Aspirin for primary prevention of cardiovascular events in patients with diabetes: a meta-analysis


CRD summary
The authors concluded that aspirin did not significantly reduce the risk of cardiovascular events without an increase in the risk of major bleeding in patients with diabetes. The reliability of these conclusions is uncertain given the potential for error and bias in the review methodology and the unclear quality of the included trials.

Authors' objectives
To assess the effect of aspirin therapy for primary prevention of cardiovascular events in patients with diabetes mellitus.

Searching
MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched up to June 2009 with no language restrictions. Search terms were not reported. Reference lists of relevant articles and meta-analyses were handsearched.

Study selection
Prospective, randomised controlled trials (RCTs) that assessed the effects of aspirin therapy for the primary prevention of cardiovascular events in patients with diabetes mellitus were eligible for inclusion. To be included, trials had to have a follow-up duration of at least 12 months and report data on major cardiovascular events (a composite of cardiovascular mortality, non-fatal myocardial infarction or non-fatal stroke), myocardial infarction, stroke, all-cause mortality, cardiovascular mortality, or major bleeding.

Included trials compared aspirin monotherapy to placebo. Aspirin doses ranged from 50mg/day to 650mg/day. The mean age ranged between 60 to 64 years (where reported). The proportion of men ranged from zero to 100%.

The authors did not state how many reviewers selected studies for inclusion.

Assessment of study quality
The authors did not report that they assessed study quality.

Data extraction
Data to permit the calculation of relative risks (RRs) with 95% confidence intervals (CIs) for the outcomes were extracted.

The authors did not state the number of reviewers who extracted data.

Methods of synthesis
Pooled relative risks and their 95% confidence intervals were calculated using a random-effects model. Heterogeneity was assessed using Cochrane’s Q and I². Analyses were based on intention-to-treat principle. Meta-regression and subgroup analyses were performed to examine sex-specific effects on myocardial infarction and stroke.

Publication bias was assessed using funnel plots and Begg’s and Egger’s tests.

Results of the review
Seven RCTs were included in the review (n=11,618 participants; range 533 to 3,711). The mean follow-up ranged from 3.7 to 10.1 years.
There was no significant effect of aspirin therapy on major cardiovascular events (six RCTs), all-cause mortality (five RCTs), cardiovascular mortality (five RCTs), stroke (six RCTs), myocardial infarction (seven RCTs) or risk of major bleeding (three RCTs). There was significant heterogeneity associated with the myocardial infarction and major bleeding analyses.

Aspirin was associated with a greater reduction of myocardial infarction in men (p=0.000) and with a significant decrease of stroke in women (p=0.000).

**Authors’ conclusions**

Aspirin therapy did not significantly reduce the risk of cardiovascular events without an increase in the risk of major bleeding in patients with diabetes, and showed sex-specific effects on myocardial infarction and stroke.

**CRD commentary**

The review question was clearly stated for eligible study designs, patients and outcome measures. Eligible comparison treatments were not clearly specified. Three relevant databases were searched with no restrictions on language or publication date, so language and publication biases were minimised. Publication bias was assessed and no evidence found. It was unclear whether the review processes were conducted in duplicate, so reviewer error and biases could not be excluded.

The quality of included trials was unknown as quality assessment was not conducted. The methods used to combine data and account for statistical heterogeneity were appropriate and justified. No attempts appear to have been made to explore the causes of heterogeneity for major bleeding outcomes.

The reliability of the authors’ conclusions is uncertain given the potential for error and bias in the conduct of review processes and the unclear trial quality.

**Implications of the review for practice and research**

**Practice:** The authors stated that lipid-lowering blood pressure control and glucose control must continue to be the main approaches to managing diabetes since no significant benefits of aspirin was found in the current review.

**Research:** The authors did not state any implications for further research, but noted the relevance of two ongoing studies (ASCEND and ACCEPT-D).

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