Do angiotensin converting enzyme inhibitors or angiotensin receptor blockers prevent diabetes mellitus? A meta-analysis
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CRD summary
The review concluded that use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers prevented new-onset diabetes mellitus. Further research was needed. Given the uncertain quality of the included trials and evidence of publication bias, caution is warranted when interpreting the authors’ results and conclusions.

Authors' objectives
To determine the impact of angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB) on the incidence of new onset diabetes mellitus.

Searching
EMBASE, MEDLINE, BIOSIS and The Cochrane Library were searched to July 2009 for articles published in any language. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) of at least one-year duration that studied ARB or ACEi and reported incidence of new onset diabetes mellitus (defined with recognised criteria) were eligible for inclusion.

The included trials studied ACEi (enalapril, ramipril, lisinopril, quinapril, trandolapril and captopril) or ARB (candesartan, losartan, valsartan and telmisartan) compared with beta-blockers, calcium channel blockers, diuretics or placebo. Mean age of patients ranged from 52.55 to 76.4 years. Patients’ body mass index (BMI) ranged from 24.55 to 31kg/m², where reported.

The authors did not state how many reviewers performed study selection.

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

Data extraction
Data were extracted on incidence of diabetes mellitus and used to calculate relative risks (RRs) with 95% confidence intervals (CIs).

One reviewer extracted data and a second checked these for accuracy.

Methods of synthesis
A random-effects meta-analysis was undertaken to calculate pooled relative risks and 95% CIs, which were based on intention-to-treat. The number needed to treat (NNT) was calculated. Statistical heterogeneity was assessed using $X^2$ and $I^2$. Publication bias was assessed using funnel plots. Subgroup analysis was undertaken for ARB and ACEi. Sensitivity analysis was undertaken for follow-up, age, pre-specified diabetes endpoint, tissue-specific ACEi and candesartan use.

Results of the review
Eighteen RCTs were included in the review (n=100,848 patients, range 392 to 33,357): 10 trials of ACEi and eight trials of ARB. Twelve trials were double-blind RCTs and six trials were open label. Follow-up ranged from one to 6.1 years.

Compared with control, use of ACEi and ARB had a statistically significantly lower risk of developing diabetes mellitus.
(RR 0.80, 95% CI 0.75 to 0.86, \(I^2=45\%\); 18 trials). Rates were similar for ACEi (RR 0.78, 95% CI 0.70 to 0.88, \(I^2=64\%\); 10 trials) and ARB subgroups (RR 0.80, 95% CI 0.75 to 0.86, \(I^2=0\%\); eight trials).

Sensitivity analysis indicated no statistically significant difference in results with any analyses. There was evidence of publication bias.

**Authors' conclusions**
The use of ARB and ACEi prevented new-onset diabetes mellitus. Further research was needed.

**CRD commentary**
Inclusion criteria for the review were broadly defined. Several relevant data sources were searched without language restrictions. Publication bias was assessed and could not be ruled out. Attempts were made to reduce reviewer error and bias during data extraction; it was unclear whether the same methods were used for study selection. No quality assessment was reported, which made determining the reliability of the included trials difficult. Trials were pooled using random-effects meta-analysis. Statistical heterogeneity was assessed, which was appropriate.

The uncertain quality of the included trials and the evidence of publication bias mean that caution is warranted when interpreting the authors’ results and conclusions.

**Implications of the review for practice and research**
**Practice:** The authors stated that it is not justified to use ARB/ACEi for simple prevention of diabetes mellitus, but use of these medications to treat hypertensive and chronic heart failure patients at risk of diabetes was highly recommended.

**Research:** The authors stated that additional prospective double-blinded RCTs were needed to confirm the importance of ACEi and ARB in preventing new-onset diabetes mellitus. Cost-effectiveness studies were needed to determine the cost-effectiveness of ACEi and ARB in preventing new-onset diabetes mellitus in a specific patient population (such as pre-diabetes or hypertension).

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