

- Research

Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis



1. [Mark J Bolland](#), senior research fellow¹,
2. [Alison Avenell](#), clinical senior lecturer²,
3. [John A Baron](#), professor³,
4. [Andrew Grey](#), associate professor¹,
5. [Graeme S MacLennan](#), senior research fellow²,
6. [Greg D Gamble](#), research fellow¹,
7. [Ian R Reid](#), professor¹

± Author Affiliations

1. ¹Department of Medicine, Faculty of Medical and Health Sciences, University of Auckland, Private Bag 92 019, Auckland 1142, New Zealand
2. ²Health Services Research Unit, University of Aberdeen
3. ³Department of Medicine, and Department of Community and Family Medicine, Dartmouth Medical School, NH, USA

1. Correspondence to: I R Reid i.reid@auckland.ac.nz

- Accepted 21 May 2010

Abstract

Objective To investigate whether calcium supplements increase the risk of cardiovascular events.

Design Patient level and trial level meta-analyses.

Data sources Medline, Embase, and Cochrane Central Register of Controlled Trials (1966-March 2010), reference lists of meta-analyses of calcium supplements, and two clinical trial registries. Initial searches were carried out in November 2007, with electronic database searches repeated in March 2010.

Study selection Eligible studies were randomised, placebo controlled trials of calcium supplements (≥ 500 mg/day), with 100 or more participants of mean age more than 40 years and study duration more than one year. The lead authors of eligible trials supplied data. Cardiovascular outcomes were obtained from self reports, hospital admissions, and death certificates.

Results 15 trials were eligible for inclusion, five with patient level data (8151 participants, median follow-up 3.6 years, interquartile range 2.7-4.3 years) and 11 with trial level data (11 921 participants, mean duration 4.0 years). In the five studies contributing patient level data, 143 people allocated to calcium had a myocardial infarction compared with 111 allocated to placebo (hazard ratio 1.31, 95% confidence interval 1.02 to 1.67, $P=0.035$). Non-significant increases occurred in the incidence of stroke (1.20, 0.96 to 1.50, $P=0.11$), the composite end point of myocardial infarction, stroke, or sudden death (1.18, 1.00 to 1.39, $P=0.057$), and death (1.09, 0.96 to 1.23, $P=0.18$). The meta-analysis of trial level data showed similar results: 296 people had a myocardial infarction (166 allocated to calcium, 130 to placebo), with an increased incidence of myocardial infarction in those allocated to calcium (pooled relative risk 1.27, 95% confidence interval 1.01 to 1.59, $P=0.038$).

Conclusions Calcium supplements (without coadministered vitamin D) are associated with an increased risk of myocardial infarction. As calcium supplements are widely used these modest increases in risk of cardiovascular disease might translate into a large burden of disease in the population. A reassessment of the role of calcium supplements in the management of osteoporosis is warranted.

Footnotes

- We thank the investigators who provided unpublished data on cardiovascular events from their studies including Larry Riggs, Richard Prince, Claire Bonithon-Kopp, Joan Lappe, Boyd Scott, and Kathy Zhu, as well as Adrian M Grant, M K Campbell, Alison M McDonald and Gladys C McPherson from the Randomised Evaluation of Calcium or Vitamin D trial.
- Contributors: MJB, AG, and IRR drafted the protocol. AA and JAB critically revised the protocol. MJB and AG carried out the literature search and event adjudication. All authors provided individual patient data from their studies. MJB and GDG did the analyses. MJB drafted the paper. All authors critically reviewed the paper. MJB had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. MJB is the guarantor.
- Funding: This review was funded by the Health Research Council of New Zealand and the University of Auckland School of Medicine Foundation. AA is funded by a career scientist award of the chief scientist office of the Scottish government health directorates. The Health Services Research Unit is funded by the chief scientist office of the Scottish government health directorates. The sponsors of the study had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript. The authors are independent from the funders.
- Competing interests: All authors have completed the unified competing interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that: (1) no author has support from companies for the submitted work; (2) IR has received research support from and acted as a consultant for Fonterra that might have an interest in the submitted work in the previous 3 years; JB, IR, AA and GM had study drugs for clinical trials of calcium supplementation supplied by Wyeth; Mission Pharmacal; Shire Pharmaceuticals and Nycomed; and Shire Pharmaceuticals and Nycomed, respectively, might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (4) no author has non-financial interests that may be relevant to the submitted work.
- Ethical approval: Not required.
- Data sharing: No additional data available.
- Accepted 21 May 2010