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# Calcium supplementation for improving bone mineral density in children (Review)

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[Intervention Review]

# Calcium supplementation for improving bone mineral density in children

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## ABSTRACT

### Background

Clinical trials have shown that calcium supplementation in children can increase bone mineral density (BMD) although this effect may not be maintained. There has been no quantitative systematic review of this intervention.

### Objectives

·To determine the effectiveness of calcium supplementation for improving BMD in children.
·To determine if any effect varies by sex, pubertal stage, ethnicity or level of physical activity, and if any effect persists after supplementation is ceased.

### Search methods

We searched CENTRAL, (Cochrane Central Register of Controlled Trials) (Issue 3, 2005), MEDLINE (1966 to 1 April 2005), EMBASE (1980 to 1 April 2005), CINAHL (1982 to 1 April 2005), AMED (1985 to 1 April 2005), MANTIS (1880 to 1 April 2005) ISI Web of Science (1945 to 1 April 2005), Food Science and Technology Abstracts (1969 to 1 April 2005) and Human Nutrition (1982 to 1 April 2005). Conference abstract books (Osteoporosis International, Journal of Bone and Mineral Research) were hand-searched.

### Selection criteria

Randomised controlled trials of calcium supplementation (including by food sources) compared with placebo, with a treatment period of at least 3 months in children without co-existent medical conditions affecting bone metabolism. Outcomes had to include areal or volumetric BMD, bone mineral content (BMC), or in the case of studies using quantitative ultrasound, broadband ultrasound attenuation and ultrasonic speed of sound, measured after at least 6 months of follow-up.

### Data collection and analysis

Two authors independently assessed trial quality and extracted data including adverse events. We contacted study authors for additional information.

### Main results

The 19 trials included 2859 participants, of which 1367 were randomised to supplementation and 1426 to placebo. There was no heterogeneity in the results of the main effects analyses to suggest that the studies were not comparable. There was no effect of calcium supplementation on femoral neck or lumbar spine BMD. There was a small effect on total body BMC (standardised mean difference (SMD) +0.14, 95% CI+0.01, +0.27) and upper limb BMD (SMD +0.14, 95%CI +0.04, +0.24). Only the effect in the upper limb persisted after supplementation ceased (SMD+0.14, 95%CI+0.01, +0.28). This effect is approximately equivalent to a 1.7% greater increase in

supplemented groups, which at best would reduce absolute fracture risk in children by 0.1-0.2%per annum. There was no evidence of effect modification by baseline calcium intake, sex, ethnicity, physical activity or pubertal stage. Adverse events were reported infrequently and were minor.

**Authors' conclusions**

While there is a small effect of calcium supplementation in the upper limb, the increase in BMD which results is unlikely to result in a clinically significant decrease in fracture risk. The results do not support the use of calcium supplementation in healthy children as a public health intervention. These results cannot be extrapolated to children with medical conditions affecting bone metabolism.

## PLAIN LANGUAGE SUMMARY

**Calcium for improving bone mineral density in children**

Do calcium supplements build stronger bones in children?

## BACKGROUND

Osteoporosis is a systemic skeletal disorder characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture (1993). It is a major and growing public health problem, particularly in women (Jones 1994; Cooley 2001; Woolf 2003). An estimated 10 million people already have osteoporosis and 18 million more have low bone mass (NIH 2000) in the United States alone. While the impact of osteoporosis is currently greatest in western population, its impact worldwide is expected to increase (Woolf 2003). Low bone mineral density (BMD) is a major risk factor for osteoporotic fracture (Marshall 1996). It is well accepted that childhood factors are likely to have an impact of future risk of osteoporosis (NIH 2000). Peak bone mass is the maximum bone mass attained by an individual and is reached in early adult life. At least 90% of peak bone mass is obtained by age 18 years (Bailey 1999). BMD in later life is a function of peak bone mass and the rate of subsequent bone loss (Hansen 1991). It has also been shown that peak bone mass is as important as rate of bone loss as a risk factor for fracture in later life (Riis 1996). Peak bone mass is influenced by genetic factors, but also modifiable lifestyle factors such as adequate nutrition, body weight and physical activity (Javaid 2002). Maximizing peak bone mass is therefore a potential way to minimise the impact of age-related bone loss. In addition, there is evidence that low BMD is a risk factor for fracture in childhood (Ma 2003; Goulding 1998; Goulding 2001), suggesting that optimising age-appropriate bone mass may also have a more immediate effect on childhood fracture rates.

Strategies to maximise peak bone mass in girls and boys have been identified as a priority area for research (NIH 2000). Bone acts as a reservoir for calcium and other ions and is the major store of calcium within the body (Favus 2003). Calcium deposition in bone leads to increased bone mineral density and bone mineral content. Clinical trials have shown that BMD in children can be increased in the short-term by physical activity interventions ( Bradney 1998; Fuchs 2001; Heinonen 2000; Morris 1997; MacKelvie 2003; Sundberg 2001) and calcium supplementation (Bonjour 1995; Johnston 1992; Lee 1994; Lee 1995; Lloyd 1993) although this effect may not be maintained (Lee 1994); and by increased dairy intake (Chan 1995). However, there has been no systematic review of effectiveness of calcium supplementation, the magnitude of its effect, the duration of any effect after supplementation ends and the impact of sex or pubertal stage on its effect.

## OBJECTIVES

·To determine the effectiveness of calcium supplementation for improving BMD in children.
·To determine if any effect varies by sex, pubertal stage, ethnicity or level of physical activity.
·To determine if any effect persists after calcium supplementation is ceased.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

All randomised controlled trials of calcium supplementation compared with placebo, with a treatment period of at least 3 months were included. The studies had to have areal or volumetric BMD, or bone mineral content (BMC) as an outcome, or in the case of studies using quantitative ultrasound, broadband ultrasound attenuation (BUA) and ultrasonic speed of sound (SOS).

#### Types of participants

Trials in children (age<18 years) without co-existent medical conditions or treatments affecting bone metabolism were included.

#### Types of interventions

Trials of calcium supplementation including supplementation by food sources. Trials of less than 3 months were excluded.

#### Types of outcome measures

Fractures in later life would be the ideal outcome measure in intervention studies for osteoporosis prevention, however for intervention studies in children this would require following large numbers of subjects for decades and these studies have not been performed. Therefore, in this review BMD was used as a surrogate outcome, as is commonly seen in intervention studies in children (Gilsanz 1998).

Data was extracted on areal BMD and BMC, measured a minimum of 6 months after the treatment was commenced. In the original review protocol, we aimed to use percentage change from baseline, but as this was available for only a small number of studies, this was not used. The available data also did not allow for calculation of volumetric BMD as was stipulated in the original review protocol. In the case of studies using quantitative ultrasound, broadband ultrasound attenuation (BUA) and ultrasonic speed of sound (SOS) were to be used, but in the absence of studies using these measures, these outcomes were not used. The outcome measures were converted to standardized mean differences (SMD) using Review Manager (version 4.2.7). We had sufficient extractable bone measurement data for meta-analysis of the following outcomes: total body BMC, femoral neck BMD; lumbar spine BMD; distal radius BMD and upper limb BMD. Upper limb BMD included those studies included in the outcome for distal radius and additional studies with upper limb outcomes at other sites. Where multiple upper limb sites were measured, we chose the distal radius or the site closest to that point as the outcome. Methods of measurement included dual energy x-ray absorptiometry (DXA), single photon absorptiometry (SPA) and dual photon absorptiometry (DPA).

Where possible we also determined sex, age, pubertal stage, physical activity, baseline height, baseline weight, dietary calcium intake, type of calcium supplement used, ethnicity and follow-up after cessation of treatment to assess possible effect modification by these variables. We also collected data on adverse effects, where available.

### Search methods for identification of studies

The search strategies included a search CENTRAL, (Cochrane Central Register of Controlled Trials) (Issue 3, 2005), MEDLINE (1966 to 1 April 2005), EMBASE (1980 to 1 April 2005), CINAHL (1982 to 1 April 2005), AMED (1985 to 1 April 2005), MANTIS (1880 to 1 April 2005) ISI Web of Science (1945 to 1 April 2005), Food Science and Technology Abstracts (1969 to 1 April 2005) and Human Nutrition (1982 to 1 April 2005). Conference abstract books (Osteoporosis

International, Journal of Bone and Mineral Research) were also hand searched.

For MEDLINE (OVID) the strategy used was:

1exp CALCIUM/
2exp Calcium, Dietary/
3calcium.tw.
4exp dairy products/
5dairy.tw.
6milk.tw.
7exp dietary supplements/
8or/1-7
9exp OSTEOPOROSIS/
10osteoporo$.tw.
11exp Bone Density/
12(bone adj2 loss).tw.
13(bone adj2 densit$).tw.
14bone mass.tw.
15bmd.tw.
16or/9-15
178 and 16
18limit 17 to all child <0 to 18 years>

The Dickersin filter (Robinson 2002) for randomised controlled trials was applied to MEDLINE, and adapted for other databases where relevant. In the absence of evidence of publication bias we did not systematically contact content experts regarding unpublished studies. Informal contacts did not yield any unpublished studies.

### Data collection and analysis

Two reviewers (TW, KS) independently reviewed relevant articles identified by the search strategy, with initial screening of abstracts according to the inclusion criteria and with full text articles being reviewed if there was insufficient information in the abstract to assess eligibility. All data was extracted by two reviewers (TW, KS). Details regarding the study population, treatment periods, baseline demographic data and baseline and end of study outcomes were extracted independently. Differences in data extraction were resolved by referring back to the original article and establishing consensus. A third reviewer (GJ) was available to assist in reaching consensus if required, but was not needed. The same two reviewers (TW,KS) performed a quality assessment independently for each trial assessing randomisation, allocation concealment, blinding of those providing treatment and of treatment subjects, and description of withdrawals and dropouts (Jadad 1996; Juni 2001).

For bone density, we calculated the SMD of the endpoints at end of trial between treatment and control groups for the various outcomes. Originally, we had planned to use percentage change from baseline as the outcome measure, but this was not possible with the data available to us, and end point data was therefore used instead. We assessed heterogeneity of the data using a Chi-square test on N-1 degrees of freedom. Meta-analysis was conducted according to a fixed-effect model for the main effect outcomes, as there was no heterogeneity for these outcomes. Where heterogeneity existed in subgroup analyses we used a random-effects model. In the absence of heterogeneity of the main effect outcomes and because of limited numbers of studies for each outcome, we did not perform meta-regression and we limited our subgroup analyses to key potential effect modifiers, namely: sex; ethnicity; baseline calcium intake; physical activity; type of supplementation (milk extract compared to other calcium supplement forms (calcium carbonate/calcium citrate malate/calcium phosphate)) and duration of supplementation. The baseline calcium subgroups were determined by whether the baseline dietary calcium intake was less than or greater than or equal to the median value of the individual study means, which was 794 mg/day. Due to study numbers, we were unable to perform analyses using other definitions of low calcium intake except in the case of upper limb BMD, where we also analysed in subgroups of baseline calcium intake of below compared to above the 25th percentile (i.e . 582 mg/day). Physical activity subgroups were chosen according to the data available in individual studies - where the studies had physical activity as a co-intervention or subgrouping, those in the low physical activity arm were included in the low physical activity subgroup for the review and those in the high physical activity arm in the high physical activity subgroup for the review. For study duration, we initially chose a cut-off of 24 months duration so as to sure of exceeding any period of rapid change from the bone remodeling transient. Because this left few studies in the longer duration subgroup, we repeated the analysis using an 18-month cut-off, which is likely to still have exceeded the time needed for the effects on bone of remodeling changes to appear and a new steady state to be reached. We also performed a subgroup analysis whether the calcium intake in the intervention group in the trial exceeded the probable threshold (approximately 1400 mg/day) below which skeletal accumulation varies with intake and above which skeletal accumulation appears constant regardless of intake (Jackman 1997; Matkovic 1992). This was an analysis additional to those specified in the original protocol.

Where necessary the authors of the primary studies were contacted to obtain additional information. We aimed to use intention-to-treat data from the individual clinical trials wherever possible. If this data was not available, we used data from available treatment analysis. If no other data were available we used data from treatment received analysis. For the single study (Wang 1996) in which upper limb outcomes were presented as percent change from baseline, and no endpoint data could be obtained from the authors, we imputed endpoint data using the formula endpoint BMD= (100% +%change) X baseline BMD and assumed the endpoint standard deviation (SD) was the same as that seen at baseline (as was observed in other studies for upper limb outcomes). Where studies reported the outcome as absolute change from baseline and endpoint data were not available (Lloyd 1993; Bonjour 1995; Chevalley 2005; Iuliano-Burns 2003; Specker 2003) we imputed the endpoint using (baseline plus change) for the mean in both treatment and control arms, and using the standard deviation of the baseline data for the endpoint SD.

Funnel plots were performed for assessment of publication bias.

Our method of imputing the standard deviation for studies which gave change rather than endpoint data was likely to result in those studies being given more rather than less weight. We therefore performed a sensitivity analysis for the main effects omitting studies for which data was imputed (Wang 1996; Lloyd 1993; Bonjour 1995; Chevalley 2005; Iuliano-Burns 2003; Specker 2003) . We also performed a sensitivity analysis omitting the study (Bonjour 1995) that used treatment received rather than intention to treat or available data analysis. In the absence of

heterogeneity of the main effect outcomes, sensitivity analyses were not performed to assess the impact of study quality on results.

Grading of evidence
We used the grading system described in the 2004 book Evidence-based Rheumatology (Tugwell 2004) and recommended by the Musculoskeletal Group:
Platinum: A published systematic review that has at least two individual controlled trials each satisfying the following :
·Sample sizes of at least 50 per group - if these do not find a statistically significant difference, they are adequately powered for a 20% relative difference in the relevant outcome.
·Blinding of patients and assessors for outcomes.
·Handling of withdrawals >80% follow up (imputations based on methods such as Last Observation Carried Forward (LOCF) are acceptable).
·Concealment of treatment allocation.

Gold: At least one randomised clinical trial meeting all of the following criteria for the major outcome(s) as reported:
·Sample sizes of at least 50 per group - if these do not find a statistically significant difference, they are adequately powered for a 20% relative difference in the relevant outcome.
·Blinding of patients and assessors for outcomes.
·Handling of withdrawals > 80% follow up (imputations based on methods such as LOCF are acceptable).
·Concealment of treatment allocation.

Silver: A randomised trial that does not meet the above criteria. Silver ranking would also include evidence from at least one study of non-randomised cohorts that did and did not receive the therapy, or evidence from at least one high quality case-control study. A randomised trial with a 'head-to-head' comparison of agents would be considered silver level ranking unless a reference were provided to a comparison of one of the agents to placebo showing at least a 20% relative difference.

Bronze: The bronze ranking is given to evidence if at least one high quality case series without controls (including simple before/after studies in which patients act as their own control) or if the conclusion is derived from expert opinion based on clinical experience without reference to any of the foregoing (for example, argument from physiology, bench research or first principles).

Clinical relevance

The SMD effect size was used to estimate an absolute benefit in mg/cm$^2$ by estimating the pooled SD from the means of the SD of the outcomes in treatment and control groups for each study, and multiplying the SMD by this (Alderson 2002). Relative difference in the change from baseline was estimated as the absolute benefit divided by the mean of all the baseline means of the control groups, expressed as a percentage. The result of this analysis is reported in the text of the review results and discussion.

The review will be updated in future according to Cochrane Collaboration recommendations .

## RESULTS

### Description of studies

We identified 233 references to potential studies. Of these, 155 were excluded as they were not randomised controlled trials. Of the remaining 78 references, 9 were to trials without calcium supplementation as an intervention, 7 were to trials in participants with conditions predisposing to osteoporosis and 3 were to studies in adults. Of the remaining 59 references to RCTs of calcium supplementation in children, the following references were excluded for the following reasons:
·16 references were to studies with either no placebo (Barker 1998; Cadogan 1997; Chan 1995; Du 2004; Fischer 1999a; Lau 1992; Lau 2004; Li 2002; Magee 1996; Merrilees 2000; Renner 1998; Specker 1997; Zhang 2003; Zhu 2003; Zhu 2004) or which used an active placebo i.e. a placebo which itself could affect bone (Gibbons 2004)
·3 were duplicate publications (Fischer 1999b; Nowson 1995; Specker 2002)
·2 did not measure BMD or BMC or ultrasound measures of bone as outcomes (Lappe 2004; Ohgitani 1997)
·1 included vitamin D with calcium as the intervention (Moyer-Mileur 2003)
·1 had inadequate randomisation (Matkovic 1990)
·1 had outcomes measured after< 6 months follow-up (Volek 2003)

The remaining 35 references to 19 studies were included in the systematic review.

Additional data was requested from authors of 8 eligible studies, of whom 5 supplied the additional information sought (Cameron 2004; Johnston 1992; Prentice 2005; Stear 2003; Courteix 2005) . In only one of the cases where additional information was not obtained, did this result in no usable data being available for the meta-analysis (Rodda 2004). All other eligible studies provided useful data for pooling.

The 19 RCTs included a total of 2859 participants, of whom 1367 were randomised to receive calcium supplementation, 1426 were randomised to placebo, and 66 withdrew from the study and the intervention group to which they were randomised was not stated. The Characteristics of Included Studies table summarises the characteristics of these studies. Studies included children as young as 3 years old, up to 18 years of age. Calcium supplementation was by calcium citrate malate, calcium carbonate, calcium phosphate, calcium lactate gluconate, calcium phosphate milk extract or milk minerals with calcium dose ranging from 300 to 1200 mg per day. No studies used ultrasound measures of bone outcomes. One study used intention-to-treat analysis (Dibba 2000); in one study the type of analysis was not stated (Rodda 2004); in one study (Bonjour 1995) only data from treatment received analysis was available for the femoral neck, lumbar spine and upper limb BMD at end of the trial. The remaining studies used available data analysis. Five studies had loss to follow-up of less than 5% (Dibba 2000; Lee 1994; Molgaard 2004; Prentice 2005; Wang 1996), 5 had a loss to follow-up of between 5 and 20% (Bonjour 1995; Iuliano-Burns 2003; Lloyd 1993; Rozen 2003; Stear 2003) and 8 had loss to follow-up of more than 20% (Cameron 2004; Chevalley 2005; Courteix 2005; Johnston 1992; Lee 1995; Matkovic 2004; Nowson 1997; Specker 2003) of their trial participants. One study did not report withdrawals and drop outs (Rodda 2004). Three studies had physical activity as a co-intervention (Iuliano-Burns 2003; Prentice 2005; Stear 2003) and one had physical activity subgroups of exercise (7.2 hours exercise per week) and sedentary (1.2 hours exercise per week) (Courteix 2005).

## Risk of bias in included studies

Two reviewers (KS, TW) independently rated the methodological quality of each eligible study. Any disagreement was resolved by consensus, with the third reviewer (GJ) not being required to contribute for these to be resolved. Adequate description of randomisation was given for four studies (Courteix 2005; Dibba 2000; Iuliano-Burns 2003; Prentice 2005), the remaining studies were stated to be randomised but randomisation procedures were not described. Four studies (Bonjour 1995; Courteix 2005; Dibba 2000; Stear 2003) described adequate allocation concealment, the description in the remainder of the studies was unclear. Adequate description of blinding of subjects was given in all studies except two (Chevalley 2005; Specker 2003) in which the description was unclear, though all were controlled with adequate placebo. Thirteen studies gave an adequate description of withdrawals and drop outs (Bonjour 1995; Cameron 2004; Chevalley 2005; Courteix 2005; Dibba 2000; Johnston 1992; Lee 1994; Lee 1995; Lloyd 1993; Molgaard 2004; Nowson 1997; Prentice 2005; Specker 2003) and six did not (Iuliano-Burns 2003; Matkovic 2004; Rodda 2004; Rozen 2003; Stear 2003; Wang 1996). Overall, the risk of bias was rated as low in two studies (Courteix 2005; Dibba 2000), moderate in twelve studies ( Bonjour 1995; Cameron 2004; Chevalley 2005; Johnston 1992; Lee 1994; Lee 1995; Lloyd 1993; Molgaard 2004; Nowson 1997; Prentice 2005; Rodda 2004; Specker 2003), and high in five studies (Iuliano-Burns 2003; Matkovic 2004; Rozen 2003; Stear 2003; Wang 1996).

## Effects of interventions

Comparison Tables 1 to 9 give the treatment effects, as standardised mean differences (SMD) at each site at the end of the period of calcium supplementation and the results at the longest period of follow-up available after calcium supplementation was ceased for each trial. There was no effect of calcium supplementation on BMD at the femoral neck (+0.07, 95%CI -0.05, +0.19) or lumbar spine BMD (+0.08, 95% CI -0.04, +0.20). There was a small effect on total body BMC (+0.14, 95% CI +0.01, +0.27) and upper limb BMD (+0.14, 95%CI +0.04, +0.24) which persisted after supplementation ceased only in the upper limb (+0.14, 95%CI +0.01, +0.28). As the effect at the distal radius alone was similar to that in the upper limb as defined in the methods, we discuss only the upper limb results in further detail. The effect at the upper limb is approximately equivalent to a treatment effect of 6.38 mg/cm$^2$ or an approximately 1.7% greater increase in supplemented groups over the course of supplementation; and to a 6.30 mg/cm$^2$ or 1.7% greater increase after follow-up after supplementation had ceased. A single study (Rozen 2003) reported on total body BMC after cessation of supplementation, and this showed no persistent effect (SMD 0.0, 95%CI -0.40, +0.40). There was no significant heterogeneity for the results at any site (p= 0.29 to p>0.99).

Subgroup Analyses

Subgroup analyses by baseline calcium intake, sex, ethnicity, physical activity, pubertal stage, type of supplementation (milk extract or other), duration of supplementation and by whether the calcium threshold was exceeded all did not demonstrate significant effect modification at any site (Comparison Tables 10 to 79). Point estimates of treatment effects during supplementation were greater at all sites in females than males (Tables 19 to 26), though these differences were not significant. At the upper limb, treatment effects during supplementation were similar in magnitude and not significant in both Caucasian and Chinese population studies but a relatively strong effect was seen in the single study in an African population (+0.44, 95%CI +0.12, +0.75). A single study described a gain in lumbar spine BMD of 0.045 g/cm$^2$ in Chinese but not Anglo-Celt girls (Rodda 2004) but the study provided insufficient data to be included in the meta-analysis. Subgroup analysis by physical activity level showed no evidence of effect modification, though there were only two studies with extractable data for the femoral neck, lumbar spine and upper limb outcomes. One study not included in the meta-analysis demonstrated interaction between calcium supplementation and physical activity using femoral BMC as an outcome but not for tibia-fibula BMC (Iuliano-Burns 2003).

Numbers of studies available for subgroup analyses were limited for some outcomes, for example subgroup analysis by baseline calcium intake using a definition of low calcium intake as the mean baseline calcium intake of the participants in the study being in the lowest quartile. Only a single study (Rozen 2003) measured TB BMC after supplementation ceased so subgroup analyses for this outcome were not possible. Only one study reported TB BMC for males (Prentice 2005) and only one reported femoral neck and lumbar spine BMD after supplementation ceased for males (Chevalley 2005). There was only a single study with any results described in purely peri-pubertal children (Matkovic 2004) and insufficient data for any subgroup analysis by pubertal stage for effects after cessation of supplementation. No studies in Chinese populations had total body BMC data, and only a single study using milk extract as a supplement had total body BMC data.

Funnel plots for each outcome did not suggest the presence of publication bias (See Additional Figures:Figure 1, Figure 2, Figure 3, Figure 4, Figure 5, Figure 6, Figure 7, Figure 8, Figure 9).

**Figure 1. Funnel plot of studies with femoral neck BMD outcome at end of supplementation period**

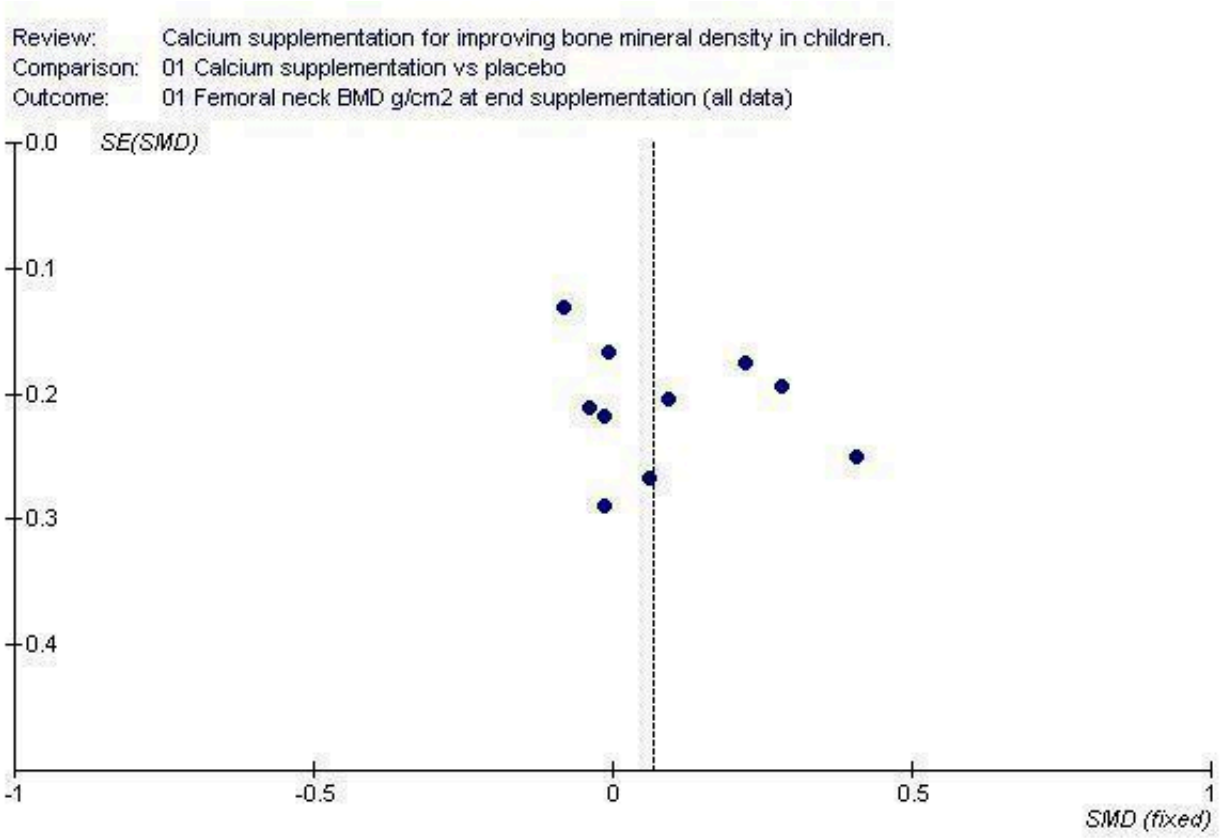


**Figure 2. Funnel plot of studies with femoral neck BMD outcome at end of longest period of follow-up after supplementation ceased**

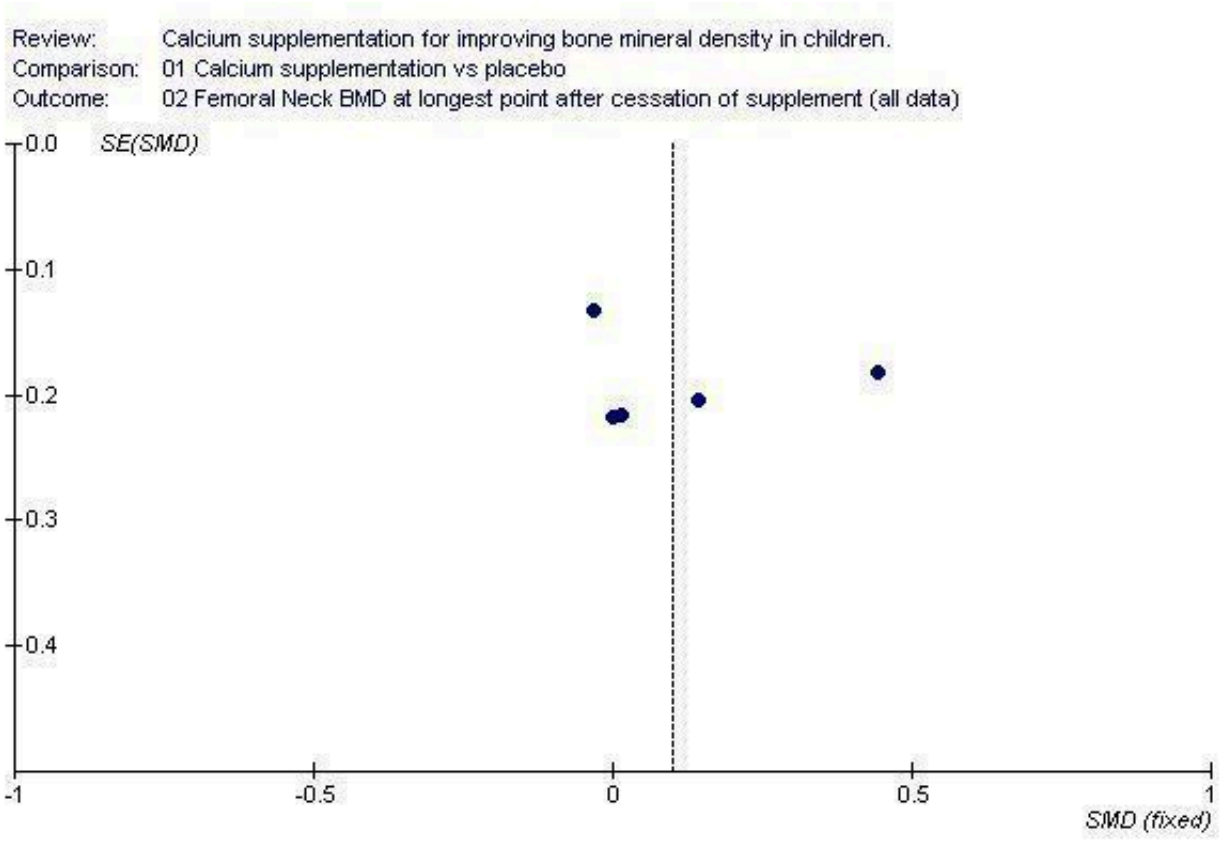


**Figure 3. Funnel plot of studies with lumbar spine BMD outcome at end of supplementation period**

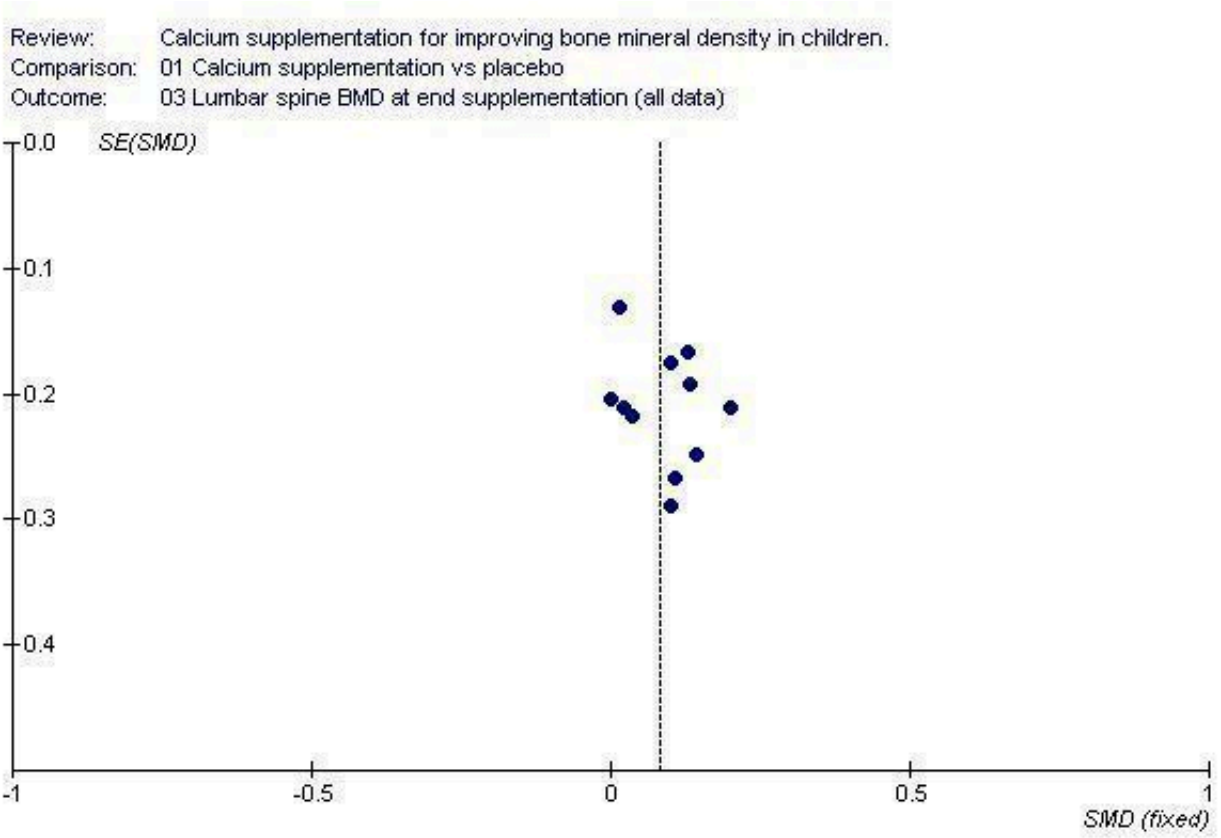


**Figure 4. Funnel plot of studies with lumbar spine BMD outcome at end of longest period of follow-up after supplementation ceased**

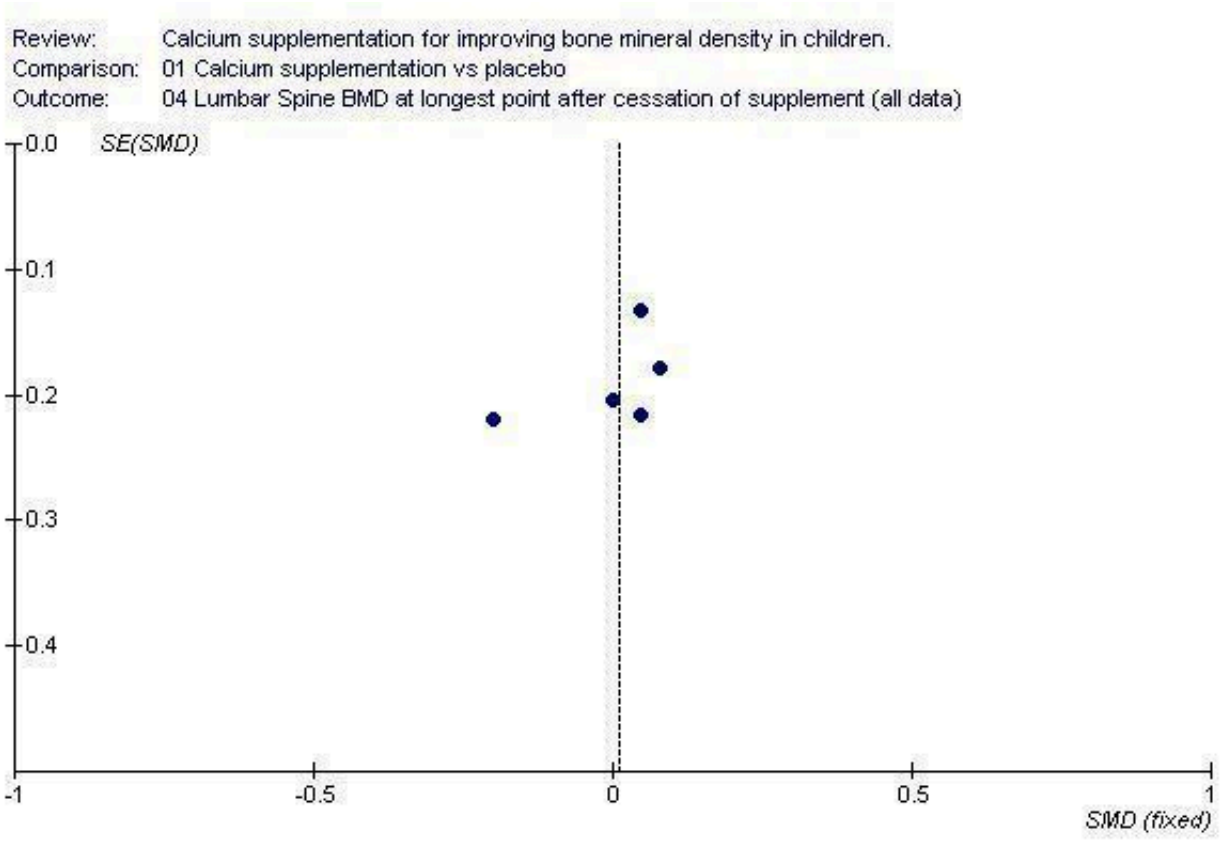


**Figure 5. Funnel plot of studies with total body BMC outcome at end of supplementation period**

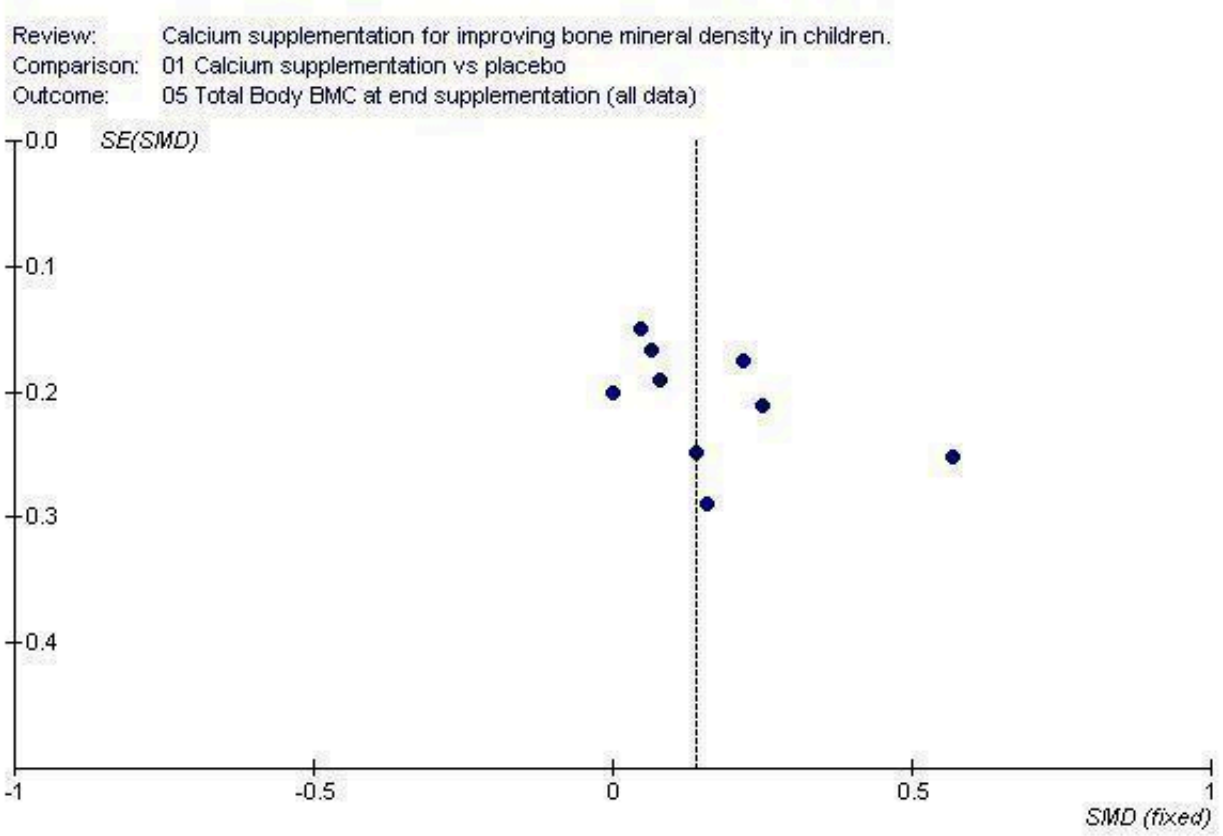


**Figure 6. Funnel plot of studies with distal radius BMD outcome at end of supplementation period**

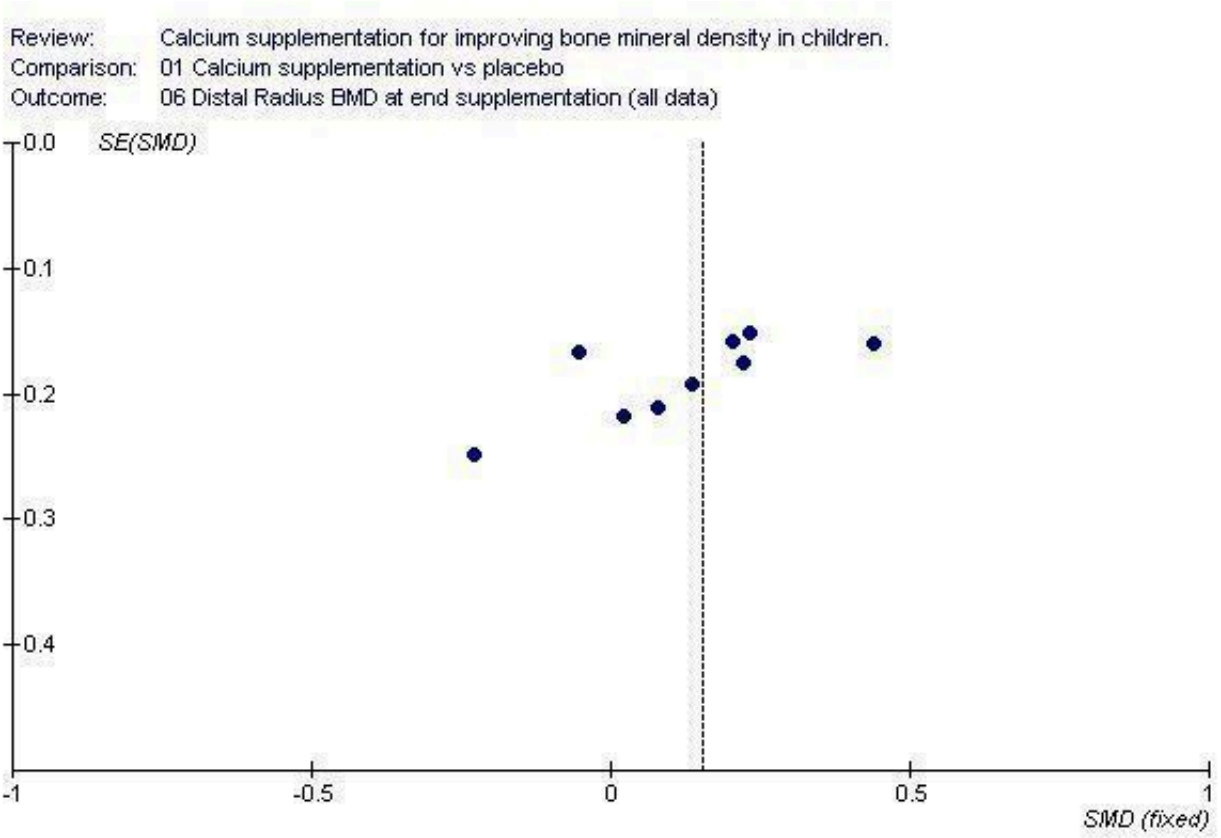


**Figure 7. Funnel plot of studies with distal radius BMD outcome at end of longest period of follow-up after supplementation ceased**

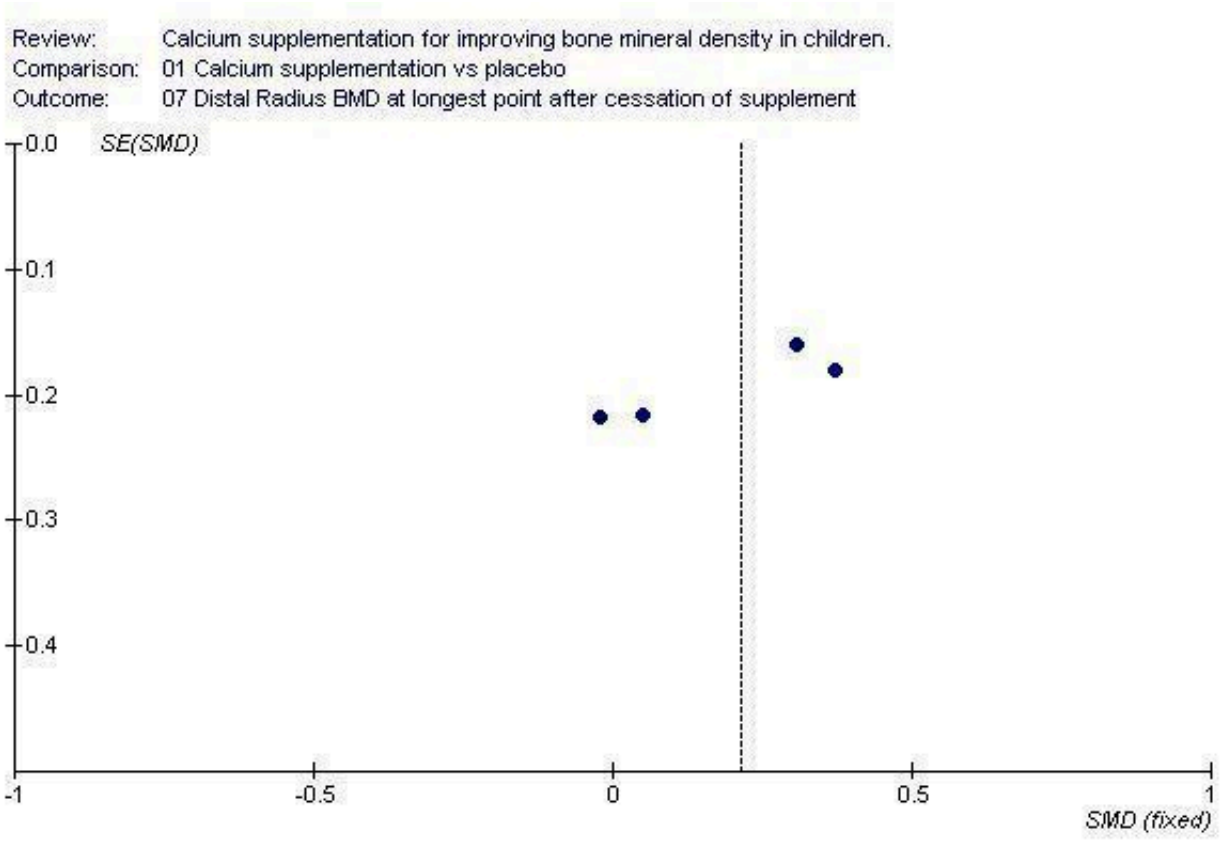


**Figure 8. Funnel plot of studies with upper limb BMD outcome at end of supplementation period**

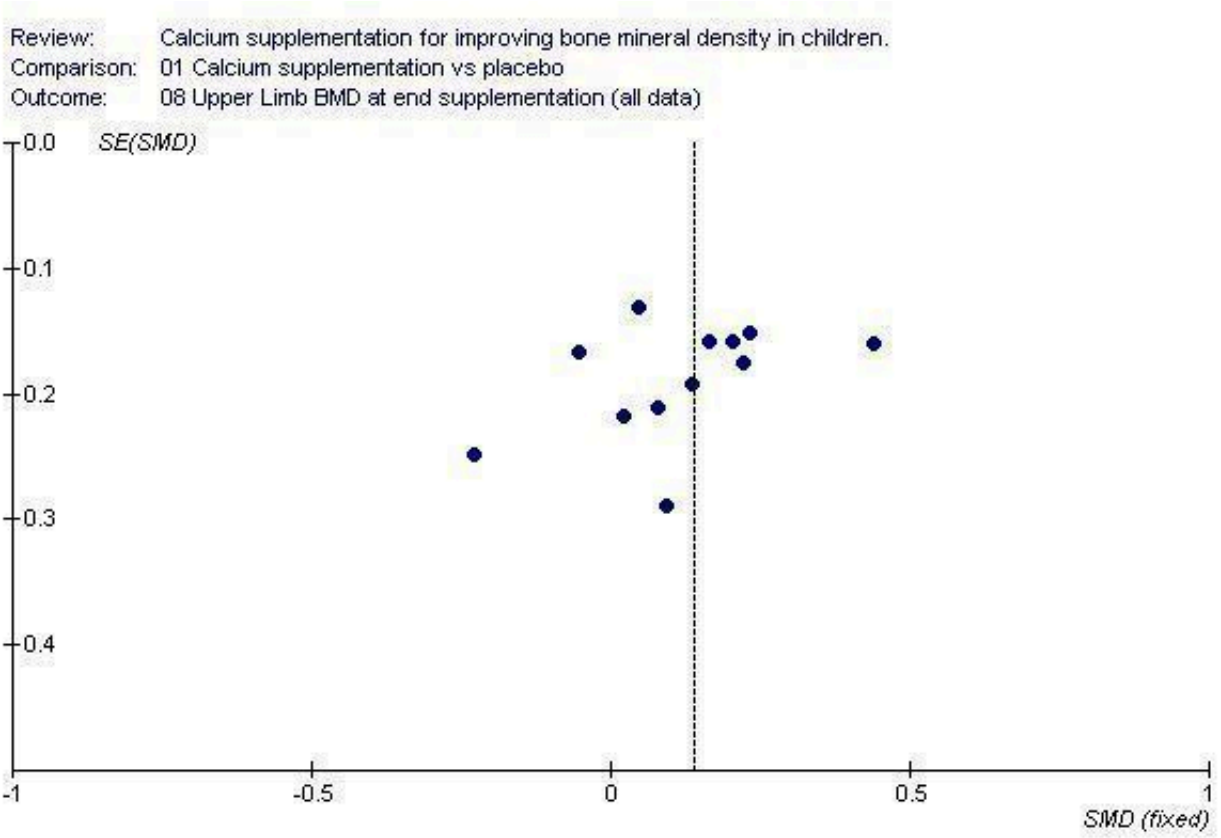
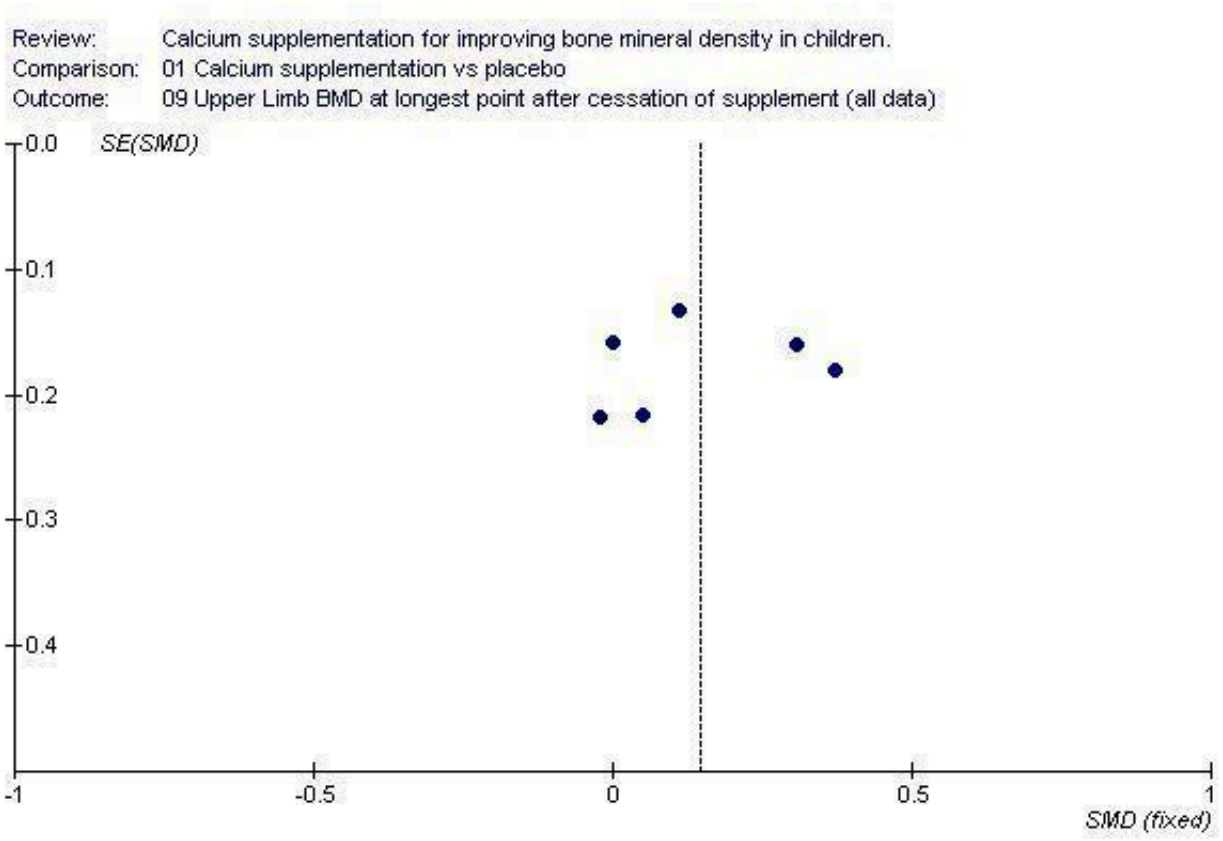


**Figure 9. Funnel plot of studies with upper limb BMD outcome at end of longest period of follow-up after supplementation ceased**




Sensitivity analyses omitting results only given from active treatment analysis (Bonjour 1995 at end of supplementation) did not substantially alter the results of the review. Omitting the studies with imputed values reduced the effect at the upper limb after cessation of supplementation from an SMD of +0.14 (95%CI +0.01, +0.28) to +0.10 (95% CI -0.07, +0.28) and marginally widened the confidence interval around the effect on total body BMC at the end of supplementation (+0.15, 95%CI -0.01, +0.31) without changing the size of the point estimate of the treatment effect. Sensitivity analyses did not substantially affect the review results for any other outcomes.

Adverse events were reported infrequently and were minor in nature, including raised urinary calcium to creatinine ratio (1 child), and gastro-intestinal side effects (4 children).

## DISCUSSION

Calcium supplementation has little effect on BMD. At the only site where an effect was demonstrated, the upper limb, the effect is small, equating to an approximately 1.7 percentage point greater increase in BMD in the supplemented compared to the control group, an effect which persists after supplementation ceases with a 1.7 percentage point greater increase. It is important to note that this effect did not remain statistically significant when the studies for which imputed outcomes were used were excluded, and it is therefore possible that the upper limb effect may be smaller than indicated in the main analysis. The small increase in BMD at the upper limb is unlikely to result in a clinically significant decrease in fracture risk. Importantly, there were no effects seen at other sites at which fracture is common, namely the femoral neck and lumbar spine.

Children with upper limb fractures have been reported to have reduced BMD at the femoral neck, lumbar spine and total body compared to controls with the difference being in the order of 1-5% depending on site of BMD measurement (Ma 2003). Other studies examining distal forearm fractures in boys and girls (Goulding 1998; Goulding 2001) have reported a reduction in ultradistal radius BMD of around 4% in girls and 5% in boys and in 33% radius BMD of around 3% in both sexes. Based on the decrease in odds ratio for wrist and forearm fractures observed for each standard deviation increase in lumbar spine BMD (Ma 2003), the treatment effect observed in this review would result in an approximately 6% decrease in the relative risk of fracture. If this were applied to the peak incidence of all fracture in childhood (about 3% per annum (p.a.) in 15-19 year old boys and 1% p.a. in 10-14 year old girls) (Jones 2002), the decrease in absolute risk would be at most 0.2% p.a. in boys and 0.1% p.a. in girls. Therefore, while it is possible that the small increase in BMD from calcium supplementation could have an effect on reduction of fracture risk in childhood, the public health impact of this is likely to be small. Extrapolating these results to assess the potential for reduction in fracture risk in adult life is more problematic. Though the increase in upper limb BMD did persist after cessation of supplementation, the maximum length of follow-up after supplementation was withdrawn was only

7 years (Bonjour 1995) and the study participants in even this study had not yet all reached adulthood. The impact of a period of supplementation in childhood on upper limb BMD and fracture risk in later life remains unknown. Even in calcium supplement trials in post-menopausal women, the effect of calcium supplementation on fracture risk is unclear. While BMD increased by around 1.6 to 2 % (Shea 2004), the point estimate from the meta-analysis of the five studies that included fracture risk as an outcome only suggested a reduction in vertebral fractures (relative risk (RR) 0.79, 95%CI 0.55 to 1.13), and a smaller reduction in risk of non-vertebral fractures (RR 0.86, 95% CI 0.43 to 1.72). However, these results were not significant, probably due to small event numbers. The two studies providing data on non-vertebral fracture did not examine upper limb fractures separately as an outcome, probably due to small events numbers. Thus, the public health benefits of calcium supplementation in children, either in childhood or in later life appear marginal at best.

The literature pertaining to calcium supplement use in children has been qualitatively reviewed previously (French 2000; Wosje 2000; Lanou 2005). These reviews reported that overall calcium supplementation did appear to have a favourable effect on bone outcomes. One review of six intervention studies published up until 1999 (French 2000) reported that calcium supplement use showed consistent positive effects on bone mass gains in children and adolescents, most consistently at the lumbar spine and total body sites. A second review (Wosje 2000) included one additional study and by contrast concluded that increases in BMD occurred mostly at cortical sites, are greater in populations with low baseline calcium intake and do not seem to persist beyond the supplementation period. The most recent review (Lanou 2005) was aimed specifically at determining whether the literature supported the suggestion that dairy products are better for promoting bone integrity that other calcium-containing food sources or supplements. As part of this review the authors described 12 randomised controlled trials with duration of calcium supplementation more than 12 months. They reported that 9 out of 10 trials of calcium supplementation by non-dairy sources showed an increase in bone outcomes and one showed no effect and that the three trials of dairy products showed slight effects. None of these latter three trials met the inclusion criteria for our review, as they were not placebo-controlled (Cadogan 1997; Chan 1995) or did not have adequate randomisation (Matkovic 1990). In our review four studies used milk extract supplementation (Bonjour 1995; Chevalley 2005; Iuliano-Burns 2003; Courteix 2005). In contrast to the qualitative reviews, the results of our quantitative review do not support the findings that calcium supplementation has significant beneficial effects in children for bone outcomes or that a particular type of calcium supplementation has any more effect on bone than any other.

Subgroup analyses demonstrated little effect modification across the subgroups tested, as one would expect given the lack of heterogeneity overall in the included studies. The consistently greater effects seen in females compared to males across all sites of bone outcome measurement at the end of supplementation, though not significant, are suggestive of a sex difference in the response of BMD and BMC to calcium supplementation. There were few studies on which to base an assessment of whether this sex difference persisted with withdrawal of supplementation, but on the available data the differences did not persist. The treatment effect on upper limb BMD in the single study performed in an African population was greater than that observed in either Caucasian or Chinese populations, but again not significantly so. Given that this was in a single study, some caution is needed in interpreting this result. The difference in effect may be explained by genetic factors, but the result could also be confounded by dietary, physical activity or other environmental factors.

It is interesting that there were no differences in treatment effects observed between shorter and longer studies. It has been hypothesised that calcium supplementation reduces bone remodeling rather than or as well as increasing bone modelling, thus accounting for the transient benefit of calcium supplementation seen in some individual studies (Heaney 2001). If bone remodeling was affected by calcium supplementation more than bone modelling, one would expect the difference between treatment effects in shorter versus longer studies to be small, in other words that as the duration of supplementation increased, the rate of increase in BMD/BMC would drop. This is consistent with our data. However, one would also expect that after supplementation ceased there would be a decrease in treatment effect. This is observed in our data for total body BMC but not at the upper limb, which is the only site where an overall treatment effect was observed during supplementation. The reason for this inconsistency between sites is not clear.

During supplementation, the magnitude of changes in bone density outcomes were similar whether the total calcium intake in the intervention arms of the studies did or did not exceed the estimated threshold below which skeletal accumulation varies with intake. This observation supports the concept of a calcium threshold: exceeding the threshold would not be expected to result in greater bone deposition. However, this analysis cannot confirm the magnitude of the threshold. It is possible that any effect of calcium supplementation ceases at a level less than the 1400 mg/day intake predicted from the literature which we tested in this analysis.

The sensitivity analyses performed indicated that the overall review results if anything may have overestimated the treatment effects for the upper limb after calcium supplementation had ceased. Otherwise, the sensitivity analyses had little effect on the review results and do not alter the overall conclusion of the review that the public health benefits of calcium supplementation in children, either in the short-term or long-term, appear marginal at best.

### Limitations

No studies in this review measured fractures as an outcome. This is not surprising as a RCT examining fracture outcomes would require a large cohort of children followed for a lengthy period of time to have sufficient power and fracture events to detect an effect on fracture risk. However, this does add to the difficulty of interpreting the clinical and public health significance of the results. This review also did not assess changes in other bone indices such as bone size or geometry. The studies selected intentionally did not include trials in children with medical conditions or on medications that might affect bone metabolism. Therefore, the results of this review should not be extrapolated to children with such conditions. Meta-regression could not be performed in this review due to the small number of studies. However, in the absence of heterogeneity this is not a significant limitation.

It has been suggested that areal BMD only partly corrects for bone size and that adjustment of BMC for bone area, weight and height is desirable (Prentice 1994). Only 3 studies provided such size adjusted data (Dibba 2000; Prentice 2005; Stear 2003) and

so this outcome was not included in the meta-analysis. However, qualitatively the outcomes of these 3 studies were similar, whether they were analysed using BMD or size-adjusted BMC.

Subgroup analyses identified areas in which there were gaps in studies in this review, particularly where studies have limited the number of sites measured for their outcomes. As a result, while there is no evidence of effect modification, in a number of areas studies are lacking, so that effect modification cannot be rule out. For example, one might expect that children with lower baseline calcium intake might benefit more from supplementation. While we did not find evidence of this, there were few studies performed in children with very low baseline calcium intake - the majority were performed in participants in whom the mean baseline calcium intake was close to or above 700 mg/day. Only three studies had baseline intakes below 500 mg/day. Our power to detect effect modification by very low baseline calcium intake (< 500 mg/day) was limited. There were also few studies in which participants could be analysed by whether they were purely post-pubertal and only a single study with only an upper limb outcome in purely peripubertal children. Given that it appears that calcium accumulation in the skeleton accelerates during puberty (Abrams 1996; Bonjour 1991), the absence of sufficient data in the peripubertal period is an important gap to be filled by further research. Other gaps were related to ethnicity and the impact of physical activity. Relatively few studies were in non-Caucasian populations, which resulted in single studies with smaller numbers of participants for some outcomes in ethnicity subgroups. For example, at the femoral neck there was only a single study of Arabs/Jews with a wide confidence interval for the point estimate, though the magnitude of the treatment effect point estimate was larger than that seen in Caucasians. While no effect modification by physical activity was observed, there were only two studies to assess this at the lumbar spine, femoral neck and upper limb. Individual results from studies which were not included in the meta-analysis suggest that effect modification could occur at other sites, but more studies are needed to assess this. The methods of assessing physical activity and calcium intake across the different studies were also variable, making classification into subgroups problematic.

## AUTHORS' CONCLUSIONS

### Implications for practice

While there is a small effect of calcium supplementation at the upper limb, the resultant increase in BMD is unlikely to result in a clinically significant decrease in fracture risk. The results of this review do not support the use of calcium supplementation in healthy children as a public health intervention. However, these results cannot be extrapolated to children with medical conditions affecting bone metabolism.

### Implications for research

While long-term fracture studies are desirable to properly assess any effect on fracture risk reduction, for reasons discussed above we recognise that these are unlikely to be feasible. The absence of sufficient data children with very low calcium intakes and in the peripubertal period are important gaps to be filled by further research. Long-term calcium supplement studies over the period of peak bone mineral content velocity, perhaps particularly in children with very low calcium intake, would be desirable. Other gaps were related to ethnicity, the impact of physical activity, and the provision of information from follow-up after supplementation ceases. Given the small treatment effects seen with calcium supplementation, it may also be appropriate to explore possible alternative nutritional interventions, such as vitamin D supplementation (Moyer-Mileur 2003; Zhu 2004 b) and fruit and vegetable intake (Jones 2001).

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* Indicates the major publication for the study

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies *[ordered by study ID]*

#### Bonjour 1995

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (Youth Health Service), Switzerland<br>DURATION OF SUPPLEMENTATION: 1 year<br>DURATION OF FOLLOW-UP: 8 years<br>QUALITY ASSESSMENT: Moderate risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Yes<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes<br><br>TYPE OF ANALYSIS: Available data and treatment received<br>COMPLIANCE: Assessed<br>CONFOUNDERS MEASURED: pubertal status, spontaneous calcium intake |
| Participants | N SCREENED: unknown<br>N RANDOMISED: 149<br>N COMPLETED: 144 (1 year); 122 (8 years)<br>M=0%<br>F=100% |

**Bonjour 1995** *(Continued)*

| | |
|---|---|
| | ETHNICITY: CAUCASIAN<br>MEAN BASELINE AGE (yrs): 7.93<br>BASELINE AGE RANGE (yrs): 6.6-9.4<br>INCLUSION CRITERIA: healthy prepubertal, Caucasian females<br>EXCLUSION CRITERIA: no parental approval, ratio weight/height < 3rd or > 97th percentile according to Geneva reference values, presence of physical signs of puberty, chronic disease, gastro-intestinal disease capable of inducing malabsorption, congenital or acquired bone disease, regular use of medication.<br>BASELINE CALCIUM INTAKE (mg/day): 752<br>PUBERTAL STATUS: prepubertal |
| Interventions | 1. Foods supplemented by milk extract (850 mg Calcium per day)<br>2. Unsupplemented foods<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: distal radial metaphysis, diaphysis of radius, femoral neck, femoral trochanter, femoral diaphysis and L2-4 vertebrae.<br>BONE MINERAL CONTENT: distal radial metaphysis, diaphysis of radius, femoral neck, femoral trochanter, femoral diaphysis and L2-4 vertebrae.<br>BONE AREA: distal radial metaphysis, diaphysis of radius, femoral neck, femoral trochanter, femoral diaphysis and L2-4 vertebrae.<br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 1, 2, 4.5, 8.5<br>OTHER OUTCOMES MEASURED: weight, height<br>BONE MEASURES INCLUDED IN STUDY ANALYSES:<br>AREAL BONE MINERAL DENSITY: distal radial metaphysis, diaphysis of radius, femoral neck, femoral trochanter, femoral diaphysis and L2-4 vertebrae, mean of the 6 sites. .<br>BONE MINERAL CONTENT: L2-4 vertebrae, mean of all 6 sites<br>BONE AREA: femoral diaphysis and L2-4 vertebrae, mean of the 6 sites.<br>SUB-GROUPS IDENTIFIED: Spontaneous calcium intake (defined by median); early vs late menarcheal age |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Low risk | A - Adequate |

**Cameron 2004**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (Twin register), Australia<br>DURATION OF SUPPLEMENTATION: 2 years<br>DURATION OF FOLLOW-UP: 2 years<br>QUALITY ASSESSMENT: Moderate risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes<br><br>TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed<br>CONFOUNDERS MEASURED: spontaneous calcium intake, physical activity, medical history and medication use. |

**Cameron 2004** *(Continued)*

| | |
|---|---|
| Participants | N SCREENED: unknown<br>N RANDOMISED: 128<br>N COMPLETED: 104 (6 months); 48 (2 years)<br>M=0%<br>F=100%<br>ETHNICITY: unknown<br>MEAN BASELINE AGE (yrs): 10.3<br>BASELINE AGE RANGE (yrs): 8-13<br>INCLUSION CRITERIA: premenarcheal female twins<br>EXCLUSION CRITERIA: nil<br>BASELINE CALCIUM INTAKE (mg/day): 716<br>PUBERTAL STAGE: prepubertal |
| Interventions | 1. Calcium carbonate 1200 mg<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: total hip, femoral neck, total forearm and L2-4 vertebrae.<br>BONE MINERAL CONTENT: total body<br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 0.5, 1, 1.5, 2<br>OTHER OUTCOMES MEASURED: weight, height, fat mass, lean mass<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: total hip, femoral neck, total forearm and L2-4 vertebrae.<br>BONE MINERAL CONTENT: total body<br>SUB-GROUPS IDENTIFIED: Menarche vs premenarche |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Chevalley 2005**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (Public Youth Health Service), Switzerland<br>DURATION OF SUPPLEMENTATION: 1 year<br>DURATION OF FOLLOW-UP: 2 years<br>QUALITY ASSESSMENT: Moderate risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Unclear<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes<br><br>TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed<br>CONFOUNDERS MEASURED: spontaneous calcium intake, physical activity, |
| Participants | N SCREENED: unknown<br>N RANDOMISED: 235<br>N COMPLETED: 232 (1 year); 172 (2 years)<br>M=100%<br>F=0% |

**Chevalley 2005** *(Continued)*

| | |
|---|---|
| | ETHNICITY: CAUCASIAN<br>MEAN BASELINE AGE (yrs): 7.44<br>BASELINE AGE RANGE (yrs): 6.5-8.5<br>INCLUSION CRITERIA: healthy prepubertal, Caucasian males with spontatneous calcium intake below the 75th centile of a community sample of 990 boys<br>EXCLUSION CRITERIA: ratio weight/height < 3rd or > 97th percentile according to Geneva reference values, presence of physical signs of puberty, chronic disease, gastro-intestinal disease capable of inducing malabsorption, congenital or acquired bone disease, regular use of medication.<br>BASELINE CALCIUM INTAKE (mg/day): 752<br>PUBERTAL STAGE: prepubertal |
| Interventions | 1. Foods supplemented by calcium phosphate milk extract (850 mg Calcium per day)<br>2. Unsupplemented foods<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES MEASURED: SITES<br>AREAL BONE MINERAL DENSITY: distal radial metaphysis, diaphysis of radius, femoral neck, femoral trochanter, femoral diaphysis and L2-4 vertebrae.<br>BONE MINERAL CONTENT: total body, distal radial metaphysis, diaphysis of radius, femoral neck, femoral trochanter, femoral diaphysis and L2-4 vertebrae.<br>BONE AREA: distal radial metaphysis, diaphysis of radius, femoral neck, femoral trochanter, femoral diaphysis and L2-4 vertebrae.<br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 1, 2<br>OTHER OUTCOMES MEASURED: weight, height<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: distal radial metaphysis, diaphysis of radius, femoral neck, femoral trochanter, femoral diaphysis and L2-4 vertebrae, mean at the 5 appendicular sites.<br>BONE MINERAL CONTENT: distal radial metaphysis, diaphysis of radius, femoral neck, femoral trochanter, femoral diaphysis and L2-4 vertebrae, mean at the 5 appendicular sites.<br>BONE AREA: distal radial metaphysis, diaphysis of radius, femoral neck, femoral trochanter, femoral diaphysis and L2-4 vertebrae, mean at the 5 appendicular sites.<br><br>SUB-GROUPS IDENTIFIED: physical activity levels and spontaneous calcium intake (defined by above and below median) |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Courteix 2005**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (school and sports clubs), France<br>DURATION OF SUPPLEMENTATION: 1 year<br>DURATION OF FOLLOW-UP: 1 year<br>QUALITY ASSESSMENT: low risk of bias<br>RANDOMISED: random and description consistent with this<br>ALLOCATION CONCEALMENT: Yes<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes<br><br>TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed |

**Courteix 2005** *(Continued)*

| | |
|---|---|
| | CONFOUNDERS MEASURED: physical activity, pubertal status, spontaneous calcium intake |
| Participants | N SCREENED: 138<br>N RANDOMISED: 113<br>N COMPLETED: 85 (1 year)<br>M=0%<br>F=100%<br>ETHNICITY: CAUCASIAN<br>MEAN BASELINE AGE (yrs): 9.91<br>BASELINE AGE RANGE (yrs): 8-13<br>INCLUSION CRITERIA: healthy Caucasian females, age 8-13, prepubescent and not expected to reach menarche before end of first year of study<br>EXCLUSION CRITERIA: children with swimming as a physical activity<br>BASELINE CALCIUM INTAKE (mg/day): 994<br>PUBERTAL STAGE: prepubertal |
| Interventions | 1. 800 mg/day calcium as calcium phosphate<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: total body, dominant hip (femoral neck, trochanter and Ward's triangle), non-dominant radius (1/3, mid and distal) and L2-4 vertebrae.<br>BONE MINERAL CONTENT: total body, dominant hip (femoral neck, trochanter and Ward's triangle), non-dominant radius (1/3, mid and distal) and L2-4 vertebrae.<br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 1<br>OTHER OUTCOMES MEASURED: BMI, height, bone age, fat mass, lean mass<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: total body, dominant hip (femoral neck, trochanter and Ward's triangle), non-dominant radius (1/3, mid and distal) and L2-4 vertebrae.<br>BONE MINERAL CONTENT: total body, dominant hip (femoral neck, trochanter and Ward's triangle), non-dominant radius (1/3, mid and distal) and L2-4 vertebrae.<br><br>SUB-GROUPS IDENTIFIED: exercise (7.2 hours exercise per week) and sedentary (1.2 hours exercise per week) |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Low risk | A - Adequate |

**Dibba 2000**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (rural village), Gambia<br>DURATION OF SUPPLEMENTATION: 1 year<br>DURATION OF FOLLOW-UP: 3 years<br>QUALITY ASSESSMENT: Low risk of bias<br>RANDOMISED: random and description consistent with this<br>ALLOCATION CONCEALMENT: Yes<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes<br><br>TYPE OF ANALYSIS: Intention-to-treat |

**Dibba 2000** *(Continued)*

| | |
|---|---|
| | COMPLIANCE: Assessed<br>CONFOUNDERS MEASURED: tanner stage status, spontaneous calcium intake, baseline serum vitamin D, grip strength |
| Participants | N SCREENED: 162<br>N RANDOMISED: 160<br>N COMPLETED: 160<br>M=50%<br>F=50%<br>ETHNICITY: Gambian<br>MEAN BASELINE AGE (yrs): 10.3<br>BASELINE AGE RANGE (yrs): 8.3-11.9<br>INCLUSION CRITERIA: 8.3-11.9 y.o children in a single rural village, healthy, no history of medical condition known to affect calcium or bone metabolism, no recent fracture, no alcohol, antacids, calcium or other nutritional supplements, non-smoking.<br>EXCLUSION CRITERIA: see inclusion criteria<br>BASELINE CALCIUM INTAKE (mg/day): 338<br>PUBERTAL STAGE: mixed |
| Interventions | 1. Calcium carbonate 1000mg 5 days per week<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: midshaft and distal radius (left arm).<br>BONE MINERAL CONTENT: midshaft and distal radius (left arm).<br>BONE WIDTH: midshaft and distal radius (left arm).<br>METHOD OF MEASUREMENT: SPA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 1, 2, 3<br>OTHER OUTCOMES MEASURED: weight, height, triceps skinfold thickness, plasma osteocalcin (n=100 only)<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: midshaft and distal radius (left arm).<br>BONE MINERAL CONTENT: midshaft and distal radius (left arm).<br>BONE WIDTH: midshaft and distal radius (left arm).<br><br>SUB-GROUPS IDENTIFIED: sex |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Low risk | A - Adequate |

**Iuliano-Burns 2003**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (school), Australia<br>DURATION OF SUPPLEMENTATION: 8.5 months<br>DURATION OF FOLLOW-UP: 8.5 months<br>QUALITY ASSESSMENT: High risk of bias<br>RANDOMISED: random and description consistent with this<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: No |

**Iuliano-Burns 2003** *(Continued)*

| | |
|---|---|
| | TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed<br>CONFOUNDERS MEASURED: Tanner stage, spontaneous calcium intake, physical activity |
| Participants | N SCREENED: 75<br>N RANDOMISED: 72<br>N COMPLETED: 66 (8.5 months)<br>M=0%<br>F=100%<br>ETHNICITY: Asian 15%, 85% not stated<br>MEAN BASELINE AGE (yrs): 8.86<br>BASELINE AGE RANGE (yrs): 7-11<br>INCLUSION CRITERIA: girls aged 7-11<br>EXCLUSION CRITERIA: BMI> 4SD above the mean; > 10 hr/week of weight-bearing exercise<br>BASELINE CALCIUM INTAKE (mg/day): 674<br>PUBERTAL STAGE: mixed |
| Interventions | 1. Foods fortified by 2 g milk minerals (400 mg calcium/day)<br>2. Unsupplemented foods<br>CO-INTERVENTIONS: Moderate-impact (ground reaction forces 2-4 times body weight) vs low-impact exercise (ground reaction forces approximately equal to body weight) 20 min 3 times per week. |
| Outcomes | BONE MEASURES: SITES<br>BONE MINERAL CONTENT: total body, leg, femur, tibia/fibula, humerus, ulna/radius and lumbar spine.<br><br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 0.7<br>OTHER OUTCOMES MEASURED: body composition, weight, sitting and standing height, limb lengths<br>BONE MEASURES INCLUDED IN ANALYSES:<br>BONE MINERAL CONTENT: total body, leg, femur, tibia/fibula, humerus, ulna/radius and lumbar spine.<br><br>SUB-GROUPS IDENTIFIED: by exercise intervention |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Johnston 1992**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (Twin register), USA<br>DURATION OF SUPPLEMENTATION: 3 years<br>DURATION OF FOLLOW-UP: 6 years<br>QUALITY ASSESSMENT: Moderate risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes<br><br>TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed<br>CONFOUNDERS MEASURED: physical activity, Tanner stage, spontaneous calcium intake, smoking, alcohol consumption |

**Johnston 1992** *(Continued)*

| | |
|---|---|
| Participants | N SCREENED: 142<br>N RANDOMISED: 140<br>N COMPLETED: 90 (3 years); 84 (6 years)<br>M=39%<br>F=61%<br>ETHNICITY: CAUCASIAN<br>MEAN BASELINE AGE (yrs): 10<br>BASELINE AGE RANGE (yrs): 6-14<br>INCLUSION CRITERIA: healthy, Caucasian, monozygotic twins aged 6-14<br>EXCLUSION CRITERIA: baseline calcium intake > 1200 mg.<br>BASELINE CALCIUM INTAKE (mg/day): 919<br>PUBERTAL STAGE: mixed |
| Interventions | 1. 1000mg calcium daily as calcium citrate malate<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: distal radius, midshaft radius, femoral neck, Ward's triangle, greater trochanter and L2-4 vertebrae.<br>BONE MINERAL CONTENT: distal radius, midshaft radius, femoral neck, Ward's triangle, greater trochanter and L2-4 vertebrae.<br>BONE AREA: distal radius, midshaft radius, femoral neck, Ward's triangle, greater trochanter and L2-4 vertebrae.<br>METHOD OF MEASUREMENT: SPA for radius, DXA for other sites<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 0.5, 1,2 and 3 for radius, 0 and 3 for other sites<br>OTHER OUTCOMES MEASURED: weight, height, urinary calcium and creatinine, serum osteocalcin, tartrate resistant acid phosphatase and dietary calcium absorption by calcium-44 enrichment.<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: distal radius, midshaft radius, femoral neck, Ward's triangle, greater trochanter and L2-4 vertebrae.<br>BONE MINERAL CONTENT: distal radius, midshaft radius, femoral neck, Ward's triangle, greater trochanter and L2-4 vertebrae.<br>BONE AREA: distal radius, midshaft radius, femoral neck, Ward's triangle, greater trochanter and L2-4 vertebrae.<br><br>SUB-GROUPS IDENTIFIED: Prepubertal vs peri/post-pubertal |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Lee 1994**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (school), China<br>DURATION OF SUPPLEMENTATION: 1.5 years<br>DURATION OF FOLLOW-UP: 2.5 years<br>QUALITY ASSESSMENT: Moderate risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes |

**Lee 1994** *(Continued)*

| | |
|---|---|
| | TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed<br>CONFOUNDERS MEASURED: physical activity, spontaneous calcium intake, baseline serum vitamin D (n=18), |
| Participants | N SCREENED: unknown<br>N RANDOMISED: 163<br>N COMPLETED: 162 (1.5 years); 159 (2.5 years)<br>M=54%<br>F=46%<br>ETHNICITY: Chinese<br>MEAN BASELINE AGE (yrs): 7.18<br>BASELINE AGE RANGE (yrs): 7 year olds only<br>INCLUSION CRITERIA:7 year old, healthy, low (< 300 mg/day) habitual calcium intake<br>EXCLUSION CRITERIA: recent fracture or metabolic disease known to affect bone mass<br>BASELINE CALCIUM INTAKE (mg/day): 277<br>PUBERTAL STAGE: |
| Interventions | 1. 300 mg/day calcium as calcium carbonate<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: midshaft radius<br>BONE MINERAL CONTENT: midshaft radius<br>BONE WIDTH : midshaft radius<br>METHOD OF MEASUREMENT: SPA<br>FOLLOW-UP ASSESSMENT POINTS: 0, 6-monthly until 2.5 years<br>OTHER OUTCOMES MEASURED: weight, height<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: midshaft radius<br>BONE MINERAL CONTENT: midshaft radius<br>BONE WIDTH : midshaft radius<br><br>SUB-GROUPS IDENTIFIED: Males and females |
| Notes | Randomised by school class. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Lee 1995**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (Well-baby clinic), hong Kong<br>DURATION OF SUPPLEMENTATION: 1.5 years<br>DURATION OF FOLLOW-UP: 3 years<br>QUALITY ASSESSMENT: Moderate risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes<br><br>TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed |

**Lee 1995** *(Continued)*

| | |
|---|---|
| | CONFOUNDERS MEASURED: physical activity, serum vitamin D (n=20), spontaneous calcium intake, dietary protein and energy intake, Tanner stage (at end of follow-up only). |
| Participants | N SCREENED: unknown<br>N RANDOMISED: 109<br>N COMPLETED: 84 (1.5 years); 84 (3 years)<br>M=57%<br>F=43%<br>ETHNICITY: Chinese<br>MEAN BASELINE AGE (yrs): not given<br>BASELINE AGE RANGE (yrs): 7 year olds only<br>INCLUSION CRITERIA: 7-year olds, no recent metabolic disorder or fracture that might directly or indirectly affect bone metabolism, normal growth since birth.<br>EXCLUSION CRITERIA: see above<br>BASELINE CALCIUM INTAKE (mg/day): 567<br>PUBERTAL STAGE: assume prepubertal (age=7) |
| Interventions | 1. Calcium 300mg/day as calcium carbonate<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: distal radius, femoral neck and L2-4 vertebrae.<br>BONE MINERAL CONTENT: distal radius, femoral neck and L2-4 vertebrae.<br>BONE AREA: distal radius, femoral neck and L2-4 vertebrae.<br>METHOD OF MEASUREMENT: SPA radius, DXA other sites<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 6-montly until 3 years<br>OTHER OUTCOMES MEASURED: weight, height<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: distal radius, femoral neck and L2-4 vertebrae.<br>BONE MINERAL CONTENT: distal radius, femoral neck and L2-4 vertebrae.<br>BONE AREA: distal radius, femoral neck and L2-4 vertebrae<br><br>SUB-GROUPS IDENTIFIED: Nil |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Lloyd 1993**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (schools), USA<br>DURATION OF SUPPLEMENTATION: 2 years<br>DURATION OF FOLLOW-UP: 2 years<br>QUALITY ASSESSMENT: Moderate risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes<br><br>TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed |

**Lloyd 1993** *(Continued)*

| | |
|---|---|
| | CONFOUNDERS MEASURED: Tanner stage, Integrated Estrogen Exposure Score, spontaneous calcium intake, Urinary estradiol, testosterone, cortisol, luteinizing hormone and follicle-stimulating hormone . |
| Participants | N SCREENED: unknown<br>N RANDOMISED: 112<br>N COMPLETED: 94 (1.5 years); 91 (2 years)<br>M=0%<br>F=100%<br>ETHNICITY: CAUCASIAN<br>MEAN BASELINE AGE (yrs): 11.9<br>BASELINE AGE RANGE (yrs): unknown<br>INCLUSION CRITERIA: white female descendants of Northern Europeans, premenarcheal<br>EXCLUSION CRITERIA: Not between 80-120% of ideal body weight for height; regular medication; medical history known to affect bone development; known eating disorder.<br>BASELINE CALCIUM INTAKE (mg/day): 976<br>PUBERTAL STAGE: mixed |
| Interventions | 1. 500 mg/day calcium as calcium citrate malate<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: Total body, pelvis and lumbar spine.<br>BONE MINERAL CONTENT: Total body, pelvis and lumbar spine.<br>BONE AREA: Total body, pelvis and lumbar spine.<br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 6-monthly to 2 years<br>OTHER OUTCOMES MEASURED: weight, height, urinary calcium & creatinine<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: Total body, pelvis and lumbar spine.<br>BONE MINERAL CONTENT: Total body, pelvis and lumbar spine.<br>BONE AREA: Total body, pelvis and lumbar spine.<br><br>SUB-GROUPS IDENTIFIED: Above and below median Tanner score and median dietary calcium intake |
| Notes | Randomisation stratified by BMI and baseline lumbar spine BMD |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Matkovic 2004**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (school), USA<br>DURATION OF SUPPLEMENTATION: 7 years<br>DURATION OF FOLLOW-UP: 7 years<br>QUALITY ASSESSMENT: High risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: No<br><br>TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed |

**Matkovic 2004** *(Continued)*

| | |
|---|---|
| | CONFOUNDERS MEASURED: physical activity; dietary calcium, protein, energy intake; 24 hour urinary sodium; skeletal age, urinary and fecal calcium, serum calcium, serum vitamin D. |
| Participants | N SCREENED: unknown<br>N RANDOMISED: 354<br>N COMPLETED: 220 (4 year); 179 (7 years)<br>M=0%<br>F=100%<br>ETHNICITY: white<br>MEAN BASELINE AGE (yrs): 10.8<br>BASELINE AGE RANGE (yrs): unknown<br>INCLUSION CRITERIA: white, normal physical and mental health, pubertal stage 2, calcium intake <1480 mg/day, female<br>EXCLUSION CRITERIA: history of metabolic bone, kidney, liver or celiac disease; use of oral corticosteroids, hormones, diuretics or antiseizure medications,; other current systemic, chronic disease; and the presence of clinically significant abnormal laboratory data on screening<br>BASELINE CALCIUM INTAKE (mg/day): 837<br>PUBERTAL STAGE: peripubertal (Tanner stage 2) |
| Interventions | 1. 1000 mg/day calcium as calcium citrate malate<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: distal radius, radius at 33% of the radius length, total body.<br>BONE AREA: distal radius, radius at 33% of the radius length, total body.<br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 1, 2, 4.5, 8.5<br>OTHER OUTCOMES MEASURED: metacarpal cortical index at 4 and 7 years, weight, height, body composition, serum osteocalcin and PTH and urinary N-telopeptides.<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: distal radius, radius at 33% of the radius length, total body.<br>BONE AREA: distal radius, radius at 33% of the radius length, total body.<br>SUB-GROUPS IDENTIFIED: nil |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Molgaard 2004**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Population-based, Denmark<br>DURATION OF SUPPLEMENTATION: 1 years<br>DURATION OF FOLLOW-UP: 2 years<br>QUALITY ASSESSMENT: Moderate risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes<br><br>TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed |

**Molgaard 2004** *(Continued)*

| | |
|---|---|
| | CONFOUNDERS MEASURED: pubertal status, spontaneous calcium intake, physical activity, serum vitamin D |
| Participants | N SCREENED: 241<br>N RANDOMISED: 113<br>N COMPLETED: 111 (1 year);<br>M=0%<br>F=100%<br>ETHNICITY: white<br>MEAN BASELINE AGE (yrs): 13.2<br>BASELINE AGE RANGE (yrs): 12-14<br>INCLUSION CRITERIA: 12 years old +/- 6 months, girls<br>EXCLUSION CRITERIA: nonwhite ethnic origin, abnormal weight for height (< 3rd, > 97th percentile), diseases or intake of drugs with a potential effect on bones. Two groups recruited by calcium intake (high between 40th and 60th percentile = 1000-1304 mg/day by FFQ; low < 20th percentile, < 713 mg/day)<br>BASELINE CALCIUM INTAKE (mg/day): 841<br>PUBERTAL STAGE: mixed |
| Interventions | 1. 500 mg/day of calcium as calcium carbonate<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: total body.<br>BONE MINERAL CONTENT: total body.<br>BONE AREA: total body.<br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 1<br>OTHER OUTCOMES MEASURED: weight, height, serum alkaline phosphatase<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: total body.<br>BONE MINERAL CONTENT: total body.<br>BONE AREA: total body.<br><br>SUB-GROUPS IDENTIFIED: Spontaneous calcium intake (defined as high between 40th and 60th percentile = 1000-1304 mg/day by FFQ; low < 20th percentile, < 713 mg/day) |
| Notes | Study also gives results as size-adjusted BMC ie BMC adjusted for bone area, weight and height.<br>In second year of follow-up, all participants were given supplements and no results are reported from the second year. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Nowson 1997**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (Twin register), Australia<br>DURATION OF SUPPLEMENTATION: 1.5 years<br>DURATION OF FOLLOW-UP: 1.5 years<br>QUALITY ASSESSMENT: Moderate risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Not described or unclear |

**Nowson 1997** *(Continued)*

| | |
|---|---|
| | BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes<br><br>TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed<br>CONFOUNDERS MEASURED: physical activity, pre vs post menarcheal, spontaneous calcium intake |
| Participants | N SCREENED: unknown<br>N RANDOMISED: 110<br>N COMPLETED: 56 (1.5 years);<br>M=0%<br>F=100%<br>ETHNICITY: not stated<br>MEAN BASELINE AGE (yrs): 14<br>BASELINE AGE RANGE (yrs): 10-17<br>INCLUSION CRITERIA: female twin pairs<br>EXCLUSION CRITERIA: none stated<br>BASELINE CALCIUM INTAKE (mg/day): 734<br>PUBERTAL STAGE: mixed |
| Interventions | 1. 1000 mg/day calcium as calcium carbonate/calcium lactate gluconate combination<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: forearm, femoral neck, Ward's triangle, total hip and L2-4 vertebrae.<br>BONE MINERAL CONTENT: total body<br><br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0 (all sites), 6-monthly to 1.5 (hip and spine)<br>OTHER OUTCOMES MEASURED: weight, height, fat mass, lean mass<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: forearm, femoral neck, Ward's triangle, total hip and L2-4 vertebrae.<br>BONE MINERAL CONTENT: total body<br>SUB-GROUPS IDENTIFIED: Pre vs post menarcheal |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Prentice 2005**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (college), UK<br>DURATION OF SUPPLEMENTATION: 1.06 years<br>DURATION OF FOLLOW-UP: 1.06 years<br>QUALITY ASSESSMENT: Moderate risk of bias<br>RANDOMISED: random and description consistent with this<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes<br><br>TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed |

**Prentice 2005** *(Continued)*

| | |
|---|---|
| | CONFOUNDERS MEASURED: physical activity, ethnic group, medical history, smoking and alcohol intake, consumption of dietary supplements and antacids, calcium intake, plasma testosterone concentration. |
| Participants | N SCREENED: unknown<br>N RANDOMISED: 150<br>N COMPLETED: 143 (1 year)<br>M=100%<br>F=0%<br>ETHNICITY: 90% white<br>MEAN BASELINE AGE (yrs): 16.8<br>BASELINE AGE RANGE (yrs): 16-18<br>INCLUSION CRITERIA: male sixth form students aged 16-18<br>EXCLUSION CRITERIA: any medical problem, history of eating disorders, medication known to affect bone metabolism<br>BASELINE CALCIUM INTAKE (mg/day): 1198<br>PUBERTAL STAGE: post-pubertal (assumed from age) |
| Interventions | 1. 1000 mg/day calcium as calcium carbonate<br>2. Placebo<br>CO-INTERVENTIONS: Exercise in low physical activity group |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: left hip (total, femoral neck, greater trochanter, intertrochanter) and non-dominant forearm (total, ultradistal and 1/3 sites of radius).<br>BONE MINERAL CONTENT: total body, left hip (total, femoral neck, greater trochanter, intertrochanter) and non-dominant forearm (total, ultradistal and 1/3 sites of radius).<br>BONE AREA: left hip (total, femoral neck, greater trochanter, intertrochanter) and non-dominant forearm (total, ultradistal and 1/3 sites of radius).<br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 0.43, 1.06<br>OTHER OUTCOMES MEASURED: weight, height, fat mass, lean mass<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: left hip (total, femoral neck, greater trochanter, intertrochanter) and non-dominant forearm (total, ultradistal and 1/3 sites of radius).<br>BONE MINERAL CONTENT: total body, left hip (total, femoral neck, greater trochanter, intertrochanter) and non-dominant forearm (total, ultradistal and 1/3 sites of radius).<br>BONE AREA: left hip (total, femoral neck, greater trochanter, intertrochanter) and non-dominant forearm (total, ultradistal and 1/3 sites of radius).<br>SUB-GROUPS IDENTIFIED: High vs low physical activity; above and below median calcium intake |
| Notes | Study also gives results as size-adjusted BMC ie BMC adjusted for bone area, weight and height |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Rodda 2004**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (schools), Australia<br>DURATION OF SUPPLEMENTATION: 1-4 years<br>DURATION OF FOLLOW-UP: 4 years<br>QUALITY ASSESSMENT: Moderate risk of bias<br>RANDOMISED: States random but no description |

**Rodda 2004** *(Continued)*

| | |
|---|---|
| | ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: No<br><br>TYPE OF ANALYSIS: not stated<br>COMPLIANCE: not stated<br>CONFOUNDERS MEASURED: Pubertal status, no others stated |
| Participants | N SCREENED: unknown<br>N RANDOMISED: 93<br>N COMPLETED: unknown<br>M=0%<br>F=100%<br>ETHNICITY: Chinese 43%, anglocelt 57%<br>MEAN BASELINE AGE (yrs): not stated<br>BASELINE AGE RANGE (yrs): 10-12<br>INCLUSION CRITERIA: healthy girls<br>EXCLUSION CRITERIA: not stated<br>BASELINE CALCIUM INTAKE (mg/day): not stated<br>PUBERTAL STAGE: not stated |
| Interventions | 1. Calcium carbonate 1200 mg/day<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: total body and lumbar spine.<br>BONE MINERAL CONTENT: total body and lumbar spine<br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, yearly up to 4 years<br>OTHER OUTCOMES MEASURED: bone age, height, weight, sitting height, date of menarche, bone age<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: total body and lumbar spine.<br>BONE MINERAL CONTENT: total body and lumbar spine<br>SUB-GROUPS IDENTIFIED: Chinese vs Anglocelt ethnicity |
| Notes | Information about this study is limited as it has only been published as an abstract and no further information was available. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Rozen 2003**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (school), Israel<br>DURATION OF SUPPLEMENTATION: 1 years<br>DURATION OF FOLLOW-UP: 4.5 years<br>QUALITY ASSESSMENT: High risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: No<br><br>TYPE OF ANALYSIS: Available Data and treatment received |

**Rozen 2003** *(Continued)*

| | |
|---|---|
| | COMPLIANCE: Assessed<br>CONFOUNDERS MEASURED: spontaneous calcium intake, serum vitamin D |
| Participants | N SCREENED: unknown<br>N RANDOMISED: 112<br>N COMPLETED: 100 (1 year); 96 (4.5 years)<br>M=0%<br>F=100%<br>ETHNICITY: 76% Jewish, 24% arab<br>MEAN BASELINE AGE (yrs): 14.85<br>BASELINE AGE RANGE (yrs): 12-17<br>INCLUSION CRITERIA: girls, calcium intake < 800 mg; >= 1 year post menarcheal, age < 15.5, no chronic disease, nonsmoking and no use of contraceptives.<br>EXCLUSION CRITERIA: Pregnancy between cessation of supplementation and follow-up (for follow-up study)<br>BASELINE CALCIUM INTAKE (mg/day): 582<br>PUBERTAL STAGE: post pubertal |
| Interventions | 1. 1000 mg/day calcium as calcium carbonate<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: total body, lumbar spine (L2-4) and femoral neck<br>BONE MINERAL CONTENT: total body, lumbar spine (L2-4) and femoral neck<br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 0.5,1, 4.5<br>OTHER OUTCOMES MEASURED: weight, height, bone-specific alkaline phosphatase, urinary de-oxypyridinline cross-links, serum PTH and osteocalcin.<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: total body, lumbar spine (L2-4) and femoral neck<br>BONE MINERAL CONTENT: total body, lumbar spine (L2-4) and femoral neck<br>SUB-GROUPS IDENTIFIED: < 24 months post-menarche vs > 24 months post-menarche |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Specker 2003**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (child care centres), USA<br>DURATION OF SUPPLEMENTATION: 1 years<br>DURATION OF FOLLOW-UP: 1 years<br>QUALITY ASSESSMENT: Moderate risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: unclear<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: Yes<br><br>TYPE OF ANALYSIS: Available Data<br>COMPLIANCE: Assessed<br>CONFOUNDERS MEASURED: spontaneous calcium intake, physical activity by accelerometer |

**Specker 2003** *(Continued)*

| | |
|---|---|
| Participants | N SCREENED: unknown<br>N RANDOMISED: 239<br>N COMPLETED: 178 (1 year)<br>M= 53%<br>F= 47%<br>ETHNICITY: white 94%, other 6%<br>MEAN BASELINE AGE (yrs): 3.92<br>BASELINE AGE RANGE (yrs): 3-5<br>INCLUSION CRITERIA: enrolled in child care centre, no known disorders that affected bone metabolism<br>EXCLUSION CRITERIA: see inclusion criteria<br>BASELINE CALCIUM INTAKE (mg/day): 946<br>PUBERTAL STAGE: prepubertal |
| Interventions | 1. 1000 mg/day calcium as calcium carbonate<br>2. Placebo<br>CO-INTERVENTIONS: Gross motor vs fine motor exercise 30 min per day 5 days per week |
| Outcomes | BONE MEASURES: SITES<br>BONE MINERAL CONTENT: total body, arm, leg<br>BONE AREA: total body, arm, leg<br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 1<br>OTHER OUTCOMES MEASURED: weight, height, fat mass, lean mass, distal tibial periosteal and endosteal circumferences, cortical thickness and cortical area.<br>BONE MEASURES INCLUDED IN ANALYSES:<br>BONE MINERAL CONTENT: total body, arm, leg<br>BONE AREA: total body, arm, leg<br><br>SUB-GROUPS IDENTIFIED: By exercise intervention |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

**Stear 2003**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (college), UK<br>DURATION OF SUPPLEMENTATION: 15.5 months<br>DURATION OF FOLLOW-UP: 15.5 months<br>QUALITY ASSESSMENT: High risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Yes<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: No<br><br>TYPE OF ANALYSIS: Available Data and treatment received<br>COMPLIANCE: Assessed<br>CONFOUNDERS MEASURED: spontaneous calcium intake and physical activity |
| Participants | N SCREENED: unknown<br>N RANDOMISED: 144 |

**Stear 2003** *(Continued)*

| | |
|---|---|
| | N COMPLETED: 131 (15.5 months)<br>M=0%<br>F=100%<br>ETHNICITY: not stated<br>MEAN BASELINE AGE (yrs): 17.3<br>BASELINE AGE RANGE (yrs): 16-18<br>INCLUSION CRITERIA: female sixth form college students<br>EXCLUSION CRITERIA: any medical problem, history of eating disorders, medication known to interfere with bone metabolism<br>BASELINE CALCIUM INTAKE (mg/day): 938<br>PUBERTAL STAGE: post pubertal |
| Interventions | 1. 1000 mg/day of calcium as calcium carbonate<br>2. Placebo<br>CO-INTERVENTIONS: exercise (45 min 3 times per week aerobics with moderate to high impact movements) and no exercise groups |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: unpublished data femoral neck, lumbar spine, distal radius.<br>BONE MINERAL CONTENT: total body, spine, radius (total, ultradistal, distal third), hip (total, femoral neck, trochanter, intertrochanter), lumbar spine<br>BONE AREA: total body, spine, radius (total, ultradistal, distal third), hip (total, femoral neck, trochanter, intertrochanter), lumbar spine<br>METHOD OF MEASUREMENT: DXA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 1.29<br>OTHER OUTCOMES MEASURED: weight, height,<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: unpublished data femoral neck, lumbar spine, distal radius.<br>BONE MINERAL CONTENT: total body, spine, radius (total, ultradistal, distal third), hip (total, femoral neck, trochanter, intertrochanter), lumbar spine<br>BONE AREA: total body, spine, radius (total, ultradistal, distal third), hip (total, femoral neck, trochanter, intertrochanter), lumbar spine<br><br>SUB-GROUPS IDENTIFIED: Exercise groups; high compliance groups for calcium and exercise |
| Notes | Compliance to exercise was poor; only 27% of subjects attended more than 50% of the intervention target.<br>Study also gives results as size-adjusted BMC ie BMC adjusted for bone area, weight and height |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Low risk | A - Adequate |

**Wang 1996**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION AND SETTING: Community (school), China<br>DURATION OF SUPPLEMENTATION: 1.5 years<br>DURATION OF FOLLOW-UP: 1.5 years<br>QUALITY ASSESSMENT: High risk of bias<br>RANDOMISED: States random but no description<br>ALLOCATION CONCEALMENT: Not described or unclear<br>BLINDING OF SUBJECT: Yes<br>DESCRIPTION OF WITHDRAWALS/DROPOUTS: No<br><br>TYPE OF ANALYSIS: Available Data |

**Wang 1996** *(Continued)*

| | |
|---|---|
| | COMPLIANCE: Not reported<br>CONFOUNDERS MEASURED: serum vitamin D, physical activity, spontaneous calcium intake |
| Participants | N SCREENED: unknown<br>N RANDOMISED: 163<br>N COMPLETED: 162 (1.5 years)<br>M=54%<br>F=46%<br>ETHNICITY: Chinese<br>MEAN BASELINE AGE (yrs): 7.2<br>BASELINE AGE RANGE (yrs): not stated<br>INCLUSION CRITERIA: healthy, no metabolic disease or recent medication related to bone metabolism<br>EXCLUSION CRITERIA: see inclusion criteria<br>BASELINE CALCIUM INTAKE (mg/day): 277<br>PUBERTAL STAGE: prepubertal (assumed from age) |
| Interventions | 1. 300 mg/day calcium as calcium carbonate<br>2. Placebo<br>CO-INTERVENTIONS: Nil |
| Outcomes | BONE MEASURES: SITES<br>AREAL BONE MINERAL DENSITY: distal radius.<br>BONE MINERAL CONTENT: distal radius.<br>BONE WIDTH: distal radius .<br>METHOD OF MEASUREMENT: SPA<br>FOLLOW-UP ASSESSMENT POINTS(yrs): 0, 1, 2, 4.5, 8.5<br>OTHER OUTCOMES MEASURED: weight, height<br>BONE MEASURES INCLUDED IN ANALYSES:<br>AREAL BONE MINERAL DENSITY: distal radius.<br>BONE MINERAL CONTENT: distal radius.<br>BONE WIDTH: distal radius .<br><br>SUB-GROUPS IDENTIFIED: nil |
| Notes | Chinese language paper. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Allocation concealment? | Unclear risk | B - Unclear |

## Characteristics of excluded studies *[ordered by study ID]*

| Study | Reason for exclusion |
|---|---|
| Abrams 2001 | Not a randomised controlled trial |
| Adiyaman 2004 | Not a randomised controlled trial |
| Albertson 1997 | Not a randomised controlled trial |
| Ali 2001 | Not a randomised controlled trial |
| Anderson 2001 | Not a randomised controlled trial |

| Study | Reason for exclusion |
|---|---|
| Andon 1994 | Not a randomised controlled trial |
| Anonymous 1992 | Not a randomised controlled trial |
| Anonymous 1993a | Not a randomised controlled trial |
| Anonymous 1993b | Not a randomised controlled trial |
| Anonymous 1994 | Not a randomised controlled trial |
| Anonymous 1997a | Not a randomised controlled trial |
| Anonymous 1997b | Not a randomised controlled trial |
| Anonymous 1998 | Not a randomised controlled trial |
| Anonymous 2000 | Not a randomised controlled trial |
| Anonymous 2004 | Not a randomised controlled trial |
| Antoniazzi 2003 | Condition predisposing to osteoporosis (participants undergoing treatment with gonadotrophin-releasing hormone agonist treatment) |
| Antoniazzi 1999 | Condition predisposing to osteoporosis (participants undergoing treatment with gonadotrophin-releasing hormone agonist treatment) |
| Appleby 1998 | Not a randomised controlled trial |
| Ausenhus 1988 | Not a randomised controlled trial |
| Badenhop 2004 | Not a randomised controlled trial |
| Barker 1998 | No placebo used |
| Barr 1998 | Not a randomised controlled trial |
| Barr 2001 | Not a randomised controlled trial |
| Bateson 2002 | Not a randomised controlled trial |
| Berthier 1994 | Not a randomised controlled trial |
| Black 2002 | Not a randomised controlled trial |
| Blalock 2002 | No calcium intervention |
| Bonjour 1999 | Not a randomised controlled trial |
| Bonofiglio 2004 | Not a randomised controlled trial |
| Boot 1997 | Not a randomised controlled trial |
| Bourges | Not a randomised controlled trial |
| Brown 2004 | No calcium intervention |

| Study | Reason for exclusion |
|---|---|
| Burckhardt 2001 | Not a randomised controlled trial |
| Cadogan 1997 | No placebo used |
| Carter 2001 | Not a randomised controlled trial |
| Chan 1987 | Trial in lactating adolscents ie condition predisposing to bone loss |
| Chan 1991 | Not a randomised controlled trial |
| Chan 1995 | No placebo used |
| Cheng 1999 | Not a randomised controlled trial |
| Chevalley 2004 | Not a randomised controlled trial |
| Clements 1991 | Not a randomised controlled trial |
| DeBar 2004 | No calcium intervention |
| DiMeglio 2005 | No calcium intervention |
| Dowd 2001 | Not a randomised controlled trial |
| Du 2002 | Not a randomised controlled trial |
| Du 2004 | No placebo used |
| Edwards 1998 | Not a randomised controlled trial |
| El-Husseini 2004 | Condition presiposing to osteoporosis (renal transplantion) |
| Elgan 2002 | Not a randomised controlled trial |
| Feskanich 1997 | Not a randomised controlled trial |
| Fischer 1999a | No placebo |
| Fischer 1999b | Duplicate paper to Fischer 1999a |
| Fisher 2004 | Not a randomised controlled trial |
| Fujita 1992 | Not a randomised controlled trial |
| Gharib 2004 | Not a randomised controlled trial |
| Gibbons 2004 | Active placebo used (400 mg calcium) |
| Ginty 2004 | Not a randomised controlled trial |
| Goulding 2004 | Not a randomised controlled trial |
| Griffiths 1998 | Not a randomised controlled trial |
| Grossklaus 1998 | Not a randomised controlled trial |

| Study | Reason for exclusion |
|---|---|
| Gulati 2005 | Not a randomised controlled trial |
| Hampton 2004 | Not a randomised controlled trial |
| Harel 1998 | Not a randomised controlled trial |
| Henderson 1994 | Not a randomised controlled trial |
| Hidvegi 2003 | Not a randomised controlled trial |
| Homik 2005 | Not a randomised controlled trial |
| Hoppe 2000 | Not a randomised controlled trial |
| Hosokawa 1996 | Not a randomised controlled trial |
| Howat 2001 | Not a randomised controlled trial |
| Iki 2003 | Not a randomised controlled trial |
| Ilich 1996 | Not a randomised controlled trial |
| Infante 2000 | Not a randomised controlled trial |
| Kalkwarf 1997 | Adult participants and participants lactating |
| Kalkwarf 2003 | Not a randomised controlled trial |
| Kalusk 2001 | Not a randomised controlled trial |
| Kanis 1994 | Not a randomised controlled trial |
| Kardinaal 1999 | Not a randomised controlled trial |
| Kasper 2001 | Not a randomised controlled trial |
| Kerstetter 1995 | Not a randomised controlled trial |
| Koenig 2000 | Not a randomised controlled trial |
| Kowalski 2004 | Not a randomised controlled trial |
| Kreipe 1995 | Not a randomised controlled trial |
| Kubota 2003 | Not a randomised controlled trial |
| Kun 2001 | Not a randomised controlled trial |
| Lappe 2004 | No bone outcome measures (trial of calcium effect on wieght gain) |
| LaRosa 2004 | Not a randomised controlled trial |
| Lau 1992 | No placebo and no randomisation |
| Lau 2004 | No placebo used |

| Study | Reason for exclusion |
|---|---|
| Lee 1993 | Not a randomised controlled trial |
| Lee 2003 | Not a randomised controlled trial |
| Levers-Landis 2003 | Not a randomised controlled trial |
| Li 2002 | No placebo used |
| Lloyd 2000 | Not a randomised controlled trial |
| Lloyd 2002 | Not a randomised controlled trial |
| Lysen 1997 | Not a randomised controlled trial |
| Ma 2004 | Not a randomised controlled trial |
| Mackelvie 2001 | Not a randomised controlled trial |
| Magee 1996 | No placebo used |
| Maggiolini 1999 | Not a randomised controlled trial |
| Mahana 1988 | Not a randomised controlled trial |
| Mallet 2000 | Not a randomised controlled trial |
| Mallet 2003 | Not a randomised controlled trial |
| Marrero 2004 | Not a randomised controlled trial |
| Martin 2004 | Not a randomised controlled trial |
| Matkovic 1990 | Inadequate randomisation |
| Matkovic 2002 | Not a randomised controlled trial |
| McCulloch 1990 | Not a randomised controlled trial |
| Meier 2004 | Participants were adults. |
| Merrilees 2000 | No placebo used |
| Meschino 2004 | Not a randomised controlled trial |
| Moelgaard 2001 | Not a randomised controlled trial |
| Monge 2001 | Not a randomised controlled trial |
| Moya 1997 | Not a randomised controlled trial |
| Moyer-Mileur 2003 | Intervention combined vitamin D and calcium with no capacity to seperate calcium effect. |
| Naunton 2004 | Not a randomised controlled trial |
| Neville 2002 | Not a randomised controlled trial |

| Study | Reason for exclusion |
|---|---|
| New 1998 | Not a randomised controlled trial |
| NIH 2001 | Not a randomised controlled trial |
| Novotny 2004 | Not a randomised controlled trial |
| Nowson 1995 | Duplicate data (conference abstract) |
| O' Brien 1998 | Not a randomised controlled trial |
| Oellingrath 1989 | Not a randomised controlled trial |
| Ohgitani 1997 | No BMD or BMC outcomes |
| Oria 2003 | Not a randomised controlled trial |
| Parr 2002 | Not a randomised controlled trial |
| Pena 2004 | Not a randomised controlled trial |
| Peterson 2000 | No calcium intervention |
| Piaseu 2002 | No calcium intervention |
| Picard 1988 | Not a randomised controlled trial |
| Portsmouth 1994 | Not a randomised controlled trial |
| Prestridge 1993 | Condition predisposing to osteoporosis (very low birth weight infants) |
| Prynne 2004 | Not a randomised controlled trial |
| Purdie 1994 | Not a randomised controlled trial |
| Recker 1993 | Not a randomised controlled trial |
| Reid 1998 | Not a randomised controlled trial |
| Remer 2002 | Not a randomised controlled trial |
| Renner 1991a | Not a randomised controlled trial |
| Renner 1991b | Not a randomised controlled trial |
| Renner 1994 | Not a randomised controlled trial |
| Renner 1998 | No placebo or randomisation |
| Roberts 2000 | Not a randomised controlled trial |
| Robertson 2005 | Not a randomised controlled study |
| Roux 1995 | Not a randomised controlled trial |
| Rozen 2001 | Not a randomised controlled trial |

| Study | Reason for exclusion |
|---|---|
| Ruiz 1995 | Not a randomised controlled trial |
| Runyan 2003 | Not a randomised controlled trial |
| Sagara 2002 | Not a randomised controlled trial |
| Saggese | Not a randomised controlled trial |
| Sakkers 2004 | No calcium intervention |
| Scholz 1993 | Not a randomised controlled trial |
| Schonau 2004 | Not a randomised controlled trial |
| Smart 1994 | Not a randomised controlled trial |
| Solomons 1996 | No a randomised controlled study |
| Soroko 1994 | Not a randomised controlled trial |
| Specker 1997 | No placebo |
| Specker 1999 | No calcium intervention |
| Specker 2002 | Duplicate data (conference abstract) |
| Stallings 1994 | Not a randomised controlled trial |
| Szumera 2004 | Not a randomised controlled trial |
| Taha 2001 | Not a randomised controlled trial |
| Teegarden 1994 | Not a randomised controlled trial |
| Teegarden 1999 | Not a randomised controlled trial |
| Teesalu 1996 | Not a randomised controlled trial |
| ter Meulen 2004 | Condition predisposing to osteoporosis (renal transplantation) |
| Torres 2004 | Condition predisposing to osteoporosis (renal transplanation) |
| Tortolani 2002 | Not a randomised controlled trial |
| Tounian 2003 | Not a randomised controlled trial |
| Tsukahara 1997 | Not a randomised controlled trial |
| Tucker 2003 | Not a randomised controlled trial |
| Turner 1992 | Not a randomised controlled trial |
| Turner 2000 | Not a randomised controlled trial |
| Tussing 2005 | Not a randomised controlled trial |

| Study | Reason for exclusion |
|---|---|
| Tylavsky 1992 | Not a randomised controlled trial |
| Ulrich 1996 | Not a randomised controlled trial |
| Valerio 2004 | Not a randomised controlled trial |
| VandenBergh 1995 | Not a randomised controlled trial |
| Vigano 2004 | Not a randomised controlled trial |
| Volek 2003 | Outcomes measured at less than 6 months from baseline |
| Wallace 2002 | Not a randomised controlled trial |
| Wang 1999 | Not a randomised controlled trial |
| Wang 2003 | Not a randomised controlled trial |
| Wastney 2003 | Not a randomised controlled trial |
| Weaver 1999 | Not a randomised controlled trial |
| Welten 1995 | Not a randomised controlled trial |
| Welten 1997 | Not a randomised controlled trial |
| Whiting 2001 | Not a randomised controlled trial |
| Whiting 2004 | Not a randomised controlled trial |
| Winters-Stone 2004 | Participants aged > 18 years |
| Yeste 2004 | Not a randomised controlled trial |
| Zacharin 2004 | Not a randomised controlled trial |
| Zanchetta 1995 | Not a randomised controlled trial |
| Zhang 2003 | No placebo used |
| Zhu 2003 | No placebo used |
| Zhu 2004 | No placebo used |
| Zhu 2004 b | Not a randomised controlled trial |
| Ziccardi 2004 | Not a randomised controlled trial |
| Zwart 2004 | No calcium intervention |
| Zwiauer 2003 | Not a randomised controlled trial |

## DATA AND ANALYSES

### Comparison 1. Calcium supplementation vs placebo

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Femoral neck BMD (mg/cm2) at end supplementation (all data) | 10 | 1073 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.07 [-0.05, 0.19] |
| 2 Femoral Neck BMD (mg/cm2) at longest point after cessation of supplement (all data) | 5 | 617 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.10 [-0.06, 0.26] |
| 3 Lumbar spine BMD (mg/cm2) at end supplementation (all data) | 11 | 1164 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.04, 0.20] |
| 4 Lumbar Spine BMD (mg/cm2) at longest point after cessation of supplement (all data) | 5 | 617 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.01 [-0.15, 0.17] |
| 5 Total Body BMC (mg) at end supplementation (all data) | 9 | 953 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.01, 0.27] |
| 6 Distal Radius BMD (mg/cm2) at end supplementation (all data) | 9 | 1140 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [0.04, 0.27] |
| 7 Distal Radius BMD (mg/cm2) at longest point after cessation of supplement | 4 | 455 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.21 [0.03, 0.40] |
| 8 Upper Limb BMD (mg/cm2) at end supplementation (all data) | 12 | 1579 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.04, 0.24] |
| 9 Upper Limb BMD (mg/cm2) at longest point after cessation of supplement (all data) | 6 | 840 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.01, 0.28] |
| 10 Femoral neck BMD (mg/cm2) (end trial) by baseline calcium intake | 10 | 1073 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.07 [-0.05, 0.19] |
| 10.1 Low baseline calcium | 5 | 516 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.02 [-0.19, 0.16] |
| 10.2 High baseline calcium | 5 | 557 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [-0.02, 0.32] |
| 11 Lumbar spine BMD (mg/cm2) (end trial) by baseline calcium intake | 11 | 1164 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.04, 0.20] |
| 11.1 Low baseline calcium | 5 | 516 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.03 [-0.14, 0.21] |
| 11.2 High baseline calcium | 6 | 648 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.12 [-0.04, 0.28] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 12 Total Body BMC (mg) (end trial) by baseline calcium intake | 9 | 953 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.01, 0.27] |
| 12.1 Low baseline calcium | 4 | 265 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.11 [-0.13, 0.35] |
| 12.2 High baseline calcium | 6 | 688 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [0.00, 0.31] |
| 13 Distal radius BMD (mg/cm2) (end trial) by baseline calcium intake | 9 | 1140 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [0.04, 0.27] |
| 13.1 Low baseline calcium | 3 | 406 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.26 [0.06, 0.45] |
| 13.2 High baseline calcium | 6 | 734 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.10 [-0.05, 0.24] |
| 14 Upper limb BMD (mg/cm2) (end trial) by baseline calcium intake | 12 | 1579 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.04, 0.24] |
| 14.1 Low baseline calcium | 6 | 845 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.17 [0.04, 0.31] |
| 14.2 High baseline calcium | 6 | 734 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.10 [-0.05, 0.24] |
| 15 Femoral neck BMD (mg/cm2) at longest point after supplement ceased by baseline calcium intake | 5 | 617 | Std. Mean Difference (IV, Random, 95% CI) | 0.11 [-0.07, 0.29] |
| 15.1 Low baseline calcium | 3 | 406 | Std. Mean Difference (IV, Random, 95% CI) | 0.02 [-0.18, 0.21] |
| 15.2 High baseline calcium | 2 | 211 | Std. Mean Difference (IV, Random, 95% CI) | 0.24 [-0.17, 0.66] |
| 16 Lumbar spine BMD (mg/cm2) at longest point after supplement ceased by baseline calcium intake | 5 | 617 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.01 [-0.15, 0.17] |
| 16.1 Low baseline calcium | 3 | 406 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.02 [-0.21, 0.18] |
| 16.2 High baseline calcium | 2 | 211 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.06 [-0.21, 0.33] |
| 17 Distal radius BMD (mg/cm2) at longest point after supplement ceased by baseline calcium intake | 4 | 455 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.21 [0.03, 0.40] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 17.1 Low baseline calcium | 2 | 244 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.19 [-0.06, 0.44] |
| 17.2 High baseline calcium | 2 | 211 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.24 [-0.03, 0.51] |
| 18 Upper limb BMD (mg/cm2) at longest point after supplement ceased by baseline calcium intake | 6 | 840 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.19 [0.05, 0.32] |
| 18.1 Low baseline calcium | 4 | 629 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.17 [0.01, 0.32] |
| 18.2 High baseline calcium | 2 | 211 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.24 [-0.03, 0.51] |
| 19 Femoral neck BMD (mg/cm2) (at end supplementation) by sex | 10 | 1073 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.07 [-0.05, 0.19] |
| 19.1 Male | 2 | 375 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.05 [-0.26, 0.15] |
| 19.2 Female | 6 | 524 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.19 [0.02, 0.37] |
| 19.3 Mixed | 2 | 174 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.03 [-0.32, 0.27] |
| 20 Lumbar spine BMD (mg/cm2) (at end supplementation) by sex | 11 | 1164 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.04, 0.20] |
| 20.1 Male | 2 | 375 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.06 [-0.14, 0.26] |
| 20.2 Female | 7 | 615 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.11 [-0.05, 0.27] |
| 20.3 Mixed | 2 | 174 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.03 [-0.27, 0.33] |
| 21 Total Body BMC (mg) (at end supplementation) by sex | 9 | 953 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.01, 0.27] |
| 21.1 Male | 1 | 143 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.06 [-0.27, 0.39] |
| 21.2 Female | 7 | 632 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.18 [0.03, 0.34] |
| 21.3 Mixed | 1 | 178 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.05 [-0.25, 0.34] |
| 22 Distal Radius BMD (mg/cm2) (at end supplementation) by sex | 9 | 1140 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [0.04, 0.27] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 22.1 Male | 1 | 143 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.05 [-0.38, 0.27] |
| 22.2 Female | 4 | 501 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [-0.04, 0.32] |
| 22.3 Mixed | 4 | 496 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.22 [0.05, 0.40] |
| 23 Upper Limb BMD (mg/cm2) (at end supplementation) by sex | 12 | 1579 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.04, 0.24] |
| 23.1 Male | 3 | 459 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.03 [-0.15, 0.21] |
| 23.2 Female | 6 | 624 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [-0.01, 0.31] |
| 23.3 Mixed | 4 | 496 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.22 [0.05, 0.40] |
| 24 Femoral neck BMD (mg/cm2) at longest point after supplement ceased by sex | 5 | 617 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.10 [-0.06, 0.26] |
| 24.1 Male | 1 | 226 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.03 [-0.29, 0.23] |
| 24.2 Female | 2 | 221 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.31 [0.04, 0.58] |
| 24.3 Mixed | 2 | 170 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.01 [-0.29, 0.31] |
| 25 Lumbar spine BMD (mg/cm2) at longest point after supplement ceased by sex | 5 | 617 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.01 [-0.15, 0.17] |
| 25.1 Male | 1 | 226 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.05 [-0.22, 0.31] |
| 25.2 Female | 2 | 221 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.04 [-0.22, 0.31] |
| 25.3 Mixed | 2 | 170 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.07 [-0.38, 0.23] |
| 26 Upper limb BMD (mg/cm2) at longest point after supplement ceased by sex | 6 | 840 | Std. Mean Difference (IV, Random, 95% CI) | 0.19 [0.05, 0.32] |
| 26.1 Male | 2 | 310 | Std. Mean Difference (IV, Random, 95% CI) | 0.08 [-0.32, 0.49] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 26.2 Female | 2 | 200 | Std. Mean Difference (IV, Random, 95% CI) | 0.30 [0.02, 0.58] |
| 26.3 Mixed | 3 | 330 | Std. Mean Difference (IV, Random, 95% CI) | 0.16 [-0.06, 0.37] |
| 27 Femoral neck BMD (mg/cm2) (at end supplementation) by pubertal status | 9 | 977 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.07 [-0.06, 0.19] |
| 27.1 Pre-pubertal | 5 | 557 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.07 [-0.10, 0.24] |
| 27.2 Peri-pubertal | 0 | 0 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.0 [0.0, 0.0] |
| 27.3 Post-pubertal | 2 | 274 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.10 [-0.14, 0.34] |
| 27.4 Mixed | 2 | 146 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.00 [-0.32, 0.33] |
| 28 Lumbar spine BMD (mg/cm2) (at end supplementation) by pubertal status | 10 | 1068 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.09 [-0.03, 0.21] |
| 28.1 Pre-pubertal | 5 | 557 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.06 [-0.10, 0.23] |
| 28.2 Peri-pubertal | 0 | 0 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.0 [0.0, 0.0] |
| 28.3 Post-pubertal | 2 | 274 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.11 [-0.12, 0.35] |
| 28.4 Mixed | 3 | 237 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.11 [-0.14, 0.37] |
| 29 Total body BMC (mg) (at end supplementation) by pubertal status | 8 | 853 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.16 [0.02, 0.29] |
| 29.1 Pre-pubertal | 3 | 311 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.18 [-0.05, 0.41] |
| 29.2 Peri-pubertal | 0 | 0 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.0 [0.0, 0.0] |
| 29.3 Post-pubertal | 2 | 274 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [-0.10, 0.37] |
| 29.4 Mixed | 3 | 268 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [-0.09, 0.39] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 30 Distal radius BMD (mg/cm2) (at end supplementation) by pubertal status | 9 | 1140 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [0.04, 0.27] |
| 30.1 Pre-pubertal | 4 | 439 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.11, 0.27] |
| 30.2 Peri-pubertal | 1 | 177 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.23 [-0.06, 0.53] |
| 30.3 Post-pubertal | 2 | 274 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.16, 0.31] |
| 30.4 Mixed | 2 | 250 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.31 [0.06, 0.56] |
| 31 Upper limb BMD (mg/cm2) (at end supplementation) by pubertal status | 12 | 1579 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.04, 0.24] |
| 31.1 Pre-pubertal | 7 | 878 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.09 [-0.05, 0.22] |
| 31.2 Peri-pubertal | 1 | 177 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.23 [-0.06, 0.53] |
| 31.3 Post-pubertal | 2 | 274 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.16, 0.31] |
| 31.4 Mixed | 2 | 250 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.31 [0.06, 0.56] |
| 32 Femoral neck BMD (mg/cm2) (at end supplementation) by ethnicity | 7 | 838 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.05 [-0.09, 0.19] |
| 32.1 Caucasian | 5 | 658 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.05 [-0.10, 0.21] |
| 32.2 Chinese | 1 | 84 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.01 [-0.44, 0.41] |
| 32.3 Other | 1 | 96 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.09 [-0.31, 0.49] |
| 33 Lumbar spine BMD (mg/cm2) (at end supplementation) by ethnicity | 8 | 929 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.05, 0.21] |
| 33.1 Caucasian | 6 | 749 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.09 [-0.06, 0.24] |
| 33.2 Chinese | 1 | 84 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.03 [-0.39, 0.46] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 33.3 Other | 1 | 96 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.0 [-0.40, 0.40] |
| 34 Total body BMC (mg) (at end supplementation) by ethnicity | 6 | 708 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.12 [-0.03, 0.27] |
| 34.1 Caucasian | 5 | 608 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [-0.02, 0.31] |
| 34.2 Other | 1 | 100 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.00 [-0.39, 0.39] |
| 35 Distal radius BMD (mg/cm2) (at end supplementation) by ethnicity | 8 | 1009 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [0.02, 0.27] |
| 35.1 Caucasian | 5 | 603 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.07 [-0.09, 0.23] |
| 35.2 Chinese | 2 | 246 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [-0.11, 0.39] |
| 35.3 Other | 1 | 160 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.44 [0.12, 0.75] |
| 36 Upper limb BMD (mg/cm2) (at end supplementation) by ethnicity | 10 | 1400 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.13 [0.03, 0.24] |
| 36.1 Caucasian | 6 | 835 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.06 [-0.08, 0.20] |
| 36.2 Chinese | 3 | 405 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [-0.04, 0.35] |
| 36.3 Other | 1 | 160 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.44 [0.12, 0.75] |
| 37 Femoral neck BMD (mg/cm2) at longest point after supplementation ceased by ethnicity | 5 | 617 | Std. Mean Difference (IV, Random, 95% CI) | 0.11 [-0.07, 0.29] |
| 37.1 Caucasian | 3 | 437 | Std. Mean Difference (IV, Random, 95% CI) | 0.13 [-0.17, 0.44] |
| 37.2 Chinese | 1 | 84 | Std. Mean Difference (IV, Random, 95% CI) | 0.0 [-0.43, 0.43] |
| 37.3 Other | 1 | 96 | Std. Mean Difference (IV, Random, 95% CI) | 0.14 [-0.26, 0.54] |
| 38 Lumbar spine BMD (mg/cm2) at longest point after supplementation ceased by ethnicity | 5 | 617 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.01 [-0.15, 0.17] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 38.1 Caucasian | 3 | 437 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.05 [-0.13, 0.24] |
| 38.2 Chinese | 1 | 84 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.20 [-0.63, 0.23] |
| 38.3 Other | 1 | 96 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.0 [-0.40, 0.40] |
| 39 Distal radius BMD (mg/cm2) at longest point after supplementation ceased by ethnicity | 4 | 455 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.21 [0.03, 0.40] |
| 39.1 Caucasian | 2 | 211 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.24 [-0.03, 0.51] |
| 39.2 Chinese | 1 | 84 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.02 [-0.45, 0.41] |
| 39.3 Other | 1 | 160 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.31 [-0.01, 0.62] |
| 40 Upper limb BMD (mg/cm2) at longest point after supplementation ceased by ethnicity | 6 | 840 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.19 [0.05, 0.32] |
| 40.1 Caucasian | 3 | 437 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.25 [0.06, 0.44] |
| 40.2 Chinese | 2 | 243 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.01 [-0.26, 0.24] |
| 40.3 Other | 1 | 160 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.31 [-0.01, 0.62] |
| 41 Femoral neck BMD (mg/cm2) (at end supplementation) by physical activity level | 2 | 216 | Std. Mean Difference (IV, Random, 95% CI) | 0.29 [-0.24, 0.83] |
| 41.1 High | 2 | 129 | Std. Mean Difference (IV, Random, 95% CI) | 0.41 [-0.65, 1.47] |
| 41.2 Low | 2 | 87 | Std. Mean Difference (IV, Random, 95% CI) | 0.20 [-0.61, 1.00] |
| 42 Lumbar spine BMD (mg/cm2) (at end supplementation) by physical activity level | 2 | 216 | Std. Mean Difference (IV, Random, 95% CI) | 0.16 [-0.34, 0.65] |
| 42.1 High | 2 | 129 | Std. Mean Difference (IV, Random, 95% CI) | 0.19 [-0.65, 1.02] |
| 42.2 Low | 2 | 87 | Std. Mean Difference (IV, Random, 95% CI) | 0.12 [-0.78, 1.01] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 43 Total body BMC (mg) (at end supplementation) by physical activity level | 4 | 463 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.18 [-0.01, 0.37] |
| 43.1 High | 4 | 254 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.22 [-0.04, 0.48] |
| 43.2 Low | 4 | 209 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.13 [-0.14, 0.41] |
| 44 Distal radius BMD (mg/cm2) (at end supplementation) by physical activity level | 2 | 216 | Std. Mean Difference (IV, Random, 95% CI) | 0.09 [-0.32, 0.50] |
| 44.1 High | 2 | 129 | Std. Mean Difference (IV, Random, 95% CI) | -0.06 [-0.43, 0.31] |
| 44.2 Low | 2 | 87 | Std. Mean Difference (IV, Random, 95% CI) | 0.22 [-0.72, 1.16] |
| 45 Upper limb BMD (mg/cm2) (at end supplementation) by physical activity level | 2 | 216 | Std. Mean Difference (IV, Random, 95% CI) | 0.09 [-0.32, 0.50] |
| 45.1 High | 2 | 129 | Std. Mean Difference (IV, Random, 95% CI) | -0.06 [-0.43, 0.31] |
| 45.2 Low | 2 | 87 | Std. Mean Difference (IV, Random, 95% CI) | 0.22 [-0.72, 1.16] |
| 46 Femoral neck BMD (mg/cm2) at end supplementation by calcium threshold | 10 | 1073 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.07 [-0.05, 0.19] |
| 46.1 Above | 8 | 893 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.07 [-0.06, 0.21] |
| 46.2 Below | 2 | 180 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.04 [-0.25, 0.33] |
| 47 Lumbar spine BMD (mg/cm2) at end supplementation by calcium threshold | 11 | 1164 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.04, 0.20] |
| 47.1 Above | 8 | 893 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.05, 0.21] |
| 47.2 Below | 3 | 271 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.16, 0.32] |
| 48 Total body BMC (mg) at end supplementation by calcium threshold | 9 | 953 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.01, 0.27] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 48.1 Above | 4 | 407 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.21 [0.01, 0.41] |
| 48.2 Below | 5 | 546 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.09 [-0.08, 0.26] |
| 49 Distal radius BMD (mg/cm2) at end supplementation by calcium threshold | 9 | 1140 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [0.04, 0.27] |
| 49.1 Above | 6 | 734 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.10 [-0.05, 0.24] |
| 49.2 Below | 3 | 406 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.26 [0.06, 0.45] |
| 50 Upper limb BMD (mg/cm2) at end supplementation by calcium threshold | 12 | 1579 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.04, 0.24] |
| 50.1 Above | 8 | 1014 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.04, 0.21] |
| 50.2 Below | 4 | 565 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.23 [0.07, 0.40] |
| 51 Femoral neck BMD (mg/cm2) at longest point after supplementation ceased end by calcium threshold | 5 | 617 | Std. Mean Difference (IV, Random, 95% CI) | 0.11 [-0.07, 0.29] |
| 51.1 Above | 3 | 437 | Std. Mean Difference (IV, Random, 95% CI) | 0.13 [-0.17, 0.44] |
| 51.2 Below | 2 | 180 | Std. Mean Difference (IV, Random, 95% CI) | 0.08 [-0.22, 0.37] |
| 52 Lumbar spine BMD (mg/cm2) at longest point after supplementation ceased end by calcium threshold | 5 | 617 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.01 [-0.15, 0.17] |
| 52.1 Above | 3 | 437 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.05 [-0.13, 0.24] |
| 52.2 Below | 2 | 180 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.09 [-0.39, 0.20] |
| 53 Distal radius BMD (mg/cm2) at longest point after supplementation ceased end by calcium threshold | 4 | 455 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.21 [0.03, 0.40] |
| 53.1 Above | 2 | 211 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.24 [-0.03, 0.51] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 53.2 Below | 2 | 244 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.19 [-0.06, 0.44] |
| 54 Upper limb BMD (mg/cm2) at longest point after supplementation ceased end by calcium threshold | 6 | 840 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.19 [0.05, 0.32] |
| 54.1 Above | 3 | 437 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.25 [0.06, 0.44] |
| 54.2 Below | 3 | 403 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.12 [-0.08, 0.31] |
| 55 Femoral neck BMD (mg/cm2) at end supplementation by duration of supplementation (< 24 months vs >= 24 months) | 10 | 1073 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.07 [-0.05, 0.19] |
| 55.1 <24 months duration | 8 | 935 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.05, 0.21] |
| 55.2 >= 24 months duration | 2 | 138 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.03 [-0.36, 0.30] |
| 56 Lumbar spine BMD (mg/cm2) at end supplementation by duration of supplementation (< 24 months vs >= 24 months) | 11 | 1164 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.04, 0.20] |
| 56.1 <24 months duration | 8 | 935 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.07 [-0.06, 0.20] |
| 56.2 >= 24 months duration | 3 | 229 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.11 [-0.15, 0.37] |
| 57 Total body BMC (mg) at end supplementation by duration of supplementation (< 24 months vs >= 24 months) | 9 | 953 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.01, 0.27] |
| 57.1 <24 months duration | 7 | 814 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.13 [-0.01, 0.27] |
| 57.2 >= 24 months duration | 2 | 139 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.22 [-0.12, 0.55] |
| 58 Distal radius BMD (mg/cm2) at end supplementation by duration of supplementation (< 24 months vs >= 24 months) | 9 | 1140 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [0.04, 0.27] |
| 58.1 <24 months duration | 7 | 873 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [0.01, 0.28] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 58.2 >= 24 months duration | 2 | 267 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.18 [-0.06, 0.42] |
| 59 Upper limb BMD (mg/cm2) at end supplementation by duration of supplementation (< 24 months vs >= 24 months) | 12 | 1579 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.04, 0.24] |
| 59.1 <24 months duration | 9 | 1264 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.13 [0.02, 0.24] |
| 59.2 >= 24 months duration | 3 | 315 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.17 [-0.06, 0.39] |
| 60 Femoral neck BMD (mg/cm2) at longest point after supplementation ceased end by duration of supplementation (24 | 5 | 617 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.10 [-0.06, 0.26] |
| 60.1 <24 months duration | 4 | 531 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.11 [-0.06, 0.28] |
| 60.2 >= 24 months duration | 1 | 86 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.01 [-0.41, 0.44] |
| 61 Lumbar spine BMD (mg/cm2) at longest point after supplementation ceased end by duration of supplementation (24 | 5 | 617 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.01 [-0.15, 0.17] |
| 61.1 <24 months duration | 4 | 531 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.01 [-0.16, 0.18] |
| 61.2 >= 24 months duration | 1 | 86 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.05 [-0.38, 0.47] |
| 62 Distal radius BMD (mg/cm2) at longest point after supplementation ceased end by duration of supplementation (2 | 4 | 455 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.21 [0.03, 0.40] |
| 62.1 <24 months duration | 3 | 369 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.25 [0.05, 0.46] |
| 62.2 >= 24 months duration | 1 | 86 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.05 [-0.37, 0.47] |
| 63 Upper limb BMD (mg/cm2) at longest point after supplementation ceased end by duration of supplementation (24) | 6 | 840 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.19 [0.05, 0.32] |
| 63.1 <24 months duration | 5 | 754 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.20 [0.06, 0.34] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 63.2 >= 24 months duration | 1 | 86 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.05 [-0.37, 0.47] |
| 64 Femoral neck BMD (mg/cm2) at end supplementation by duration of supplementation (< 18months vs >= 18months) | 10 | 1073 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.07 [-0.05, 0.19] |
| 64.1 <18months duration | 6 | 795 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.10 [-0.05, 0.24] |
| 64.2 >= 18 months duration | 4 | 278 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.01 [-0.24, 0.23] |
| 65 Lumbar spine BMD (mg/cm2) at end supplementation by duration of supplementation (< 18months vs >= 18months) | 11 | 1164 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.04, 0.20] |
| 65.1 <18months duration | 6 | 795 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.07, 0.22] |
| 65.2 >= 18 months duration | 5 | 369 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.09 [-0.11, 0.30] |
| 66 Total body BMC (mg) at end supplementation by duration of supplementation (< 18months vs >= 18months) | 9 | 953 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.01, 0.27] |
| 66.1 <18months duration | 7 | 814 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.13 [-0.01, 0.27] |
| 66.2 >= 18 months duration | 2 | 139 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.22 [-0.12, 0.55] |
| 67 Distal radius BMD (mg/cm2) at end supplementation by duration of supplementation (< 18months vs >= 18months) | 9 | 1140 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [0.04, 0.27] |
| 67.1 <18 months duration | 5 | 627 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.15 [-0.01, 0.31] |
| 67.2 >= 18 months duration | 4 | 513 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.16 [-0.01, 0.34] |
| 68 Upper limb BMD (mg/cm2) at end supplementation by duration of supplementation (< 18months vs >= 18months) | 12 | 1579 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.04, 0.24] |
| 68.1 <18 months duration | 6 | 859 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.12 [-0.02, 0.26] |

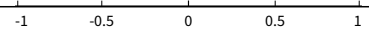
| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 68.2 >= 18 months duration | 6 | 720 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.16 [0.01, 0.30] |
| 69 Femoral neck BMD (mg/cm2) at longest point after cessation of supplementation by duration of supplementation | 5 | 617 | Std. Mean Difference (IV, Random, 95% CI) | 0.11 [-0.07, 0.29] |
| 69.1 <18 months duration | 3 | 447 | Std. Mean Difference (IV, Random, 95% CI) | 0.17 [-0.12, 0.46] |
| 69.2 >= 18 months duration | 2 | 170 | Std. Mean Difference (IV, Random, 95% CI) | 0.01 [-0.29, 0.31] |
| 70 Lumbar spine BMD (mg/cm2) at longest point after cessation of supplementation by duration of supplementation | 5 | 617 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.01 [-0.15, 0.17] |
| 70.1 <18 months duration | 3 | 447 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.04 [-0.14, 0.23] |
| 70.2 >= 18 months duration | 2 | 170 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.07 [-0.38, 0.23] |
| 71 Distal radius BMD (mg/cm2) at longest point after cessation of supplementation by duration of supplementation | 4 | 455 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.21 [0.03, 0.40] |
| 71.1 <18 months duration | 2 | 285 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.33 [0.10, 0.57] |
| 71.2 >= 18 months duration | 2 | 170 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.02 [-0.29, 0.32] |
| 72 Upper limb BMD (mg/cm2) at longest point after cessation of supplementation by duration of supplementation | 6 | 840 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.19 [0.05, 0.32] |
| 72.1 <18 months duration | 3 | 511 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.30 [0.13, 0.48] |
| 72.2 >= 18 months duration | 3 | 329 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.01 [-0.21, 0.22] |
| 73 Femoral neck BMD (mg/cm2) at end supplementation by milk extract vs other calcium supplement | 10 | 1073 | Std. Mean Difference (IV, Random, 95% CI) | 0.07 [-0.05, 0.19] |
| 73.1 milk extract | 3 | 425 | Std. Mean Difference (IV, Random, 95% CI) | 0.15 [-0.16, 0.46] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 73.2 other calcium supplementation | 7 | 648 | Std. Mean Difference (IV, Random, 95% CI) | 0.05 [-0.10, 0.21] |
| 74 Lumbar spine BMD (mg/cm2) at end supplementation by milk extract vs other calcium supplement | 11 | 1164 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.04, 0.20] |
| 74.1 milk extract | 3 | 425 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.07 [-0.13, 0.26] |
| 74.2 other calcium supplementation | 8 | 739 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.09 [-0.06, 0.23] |
| 75 Upper limb BMD (mg/cm2) at end supplementation by milk extract vs other calcium supplement | 12 | 1579 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.04, 0.24] |
| 75.1 milk extract | 3 | 425 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.03 [-0.17, 0.22] |
| 75.2 other calcium supplementation | 9 | 1154 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.18 [0.06, 0.29] |
| 76 Femoral neck BMD (mg/cm2) after supplementation ceased by milk extract vs other calcium supplement | 5 | 617 | Std. Mean Difference (IV, Random, 95% CI) | 0.11 [-0.07, 0.29] |
| 76.1 milk extract | 2 | 351 | Std. Mean Difference (IV, Random, 95% CI) | 0.19 [-0.28, 0.65] |
| 76.2 other calcium supplementation | 3 | 266 | Std. Mean Difference (IV, Random, 95% CI) | 0.06 [-0.18, 0.30] |
| 77 Lumbar spine BMD (mg/cm2) after supplementation ceased by milk extract vs other calcium supplement | 5 | 617 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.01 [-0.15, 0.17] |
| 77.1 milk extract | 2 | 351 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.06 [-0.15, 0.27] |
| 77.2 other calcium supplementation | 3 | 266 | Std. Mean Difference (IV, Fixed, 95% CI) | -0.05 [-0.29, 0.19] |
| 78 Upper limb BMD (mg/cm2) after supplementation ceased by milk extract vs other calcium supplement | 6 | 840 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.01, 0.28] |
| 78.1 milk extract | 2 | 351 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.20 [-0.01, 0.41] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 78.2 other calcium supplementation | 4 | 489 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.10 [-0.07, 0.28] |
| 79 Upper limb BMD (mg/cm2) by calcium intake (lowest quartile vs above lowest quartile) | 12 | 1579 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.14 [0.04, 0.24] |
| 79.1 Lowest quartile | 4 | 565 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.23 [0.07, 0.40] |
| 79.2 Above lowest quartile | 8 | 1014 | Std. Mean Difference (IV, Fixed, 95% CI) | 0.08 [-0.04, 0.21] |

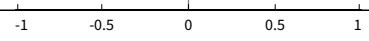
**Analysis 1.1. Comparison 1 Calcium supplementation vs placebo, Outcome 1 Femoral neck BMD (mg/cm2) at end supplementation (all data).**

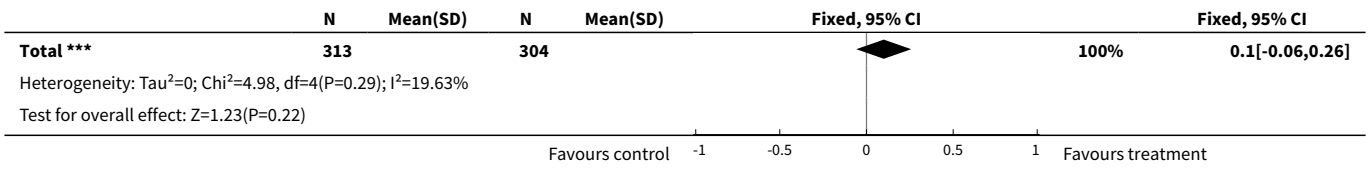
| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Bonjour 1995 | 55 | 656 (81.6) | 53 | 635 (65.5) | | 10.18% | 0.28[-0.1,0.66] |
| Cameron 2004 | 24 | 814 (131) | 24 | 816 (131) | | 4.57% | -0.02[-0.58,0.55] |
| Chevalley 2005 | 114 | 698 (70) | 118 | 703.7 (68) | | 22.08% | -0.08[-0.34,0.18] |
| Courteix 2005 | 22 | 772.5 (57.4) | 63 | 737 (93.8) | | 6.11% | 0.41[-0.08,0.9] |
| Johnston 1992 | 45 | 847.7 (128.1) | 45 | 852.9 (144) | | 8.57% | -0.04[-0.45,0.38] |
| Lee 1995 | 44 | 592 (74) | 40 | 593 (65) | | 7.99% | -0.01[-0.44,0.41] |
| Nowson 1997 | 28 | 877 (90) | 28 | 871 (100.5) | | 5.33% | 0.06[-0.46,0.59] |
| Prentice 2005 | 73 | 1001 (134) | 70 | 1002 (129) | | 13.62% | -0.01[-0.34,0.32] |
| Rozen 2003 | 49 | 1010 (70) | 47 | 1000 (137) | | 9.13% | 0.09[-0.31,0.49] |
| Stear 2003 | 65 | 870 (100) | 66 | 847 (107) | | 12.4% | 0.22[-0.12,0.56] |
| **Total ***** | **519** | | **554** | | | **100%** | **0.07[-0.05,0.19]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=5.83, df=9(P=0.76); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.11(P=0.27) | | | | | | | |



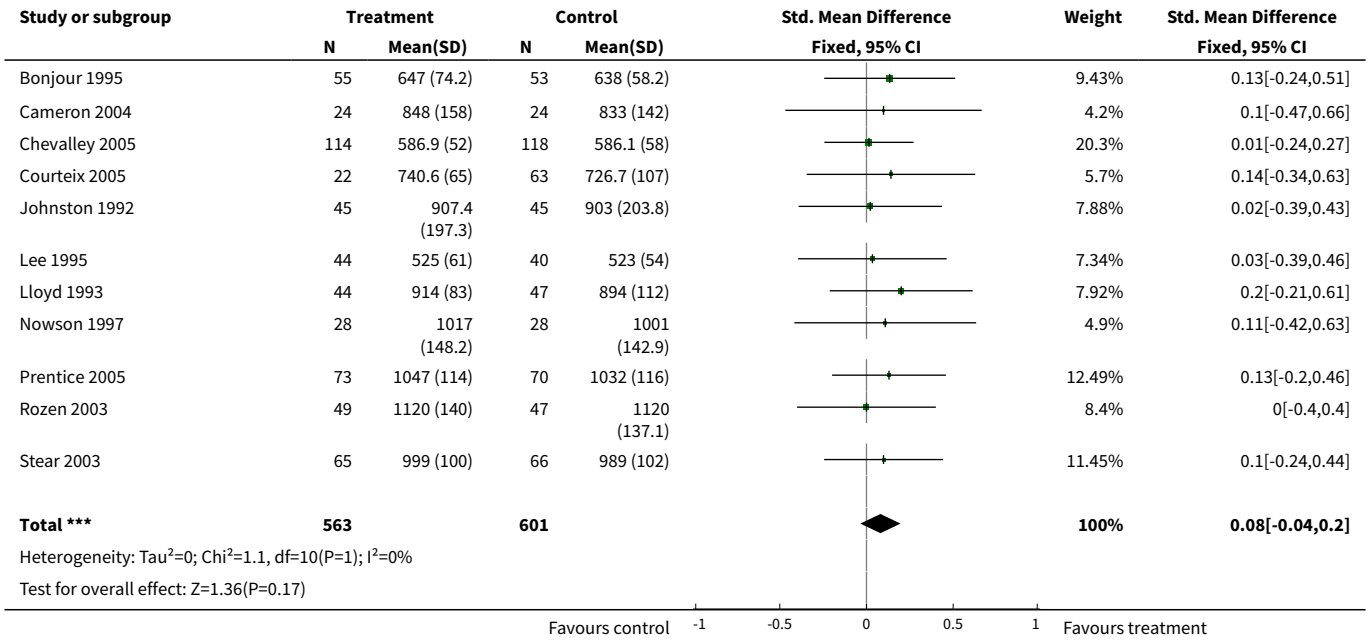

**Analysis 1.2. Comparison 1 Calcium supplementation vs placebo, Outcome 2 Femoral Neck BMD (mg/cm2) at longest point after cessation of supplement (all data).**

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Bonjour 1995 | 67 | 885 (70.2) | 58 | 853 (73.7) | | 19.8% | 0.44[0.09,0.8] |
| Chevalley 2005 | 110 | 722.4 (70) | 116 | 724.7 (68) | | 36.86% | -0.03[-0.29,0.23] |
| Johnston 1992 | 43 | 956.1 (136.7) | 43 | 954.1 (140.9) | | 14.04% | 0.01[-0.41,0.44] |
| Lee 1995 | 44 | 603 (76) | 40 | 603 (64) | | 13.68% | 0[-0.43,0.43] |
| Rozen 2003 | 49 | 1010 (140) | 47 | 990 (137.1) | | 15.62% | 0.14[-0.26,0.54] |

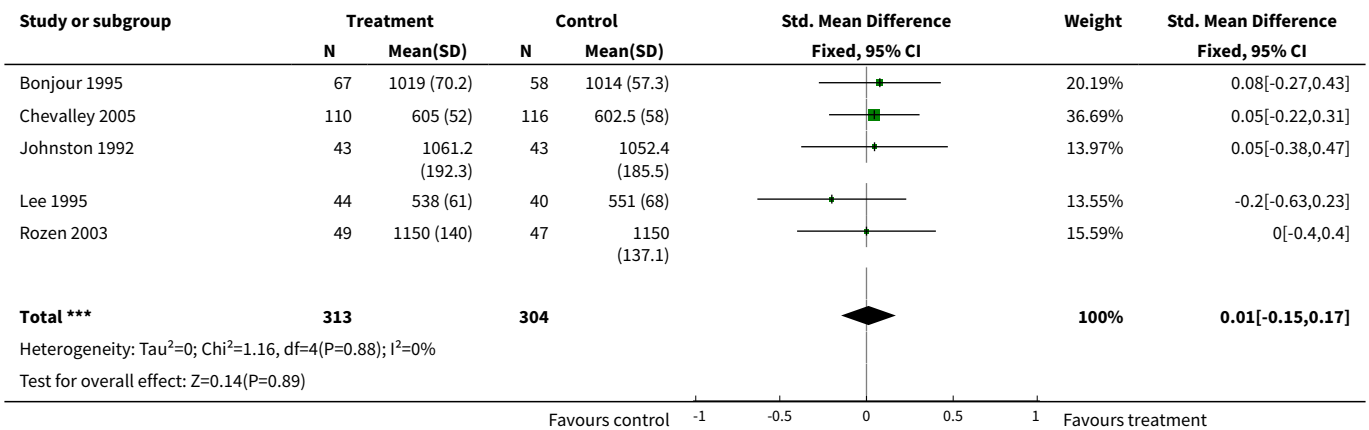





## Analysis 1.3. Comparison 1 Calcium supplementation vs placebo, Outcome 3 Lumbar spine BMD (mg/cm2) at end supplementation (all data).

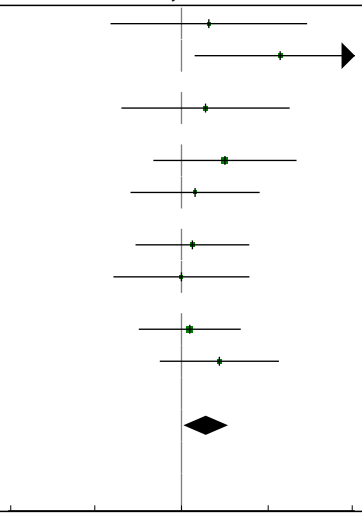



## Analysis 1.4. Comparison 1 Calcium supplementation vs placebo, Outcome 4 Lumbar Spine BMD (mg/cm2) at longest point after cessation of supplement (all data).



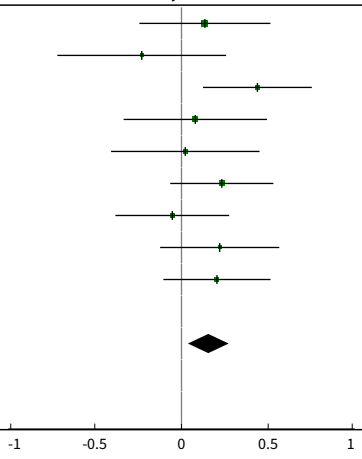
## Analysis 1.5. Comparison 1 Calcium supplementation vs placebo, Outcome 5 Total Body BMC (mg) at end supplementation (all data).

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Cameron 2004 | 24 | 1583 (504) | 24 | 1512 (372) | | 5.15% | 0.16[-0.41,0.72] |
| Courteix 2005 | 22 | 1340.9 (216.4) | 63 | 1186.1 (285.3) | | 6.81% | 0.57[0.08,1.06] |
| Iuliano-Burns 2003 | 30 | 1179.6 (209) | 36 | 1151.3 (195.6) | | 7.03% | 0.14[-0.35,0.62] |
| Lloyd 1993 | 44 | 1783 (238) | 47 | 1714 (302) | | 9.71% | 0.25[-0.16,0.66] |
| Molgaard 2004 | 54 | 1932.1 (292.3) | 57 | 1907.5 (328.8) | | 11.94% | 0.08[-0.29,0.45] |
| Prentice 2005 | 73 | 2796 (415) | 70 | 2770 (407) | | 15.39% | 0.06[-0.27,0.39] |
| Rozen 2003 | 49 | 860.3 (134.2) | 51 | 860.3 (138.7) | | 10.77% | -0[-0.39,0.39] |
| Specker 2003 | 88 | 685.6 (88) | 90 | 681.5 (80.6) | | 19.17% | 0.05[-0.25,0.34] |
| Stear 2003 | 65 | 2143 (265) | 66 | 2088 (235) | | 14.03% | 0.22[-0.13,0.56] |
| **Total ***** | **449** | | **504** | | | **100%** | **0.14[0.01,0.27]** |
| Heterogeneity: $Tau^2=0$; $Chi^2=4.58$, df=8(P=0.8); $I^2=0\%$ | | | | | | | |
| Test for overall effect: Z=2.13(P=0.03) | | | | | | | |



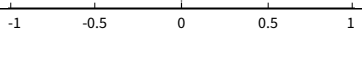

## Analysis 1.6. Comparison 1 Calcium supplementation vs placebo, Outcome 6 Distal Radius BMD (mg/cm2) at end supplementation (all data).

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 9.7% | 0.14[-0.24,0.51] |
| Courteix 2005 | 22 | 336.2 (43.2) | 63 | 351 (69.8) | | 5.84% | -0.23[-0.72,0.26] |
| Dibba 2000 | 80 | 253 (50) | 80 | 231 (50) | | 14.06% | 0.44[0.12,0.75] |
| Johnston 1992 | 45 | 317.1 (69.4) | 45 | 311.5 (69.7) | | 8.1% | 0.08[-0.33,0.49] |
| Lee 1995 | 44 | 492 (39) | 40 | 491 (51) | | 7.55% | 0.02[-0.41,0.45] |
| Matkovic 2004 | 79 | 450 (53) | 98 | 438 (50) | | 15.65% | 0.23[-0.06,0.53] |
| Prentice 2005 | 73 | 479 (61) | 70 | 482 (51) | | 12.87% | -0.05[-0.38,0.27] |
| Stear 2003 | 65 | 427 (38) | 66 | 418 (43) | | 11.72% | 0.22[-0.12,0.56] |
| Wang 1996 | 79 | 486 (37) | 83 | 479 (31) | | 14.5% | 0.2[-0.1,0.51] |
| **Total ***** | **542** | | **598** | | | **100%** | **0.15[0.04,0.27]** |
| Heterogeneity: $Tau^2=0$; $Chi^2=8.07$, df=8(P=0.43); $I^2=0.91\%$ | | | | | | | |
| Test for overall effect: Z=2.57(P=0.01) | | | | | | | |




## Analysis 1.7. Comparison 1 Calcium supplementation vs placebo, Outcome 7 Distal Radius BMD (mg/cm2) at longest point after cessation of supplement.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Bonjour 1995 | 67 | 429 (26.3) | 58 | 418 (32.7) | | 27.15% | 0.37[0.02,0.73] |



| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Dibba 2000 | 80 | 256 (43) | 80 | 242 (48) | | 35.13% | 0.31[-0.01,0.62] |
| Johnston 1992 | 43 | 365.2 (77.1) | 43 | 361.3 (74.8) | | 19.1% | 0.05[-0.37,0.47] |
| Lee 1995 | 44 | 516 (44) | 40 | 517 (49) | | 18.62% | -0.02[-0.45,0.41] |
| **Total ***** | **234** | | **221** | | | **100%** | **0.21[0.03,0.4]** |

Heterogeneity: $Tau^2=0$; $Chi^2=2.82$, df=3(P=0.42); $I^2=0\%$

Test for overall effect: Z=2.27(P=0.02)

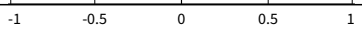



## Analysis 1.8. Comparison 1 Calcium supplementation vs placebo, Outcome 8 Upper Limb BMD (mg/cm2) at end supplementation (all data).

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 6.96% | 0.14[-0.24,0.51] |
| Cameron 2004 | 24 | 418 (43) | 24 | 414 (42) | | 3.1% | 0.09[-0.47,0.66] |
| Chevalley 2005 | 114 | 309.6 (28) | 118 | 308.2 (32) | | 14.97% | 0.05[-0.21,0.3] |
| Courteix 2005 | 22 | 336.2 (43.2) | 63 | 351 (69.8) | | 4.19% | -0.23[-0.72,0.26] |
| Dibba 2000 | 80 | 253 (50) | 80 | 231 (50) | | 10.09% | 0.44[0.12,0.75] |
| Johnston 1992 | 45 | 317.1 (69.4) | 45 | 311.5 (69.7) | | 5.81% | 0.08[-0.33,0.49] |
| Lee 1994 | 77 | 487 (41) | 82 | 480 (43) | | 10.22% | 0.17[-0.15,0.48] |
| Lee 1995 | 44 | 492 (39) | 40 | 491 (51) | | 5.41% | 0.02[-0.41,0.45] |
| Matkovic 2004 | 79 | 450 (53) | 98 | 438 (50) | | 11.22% | 0.23[-0.06,0.53] |
| Prentice 2005 | 73 | 479 (61) | 70 | 482 (51) | | 9.23% | -0.05[-0.38,0.27] |
| Stear 2003 | 65 | 427 (38) | 66 | 418 (43) | | 8.41% | 0.22[-0.12,0.56] |
| Wang 1996 | 79 | 486 (37) | 83 | 479 (31) | | 10.4% | 0.2[-0.1,0.51] |
| **Total ***** | **757** | | **822** | | | **100%** | **0.14[0.04,0.24]** |

Heterogeneity: $Tau^2=0$; $Chi^2=8.69$, df=11(P=0.65); $I^2=0\%$

Test for overall effect: Z=2.71(P=0.01)

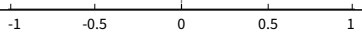



## Analysis 1.9. Comparison 1 Calcium supplementation vs placebo, Outcome 9 Upper Limb BMD (mg/cm2) at longest point after cessation of supplement (all data).

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Bonjour 1995 | 67 | 429 (26.3) | 58 | 418 (32.7) | | 14.64% | 0.37[0.02,0.73] |
| Chevalley 2005 | 110 | 319.7 (28) | 116 | 316.4 (32) | | 27.02% | 0.11[-0.15,0.37] |
| Dibba 2000 | 80 | 256 (43) | 80 | 242 (48) | | 18.95% | 0.31[-0.01,0.62] |
| Johnston 1992 | 43 | 365.2 (77.1) | 43 | 361.3 (74.8) | | 10.3% | 0.05[-0.37,0.47] |
| Lee 1994 | 77 | 505 (45) | 82 | 505 (40) | | 19.04% | 0[-0.31,0.31] |
| Lee 1995 | 44 | 516 (44) | 40 | 517 (49) | | 10.04% | -0.02[-0.45,0.41] |
| **Total ***** | **421** | | **419** | | | **100%** | **0.14[0.01,0.28]** |

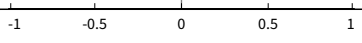
Heterogeneity: $Tau^2=0$; $Chi^2=4.26$, df=5(P=0.51); $I^2=0\%$

Test for overall effect: Z=2.09(P=0.04)



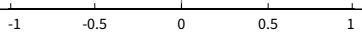
## Analysis 1.10. Comparison 1 Calcium supplementation vs placebo, Outcome 10 Femoral neck BMD (mg/cm2) (end trial) by baseline calcium intake.

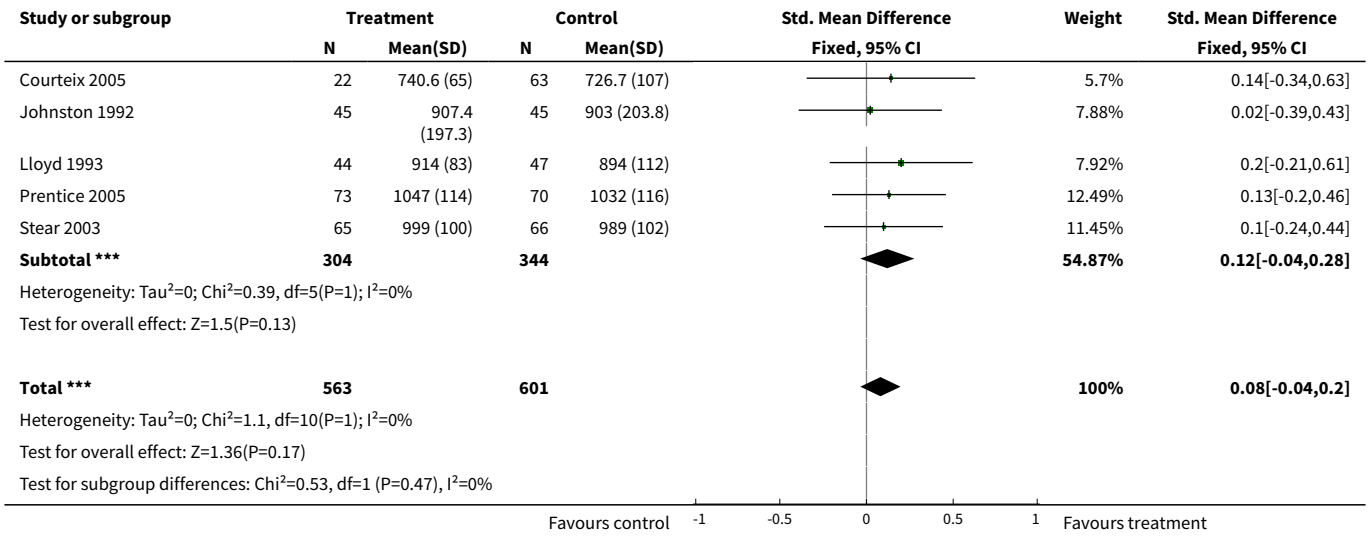
| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.10.1 Low baseline calcium** | | | | | | | |
| Cameron 2004 | 24 | 814 (131) | 24 | 816 (131) | | 4.57% | -0.02[-0.58,0.55] |
| Chevalley 2005 | 114 | 698 (70) | 118 | 703.7 (68) | | 22.08% | -0.08[-0.34,0.18] |
| Lee 1995 | 44 | 592 (74) | 40 | 593 (65) | | 7.99% | -0.01[-0.44,0.41] |
| Nowson 1997 | 28 | 877 (90) | 28 | 871 (100.5) | | 5.33% | 0.06[-0.46,0.59] |
| Rozen 2003 | 49 | 1010 (70) | 47 | 1000 (137) | | 9.13% | 0.09[-0.31,0.49] |
| **Subtotal ***** | **259** | | **257** | | | **49.11%** | **-0.02[-0.19,0.16]** |
| Heterogeneity: Tau²=0; Chi²=0.62, df=4(P=0.96); I²=0% | | | | | | | |
| Test for overall effect: Z=0.19(P=0.85) | | | | | | | |
| **1.10.2 High baseline calcium** | | | | | | | |
| Bonjour 1995 | 55 | 656 (81.6) | 53 | 635 (65.5) | | 10.18% | 0.28[-0.1,0.66] |
| Courteix 2005 | 22 | 772.5 (57.4) | 63 | 737 (93.8) | | 6.11% | 0.41[-0.08,0.9] |
| Johnston 1992 | 45 | 847.7 (128.1) | 45 | 852.9 (144) | | 8.57% | -0.04[-0.45,0.38] |
| Prentice 2005 | 73 | 1001 (134) | 70 | 1002 (129) | | 13.62% | -0.01[-0.34,0.32] |
| Stear 2003 | 65 | 870 (100) | 66 | 847 (107) | | 12.4% | 0.22[-0.12,0.56] |
| **Subtotal ***** | **260** | | **297** | | | **50.89%** | **0.15[-0.02,0.32]** |
| Heterogeneity: Tau²=0; Chi²=3.37, df=4(P=0.5); I²=0% | | | | | | | |
| Test for overall effect: Z=1.74(P=0.08) | | | | | | | |
| **Total ***** | **519** | | **554** | | | **100%** | **0.07[-0.05,0.19]** |
| Heterogeneity: Tau²=0; Chi²=5.83, df=9(P=0.76); I²=0% | | | | | | | |
| Test for overall effect: Z=1.11(P=0.27) | | | | | | | |
| Test for subgroup differences: Chi²=1.84, df=1 (P=0.17), I²=45.76% | | | | | | | |



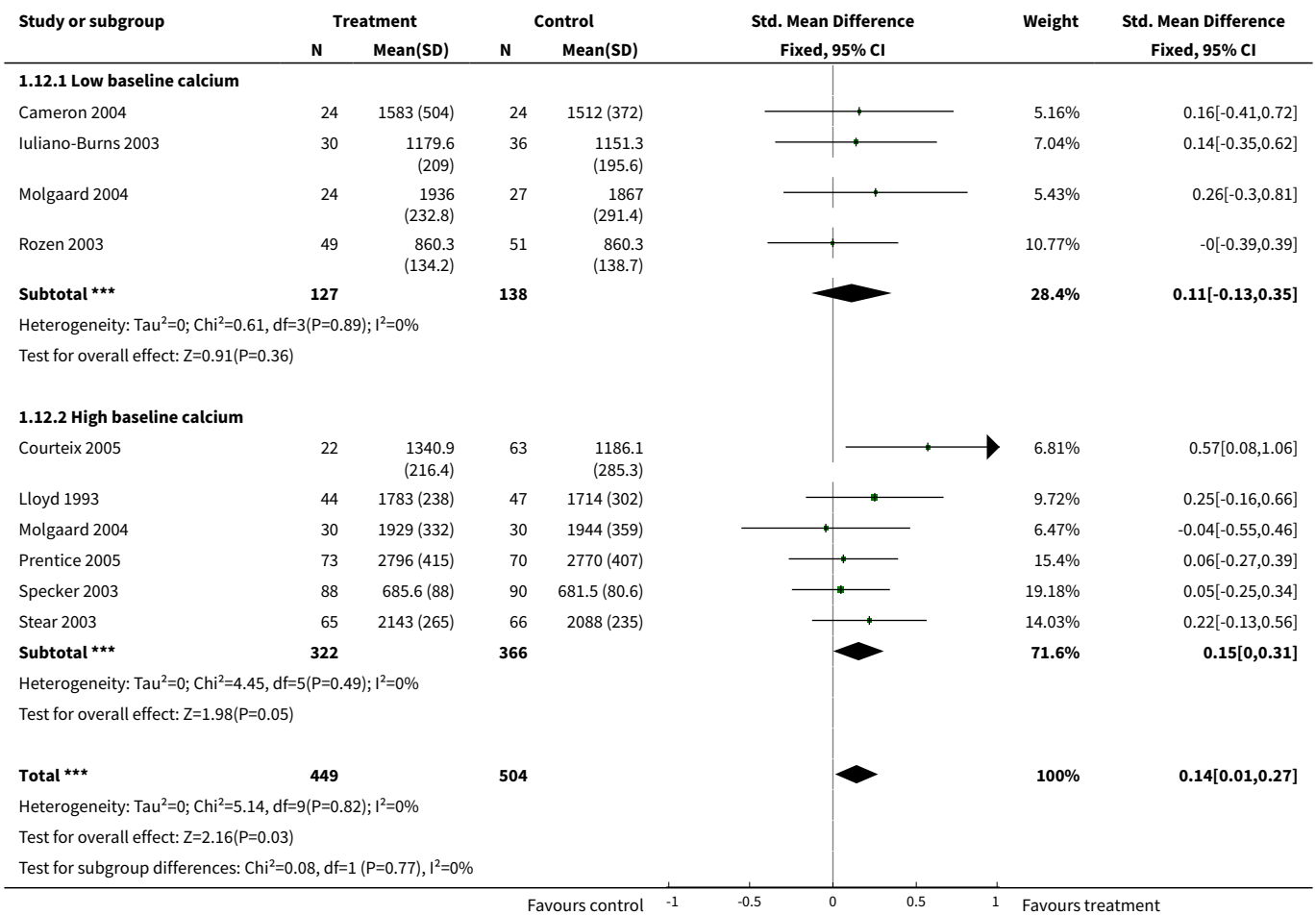

## Analysis 1.11. Comparison 1 Calcium supplementation vs placebo, Outcome 11 Lumbar spine BMD (mg/cm2) (end trial) by baseline calcium intake.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.11.1 Low baseline calcium** | | | | | | | |
| Cameron 2004 | 24 | 848 (158) | 24 | 833 (142) | | 4.2% | 0.1[-0.47,0.66] |
| Chevalley 2005 | 114 | 586.9 (52) | 118 | 586.1 (58) | | 20.3% | 0.01[-0.24,0.27] |
| Lee 1995 | 44 | 525 (61) | 40 | 523 (54) | | 7.34% | 0.03[-0.39,0.46] |
| Nowson 1997 | 28 | 1017 (148.2) | 28 | 1001 (142.9) | | 4.9% | 0.11[-0.42,0.63] |
| Rozen 2003 | 49 | 1120 (140) | 47 | 1120 (137.1) | | 8.4% | 0[-0.4,0.4] |
| **Subtotal ***** | **259** | | **257** | | | **45.13%** | **0.03[-0.14,0.21]** |
| Heterogeneity: Tau²=0; Chi²=0.18, df=4(P=1); I²=0% | | | | | | | |
| Test for overall effect: Z=0.37(P=0.71) | | | | | | | |
| **1.11.2 High baseline calcium** | | | | | | | |
| Bonjour 1995 | 55 | 647 (74.2) | 53 | 638 (58.2) | | 9.43% | 0.13[-0.24,0.51] |



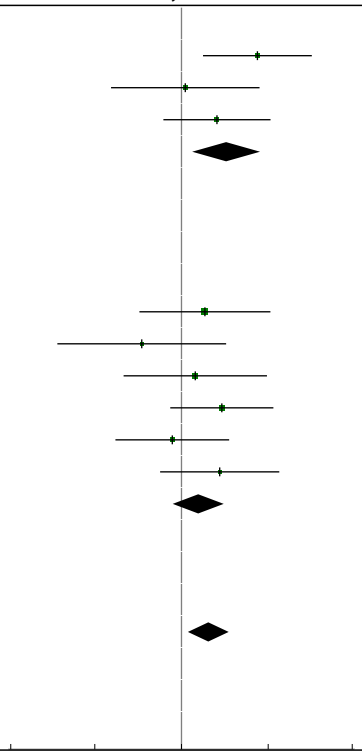



## Analysis 1.12. Comparison 1 Calcium supplementation vs placebo, Outcome 12 Total Body BMC (mg) (end trial) by baseline calcium intake.



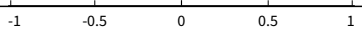
## Analysis 1.13. Comparison 1 Calcium supplementation vs placebo, Outcome 13 Distal radius BMD (mg/cm2) (end trial) by baseline calcium intake.

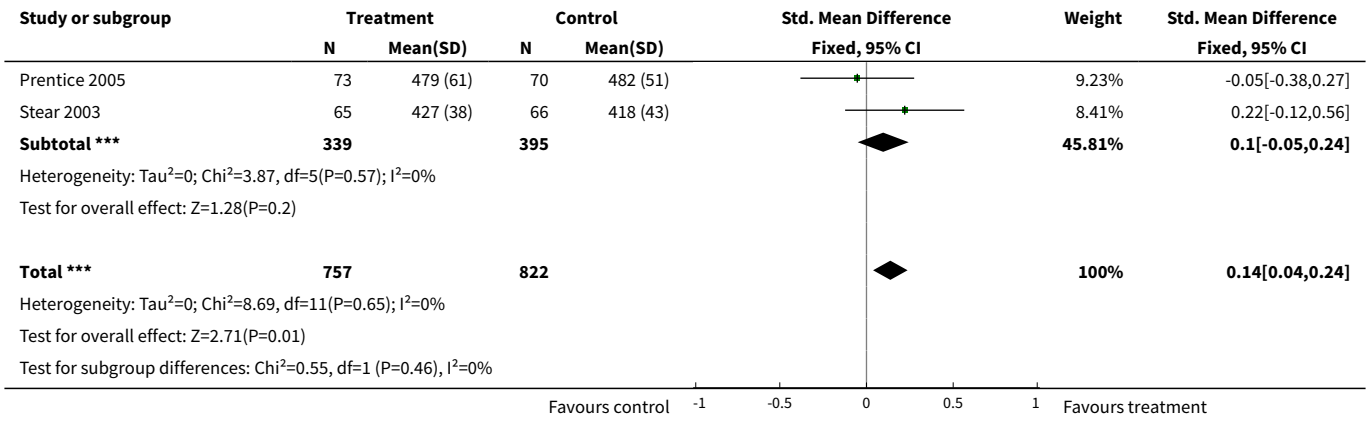
| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.13.1 Low baseline calcium** | | | | | | | |
| Dibba 2000 | 80 | 253 (50) | 80 | 231 (50) | | 14.06% | 0.44[0.12,0.75] |
| Lee 1995 | 44 | 492 (39) | 40 | 491 (51) | | 7.55% | 0.02[-0.41,0.45] |
| Wang 1996 | 79 | 486 (37) | 83 | 479 (31) | | 14.5% | 0.2[-0.1,0.51] |
| **Subtotal ***** | **203** | | **203** | | | **36.12%** | **0.26[0.06,0.45]** |
| Heterogeneity: Tau²=0; Chi²=2.55, df=2(P=0.28); I²=21.44% | | | | | | | |
| Test for overall effect: Z=2.58(P=0.01) | | | | | | | |
| **1.13.2 High baseline calcium** | | | | | | | |
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 9.7% | 0.14[-0.24,0.51] |
| Courteix 2005 | 22 | 336.2 (43.2) | 63 | 351 (69.8) | | 5.84% | -0.23[-0.72,0.26] |
| Johnston 1992 | 45 | 317.1 (69.4) | 45 | 311.5 (69.7) | | 8.1% | 0.08[-0.33,0.49] |
| Matkovic 2004 | 79 | 450 (53) | 98 | 438 (50) | | 15.65% | 0.23[-0.06,0.53] |
| Prentice 2005 | 73 | 479 (61) | 70 | 482 (51) | | 12.87% | -0.05[-0.38,0.27] |
| Stear 2003 | 65 | 427 (38) | 66 | 418 (43) | | 11.72% | 0.22[-0.12,0.56] |
| **Subtotal ***** | **339** | | **395** | | | **63.88%** | **0.1[-0.05,0.24]** |
| Heterogeneity: Tau²=0; Chi²=3.87, df=5(P=0.57); I²=0% | | | | | | | |
| Test for overall effect: Z=1.28(P=0.2) | | | | | | | |
| **Total ***** | **542** | | **598** | | | **100%** | **0.15[0.04,0.27]** |
| Heterogeneity: Tau²=0; Chi²=8.07, df=8(P=0.43); I²=0.91% | | | | | | | |
| Test for overall effect: Z=2.57(P=0.01) | | | | | | | |
| Test for subgroup differences: Chi²=1.66, df=1 (P=0.2), I²=39.67% | | | | | | | |



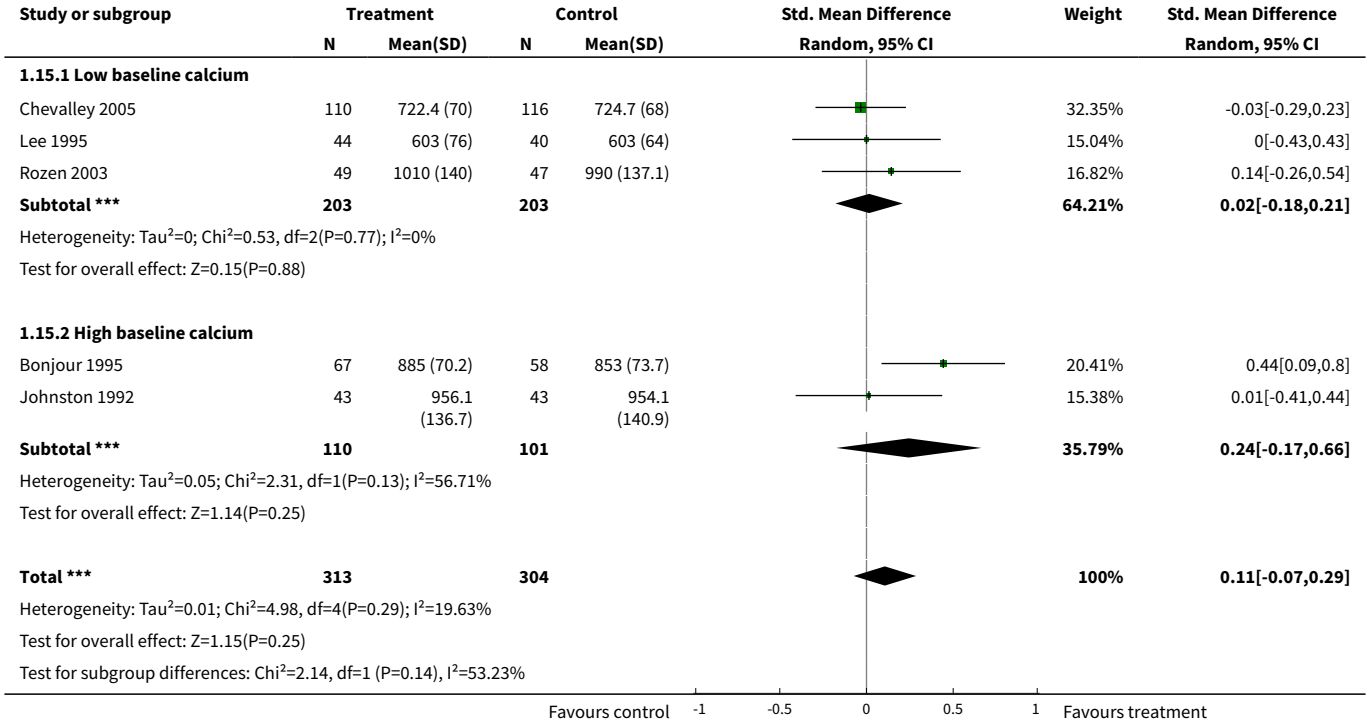

## Analysis 1.14. Comparison 1 Calcium supplementation vs placebo, Outcome 14 Upper limb BMD (mg/cm2) (end trial) by baseline calcium intake.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.14.1 Low baseline calcium** | | | | | | | |
| Cameron 2004 | 24 | 418 (43) | 24 | 414 (42) | | 3.1% | 0.09[-0.47,0.66] |
| Chevalley 2005 | 114 | 309.6 (28) | 118 | 308.2 (32) | | 14.97% | 0.05[-0.21,0.3] |
| Dibba 2000 | 80 | 253 (50) | 80 | 231 (50) | | 10.09% | 0.44[0.12,0.75] |
| Lee 1994 | 77 | 487 (41) | 82 | 480 (43) | | 10.22% | 0.17[-0.15,0.48] |
| Lee 1995 | 44 | 492 (39) | 40 | 491 (51) | | 5.41% | 0.02[-0.41,0.45] |
| Wang 1996 | 79 | 486 (37) | 83 | 479 (31) | | 10.4% | 0.2[-0.1,0.51] |
| **Subtotal ***** | **418** | | **427** | | | **54.19%** | **0.17[0.04,0.31]** |
| Heterogeneity: Tau²=0; Chi²=4.27, df=5(P=0.51); I²=0% | | | | | | | |
| Test for overall effect: Z=2.5(P=0.01) | | | | | | | |
| **1.14.2 High baseline calcium** | | | | | | | |
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 6.96% | 0.14[-0.24,0.51] |
| Courteix 2005 | 22 | 336.2 (43.2) | 63 | 351 (69.8) | | 4.19% | -0.23[-0.72,0.26] |
| Johnston 1992 | 45 | 317.1 (69.4) | 45 | 311.5 (69.7) | | 5.81% | 0.08[-0.33,0.49] |
| Matkovic 2004 | 79 | 450 (53) | 98 | 438 (50) | | 11.22% | 0.23[-0.06,0.53] |

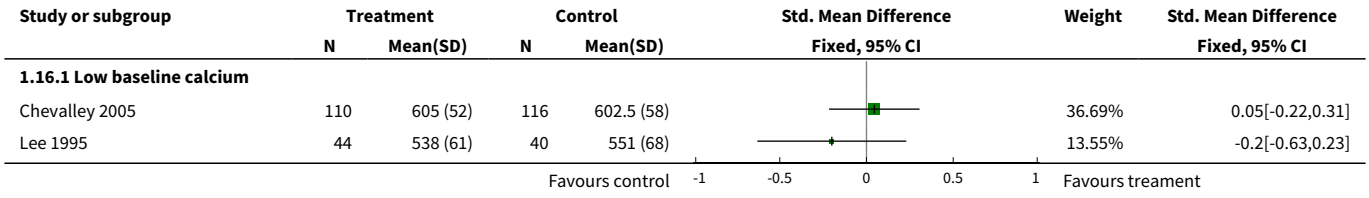


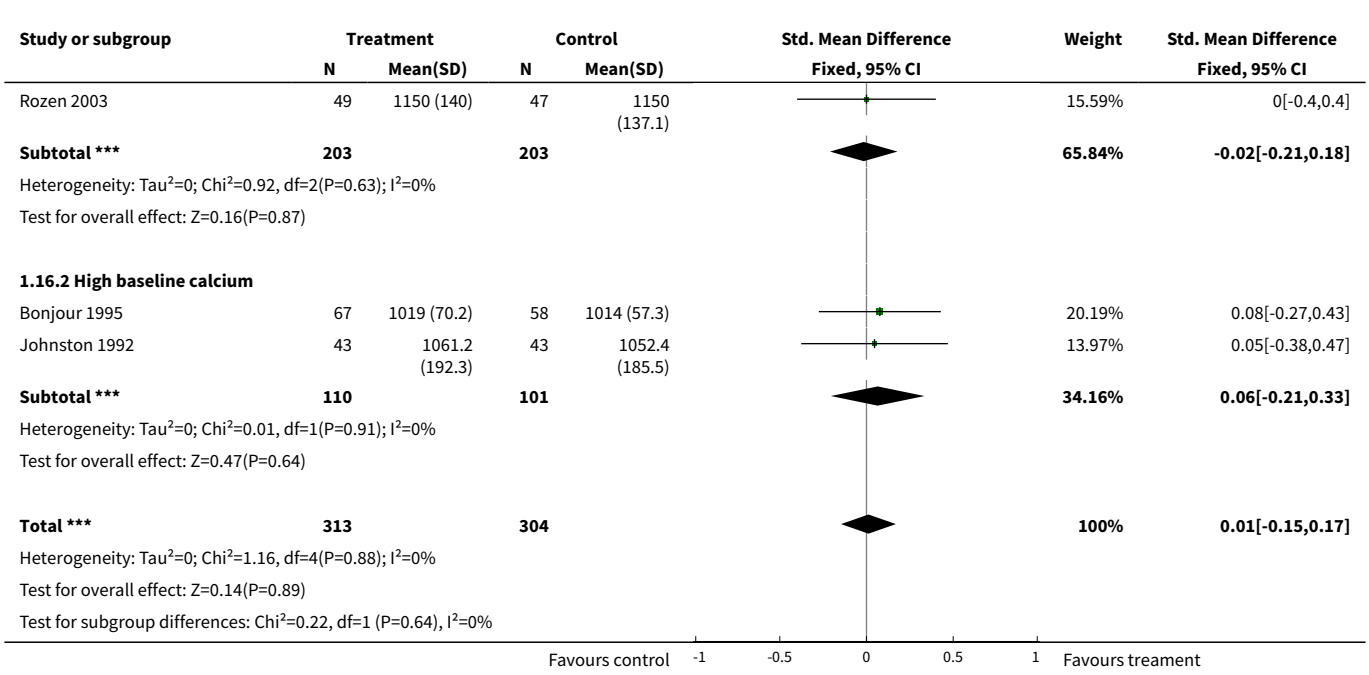



## Analysis 1.15. Comparison 1 Calcium supplementation vs placebo, Outcome 15 Femoral neck BMD (mg/cm2) at longest point after supplement ceased by baseline calcium intake.

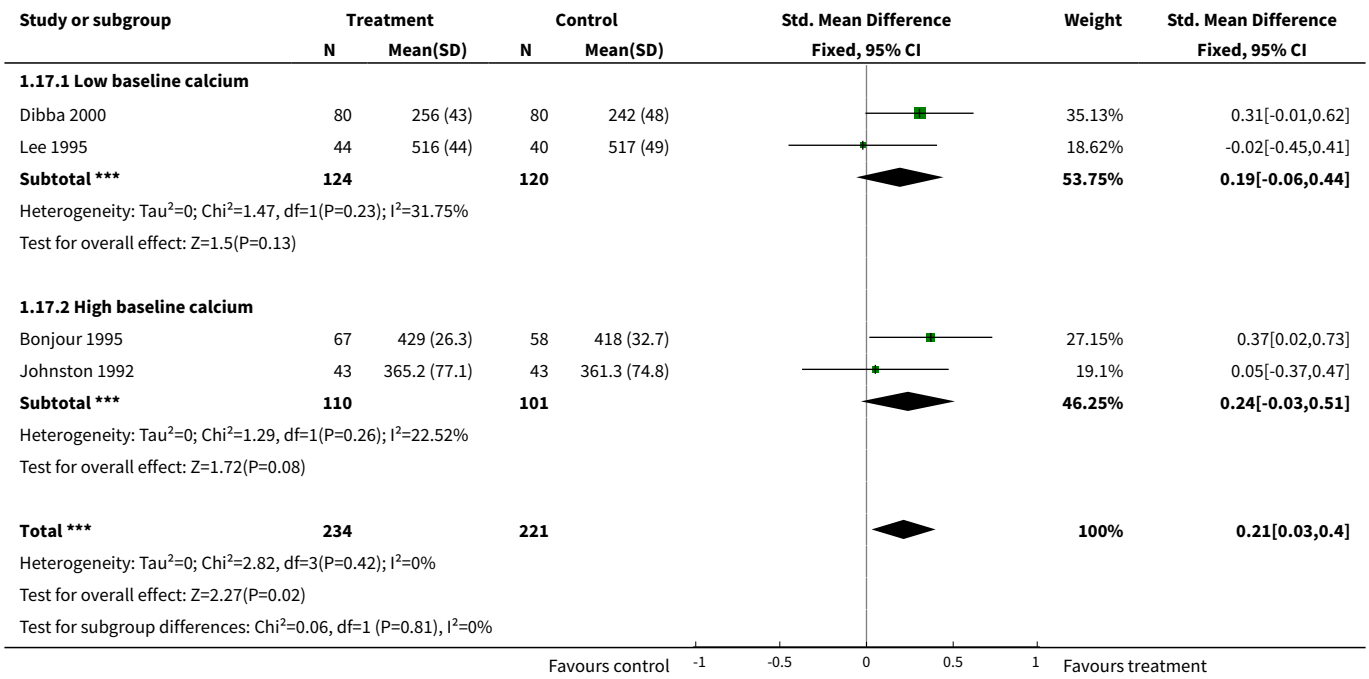



## Analysis 1.16. Comparison 1 Calcium supplementation vs placebo, Outcome 16 Lumbar spine BMD (mg/cm2) at longest point after supplement ceased by baseline calcium intake.






## Analysis 1.17. Comparison 1 Calcium supplementation vs placebo, Outcome 17 Distal radius BMD (mg/cm2) at longest point after supplement ceased by baseline calcium intake.



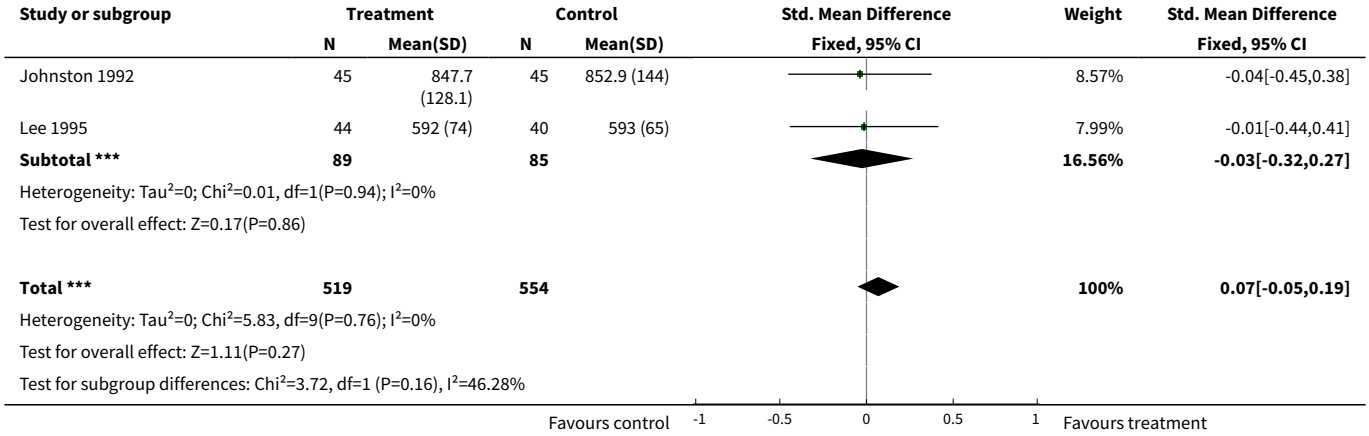
## Analysis 1.18. Comparison 1 Calcium supplementation vs placebo, Outcome 18 Upper limb BMD (mg/cm2) at longest point after supplement ceased by baseline calcium intake.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.18.1 Low baseline calcium** | | | | | | | |
| Chevalley 2005 | 110 | 24.7 (21.7) | 116 | 19.4 (19.2) | | 26.89% | 0.26[-0,0.52] |
| Dibba 2000 | 80 | 256 (43) | 80 | 242 (48) | | 18.98% | 0.31[-0.01,0.62] |
| Lee 1994 | 77 | 505 (45) | 82 | 505 (40) | | 19.07% | 0[-0.31,0.31] |
| Lee 1995 | 44 | 516 (44) | 40 | 517 (49) | | 10.06% | -0.02[-0.45,0.41] |
| **Subtotal ***** | **311** | | **318** | | | **75.01%** | **0.17[0.01,0.32]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=3.08, df=3(P=0.38); $I^2$=2.53% | | | | | | | |
| Test for overall effect: Z=2.09(P=0.04) | | | | | | | |
| **1.18.2 High baseline calcium** | | | | | | | |
| Bonjour 1995 | 67 | 429 (26.3) | 58 | 418 (32.7) | | 14.67% | 0.37[0.02,0.73] |
| Johnston 1992 | 43 | 365.2 (77.1) | 43 | 361.3 (74.8) | | 10.32% | 0.05[-0.37,0.47] |
| **Subtotal ***** | **110** | | **101** | | | **24.99%** | **0.24[-0.03,0.51]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=1.29, df=1(P=0.26); $I^2$=22.52% | | | | | | | |
| Test for overall effect: Z=1.72(P=0.08) | | | | | | | |
| **Total ***** | **421** | | **419** | | | **100%** | **0.19[0.05,0.32]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=4.57, df=5(P=0.47); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=2.67(P=0.01) | | | | | | | |
| Test for subgroup differences: $Chi^2$=0.2, df=1 (P=0.65), $I^2$=0% | | | | | | | |

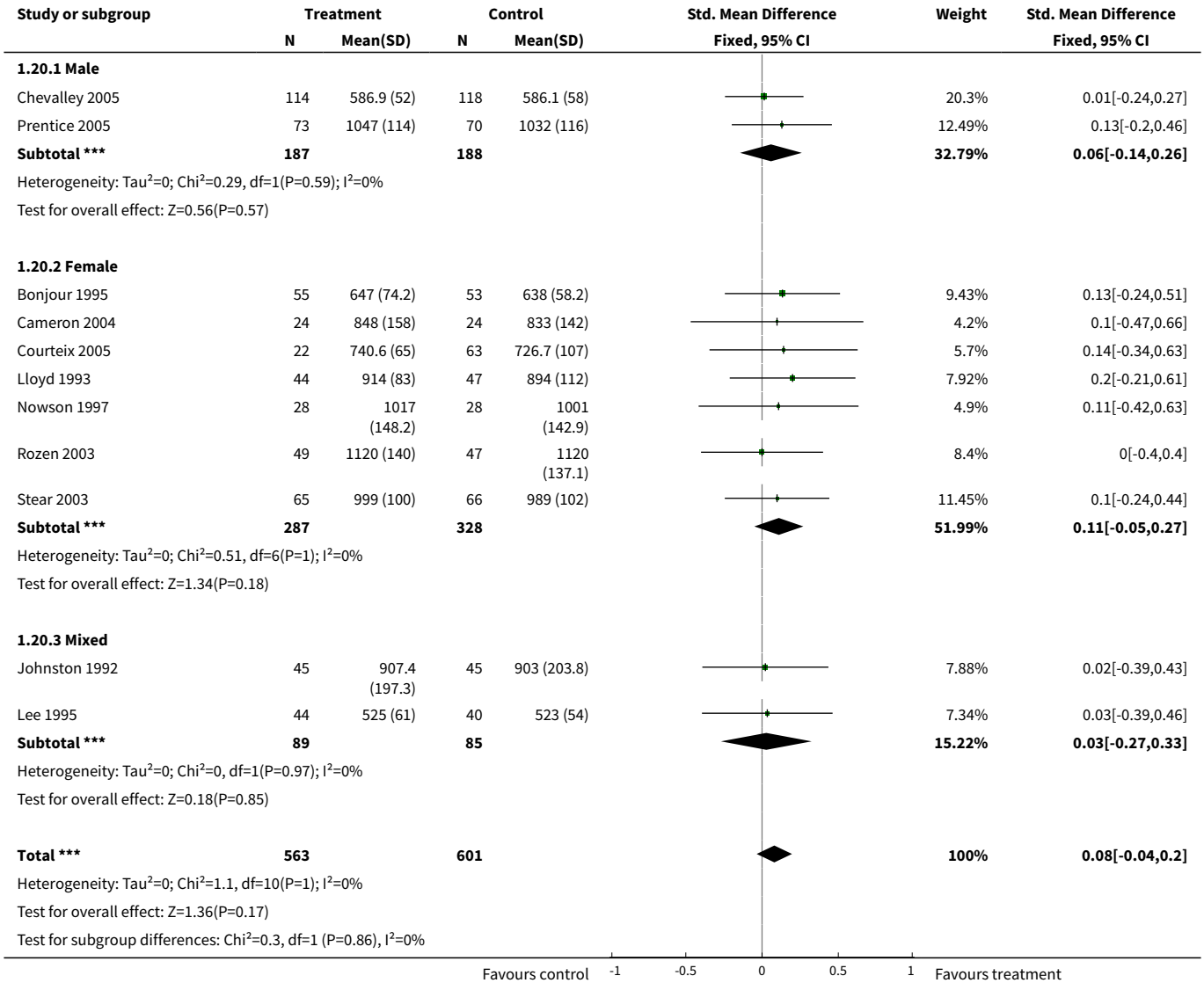



## Analysis 1.19. Comparison 1 Calcium supplementation vs placebo, Outcome 19 Femoral neck BMD (mg/cm2) (at end supplementation) by sex.

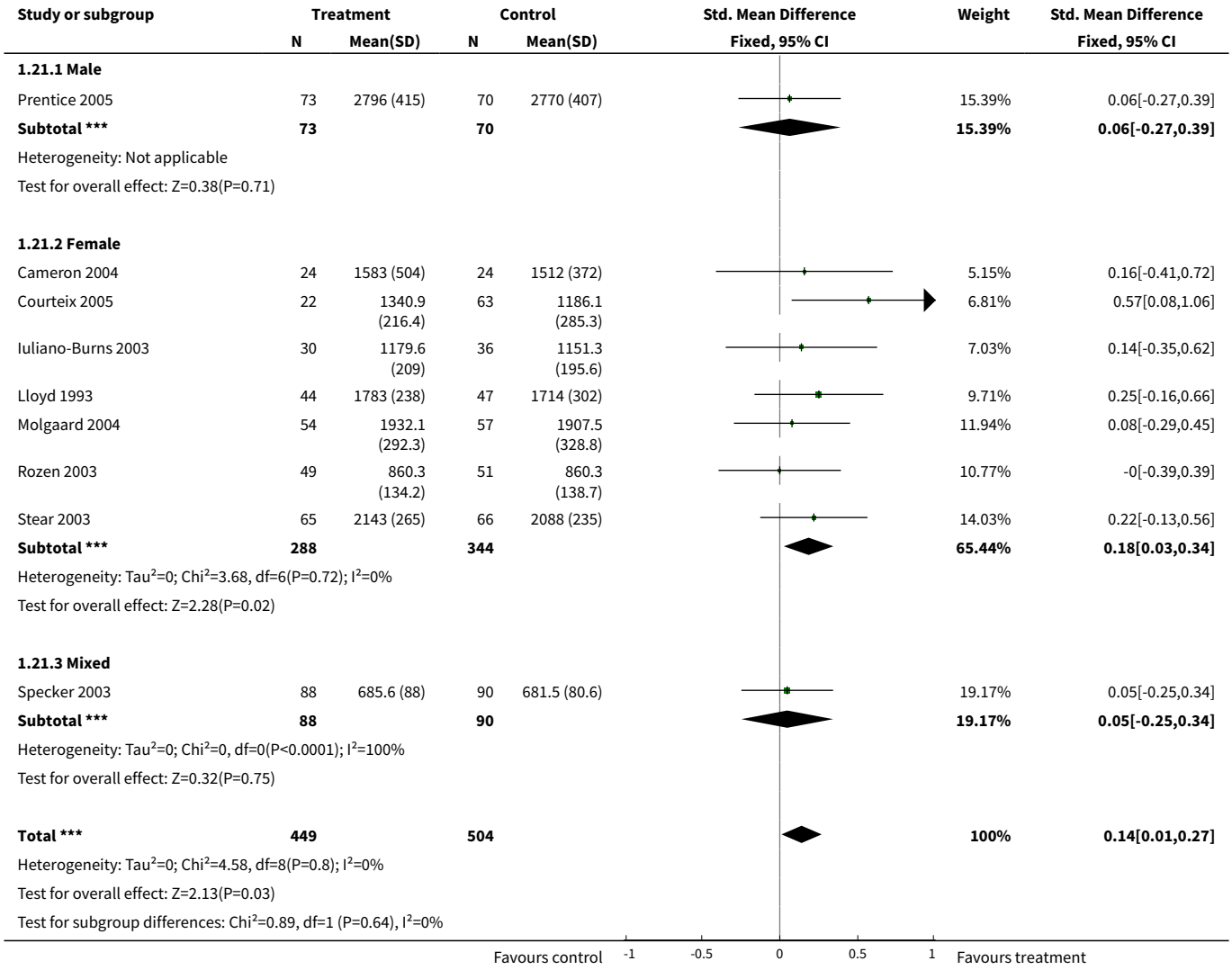
| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.19.1 Male** | | | | | | | |
| Chevalley 2005 | 114 | 698 (70) | 118 | 703.7 (68) | | 22.08% | -0.08[-0.34,0.18] |
| Prentice 2005 | 73 | 1001 (134) | 70 | 1002 (129) | | 13.62% | -0.01[-0.34,0.32] |
| **Subtotal ***** | **187** | | **188** | | | **35.7%** | **-0.05[-0.26,0.15]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.12, df=1(P=0.73); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.52(P=0.6) | | | | | | | |
| **1.19.2 Female** | | | | | | | |
| Bonjour 1995 | 55 | 656 (81.6) | 53 | 635 (65.5) | | 10.18% | 0.28[-0.1,0.66] |
| Cameron 2004 | 24 | 814 (131) | 24 | 816 (131) | | 4.57% | -0.02[-0.58,0.55] |
| Courteix 2005 | 22 | 772.5 (57.4) | 63 | 737 (93.8) | | 6.11% | 0.41[-0.08,0.9] |
| Nowson 1997 | 28 | 877 (90) | 28 | 871 (100.5) | | 5.33% | 0.06[-0.46,0.59] |
| Rozen 2003 | 49 | 1010 (70) | 47 | 1000 (137) | | 9.13% | 0.09[-0.31,0.49] |
| Stear 2003 | 65 | 870 (100) | 66 | 847 (107) | | 12.4% | 0.22[-0.12,0.56] |
| **Subtotal ***** | **243** | | **281** | | | **47.74%** | **0.19[0.02,0.37]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=1.98, df=5(P=0.85); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=2.16(P=0.03) | | | | | | | |
| **1.19.3 Mixed** | | | | | | | |



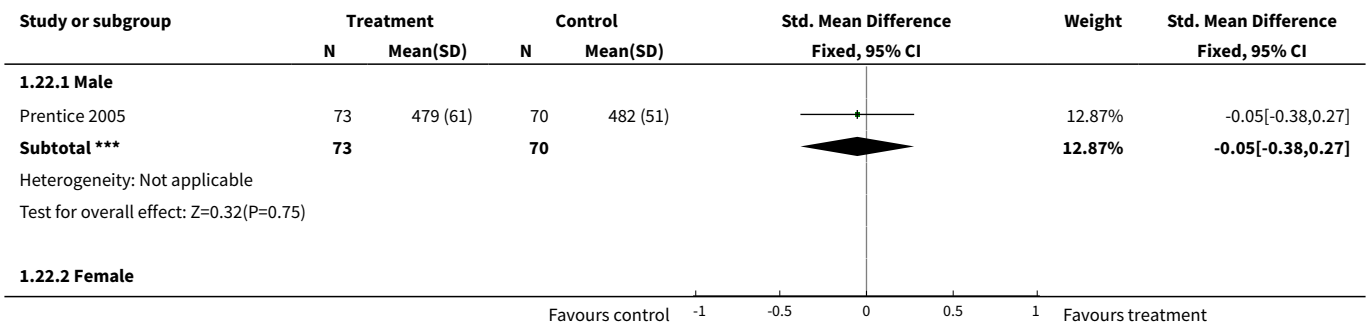

## Analysis 1.20. Comparison 1 Calcium supplementation vs placebo, Outcome 20 Lumbar spine BMD (mg/cm2) (at end supplementation) by sex.

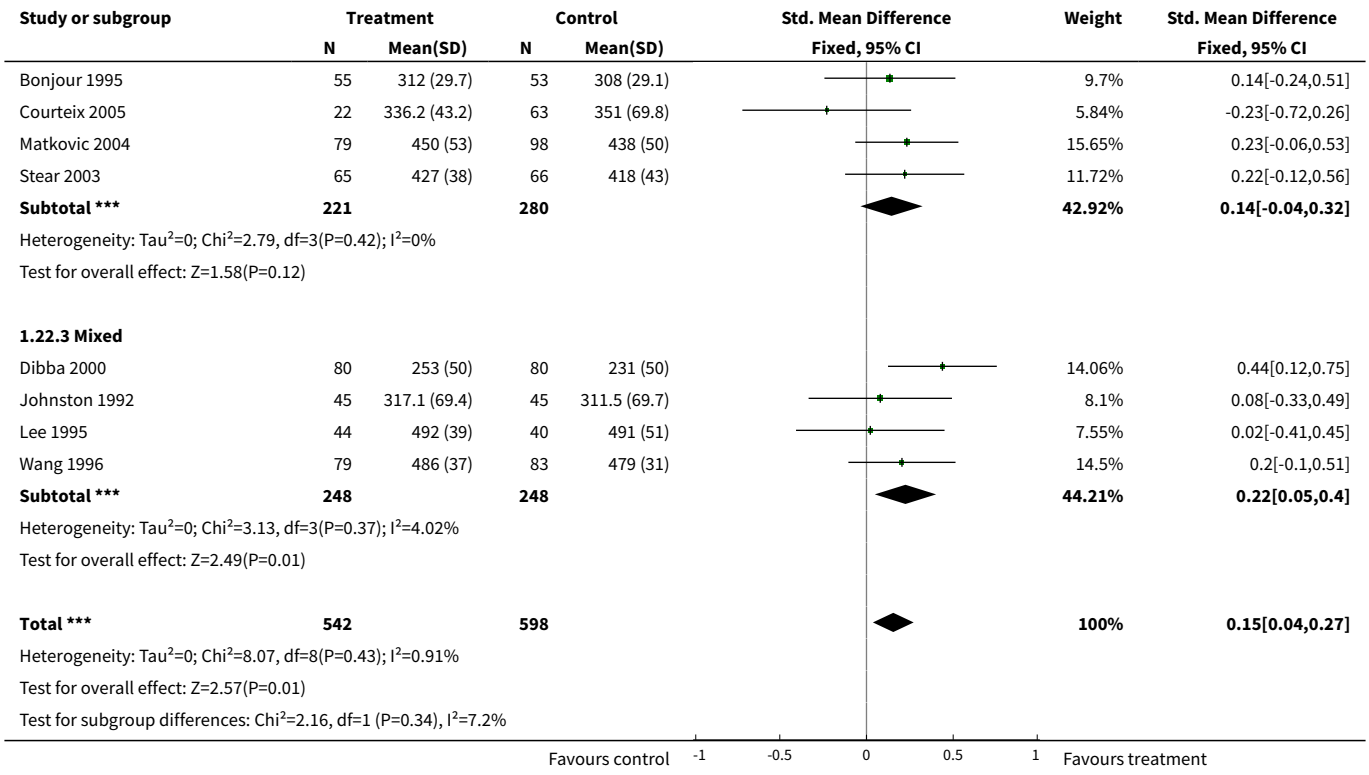


## Analysis 1.21. Comparison 1 Calcium supplementation vs placebo, Outcome 21 Total Body BMC (mg) (at end supplementation) by sex.




## Analysis 1.22. Comparison 1 Calcium supplementation vs placebo, Outcome 22 Distal Radius BMD (mg/cm2) (at end supplementation) by sex.

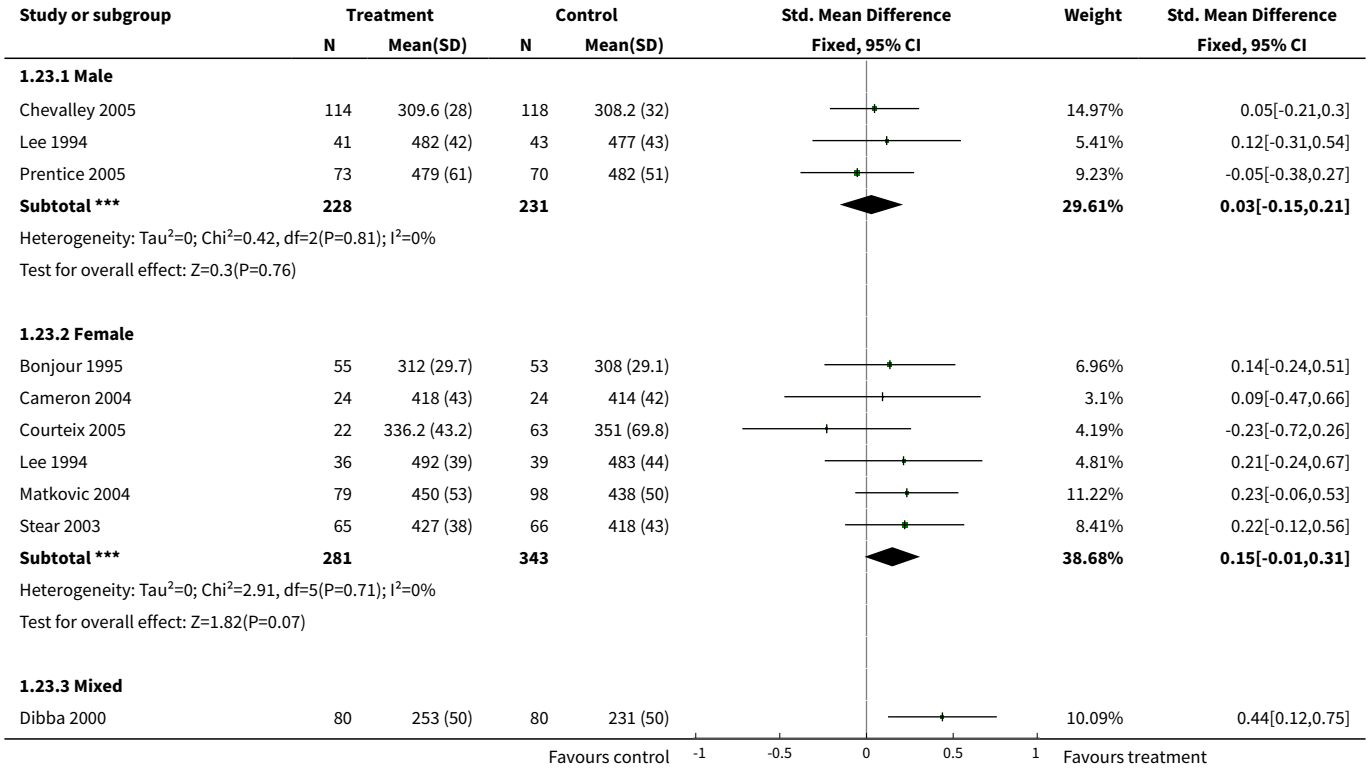




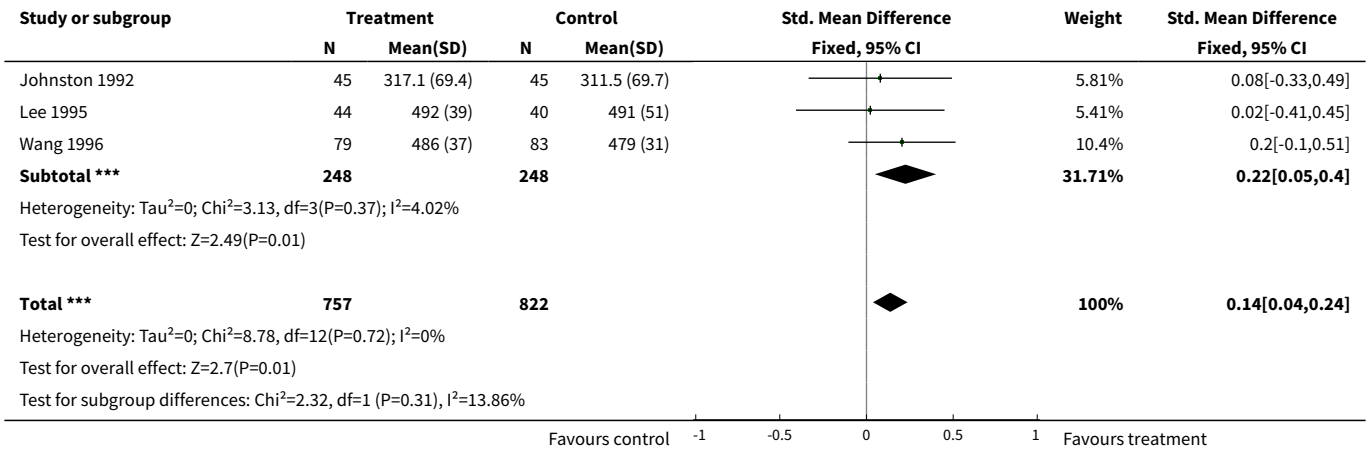
| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 9.7% | 0.14[-0.24,0.51] |
| Courteix 2005 | 22 | 336.2 (43.2) | 63 | 351 (69.8) | | 5.84% | -0.23[-0.72,0.26] |
| Matkovic 2004 | 79 | 450 (53) | 98 | 438 (50) | | 15.65% | 0.23[-0.06,0.53] |
| Stear 2003 | 65 | 427 (38) | 66 | 418 (43) | | 11.72% | 0.22[-0.12,0.56] |
| **Subtotal *** ** | **221** | | **280** | | | **42.92%** | **0.14[-0.04,0.32]** |
| Heterogeneity: Tau²=0; Chi²=2.79, df=3(P=0.42); I²=0% | | | | | | | |
| Test for overall effect: Z=1.58(P=0.12) | | | | | | | |
| **1.22.3 Mixed** | | | | | | | |
| Dibba 2000 | 80 | 253 (50) | 80 | 231 (50) | | 14.06% | 0.44[0.12,0.75] |
| Johnston 1992 | 45 | 317.1 (69.4) | 45 | 311.5 (69.7) | | 8.1% | 0.08[-0.33,0.49] |
| Lee 1995 | 44 | 492 (39) | 40 | 491 (51) | | 7.55% | 0.02[-0.41,0.45] |
| Wang 1996 | 79 | 486 (37) | 83 | 479 (31) | | 14.5% | 0.2[-0.1,0.51] |
| **Subtotal *** ** | **248** | | **248** | | | **44.21%** | **0.22[0.05,0.4]** |
| Heterogeneity: Tau²=0; Chi²=3.13, df=3(P=0.37); I²=4.02% | | | | | | | |
| Test for overall effect: Z=2.49(P=0.01) | | | | | | | |
| **Total *** ** | **542** | | **598** | | | **100%** | **0.15[0.04,0.27]** |
| Heterogeneity: Tau²=0; Chi²=8.07, df=8(P=0.43); I²=0.91% | | | | | | | |
| Test for overall effect: Z=2.57(P=0.01) | | | | | | | |
| Test for subgroup differences: Chi²=2.16, df=1 (P=0.34), I²=7.2% | | | | | | | |



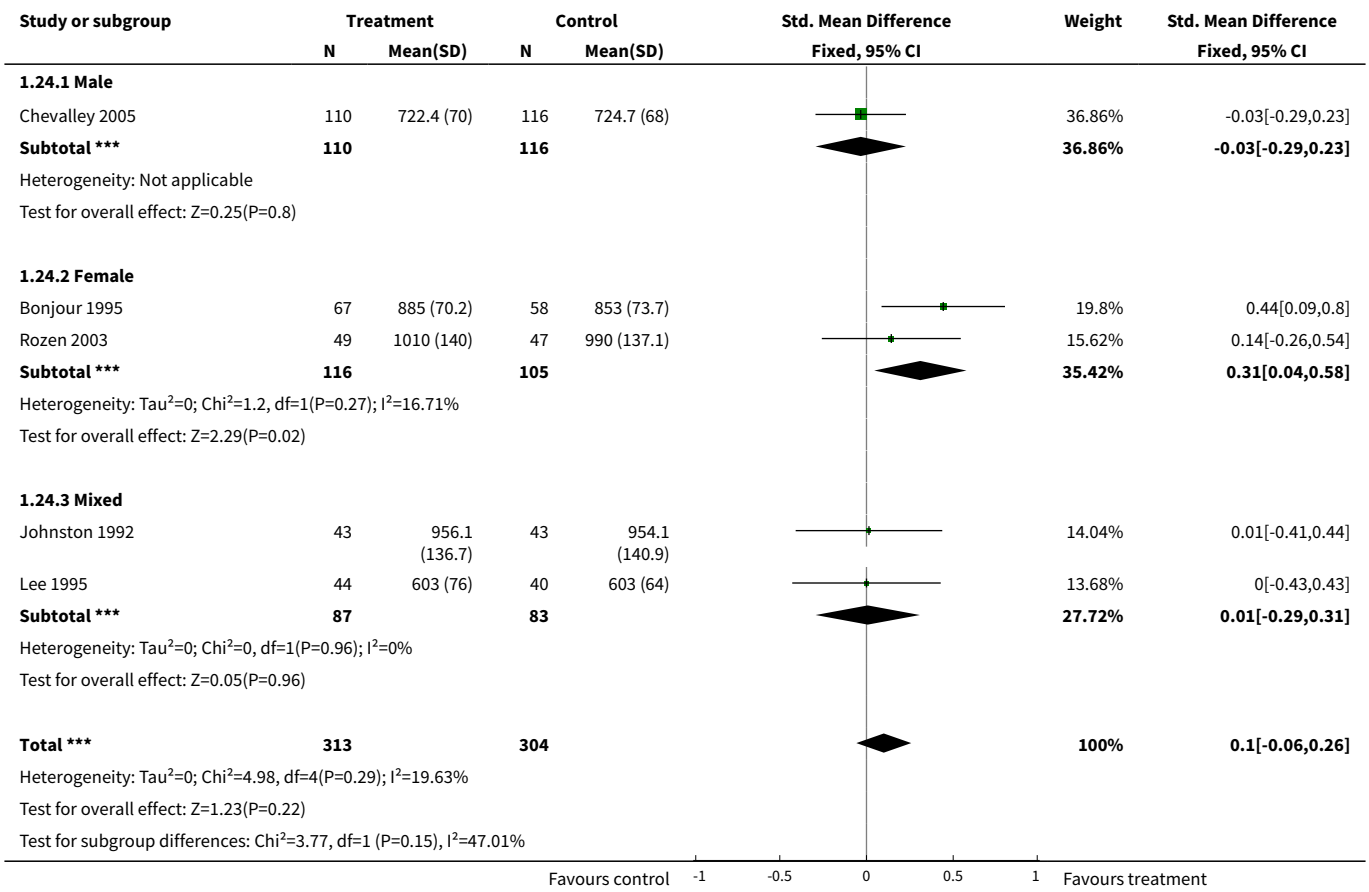
## Analysis 1.23. Comparison 1 Calcium supplementation vs placebo, Outcome 23 Upper Limb BMD (mg/cm2) (at end supplementation) by sex.



| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.23.1 Male** | | | | | | | |
| Chevalley 2005 | 114 | 309.6 (28) | 118 | 308.2 (32) | | 14.97% | 0.05[-0.21,0.3] |
| Lee 1994 | 41 | 482 (42) | 43 | 477 (43) | | 5.41% | 0.12[-0.31,0.54] |
| Prentice 2005 | 73 | 479 (61) | 70 | 482 (51) | | 9.23% | -0.05[-0.38,0.27] |
| **Subtotal *** ** | **228** | | **231** | | | **29.61%** | **0.03[-0.15,0.21]** |
| Heterogeneity: Tau²=0; Chi²=0.42, df=2(P=0.81); I²=0% | | | | | | | |
| Test for overall effect: Z=0.3(P=0.76) | | | | | | | |
| **1.23.2 Female** | | | | | | | |
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 6.96% | 0.14[-0.24,0.51] |
| Cameron 2004 | 24 | 418 (43) | 24 | 414 (42) | | 3.1% | 0.09[-0.47,0.66] |
| Courteix 2005 | 22 | 336.2 (43.2) | 63 | 351 (69.8) | | 4.19% | -0.23[-0.72,0.26] |
| Lee 1994 | 36 | 492 (39) | 39 | 483 (44) | | 4.81% | 0.21[-0.24,0.67] |
| Matkovic 2004 | 79 | 450 (53) | 98 | 438 (50) | | 11.22% | 0.23[-0.06,0.53] |
| Stear 2003 | 65 | 427 (38) | 66 | 418 (43) | | 8.41% | 0.22[-0.12,0.56] |
| **Subtotal *** ** | **281** | | **343** | | | **38.68%** | **0.15[-0.01,0.31]** |
| Heterogeneity: Tau²=0; Chi²=2.91, df=5(P=0.71); I²=0% | | | | | | | |
| Test for overall effect: Z=1.82(P=0.07) | | | | | | | |
| **1.23.3 Mixed** | | | | | | | |
| Dibba 2000 | 80 | 253 (50) | 80 | 231 (50) | | 10.09% | 0.44[0.12,0.75] |

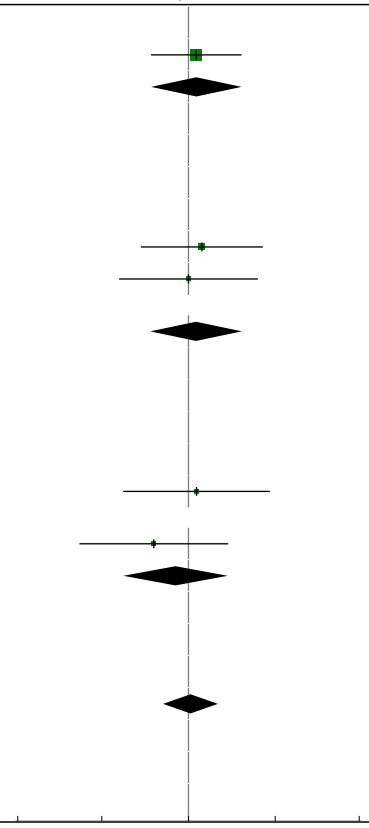



## Analysis 1.24. Comparison 1 Calcium supplementation vs placebo, Outcome 24 Femoral neck BMD (mg/cm2) at longest point after supplement ceased by sex.



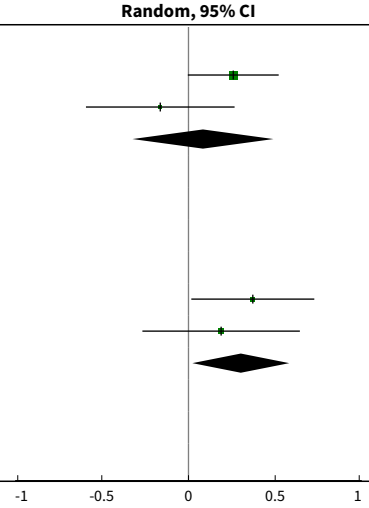
## Analysis 1.25. Comparison 1 Calcium supplementation vs placebo, Outcome 25 Lumbar spine BMD (mg/cm2) at longest point after supplement ceased by sex.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.25.1 Male** | | | | | | | |
| Chevalley 2005 | 110 | 605 (52) | 116 | 602.5 (58) | | 36.69% | 0.05[-0.22,0.31] |
| **Subtotal ***** | **110** | | **116** | | | **36.69%** | **0.05[-0.22,0.31]** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z=0.34(P=0.73) | | | | | | | |
| **1.25.2 Female** | | | | | | | |
| Bonjour 1995 | 67 | 1019 (70.2) | 58 | 1014 (57.3) | | 20.19% | 0.08[-0.27,0.43] |
| Rozen 2003 | 49 | 1150 (140) | 47 | 1150 (137.1) | | 15.59% | 0[-0.4,0.4] |
| **Subtotal ***** | **116** | | **105** | | | **35.79%** | **0.04[-0.22,0.31]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.08, df=1(P=0.78); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.32(P=0.75) | | | | | | | |
| **1.25.3 Mixed** | | | | | | | |
| Johnston 1992 | 43 | 1061.2 (192.3) | 43 | 1052.4 (185.5) | | 13.97% | 0.05[-0.38,0.47] |
| Lee 1995 | 44 | 538 (61) | 40 | 551 (68) | | 13.55% | -0.2[-0.63,0.23] |
| **Subtotal ***** | **87** | | **83** | | | **27.52%** | **-0.07[-0.38,0.23]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.64, df=1(P=0.42); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.49(P=0.63) | | | | | | | |
| **Total ***** | **313** | | **304** | | | **100%** | **0.01[-0.15,0.17]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=1.16, df=4(P=0.88); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.14(P=0.89) | | | | | | | |
| Test for subgroup differences: $Chi^2$=0.44, df=1 (P=0.8), $I^2$=0% | | | | | | | |




## Analysis 1.26. Comparison 1 Calcium supplementation vs placebo, Outcome 26 Upper limb BMD (mg/cm2) at longest point after supplement ceased by sex.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Random, 95% CI | Weight | Std. Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.26.1 Male** | | | | | | | |
| Chevalley 2005 | 110 | 24.7 (21.7) | 116 | 19.4 (19.2) | | 26.91% | 0.26[-0,0.52] |
| Lee 1994 | 41 | 497 (47) | 43 | 504 (38) | | 10.05% | -0.16[-0.59,0.27] |
| **Subtotal ***** | **151** | | **159** | | | **36.96%** | **0.08[-0.32,0.49]** |
| Heterogeneity: $Tau^2$=0.06; $Chi^2$=2.7, df=1(P=0.1); $I^2$=62.94% | | | | | | | |
| Test for overall effect: Z=0.4(P=0.69) | | | | | | | |
| **1.26.2 Female** | | | | | | | |
| Bonjour 1995 | 67 | 429 (26.3) | 58 | 418 (32.7) | | 14.68% | 0.37[0.02,0.73] |
| Lee 1994 | 36 | 514 (41) | 39 | 506 (43) | | 8.96% | 0.19[-0.27,0.64] |
| **Subtotal ***** | **103** | | **97** | | | **23.64%** | **0.3[0.02,0.58]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.39, df=1(P=0.53); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=2.12(P=0.03) | | | | | | | |



| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Random, 95% CI | Weight | Std. Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.26.3 Mixed** | | | | | | | |
| Dibba 2000 | 80 | 256 (43) | 80 | 242 (48) | | 19% | 0.31[-0.01,0.62] |
| Johnston 1992 | 43 | 365.2 (77.1) | 43 | 361.3 (74.8) | | 10.33% | 0.05[-0.37,0.47] |
| Lee 1995 | 44 | 516 (44) | 40 | 517 (49) | | 10.07% | -0.02[-0.45,0.41] |
| **Subtotal ***** | **167** | | **163** | | | **39.4%** | **0.16[-0.06,0.37]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=1.78, df=2(P=0.41); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.41(P=0.16) | | | | | | | |
| **Total ***** | **421** | | **419** | | | **100%** | **0.19[0.05,0.32]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=5.74, df=6(P=0.45); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=2.68(P=0.01) | | | | | | | |
| Test for subgroup differences: $Chi^2$=0.87, df=1 (P=0.65), $I^2$=0% | | | | | | | |




## Analysis 1.27. Comparison 1 Calcium supplementation vs placebo, Outcome 27 Femoral neck BMD (mg/cm2) (at end supplementation) by pubertal status.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.27.1 Pre-pubertal** | | | | | | | |
| Bonjour 1995 | 55 | 656 (81.6) | 53 | 635 (65.5) | | 11.21% | 0.28[-0.1,0.66] |
| Cameron 2004 | 24 | 814 (131) | 24 | 816 (131) | | 5.03% | -0.02[-0.58,0.55] |
| Chevalley 2005 | 114 | 698 (70) | 118 | 703.7 (68) | | 24.3% | -0.08[-0.34,0.18] |
| Courteix 2005 | 22 | 772.5 (57.4) | 63 | 737 (93.8) | | 6.73% | 0.41[-0.08,0.9] |
| Lee 1995 | 44 | 592 (74) | 40 | 593 (65) | | 8.79% | -0.01[-0.44,0.41] |
| **Subtotal ***** | **259** | | **298** | | | **56.06%** | **0.07[-0.1,0.24]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=4.61, df=4(P=0.33); $I^2$=13.14% | | | | | | | |
| Test for overall effect: Z=0.76(P=0.45) | | | | | | | |
| **1.27.2 Peri-pubertal** | | | | | | | |
| **Subtotal ***** | **0** | | **0** | | | | **Not estimable** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Not applicable | | | | | | | |
| **1.27.3 Post-pubertal** | | | | | | | |
| Prentice 2005 | 73 | 1001 (134) | 70 | 1002 (129) | | 14.99% | -0.01[-0.34,0.32] |
| Stear 2003 | 65 | 870 (100) | 66 | 847 (107) | | 13.65% | 0.22[-0.12,0.56] |
| **Subtotal ***** | **138** | | **136** | | | **28.64%** | **0.1[-0.14,0.34]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.89, df=1(P=0.35); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.84(P=0.4) | | | | | | | |
| **1.27.4 Mixed** | | | | | | | |
| Johnston 1992 | 45 | 847.7 (128.1) | 45 | 852.9 (144) | | 9.44% | -0.04[-0.45,0.38] |
| Nowson 1997 | 28 | 877 (90) | 28 | 871 (100.5) | | 5.87% | 0.06[-0.46,0.59] |
| **Subtotal ***** | **73** | | **73** | | | **15.31%** | **0[-0.32,0.33]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.09, df=1(P=0.77); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0(P=1) | | | | | | | |

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **Total ***** | **470** | | **507** | | | **100%** | **0.07[-0.06,0.19]** |
| Heterogeneity: Tau²=0; Chi²=5.82, df=8(P=0.67); I²=0% | | | | | | | |
| Test for overall effect: Z=1.02(P=0.31) | | | | | | | |
| Test for subgroup differences: Chi²=0.24, df=1 (P=0.89), I²=0% | | | | | | | |

Favours control -1 -0.5 0 0.5 1 Favours treatment

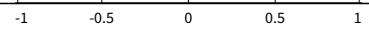
## Analysis 1.28. Comparison 1 Calcium supplementation vs placebo, Outcome 28 Lumbar spine BMD (mg/cm2) (at end supplementation) by pubertal status.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.28.1 Pre-pubertal** | | | | | | | |
| Bonjour 1995 | 55 | 647 (74.2) | 53 | 638 (58.2) | | 10.3% | 0.13[-0.24,0.51] |
| Cameron 2004 | 24 | 848 (158) | 24 | 833 (142) | | 4.58% | 0.1[-0.47,0.66] |
| Chevalley 2005 | 114 | 586.9 (52) | 118 | 586.1 (58) | | 22.17% | 0.01[-0.24,0.27] |
| Courteix 2005 | 22 | 740.6 (65) | 63 | 726.7 (107) | | 6.22% | 0.14[-0.34,0.63] |
| Lee 1995 | 44 | 525 (61) | 40 | 523 (54) | | 8.01% | 0.03[-0.39,0.46] |
| **Subtotal ***** | **259** | | **298** | | | **51.27%** | **0.06[-0.1,0.23]** |
| Heterogeneity: Tau²=0; Chi²=0.4, df=4(P=0.98); I²=0% | | | | | | | |
| Test for overall effect: Z=0.75(P=0.46) | | | | | | | |
| **1.28.2 Peri-pubertal** | | | | | | | |
| **Subtotal ***** | **0** | | **0** | | | | **Not estimable** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Not applicable | | | | | | | |
| **1.28.3 Post-pubertal** | | | | | | | |
| Prentice 2005 | 73 | 1047 (114) | 70 | 1032 (116) | | 13.63% | 0.13[-0.2,0.46] |
| Stear 2003 | 65 | 999 (100) | 66 | 989 (102) | | 12.5% | 0.1[-0.24,0.44] |
| **Subtotal ***** | **138** | | **136** | | | **26.14%** | **0.11[-0.12,0.35]** |
| Heterogeneity: Tau²=0; Chi²=0.02, df=1(P=0.9); I²=0% | | | | | | | |
| Test for overall effect: Z=0.95(P=0.34) | | | | | | | |
| **1.28.4 Mixed** | | | | | | | |
| Johnston 1992 | 45 | 907.4 (197.3) | 45 | 903 (203.8) | | 8.6% | 0.02[-0.39,0.43] |
| Lloyd 1993 | 44 | 914 (83) | 47 | 894 (112) | | 8.64% | 0.2[-0.21,0.61] |
| Nowson 1997 | 28 | 1017 (148.2) | 28 | 1001 (142.9) | | 5.34% | 0.11[-0.42,0.63] |
| **Subtotal ***** | **117** | | **120** | | | **22.59%** | **0.11[-0.14,0.37]** |
| Heterogeneity: Tau²=0; Chi²=0.36, df=2(P=0.84); I²=0% | | | | | | | |
| Test for overall effect: Z=0.85(P=0.4) | | | | | | | |
| **Total ***** | **514** | | **554** | | | **100%** | **0.09[-0.03,0.21]** |
| Heterogeneity: Tau²=0; Chi²=0.93, df=9(P=1); I²=0% | | | | | | | |
| Test for overall effect: Z=1.42(P=0.15) | | | | | | | |
| Test for subgroup differences: Chi²=0.15, df=1 (P=0.93), I²=0% | | | | | | | |

Favours control -1 -0.5 0 0.5 1 Favours treatment

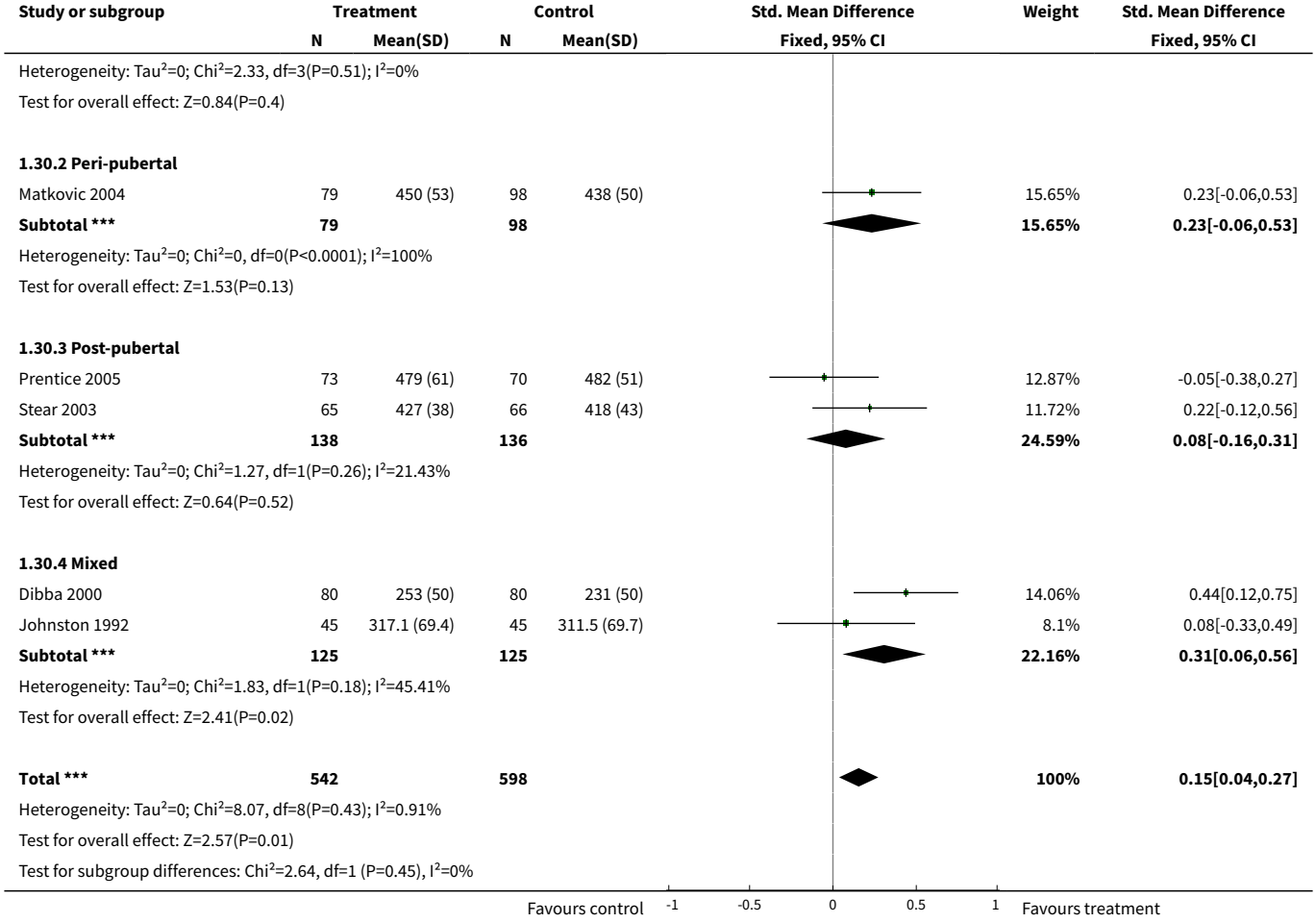
## Analysis 1.29. Comparison 1 Calcium supplementation vs placebo, Outcome 29 Total body BMC (mg) (at end supplementation) by pubertal status.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.29.1 Pre-pubertal** | | | | | | | |
| Cameron 2004 | 24 | 1583 (504) | 24 | 1512 (372) | | 5.78% | 0.16[-0.41,0.72] |
| Courteix 2005 | 22 | 1340.9 (216.4) | 63 | 1186.1 (285.3) | | 7.63% | 0.57[0.08,1.06] |
| Specker 2003 | 88 | 685.6 (88) | 90 | 681.5 (80.6) | | 21.48% | 0.05[-0.25,0.34] |
| **Subtotal ***** | **134** | | **177** | | | **34.88%** | **0.18[-0.05,0.41]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=3.17, df=2(P=0.2); $I^2$=36.98% | | | | | | | |
| Test for overall effect: Z=1.53(P=0.13) | | | | | | | |
| **1.29.2 Peri-pubertal** | | | | | | | |
| **Subtotal ***** | **0** | | **0** | | | | **Not estimable** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Not applicable | | | | | | | |
| **1.29.3 Post-pubertal** | | | | | | | |
| Prentice 2005 | 73 | 2796 (415) | 70 | 2770 (407) | | 17.25% | 0.06[-0.27,0.39] |
| Stear 2003 | 65 | 2143 (265) | 66 | 2088 (235) | | 15.72% | 0.22[-0.13,0.56] |
| **Subtotal ***** | **138** | | **136** | | | **32.97%** | **0.14[-0.1,0.37]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.41, df=1(P=0.52); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.13(P=0.26) | | | | | | | |
| **1.29.4 Mixed** | | | | | | | |
| Iuliano-Burns 2003 | 30 | 1179.6 (209) | 36 | 1151.3 (195.6) | | 7.88% | 0.14[-0.35,0.62] |
| Lloyd 1993 | 44 | 1783 (238) | 47 | 1714 (302) | | 10.89% | 0.25[-0.16,0.66] |
| Molgaard 2004 | 54 | 1932.1 (292.3) | 57 | 1907.5 (328.8) | | 13.38% | 0.08[-0.29,0.45] |
| **Subtotal ***** | **128** | | **140** | | | **32.15%** | **0.15[-0.09,0.39]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.37, df=2(P=0.83); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.24(P=0.22) | | | | | | | |
| **Total ***** | **400** | | **453** | | | **100%** | **0.16[0.02,0.29]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=4.03, df=7(P=0.78); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=2.25(P=0.02) | | | | | | | |
| Test for subgroup differences: $Chi^2$=0.07, df=1 (P=0.97), $I^2$=0% | | | | | | | |

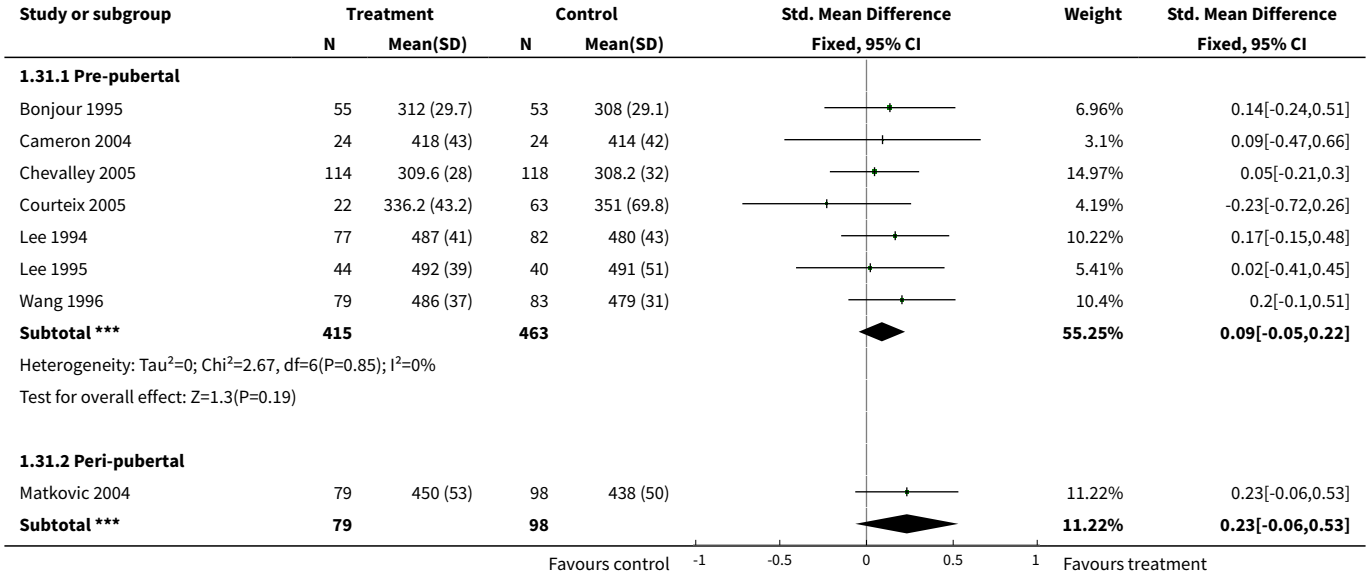


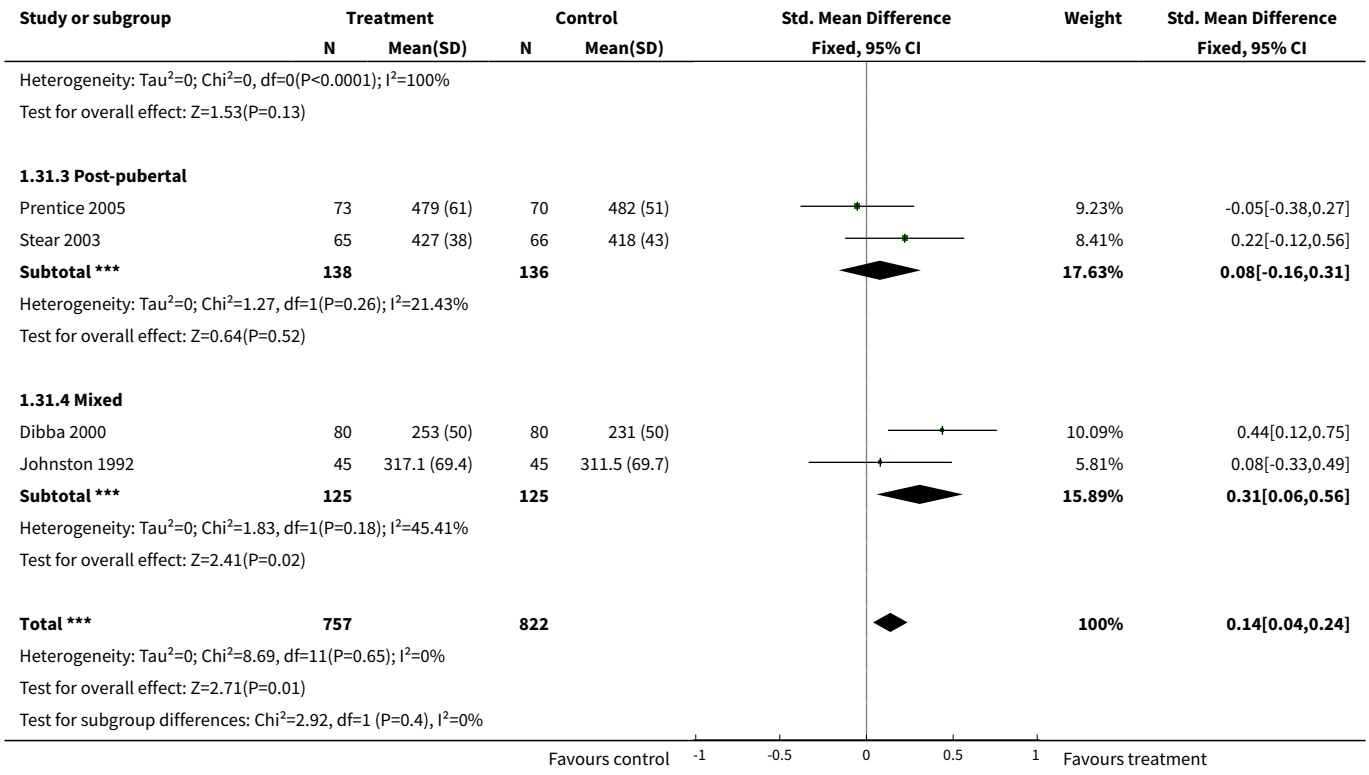

## Analysis 1.30. Comparison 1 Calcium supplementation vs placebo, Outcome 30 Distal radius BMD (mg/cm2) (at end supplementation) by pubertal status.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.30.1 Pre-pubertal** | | | | | | | |
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 9.7% | 0.14[-0.24,0.51] |
| Courteix 2005 | 22 | 336.2 (43.2) | 63 | 351 (69.8) | | 5.84% | -0.23[-0.72,0.26] |
| Lee 1995 | 44 | 492 (39) | 40 | 491 (51) | | 7.55% | 0.02[-0.41,0.45] |
| Wang 1996 | 79 | 486 (37) | 83 | 479 (31) | | 14.5% | 0.2[-0.1,0.51] |
| **Subtotal ***** | **200** | | **239** | | | **37.59%** | **0.08[-0.11,0.27]** |

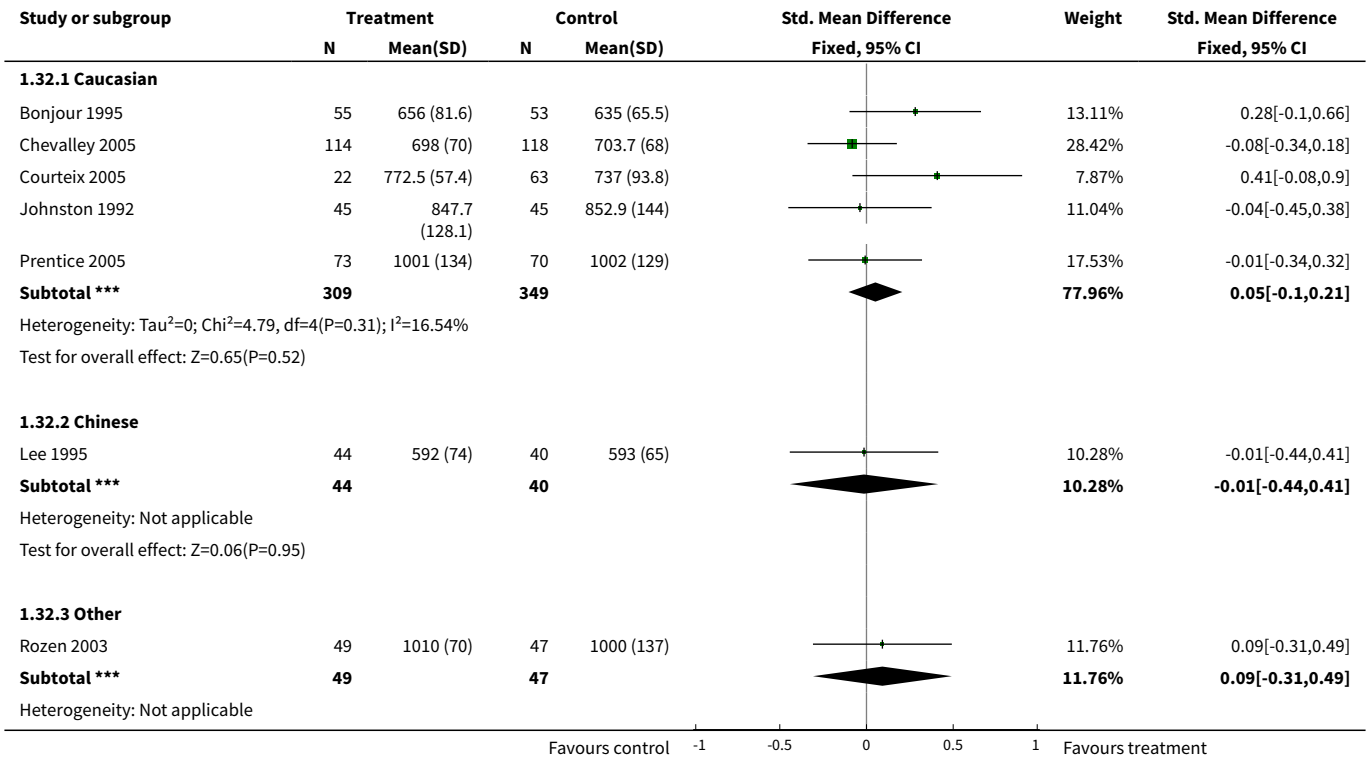



## Analysis 1.31. Comparison 1 Calcium supplementation vs placebo, Outcome 31 Upper limb BMD (mg/cm2) (at end supplementation) by pubertal status.

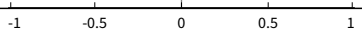





## Analysis 1.32. Comparison 1 Calcium supplementation vs placebo, Outcome 32 Femoral neck BMD (mg/cm2) (at end supplementation) by ethnicity.

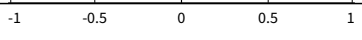


| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Test for overall effect: Z=0.45(P=0.65) | | | | | | | |
| **Total ***** | **402** | | **436** | | | **100%** | **0.05[-0.09,0.19]** |
| Heterogeneity: Tau²=0; Chi²=4.92, df=6(P=0.55); I²=0% | | | | | | | |
| Test for overall effect: Z=0.71(P=0.48) | | | | | | | |
| Test for subgroup differences: Chi²=0.13, df=1 (P=0.94), I²=0% | | | | | | | |



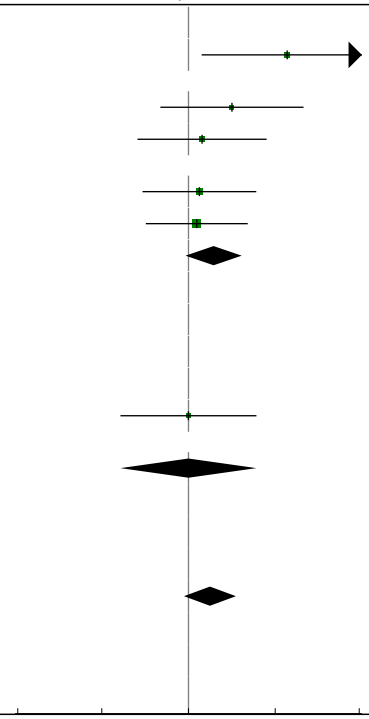

## Analysis 1.33. Comparison 1 Calcium supplementation vs placebo, Outcome 33 Lumbar spine BMD (mg/cm2) (at end supplementation) by ethnicity.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.33.1 Caucasian** | | | | | | | |
| Bonjour 1995 | 55 | 647 (74.2) | 53 | 638 (58.2) | | 11.87% | 0.13[-0.24,0.51] |
| Chevalley 2005 | 114 | 586.9 (52) | 118 | 586.1 (58) | | 25.56% | 0.01[-0.24,0.27] |
| Courteix 2005 | 22 | 740.6 (65) | 63 | 726.7 (107) | | 7.17% | 0.14[-0.34,0.63] |
| Johnston 1992 | 45 | 907.4 (197.3) | 45 | 903 (203.8) | | 9.92% | 0.02[-0.39,0.43] |
| Lloyd 1993 | 44 | 914 (83) | 47 | 894 (112) | | 9.96% | 0.2[-0.21,0.61] |
| Prentice 2005 | 73 | 1047 (114) | 70 | 1032 (116) | | 15.72% | 0.13[-0.2,0.46] |
| **Subtotal ***** | **353** | | **396** | | | **80.19%** | **0.09[-0.06,0.24]** |
| Heterogeneity: Tau²=0; Chi²=0.86, df=5(P=0.97); I²=0% | | | | | | | |
| Test for overall effect: Z=1.21(P=0.22) | | | | | | | |
| **1.33.2 Chinese** | | | | | | | |
| Lee 1995 | 44 | 525 (61) | 40 | 523 (54) | | 9.23% | 0.03[-0.39,0.46] |
| **Subtotal ***** | **44** | | **40** | | | **9.23%** | **0.03[-0.39,0.46]** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z=0.16(P=0.88) | | | | | | | |
| **1.33.3 Other** | | | | | | | |
| Rozen 2003 | 49 | 1120 (140) | 47 | 1120 (137.1) | | 10.57% | 0[-0.4,0.4] |
| **Subtotal ***** | **49** | | **47** | | | **10.57%** | **0[-0.4,0.4]** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Not applicable | | | | | | | |
| **Total ***** | **446** | | **483** | | | **100%** | **0.08[-0.05,0.21]** |
| Heterogeneity: Tau²=0; Chi²=1.07, df=7(P=0.99); I²=0% | | | | | | | |
| Test for overall effect: Z=1.14(P=0.26) | | | | | | | |
| Test for subgroup differences: Chi²=0.21, df=1 (P=0.9), I²=0% | | | | | | | |



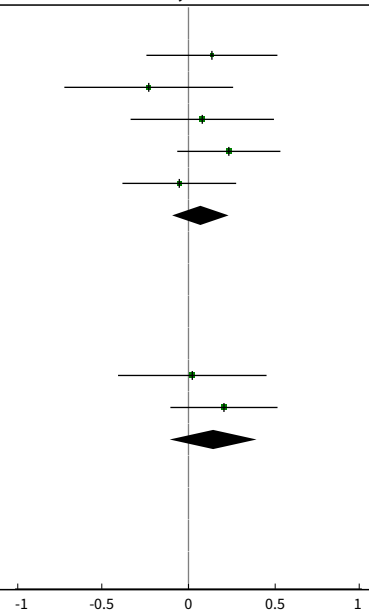
## Analysis 1.34. Comparison 1 Calcium supplementation vs placebo, Outcome 34 Total body BMC (mg) (at end supplementation) by ethnicity.

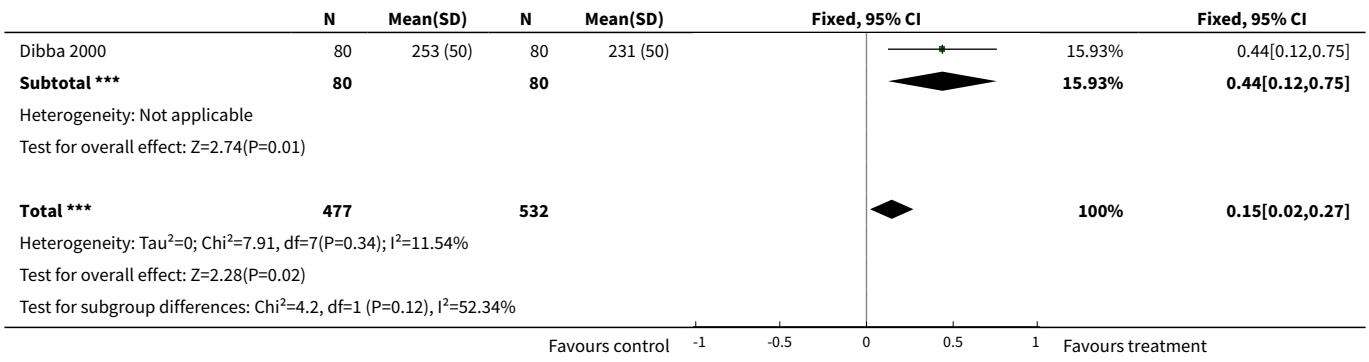
| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.34.1 Caucasian** | | | | | | | |
| Courteix 2005 | 22 | 1340.9 (216.4) | 63 | 1186.1 (285.3) | | 9.22% | 0.57[0.08,1.06] |
| Lloyd 1993 | 44 | 1783 (238) | 47 | 1714 (302) | | 13.16% | 0.25[-0.16,0.66] |
| Molgaard 2004 | 54 | 1932.1 (292.3) | 57 | 1907.5 (328.8) | | 16.18% | 0.08[-0.29,0.45] |
| Prentice 2005 | 73 | 2796 (415) | 70 | 2770 (407) | | 20.86% | 0.06[-0.27,0.39] |
| Specker 2003 | 88 | 685.6 (88) | 90 | 681.5 (80.6) | | 25.98% | 0.05[-0.25,0.34] |
| **Subtotal ***** | **281** | | **327** | | | **85.41%** | **0.14[-0.02,0.31]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=3.88, df=4(P=0.42); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.75(P=0.08) | | | | | | | |
| **1.34.2 Other** | | | | | | | |
| Rozen 2003 | 49 | 860.3 (134.2) | 51 | 860.3 (138.7) | | 14.59% | -0[-0.39,0.39] |
| **Subtotal ***** | **49** | | **51** | | | **14.59%** | **-0[-0.39,0.39]** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z=0(P=1) | | | | | | | |
| **Total ***** | **330** | | **378** | | | **100%** | **0.12[-0.03,0.27]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=4.33, df=5(P=0.5); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.62(P=0.11) | | | | | | | |
| Test for subgroup differences: $Chi^2$=0.45, df=1 (P=0.5), $I^2$=0% | | | | | | | |



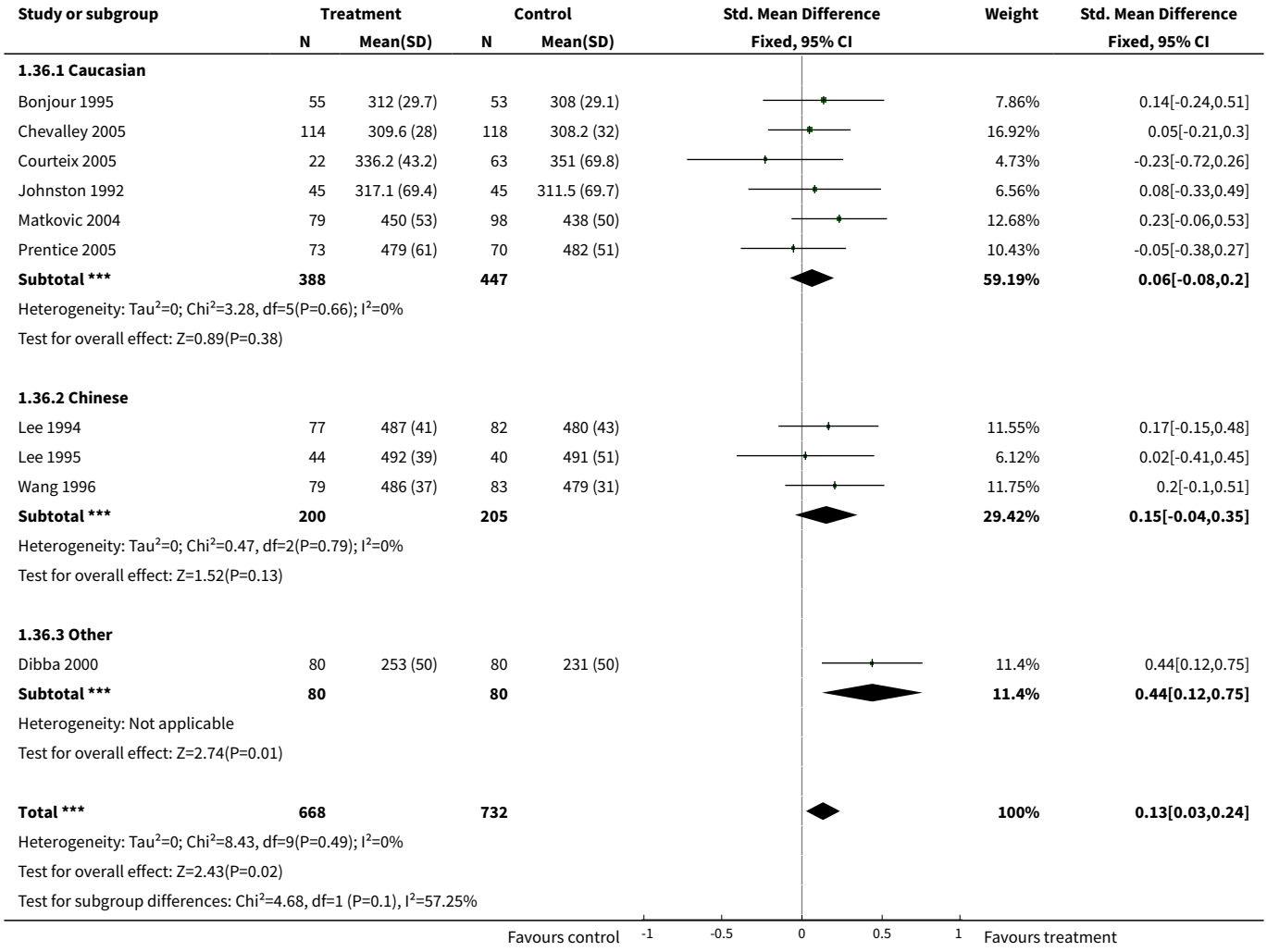

## Analysis 1.35. Comparison 1 Calcium supplementation vs placebo, Outcome 35 Distal radius BMD (mg/cm2) (at end supplementation) by ethnicity.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.35.1 Caucasian** | | | | | | | |
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 10.99% | 0.14[-0.24,0.51] |
| Courteix 2005 | 22 | 336.2 (43.2) | 63 | 351 (69.8) | | 6.62% | -0.23[-0.72,0.26] |
| Johnston 1992 | 45 | 317.1 (69.4) | 45 | 311.5 (69.7) | | 9.17% | 0.08[-0.33,0.49] |
| Matkovic 2004 | 79 | 450 (53) | 98 | 438 (50) | | 17.73% | 0.23[-0.06,0.53] |
| Prentice 2005 | 73 | 479 (61) | 70 | 482 (51) | | 14.58% | -0.05[-0.38,0.27] |
| **Subtotal ***** | **274** | | **329** | | | **59.09%** | **0.07[-0.09,0.23]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=3.26, df=4(P=0.52); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.82(P=0.41) | | | | | | | |
| **1.35.2 Chinese** | | | | | | | |
| Lee 1995 | 44 | 492 (39) | 40 | 491 (51) | | 8.55% | 0.02[-0.41,0.45] |
| Wang 1996 | 79 | 486 (37) | 83 | 479 (31) | | 16.43% | 0.2[-0.1,0.51] |
| **Subtotal ***** | **123** | | **123** | | | **24.98%** | **0.14[-0.11,0.39]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.46, df=1(P=0.5); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.11(P=0.27) | | | | | | | |
| **1.35.3 Other** | | | | | | | |



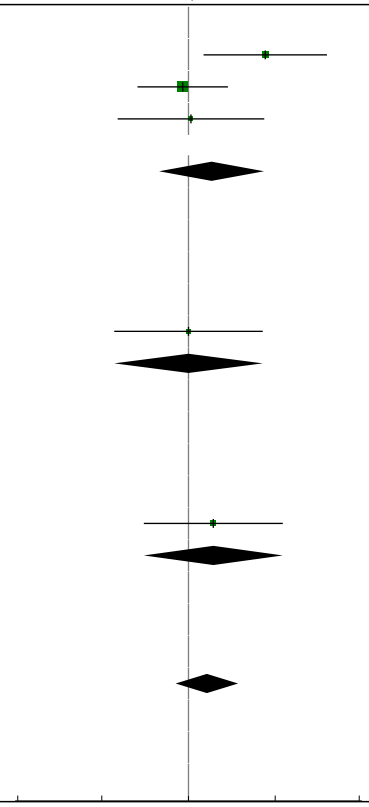



## Analysis 1.36. Comparison 1 Calcium supplementation vs placebo, Outcome 36 Upper limb BMD (mg/cm2) (at end supplementation) by ethnicity.



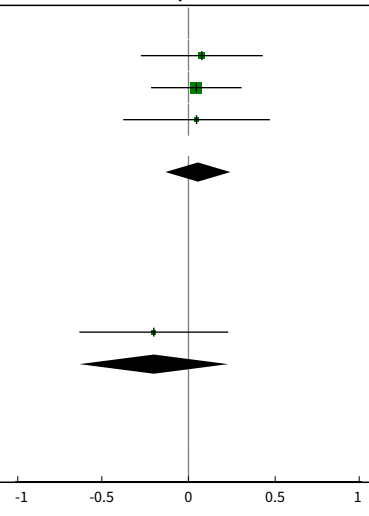
## Analysis 1.37. Comparison 1 Calcium supplementation vs placebo, Outcome 37 Femoral neck BMD (mg/cm2) at longest point after supplementation ceased by ethnicity.

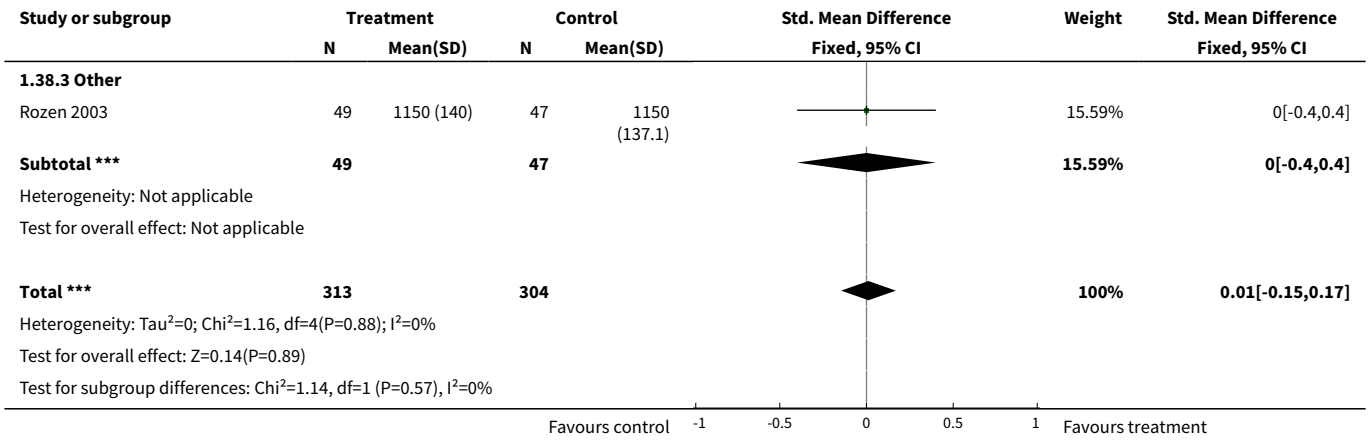
| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Random, 95% CI | Weight | Std. Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.37.1 Caucasian** | | | | | | | |
| Bonjour 1995 | 67 | 885 (70.2) | 58 | 853 (73.7) | | 20.41% | 0.44[0.09,0.8] |
| Chevalley 2005 | 110 | 722.4 (70) | 116 | 724.7 (68) | | 32.35% | -0.03[-0.29,0.23] |
| Johnston 1992 | 43 | 956.1 (136.7) | 43 | 954.1 (140.9) | | 15.38% | 0.01[-0.41,0.44] |
| **Subtotal ***** | **220** | | **217** | | | **68.14%** | **0.13[-0.17,0.44]** |
| Heterogeneity: $Tau^2$=0.04; $Chi^2$=4.71, df=2(P=0.09); $I^2$=57.57% | | | | | | | |
| Test for overall effect: Z=0.86(P=0.39) | | | | | | | |
| **1.37.2 Chinese** | | | | | | | |
| Lee 1995 | 44 | 603 (76) | 40 | 603 (64) | | 15.04% | 0[-0.43,0.43] |
| **Subtotal ***** | **44** | | **40** | | | **15.04%** | **0[-0.43,0.43]** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Not applicable | | | | | | | |
| **1.37.3 Other** | | | | | | | |
| Rozen 2003 | 49 | 1010 (140) | 47 | 990 (137.1) | | 16.82% | 0.14[-0.26,0.54] |
| **Subtotal ***** | **49** | | **47** | | | **16.82%** | **0.14[-0.26,0.54]** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z=0.7(P=0.48) | | | | | | | |
| **Total ***** | **313** | | **304** | | | **100%** | **0.11[-0.07,0.29]** |
| Heterogeneity: $Tau^2$=0.01; $Chi^2$=4.98, df=4(P=0.29); $I^2$=19.63% | | | | | | | |
| Test for overall effect: Z=1.15(P=0.25) | | | | | | | |
| Test for subgroup differences: $Chi^2$=0.26, df=1 (P=0.88), $I^2$=0% | | | | | | | |



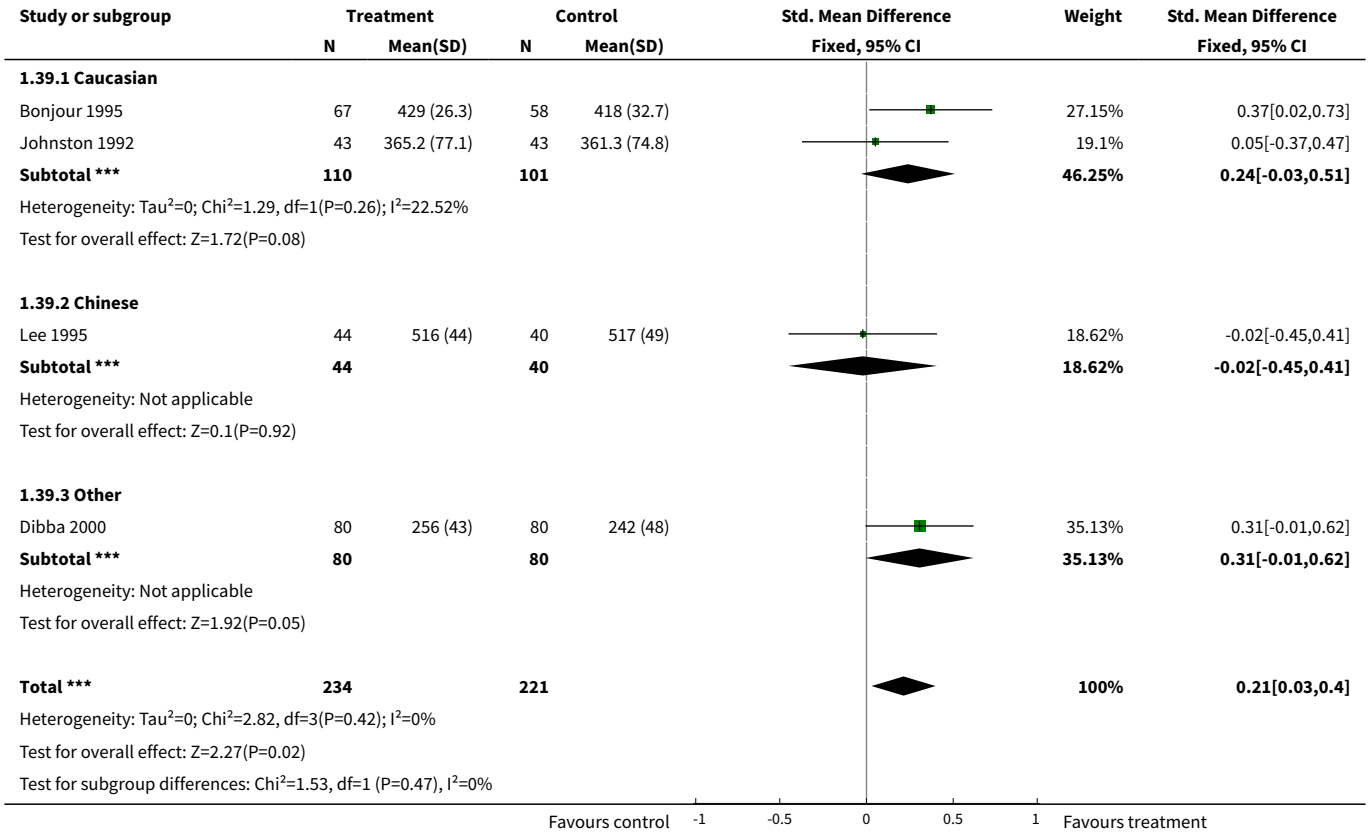

## Analysis 1.38. Comparison 1 Calcium supplementation vs placebo, Outcome 38 Lumbar spine BMD (mg/cm2) at longest point after supplementation ceased by ethnicity.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.38.1 Caucasian** | | | | | | | |
| Bonjour 1995 | 67 | 1019 (70.2) | 58 | 1014 (57.3) | | 20.19% | 0.08[-0.27,0.43] |
| Chevalley 2005 | 110 | 605 (52) | 116 | 602.5 (58) | | 36.69% | 0.05[-0.22,0.31] |
| Johnston 1992 | 43 | 1061.2 (192.3) | 43 | 1052.4 (185.5) | | 13.97% | 0.05[-0.38,0.47] |
| **Subtotal ***** | **220** | | **217** | | | **70.86%** | **0.05[-0.13,0.24]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.02, df=2(P=0.99); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.57(P=0.57) | | | | | | | |
| **1.38.2 Chinese** | | | | | | | |
| Lee 1995 | 44 | 538 (61) | 40 | 551 (68) | | 13.55% | -0.2[-0.63,0.23] |
| **Subtotal ***** | **44** | | **40** | | | **13.55%** | **-0.2[-0.63,0.23]** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z=0.91(P=0.36) | | | | | | | |



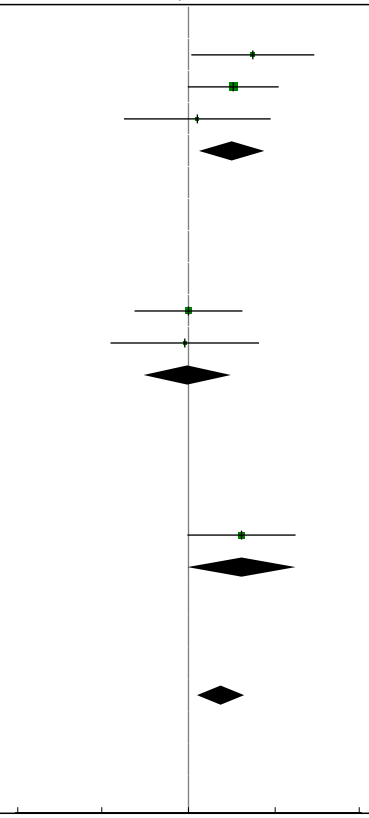



## Analysis 1.39. Comparison 1 Calcium supplementation vs placebo, Outcome 39 Distal radius BMD (mg/cm2) at longest point after supplementation ceased by ethnicity.



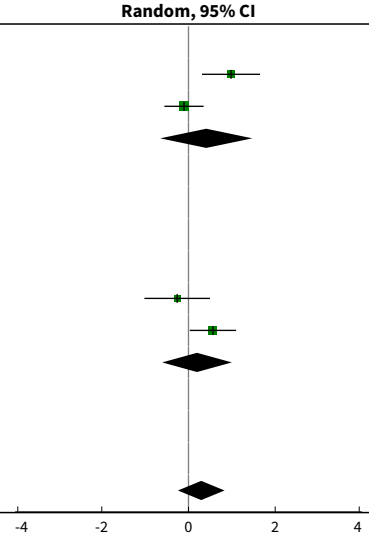
## Analysis 1.40. Comparison 1 Calcium supplementation vs placebo, Outcome 40 Upper limb BMD (mg/cm2) at longest point after supplementation ceased by ethnicity.

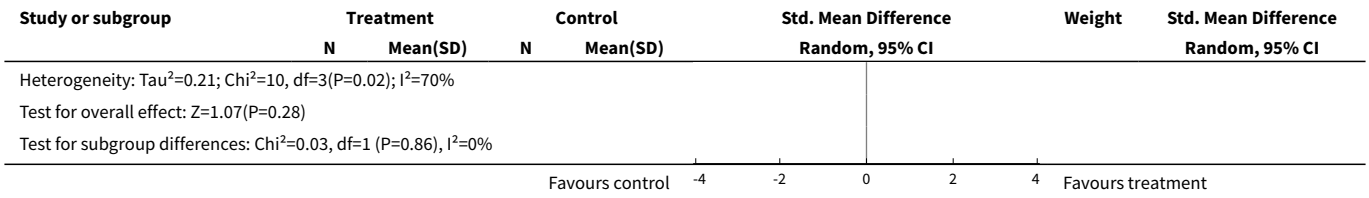
| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.40.1 Caucasian** | | | | | | | |
| Bonjour 1995 | 67 | 429 (26.3) | 58 | 418 (32.7) | | 14.67% | 0.37[0.02,0.73] |
| Chevalley 2005 | 110 | 24.7 (21.7) | 116 | 19.4 (19.2) | | 26.89% | 0.26[-0,0.52] |
| Johnston 1992 | 43 | 365.2 (77.1) | 43 | 361.3 (74.8) | | 10.32% | 0.05[-0.37,0.47] |
| **Subtotal ***** | **220** | | **217** | | | **51.88%** | **0.25[0.06,0.44]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=1.3, df=2(P=0.52); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=2.59(P=0.01) | | | | | | | |
| **1.40.2 Chinese** | | | | | | | |
| Lee 1994 | 77 | 505 (45) | 82 | 505 (40) | | 19.07% | 0[-0.31,0.31] |
| Lee 1995 | 44 | 516 (44) | 40 | 517 (49) | | 10.06% | -0.02[-0.45,0.41] |
| **Subtotal ***** | **121** | | **122** | | | **29.13%** | **-0.01[-0.26,0.24]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.01, df=1(P=0.94); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.06(P=0.95) | | | | | | | |
| **1.40.3 Other** | | | | | | | |
| Dibba 2000 | 80 | 256 (43) | 80 | 242 (48) | | 18.98% | 0.31[-0.01,0.62] |
| **Subtotal ***** | **80** | | **80** | | | **18.98%** | **0.31[-0.01,0.62]** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z=1.92(P=0.05) | | | | | | | |
| **Total ***** | **421** | | **419** | | | **100%** | **0.19[0.05,0.32]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=4.57, df=5(P=0.47); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=2.67(P=0.01) | | | | | | | |
| Test for subgroup differences: $Chi^2$=3.26, df=1 (P=0.2), $I^2$=38.7% | | | | | | | |



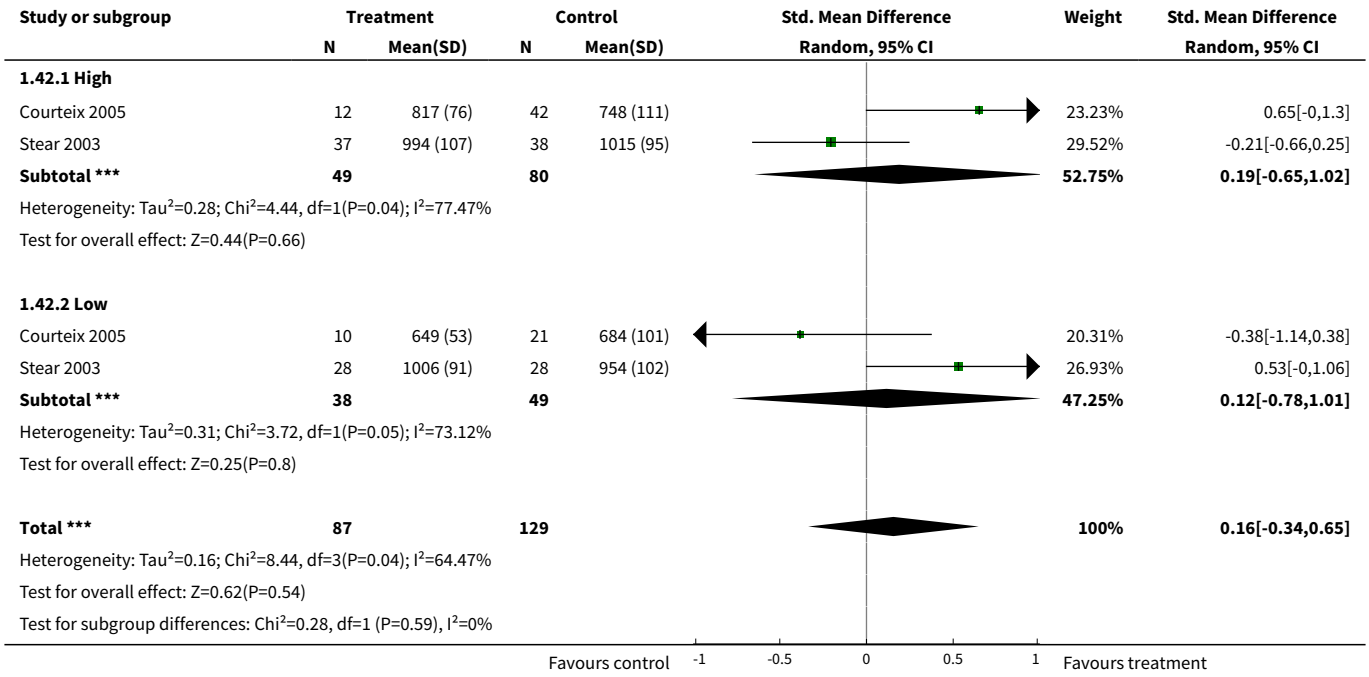

## Analysis 1.41. Comparison 1 Calcium supplementation vs placebo, Outcome 41 Femoral neck BMD (mg/cm2) (at end supplementation) by physical activity level.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Random, 95% CI | Weight | Std. Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.41.1 High** | | | | | | | |
| Courteix 2005 | 12 | 847 (49) | 42 | 754 (102) | | 23.24% | 0.98[0.31,1.65] |
| Stear 2003 | 37 | 858 (110) | 38 | 869 (101) | | 28.89% | -0.1[-0.56,0.35] |
| **Subtotal ***** | **49** | | **80** | | | **52.13%** | **0.41[-0.65,1.47]** |
| Heterogeneity: $Tau^2$=0.5; $Chi^2$=6.92, df=1(P=0.01); $I^2$=85.55% | | | | | | | |
| Test for overall effect: Z=0.76(P=0.45) | | | | | | | |
| **1.41.2 Low** | | | | | | | |
| Courteix 2005 | 10 | 683 (69) | 21 | 703 (77) | | 21.15% | -0.26[-1.02,0.5] |
| Stear 2003 | 28 | 876 (88) | 28 | 819 (110) | | 26.73% | 0.56[0.03,1.1] |
| **Subtotal ***** | **38** | | **49** | | | **47.87%** | **0.2[-0.61,1]** |
| Heterogeneity: $Tau^2$=0.23; $Chi^2$=3.05, df=1(P=0.08); $I^2$=67.21% | | | | | | | |
| Test for overall effect: Z=0.48(P=0.63) | | | | | | | |
| **Total ***** | **87** | | **129** | | | **100%** | **0.29[-0.24,0.83]** |

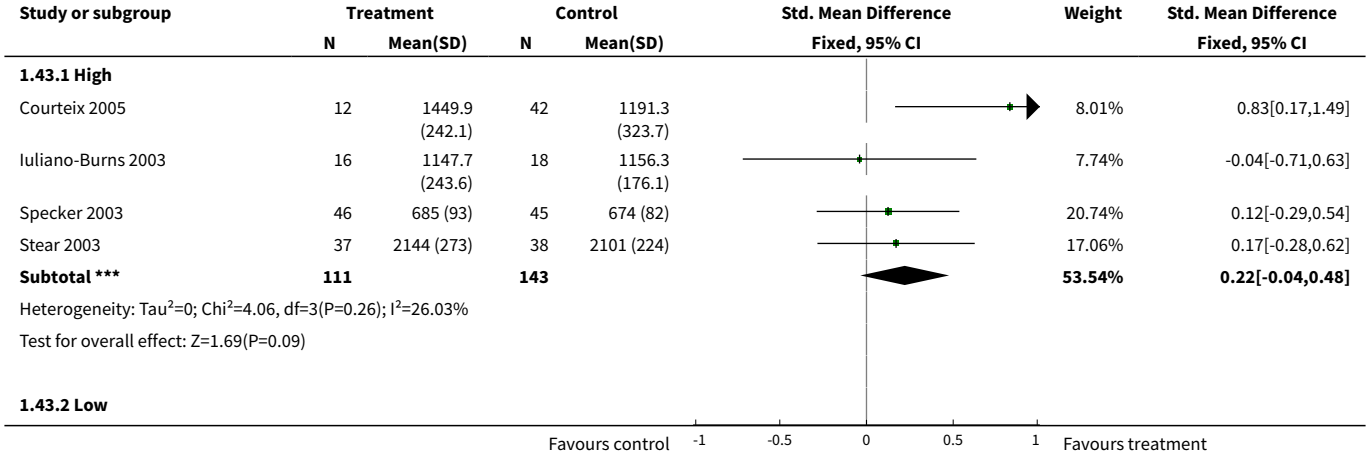


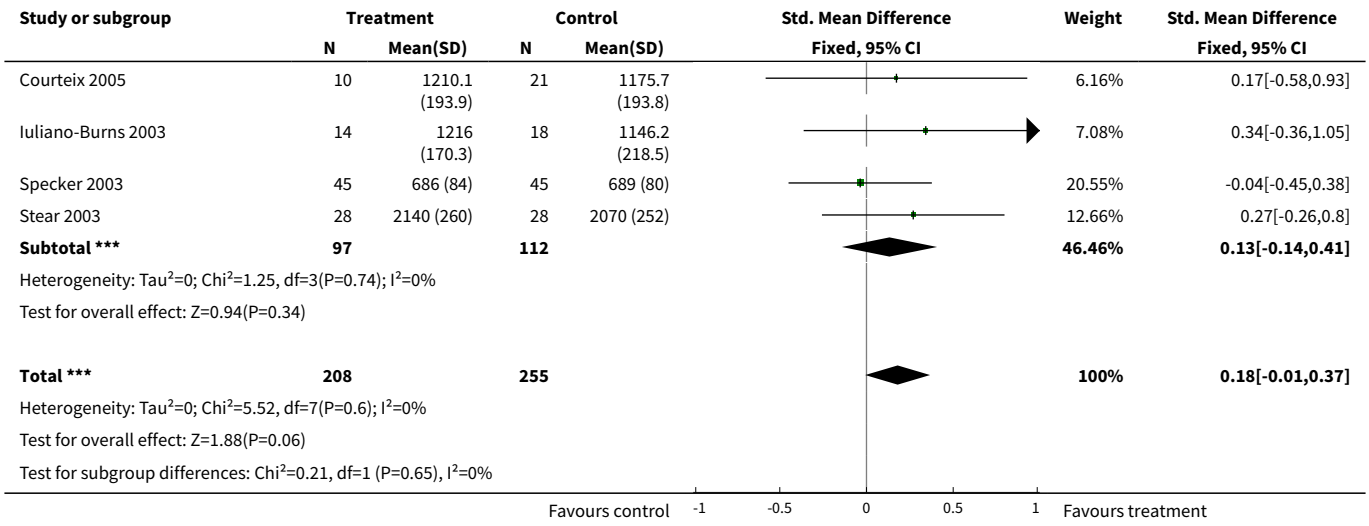



## Analysis 1.42. Comparison 1 Calcium supplementation vs placebo, Outcome 42 Lumbar spine BMD (mg/cm2) (at end supplementation) by physical activity level.

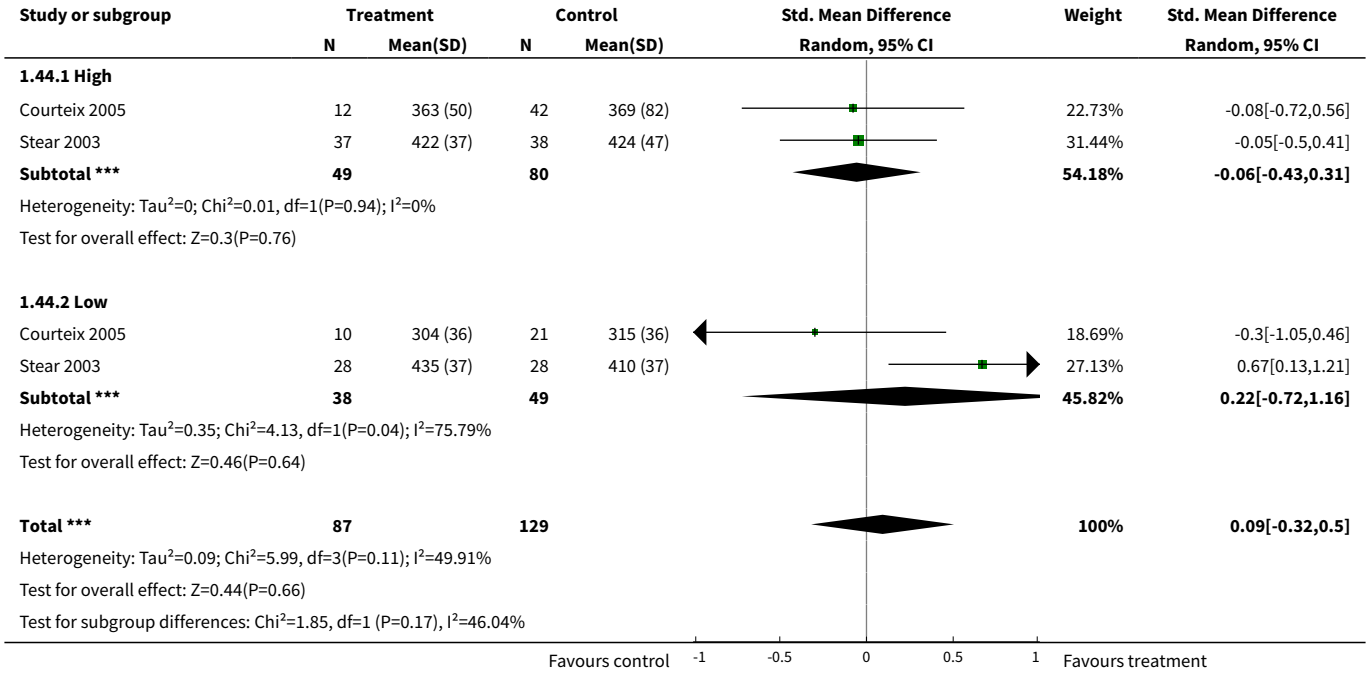



## Analysis 1.43. Comparison 1 Calcium supplementation vs placebo, Outcome 43 Total body BMC (mg) (at end supplementation) by physical activity level.

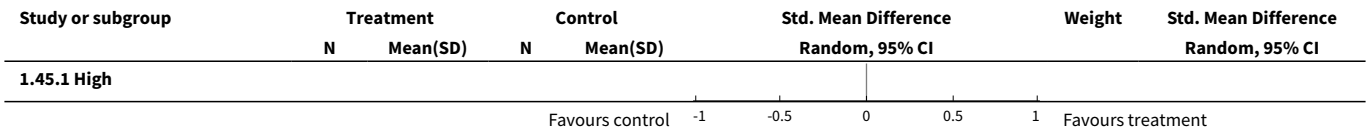


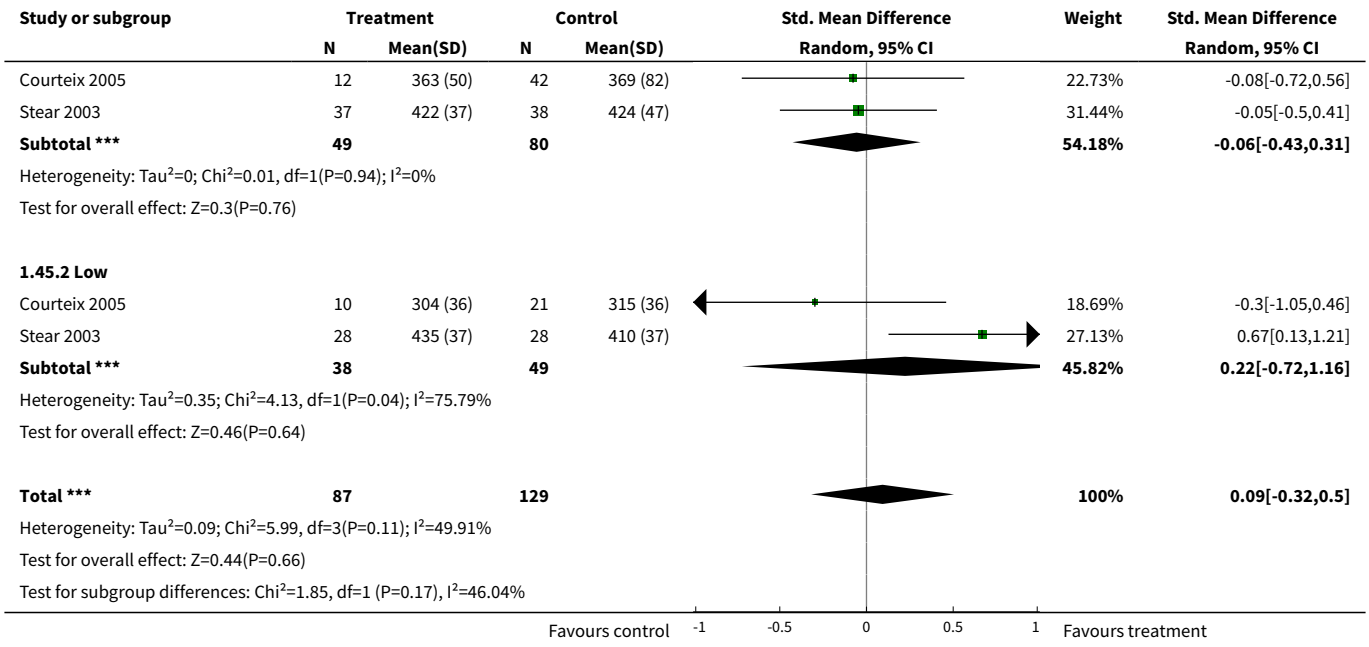



## Analysis 1.44. Comparison 1 Calcium supplementation vs placebo, Outcome 44 Distal radius BMD (mg/cm2) (at end supplementation) by physical activity level.

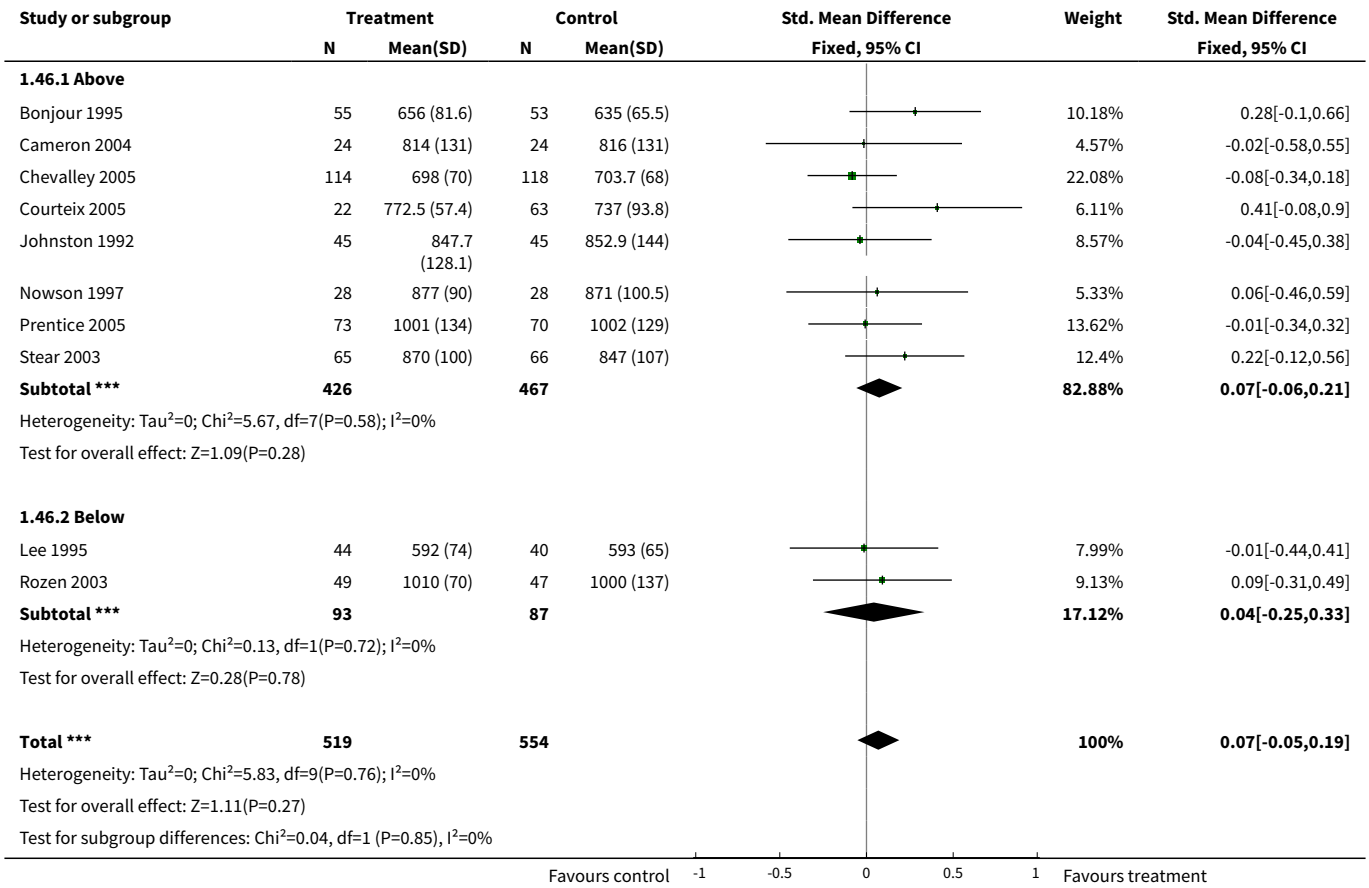



## Analysis 1.45. Comparison 1 Calcium supplementation vs placebo, Outcome 45 Upper limb BMD (mg/cm2) (at end supplementation) by physical activity level.



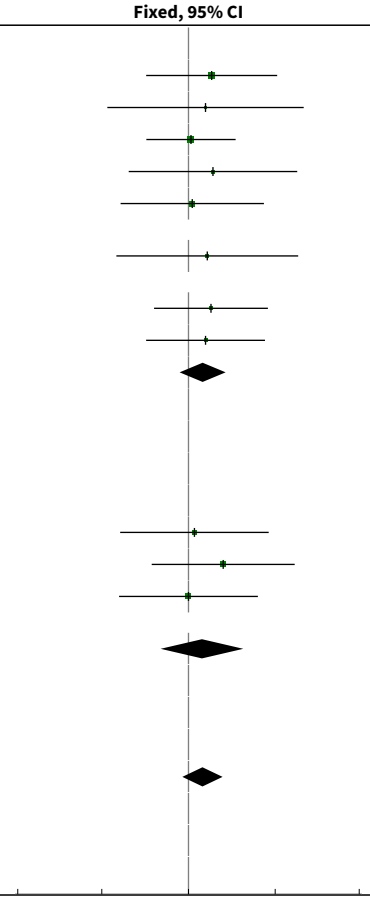



## Analysis 1.46. Comparison 1 Calcium supplementation vs placebo, Outcome 46 Femoral neck BMD (mg/cm2) at end supplementation by calcium threshold.



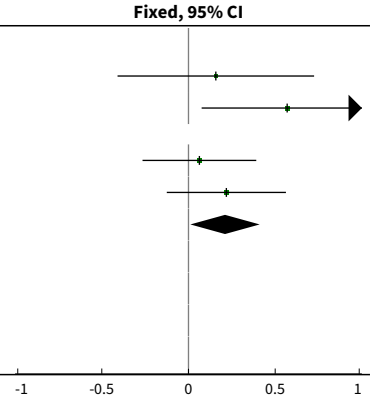
## Analysis 1.47. Comparison 1 Calcium supplementation vs placebo, Outcome 47 Lumbar spine BMD (mg/cm2) at end supplementation by calcium threshold.

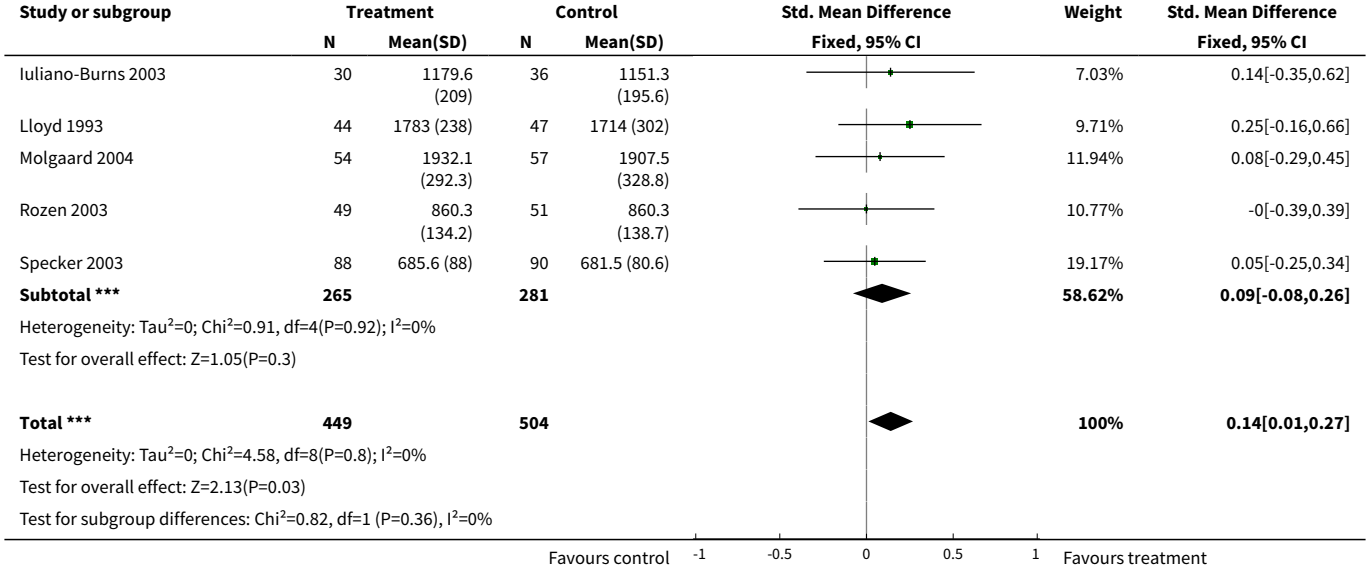
| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.47.1 Above** | | | | | | | |
| Bonjour 1995 | 55 | 647 (74.2) | 53 | 638 (58.2) | | 9.43% | 0.13[-0.24,0.51] |
| Cameron 2004 | 24 | 848 (158) | 24 | 833 (142) | | 4.2% | 0.1[-0.47,0.66] |
| Chevalley 2005 | 114 | 586.9 (52) | 118 | 586.1 (58) | | 20.3% | 0.01[-0.24,0.27] |
| Courteix 2005 | 22 | 740.6 (65) | 63 | 726.7 (107) | | 5.7% | 0.14[-0.34,0.63] |
| Johnston 1992 | 45 | 907.4 (197.3) | 45 | 903 (203.8) | | 7.88% | 0.02[-0.39,0.43] |
| Nowson 1997 | 28 | 1017 (148.2) | 28 | 1001 (142.9) | | 4.9% | 0.11[-0.42,0.63] |
| Prentice 2005 | 73 | 1047 (114) | 70 | 1032 (116) | | 12.49% | 0.13[-0.2,0.46] |
| Stear 2003 | 65 | 999 (100) | 66 | 989 (102) | | 11.45% | 0.1[-0.24,0.44] |
| **Subtotal ***** | **426** | | **467** | | | **76.35%** | **0.08[-0.05,0.21]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.58, df=7(P=1); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.2(P=0.23) | | | | | | | |
| **1.47.2 Below** | | | | | | | |
| Lee 1995 | 44 | 525 (61) | 40 | 523 (54) | | 7.34% | 0.03[-0.39,0.46] |
| Lloyd 1993 | 44 | 914 (83) | 47 | 894 (112) | | 7.92% | 0.2[-0.21,0.61] |
| Rozen 2003 | 49 | 1120 (140) | 47 | 1120 (137.1) | | 8.4% | 0[-0.4,0.4] |
| **Subtotal ***** | **137** | | **134** | | | **23.65%** | **0.08[-0.16,0.32]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.52, df=2(P=0.77); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.64(P=0.52) | | | | | | | |
| **Total ***** | **563** | | **601** | | | **100%** | **0.08[-0.04,0.2]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=1.1, df=10(P=1); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.36(P=0.17) | | | | | | | |
| Test for subgroup differences: $Chi^2$=0, df=1 (P=0.98), $I^2$=0% | | | | | | | |



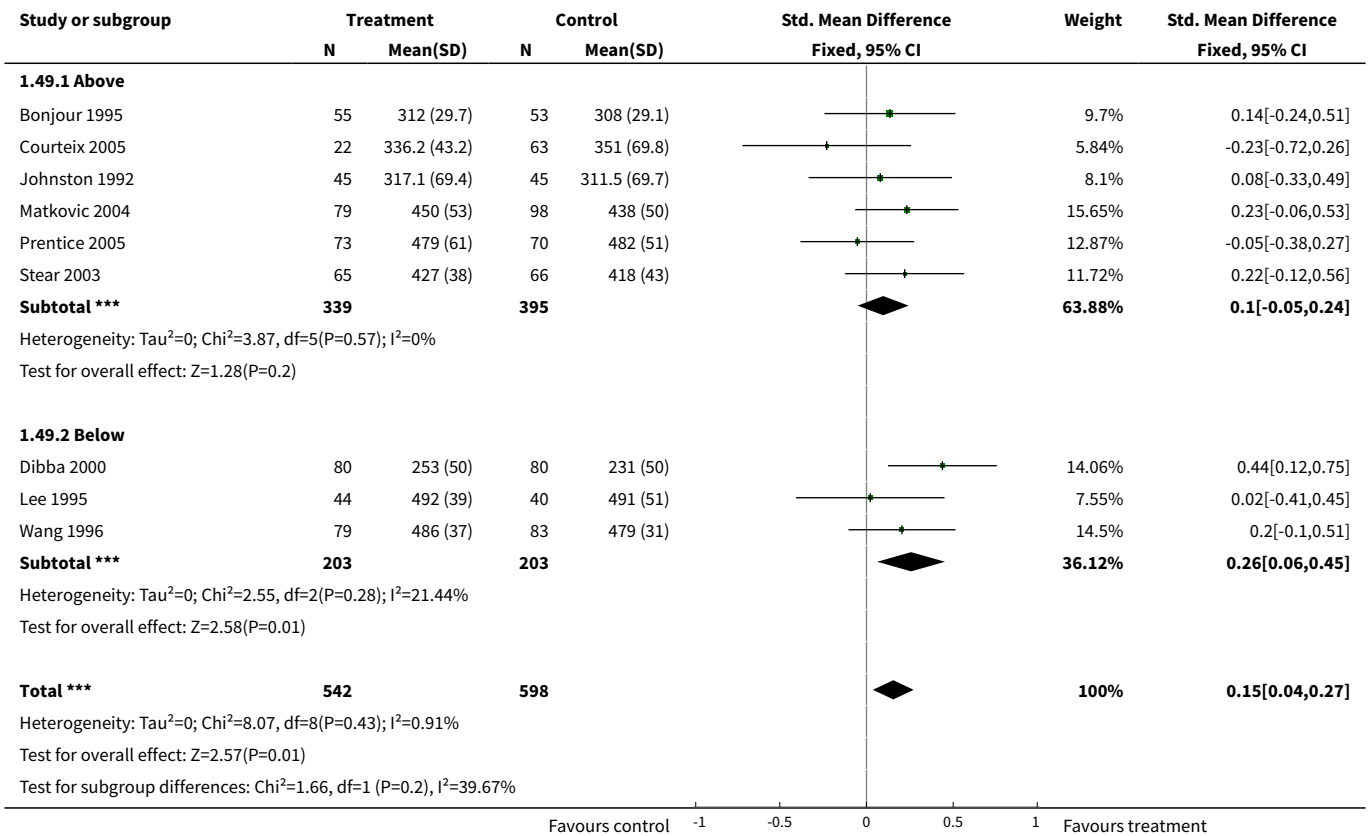

## Analysis 1.48. Comparison 1 Calcium supplementation vs placebo, Outcome 48 Total body BMC (mg) at end supplementation by calcium threshold.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.48.1 Above** | | | | | | | |
| Cameron 2004 | 24 | 1583 (504) | 24 | 1512 (372) | | 5.15% | 0.16[-0.41,0.72] |
| Courteix 2005 | 22 | 1340.9 (216.4) | 63 | 1186.1 (285.3) | | 6.81% | 0.57[0.08,1.06] |
| Prentice 2005 | 73 | 2796 (415) | 70 | 2770 (407) | | 15.39% | 0.06[-0.27,0.39] |
| Stear 2003 | 65 | 2143 (265) | 66 | 2088 (235) | | 14.03% | 0.22[-0.13,0.56] |
| **Subtotal ***** | **184** | | **223** | | | **41.38%** | **0.21[0.01,0.41]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=2.84, df=3(P=0.42); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=2.06(P=0.04) | | | | | | | |
| **1.48.2 Below** | | | | | | | |



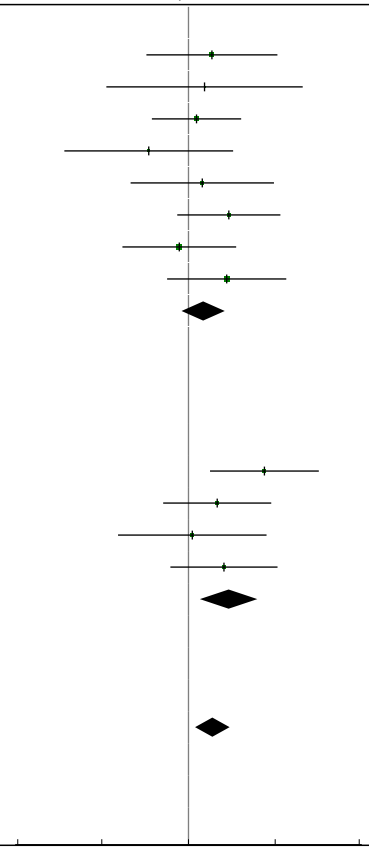



## Analysis 1.49. Comparison 1 Calcium supplementation vs placebo, Outcome 49 Distal radius BMD (mg/cm2) at end supplementation by calcium threshold.



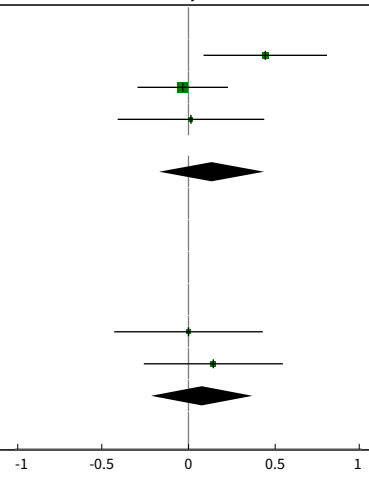
## Analysis 1.50. Comparison 1 Calcium supplementation vs placebo, Outcome 50 Upper limb BMD (mg/cm2) at end supplementation by calcium threshold.

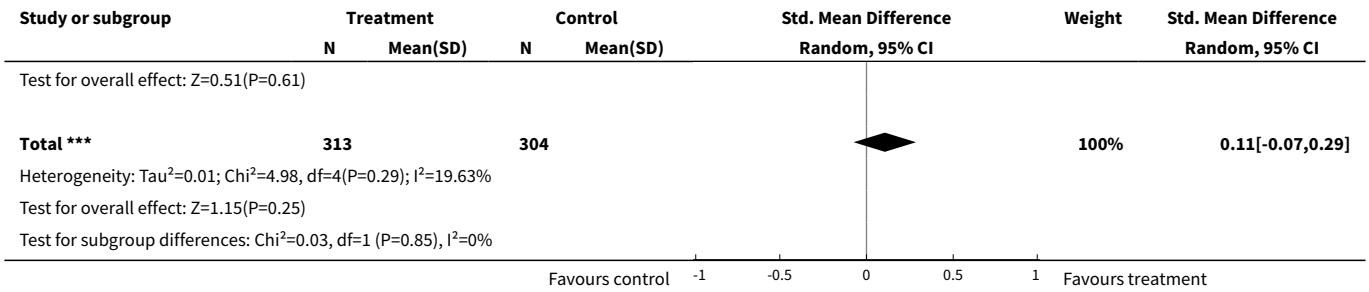
| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.50.1 Above** | | | | | | | |
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 6.96% | 0.14[-0.24,0.51] |
| Cameron 2004 | 24 | 418 (43) | 24 | 414 (42) | | 3.1% | 0.09[-0.47,0.66] |
| Chevalley 2005 | 114 | 309.6 (28) | 118 | 308.2 (32) | | 14.97% | 0.05[-0.21,0.3] |
| Courteix 2005 | 22 | 336.2 (43.2) | 63 | 351 (69.8) | | 4.19% | -0.23[-0.72,0.26] |
| Johnston 1992 | 45 | 317.1 (69.4) | 45 | 311.5 (69.7) | | 5.81% | 0.08[-0.33,0.49] |
| Matkovic 2004 | 79 | 450 (53) | 98 | 438 (50) | | 11.22% | 0.23[-0.06,0.53] |
| Prentice 2005 | 73 | 479 (61) | 70 | 482 (51) | | 9.23% | -0.05[-0.38,0.27] |
| Stear 2003 | 65 | 427 (38) | 66 | 418 (43) | | 8.41% | 0.22[-0.12,0.56] |
| **Subtotal ***** | **477** | | **537** | | | **63.88%** | **0.08[-0.04,0.21]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=3.98, df=7(P=0.78); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.33(P=0.18) | | | | | | | |
| **1.50.2 Below** | | | | | | | |
| Dibba 2000 | 80 | 253 (50) | 80 | 231 (50) | | 10.09% | 0.44[0.12,0.75] |
| Lee 1994 | 77 | 487 (41) | 82 | 480 (43) | | 10.22% | 0.17[-0.15,0.48] |
| Lee 1995 | 44 | 492 (39) | 40 | 491 (51) | | 5.41% | 0.02[-0.41,0.45] |
| Wang 1996 | 79 | 486 (37) | 83 | 479 (31) | | 10.4% | 0.2[-0.1,0.51] |
| **Subtotal ***** | **280** | | **285** | | | **36.12%** | **0.23[0.07,0.4]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=2.78, df=3(P=0.43); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=2.74(P=0.01) | | | | | | | |
| **Total ***** | **757** | | **822** | | | **100%** | **0.14[0.04,0.24]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=8.69, df=11(P=0.65); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=2.71(P=0.01) | | | | | | | |
| Test for subgroup differences: $Chi^2$=1.93, df=1 (P=0.17), $I^2$=48.1% | | | | | | | |



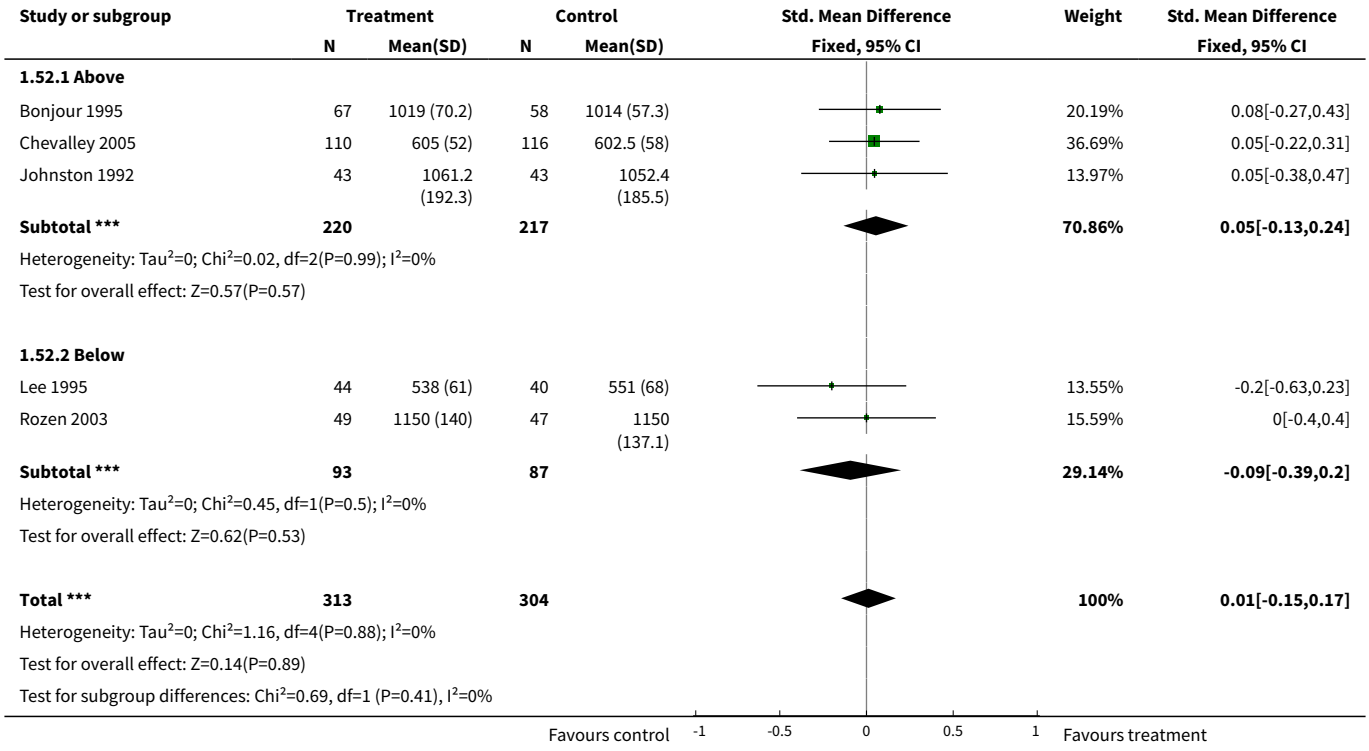

## Analysis 1.51. Comparison 1 Calcium supplementation vs placebo, Outcome 51 Femoral neck BMD (mg/cm2) at longest point after supplementation ceased end by calcium threshold.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Random, 95% CI | Weight | Std. Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.51.1 Above** | | | | | | | |
| Bonjour 1995 | 67 | 885 (70.2) | 58 | 853 (73.7) | | 20.41% | 0.44[0.09,0.8] |
| Chevalley 2005 | 110 | 722.4 (70) | 116 | 724.7 (68) | | 32.35% | -0.03[-0.29,0.23] |
| Johnston 1992 | 43 | 956.1 (136.7) | 43 | 954.1 (140.9) | | 15.38% | 0.01[-0.41,0.44] |
| **Subtotal ***** | **220** | | **217** | | | **68.14%** | **0.13[-0.17,0.44]** |
| Heterogeneity: $Tau^2$=0.04; $Chi^2$=4.71, df=2(P=0.09); $I^2$=57.57% | | | | | | | |
| Test for overall effect: Z=0.86(P=0.39) | | | | | | | |
| **1.51.2 Below** | | | | | | | |
| Lee 1995 | 44 | 603 (76) | 40 | 603 (64) | | 15.04% | 0[-0.43,0.43] |
| Rozen 2003 | 49 | 1010 (140) | 47 | 990 (137.1) | | 16.82% | 0.14[-0.26,0.54] |
| **Subtotal ***** | **93** | | **87** | | | **31.86%** | **0.08[-0.22,0.37]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.23, df=1(P=0.63); $I^2$=0% | | | | | | | |

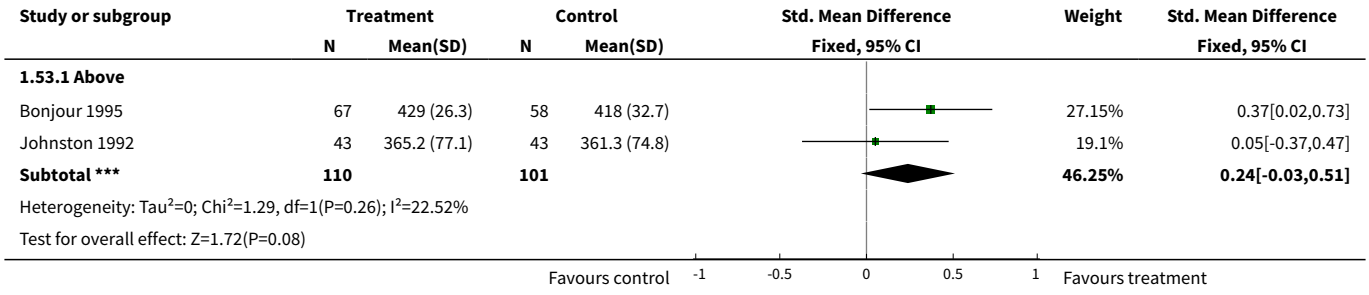


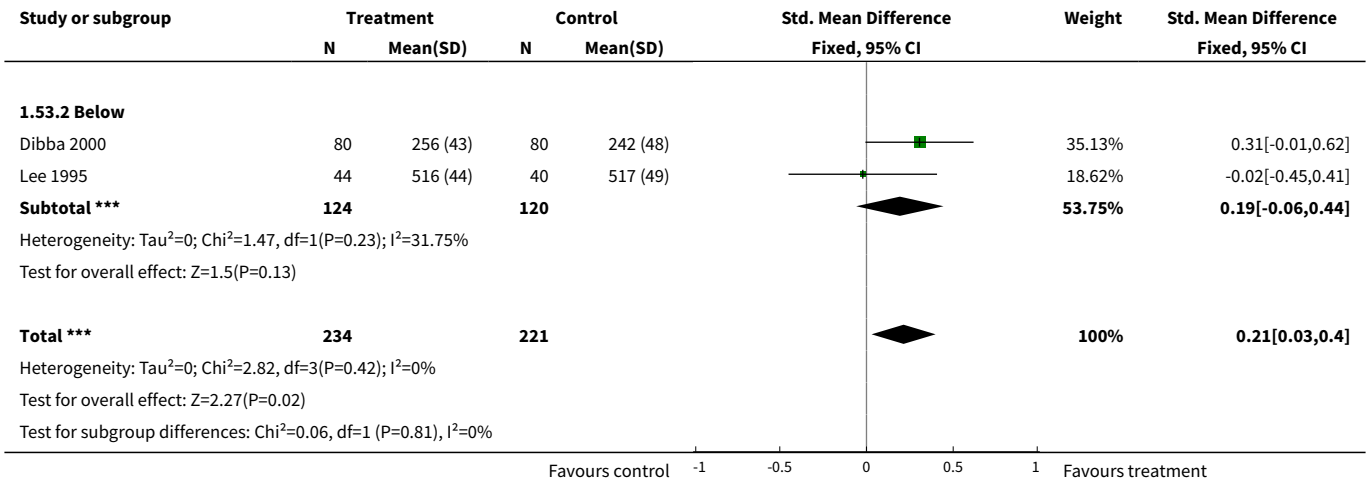



## Analysis 1.52. Comparison 1 Calcium supplementation vs placebo, Outcome 52 Lumbar spine BMD (mg/cm2) at longest point after supplementation ceased end by calcium threshold.

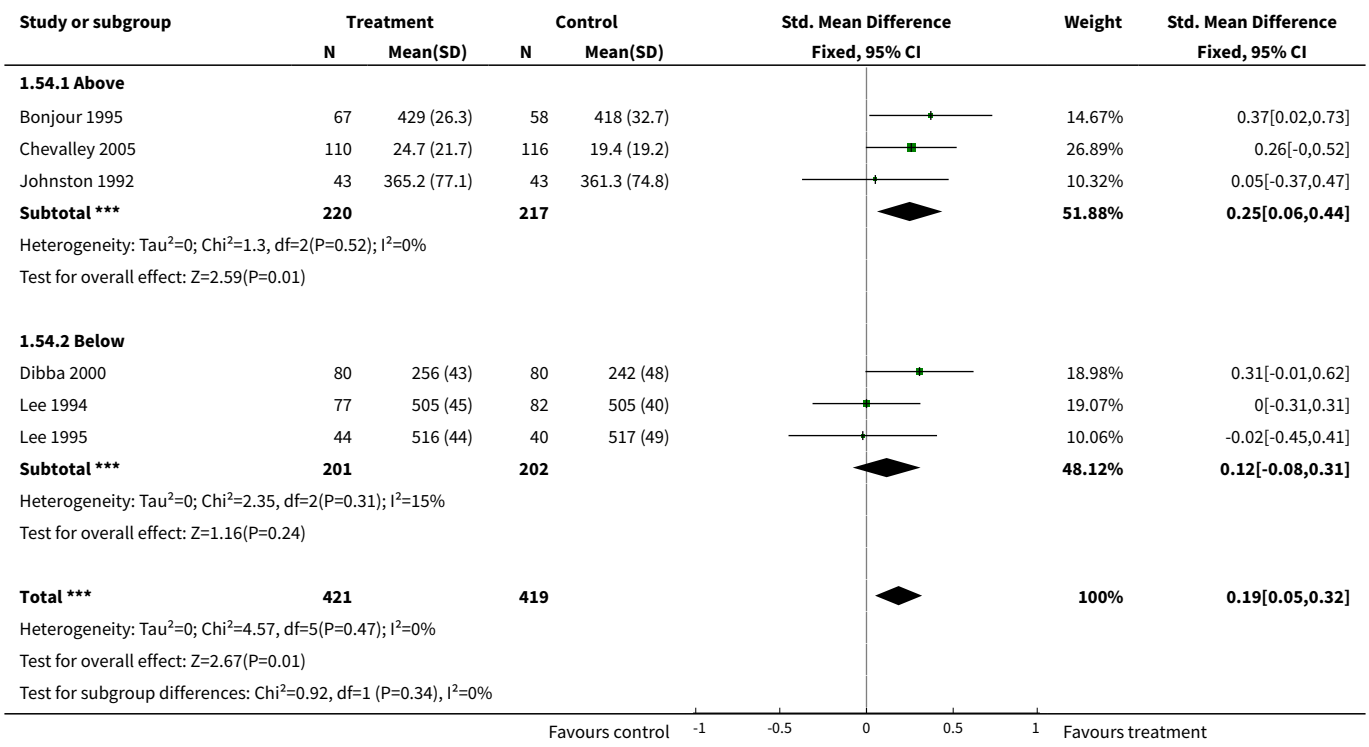



## Analysis 1.53. Comparison 1 Calcium supplementation vs placebo, Outcome 53 Distal radius BMD (mg/cm2) at longest point after supplementation ceased end by calcium threshold.

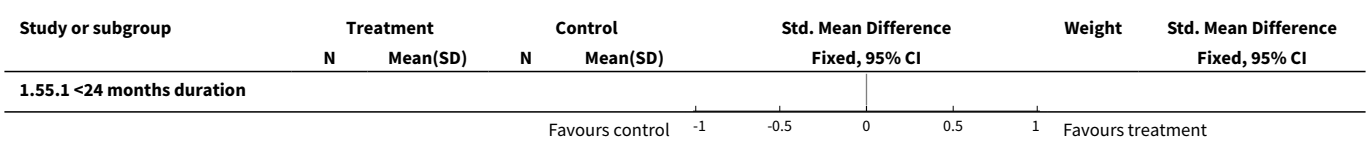





## Analysis 1.54. Comparison 1 Calcium supplementation vs placebo, Outcome 54 Upper limb BMD (mg/cm2) at longest point after supplementation ceased end by calcium threshold.




## Analysis 1.55. Comparison 1 Calcium supplementation vs placebo, Outcome 55 Femoral neck BMD (mg/cm2) at end supplementation by duration of supplementation (< 24 months vs >= 24 months).

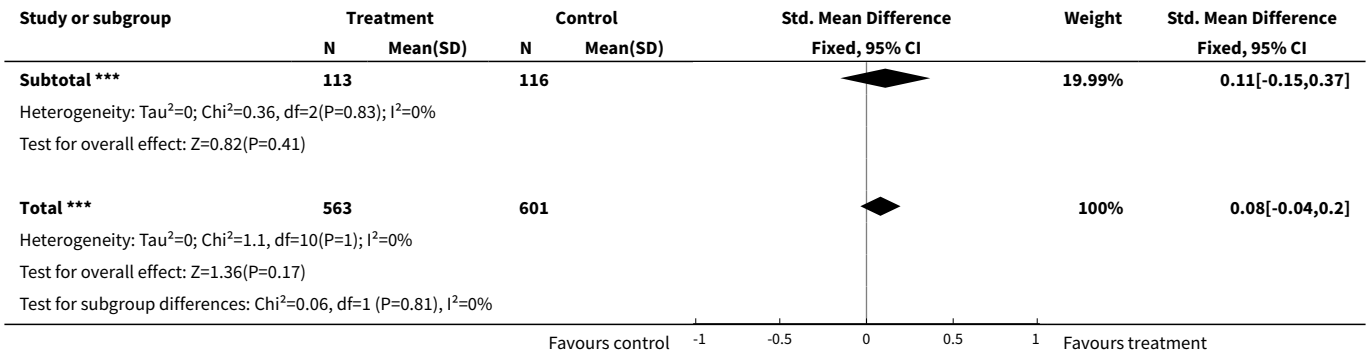


| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Bonjour 1995 | 55 | 656 (81.6) | 53 | 635 (65.5) | | 10.18% | 0.28[-0.1,0.66] |
| Chevalley 2005 | 114 | 698 (70) | 118 | 703.7 (68) | | 22.08% | -0.08[-0.34,0.18] |
| Courteix 2005 | 22 | 772.5 (57.4) | 63 | 737 (93.8) | | 6.11% | 0.41[-0.08,0.9] |
| Lee 1995 | 44 | 592 (74) | 40 | 593 (65) | | 7.99% | -0.01[-0.44,0.41] |
| Nowson 1997 | 28 | 877 (90) | 28 | 871 (100.5) | | 5.33% | 0.06[-0.46,0.59] |
| Prentice 2005 | 73 | 1001 (134) | 70 | 1002 (129) | | 13.62% | -0.01[-0.34,0.32] |
| Rozen 2003 | 49 | 1010 (70) | 47 | 1000 (137) | | 9.13% | 0.09[-0.31,0.49] |
| Stear 2003 | 65 | 870 (100) | 66 | 847 (107) | | 12.4% | 0.22[-0.12,0.56] |
| **Subtotal ***** | **450** | | **485** | | | **86.85%** | **0.08[-0.05,0.21]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=5.45, df=7(P=0.61); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.26(P=0.21) | | | | | | | |
| **1.55.2 >= 24 months duration** | | | | | | | |
| Cameron 2004 | 24 | 814 (131) | 24 | 816 (131) | | 4.57% | -0.02[-0.58,0.55] |
| Johnston 1992 | 45 | 847.7 (128.1) | 45 | 852.9 (144) | | 8.57% | -0.04[-0.45,0.38] |
| **Subtotal ***** | **69** | | **69** | | | **13.15%** | **-0.03[-0.36,0.3]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0, df=1(P=0.95); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.17(P=0.86) | | | | | | | |
| **Total ***** | **519** | | **554** | | | **100%** | **0.07[-0.05,0.19]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=5.83, df=9(P=0.76); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.11(P=0.27) | | | | | | | |
| Test for subgroup differences: $Chi^2$=0.38, df=1 (P=0.54), $I^2$=0% | | | | | | | |

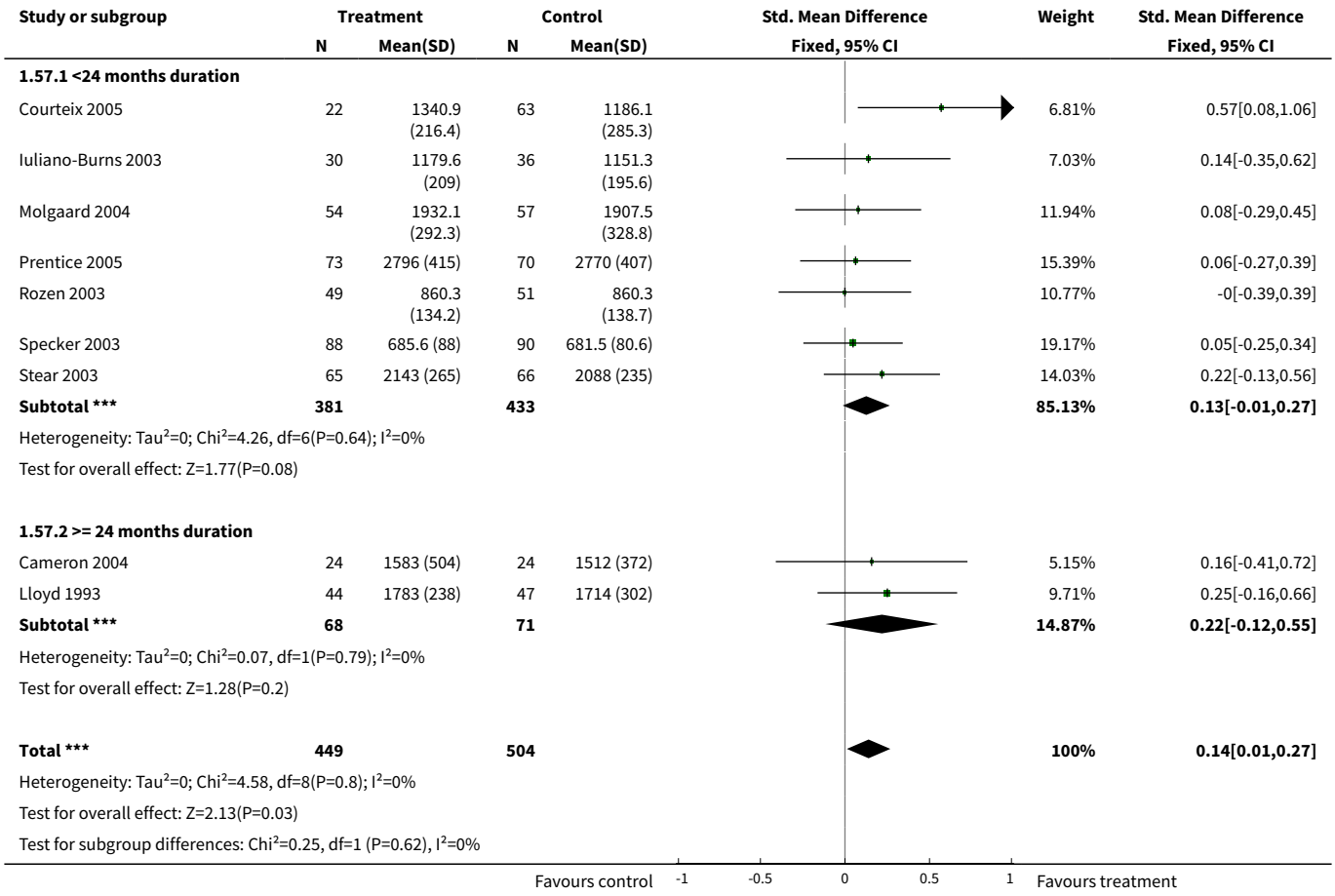



## Analysis 1.56. Comparison 1 Calcium supplementation vs placebo, Outcome 56 Lumbar spine BMD (mg/cm2) at end supplementation by duration of supplementation (< 24 months vs >= 24 months).

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.56.1 <24 months duration** | | | | | | | |
| Bonjour 1995 | 55 | 647 (74.2) | 53 | 638 (58.2) | | 9.43% | 0.13[-0.24,0.51] |
| Chevalley 2005 | 114 | 586.9 (52) | 118 | 586.1 (58) | | 20.3% | 0.01[-0.24,0.27] |
| Courteix 2005 | 22 | 740.6 (65) | 63 | 726.7 (107) | | 5.7% | 0.14[-0.34,0.63] |
| Lee 1995 | 44 | 525 (61) | 40 | 523 (54) | | 7.34% | 0.03[-0.39,0.46] |
| Nowson 1997 | 28 | 1017 (148.2) | 28 | 1001 (142.9) | | 4.9% | 0.11[-0.42,0.63] |
| Prentice 2005 | 73 | 1047 (114) | 70 | 1032 (116) | | 12.49% | 0.13[-0.2,0.46] |
| Rozen 2003 | 49 | 1120 (140) | 47 | 1120 (137.1) | | 8.4% | 0[-0.4,0.4] |
| Stear 2003 | 65 | 999 (100) | 66 | 989 (102) | | 11.45% | 0.1[-0.24,0.44] |
| **Subtotal ***** | **450** | | **485** | | | **80.01%** | **0.07[-0.06,0.2]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.69, df=7(P=1); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.11(P=0.27) | | | | | | | |
| **1.56.2 >= 24 months duration** | | | | | | | |
| Cameron 2004 | 24 | 848 (158) | 24 | 833 (142) | | 4.2% | 0.1[-0.47,0.66] |
| Johnston 1992 | 45 | 907.4 (197.3) | 45 | 903 (203.8) | | 7.88% | 0.02[-0.39,0.43] |
| Lloyd 1993 | 44 | 914 (83) | 47 | 894 (112) | | 7.92% | 0.2[-0.21,0.61] |

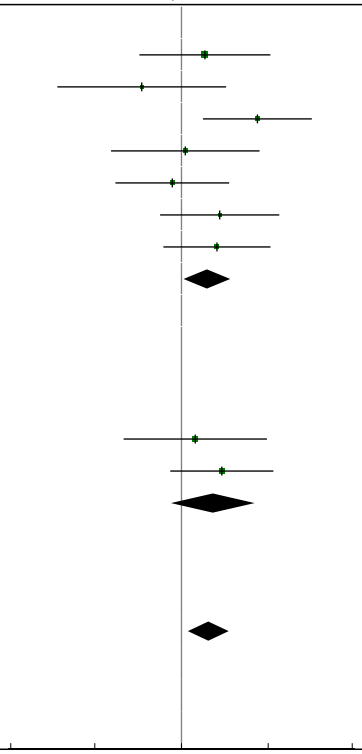



## Analysis 1.57. Comparison 1 Calcium supplementation vs placebo, Outcome 57 Total body BMC (mg) at end supplementation by duration of supplementation (< 24 months vs >= 24 months).



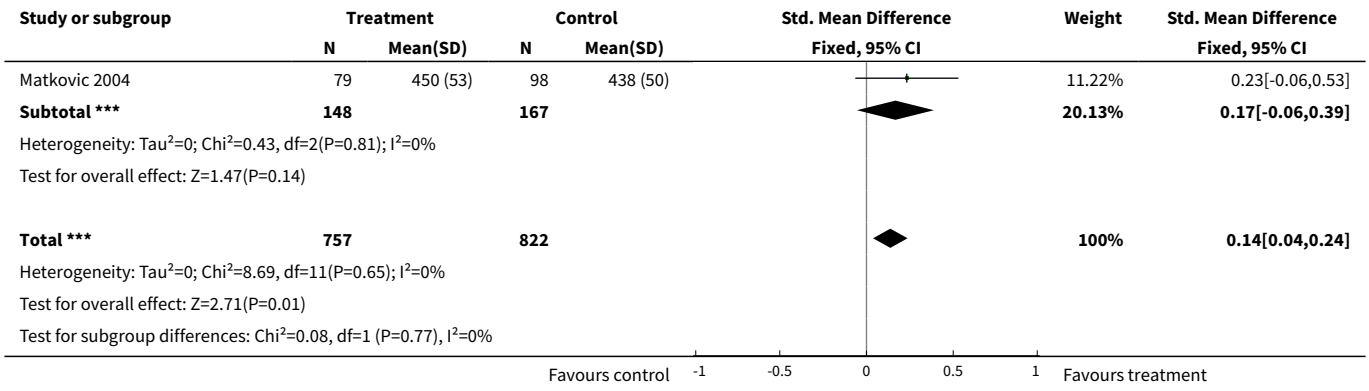
## Analysis 1.58. Comparison 1 Calcium supplementation vs placebo, Outcome 58 Distal radius BMD (mg/cm2) at end supplementation by duration of supplementation (< 24 months vs >= 24 months).

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.58.1 <24 months duration** | | | | | | | |
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 9.7% | 0.14[-0.24,0.51] |
| Courteix 2005 | 22 | 336.2 (43.2) | 63 | 351 (69.8) | | 5.84% | -0.23[-0.72,0.26] |
| Dibba 2000 | 80 | 253 (50) | 80 | 231 (50) | | 14.06% | 0.44[0.12,0.75] |
| Lee 1995 | 44 | 492 (39) | 40 | 491 (51) | | 7.55% | 0.02[-0.41,0.45] |
| Prentice 2005 | 73 | 479 (61) | 70 | 482 (51) | | 12.87% | -0.05[-0.38,0.27] |
| Stear 2003 | 65 | 427 (38) | 66 | 418 (43) | | 11.72% | 0.22[-0.12,0.56] |
| Wang 1996 | 79 | 486 (37) | 83 | 479 (31) | | 14.5% | 0.2[-0.1,0.51] |
| **Subtotal ***** | **418** | | **455** | | | **76.25%** | **0.15[0.01,0.28]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=7.67, df=6(P=0.26); $I^2$=21.75% | | | | | | | |
| Test for overall effect: Z=2.13(P=0.03) | | | | | | | |
| **1.58.2 >= 24 months duration** | | | | | | | |
| Johnston 1992 | 45 | 317.1 (69.4) | 45 | 311.5 (69.7) | | 8.1% | 0.08[-0.33,0.49] |
| Matkovic 2004 | 79 | 450 (53) | 98 | 438 (50) | | 15.65% | 0.23[-0.06,0.53] |
| **Subtotal ***** | **124** | | **143** | | | **23.75%** | **0.18[-0.06,0.42]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.35, df=1(P=0.56); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.47(P=0.14) | | | | | | | |
| **Total ***** | **542** | | **598** | | | **100%** | **0.15[0.04,0.27]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=8.07, df=8(P=0.43); $I^2$=0.91% | | | | | | | |
| Test for overall effect: Z=2.57(P=0.01) | | | | | | | |
| Test for subgroup differences: $Chi^2$=0.06, df=1 (P=0.81), $I^2$=0% | | | | | | | |

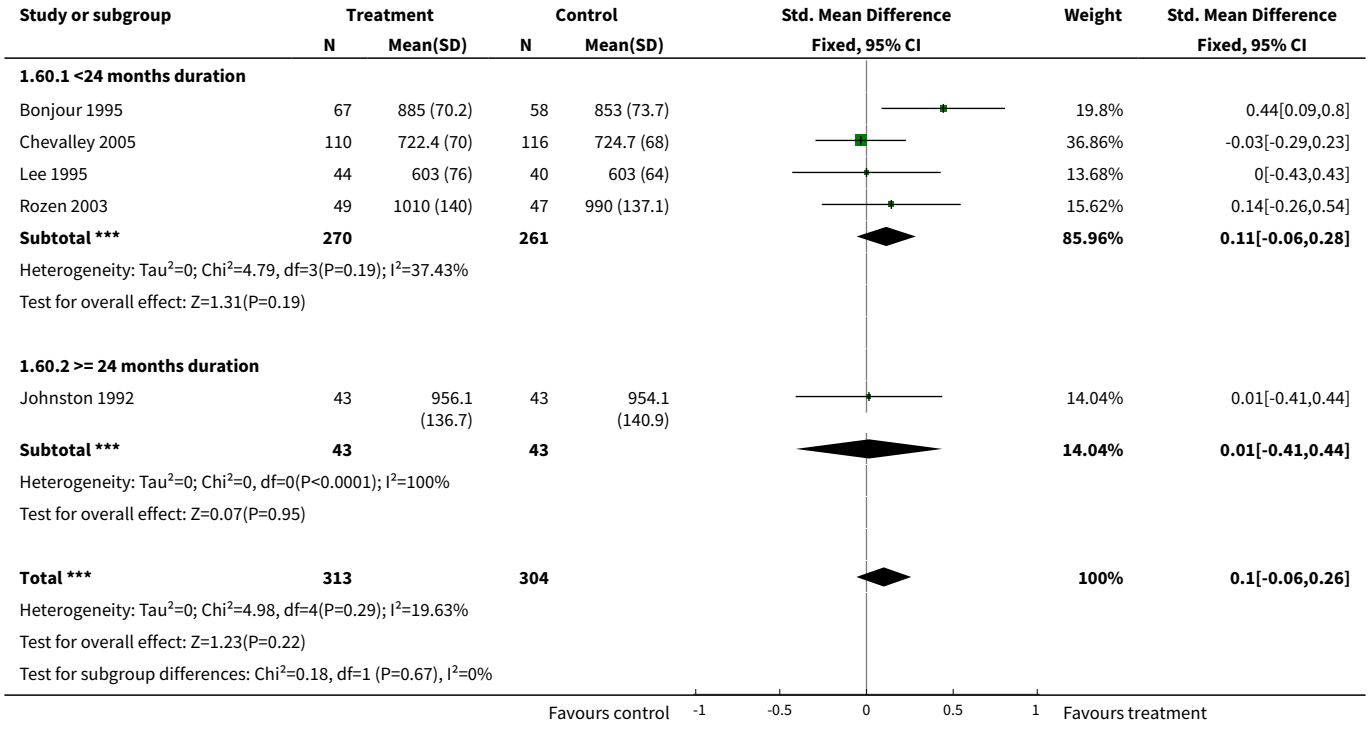



## Analysis 1.59. Comparison 1 Calcium supplementation vs placebo, Outcome 59 Upper limb BMD (mg/cm2) at end supplementation by duration of supplementation (< 24 months vs >= 24 months).

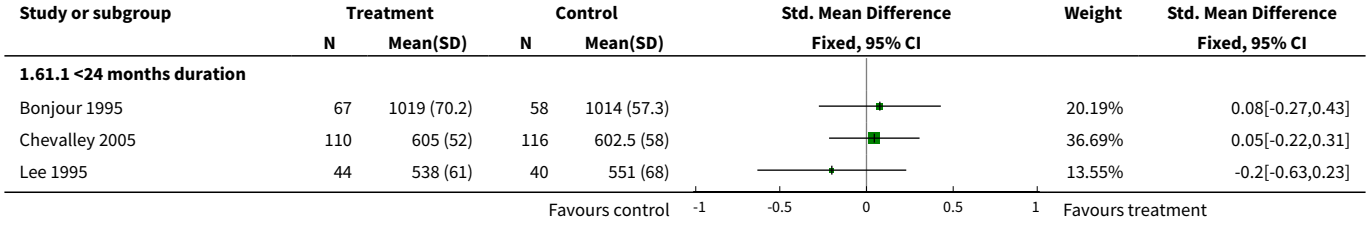
| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.59.1 <24 months duration** | | | | | | | |
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 6.96% | 0.14[-0.24,0.51] |
| Chevalley 2005 | 114 | 309.6 (28) | 118 | 308.2 (32) | | 14.97% | 0.05[-0.21,0.3] |
| Courteix 2005 | 22 | 336.2 (43.2) | 63 | 351 (69.8) | | 4.19% | -0.23[-0.72,0.26] |
| Dibba 2000 | 80 | 253 (50) | 80 | 231 (50) | | 10.09% | 0.44[0.12,0.75] |
| Lee 1994 | 77 | 487 (41) | 82 | 480 (43) | | 10.22% | 0.17[-0.15,0.48] |
| Lee 1995 | 44 | 492 (39) | 40 | 491 (51) | | 5.41% | 0.02[-0.41,0.45] |
| Prentice 2005 | 73 | 479 (61) | 70 | 482 (51) | | 9.23% | -0.05[-0.38,0.27] |
| Stear 2003 | 65 | 427 (38) | 66 | 418 (43) | | 8.41% | 0.22[-0.12,0.56] |
| Wang 1996 | 79 | 486 (37) | 83 | 479 (31) | | 10.4% | 0.2[-0.1,0.51] |
| **Subtotal ***** | **609** | | **655** | | | **79.87%** | **0.13[0.02,0.24]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=8.18, df=8(P=0.42); $I^2$=2.21% | | | | | | | |
| Test for overall effect: Z=2.29(P=0.02) | | | | | | | |
| **1.59.2 >= 24 months duration** | | | | | | | |
| Cameron 2004 | 24 | 418 (43) | 24 | 414 (42) | | 3.1% | 0.09[-0.47,0.66] |
| Johnston 1992 | 45 | 317.1 (69.4) | 45 | 311.5 (69.7) | | 5.81% | 0.08[-0.33,0.49] |

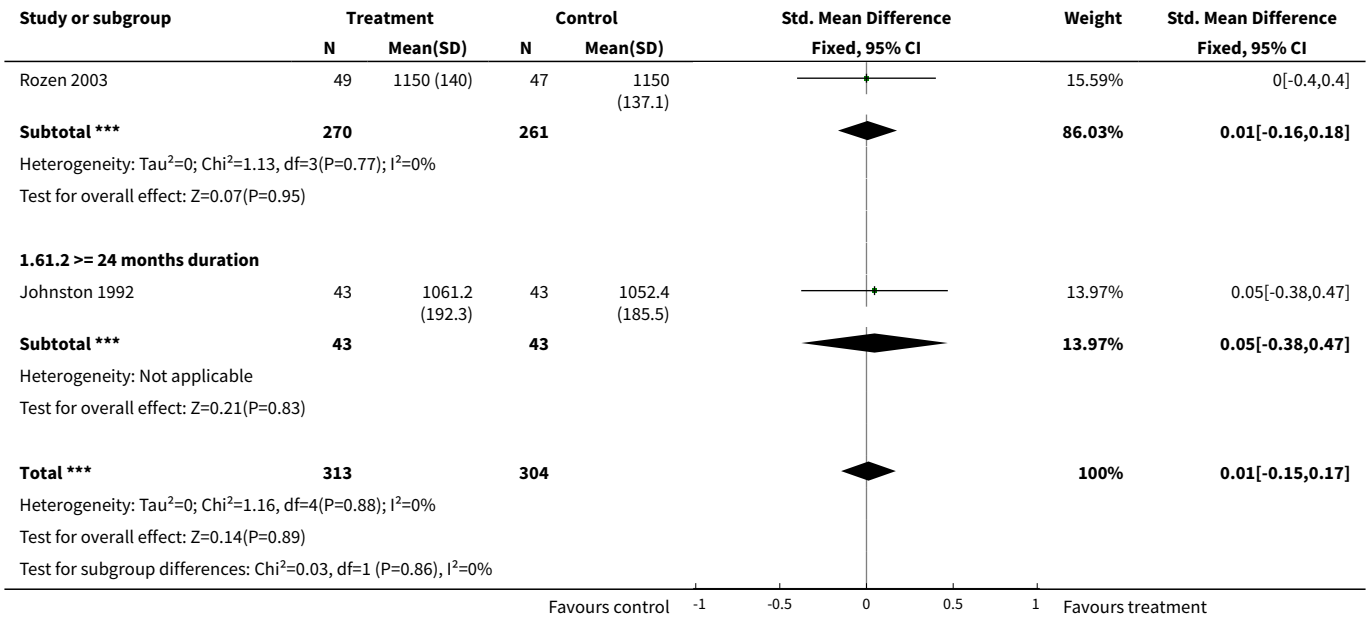



## Analysis 1.60. Comparison 1 Calcium supplementation vs placebo, Outcome 60 Femoral neck BMD (mg/cm2) at longest point after supplementation ceased end by duration of supplementation (24.

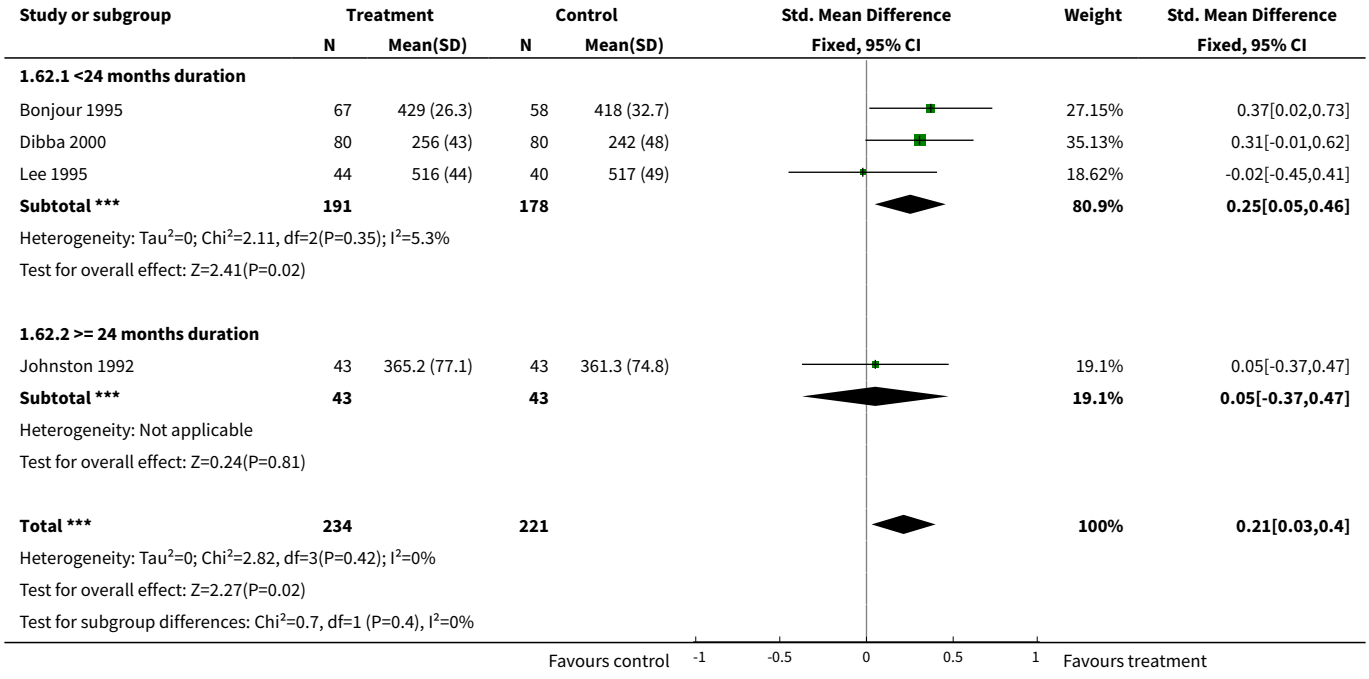



## Analysis 1.61. Comparison 1 Calcium supplementation vs placebo, Outcome 61 Lumbar spine BMD (mg/cm2) at longest point after supplementation ceased end by duration of supplementation (24.



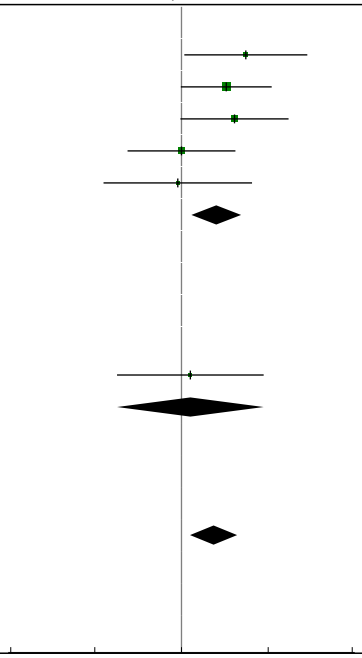



## Analysis 1.62. Comparison 1 Calcium supplementation vs placebo, Outcome 62 Distal radius BMD (mg/cm2) at longest point after supplementation ceased end by duration of supplementation (2.



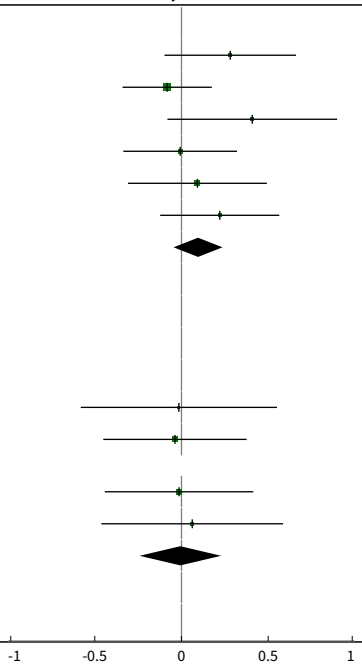
## Analysis 1.63. Comparison 1 Calcium supplementation vs placebo, Outcome 63 Upper limb BMD (mg/cm2) at longest point after supplementation ceased end by duration of supplementation (24).

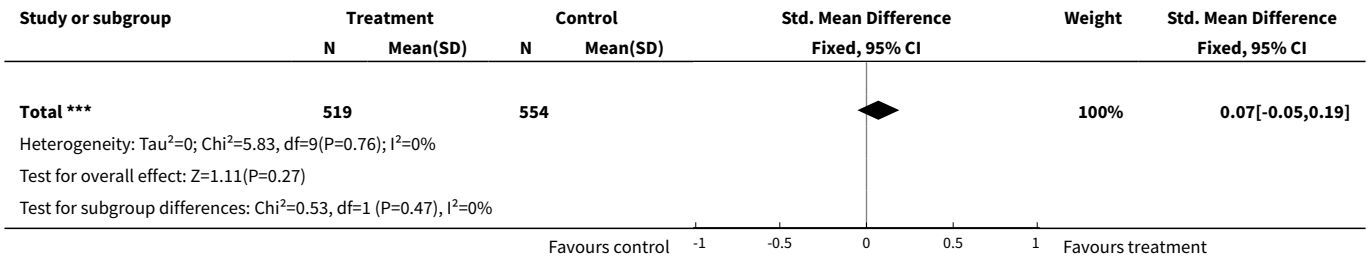
| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.63.1 <24 months duration** | | | | | | | |
| Bonjour 1995 | 67 | 429 (26.3) | 58 | 418 (32.7) | | 14.67% | 0.37[0.02,0.73] |
| Chevalley 2005 | 110 | 24.7 (21.7) | 116 | 19.4 (19.2) | | 26.89% | 0.26[-0,0.52] |
| Dibba 2000 | 80 | 256 (43) | 80 | 242 (48) | | 18.98% | 0.31[-0.01,0.62] |
| Lee 1994 | 77 | 505 (45) | 82 | 505 (40) | | 19.07% | 0[-0.31,0.31] |
| Lee 1995 | 44 | 516 (44) | 40 | 517 (49) | | 10.06% | -0.02[-0.45,0.41] |
| **Subtotal ***** | **378** | | **376** | | | **89.68%** | **0.2[0.06,0.34]** |
| Heterogeneity: Tau²=0; Chi²=4.14, df=4(P=0.39); I²=3.38% | | | | | | | |
| Test for overall effect: Z=2.74(P=0.01) | | | | | | | |
| **1.63.2 >= 24 months duration** | | | | | | | |
| Johnston 1992 | 43 | 365.2 (77.1) | 43 | 361.3 (74.8) | | 10.32% | 0.05[-0.37,0.47] |
| **Subtotal ***** | **43** | | **43** | | | **10.32%** | **0.05[-0.37,0.47]** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z=0.24(P=0.81) | | | | | | | |
| **Total ***** | **421** | | **419** | | | **100%** | **0.19[0.05,0.32]** |
| Heterogeneity: Tau²=0; Chi²=4.57, df=5(P=0.47); I²=0% | | | | | | | |
| Test for overall effect: Z=2.67(P=0.01) | | | | | | | |
| Test for subgroup differences: Chi²=0.43, df=1 (P=0.51), I²=0% | | | | | | | |



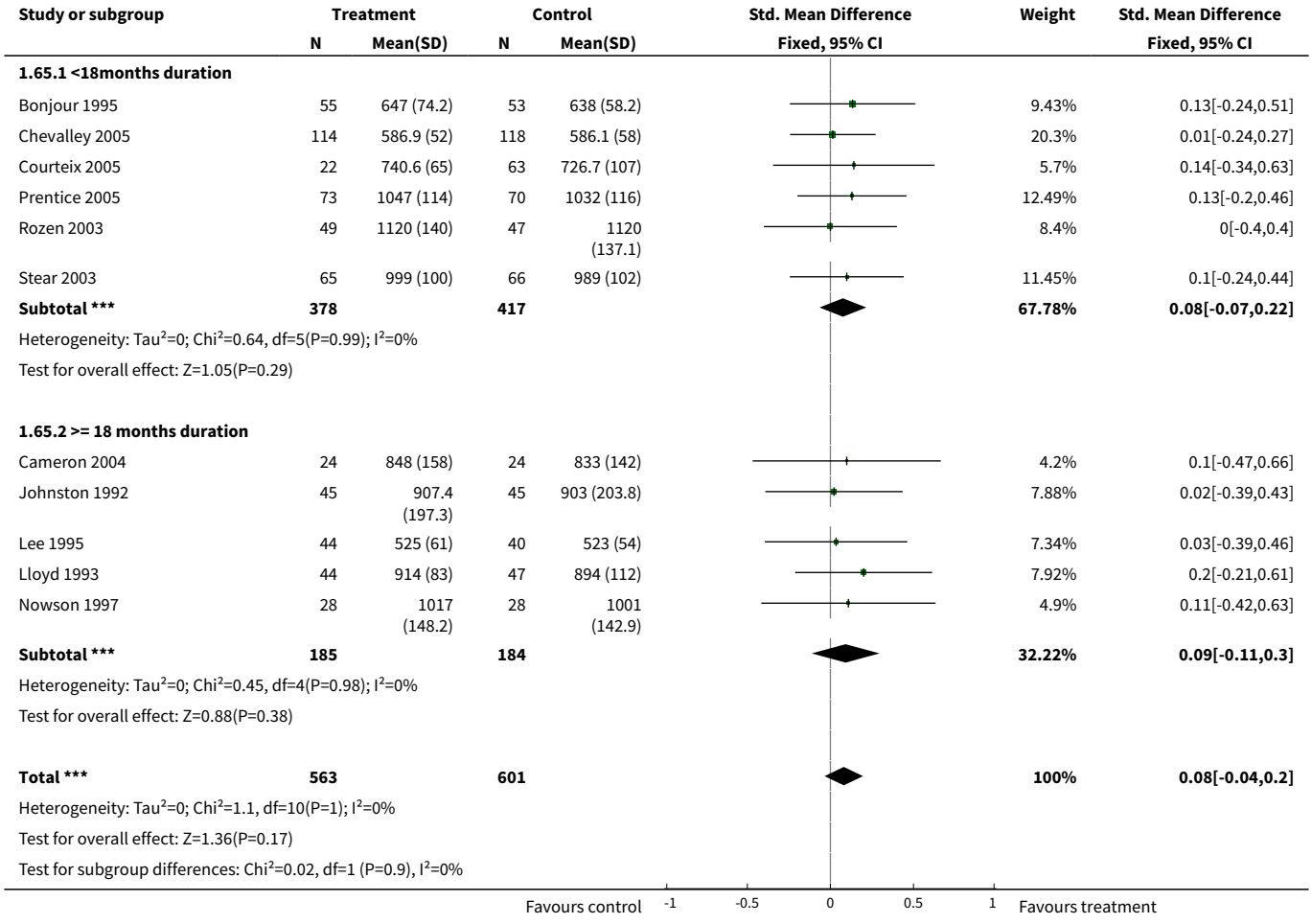

## Analysis 1.64. Comparison 1 Calcium supplementation vs placebo, Outcome 64 Femoral neck BMD (mg/cm2) at end supplementation by duration of supplementation (< 18months vs >= 18months).

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.64.1 <18months duration** | | | | | | | |
| Bonjour 1995 | 55 | 656 (81.6) | 53 | 635 (65.5) | | 10.18% | 0.28[-0.1,0.66] |
| Chevalley 2005 | 114 | 698 (70) | 118 | 703.7 (68) | | 22.08% | -0.08[-0.34,0.18] |
| Courteix 2005 | 22 | 772.5 (57.4) | 63 | 737 (93.8) | | 6.11% | 0.41[-0.08,0.9] |
| Prentice 2005 | 73 | 1001 (134) | 70 | 1002 (129) | | 13.62% | -0.01[-0.34,0.32] |
| Rozen 2003 | 49 | 1010 (70) | 47 | 1000 (137) | | 9.13% | 0.09[-0.31,0.49] |
| Stear 2003 | 65 | 870 (100) | 66 | 847 (107) | | 12.4% | 0.22[-0.12,0.56] |
| **Subtotal ***** | **378** | | **417** | | | **73.53%** | **0.1[-0.05,0.24]** |
| Heterogeneity: Tau²=0; Chi²=5.21, df=5(P=0.39); I²=4.1% | | | | | | | |
| Test for overall effect: Z=1.32(P=0.19) | | | | | | | |
| **1.64.2 >= 18 months duration** | | | | | | | |
| Cameron 2004 | 24 | 814 (131) | 24 | 816 (131) | | 4.57% | -0.02[-0.58,0.55] |
| Johnston 1992 | 45 | 847.7 (128.1) | 45 | 852.9 (144) | | 8.57% | -0.04[-0.45,0.38] |
| Lee 1995 | 44 | 592 (74) | 40 | 593 (65) | | 7.99% | -0.01[-0.44,0.41] |
| Nowson 1997 | 28 | 877 (90) | 28 | 871 (100.5) | | 5.33% | 0.06[-0.46,0.59] |
| **Subtotal ***** | **141** | | **137** | | | **26.47%** | **-0.01[-0.24,0.23]** |
| Heterogeneity: Tau²=0; Chi²=0.09, df=3(P=0.99); I²=0% | | | | | | | |
| Test for overall effect: Z=0.05(P=0.96) | | | | | | | |

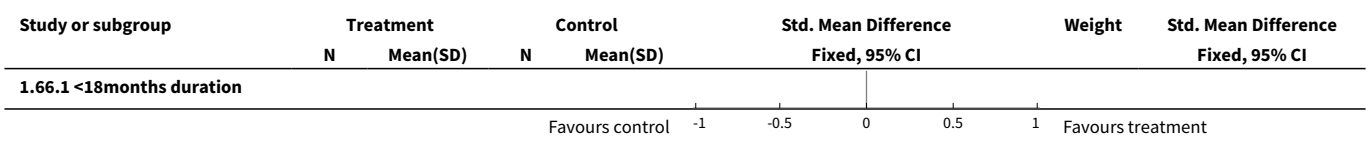


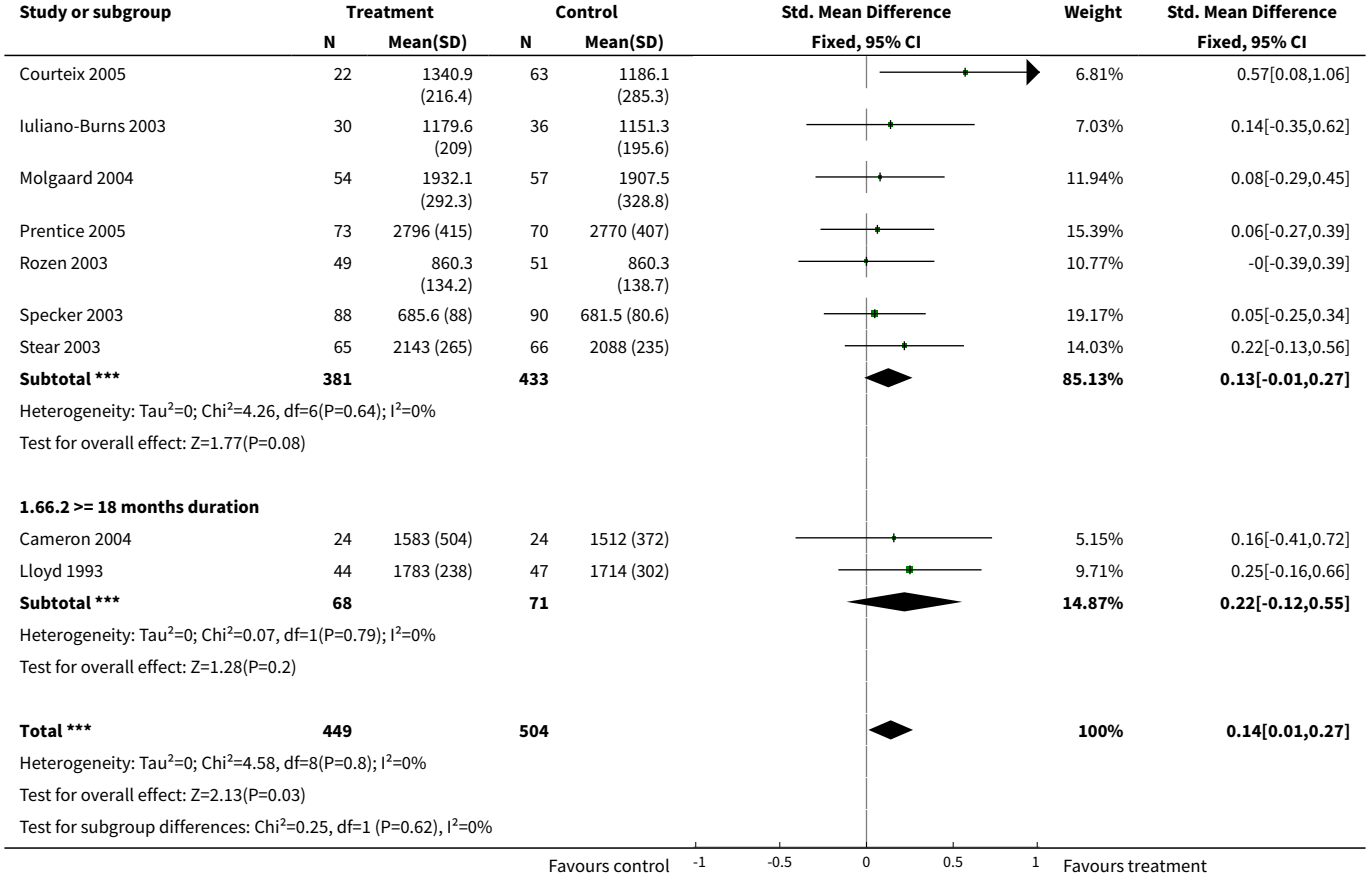



## Analysis 1.65. Comparison 1 Calcium supplementation vs placebo, Outcome 65 Lumbar spine BMD (mg/cm2) at end supplementation by duration of supplementation (< 18months vs >= 18months).

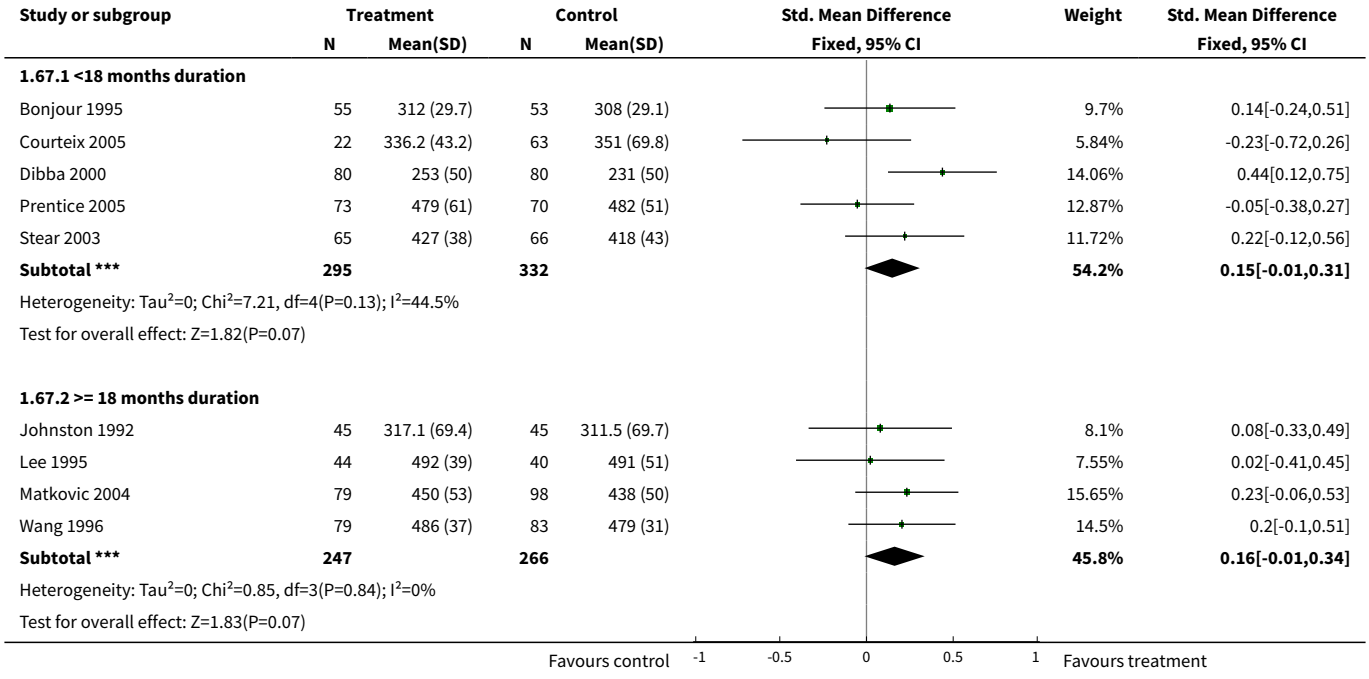



## Analysis 1.66. Comparison 1 Calcium supplementation vs placebo, Outcome 66 Total body BMC (mg) at end supplementation by duration of supplementation (< 18months vs >= 18months).

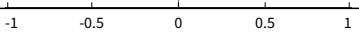





## Analysis 1.67. Comparison 1 Calcium supplementation vs placebo, Outcome 67 Distal radius BMD (mg/cm2) at end supplementation by duration of supplementation (< 18months vs >= 18months).



| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **Total ***** | **542** | | **598** | | | **100%** | **0.15[0.04,0.27]** |
| Heterogeneity: Tau²=0; Chi²=8.07, df=8(P=0.43); I²=0.91% | | | | | | | |
| Test for overall effect: Z=2.57(P=0.01) | | | | | | | |
| Test for subgroup differences: Chi²=0.01, df=1 (P=0.91), I²=0% | | | | | | | |



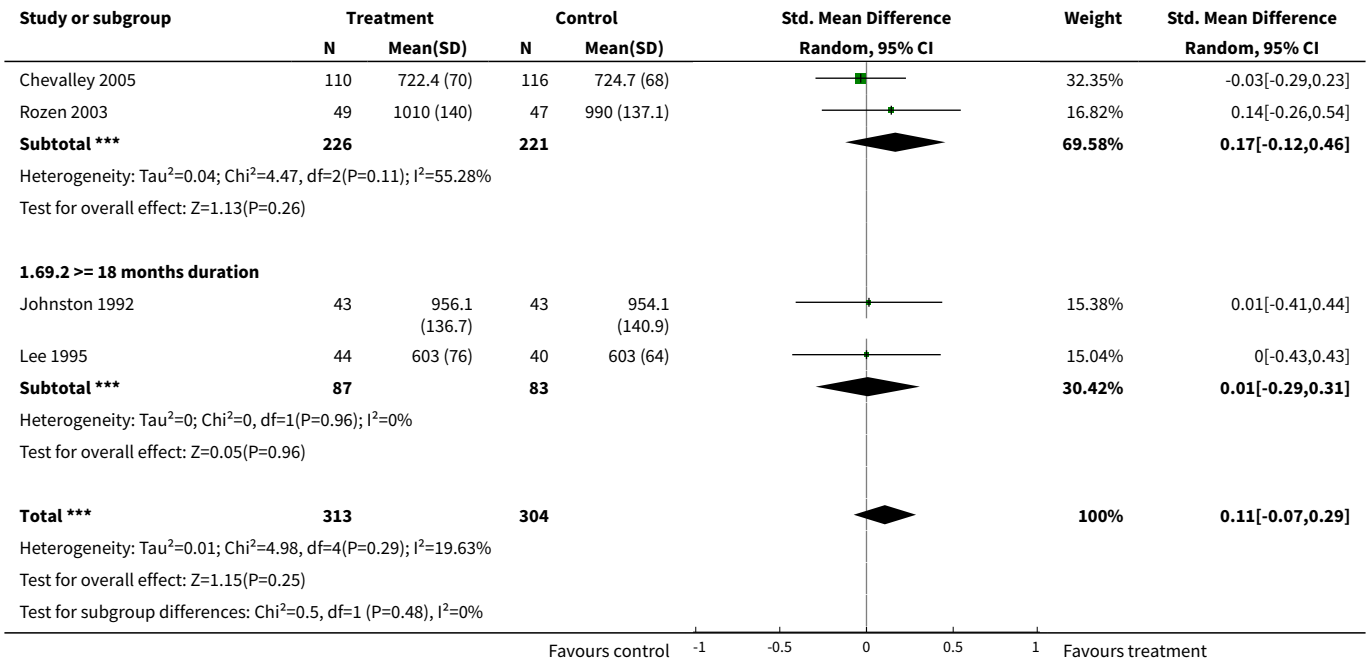

## Analysis 1.68. Comparison 1 Calcium supplementation vs placebo, Outcome 68 Upper limb BMD (mg/cm2) at end supplementation by duration of supplementation (< 18months vs >= 18months).

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.68.1 <18 months duration** | | | | | | | |
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 6.96% | 0.14[-0.24,0.51] |
| Chevalley 2005 | 114 | 309.6 (28) | 118 | 308.2 (32) | | 14.97% | 0.05[-0.21,0.3] |
| Courteix 2005 | 22 | 336.2 (43.2) | 63 | 351 (69.8) | | 4.19% | -0.23[-0.72,0.26] |
| Dibba 2000 | 80 | 253 (50) | 80 | 231 (50) | | 10.09% | 0.44[0.12,0.75] |
| Prentice 2005 | 73 | 479 (61) | 70 | 482 (51) | | 9.23% | -0.05[-0.38,0.27] |
| Stear 2003 | 65 | 427 (38) | 66 | 418 (43) | | 8.41% | 0.22[-0.12,0.56] |
| **Subtotal ***** | **409** | | **450** | | | **53.84%** | **0.12[-0.02,0.26]** |
| Heterogeneity: Tau²=0; Chi²=7.64, df=5(P=0.18); I²=34.56% | | | | | | | |
| Test for overall effect: Z=1.73(P=0.08) | | | | | | | |
| **1.68.2 >= 18 months duration** | | | | | | | |
| Cameron 2004 | 24 | 418 (43) | 24 | 414 (42) | | 3.1% | 0.09[-0.47,0.66] |
| Johnston 1992 | 45 | 317.1 (69.4) | 45 | 311.5 (69.7) | | 5.81% | 0.08[-0.33,0.49] |
| Lee 1994 | 77 | 487 (41) | 82 | 480 (43) | | 10.22% | 0.17[-0.15,0.48] |
| Lee 1995 | 44 | 492 (39) | 40 | 491 (51) | | 5.41% | 0.02[-0.41,0.45] |
| Matkovic 2004 | 79 | 450 (53) | 98 | 438 (50) | | 11.22% | 0.23[-0.06,0.53] |
| Wang 1996 | 79 | 486 (37) | 83 | 479 (31) | | 10.4% | 0.2[-0.1,0.51] |
| **Subtotal ***** | **348** | | **372** | | | **46.16%** | **0.16[0.01,0.3]** |
| Heterogeneity: Tau²=0; Chi²=0.91, df=5(P=0.97); I²=0% | | | | | | | |
| Test for overall effect: Z=2.11(P=0.03) | | | | | | | |
| **Total ***** | **757** | | **822** | | | **100%** | **0.14[0.04,0.24]** |
| Heterogeneity: Tau²=0; Chi²=8.69, df=11(P=0.65); I²=0% | | | | | | | |
| Test for overall effect: Z=2.71(P=0.01) | | | | | | | |
| Test for subgroup differences: Chi²=0.14, df=1 (P=0.71), I²=0% | | | | | | | |

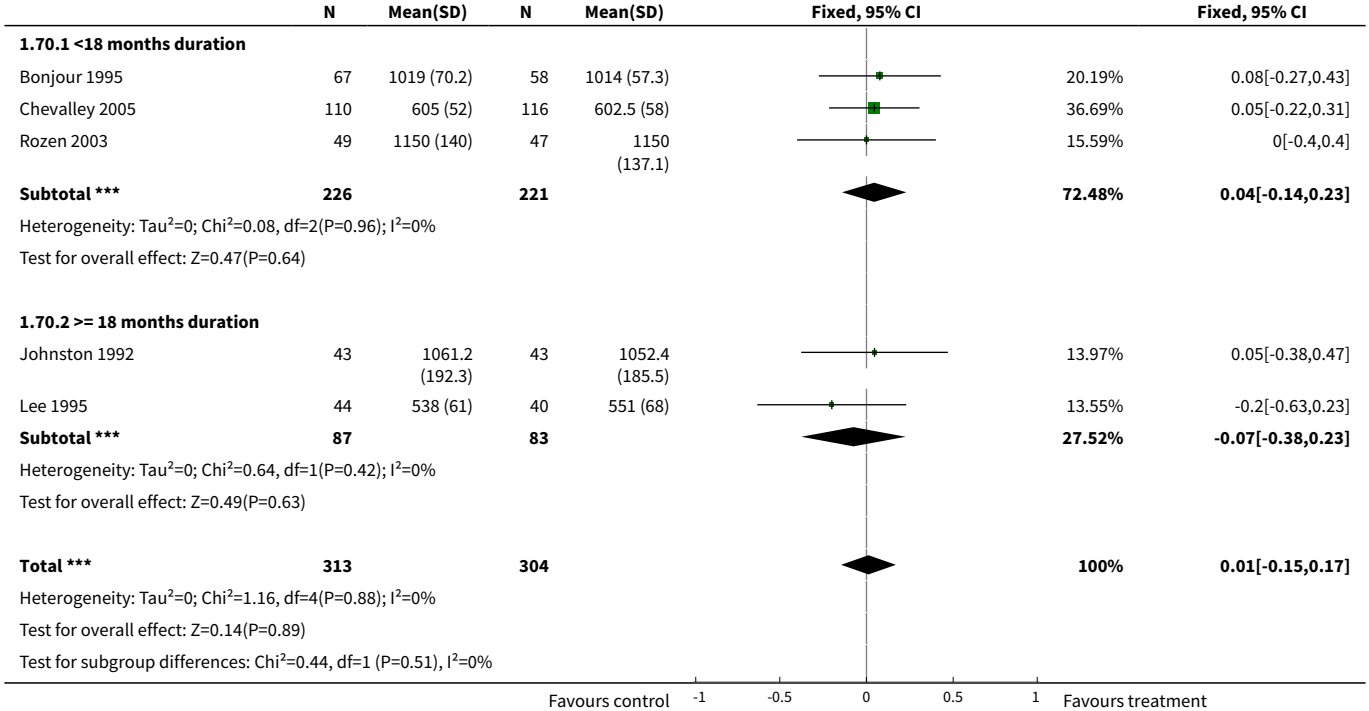



## Analysis 1.69. Comparison 1 Calcium supplementation vs placebo, Outcome 69 Femoral neck BMD (mg/cm2) at longest point after cessation of supplementation by duration of supplementation.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Random, 95% CI | Weight | Std. Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.69.1 <18 months duration** | | | | | | | |
| Bonjour 1995 | 67 | 885 (70.2) | 58 | 853 (73.7) | | 20.41% | 0.44[0.09,0.8] |

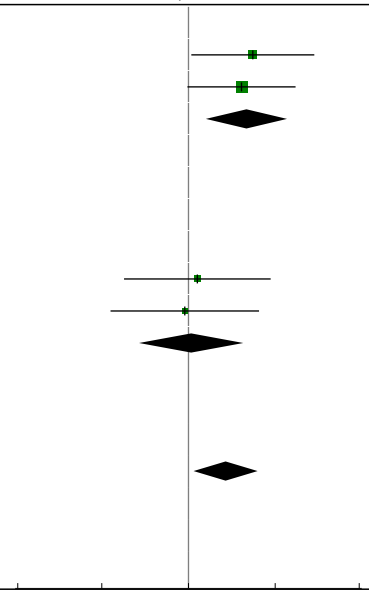



## Analysis 1.70. Comparison 1 Calcium supplementation vs placebo, Outcome 70 Lumbar spine BMD (mg/cm2) at longest point after cessation of supplementation by duration of supplementation.



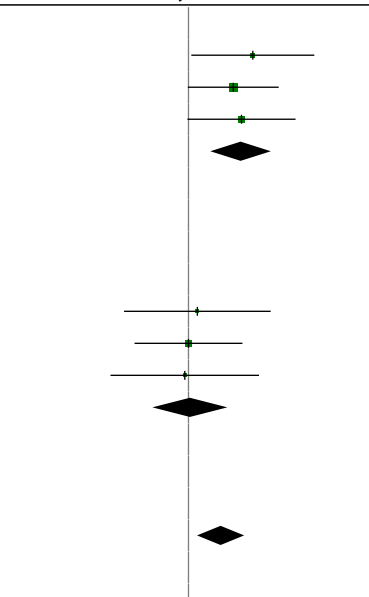
## Analysis 1.71. Comparison 1 Calcium supplementation vs placebo, Outcome 71 Distal radius BMD (mg/cm2) at longest point after cessation of supplementation by duration of supplementation.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.71.1 <18 months duration** | | | | | | | |
| Bonjour 1995 | 67 | 429 (26.3) | 58 | 418 (32.7) | | 27.15% | 0.37[0.02,0.73] |
| Dibba 2000 | 80 | 256 (43) | 80 | 242 (48) | | 35.13% | 0.31[-0.01,0.62] |
| **Subtotal ***** | **147** | | **138** | | | **62.28%** | **0.33[0.1,0.57]** |
| Heterogeneity: Tau²=0; Chi²=0.07, df=1(P=0.79); I²=0% | | | | | | | |
| Test for overall effect: Z=2.8(P=0.01) | | | | | | | |
| **1.71.2 >= 18 months duration** | | | | | | | |
| Johnston 1992 | 43 | 365.2 (77.1) | 43 | 361.3 (74.8) | | 19.1% | 0.05[-0.37,0.47] |
| Lee 1995 | 44 | 516 (44) | 40 | 517 (49) | | 18.62% | -0.02[-0.45,0.41] |
| **Subtotal ***** | **87** | | **83** | | | **37.72%** | **0.02[-0.29,0.32]** |
| Heterogeneity: Tau²=0; Chi²=0.06, df=1(P=0.81); I²=0% | | | | | | | |
| Test for overall effect: Z=0.1(P=0.92) | | | | | | | |
| **Total ***** | **234** | | **221** | | | **100%** | **0.21[0.03,0.4]** |
| Heterogeneity: Tau²=0; Chi²=2.82, df=3(P=0.42); I²=0% | | | | | | | |
| Test for overall effect: Z=2.27(P=0.02) | | | | | | | |
| Test for subgroup differences: Chi²=2.69, df=1 (P=0.1), I²=62.78% | | | | | | | |



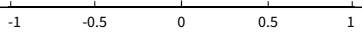

## Analysis 1.72. Comparison 1 Calcium supplementation vs placebo, Outcome 72 Upper limb BMD (mg/cm2) at longest point after cessation of supplementation by duration of supplementation.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.72.1 <18 months duration** | | | | | | | |
| Bonjour 1995 | 67 | 429 (26.3) | 58 | 418 (32.7) | | 14.67% | 0.37[0.02,0.73] |
| Chevalley 2005 | 110 | 24.7 (21.7) | 116 | 19.4 (19.2) | | 26.89% | 0.26[-0,0.52] |
| Dibba 2000 | 80 | 256 (43) | 80 | 242 (48) | | 18.98% | 0.31[-0.01,0.62] |
| **Subtotal ***** | **257** | | **254** | | | **60.54%** | **0.3[0.13,0.48]** |
| Heterogeneity: Tau²=0; Chi²=0.25, df=2(P=0.88); I²=0% | | | | | | | |
| Test for overall effect: Z=3.37(P=0) | | | | | | | |
| **1.72.2 >= 18 months duration** | | | | | | | |
| Johnston 1992 | 43 | 365.2 (77.1) | 43 | 361.3 (74.8) | | 10.32% | 0.05[-0.37,0.47] |
| Lee 1994 | 77 | 505 (45) | 82 | 505 (40) | | 19.07% | 0[-0.31,0.31] |
| Lee 1995 | 44 | 516 (44) | 40 | 517 (49) | | 10.06% | -0.02[-0.45,0.41] |
| **Subtotal ***** | **164** | | **165** | | | **39.46%** | **0.01[-0.21,0.22]** |
| Heterogeneity: Tau²=0; Chi²=0.06, df=2(P=0.97); I²=0% | | | | | | | |
| Test for overall effect: Z=0.07(P=0.94) | | | | | | | |
| **Total ***** | **421** | | **419** | | | **100%** | **0.19[0.05,0.32]** |
| Heterogeneity: Tau²=0; Chi²=4.57, df=5(P=0.47); I²=0% | | | | | | | |
| Test for overall effect: Z=2.67(P=0.01) | | | | | | | |
| Test for subgroup differences: Chi²=4.26, df=1 (P=0.04), I²=76.51% | | | | | | | |



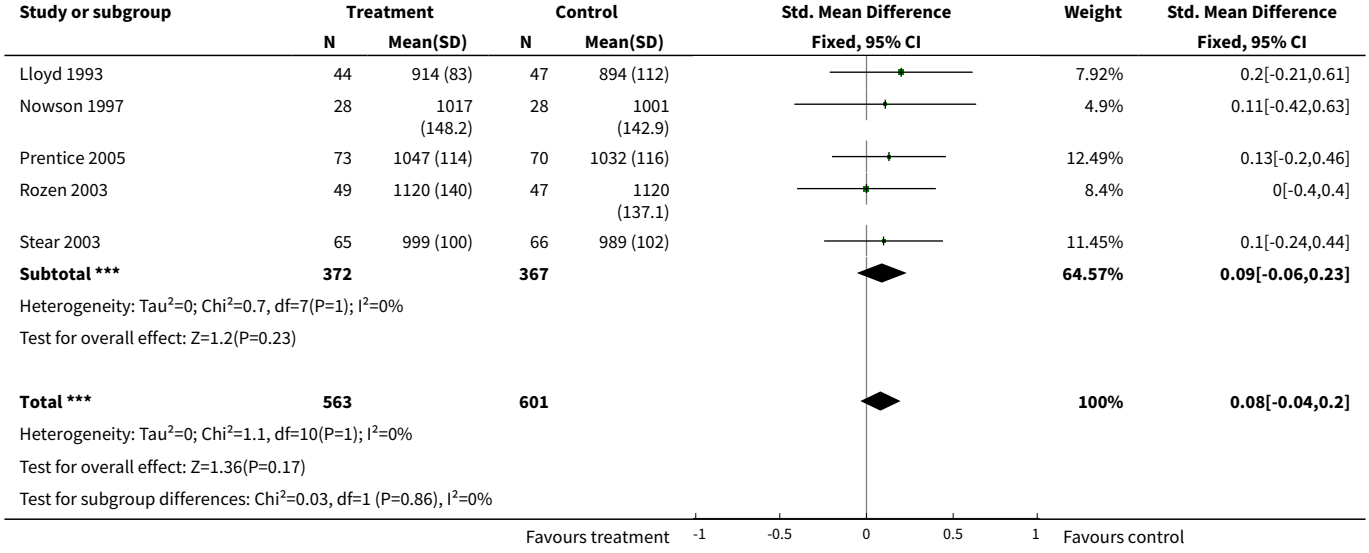
## Analysis 1.73. Comparison 1 Calcium supplementation vs placebo, Outcome 73 Femoral neck BMD (mg/cm2) at end supplementation by milk extract vs other calcium supplement.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Random, 95% CI | Weight | Std. Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.73.1 milk extract** | | | | | | | |
| Bonjour 1995 | 55 | 656 (81.6) | 53 | 635 (65.5) | | 10.18% | 0.28[-0.1,0.66] |
| Chevalley 2005 | 114 | 698 (70) | 118 | 703.7 (68) | | 22.08% | -0.08[-0.34,0.18] |
| Courteix 2005 | 22 | 772.5 (57.4) | 63 | 737 (93.8) | | 6.11% | 0.41[-0.08,0.9] |
| **Subtotal ***** | **191** | | **234** | | | **38.38%** | **0.15[-0.16,0.46]** |
| Heterogeneity: $Tau^2$=0.04; $Chi^2$=4.32, df=2(P=0.12); $I^2$=53.73% | | | | | | | |
| Test for overall effect: Z=0.98(P=0.33) | | | | | | | |
| **1.73.2 other calcium supplementation** | | | | | | | |
| Cameron 2004 | 24 | 814 (131) | 24 | 816 (131) | | 4.57% | -0.02[-0.58,0.55] |
| Johnston 1992 | 45 | 847.7 (128.1) | 45 | 852.9 (144) | | 8.57% | -0.04[-0.45,0.38] |
| Lee 1995 | 44 | 592 (74) | 40 | 593 (65) | | 7.99% | -0.01[-0.44,0.41] |
| Nowson 1997 | 28 | 877 (90) | 28 | 871 (100.5) | | 5.33% | 0.06[-0.46,0.59] |
| Prentice 2005 | 73 | 1001 (134) | 70 | 1002 (129) | | 13.62% | -0.01[-0.34,0.32] |
| Rozen 2003 | 49 | 1010 (70) | 47 | 1000 (137) | | 9.13% | 0.09[-0.31,0.49] |
| Stear 2003 | 65 | 870 (100) | 66 | 847 (107) | | 12.4% | 0.22[-0.12,0.56] |
| **Subtotal ***** | **328** | | **320** | | | **61.62%** | **0.05[-0.1,0.21]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=1.42, df=6(P=0.96); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.68(P=0.5) | | | | | | | |
| **Total ***** | **519** | | **554** | | | **100%** | **0.07[-0.05,0.19]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=5.83, df=9(P=0.76); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.11(P=0.27) | | | | | | | |
| Test for subgroup differences: $Chi^2$=0.09, df=1 (P=0.76), $I^2$=0% | | | | | | | |

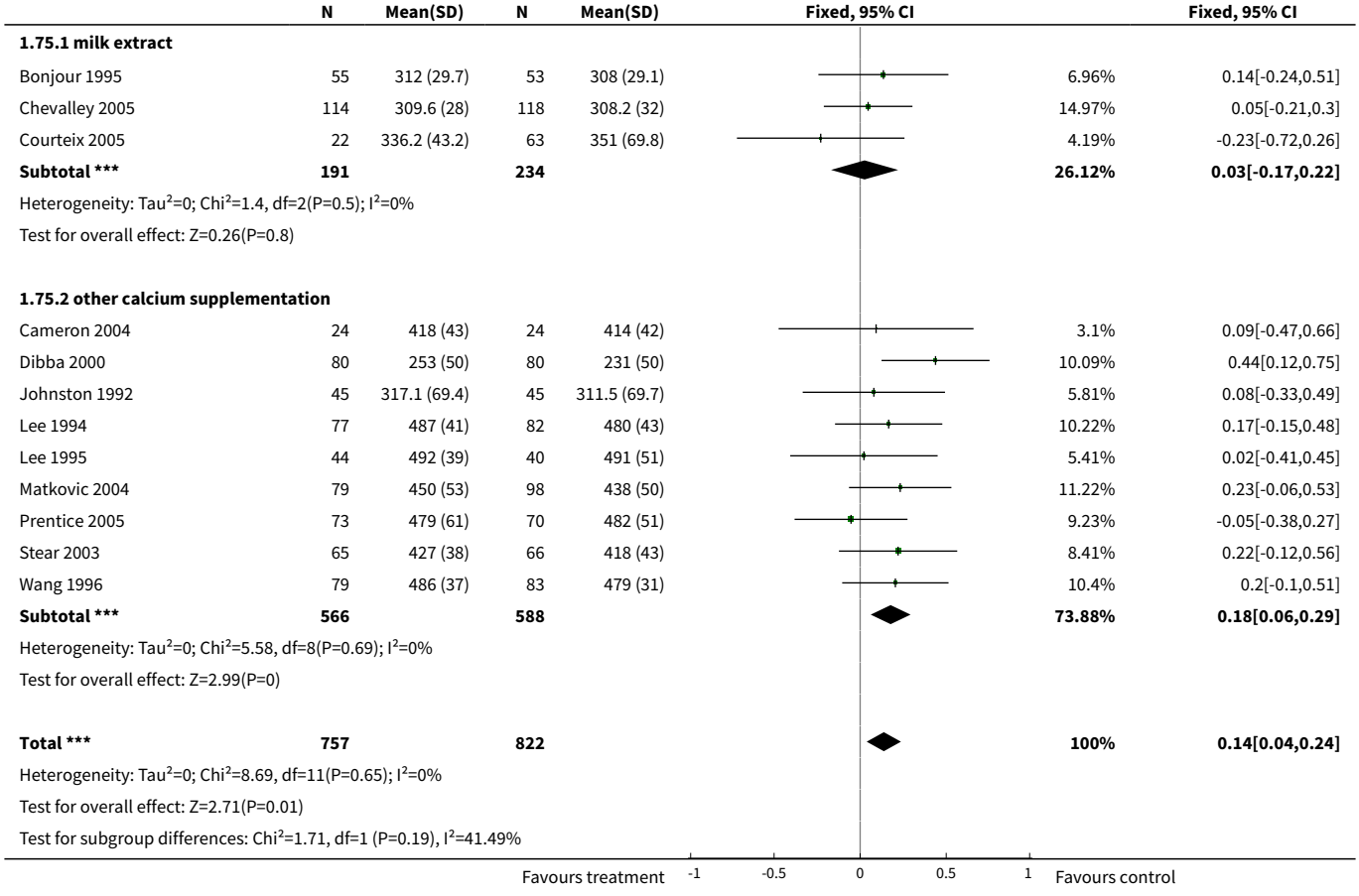



## Analysis 1.74. Comparison 1 Calcium supplementation vs placebo, Outcome 74 Lumbar spine BMD (mg/cm2) at end supplementation by milk extract vs other calcium supplement.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.74.1 milk extract** | | | | | | | |
| Bonjour 1995 | 55 | 647 (74.2) | 53 | 638 (58.2) | | 9.43% | 0.13[-0.24,0.51] |
| Chevalley 2005 | 114 | 586.9 (52) | 118 | 586.1 (58) | | 20.3% | 0.01[-0.24,0.27] |
| Courteix 2005 | 22 | 740.6 (65) | 63 | 726.7 (107) | | 5.7% | 0.14[-0.34,0.63] |
| **Subtotal ***** | **191** | | **234** | | | **35.43%** | **0.07[-0.13,0.26]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.37, df=2(P=0.83); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.67(P=0.5) | | | | | | | |
| **1.74.2 other calcium supplementation** | | | | | | | |
| Cameron 2004 | 24 | 848 (158) | 24 | 833 (142) | | 4.2% | 0.1[-0.47,0.66] |
| Johnston 1992 | 45 | 907.4 (197.3) | 45 | 903 (203.8) | | 7.88% | 0.02[-0.39,0.43] |
| Lee 1995 | 44 | 525 (61) | 40 | 523 (54) | | 7.34% | 0.03[-0.39,0.46] |

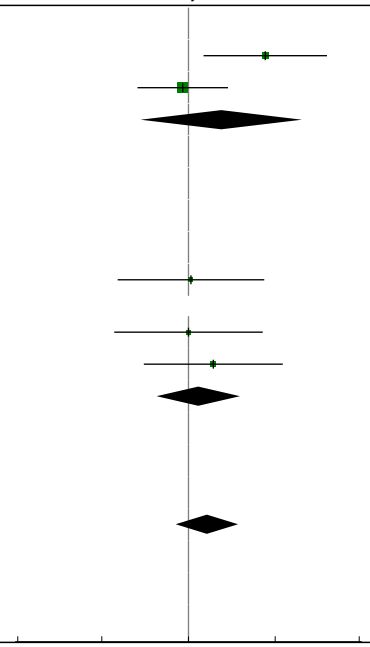



## Analysis 1.75. Comparison 1 Calcium supplementation vs placebo, Outcome 75 Upper limb BMD (mg/cm2) at end supplementation by milk extract vs other calcium supplement.



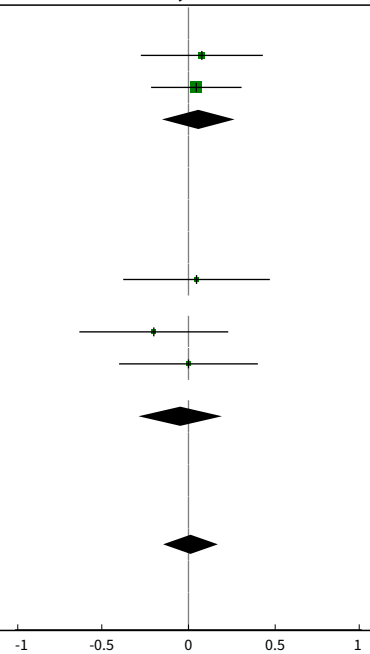
## Analysis 1.76. Comparison 1 Calcium supplementation vs placebo, Outcome 76 Femoral neck BMD (mg/cm2) after supplementation ceased by milk extract vs other calcium supplement.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Random, 95% CI | Weight | Std. Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.76.1 milk extract** | | | | | | | |
| Bonjour 1995 | 67 | 885 (70.2) | 58 | 853 (73.7) | | 20.41% | 0.44[0.09,0.8] |
| Chevalley 2005 | 110 | 722.4 (70) | 116 | 724.7 (68) | | 32.35% | -0.03[-0.29,0.23] |
| **Subtotal ***** | **177** | | **174** | | | **52.76%** | **0.19[-0.28,0.65]** |
| Heterogeneity: $Tau^2$=0.09; $Chi^2$=4.47, df=1(P=0.03); $I^2$=77.63% | | | | | | | |
| Test for overall effect: Z=0.79(P=0.43) | | | | | | | |
| **1.76.2 other calcium supplementation** | | | | | | | |
| Johnston 1992 | 43 | 956.1 (136.7) | 43 | 954.1 (140.9) | | 15.38% | 0.01[-0.41,0.44] |
| Lee 1995 | 44 | 603 (76) | 40 | 603 (64) | | 15.04% | 0[-0.43,0.43] |
| Rozen 2003 | 49 | 1010 (140) | 47 | 990 (137.1) | | 16.82% | 0.14[-0.26,0.54] |
| **Subtotal ***** | **136** | | **130** | | | **47.24%** | **0.06[-0.18,0.3]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.28, df=2(P=0.87); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.46(P=0.65) | | | | | | | |
| **Total ***** | **313** | | **304** | | | **100%** | **0.11[-0.07,0.29]** |
| Heterogeneity: $Tau^2$=0.01; $Chi^2$=4.98, df=4(P=0.29); $I^2$=19.63% | | | | | | | |
| Test for overall effect: Z=1.15(P=0.25) | | | | | | | |
| Test for subgroup differences: $Chi^2$=0.22, df=1 (P=0.64), $I^2$=0% | | | | | | | |




## Analysis 1.77. Comparison 1 Calcium supplementation vs placebo, Outcome 77 Lumbar spine BMD (mg/cm2) after supplementation ceased by milk extract vs other calcium supplement.

| Study or subgroup | Treatment N | Treatment Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.77.1 milk extract** | | | | | | | |
| Bonjour 1995 | 67 | 1019 (70.2) | 58 | 1014 (57.3) | | 20.19% | 0.08[-0.27,0.43] |
| Chevalley 2005 | 110 | 605 (52) | 116 | 602.5 (58) | | 36.69% | 0.05[-0.22,0.31] |
| **Subtotal ***** | **177** | | **174** | | | **56.88%** | **0.06[-0.15,0.27]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.02, df=1(P=0.89); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.53(P=0.6) | | | | | | | |
| **1.77.2 other calcium supplementation** | | | | | | | |
| Johnston 1992 | 43 | 1061.2 (192.3) | 43 | 1052.4 (185.5) | | 13.97% | 0.05[-0.38,0.47] |
| Lee 1995 | 44 | 538 (61) | 40 | 551 (68) | | 13.55% | -0.2[-0.63,0.23] |
| Rozen 2003 | 49 | 1150 (140) | 47 | 1150 (137.1) | | 15.59% | 0[-0.4,0.4] |
| **Subtotal ***** | **136** | | **130** | | | **43.12%** | **-0.05[-0.29,0.19]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.73, df=2(P=0.69); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.39(P=0.7) | | | | | | | |
| **Total ***** | **313** | | **304** | | | **100%** | **0.01[-0.15,0.17]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=1.16, df=4(P=0.88); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.14(P=0.89) | | | | | | | |



| Study or subgroup | Treatment N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Test for subgroup differences: Chi²=0.41, df=1 (P=0.52), I²=0% | | | | | | | |

Favours treatment -1 -0.5 0 0.5 1 Favours control

## Analysis 1.78. Comparison 1 Calcium supplementation vs placebo, Outcome 78 Upper limb BMD (mg/cm2) after supplementation ceased by milk extract vs other calcium supplement.

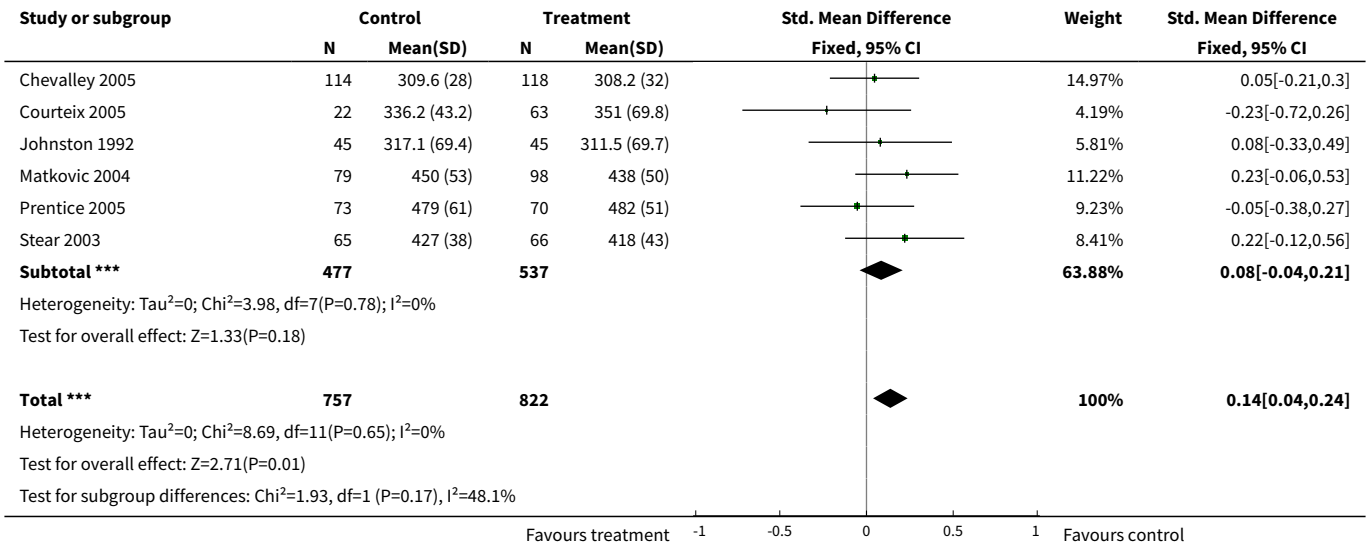
| Study or subgroup | Treatment N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.78.1 milk extract** | | | | | | | |
| Bonjour 1995 | 67 | 429 (26.3) | 58 | 418 (32.7) | | 14.64% | 0.37[0.02,0.73] |
| Chevalley 2005 | 110 | 319.7 (28) | 116 | 316.4 (32) | | 27.02% | 0.11[-0.15,0.37] |
| **Subtotal ***** | **177** | | **174** | | | **41.67%** | **0.2[-0.01,0.41]** |
| Heterogeneity: Tau²=0; Chi²=1.36, df=1(P=0.24); I²=26.35% | | | | | | | |
| Test for overall effect: Z=1.88(P=0.06) | | | | | | | |
| **1.78.2 other calcium supplementation** | | | | | | | |
| Dibba 2000 | 80 | 256 (43) | 80 | 242 (48) | | 18.95% | 0.31[-0.01,0.62] |
| Johnston 1992 | 43 | 365.2 (77.1) | 43 | 361.3 (74.8) | | 10.3% | 0.05[-0.37,0.47] |
| Lee 1994 | 77 | 505 (45) | 82 | 505 (40) | | 19.04% | 0[-0.31,0.31] |
| Lee 1995 | 44 | 516 (44) | 40 | 517 (49) | | 10.04% | -0.02[-0.45,0.41] |
| **Subtotal ***** | **244** | | **245** | | | **58.33%** | **0.1[-0.07,0.28]** |
| Heterogeneity: Tau²=0; Chi²=2.43, df=3(P=0.49); I²=0% | | | | | | | |
| Test for overall effect: Z=1.15(P=0.25) | | | | | | | |
| **Total ***** | **421** | | **419** | | | **100%** | **0.14[0.01,0.28]** |
| Heterogeneity: Tau²=0; Chi²=4.26, df=5(P=0.51); I²=0% | | | | | | | |
| Test for overall effect: Z=2.09(P=0.04) | | | | | | | |
| Test for subgroup differences: Chi²=0.47, df=1 (P=0.49), I²=0% | | | | | | | |

Favours treatment -1 -0.5 0 0.5 1 Favours control

## Analysis 1.79. Comparison 1 Calcium supplementation vs placebo, Outcome 79 Upper limb BMD (mg/cm2) by calcium intake (lowest quartile vs above lowest quartile).

| Study or subgroup | Control N | Mean(SD) | Treatment N | Mean(SD) | Std. Mean Difference Fixed, 95% CI | Weight | Std. Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.79.1 Lowest quartile** | | | | | | | |
| Dibba 2000 | 80 | 253 (50) | 80 | 231 (50) | | 10.09% | 0.44[0.12,0.75] |
| Lee 1994 | 77 | 487 (41) | 82 | 480 (43) | | 10.22% | 0.17[-0.15,0.48] |
| Lee 1995 | 44 | 492 (39) | 40 | 491 (51) | | 5.41% | 0.02[-0.41,0.45] |
| Wang 1996 | 79 | 486 (37) | 83 | 479 (31) | | 10.4% | 0.2[-0.1,0.51] |
| **Subtotal ***** | **280** | | **285** | | | **36.12%** | **0.23[0.07,0.4]** |
| Heterogeneity: Tau²=0; Chi²=2.78, df=3(P=0.43); I²=0% | | | | | | | |
| Test for overall effect: Z=2.74(P=0.01) | | | | | | | |
| **1.79.2 Above lowest quartile** | | | | | | | |
| Bonjour 1995 | 55 | 312 (29.7) | 53 | 308 (29.1) | | 6.96% | 0.14[-0.24,0.51] |
| Cameron 2004 | 24 | 418 (43) | 24 | 414 (42) | | 3.1% | 0.09[-0.47,0.66] |

Favours treatment -1 -0.5 0 0.5 1 Favours control




## FEEDBACK

### Feedback from Tanis Fenton, 5 January 2010

#### Summary

Date of Submission: 05-Jan-2010

Name: Tanis Fenton

Email Address: tanisfenton@shaw.ca

Personal Description: Occupation Nutrition Researcher

Feedback: To the Editor:

In the meta-analysis on role of calcium supplementation in children, Winzenberg et al (1) used standardised mean differences (SMD) to summarize their results and to base their conclusions. Although the use of SMD is recognized as a valid approach in summarizing mean differences across trials in the Cochrane Review methodology (1), its primary purpose is for comparing variables with different units and measurement scales of different length (2). The SMD is calculated by dividing the group differences by the standard deviation. This converts a variable which has units to a unitless score. In other words, a variable which once had clinical meaning becomes clinically meaningless.

In Winzenberg et al.?s meta-analysis, all measurements of bone mineral density (BMD) by the included studies were reported as grams per square centimetre (mg/cm2). Under these circumstances, we believe that the use of SMDs is unnecessary. An alternate approach is to summarize the treatment effects as absolute differences. We have re-constructed Table 2 from the meta-analysis by calculating the effect size at the end of supplementation period in terms of g/cm2, the usual units of measurement for BMD (published on-line at: http://www.bmj.com/cgi/eletters/333/7572/775). We hope that our re-constructed Table will help clinicians better-appraise the magnitude of effect size for this meta-analysis.

In regards to interpreting the results from the Table, all bone sites show consistent increase in BMD at the end of a median calcium supplementation period of one year. We disagree with Winzenberg et al.?s claim that the observed relative increase in upper limb body BMD is not clinically important. Not only is this result statistically significant, but a yearly 0.007 g/cm2 increase (or a 1.8% relative increase) in BMD is a clinically meaningful change. If this increase continued throughout childhood, it would likely translate to a substantial gain in bone strength.

We are concerned that the results of Winzenberg et al.?s meta-analysis could be construed to imply calcium is not important in childhood, even though the meta-analysis focused on the role of calcium supplementation and did not address calcium requirements. This interpretation of the results was promoted by the accompanying Editorial in the BMJ(3). It was written by a member of the Physicians Committee for Responsible Medicine, a group that promotes vegan diets devoid of dairy products. This thinking is at odds with the American Association of Clinical Endocrinologists (4), the National Institutes of Health Consensus Development Panel on Osteoporosis

Prevention, Diagnosis and Therapy (5), the Institute of Medicine (6), and the Scientific Advisory Council of Osteoporosis Canada (7). These groups recommend adequate intakes of calcium and vitamin D, combined with weight bearing physical activity, throughout childhood to promote the attainment of an optimal peak bone mass. It is likely that calcium intake is a necessary but not sufficient condition for the development of a strong skeleton, as physical activity and calcium both play key roles in the attainment of a high peak bone mass (8).

Until we are absolutely certain about what the minimum and optimum combinations of calcium, vitamin D, foods from plant sources and physical activity are required to achieve a bone mass that will sustain the bones of individuals through their older ages without fragility fractures, it seems prudent to continue to follow the consensus-based recommendations for intakes of calcium and vitamin D.

Sincerely,

Tanis R. Fenton, PhD, RD

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**Reply**

To the editor

Thank you for the opportunity to respond to the letter from your e-mail of 5th January 2010.

Addressing the points raised in the letter:

It is valid to use SMDs. While SMDs require a greater degree of interpretation, because of the recognised variation between methods of measuring bone density we remain of the opinion that this was the most appropriate approach to use in our analysis.

We were surprised at the marked difference in results described by the letter authors in their table compared to our findings. We therefore repeated our analyses for these three outcomes using the alternative method of weighted mean differences using the inverse variance method and using a fixed effect model as there was no statistical heterogeneity for any result[1]. The results of these analyses are given in detail in figures 1-3 and are entirely consistent with our original analyses using SMDs[2,3]. Results at the femoral neck and lumbar spine were not statistically significant (p=0.2 and 0.22 respectively) but the distal radius result was significant (p=0.01). This contrasts with the p-values reported in the letter. Moreover, our re-analysis gives weighted mean differences substantially less for femoral neck and lumbar spine than provided by the letter authors (6.83 and 5.73 g/cm$^2$ compared to the results given in the letter of 11.7 and 15.2 for femoral neck and lumbar spine respectively) and somewhat less at the upper limb (5.52 g/cm$^2$ vs. 7.0 g/cm$^2$).

As we do not have details of the letter authors' analysis approach, we cannot be certain of the reason for the differences between their analyses and ours. We, however, do stand by our results which are consistent regardless of whether standardised or weighted mean differences are used and which use well established methods as outlined in the Cochrane handbook of Systematic Reviews[1].

The remaining issues raised in the letter relate to interpretation of our original findings. We argue in our original paper and continue to maintain that:

- There are no statistically significant effects of calcium supplementation at the femoral neck or lumbar, two sites of key clinical importance.
- The small persistent increase seen at the distal radius is not clinically significant in terms of reducing childhood fracture risk.
- Our subgroup analyses by study duration (<24 months compared to 24 months or more) do not support additive effects on BMD occurring with increased duration of supplementation (as postulated by the letter authors).

We cannot speak for the authors of BMJ editorials accompanying the version of our review published in the BMJ. However, none of the authors of our review have any conflict of interest with our published work, including membership of the Physicians Committee for Responsible Medicine.

We agree that calcium is important for bone health. However, our data do not demonstrate improvements in BMD likely to be of clinical or public health significance from calcium supplementation even with dietary calcium intakes as low as 594 mg/day. Thus, we maintain that potential measures for improving peak bone mass besides calcium supplementation merit urgent exploration.

Yours sincerely

Dr Tania Winzenberg

Professor Graeme Jones

Ms Jayne Fryer

Dr Kelly Shaw

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**Contributors**

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Professor Graeme Jones

Ms Jayne Fryer

Dr Kelly Shaw

## WHAT'S NEW

| Date | Event | Description |
|---|---|---|
| 19 February 2010 | Feedback has been incorporated | Feedback from Tanis Fenton, 05 January 2010 |
| 3 October 2008 | Amended | CMSG ID: A005-R |

## HISTORY

Protocol first published: Issue 1, 2005
Review first published: Issue 2, 2006

| Date | Event | Description |
|---|---|---|
| 3 October 2008 | Amended | Converted to new review format. |

## CONTRIBUTIONS OF AUTHORS

Tania Winzenberg - wrote review protocol, reviewed articles to decide on inclusion, performed data extraction and quality assessment of articles, performed the analysis and wrote the discussion of review results with the input of other authors. She will also be responsible for regularly updating and improving the review, as per Cochrane requirements.

Kelly Shaw - reviewed articles to decide on inclusion, performed data extraction and quality assessment of articles, and had input into writing of discussion of review results.

Jayne Fryer - provided advice on statistical analysis and input into writing of review methods, results and discussion.

Graeme Jones - is the content expert in pediatric bone health for the review. He provided input into design of the protocol, was the deciding reviewer for any differences in data extraction between TW and KS, assisted with the analysis and with writing the discussion of review results.

## DECLARATIONS OF INTEREST

None known.

## SOURCES OF SUPPORT

### Internal sources

- Menzies Research Institute, Australia.

### External sources

- No sources of support supplied

## INDEX TERMS

### Medical Subject Headings (MeSH)

*Dietary Supplements; Bone Density [*drug effects]; Calcium, Dietary [*administration & dosage]; Randomized Controlled Trials as Topic

## MeSH check words

Adolescent; Child; Child, Preschool; Female; Humans; Male