Calcium does not protect against colorectal neoplasia

Authors' objectives
To assess whether calcium decreases the risk of colorectal neoplasia by binding bowel-irritating compounds and diminishing mucosal proliferation.

Searching
MEDLINE was searched from January 1980 to September 1994 with the following keywords: 'site' ('colon', 'rectum', 'colorectal'), 'endpoint' ('cancer', 'carcinoma', 'tumour', 'polyps', 'hyperproliferation') and 'calcium' ('calcium diet', 'dietary', 'dairy'). Current Contents for 1994 (July to September) and the reference lists of retrieved papers were also examined.

Study selection
Study designs of evaluations included in the review
Cohort and case-control studies were included.

Specific interventions included in the review
Calcium intake.

Participants included in the review
Men and women were included.

Outcomes assessed in the review
The outcome was colorectal cancer or colorectal adenoma.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection. Studies had to be published in English, and designed as a cohort or case-control that estimated the association between calcium intake and risk of colon and/or rectal cancer or polyps.

Assessment of study quality
Information relating to, e.g. study design and confounding was collected. Quality scores were not applied to the individual studies.

Data extraction
The data were abstracted by one reviewer using a prior drafted scoring form, and checked by a second reviewer. The form included information about the publication, study population, design, descriptive data, analysis and results.

Methods of synthesis
How were the studies combined?
Summary RRs (measures of association for highest versus lowest category of calcium intake) were calculated as the antilog of weighted mean of the natural logarithms. When studies were homogeneous, the inverse of the sampling variance was used as a weighting factor to calculate summary RRs. When heterogeneity was present in a study, the weighting factor also included a variance component for the random effect to account for between-study variability. Weighted regression analysis was also used.

How were differences between studies investigated?
Heterogeneity was evaluated using a chi-squared test. Stratum-specific RRs were also calculated, according to study design and the hypothesis of the review (calcium could decrease risk of colorectal neoplasia by binding bowel-irritating compounds and diminishing mucosal proliferation). When heterogeneity was found, a random-effect measure was used as a measure of deviation to quantify between-study intervals, thus allowing assessment of between-study variation.

**Results of the review**

Twenty-four studies were included: 8 cohort (n=135,717) and 14 case-control (n=19,554) studies, with a total of 43 measures of relative risks (RRs).

The weighted mean, according to a random-effects model, did not indicate substantial protection by calcium (RR 0.89, 95% confidence interval, CI: 0.79, 1.01). Summary RRs for cohort and case-control studies were 0.90 (0.78 to 1.05) and 0.88 (0.73 to 1.04), respectively. Substantial heterogeneity was found between studies. For adenomas, the RR from 6 estimates was 1.13 (0.91 to 1.39), and for cancer, the RR based on 37 estimates was 0.86 (0.74 to 0.98). Stratification on study characteristics and weighted regression analysis yielded RRs slightly below 1.0 with considerable heterogeneity.

**Authors' conclusions**

The present analysis of epidemiological studies does not indicate a substantial protective effect of calcium on colorectal cancer or colorectal adenoma risk. We observed considerable heterogeneity among study results, which could not be explained by end point, subsite, gender, exposure level, or methodological characteristics related to study design and exposure assessment.

**CRD commentary**

Detailed information is presented about the methods of this review and the individual studies included. The search strategy appears limited and only English language studies were included.

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contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.