Aspirin for the chemoprevention of colorectal adenomas: meta-analysis of the randomized trials

Cole BF, Logan RF, Halabi S, Benamouzig R, Sandler RS, Grainge MJ, Chaussade S, Baron JA

CRD summary
The review concluded that aspirin was effective for prevention of colorectal adenomas in individuals with a history of such lesions. Limited reporting of several aspects of the review means the authors' conclusions should be interpreted with caution.

Authors' objectives
To investigate whether aspirin reduced the risk of colorectal adenomas.

Searching
MEDLINE and Web of Science were searched. Search terms were reported. Colleagues were consulted to help identify unpublished studies.

Study selection
Double-blinded randomised controlled trials (RCTs) of aspirin (any dose given for at least one year) as a chemopreventive agent for sporadic large-bowel adenomas were eligible. Studies had to be placebo-controlled. Patients with familial adenomatous polyposis were excluded. Colorectal polyp status at baseline had to be assessed with complete colonoscopy with no polyps knowingly left in the bowel. Colorectal polyp occurrence after randomisation had to be assessed by colonoscopic follow-up. The primary outcome was occurrence of any colorectal adenoma.

The mean age of included participants was around 58 years. Approximately 60% of patients were male. Studies recruited patients between 1993 and 2001. Half of the trials studied low-dose aspirin (81mg/d or 160mg/d). All trials studied high-dose aspirin (300mg/d or 325 mg/d). Treatments were given for three or four years.

The authors did not state how many reviewers selected studies.

Assessment of study quality
The authors did not state that they assessed study quality and verified or checked the integrity of the data.

Data extraction
Participant-level data from each trial were obtained from individual trial authors in order to calculate risk ratios (RR) and absolute risk reductions with 95% confidence intervals (CI).

The authors did not state how many reviewers performed data extraction.

Methods of synthesis
Data were pooled by meta-analysis using a random-effects model. Only data from patients with at least one follow-up colonoscopy were analysed. Statistical heterogeneity was assessed using Cochran's Q and $I^2$. Predefined subgroup analyses examined age, gender, body mass index (BMI), family history of colorectal cancer, number of lifetime adenomas and presence of advanced lesions at baseline. Effects of follow-up time point and dose were explored.

Results of the review
Four RCTs (n=2,967 participants, range 272 to 1,121) were included. Median follow-up was around 33 months. Mean treatment compliance rates ranged between 69% and 92%.

There was a statistically significant reduction in risk of any adenoma for aspirin (any dose) compared with placebo.
(RR 0.83, 95% CI 0.72 to 0.96, I²=41.5%; four RCTs). The benefit was significantly better for lower doses than higher doses (RR 1.18, 95% CI 1.01 to 1.37; two RCTs). For advanced lesions, the pooled risk ratio was 0.72 (95% CI 0.57 to 0.90, I²=0%; four RCTs). The largest reduction in risk for all adenomas occurred during the first year of follow-up (RR 0.62, 95% CI 0.48 to 0.81; three RCTs). Aspirin had no effect on risk beyond 38 months (RR 0.99, 95% CI 0.78 to 1.26; four RCTs).

No statistically significant effect modification was found for any of the baseline variables studied, although the effect of aspirin (any dose) on advanced lesions was greater in those with a family history of colorectal cancer (RR 0.53, 95% CI 0.33 to 0.83) than in those without (RR 0.92, 95% CI 0.67 to 1.28). There were no differences between groups in adverse events (reported in three RCTs) for mortality, myocardial infarction, major bleeding and all-site invasive cancer, but there was a statistically significantly higher rate of strokes (most of which were thought to be ischaemic) among aspirin-treated participants than among those who received placebo. In the three studies that reported incidence of colorectal cancer (in patients with no history of colorectal cancer) there was no significant difference between treatment groups. Further results were reported.

Authors' conclusions
Aspirin was effective for prevention of colorectal adenomas in individuals with a history of such lesions.

CRD commentary
The review addressed a clear question and was supported by appropriate inclusion criteria. The search was not comprehensive: only two electronic databases were searched; and it was unclear whether language and date restrictions were used, so it was possible that relevant studies may have been missed. It was unclear whether suitable methods (such as independent duplicate processes) were employed to reduce the risks of reviewer error and bias when selecting studies for inclusion and extracting data. No assessment of study quality or data checking/verification was reported, which made it difficult to assess the reliability of the primary studies. Follow-up periods were generally quite short. One study was stopped early due to intervention efficacy. Sufficient study details were provided and appropriate methods were used to synthesise data and assess heterogeneity.

Limited reporting of several aspects of the review means that the authors' conclusions should be interpreted with caution.

Implications of the review for practice and research
The authors made no explicit recommendations for practice and research.

Funding
Bayer AG.

Bibliographic details

PubMedID
19211452

DOI
10.1093/jnci/djn485

Original Paper URL
http://jnci.oxfordjournals.org/content/101/4/256.abstract

Indexing Status
Subject indexing assigned by NLM
MeSH
Adenoma /prevention & control; Aged; Anti-Inflammatory Agents, Non-Steroidal /administration & dosage /adverse effects; Anticarcinogenic Agents /administration & dosage /adverse effects; Aspirin /administration & dosage /adverse effects; Colorectal Neoplasms /prevention & control; Confidence Intervals; Dose-Response Relationship, Drug; Double-Blind Method; Female; Humans; Male; Medication Adherence; Middle Aged; Neoplasm Recurrence, Local /prevention & control; Odds Ratio; Randomized Controlled Trials as Topic; Research Design

AccessionNumber
12009103390

Date bibliographic record published
07/10/2009

Date abstract record published
20/07/2011

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract 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.