Efficacy of calcium supplementation for management of overweight and obesity: systematic review of randomized clinical trials

Igho J Onakpoya, Rachel Perry, Junhua Zhang, and Edzard Ernst

Numerous dietary supplements are marketed as slimming aids, but the efficacy of most has not been proven. One such slimming aid is calcium. Presented here are the results of a systematic review that aimed to evaluate the evidence for or against the efficacy of calcium supplements for body-weight reduction in overweight and obese individuals. Electronic searches were conducted to identify relevant randomized clinical trials of at least 6 months duration. No restrictions of age, gender, language, or time of publication were imposed. Two reviewers independently determined the eligibility of studies, assessed the reporting quality of the studies included, and extracted data. Twenty-four eligible trials were identified, and seven were included. Five of the randomized clinical trials included were not of good reporting quality. A meta-analysis revealed a small, significant reduction in body weight for calcium compared with placebo (mean difference, ⁻0.74 kg; 95% confidence interval, ⁻1.00–⁻0.48). A small, significant reduction in body fat favoring calcium over placebo was also noted (mean difference, ⁻0.93 kg; 95% confidence interval, ⁻1.16–⁻0.71). In conclusion, the evidence from randomized clinical trials suggests calcium supplementation generates small, statistically significant weight loss in overweight and obese individuals, but the clinical relevance of this finding is uncertain.

INTRODUCTION

The prevalence of overweight and obesity has increased dramatically worldwide.[1] Different weight-management options are available, and a variety of dietary supplements are being marketed as slimming aids. However, the efficacy of many of these supplements is far from certain. One such supplement is calcium.

Calcium is the most abundant macroelement in the human body and can be found in a variety of foods as well as drugs, e.g., antacids.[2] Calcium is required for numerous physiological functions, including contraction of muscles and blood vessels, secretion of hormones and enzymes, and transmission of impulses in the nervous system.[3] Most of the calcium in the body is stored in bones and teeth.[4] Some authors have suggested that calcium intake could cause changes in body weight via a decrease in the production of parathyroid hormone and vitamin D.[5] This is thought to increase the breakdown of fat and to decrease fat accumulation. Calcium has also been demonstrated to increase fecal fat excretion, which could lead to a reduction of body weight.[6]

Calcium carbonate and calcium citrate are commonly used supplements. Some researchers have hypothesized that calcium supplementation may help with shedding excess body weight and body fat,[5,7] but a previous systematic review reported no beneficial effects on body weight.[8] Several long-term clinical trials of calcium supplementation on body composition have recently become available.

The objective of the systematic review presented here was to critically evaluate the evidence from randomized

Affiliations: *IJ Onakpoya*, *R Perry*, *J Zhang,* and *E Ernst* are with Complementary Medicine, Peninsula College of Medicine and Dentistry, University of Exeter, Exeter, Devon, United Kingdom.

Correspondence: *IJ Onakpoya*, Department of Complementary Medicine, Peninsula Medical School, University of Exeter, 25 Victoria Park Road, Exeter, Devon, UK. E-mail: igho.onakpoya@pcmd.ac.uk, Phone: +44-1392-424872; Fax: +44-1392-427562.

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clinical trials (RCTs) regarding the efficacy of calcium supplementation for reducing human body weight.

LITERATURE SEARCH METHODS

Electronic searches were conducted using the following databases: Medline, Embase, Amed, Cinahl, and the Cochrane Library. Each database was searched from inception up until September 2010. The following search terms were used: dietary supplement; food supplement; nutritional supplement; nutraceutical; anti-obesity agent; appetite suppressant; overweight; obesity; weight loss; slimming; body weight; body fat; BMI; calcium; calcium supplement; calcium carbonate; calcium citrate; calcium phosphate; calcium chelates; calcium malate; calcium aspartate; calcium fumarate; dairy; dairy supplement; and milk supplement. Derivatives of these were also used. The Internet was searched for relevant conference proceedings, and relevant medical journals and the authors' personal files were hand searched. The bibliographies of all articles located were also searched. No age, gender, language, or time restrictions were imposed.

Only randomized, double-blind, placebo-controlled trials were included as RCTs in this review. To be considered for inclusion, RCTs had to test the efficacy of orally administered calcium for body-weight reduction in overweight or obese human volunteers. Body weight or body composition had to be included as an outcome measure. Studies testing calcium as part of a combination supplement, i.e., dietary interventions containing other supplements in addition to calcium, were excluded. Studies had to have treatment periods of at least 6 months.

Two reviewers (IO and RP) independently assessed the eligibility of studies. The same reviewers extracted data systematically according to patient characteristics, interventions, and results. Finally, the reporting quality of all studies included was assessed using a quality assessment checklist adapted from the Consolidated Standard of Reporting Trials (CONSORT) guidelines.[9,10] Disagreements were resolved through discussion.

Data were presented as means with standard deviations. Mean changes in body weight, body fat, and body mass index (BMI) were used as common endpoints to assess the differences between calcium and placebo groups. Using standard meta-analysis software,[11] mean differences (MDs) and 95% confidence intervals (CIs) were calculated for studies with adequate data for statistical pooling. The I^2 statistic was used to assess for statistical heterogeneity among studies, with values of 25%, 50%, and 75% indicating low, medium, and high statistical heterogeneity, respectively. In addition, sensitivity and subgroup analyses were carried out to test the robustness of overall analysis.

SCREENING AND ANALYSES

The electronic searches returned 4,960 "hits"; among them, 24 potentially relevant articles were identified after screening of abstracts (Figure 1). The full-text copies of these articles were subsequently retrieved. Three articles were excluded because they were open trials,[12–14] and one study was excluded because it involved only normal-weight individuals.[15] Six articles were excluded because they involved both normal and overweight individuals[16–21] and one because the subjects were not described as overweight or obese.[22] Four studies were excluded because they were not described as double blinded,[23–26] one because it was only partially blinded,[27] and another because it was not placebo controlled.[28] Thus, seven RCTs[29–35] that included a total of 794 participants met the inclusion criteria. The key data from these RCTs are summarized in Tables 1 and 2.

There was variation in the reporting quality of the RCTs included (Table 1). Only two studies reported adequate randomization and allocation concealment procedures, and only these studies reported adequate sample-size calculation.[33,35] Only one trial reported adequate blinding of outcome assessors,[35] and intention-to-treat-analysis was adequately reported in only one trial.[35]

A forest plot (fixed-effects model) of the seven RCTs included in the review (Figure 2) revealed a small, significantly greater weight loss for calcium than for placebo (MD, ⁻0.74 kg; 95% CI, ⁻1.00–⁻0.48); heterogeneity was minimal ($I^2 = 0\%$). This translates to about a 0.9% loss of body weight in the calcium group compared with the placebo group. A funnel plot of the MDs plotted against sample size (Figure 3) indicated that most were distributed around the weighted MD for all trials. However, one RCT with >90% of the weight[33] was an outlier, which caused some asymmetry and suggests some evidence of publication bias. A meta-analysis performed without this study revealed a nonsignificant difference in weight reduction between calcium and placebo (MD, ⁻0.09 kg; 95% CI, ⁻0.98–0.80; I^2 value, 0%). A forest plot of the two studies with the highest reporting quality (and largest sample sizes) revealed that a small but significantly greater weight loss was associated with calcium compared with placebo (MD, ⁻0.78 kg; 95% CI, ⁻1.05–⁻0.51; I^2 value, 0%).

A subgroup analysis of three RCTs[29,33,34] involving premenopausal women revealed significantly greater weight loss in the calcium group compared with the placebo group (MD, ⁻1.32 kg; 95% CI, ⁻2.58–⁻0.06; I^2 value, 0%). A forest plot of three RCTs involving postmenopausal women[30,31,34] did not reveal any weight loss in the calcium and placebo groups (MD, 0.58 kg; 95% CI, ⁻0.70–1.87; I^2 value, 0%).

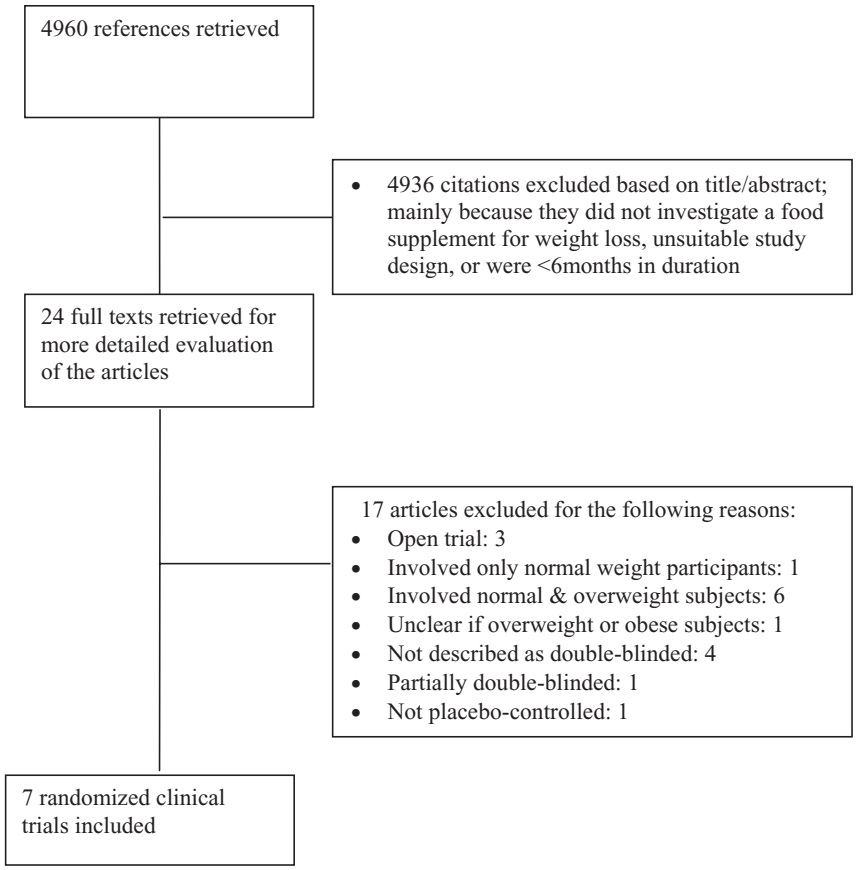

Figure 1 **Flow chart of process for inclusion of randomized clinical trials.**

A forest plot of all seven RCTs (Figure 4) revealed a small, significantly greater reduction in body fat associated with calcium compared with placebo (MD, ⁻0.93 kg; 95% CI, ⁻1.16–⁻0.71; I^2 value, 44%). Finally, a forest plot of four RCTs (Figure 5) that included 434 participants[31,32,34,35] revealed no significant difference in BMI between calcium and placebo (MD, 0.23 kg/m^2; 95% CI, ⁻0.29–0.75; I^2 value, =42%).

Adverse events were reported from only one RCT, and the events reported were not deemed to be causally related to calcium intake.[35] In total, there were 203 dropouts/attritions. In some RCTs, it was not clear to which group the dropouts belonged.

DISCUSSION OF FINDINGS

The objective of the present systematic review was to critically evaluate the evidence from RCTs of calcium supplements for reducing body weight. The meta-analysis suggested that calcium intake generates a significant weight loss when compared with placebo. However, the magnitude of the effect is small and does not seem to be clinically relevant.[36] A weight loss of 0.74 kg translates to less than 5% of body weight loss from baseline. These findings corroborate those from a previous systematic review, which reported a small reduction of body weight associated with calcium supplements or increased calcium intake via dairy products.[8] The presently reported result of the meta-analysis for fat mass indicates a small but significant reduction in weight loss favoring calcium over placebo. Again, the clinical relevance of this difference is debatable. The meta-analytic result for fat mass seems to corroborate a finding reported in a previous review article, which suggested that calcium intake causes a reduction in body fat mass.[37] The BMI did not seem to be affected by the intake of calcium supplements. All of these meta-analytic results should be interpreted with great caution because of the often poor reporting quality of the primary studies. It should also be noted that the present review examined RCTs of obese and overweight individuals exclusively.

The subgroup analysis revealed a statistically significant decrease in body weight in premenopausal women favoring calcium over placebo (which supports the overall meta-analysis), but no decrease in body weight in postmenopausal women. This seems to suggest that calcium supplementation may be efficacious for body

Table 1 **Reporting quality of the RCTs included in the analysis.**

Reference	Main outcome(s)	Main diagnoses of study participants	Study design	Gender (M/F)	Randomization appropriate?	Allocation concealed?	Sample size determined?	Groups similar at baseline?	Outcome assessor blinded?	Care provider blinded?	Patients blinded?	Attrition bias?	ITT analysis?
Riedt (2007), USA[29]	BMD, body weight, fat mass	Premenopausal overweight/obese subjects	Parallel	0/52	NS	NS	NS	Yes	NS	NS	NS	No	No
Riedt (2005), USA[30]	BMD, body weight, fat mass	Postmenopausal overweight subjects	Parallel	0/87	NS	NS	NS	Yes	NS	NS	NS	NS	No
Ricci (1998), USA[31]	BMD, body weight, fat mass	Postmenopausal overweight/obese subjects	Parallel	0/43	NS	NS	No	Yes	NS	NS	NS	No	No
Shalileh (2010), Iran[32]	Body weight, fat mass	Overweight volunteers	Parallel	0/47	NS	NS	NS	Yes	NS	NS	Yes	NS	No
Shapses (2004), USA[33]	Body weight, body fat	Overweight/obese females	Parallel	0/165	Yes	Yes	Yes	No	NS	Yes	Yes	NS	No
Shapses (2001), USA[34]	BMD, body weight, body fat	Premenopausal overweight/obese subjects	Parallel	0/60	NS	NS	No	NS	NS	NS	NS	NS	No
Yanovski (2009), USA[35]	Body weight, adiposity	Healthy obese and overweight volunteers	Parallel	95/245	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes

Abbreviations: BMD, bone mineral density; ITT, intention-to-treat; M/F, males/females; NS, not specified.

weight reduction in the premenopausal period. On average, weight gain in the perimenopausal period is between 2.2 kg and 3.2 kg,[38] and it has been reported that calcium supplementation could be beneficial for preventing weight gain in menopause.[39] However, the beneficial effects of calcium supplementation in preventing weight gain are still largely controversial.[40]

Calcium has been postulated to cause reductions in body weight and fat via a variety of biochemical pathways. Some authors have suggested dietary calcium intake could result in decreased 1,25-vitamin D levels, which results in reduction of intracellular calcium levels.[41] This is believed to stimulate lipolysis as well as inhibit lipogenesis in adipocytes. Reports from human studies have also indicated that a calcium-rich diet increases fat oxidation, resulting in the removal of additional amounts of calories from the body.[16] Calcium has also been purported to decrease calcitriol levels, thereby reducing the capacity of adipocytes to store lipids.[42] The results presented above do not, however, indicate that these effects cause clinically relevant reductions in body weight or fat in obese and overweight individuals.

Most of the studies included in this review were unclear regarding how the randomization procedures were carried out and how allocation concealment was achieved. Only one study demonstrated appropriate intention-to-treat analyses,[35] and only two reported that a sample-size calculation was performed.[33,35] Furthermore, most of the studies had small sizes, ranging from 43 to 87 subjects. In some of the RCTs,[30–32,34] the number of dropouts/attritions in the calcium and placebo groups, respectively, was not specified. The poor reporting of blinding procedures in most of the RCTs casts some doubt on the internal and external validity of the studies. The small sample sizes of most of the studies increases the risk of bias and unreliable findings. The poor reporting quality of some of the RCTs is a poignant reminder for investigators to adhere to standardized reporting guidelines.[9,10]

Variations in lifestyle factors in the different studies should also be considered. The daily caloric intake ranged from 942 to over 2,000 kcal. The estimated dietary calcium intake varied from 600 mg to over 1,000 mg daily. Though dairy products are a good dietary source of calcium, other components such as magnesium, lactose, or casein may also play a role in fat and lipid metabolism.[43] All except one of the included RCTs[31] reported the use of registered dieticians for assessing dietary compliance, and all except one[32] reported using nutritional software to assess the dietary intake of study subjects. In two RCTs, the placebo groups were supplemented with 200 mg of calcium daily.[29,30] The extent to which these factors influenced the outcome of the study results is not clear. A dose-response curve (Figure 6) did not reveal a

Table 2 **Main results of RCTs on calcium supplementation and weight management.**

Reference	Calcium daily dosage and formulation	Randomized/ analyzed	Age in years	Body weight at baseline (kg)	Treatment duration	Main results; reported as means ± standard deviations	Adverse events	Control for lifestyle factors
*Riedt (2007)[29]	1,000 mg tablets	52/52	38.0 ± 6.4 for all subjects	73.2 ± 4.4 (Ca) 73.4 ± 2.4 (PLA)	6 months	Mean weight loss 5.93 ± 2.93 kg and 4.71 ± 1.71 kg for Ca and PLA groups, respectively	Not reported	Normal lifestyle, 1,200–1,500 kcal daily, 600 mg dietary Ca daily
*Riedt (2005)[30]	1,000 mg tablets	87/66	61.3 ± 6.7 (Ca) 61.6 ± 6.4 (PLA)	71.3 ± 6.4 (Ca) 73.8 ± 6.9 (PLA)	6 months	Mean weight loss 6.2 ± 2.8 kg and 7.38 ± 2.9 kg for Ca and PLA groups, respectively	Not reported	Normal lifestyle, 1,200–1,500 kcal daily, 600 mg dietary Ca daily
Ricci (1998)[31]	1,000 mg tablets	43/31	58.3 ± 9.1 for all subjects	88.5 ± 12.9 (Ca) 88.0 ± 9.9 (PLA)	6 months	Mean weight loss 11.5 ± 6.0 kg and 11.4 ± 5.9 kg for Ca and PLA groups, respectively	Not reported	Dietary counseling, 942–1,544 kcal daily, 600–700 mg dietary Ca daily
Shalileh (2010)[32]	1,000 mg tablets	47/40	36.6 ± 7.8 (Ca) 36.6 ± 8.0 (PLA)	77.7 ± 16.8 (Ca) 76.3 ± 8.2 (PLA)	6 months	Mean weight loss 4.1 ± 17.0 kg and 3.1 ± 8.7 kg for Ca and PLA groups, respectively	Not reported	Normal lifestyle, 500 kcal deficit daily, 308–581 mg dietary Ca daily
†Shapses (2004)[33]	1,000 mg tablets	165/100	35.0 – 70.2 (Ca) 34.7 – 65.2 (PLA)	74.7 – 107.3 (Ca) 79.1 – 109.9 (PLA)	6 months	Mean weight loss 7.0 ± 0.7 kg and 6.2 ± 0.7 kg for Ca and PLA groups, respectively	Not reported	Normal lifestyle, 2,100 KJ deficit daily, 700 mg dietary Ca daily
*Shapses (2001)[34]	1,000 mg tablets	60/38	42.1 ± 6.2 for all subjects	94.9 ± 14.9 (Ca) 93.8 ± 13.0 (PLA)	6 months	Mean weight loss 7.5 ± 3.9 kg and 6.7 ± 2.4 kg for Ca and PLA groups, respectively	Not reported	Normal lifestyle, 1,263–1,281 kcal daily, 810–1,005 dietary Ca daily
‡Yanovski (2009)[35]	1,500 mg tablets	340/335	38.7 ± 10.4 for all subjects	94.5 ± 20.5 kg (Ca) 94.0 ± 20.5 kg (PLA)	24 months	Mean weight loss 0.54 ± 8.3 kg and 0.52 ± 8.84 kg for Ca and PLA groups, respectively	None related to trial participation	Normal lifestyle, 2,110–2,190 kcal daily, 878–887 mg dietary Ca daily

* Studies had three comparative groups.
† Study had three subgroups: postmenopausal, postmenopausal special diet, and premenopausal. Calcium supplementation did not affect weight differentially ($P = 0.48$).
‡ Five participants were excluded from analyses because they joined commercial weight-loss programs.
Abbreviations: Ca, calcium; PLA, placebo.

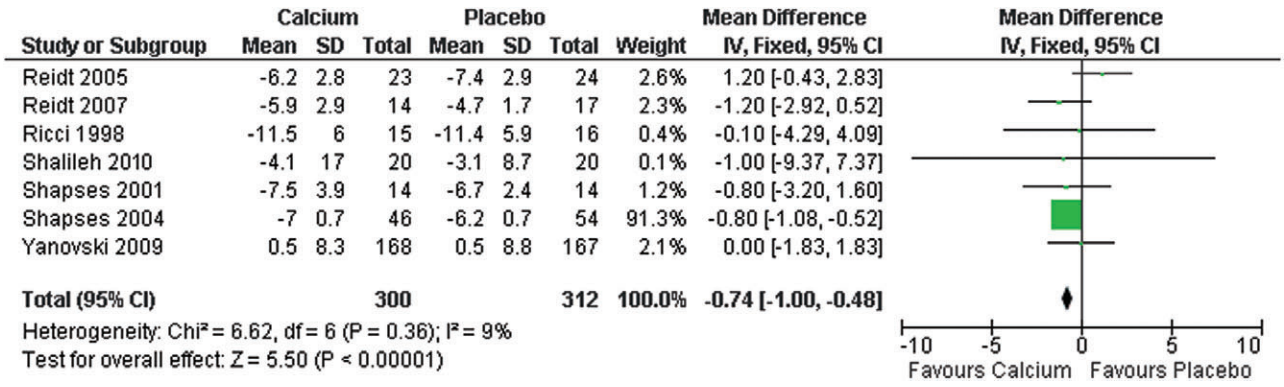

Figure 2 **Forest plot of effect of calcium supplementation on body weight.**

linear relationship between dosage and body weight loss ($P > 0.05$).

Adverse effects of calcium were not reported. The recommended daily requirement for calcium in adults is between 1,000 mg and 1,300 mg.[2] The total intake of calcium among study participants (including dietary sources) ranged from 1,600 mg to over 2,500 mg, which exceeds the recommended daily allowance. Just because

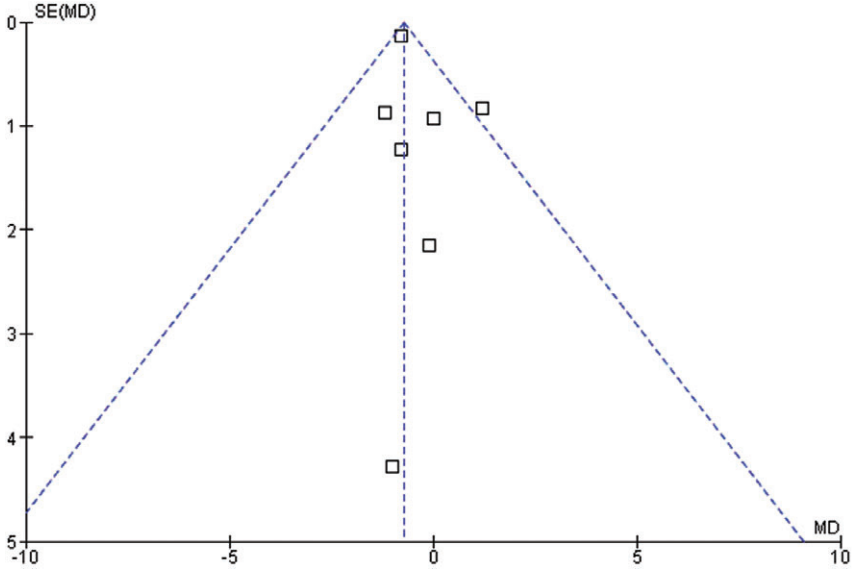

Figure 3 **Funnel plot of comparison of effect of calcium supplementation on body weight.**

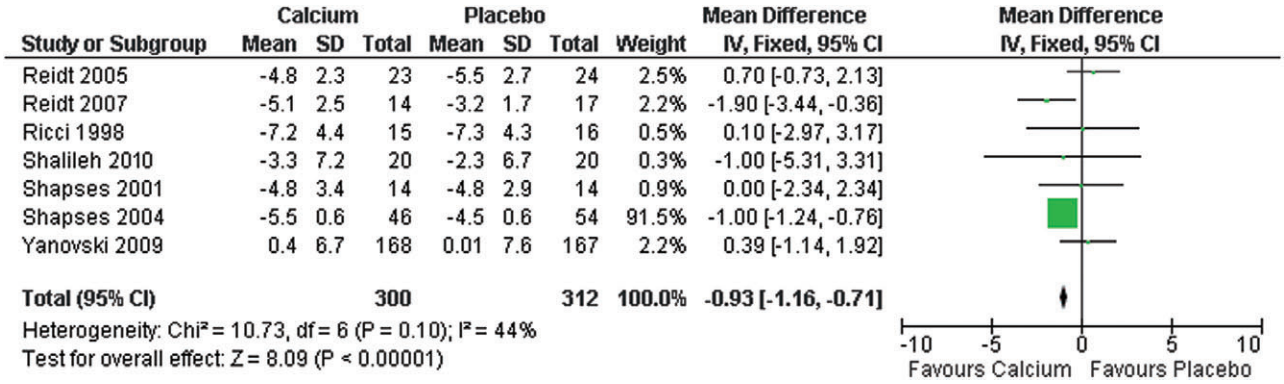

Figure 4 **Forest plot of comparison of effect of calcium supplementation on body fat.**

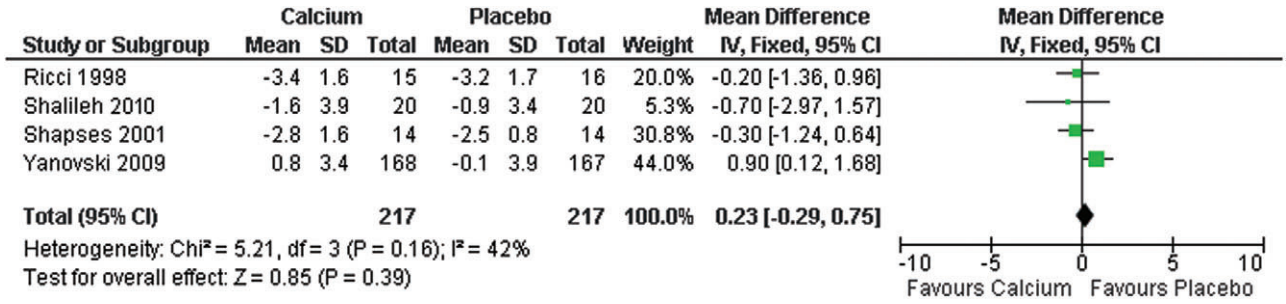

Figure 5 **Forest plot of comparison of effect of calcium supplementation on BMI.**

none of the RCTs reported adverse events does not necessarily mean that calcium supplementation is entirely risk-free. In fact, calcium supplementation has been reported to be associated with an increased risk of myocardial infarction and cardiovascular events.[44] Considering the duration of most of the studies was 6 months, it is questionable whether this was long enough to ascertain if the supplement has any negative effects on the human body. When designing future trials, it will be prudent for study investigators to institute surveillance timeframes beyond the period of intervention to monitor for adverse events.[45]

Calcium supplementation is beneficial for increasing bone mass as well as preventing fractures.[18] This is particularly important for postmenopausal women, who have decreased bone turnover as a consequence of hormonal changes accompanying menopause. Four of the RCTs included in this review measured bone mineral density[29–31,34] and all reported that calcium had beneficial effects of calcium on this measure.

The present systematic review has several important limitations. Even though great effort was expended in searching electronic and non-electronic sources, it is possible that not all relevant RCTs were identified. Furthermore, only a few of the RCTs identified were appropriate for inclusion, and the reporting quality of some of the trials was poor. Collectively, these drawbacks limit the conclusiveness of the findings.

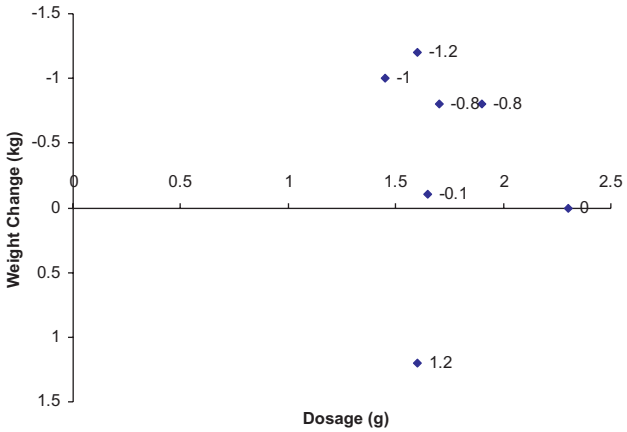

Figure 6 **Dose effect of calcium on body weight, with coefficient of correlation as ⁻0.15.**
Values above and below 0 on the y axis represent weight loss and weight gain, respectively.

CONCLUSION

The present analysis indicates that evidence on calcium supplementation and weight management from published RCTs is scarce, and most RCTs have not been rigorously reported. While the findings suggest that calcium supplementation for at least 6 months results in a statistically significant weight loss in obese and overweight individuals, the clinical relevance of this finding is uncertain.

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