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 examined the use of 300 mg/day acarbose, an alpha-glucosidase inhibitor, in patients with impaired glucose tolerance (IGT) to prevent progression to Type 2 diabetes (T2D).

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients diagnosed with IGT. IGT was defined as a 2-hour plasma glucose level of between 7.8 and 11.1 mmol/L after a 75-g oral glucose load.

Setting
The setting was the community. The economic study was carried out in Sweden.

Dates to which data relate
The effectiveness data referred to 2002 to 2003, while the resource use data referred to 1999 to 2004. The price year was 2003.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The resource use data for treatment with acarbose and IGT management were derived from the same patient sample as that used in the effectiveness study. These resource use data were based on protocol-driven items. The resource use data, costs of T2D management and treatment of CV events were derived from published studies.

Study sample
Further details of the clinical study can be found elsewhere (Chiasson et al. 2002, see ‘Other Publications of Related Interest’ below for bibliographic details). The study sample consisted of 1,429 patients from nine countries. The sample had a mean age of 54.5 (standard deviation 7.9) years and 51% were female. The final study sample consisted of 1,368 patients, 682 of whom were randomised to acarbose and 686 to placebo. The reasons for the exclusion of some patients were not provided.
Study design
The study was a double-blind, multi-centre, international, randomised controlled trial. The study had centres in Canada, Germany, Austria, Spain, Israel, Finland, Norway, Sweden and Denmark. The method of randomisation was not reported in this study, nor was the method of blinding. The patients were followed for a mean 3.3-year period. Loss to follow-up was not reported in this study.

Analysis of effectiveness
The analysis of effectiveness was conducted on an intention to treat basis. The primary health outcome in the clinical study was the development of T2D, based on an annual oral glucose tolerance test. The occurrence of CV events and hypertension were secondary end points. The patient groups were shown to be comparable in terms of their baseline characteristics.

Effectiveness results
The relative risk reductions were:

- 25% for progression to T2D, (p=0.0015);
- 34% for the development of hypertension, (p=0.006); and
- 49% for the occurrence of CV events, (p=0.03).

Clinical conclusions
The authors concluded that acarbose is associated with fewer progressions to T2D and CV events than placebo.

Modelling
A Cox regression model was used to predict the monthly probability of progression to T2D and occurrence of CV events. This was used to calculate the costs of treatment with acarbose and no treatment.

Measure of benefits used in the economic analysis
The measures of benefits used were freedom from T2D or freedom from CV events at 40 months, and the number of months prior to progression to T2D or the number of months prior to a CV event.

Direct costs
The resource use quantities and costs were reported separately. The study included direct health service costs related to acarbose, IGT management, T2D, CV events and hypertension. The resource use items included medication, consultations (with nurses, doctors and dieticians), diagnostic tests, hospital care, revascularisation and ambulatory care. The unit costs were based on national databases and on diagnosis-related group (DRG) reimbursement rates. The use of DRG data may not reflect the opportunity cost of the resources used. The costs were discounted at a rate of 3% per annum, which was appropriate given that the time horizon for the study was greater than 1 year. The study reported the average costs adjusted to the price year 2003. Where necessary, the prices were adjusted to year 2003 using a rate from Sweden's statistical database, although it was not specified whether this was the general inflation rate or a health care-specific inflation rate. The study included the protocol-driven costs of managing IGT, and it is not clear whether these are representative of IGT management in the general population.

Statistical analysis of costs
Resource use and cost data were modelled as they were not recorded in the clinical trial. Due to the lack of individual patient data, statistical analysis of the costs was not relevant.
Indirect Costs
The indirect costs were not included in the analysis as the authors stated they were beyond the scope of the study.

Currency
Swedish kronor (SEK).

Sensitivity analysis
The authors performed a one-way sensitivity analysis around the efficacy of acarbose, the dose of acarbose, the costs of T2D, the discount rate, the costs of CV events and the survival estimates. The sensitivity analyses explored parameter and structural uncertainty and generalisability of the model results. The range tested for the efficacy of acarbose was based on the 95% confidence interval, while that for the dose was based on differences between the protocol dose of acarbose and the actual dose received. The justification for the other ranges tested was unclear.

Estimated benefits used in the economic analysis
The probability of being free from T2D at 40 months was 0.607 for patients receiving acarbose and 0.535 for patients receiving placebo.

The probability of being free from CV events at 40 months was 0.888 for patients receiving acarbose and 0.868 for patients receiving placebo.

The number of months prior to progression to T2D was 32.04 with acarbose and 30.44 with placebo.

The number of months prior to the occurrence of a CV event was 37.73 with acarbose and 37.32 with placebo.

The uncertainty around these estimates was not reported. The time horizon for the analysis was 40 months, which was no longer than the clinical trial. The benefits were discounted at a rate of 3% per annum. The side effects of treatment do not appear to have been included in the analysis.

Cost results
The expected average cost per patient over 40 months, using a discount rate of 3% per annum, was SEK 41,829 with acarbose and SEK 39,810 with placebo. The side effects of treatment do not appear to have been incorporated into the analysis.

Synthesis of costs and benefits
The costs and benefits were combined to calculate incremental cost-effectiveness ratios (ICERs).

The cost per additional patient free from T2D was SEK 28,009 for acarbose compared with placebo.

The cost per additional patient free from a CV event was SEK 101,375.

The cost per month prior to progression to T2D was SEK 1,259 for acarbose compared with placebo.

The cost per month prior to the occurrence of a CV event was SEK 4,985.

The relevant time horizon for these ICERs was 40 months and a discount rate of 3% per annum was used. The authors stated that the results were particularly sensitive to the efficacy and daily dose of acarbose.

Authors' conclusions
Acarbose is likely to be cost-effective in the management of impaired glucose tolerance (IGT).
CRD COMMENTARY - Selection of comparators
The study was a trial-based economic evaluation, so the comparators were taken from the clinical trial. There are other relevant alternatives available for the management of IGT, including exercise and diet modification. This study therefore compared a sub-set of the relevant alternatives. You must consider whether this is a relevant comparison in your own setting.

Validity of estimate of measure of effectiveness
The estimate of effectiveness was based on a single clinical trial. The analysis was conducted on an intention to treat population from a double-blind, randomised controlled trial, which was appropriate for the study question. The study sample included patients from multiple countries. The authors stated that the countries involved should be relatively homogeneous in terms of alignment with international best clinical practice and economic development, but they did not rule out the potential for important variations between countries. They pointed out that the trial was not powered to allow country-by-country analysis. The patient groups were shown to be comparable with respect to baseline covariates at analysis. A sensitivity analysis showed that the results were very sensitive to the efficacy of acarbose.

Validity of estimate of measure of benefit
A Cox regression model was used to calculate the monthly probabilities of events. This model estimated slightly delayed rates of progression compared with the observed progressions, and the authors stated that this resulted in an underestimation of the benefits of acarbose. The authors did not adequately explore the uncertainty in the model results.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. However, since protocol-driven costs appear to have been included for the management of IGT, this may mean that these costs are not representative of IGT management in general practice. The costs and the quantities were reported separately, which improves the generalisability of the study results and should allow readers to assess the impact of the protocol-driven elements. The resource use quantities were taken from the trial protocol and from published studies. Some one-way sensitivity analyses around the costs were conducted, but the justification for some of the ranges explored was unclear. The unit costs were derived from the authors' setting, including some prices based on DRGs. The authors believed that the economic results should be broadly representative of the other countries in the multi-national trial, even though country-specific costs were used. The authors inflated all costs to the same price year, and discounted the model results appropriately.

Other issues
The authors made appropriate comparisons of their findings with those from other studies of interventions in IGT. The issue of generalisability to other settings was addressed in detail. The authors do not appear to have presented their results selectively, but they could have provided more information on the uncertainty surrounding the estimated costs and benefits. The authors' conclusions might have exceeded the scope of the analysis. They concluded that acarbose is likely to be cost-effective, but did not discuss the appropriate cost-effectiveness threshold for the disease-specific measure of health benefit they had chosen. In addition, the results of the study were shown to be sensitive to the efficacy of acarbose. The authors stated that some of the published cost estimates used in the study may be considered out of date.

Implications of the study
The authors recommended that country-specific assessments of the cost-effectiveness of acarbose be conducted to assess whether the results of this study are transferable to other settings.

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Other publications of related interest

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