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Dietary calcium supplements for prevention/ progression of colorectal carcinoma, adenomas and polyps: meta-analysis of randomized controlled trials

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 July 2023 and was last updated on 08 July 2023.

INTRODUCTION

Review question / Objective The aim of this meta-analysis of randomized controlled trials is to evaluate the effect of calcium supplementation on the risk of CRC(including adenomas and polyps) incidence or recurrence.

Rationale Extant research suggests that calcium and calcium supplements may inhibit the occurrence/progression of colorectal cancer. However, recent data provide a controversial picture of this topic.

Condition being studied Colorectal cancer (CRC) is the third most frequent cancer diagnosed worldwide and the second major cause of cancer death. It is also the third most common disease in males and the second most common cancer in women. The International Agency for Research on Cancer reported that in 2020, 1.9 million new instances of CRC, representing 10% of all new cancer cases, and 930,000 deaths from CRC, accounting for 9.4% of all cancer deaths, recorded globally. Despite the various therapeutic methods that have been developed and applied in clinical practice, the five-year survival rate of people diagnosed with metastatic CRC is less than 20%.

METHODS

Search strategy From January 2000 to May 2022, a literature search was conducted on PubMed and OVID (Embase, Medline, Cochrane) databases. The search was limited to human studies, and the language was restricted to English. Abstracts and unpublished results were excluded.
The following medical subject headings (MeSH) and non-MeSH terms were used: (1) “colonic neoplasms [mesh]” or “colonic polyps [mesh]” or “rectal neoplasms [mesh]” or “colorectal neoplasms [mesh]”; (2) (“colonic” or “colorectal” or “rectum”) and (“cancer” or “neoplasms” “adenomas” or “polyps” or “carcinoma”); (3) “calcium”; (4) “human”; and (5) “randomized controlled trials.” A search was also performed using adenoma*, colo*, rectal*, and polyp*.

Participant or population Healthy adults or adults who have been diagnosed with colorectal cancer (including adenomas or polyps) but have recovered from surgery (as diagnosed by a clinician, or using any recognized diagnostic criteria) will be included.

Intervention Different forms of calcium supplements (e.g. calcium carbonate, calcium citrate)was the main intervention.

Comparator Placebo was a Comparator.

Study designs to be included Randomized controlled trials (RCTs) will be included.

Eligibility criteria Studies were included when they satisfied the following criteria: (1) randomized, placebo-controlled trials examining supplemental calcium intake to prevent the development or recurrence of CRC (including adenomas and polyps); (2) all studies must include follow-up assessments, that is, if the results of a study were published in multiple publications or at various times, only the most recent publication and the longest follow-up period were chosen for data extraction; (3) CRC (including adenomas and polyps) with a precise diagnosis; and(4) sufficient research information can be provided, with no missing data.Studies were excluded when they met the following exclusion criteria: (1) observational studies, opinion articles, news reports, bibliographies, conference abstracts, data compilations, and reviews; (2) non-compliant literature; and (3) calcium supplementation via non-oral routes.

Information sources Electronic databases, trial registers.

Main outcome(s) Occurrence of CRC, Recurrence of CRC (including colorectal adenoma, advanced/ multiple adenomas and hyperplastic polyps) and Delayed effects.

Additional outcome(s) Adverse events.

Data management Endnote.

Quality assessment / Risk of bias analysis The risk of bias assessment tool in RevMan 5.4.1 was utilized for analysis. Risk assessment was performed for each study from seven aspects: random sequence generation, allocation concealment, quality of blinding, outcome assessment, incomplete outcome data, selective reporting, and other biases. GRADE profiler (version 3.6.1) was used to assess the quality of evidence.

Strategy of data synthesis The risk ratio (RR) and 95% confidence interval (95% CI) were utilized to measure the treatment effect. The I-square (I2) test was performed to assess the heterogeneity among the included studies. In accordance with the Cochrane review guidelines, random-effects models were selected when heterogeneity was higher than I2 >50%. Other-wise, a fixed-effects model was used.

Subgroup analysis We will consider subgroups such as dose of calcium supplements.

Sensitivity analysis A sensitivity analysis was conducted by removing each study separately to examine the validity and consistency of the data. Potential publication bias was tested by evaluating the symmetry of the funnel plot. Review Manager 5.4.1 was used to examine the data. The results of the analysis are shown as a forest plot, and publication bias is shown as a funnel plot.

Language restriction English.

Country(ies) involved China.

Keywords calcium supplements; colorectal cancer; colorectal adenoma; meta-analysis.

Contributions of each author

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