

## **Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus: results of prospectively designed overviews of randomized trials**

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### **CRD summary**

This review compared the effects of different blood pressure-lowering regimens on cardiovascular events and death in people with and without diabetes. The authors concluded that the short- to medium-term effects on major cardiovascular events were broadly comparable for patients with and without diabetes. The lack of information on trial selection and validity checks makes the reliability of the results uncertain.

### **Authors' objectives**

To compare the effects of different blood pressure (BP)-lowering regimens on cardiovascular events and death in people with and without diabetes.

### **Searching**

The authors stated that computer databases were searched, but did not specify which ones were searched. They also checked the reference lists of retrieved articles and reviews, searched abstract and meeting proceedings, and contacted experts. The authors contacted trial investigators for summary and individual patient data. Studies that finalised or published their main results between July 1995 and the end of 2003 were eligible for inclusion.

### **Study selection**

#### **Study designs of evaluations included in the review**

The review included individual patient data from randomised controlled trials (RCTs) that had a minimum of 1,000 patient-years of planned follow-up in each group. Sixteen of the studies were double-blinded. The duration of follow-up ranged from 2.6 to 8.4 years.

#### **Specific interventions included in the review**

Studies of BP-lowering drugs, either compared with each other or with a placebo, were eligible for inclusion. Studies of BP-lowering treatments in combination with other interventions, such as aspirin or cholesterol-lowering drugs, were excluded. The included studies evaluated ramipril, perindopril, enalapril maleate, amlodipine, nisoldipine and nitrendipine in comparison with placebo, beta-blockers and/or diuretics, or each other.

#### **Participants included in the review**

Studies providing separate results for people with and without diabetes were eligible for inclusion. Patients were categorised as diabetic or not according to the definition used by the original trial authors. Two of the included studies were restricted to patients with diabetes, one to patients without diabetes and the remainder included both, with the proportion of people with diabetes ranging from 4 to 38%.

#### **Outcomes assessed in the review**

Studies reporting fatal or nonfatal stroke, myocardial infarction (MI), heart failure or coronary heart disease events, and total mortality were eligible for inclusion.

#### **How were decisions on the relevance of primary studies made?**

The authors contacted trial investigators to request data on patient characteristics, measurements made during follow-up and the occurrence of the outcome.

#### **Assessment of study quality**

The authors did not state that they cross-checked the data with summary data or trial investigators. The authors did not state how decisions were made to include or exclude studies, or who was involved in making the decision. Two trials were excluded as they

did not provide separate data for patients with and without diabetes.

## Data extraction

The BP reduction was calculated as the difference between mean post-treatment and mean baseline BP for diabetic and non-diabetic patients in each arm of the trials.

## Methods of synthesis

### How were the studies combined?

The relative risk (RR) and 95% confidence intervals (CIs) were calculated for diabetic and non-diabetic patients in each trial, using an intention-to-treat analysis. The pooled RR and 95% CI were calculated using a random-effects meta-analysis, weighted by the inverse of the variance.

### How were differences between studies investigated?

Heterogeneity between the diabetic and non-diabetic groups was assessed using the chi-squared statistic.

## Results of the review

Twenty-seven trials (n=158,709) were included in the review.

The response to most of the BP-lowering regimes was similar in diabetic and non-diabetic patients. For the outcomes of stroke, coronary heart disease events and heart failure, there were no differences between diabetic and non-diabetic patients for any comparison that did not include angiotensin receptor blockers. When angiotensin receptor blocker-based regimes were used, people with diabetes had a statistically significant increase in protection from heart failure compared with the controls (chi-squared,  $P=0.002$ ), but less protection from stroke (chi-squared,  $P=0.05$ ) than people without diabetes.

People with diabetes had a statistically significant increase in protection from major cardiovascular events (chi-squared,  $P=0.03$ ) and cardiovascular deaths (chi-squared,  $P=0.02$ ) with more intensive angiotensin-converting enzyme (ACE) inhibitor treatments versus less intensive treatments, and reduced total mortality with ACE inhibitor versus placebo (chi-squared,  $P=0.03$ ) in comparison with patients without diabetes.

## Authors' conclusions

The short- to medium-term effects on major cardiovascular events of BP-lowering regimens were broadly comparable for patients with and without diabetes.

## CRD commentary

The research question and inclusion criteria were clearly reported. The authors did not state how the trials were selected for the review. The authors obtained individual patient data but, since they did not state whether the data were cross-checked with trial investigators, the validity of the data is uncertain. Appropriate measures of effect were used, and the results presented as forest plots. Although the review was based on a large number of patients, the lack of information on the selection of trials and validity checks makes the reliability of the results uncertain.

## Implications of the review for practice and research

Practice: The authors stated that clinicians may choose from a wide range of BP-lowering agents to reduce short- to medium-term risks of macrovascular complications in patients with diabetes.

Research: The authors stated that the effects of different BP-lowering regimes on intermediate renal outcomes, or longer term effects, were not investigated.

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## Bibliographic details

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## 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.

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CRD has determined that this article meets the DARE scientific quality criteria for a systematic review.

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