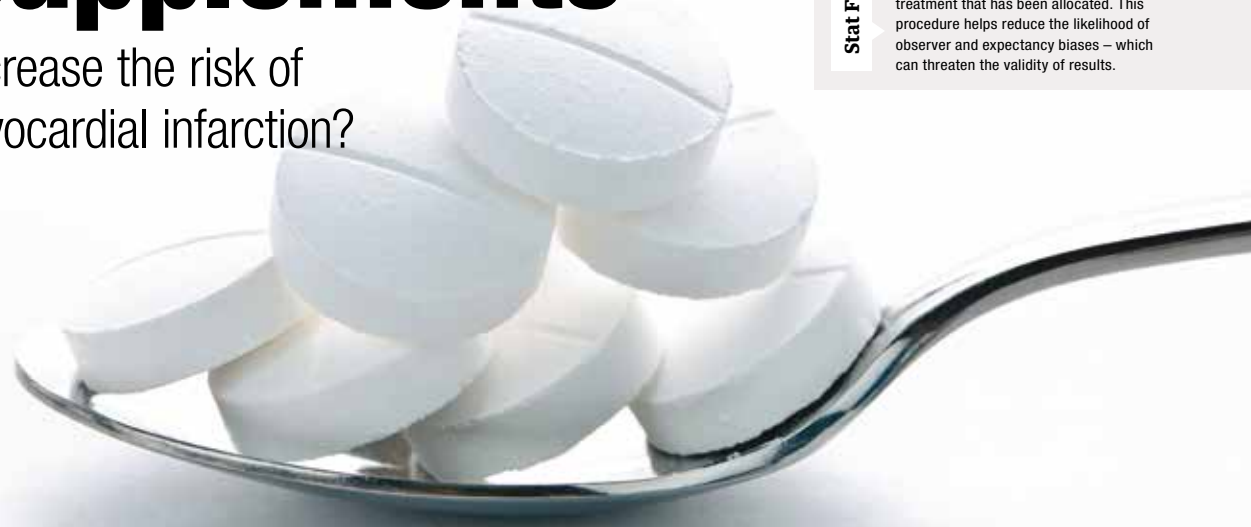


Do calcium supplements

increase the risk of myocardial infarction?



Stat Facts

BLINDING

THIS is a process used during experiments in which the participants (single blind), or both participants and investigators (double blind), remain unaware of the treatment that has been allocated. This procedure helps reduce the likelihood of observer and expectancy biases – which can threaten the validity of results.



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Clinical Scenario

NANAKO, a fit and well 56-year-old patient recently asked for my advice. She had been taking OTC calcium supplements since the onset of menopause. She was concerned about the risk of "heart attacks" and brought along a printed copy of a newspaper article she had read.¹

This topic had recently been reported in the medical news,^{2,3} but I realised I wasn't really sure of the evidence.

WHAT DOES THE RESEARCH EVIDENCE SAY?

Step 1: Clinical evidence resources
A visit to the Cochrane Library (<http://www.thecochranelibrary.com>) revealed there were no reviews on this topic. I proceeded to Trip Database (<http://www.tripdatabase.com>) and used the 'PICO search' tool:

P: women; I: calcium supplement; C: placebo; O: myocardial infarction

There were 37 hits – the first result was a critical abstract of a meta-analysis by Bolland et al. (2010) that seemed promising.⁴

Step 2: PubMed
To see if there were newer important papers, I used the search strategy: "(calcium supplements) and (myocardial infarction); limited to clinical trial OR systematic reviews". The aforementioned article appeared to be the most appropriate publication to answer the question so it is examined here more closely.

CRITICAL APPRAISAL

This article is similar to a systematic review so the appraisal sheet for systematic reviews available from the Centre for Evidence Based Medicine is appropriate.⁵

What PICO question does the systematic review ask?

In people with a mean age over 40 years (Participants); what is the effect of calcium supplements ($\geq 500\text{mg/d}$) without vitamin D (Intervention); compared to placebo (Comparator); on time

to first myocardial infarction, time to first stroke, and time to a composite endpoint (myocardial infarction, stroke, sudden death) (Outcome).

Is it clearly stated?

Yes.

Is it unlikely that important studies were missed?

Probably, but unclear.

The authors searched the major bibliographic databases. They did not describe manually searching the reference lists of selected papers, but did do this for meta-analyses of calcium supplements on a number of other conditions. They did not describe contacting other content experts for unpublished data.

Were the criteria used to select articles for inclusion appropriate? Probably yes.

The authors included double-blinded, randomised placebo-controlled trials (RCTs), where the mean age at baseline was more than 40 years, 100 or more participants were randomised, and the trial duration was more than one year. They excluded trials if vitamin D was co-administered only in the intervention group, if calcium was administered as a

dietary modification or as a complex nutritional supplement, or if the participants had a major systemic disease other than osteoporosis.

Were the included studies sufficiently valid for the question asked?

Unclear.

The authors do not clearly describe their procedure of assessing the quality of the included studies. Randomisation was likely adequate in most of the included studies. Some of the outcome data might not have been from reliable sources, e.g. patient self-reports.

Were the results similar between studies?

Yes.

There was minimal heterogeneity between trials for myocardial infarction.

RESULTS

The authors identified 11 eligible trials - five trials contributed patient-level data. Most of the participants were older women, with a mean age of about 70 years. Taking calcium supplements as compared to placebo increased the likelihood of a myocardial infarction by 31% (hazard ratio 1.31, 95% confidence interval 1.02 to 1.67, $P=0.035$).

CONCLUSION

This meta-analysis suggests that calcium supplements may increase the risk of myocardial infarction, but, there is substantial uncertainty. The authors calculated that for every 69 patients treated with calcium supplements for five years rather than placebo, there would be one extra myocardial infarction, i.e. the number needed to harm (NNH) is 69.³ However, the confidence interval is broad and by my calculation, the conceivable real five-year NNH is in a range from about 30 to over 1000 patients.

Interestingly, an update to this meta-analysis seems to suggest that co-administration of vitamin D does not change this risk.⁶ A recent cohort study seems to support this finding of increased cardiovascular risk with calcium supplements, but not from dietary calcium.⁷

I advised Nanako that the evidence wasn't clear. Calcium supplements might increase the risk of myocardial infarction, but the magnitude of the risk is uncertain. Also, most of the research was in older women. However, since she had no compelling indication for calcium supplements, it would be reasonable using the precautionary approach to discontinue the tablets.