Acarbose for the prevention of diabetes, hypertension, and cardiovascular disease in subjects with impaired glucose tolerance: the Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM) Trial

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study investigated the use of acarbose on the rate of progression of impaired glucose tolerance (IGT) to Type2 diabetes. Placebo was used as a comparator. Acarbose was administered at a dose of 100 mg three times a day.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis

Study population
The study population comprised patients with IGT. Further inclusion or exclusion criteria were not reported. However, the analysis was based on a separate parent clinical trial, the Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM). Details of the study have been published elsewhere (Chiasson et al. 1998 and 2002, see 'Other Publications of Related Interest' below for bibliographic details).

Setting
The setting was not explicitly stated, but it appears to have been primary care. The economic study was carried out in Sweden.

Dates to which data relate
The effectiveness data were collected from December 1995 to August 2001. Dates relating to resource use data and the price year were not explicitly reported.

Link between effectiveness and cost data
It appears that the costing has been carried out prospectively on the same sample of patients that provided the effectiveness data.

Study sample
The author reported only limited information around the study sample; further details can be obtained from the papers reporting the parent clinical trial (Chiasson et al. 1998 and 2002). It was reported in the paper that the initial sample comprised 1,429 patients with IGT of whom 714 were randomly assigned to acarbose and 715 to placebo. However, following randomisation, 61 patients (4%) were excluded from the study because they did not suffer from IGT, and 44 patients had no post-randomisation data. The final study sample thus comprised 682 patients in the acarbose group and 686 patients in the placebo group.

Study design
The analysis was based on an international, multi-centre, double-blind, placebo-controlled, randomised trial. The study was undertaken in nine countries (Canada, Germany, Austria, Norway, Denmark, Sweden, Finland, Spain and Israel). Other reported details were sparse (see Chiasson et al. 1998 and 2002 for further details). The author only reported that the mean duration of follow-up was 3.3 years. It was reported that 211 patients (31%) in the acarbose group and 130 (19%) patients in the placebo group discontinued treatment; however, the follow-up of these patients was not
interrupted. No patients were reported to have been lost to follow-up.

**Analysis of effectiveness**

The analysis was conducted on an intention to treat basis. The primary outcomes were the number of patients progressing from IGT to type2 diabetes, reversion rate from IGT to normal glucose tolerance, cases of hypertension and number of cardiovascular events. Type2 diabetes was diagnosed using a yearly (or two) oral glucose tolerance test (OGTT). Cardiovascular events were documented by an independent "Cardiovascular Event Adjudicating Committee" that consisted of three independent cardiologists who were blinded to the treatment. In addition, all patients were administered an electrocardiogram before randomisation and at the end of the study, and these were interpreted by two independent cardiologists blinded to the treatment. Patient characteristics were not discussed in the current paper (see Chiasson et al. 1998 and 2002 for further details).

**Effectiveness results**

Based on a single OGTT, Type2 diabetes developed in 221 (31%) patients in the acarbose group and 285 (42%) patients in the placebo group. The hazard ratio (HR) was 0.75 (95% confidence interval, CI: 0.63 to 0.90; p=0.0015).

Based on two OGTTs, the number of patients who developed Type 2 diabetes decreased to 105 (15%) in the acarbose group and 165 (24%) in the placebo group. The HR was 0.64 (95% CI: 0.49 to 0.85), for an absolute risk reduction of 8.7% and a relative risk reduction of 36%.

Acarbose was also effective in reversing IGT cases to normal glucose tolerance compared with placebo, (p<0.0001).

Seventy-eight patients in the acarbose group and 115 in the placebo group developed hypertension (HR 0.66, 95% CI: 0.49 to 0.89; p=0.0059).

Thirty-two patients in the placebo group and 15 in the acarbose group had at least one cardiovascular event. There was a 49% relative risk reduction in the incidence of cardiovascular events (HR 0.51, 95% CI: 0.28 to 0.95; p=0.03).

Based on the results of the electrocardiogram, the greatest reduction of cardiovascular events was in the risk of acute myocardial infarction: 19 myocardial infarctions in the placebo group compared with 2 in the acarbose group, (p=0.001 with Fisher exact test).

**Clinical conclusions**

Based on the analysis, the author concluded that acarbose treatment was effective in reducing the risk of Type2 diabetes and in reducing the incidence of hypertension as well as cardiovascular events.

**Measure of benefits used in the economic analysis**

The author did not derive a summary measure of benefit in the economic analysis. In effect, a cost-consequences analysis was performed.

**Direct costs**

The perspective adopted in the economic analysis was not clear. The direct costs included in the analysis were for laboratory tests, physicians visits, treatment and follow-up costs for Type2 diabetes without complications, hypertension and cardiovascular events. The latter treatment costs accounted for a period of 40 months. Long-term follow-up costs were not taken into account in the analysis. Although it was reported that the cost data were based on Swedish costs, neither the source of the unit costs nor their values were reported. The quantities of resources used were also not reported. The costs were not discounted and the price year was not stated.

**Statistical analysis of costs**

No statistical analysis was undertaken.

**Indirect Costs**

Productivity costs were not included in the analysis.
Currency
Euros (EUR).

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
For the 40-month period, the total cost was EUR 4,310 for the placebo group and EUR 4,528 for the acarbose group.

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
The author concluded "it can be predicted that acarbose is likely to be cost-effective in the management of subjects with IGT (impaired glucose tolerance)."

CRD COMMENTARY - Selection of comparators
Acarbose was chosen because of its effectiveness, with reference to published clinical literature. The author chose placebo as a comparator for the intervention treatment, thus allowing the active value of the treatment to be evaluated, although this means that no active agent was included as an alternative. Current practice should ideally be included in an analysis.

Validity of estimate of measure of effectiveness
The analysis was based on an international, multi-centre, double-blind, placebo-controlled, randomised trial, which seems to have been appropriate. However, the author reported very limited information about the study sample, methods of randomisation and blinding methods, which makes it difficult to comment on the internal validity of the estimate measures of effectiveness. The reader is referred to two published studies (Chiasson et al. 1998 and 2002) for relevant details.

Validity of estimate of measure of benefit
The author did not derive a summary measure of benefit in the economic analysis. Therefore, the study is characterised as a cost-consequence analysis.

Validity of estimate of costs
Although the perspective from which the costing was carried out was not specified, it appears to have been that of the health care provider. However, the author reported very limited information on the costing study. Consequently, from the present paper, it is not possible to determine whether all the major categories of costs were included. The exclusion of complications, hypertension treatment and cardiovascular events would bias against acarbose. In addition, the source of the unit costs, their values and the quantities of resources used were not reported. The costs were based on Swedish cost data, but no sensitivity analysis was performed to assess the robustness of the estimates used. Discounting of the costs was not undertaken and the price year was not reported. The absence of these details will limit the generalisability and the internal validity of the authors' results.

Other issues
The author did not compare the results with those from other studies that had evaluated the same interventions, so it is not possible to determine the degree to which the results agree with other published studies. The author did not directly address the issue of the generalisability of the results to other settings, and the impact of variation in the cost data between the different settings on the economic results was not evaluated through a sensitivity analysis. The results do not appear to have been presented selectively. Although the study evaluated the use of acarbose in the secondary prevention of Type2 diabetes, the author generalised the conclusions across other preventive interventions as well, without specifying particular interventions and without explicit references to the relevant trials on the prevention of Type2 diabetes. The author did not explicitly report any limitations of the study.
Implications of the study
The author recommended that interventions on the prevention of Type 2 diabetes should precede the actual diagnosis of diabetes. However, it was also recommended that a well-designed, adequately powered, prospective intervention study should be conducted to ascertain the impact of acarbose on cardiovascular events.

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Other publications of related interest
Because readers are likely to encounter and assess individual publications, NHS EED abstracts reflect the original publication as it is written, as a stand-alone paper. Where NHS EED abstractors are able to identify positively that a publication is significantly linked to or informed by other publications, these will be referenced in the text of the abstract and their bibliographic details recorded here for information.


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Subject indexing assigned by NLM

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Acarbose /economics /therapeutic use; Cardiovascular Diseases /prevention & control; Cost-Benefit Analysis; Diabetes Mellitus, Type 2 /prevention & control; Double-Blind Method; Glucose Intolerance /prevention & control; Glucose Tolerance Test; Humans; Hypertension /prevention & control; Hypoglycemic Agents /therapeutic use; Insulin Resistance; Multicenter Studies as Topic; Placebos; Randomized Controlled Trials as Topic

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