 to <30 kg/m²) and obese (BMI ≥30 kg/m²) adults (mean age, 38.8 years [SD, 10.5]).

Intervention: Calcium carbonate (elemental calcium, 1500 mg/d) (n = 170) or placebo (n = 170) with meals for 2 years.

Measurements: Changes in body weight and fat mass (primary outcomes).

Results: Seventy-five percent of participants completed the trial (78% received calcium; 73% received placebo). There were no statistically or clinically significant differences between the calcium and placebo groups in change in body weight (difference, 0.02 kg [95% CI, –1.64 to 1.69 kg]; P = 0.98), BMI (difference, 0.32 kg/m² [CI, –0.41 to 1.02 kg/m²]; P = 0.39), or body fat mass (difference, 0.39 kg [CI, –1.04 to 1.92 kg]; P = 0.55). Parathyroid hormone concentrations decreased in the calcium group compared with the placebo group (difference, –0.71 pmol/L [CI, –1.28 to –0.13 pmol/L]).

Limitation: The study took place at a research center, and its sample was mostly women.

Conclusion: Dietary supplementation with elemental calcium, 1500 mg/d, for 2 years had no statistically or clinically significant effects on weight in overweight and obese adults. Calcium supplementation is unlikely to have clinically significant efficacy as a preventive measure against weight gain in such patients.

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ClinicalTrials.gov registration number: NCT00030238.
Calcium Supplementation and Weight Change

Context

Some data suggest that body weight is inversely associated with calcium intake, increasing the possibility that supplemental calcium might facilitate weight loss or prevent weight gain.

Contribution

Researchers randomly assigned overweight and obese patients to supplemental calcium or placebo and found no between-group differences in measures of weight change.

Caution

Trial participants were almost all women.

Implication

Calcium supplementation is unlikely to prevent weight gain in persons who are overweight or obese.

—The Editors

newspaper and radio advertising in the Washington, DC, metropolitan area seeking healthy adult volunteers for a project to study the “health effects of calcium supplementation.” Men and women age 18 to 80 years were eligible to enroll if they had a body mass index (BMI) of 25 kg/m² or more and did not have cerebrovascular, cardiovascular, pulmonary, renal, hepatic, endocrinologic, or other substantial medical disease. Women were ineligible if they were pregnant, were breastfeeding, or had received a recommendation from a health care professional to take calcium supplements for any condition. We excluded persons who regularly used medications known to affect body weight, had a weight loss of 3% or more in the preceding 3 months, reported total calcium intake in excess of 3.5 g/d, used supplemental calcium in excess of 300 mg/d, used vitamin D supplements in excess of 400 IU/d, or had a history of renal stones.

The institutional review board of the National Institute of Child Health and Human Development, National Institutes of Health, approved the research protocol. Each participant provided signed consent. We provided financial compensation for participants’ time and inconvenience.

Design Overview

We conducted a single-center, randomized, double-blind, placebo-controlled trial from March 2002 to April 2006. After an outpatient visit to determine eligibility and obtain initial assessments, participants entered a 2-year, double-blind treatment period.

Randomization and Interventions

We randomly assigned participants, in a 1:1 ratio, to receive either elemental calcium, 1500 mg/d (calcium carbonate, purchased from Particle Dynamics, St. Louis, Missouri), or placebo, administered as 2 divided doses with meals. Investigators assigned consecutive code numbers to participants from prespecified lists stratified by race or ethnicity, sex, and BMI (25 to 26.99, 27 to 29.99, 30 to 34.99, and ≥35 kg/m²). The National Institutes of Health Clinical Center Pharmaceutical Development Section used permuted blocks with stratification to generate the allocations that translated code numbers into study group assignments by using a pseudo-random number program. The Pharmaceutical Development Section prepared placebo and calcium capsules to appear identical. Pharmacy personnel, not otherwise involved with the conduct of the study, dispensed study capsules with medication placed in containers that appeared identical and differed only by the individual participant code number. No participant, investigator, or other medical or nursing staff interacting with participants was aware of study group assignments for the duration of the trial.

Initial Assessment

At their prerandomization evaluation, participants reported after an overnight fast and were weighed in hospital gowns by using a digital scale (Life Measurement Instruments, Concord, California) that was calibrated with a known weight before each participant’s measurement. We measured height by using a stadiometer calibrated before each measurement (Holtain, Crymych, United Kingdom). Research dietitians assessed abdominal and hip circumferences in triplicate to the nearest 0.1 cm, as recommended (50, 51), and measured triceps skinfold thickness to the nearest 0.5 mm by using Lange calipers (Cambridge Scientific Industries, Cambridge, Maryland). We measured blood pressure, obtained after a 5-minute rest period, 3 times at 5-minute intervals from seated participants by using an automated sphygmomanometer (Dinamap-Plus, Critikon, Tampa, Florida). We did whole-body dual-energy x-ray absorptiometry to estimate total body fat mass (Delphi A, software version 11.2, Hologic, Bedford, Massachusetts). We measured intact parathyroid hormone concentrations with 2-site immunochromeluminometric assays (52), and serum 25-hydroxy vitamin D levels by using a competitive binding assay (Nichols Advantage, Nichols Diagnostic, San Clemente, California) (53). We asked participants with substantial vitamin D deficiency (serum 25-hydroxy vitamin D level <25.0 nmol/L) to take vitamin D, 400 IU/d (ergocalciferol), in a multivitamin. We assessed baseline dietary calcium intake by using a 7-day food record that a registered dietitian reviewed with each participant to maximize accuracy and completeness, and analyzed for dietary calcium intake by using the Nutrition Data System for Research software, versions 4.04_32 and 4.05_33 (University of Minnesota, Minneapolis, Minnesota) (54). We measured calcium intake from multivitamins or calcium supplements with a validated calcium questionnaire (55) that was reviewed for completeness through an interview with a registered dietitian. We recorded the calcium content as it was listed on the label of each multivitamin or calcium supplement. We measured dietary and supplemental vitamin D intakes in the same

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manner. We estimated energy intake at baseline and at 2 years by using a food-frequency questionnaire that assessed total diet (55–57). We measured socioeconomic status by using the Hollingshead score (58).

Outcomes and Follow-up

Primary efficacy end points were change in body weight and body fat mass at the end of 2 years of treatment. Secondary outcomes were fasting anthropometric measurements, body composition by dual-energy x-ray absorptiometry, and change in blood pressure, assessed yearly, along with questionnaire data on dietary and supplemental calcium intake (55).

In addition, we contacted participants every 3 months to complete questionnaires about their adherence to the medication regimen; assess their general health; and obtain self-reports of mood, stress, physical activity, and hunger. Every 6 months, participants returned to the clinic to exchange their unused study medication for a new supply. We used the tally of returned capsules to assess adherence. To examine adequacy of the masking procedure, participants completed a questionnaire at the end of the study that requested they report their best guess about their study group assignment.

Statistical Analysis

All reported primary data analyses were prespecified. On the basis of our previous study of observed yearly changes in body weight over time (59), we needed a total sample size of 256 participants to detect a 0.35-kg difference per year in weight change (that is, 0.7 kg over 2 years) between groups with 80% power. Participant accrual was set at 340 participants to allow 25% loss to follow-up. We analyzed data by using SPSS, version 14.0 (SPSS, Chicago, Illinois). We assessed efficacy in the intention-to-treat sample of all randomly assigned participants. We did 2 efficacy analyses. The primary analysis used a multiple imputation model for missing data under a missing-at-random assumption (60). By using NORM, version 2.03 (The Pennsylvania State University, State College, Pennsylvania) (61, 62), we included all available baseline, 1-year, and 2-year outcome measures in an imputation model along with age, sex, race, baseline serum 25-hydroxy vitamin D concentration, baseline calcium intake, and study group. We then combined the coefficients from analyses of 20 imputed data sets into a single set of estimates according to Shafer (62) and the Rubin rules (63). To assess sensitivity of these results to the missing-at-random assumption, we conducted 3 additional analyses: assuming that all participants who withdrew from the study had major weight gain (≥2.27 kg [≥5 lb]) (59); that those who received calcium had no weight gain, whereas those who received placebo had major weight gain; and that those who received placebo had no weight gain, whereas those who received calcium had major weight gain. We used multiple imputations to impute the missing 2-year weight measurements by using the same imputation model used for the main analysis. For the 3 scenarios, we added fixed amounts to the imputed values, reanalyzed the results by using analysis of covariance, and combined them by using the Rubin rules (63). A second, confirmatory analysis used the last-observation-carried-forward method for participants who did not complete the study. Unadjusted analyses were also run for both the imputation and the last-observation-carried-forward models. Because all of these methods yielded similar results (that is, finding no statistically significant effect of calcium supplementation on weight or fat change), we present only the imputation analyses. We did not do any interim efficacy analyses. We examined baseline characteristics by simple t tests or, in the case of categorical data, with contingency table analysis.

Role of the Funding Source

The Intramural Research Program and the Office of Dietary Supplements, National Institutes of Health, supported the study. The funding sources played no role in study design or conduct; data collection, management, analysis, or interpretation; manuscript development or approval; or in the decision to submit the article for publication.

RESULTS

A total of 1904 persons responded to advertisements for the study, and 1038 completed a telephone interview, seemed to meet eligibility requirements, and received a consent form by mail. A total of 482 subsequently agreed to attend a clinic visit, during which we determined eligibility (Figure 1). Sixty-seven of the patients elected not to participate, and we excluded 75 because of medical conditions found during evaluation. We randomly assigned 245 women and 95 men (mean age, 38.8 years [SD, 10.5]; range, 18 to 71 years) to calcium carbonate or placebo from April 2002 to January 2004.

Baseline Characteristics

Among enrolled participants, 39% were overweight (BMI, 25 to <30 kg/m²) and 61% were obese (BMI ≥30 kg/m²); 23% reported dietary calcium intake less than 600 mg/d and 75% reported dietary calcium intake less than the U.S. dietary reference intake for persons age 51 to 70 years (1200 mg/d) (64). At baseline, age, sex, race or ethnicity, weight, BMI, body fat mass, indices of calcium intake, energy intake, or serum 25-hydroxy vitamin D or parathyroid hormone concentrations did not significantly differ between groups (Table 1). We prescribed multivitamin supplements to 36 participants because of vitamin D deficiency at baseline assessment.

Changes in Body Weight and Fat Mass

Eighty-two percent of participants had body weight assessed 1 year after randomization, and 75% completed the 2-year trial (78% who received calcium; 73% who received placebo [P = 0.38]). Sociodemographic, anthropometric, or laboratory indices did not significantly differ...
between participants who did and those who did not complete the study ($P$ for all $> 0.35$). We excluded data from 5 participants who participated in formal weight-loss programs and lost more than 15 kg because their weight loss, which was due to marked changes in their dietary and physical activity habits, deviated markedly from that of other trial participants and were statistical outliers (65). Participants’ body weight, BMI, and body fat mass during the study are shown in Figure 2.

The measured change in body weight among all participants who completed the 2-year trial was 1.31 kg (SD, 6.5) ($P < 0.001$ vs. baseline weight); fat mass increased by 0.82 kg (SD, 4.3) ($P = 0.004$ vs. baseline fat mass), which was similar to expectations for an observational study (59). However, we found no statistically or clinically significant between-group differences in change in body weight (difference between calcium and placebo groups, 0.02 kg [95% CI, −1.64 to 1.69 kg]; $P = 0.98$), BMI (difference, 0.32 kg/m$^2$ [CI, −0.41 to 1.02 kg/m$^2$]; $P = 0.39$), or body fat mass (difference, 0.39 kg [CI, −1.04 to 1.92 kg]; $P = 0.55$) over 2 years in analyses adjusted for age, race, and sex (Table 2) or in unadjusted analyses ($P > 0.40$ for all). No statistically significant between-group differences were found in abdominal circumference, hip circumference, or triceps skinfold thickness (Table 2) or in body weight, fat mass, or other body composition variables using the last-observation-carried-forward method with and without adjustment for covariates ($P > 0.35$ for all).

**Post Hoc Analyses**

Because previous studies (18, 36) have suggested calcium might alter weight gain to a greater extent in women...
or in non-Hispanic black persons, we also did post hoc analyses that included terms for group-by-sex and group-by-race interactions (Appendix Table 1, available at www.annals.org). We found no substantial effects on change in body weight or fat mass of calcium supplementation by sex or race. Analyses restricted to participants with low baseline calcium intake (who might garner greater benefit from supplementation) (22), participants who were obese rather than overweight, and participants who had more than 90% adherence by capsule counts throughout the study also found no significant effects of calcium supplementation for either weight change or fat mass change (Appendix Table 1). Calcium supplementation did not affect weight change after exclusion of all participants who reported joining a commercial weight-loss program (Appendix Table 1). Baseline 25-hydroxy vitamin D concentration was unrelated to weight or fat mass change in all models ($P > 0.21$ for all). An exploratory logistic regression model, based on the analysis presented by Caan and coworkers (22), that examined the effect of calcium supplementation on the likelihood for weight change among those with lower initial dietary calcium intake ($<1200$ mg/d), also found no significant association between calcium supplementation and weight gain of 1 to 3 kg ($P > 0.89$) or greater ($P > 0.11$).

### Missing Data Sensitivity Analysis

The analyses for assessing the sensitivity of the results to the missing-at-random assumption (Appendix Table 2, available at www.annals.org) showed that the results were largely unchanged under the “major weight gain” scenario—a model that assumes nonresponse bias is nondifferential (that is, the same in each group). This result is expected because the proportion of patients with missing data was fairly similar in both groups. When we assumed a differ-

### Table 1. Baseline Participant Characteristics*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Calcium Group (n = 170)</th>
<th>Placebo Group (n = 170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD), y</td>
<td>38.9 (10.5)</td>
<td>38.7 (10.4)</td>
</tr>
<tr>
<td>Women, %</td>
<td>72.9</td>
<td>72.4</td>
</tr>
<tr>
<td>Race or ethnicity, %†</td>
<td>60</td>
<td>62</td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>60</td>
<td>62</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>30</td>
<td>32</td>
</tr>
<tr>
<td>Hispanic white</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Mean weight (SD), kg</td>
<td>94.5 (20.5)</td>
<td>94.0 (20.5)</td>
</tr>
<tr>
<td>Mean body mass index (SD), kg/m²</td>
<td>33.2 (6.8)</td>
<td>33.6 (6.8)</td>
</tr>
<tr>
<td>Overweight/obese, %/%‡</td>
<td>38/62</td>
<td>40/60</td>
</tr>
<tr>
<td>Mean fat mass (SD), kg</td>
<td>35.5 (11.7)</td>
<td>34.8 (11.8)</td>
</tr>
<tr>
<td>Median Hollingshead score (range)</td>
<td>3 (1–5)</td>
<td>3 (1–5)</td>
</tr>
<tr>
<td>Mean energy intake (SD), kcal/d</td>
<td>2110 (1238)</td>
<td>2190 (1846)</td>
</tr>
<tr>
<td>Mean calcium intake (SD), mg/d</td>
<td>878 (430)</td>
<td>887 (390)</td>
</tr>
<tr>
<td>Calcium intake &lt;600 mg/d, %</td>
<td>24.4</td>
<td>22.7</td>
</tr>
<tr>
<td>Calcium intake less than dietary reference intake, %§</td>
<td>75.5</td>
<td>74.4</td>
</tr>
<tr>
<td>Mean serum 25-hydroxy vitamin D concentration (SD), nmol/L</td>
<td>58.9 (29.5)</td>
<td>62.6 (33.7)</td>
</tr>
<tr>
<td>Mean serum parathyroid hormone concentration (SD), pmol/L</td>
<td>4.25 (1.94)</td>
<td>4.42 (1.93)</td>
</tr>
</tbody>
</table>

* At baseline, there were no significant differences between treatment groups ($P > 0.31$ for all).
† Race and ethnicity were self-reported.
‡ Overweight was defined as a body mass index from 25 to $<30$ kg/m², and obesity was defined as body mass index $\geq 30$ kg/m².
§ The U.S. dietary reference intake for persons age 51 to 70 years is 1200 mg/d (64).

Figure 2. Weight, BMI, and fat mass in study participants.

Measured means (95% CIs) for weight (top), BMI (middle), and fat mass (bottom) in participants randomly assigned to calcium or placebo are shown. There were no significant differences between groups at any time point. BMI = body mass index.
Calcium Supplementation and Weight Change

**Table 2. Changes in Variables at Conclusion of the Study***

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Calcium Group (n = 168)</th>
<th>Placebo Group (n = 167)</th>
<th>Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
<td>0.54 (−0.70 to 1.79)</td>
<td>0.52 (−0.82 to 1.86)</td>
<td>0.02 (−1.64 to 1.69)</td>
<td>0.98</td>
</tr>
<tr>
<td>Fat mass, kg</td>
<td>0.40 (−0.61 to 1.41)</td>
<td>0.01 (−1.15 to 1.06)</td>
<td>0.39 (−1.04 to 1.92)</td>
<td>0.55</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>0.18 (−0.33 to 0.69)</td>
<td>−0.14 (−0.73 to 0.45)</td>
<td>0.32 (−0.41 to 1.02)</td>
<td>0.39</td>
</tr>
<tr>
<td>Abdominal circumference, cm</td>
<td>0.95 (−1.43 to 3.34)</td>
<td>1.01 (−1.51 to 3.53)</td>
<td>−0.06 (−2.34 to 2.23)</td>
<td>0.90</td>
</tr>
<tr>
<td>Hip circumference, cm</td>
<td>−0.80 (−3.21 to 1.62)</td>
<td>−1.87 (−4.41 to 0.68)</td>
<td>1.07 (−1.24 to 3.39)</td>
<td>0.36</td>
</tr>
<tr>
<td>Triceps skinfold thickness, mm</td>
<td>−2.39 (−3.87 to −0.92)</td>
<td>−2.53 (−4.08 to −0.97)</td>
<td>0.13 (−1.28 to 1.54)</td>
<td>0.85</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>−3.2 (−6.8 to 0.3)</td>
<td>−4.3 (−8.0 to −0.5)</td>
<td>1.0 (−2.4 to 4.4)</td>
<td>0.55</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>−1.8 (−4.0 to 0.3)</td>
<td>−2.5 (−4.8 to −0.2)</td>
<td>0.7 (−1.4 to 2.7)</td>
<td>0.76</td>
</tr>
</tbody>
</table>

* Estimated marginal means (95% CIs), adjusted for age, race, sex, baseline serum 25-hydroxy vitamin D concentration, and baseline calcium intake, reported from imputation analyses.

The estimated nonresponse bias, the estimates of calcium-versus-placebo difference in weight change ranged from −0.79 kg (CI, −2.18 to 0.59 kg) to 0.32 kg (CI, −1.07 to 1.71 kg). The “major weight gain” scenario is considered much more plausible than the best- or worst-case scenario, because nonresponse (insufficient weight loss) is a common reason for withdrawing from obesity studies (66).

**Questionnaire Data**

As assessed by self-report questionnaires completed every 3 months, no between-group differences in general health, mood, stress, physical activity, or hunger occurred (P > 0.09 for all). No statistically significant between-group differences in change in reported energy intake at 2-year follow-up (difference between calcium and placebo groups, 28 kcal [CI, −244 to 300 kcal]; P = 0.84) or in reported dietary, nonprescribed, supplemental calcium intake (difference, 18.6 mg/d [CI, −93 to 130 mg/d]; P = 0.74) occurred. Reported vitamin D intake derived from the diet or supplements did not change significantly during the study (P > 0.40 for all).

**Laboratory Data**

Parathyroid hormone concentrations decreased to a statistically significantly greater extent in the calcium group than in the placebo group (difference, −0.71 pmol/L [CI, −1.28 to −0.13 pmol/L]; P < 0.001), suggesting that participants adhered to their prescribed regimen. Serum 25-hydroxy vitamin D concentrations at the end of the study (difference from baseline for calcium, −8.2 nmol/L [CI, −13.2 to 3.5 nmol/L]; difference from baseline for placebo, −4.5 ng/mL [CI, −10.0 to 1.2 ng/mL]) did not significantly differ between groups (difference, −3.7 ng/mL [CI, −11.5 to 3.5 ng/mL]; P = 0.24).

**Adverse Events and Adherence**

Adverse events leading to study discontinuation were infrequent (Figure 1). Only 1 clinically significant adverse event that was not attributed to trial participation was observed during the study (foot surgery in a participant who received placebo), and reports of any adverse event during the study did not significantly differ between groups (P > 0.41 for all). Adherence and change over time in adherence (measured by tallies of returned medication) did not differ between groups at any study interval from 6 months to 2 years (P ≥ 0.78 for all). Among all participants, however, adherence decreased significantly during the trial from 92% of prescribed doses at 6 months to 82% at 2 years (P = 0.014; 6-month vs. 2-year comparison).

**DISCUSSION**

On the basis of preliminary evidence suggesting that increasing calcium intake might lead to reduced weight gain, we tested the hypothesis that dietary calcium could prevent weight and body fat gain in overweight and obese patients. We found that 2 years of calcium supplementation, taken as capsules at meals, led to no clinically or statistically significant change in body weight or body fat in this sample. Overweight and obese adults were selected as participants because when heavier persons are followed longitudinally, they tend to show greater weight gain over time than do adults at normal weight (59, 67) and are at greater risk for complications from excessive body weight gain (68–71).

Previously published large trials of calcium supplementation were not designed with body weight as the primary end point; however, most have reported that additional calcium had insignificant effects on body weight (26, 28, 34, 72). Reid and colleagues (26) reported no difference in body weight or fat mass among 1471 women randomly assigned to take 1 g of elemental calcium (as calcium citrate or placebo) for 30 months to prevent fracture. However, a tertiary analysis of the 36 282 women who participated in the WHI (Women’s Health Initiative) trial (22) found that supplementation with calcium, 1000 mg, plus cholecalciferol, 400 IU, was associated with a small difference in body weight in the cohort (0.13 kg) and lower risks for substantial weight gain (1 to 3 kg or ≥3 kg) among persons with dietary calcium intake less than 1200...
mg/d. The data for an effect of dairy or supplemental calcium on body weight from smaller clinical trials, many of which have also involved weight-loss programs, have been mixed (73), with some studies finding a substantial effect (18, 35–37) and others not showing any differences (30, 74–78). Similar heterogeneity in results has been found when the effect of supplemental calcium on blood pressure is examined (79). To our knowledge, our study is the first large, randomized investigation specifically designed to examine whether supplemental calcium could prevent weight gain. Given the relatively small effect of calcium on body weight found in the WHI and most other trials, we believe all of the data are consistent in suggesting limited efficacy for preventing weight gain among overweight or obese persons. We did not replicate the WHI findings of lower odds for gaining weight among persons with low calcium intake who received calcium and vitamin D supplements (22). One limitation that may explain why we did not reproduce the WHI findings is that this study was not powered to detect very small differences in body weight that could be attributable to calcium. However, it would seem to be of little clinical importance to determine whether a supplement could change average body weight by a fraction of a pound over several years, as suggested by the WHI trial. A difference attributable to calcium of $-0.15$ kg is well within the 95% CI for weight change in our trial. Another possibility why the WHI regimen, which included vitamin D supplementation as well as calcium, was associated with weight change is that adequate vitamin D is required for calcium to be well absorbed. However, we found no effect of baseline 25-hydroxy vitamin D concentrations on weight change in this study. Substantial changes in dietary or supplemental calcium and vitamin D intakes could therefore also conceivably affect study results. Total intakes were formally assessed by validated questionnaires once yearly, and we assessed changes in supplemental intakes every 3 months, but we cannot rule out changes in intakes not detected by these methods. A final possibility is that, because the WHI findings were tertiary reanalyses and not the primary or even secondary purposes of the study, the WHI’s positive results may have occurred by chance.

Some investigators have suggested that dairy products, rather than calcium alone, may have greater effects on body weight (35, 37) and lipid metabolism (80). A limitation of our study is that we did not include participants randomly assigned to a high dairy calcium diet. Some participants’ dietary calcium intake may have been insufficiently low to demonstrate the effect of calcium supplementation. However, 75% of participants consumed less than the daily recommended calcium intake, and one quarter reported calcium intake less than 600 mg/d. Analyses restricted to either of these groups did not show trends consistent with an effect of calcium on body weight gain. Another limitation is that adherence was measured only through counts of returned capsules and was not confirmed by other measurements. However, parathyroid hormone concentrations decreased in the calcium group, suggesting an effect of the supplements. Finally, although this study’s participant demographic characteristics were similar to those reported for overweight persons in the United States, participants were not recruited in a truly population-based manner. Persons who participate in research projects that involve randomization may be more health-conscious than the general population, and the trial sample comprised mostly women. However, mean weight change in participants who completed the study (1.6 kg over 2 years) was similar to that reported in previous epidemiologic studies of broader samples of adults measured longitudinally (81, 82).

In summary, supplementation with elemental calcium, 1500 mg/d, did not substantially alter weight or fat gain over 2 years in overweight and obese adults. Thus, even though there may be other important reasons, such as fracture prevention (83), to recommend dietary calcium supplementation, we conclude that the extant data suggest that calcium supplementation is unlikely to have clinically significant efficacy as a preventive measure against weight gain in persons who are already overweight or obese.

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Note: Dr. Yanovski, Ms. Denkinger, and Ms. Sebring are Commissioned Officers in the U.S. Public Health Service.

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Drafting of the article: J.A. Yanovski, L.B. Yanoff.
Statistical expertise: J.A. Yanovski.
Obtaining of funding: J.A. Yanovski.
## Appendix Table 1. Post Hoc Analyses*

<table>
<thead>
<tr>
<th>Sample Evaluated</th>
<th>Change in Body Weight, kg</th>
<th>Change in Fat Mass, kg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Calcium Group</td>
<td>Placebo Group</td>
</tr>
<tr>
<td>Model including group-by-race and group-by-sex interactions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All participants (n = 335)</td>
<td>0.42 (−1.10 to 1.95)</td>
<td>−0.54 (−2.44 to 1.36)</td>
</tr>
<tr>
<td>Non-Hispanic black (n = 101)</td>
<td>0.73 (−1.99 to 3.44)</td>
<td>−0.12 (−2.41 to 2.22)</td>
</tr>
<tr>
<td>Women (n = 244)</td>
<td>0.55 (−1.12 to 2.22)</td>
<td>−0.37 (−2.46 to 1.73)</td>
</tr>
</tbody>
</table>

**Subgroup analyses**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Calcium Group</th>
<th>Placebo Group</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium intake &lt;600 mg/d (n = 80)</td>
<td>−0.79 (−3.87 to 2.27)</td>
<td>−0.64 (−3.94 to 2.65)</td>
<td>0.89</td>
</tr>
<tr>
<td>Calcium intake &lt;1200 mg/d (n = 251)</td>
<td>0.15 (−0.37 to 0.66)</td>
<td>−0.05 (−0.57 to 0.48)</td>
<td>0.45</td>
</tr>
<tr>
<td>Obesity (BMI ≥30 kg/m²) (n = 203)</td>
<td>0.13 (−1.86 to 2.11)</td>
<td>0.46 (−1.62 to 2.53)</td>
<td>0.72</td>
</tr>
<tr>
<td>≥90% adherence to study medication (calcium or placebo) (n = 152)</td>
<td>−1.21 (−3.39 to 0.97)</td>
<td>−1.16 (−3.74 to 1.15)</td>
<td>0.96</td>
</tr>
<tr>
<td>Did not participate in a commercial weight-loss program (n = 304)</td>
<td>0.22 (−1.42 to 1.86)</td>
<td>0.02 (−1.60 to 1.65)</td>
<td>0.75</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Calcium Group</th>
<th>Placebo Group</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major weight gain scenario: model assuming that participants with major weight gain (2.27 kg) withdraw from the study</td>
<td>0.50 (−0.71 to 1.70)</td>
<td>0.77 (−0.37 to 1.91)</td>
<td>−0.27 (−1.66 to 1.12)</td>
</tr>
<tr>
<td>Best-case scenario for calcium: model assuming that participants receiving calcium who withdraw from the study gain no weight, but participants receiving placebo who withdraw from the study have major (2.27 kg) weight gain</td>
<td>−0.01 (−1.22 to 1.19)</td>
<td>0.78 (−0.36 to 1.92)</td>
<td>−0.79 (−2.18 to 0.59)</td>
</tr>
<tr>
<td>Worst-case scenario for calcium: model assuming that participants receiving placebo who withdraw from the study gain no weight, but participants receiving calcium who withdraw from the study have major (2.27 kg) weight gain</td>
<td>0.46 (−0.75 to 1.67)</td>
<td>0.14 (−1 to 1.29)</td>
<td>0.32 (−1.07 to 1.71)</td>
</tr>
</tbody>
</table>

**BMI = body mass index.**

* Estimated marginal means (95% CIs).

---

## Appendix Table 2. Sensitivity to Missing Values of Estimated Intervention Effects on Change in Body Weight at 2 Years*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Calcium Group (n = 168)</th>
<th>Placebo Group (n = 167)</th>
<th>Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major weight gain scenario: model assuming that participants with major weight gain (2.27 kg) withdraw from the study</td>
<td>0.50 (−0.71 to 1.70)</td>
<td>0.77 (−0.37 to 1.91)</td>
<td>−0.27 (−1.66 to 1.12)</td>
<td>0.70</td>
</tr>
<tr>
<td>Best-case scenario for calcium: model assuming that participants receiving calcium who withdraw from the study gain no weight, but participants receiving placebo who withdraw from the study have major (2.27 kg) weight gain</td>
<td>−0.01 (−1.22 to 1.19)</td>
<td>0.78 (−0.36 to 1.92)</td>
<td>−0.79 (−2.18 to 0.59)</td>
<td>0.26</td>
</tr>
<tr>
<td>Worst-case scenario for calcium: model assuming that participants receiving placebo who withdraw from the study gain no weight, but participants receiving calcium who withdraw from the study have major (2.27 kg) weight gain</td>
<td>0.46 (−0.75 to 1.67)</td>
<td>0.14 (−1 to 1.29)</td>
<td>0.32 (−1.07 to 1.71)</td>
<td>0.65</td>
</tr>
</tbody>
</table>

* Estimated marginal means (95% CIs) for weight gain in kilograms, adjusted for age, race, sex, baseline serum 25-hydroxy vitamin D concentration, and baseline calcium intake, reported from imputation analyses.