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Can Calcium Make you Skinny?

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INTRODUCTION

With over one-third of US adults being overweight, the obesity epidemic is undeniable and multi-factorial. Diet, genetics, exercise habits, socioeconomic and systemic considerations are all factors implicated in the ongoing national crisis. In the context of our nation's increased concern with healthcare spending, and with the rising cost of treating obesity and its many related and preventable conditions such as type 2 diabetes, high blood pressure, and cardiovascular disease, there has been a concerted movement toward obesity prevention. Based on several observational studies conducted over the past several decades, it has been reported that increasing calcium intake could be a viable component of an obesity prevention regimen. The implications of these observations necessitated further analysis. Thus, several randomized-controlled clinical trials (RCTs) were conducted to this end. The RCTs demonstrate no significant correlation between calcium intake and anthropomorphic measurements such as weight, BMI, and percent body fat. Those studies are reviewed here.

METHODS

PROCEDURE

To identify relevant studies on calcium's effect on physiological parameters, an electronic search of the PubMed Clinical Queries and GoogleScholar databases was conducted from the years 2000 to 2012. The search strategy consisted of the following keyword combinations: 'micronutrients,' 'weight,' and 'obesity;' 'calcium' and 'calcium intake' with 'visceral fat' and/or 'obesity;' and 'CaSR' with 'adipocytes.' Later search strategies consisted of 'interactions' with 'calcium' and 'vitamin D' and another with 'calcium physiology.' The bibliographies of relevant papers were also screened for pertinent studies. Additionally, a minority of studies with relevant background information that were compiled in earlier stages of the Energetics Study were received from collaborators.

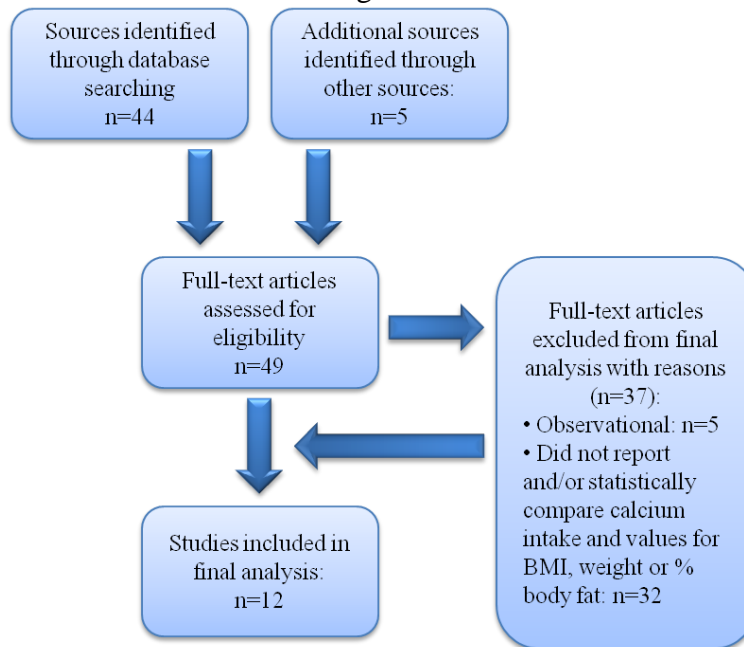
INCLUSION CRITERIA

Studies compiled for final inclusion in this evidence-based literature review included primary literature in which calcium intake and BMI, weight, percent body fat, or energy expenditure were recorded and statistically compared, with the primary variables of interest being weight and BMI (see Figure 1). Studies that included calcium supplements were included while observational studies were excluded.

DATA EXTRACTION

Studies eligible for analysis had data extracted on calcium intake, the assessment of that intake, BMI, fecal fat excretion, study design, study population, and methods of statistical analysis.

Figure 1



RESULTS

The literature search identified 12 randomized-controlled clinical trials that statistically compared calcium intake and anthropomorphic variables of interest.^{5, 18-23, 25-27, 32, 35} Of those 12, three reported statistically significant results: two with a significantly negative correlation and one with a significantly positive one. Of the remaining studies, two did not report on significance and seven reported a lack thereof. Nonetheless, six studies reported a positive association between calcium intake and weight.^{19-21, 25-26, 35}

Cadogan et al., Merrilees et al., and Yanovski et al. demonstrate non-significant positive correlations between calcium intake and weight.^{19, 20, 35} Cadogan et al. divided 82 White women into a placebo group consuming 703mg Ca/d and a calcium-supplemented group consuming 1125mg Ca/d. The placebo group gained an average of 7.2kg and the calcium supplemented group gained an average of 8.0kg during the 18-month trial.¹⁹ Merrilees reported on 91 White women from New Zealand with the placebo group consumed an average of 683mg Ca/d and the supplemented group consumed 1155mg Ca/d. The placebo group gained an average of 4.0kg while the supplemented group gained 4.6kg during the 2-year study.²⁰ Yanovski divided 340 men and women ages 18-80 into placebo-controlled and calcium-supplemented groups. The calcium group was supplemented with 1500mg of elemental calcium as calcium carbonate. At the conclusion of the study, weight (kg), fat mass (kg), and BMI (kg/m²) all had a greater increase in the calcium group than the placebo. Weight increased 0.52kg (-0.82 to +1.86) in the placebo group and 0.54kg (-0.70 to +1.79) in the calcium-supplemented group. Fat mass increased 0.01kg (-1.15 to +1.16) in the placebo group and increased 0.40kg (-0.61 to +1.41) in the calcium group. BMI decreased 0.14kg/m² (-0.73 to +0.45) in the placebo group and increased 0.18kg/m² (-0.33 to +0.69) in the calcium group at the conclusion of the study.³⁵

In similar designs, Barr et al. and Lau et al. demonstrate significantly greater weight and fat gain in supplemented groups.²⁵⁻²⁶ Barr collected data on 200 subjects (65% women and 35% men). Participants were part of a placebo group that consumed fewer than 1.5 dairy servings/day or a supplemented group that consumed 3 eight-oz. servings of skim or 1% fluid milk in addition

to baseline calcium intake. The placebo-controlled men were reported to gain 1kg and the women 0.4kg during the 12-week trial. The supplemented men gained 1.6kg while the women gained 1.9kg ($P<0.005$).²⁵ Lau separated 185 Chinese women into a placebo group consuming an average of 390mg Ca/d and a supplemented group consuming an average of 1046mg Ca/d derived from a low fat milk powder. The placebo group lost an average of 0.26kg and the supplemented group gained an average of 0.52kg during the course of the 2-year randomized control trial ($P<0.001$).²⁶ Baran et al., which does not report on significance, separated 37 women into a placebo and control group and followed them in a 3-year randomized trial. Those in the control group averaged 810mg Ca/d while the supplemented group consumed an average of 1572mg Ca/d. The control group gained 3.4kg while the supplemented group gained 4.2kg.²¹

Two studies, Prince et al. and Devine et al. both fail to demonstrate any significant change in BMI in either the placebo or the control groups during their 2-year intervention.²²⁻²³ Prince analyzed 168 women. The baseline intakes for the control group are not reported and the supplemented group is reported to have consumed 1g Ca/d. Without reporting the actual change in BMI, they state that no significant change in BMI was noted between groups.²² Devine placed 168 women into three groups: a control group with a baseline dietary intake not reported, a group supplemented with milk powder that consumed an average of 942mg Ca/d, and a Ca-tablet supplemented group that consumed an average of 1346mg Ca/d. Although weight data is not presented, Devine notes no significant change in BMI during the intervention for any of the three groups.²³

In the minority of the studies reviewed here, are those demonstrating an inverse association between calcium intake and weight.^{18, 5, 32} Chan et al. conducted a RCT involving 48 pubertal White girls separated into a control group consuming an average of 728mg Ca/d and a calcium-supplemented group consuming an average of 1437mg Ca/d. The placebo group was reported to have gained an average of 7.2kg at the end of the 12-month follow up while the calcium-supplemented group gained 6.4kg. These associations are reported to be non-significant, although the inverse correlation result reported by Zemel et al. did have statistical significance.¹⁸ Zemel put 32 obese adults (84% men and 16% women) on balanced calorie-deficit diets (500kcal/d deficit) and then divided them into three groups: a control group, a high calcium group, and a high dairy group. The control group had an average calcium intake of 430mg. The high calcium group consumed an 800mg/d supplement in addition to their baseline calcium intake and had an average intake of 1256mg/d. The high dairy group consumed 1200-1300mg of calcium in addition to their baseline intake and averaged 1137mg/d. Outcomes were reported in weight change as percentage of initial weight. The control group lost an average of 6.4% of initial weight, the high calcium lost 8.6%, and the high dairy lost 10.9% of initial weight over the course of the 24-week study. All losses were reported to be statistically significant ($p<0.01$).⁵ Similarly, Recker et al. studied 197 women of European ancestry randomized into a control group and a group that consumed a 1200mg/d supplement in addition to their baseline dietary calcium intake. Those who had a baseline dietary intake over 1g/d were excluded. The placebo-controlled group lost an average of 0.325kg/yr while the supplemented group lost 0.671kg/yr resulting in a significant treatment difference of 0.346kg/yr ($p<0.025$). This difference translates to a loss of approximately 0.052kg/yr/100mg Ca intake.³²

Cleghorn et al. is a crossover study involving 115 Australian women at least five years post-menopausal. During the two-year study, there was a 0.06kg difference noted between the two treatment groups that was not reported to be significant (95% CI: -0.71-0.83).²⁷

Data reported at the conclusion of the study conducted by Yanovski et al. support a positive association between calcium intake and weight, and therefore reinforce the general thrust of the clinical data. In a post-hoc analysis, however, Yanovski et al demonstrated mixed results. A subgroup analysis of a group consuming less than 600mg/d and one consuming less than 1200mg/d demonstrated that within the group consuming less than 600mg/d, the calcium group lost more weight, but within the group consuming less than 1200mg/d, the calcium group gained more weight relative to subjects in the placebo group.³⁵

TABLE 1: Human Experimental Studies including Calcium Supplementation and Body Weight Change: Calories consumed ad libitum unless otherwise noted.

Author	Yr	N	Gender	Country	How is Intake Assessed?	Ca Intake (Mean ± SD)	Weight Change (unless otherwise noted)	Significant	Duration
Baran, et al. ²¹	1989	37	W	United States	3-day diet histories & 24-h urinary calcium excretion	Placebo-Controlled Group: 810 ± 367 mg Ca-Supplemented Group: 1572 ± 920 mg	Placebo-Controlled Group: +3.4 kg [†] Ca-Supplemented Group: +4.2 kg	Not Reported	3 yrs
Chan, et al. ¹⁸	1995	48 pubertal girls	W	United States	3-day dietary history & food frequency at the beginning and after 3,6,9, and 12 months of study	Placebo-Controlled Group: 728 ± 321 mg Ca-Supplemented Group: 1437 ± 366 mg (P=0.0001)	Placebo-Controlled Group: +7.2 mg [†] Ca-Supplemented Group: +6.4 mg	No	1 yr
Prince, et al. ²²	1995	168	W	Australia	Tablet compliance checked by tablet counting. Milk powder compliance checked by weighing returned packets. Compliance set to 85%	Placebo-Controlled Group: Baseline intake not reported Ca-Supplemented Groups: 1g	BMI Not Reported	No	2 yrs
Devine, et al. ²³	1996	168	W	United States	4-day weighed diet records at baseline, year 1, 2, and 4	Placebo-Controlled Group: Baseline dietary intake (not reported) Ca-Supplemented Group (milk-powder): 942 ± 434 mg Ca-Supplemented Group (Ca tablet): 1346 ± 512 mg	BMI Not Reported	No	4yrs (2 intervention, 2 follow-up)
Recker, et al. ³²	1996	216	W	Europe	Questionnaire, 7-day diet diary [‡]	Placebo-Controlled Group: baseline dietary intake (<1g/day) Ca-Supplemented group: 1200 mg/d supplement + Baseline dietary intake	Placebo-Controlled Group: -0.33 kg/yr (± 0.110) ^{‡‡‡} Ca-Supplemented Group: -0.67 kg/yr (± 0.112) Tx Difference: 0.35 kg/yr Translate to: -0.05 kg/yr/100mg Ca Intake	Yes Negative P<0.025	4.3 ± 1.1 yrs
Cadogan, et al. ¹⁹	1997	82	W	United Kingdom	7 day weighed intake method	Placebo-Controlled Group: 703 ± 205 mg Ca-Supplemented Group: 1125 ± 294 mg	Placebo-Controlled Group: +7.2 kg Ca-Supplemented Group: +8.0 kg	No	18 months
Barr, et al. ²⁵	2000	200	65% W 35% M	United States	3-day food records	Placebo-Controlled Group: fewer than 1.5 dairy servings/d Supplemented Group: baseline intake + 3 eight-oz servings of skim or 1% fluid milk	Placebo-Controlled Group: +0.4 kg (w), +1.0 kg (m) Ca-Supplemented Group: +1.9 kg (w), +1.6 kg (m)	Yes Positive P<0.005	12 wks (after 4 wk baseline)
Merrilees, et al. ²⁰	2000	91	W	New Zealand	3-day food record & Ca food frequency questionnaire	Placebo-Controlled Group: 683 ± 47.1 mg Ca-Supplemented Group: 1155.1 ± 52.3 mg (P<0.001)	Placebo-Controlled Group: +4.0 kg [†] Ca-Supplemented Group: +4.6 kg	No	2 yrs
Cleghorn, et al. ^{27,iv}	2001	115	W	Australia	Compliance monitored by telephone at beginning, middle, and end of trial. Early in first year, w supplied fasting and 24 hr urine samples	Intake as mean CA 24-hr urinary excretion (95% CI) Placebo-Controlled Group: 3.78 mmol (3.21-4.35) Ca-Supplemented Group: 5.41 mmol (4.54-6.37) (P=0.0003)	0.06 kg difference between on/off added dairy products (95% CI: -0.71 to 0.83 kg) [†]	No	2 yrs
Lau, et al. ²⁶	2001	185	W	China	7-day food diaries repeated at 12-month intervals (2-yr study)	Placebo-Controlled Group: 390 ± 147 mg Ca-Supplemented Group: 1046 ± 347 mg	Placebo-Controlled Group: -0.26 kg [†] Ca-Supplemented Group: +0.52 kg P<0.001 Fat change: Placebo-Controlled Group: -0.14 kg [†] Ca-Supplemented Group: +0.42 kg	Not Reported Not Reported	1 yr
Zemel, et al. ⁵	2004	32 obese	84% W 16% M	United States	Adherence to group diet determined by diet diary & pill counts	400-500 (+ placebo) 400-500 (+ 800mg/d supp) 1200-1300 ^v	Weight change (kg) ^{vi} 4.8±1.2 6.6 ± 2.6 ^{vii} 8.6 ± 1.6 11.7 ± 1.6 Fat Change (kg) 1.4±0.6 5.6±1.0 7.2±1.2 Trunk Fat Change (kg) 1.4±0.6 2.9±0.7 3.7±0.6	Yes Negative P<0.01 ^{viii}	24 wks (after 2 wk baseline)
Yanovski, et al. ³⁶	2010	340 obese & overweight	72% W 28% M	United States	Ca Intake Questionnaire	Placebo-Controlled Group: 887 mg/d Ca-Supplemented Group: baseline + 1500 mg/d elemental ca (calcium carbonate)	Placebo-Controlled Group: +0.52 (-0.82 to +1.86), BMI Change: -0.14 (-0.73 to +0.45) Ca-Supplemented Group: +0.54 (-0.70 to +1.79) BMI Change: +0.18 (-0.33 to +0.69)	No	2 yrs

[†]Data derived from Barr, et al.²⁵

[‡] Estimate of calcium intake from food, med, & supplements was made prior to entry into study by a questionnaire (can only participate in study if calcium intake is estimated to be <1 g/day). If there was uncertainty about validity of responses, volunteers were instructed to keep 7-day diet diary

^{‡‡‡}Data derived from Davies, et al.¹

^{iv} Crossover study

^v Calcium from food, no supplement (high dairy)

^{vi} Balanced deficit diet: 500 kcal/day deficit

^{vii} Weight change as % of initial

^{viii} Weight change, fat change, and trunk fat change between low calcium and high calcium from either supplement or dairy source of calcium

DISCUSSION

Despite the six observational studies reporting decreased weight or BMI with increased calcium intake^{1-2, 4, 17, 29, 34}, randomized controlled trials evaluated in this review support the opposite trend.^{19-21, 25-26, 35} The RCTs reviewed here indicate that increased calcium intake may result in increased BMI. The trials evaluated here varied in length from 12 weeks to three years and included calcium intakes ranging from a lower limit of approximately 400mg/d in obese subjects to an upper limit of 1572mg/d in calcium-supplemented groups.^{5, 18-23, 25-27, 32, 35} Nine of the 12 trials failed to demonstrate any significant correlation.^{18-23, 26-27, 35} Of the remaining three, two trials demonstrated a significant negative correlation with increased calcium intake being associated with decreased weight^{5, 32}, while the third study demonstrated a significant positive association.²⁵

In those studies that showed weight loss, Zemel's differed from all other studies in that its subjects were obese adults maintained on a balanced deficit diet (500 kcal/d deficit).⁵ Subjects showed greater weight, fat, and trunk fat loss when given calcium in the form of either supplement or dairy products. It is unclear, however, whether the obese nature of the subjects and the energy deficient nature of their diets may have contributed to the seemingly protective effect of calcium in regards to weight.⁵

In summary, based on randomized-clinical trials presented by Barr in their meta-analysis and those published since, it does not appear that calcium is protective against weight gain, but rather, calcium intake may be positively correlated with weight gain. Yanovski postulates that calcium may be protective up to a threshold after which it may begin to contribute to weight gain either intrinsically or due to other bioactive compounds consumed concomitantly in dairy products. While Yanovski's post hoc analysis supported this threshold hypothesis, her initial results were consistent with the majority of studies reviewed, showing no significant change in fat between groups.³⁵ Zemel's and Recker's results were the two studies out of the 12 evaluated here to contradict this trend, with Ca intakes up to 1300mg showing significant weight loss.^{5, 32} Therefore, based on the literature review, many studies have tried to increase calcium intake in different populations and to differing degrees and have showed no significant impact on weight loss.

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