Trials review: cardiovascular outcome with intensive glycemic control and implications for patients with type 2 diabetes

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CRD summary
The review concluded that compared to standard treatment, intensive glycaemic control could reduce the risk of cardiovascular complications in people with diabetes who were younger, had recently been diagnosed or had few cardiovascular risk factors. Substantial differences between trials, uncertain quality of included trials and potential for missed studies meant that the conclusions should be treated with some caution.

Authors' objectives
To compare the effectiveness of intensive glycaemic control with standard treatments for adults with Type 2 diabetes.

Searching
MEDLINE and EMBASE were searched from inception to June 2009 for English-language studies. Search terms were specified. Citations in retrieved articles were handsearched.

Study selection
Randomised clinical trials (RCTs) were included if: patients had type 2 diabetes; clinical outcomes with endpoints were specified involving vascular complications; patients had stable diabetes; and patients were not in an acute hospital setting.

Where reported, mean age ranged from 49 to 66 years, males comprised 29% to 100% of patients and duration of diabetes ranged from newly diagnosed to a mean of 11.5 years. Most participants were from UK and North America; ethnicity was not reported.

Two authors reviewed the studies; disagreements were resolved by consensus.

Assessment of study quality
An assessment of study quality was not reported.

Data extraction
Two authors independently extracted data in three main categories: baseline data; hemoglobin A1c (HbA1c) values at start and end of study; and outcome measures. For older studies, rates and risk differences for all-cause and cardiac mortality, retinopathy, nephropathy, cardiovascular events, microvascular complications and myocardial infarction were extracted. For recent studies, relative risk reduction, with 95% confidence intervals (CI) for combined macro-microvascular events, major and minor macrovascular events, all-cause and cardiovascular mortality, heart failure, time to major cardiovascular event, any diabetes-related endpoint and stroke were extracted. Disagreements were resolved by consensus.

Methods of synthesis
A narrative synthesis was presented. Each study was described in detail. Some study details were tabulated. Studies were categorised by date of publication into two main groups: earlier studies (1970 to 1999) and recent studies (2008 to 2009).

Results of the review
Eight RCTs were included in the review (n=29,734): five were categorised as earlier studies (n=6,552); and five as recent studies (n=26,619), two of which were follow-ups of earlier studies.

A metformin subgroup from one earlier RCT and two recent RCTs showed a benefit of intensive glycaemic control on macrovascular outcomes. Results for all-cause, diabetes-related and cardiovascular mortality, cardiovascular events and
disease, retinopathy and nephropathy were presented where reported in individual studies. Intensive glycaemic control may be reasonable in healthier older patients, but risks may outweigh the benefits in frail older patients.

Authors' conclusions
Intensive glycaemic control reduced cardiovascular complications in people who were recently diagnosed with diabetes, in younger people with diabetes and in people with a low prevalence of cardiovascular risk factors. The risk reduction took some time to develop.

CRD commentary
The research question was clear and supported by relevant inclusion criteria. More than one database was searched and additional handsearching was conducted. Searches were restricted to those in English and there was no specific search for unpublished studies, so language and publication biases could not be ruled out. Study selection and data extraction were conducted in duplicate, which reduced risks of error and bias. There was considerable clinical heterogeneity between trials in terms of populations, comparators, outcomes and interventions, so a narrative synthesis approach appeared justified. There was no assessment of study quality. Insufficient information related to study methodology was reported to allow the reader to make a judgement. The reliability of the conclusions is uncertain.

Implications of the review for practice and research
There were no implications for practice or research.

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