Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis


CRD summary
This review concluded that lifestyle and pharmacological interventions reduce the rate of progress to type 2 diabetes in people with impaired glucose intolerance, and that lifestyle interventions seem to be at least as effective as drug treatment. The authors’ conclusions are likely to be reliable.

Authors’ objectives
To investigate the effectiveness of lifestyle and pharmacological interventions in the prevention or delay of type 2 diabetes in people with impaired glucose tolerance.

Searching
MEDLINE and EMBASE were searched up to July 2006; the search strategies were reported. Also searched were the Cochrane CENTRAL Register and the Cochrane Database of Systematic Reviews (Issue 2, 2006). The references of included studies and reviews were checked and experts in the field were contacted. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials were eligible for inclusion.

Specific interventions included in the review
Studies of interventions aimed at delaying or preventing type 2 diabetes were eligible for inclusion. The included studies investigated lifestyle interventions (diet or exercise alone, and diet plus exercise) compared with standard advice, pharmacological interventions compared with placebo, and the herbal remedy jiantang bushen compared with standard advice. The pharmacological interventions were the obesity drug orlistat and oral diabetes drugs acarbose, flumamine, glipizide, metformin and phenformin. Studies of troglitazone were included in the review, but were not included in the meta-analysis as it was no longer a viable treatment option and had been withdrawn from several markets due to risks of liver toxicity.

Participants included in the review
Studies of people with impaired glucose tolerance, or studies with a sub-sample of this patient group, were eligible for inclusion. In the included studies, the baseline risk of type 2 diabetes per 100 person-years ranged from 2.6 to 30.

Outcomes assessed in the review
To be included, studies had to measure the development of type 2 diabetes. The included studies used several definitions of type 2 diabetes, though most definitions were similar. The average length of follow-up ranged from 0.37 to 4.62 years.

How were decisions on the relevance of primary studies made?
Three authors assessed studies for relevance; trial inclusion was based on consensus.

Assessment of study quality
The Jadad scale was used to assess study quality. This scale assesses randomisation, blinding and withdrawals. An additional criterion for adequacy of allocation concealment was used. Two authors independently conducted the quality assessment.
Data extraction
Two authors independently extracted the data and any disagreements were resolved through consensus. The log hazard ratio (HR) and standard error were estimated for individual trials. Where necessary, this was based on transformed data (full details were provided in the paper). Authors were contacted where insufficient data were reported. Three studies were excluded because sufficient data were not available.

Methods of synthesis
How were the studies combined?
The studies were pooled using random-effects meta-analyses to obtain estimates and 95% confidence intervals (CIs) for each type of intervention, and the number-needed-to-treat to estimate the effect of the intervention in the 5-year cumulative incidence of developing diabetes. The risk of publication bias was assessed using Begg's and Egger's tests.

How were differences between studies investigated?
In addition to pooling the different interventions separately, the impact of mean age, body mass index and length of follow-up on the treatment effect was estimated separately using meta-regression. A Bayesian meta-analysis was used to investigate the effect of baseline risk of type 2 diabetes on the intervention effect. A cumulative analysis was used to investigate the impact of study quality using the Jadad score. In addition, the impact of removing studies with concealment of allocation from the analysis was investigated. The effect of removing studies using the newer, lower threshold for fasting plasma glucose from the analysis and the influence of individual trials on the results were also investigated. Statistical heterogeneity was investigated using the I-squared statistic.

Results of the review
Twenty-one trials met the inclusion criteria; 17 (n=8,084) were included in the meta-analyses.

The quality scores ranged from 1 to 4 out of a possible 5, with the majority reaching a score of 2 or 3.

Based on the meta-analyses, all the interventions showed a benefit in preventing or delaying type 2 diabetes.

There was a 49% relative reduction in the risk of type 2 diabetes when all the lifestyle interventions were pooled (HR 0.51, 95% CI: 0.44, 0.60, p<0.001). The findings were similar when the different lifestyle interventions were pooled separately: the HR was 0.67 (95% CI: 0.49, 0.92) for diet alone (3 studies), 0.49 (95% CI: 0.32, 0.74) for exercise alone (2 studies) and 0.49 (95% CI: 0.40, 0.59) for diet and exercise combined (7 studies).

There was a 30% relative reduction in risk when all the oral diabetes drugs were pooled (9 studies; HR 0.70, 95% CI: 0.62, 0.79, p<0.001). There was a 66% relative reduction in risk when the anti-obesity studies were pooled (2 studies; HR 0.44, 95% CI: 0.28, 0.69, p<0.001). The single trial assessing jiantang bushen had an HR in favour of the intervention, though this was not statistically significant (HR 0.32, 95% CI: 0.03, 3.07). Statistical heterogeneity was low, ranging from 0 to 8.8%.

The number of adverse events reported in the pharmacological trials varied widely between studies: most of the events were gastrointestinal and were more common in the intervention groups than in the control groups. There was a decline in liver function with troglitazone.

There was evidence from the meta-regression that lifestyle interventions were more effective in trials of participants with higher body mass index. There was no evidence of an interaction between baseline risk of type 2 diabetes and the intervention effect. The removal of trials that used newer diagnostic criteria had a minimal effect on the results, as did the removal of studies with low Jadad scores.

There was evidence from the Begg's and Egger's tests that publication bias may be a problem for the analysis of diabetes drugs.

The 2 trials of troglitazone not included in the meta-analysis showed a significant reduction in the development of diabetes compared with control.
Authors' conclusions
Lifestyle and pharmacological interventions reduced the progression rate to type 2 diabetes in people with impaired glucose intolerance. Lifestyle interventions appeared to be at least as effective as drug treatment.

CRD commentary
The review addressed a clear research question using defined inclusion criteria. Appropriate sources were searched for studies, no language restrictions were applied, and the risk of publication bias was investigated. Appropriate measures were used to reduce error and bias in the review methods. The methodological quality of the primary studies was assessed and its impact on the results of the review was investigated. The analyses were clearly described and justified. Sensitivity analyses found the review findings to be robust. Overall, the authors' conclusions are likely to be reliable. It is, however, noteworthy that the conclusion about lifestyle interventions being at least as effective as drug treatment was not based on a direct comparison of the two interventions and both study groups had different comparator interventions.

Implications of the review for practice and research
Practice: The authors raised the issue whether it was appropriate to treat what is basically a lifestyle issue with a lifelong course of medication. They also stated that strategies to ensure adherence to lifestyle interventions over the long term are required.

Research: The authors stated that further evidence on the adverse effects of pharmacological interventions is required.

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Other publications of related interest
This additional published commentary may also be of interest. Upchurch SL. Review: lifestyle or pharmacological interventions prevent or delay type 2 diabetes in people with impaired glucose tolerance. Evid Based Nurs 2007;10:78.

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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.