The cost-effectiveness of lifestyle modification or metformin in preventing Type 2 diabetes in adults with impaired glucose tolerance

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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

Two interventions for the prevention of Type 2 diabetes in adults with impaired glucose tolerance were examined. The interventions were intensive lifestyle modification (ILM) and metformin (MET). ILM involved a healthy, low-calorie, low-fat diet and moderate physical activity, such as brisk walking. ILM was implemented with a 16-lesson core curriculum covering diet, exercise and behaviour modification, which was taught by case managers on a one-on-one basis, followed by individual sessions and group sessions with case managers. MET was initiated at a dosage of 850 mg once daily and was increased to 850 mg twice daily after one month. Case managers reinforced adherence during individual quarterly sessions.

Type of intervention

Primary prevention.

Economic study type

Cost-utility analysis.

Study population

The study population comprised persons of 25 years of age or older with impaired glucose tolerance. Impaired glucose tolerance was defined by a plasma glucose level between 7.77 mmol/L (140 mg/dL) and 11.04 mmol/L (199 mg/dL) 2 hours after a 75-g oral glucose load.

Setting

The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate

The effectiveness data and some resource use data were derived from studies published between 1992 and 2003. The costs came from a study published in 2003. The price year was 2000.

Source of effectiveness data

The effectiveness evidence was derived from a synthesis of published studies and authors' assumptions.

Modelling

A Markov simulation model was constructed on the basis of a published decision model to estimate the onset and progression of diabetes, costs, and quality of life in adult patients with impaired glucose tolerance. The model was populated with annual transitional probabilities between disease states and a lifetime horizon was considered. The model used trial-based data for the first 3 years of the simulation (corresponding to the follow-up of the clinical trial) and then extrapolated clinical and economic data using multiplicative models.

Outcomes assessed in the review
The values derived from the literature were:

the annual probability of diabetes onset;

the hazard rates for hypertension and high cholesterol level;

coronary heart disease (CHD) and stroke risk factor in the pre-diabetes period;

diabetes, hypertension, and high cholesterol onset risk reduction with MET and ILM;

variables specific to disease progression, including nephropathy, neuropathy, retinopathy and stroke hazard rates;

variables specific to moderate hypertension control;

utility weights associated with the interventions;

penalty scores for utility values; and

variables specific to the quality of life model, which was used to estimate utility weights after the first 3 years of treatment.

Study designs and other criteria for inclusion in the review
A systematic review of the literature does not appear to have been undertaken and the primary studies appear to have been identified selectively. Most of the evidence came from the DPP trial, which was accurately described. Some evidence came also from the UK Prospective Diabetes Study. However, there was limited information on the design and characteristics of the other studies.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Ten primary studies provided the evidence.

Methods of combining primary studies
In general, each primary study provided a set of model inputs, which were not combined with each other.

Investigation of differences between primary studies
Not stated.

Results of the review

The annual probability of diabetes onset was 0.108.

In the pre-diabetes period, the hazard rates were 0.0506 for hypertension and 0.0375 for high cholesterol level, while CHD and stroke risk factors were 0.58 and 0.56, respectively.

In the first 3 years, the diabetes onset risk reduction was 29.9% with MET and 55.3% with ILM over placebo. The hypertension onset risk reduction was 0% with MET and 100% with ILM over placebo. The high cholesterol onset risk reduction was 0% with MET and 22.6% with ILM over placebo.

The utility scores were 0.72 for men and 0.68 for women with ILM, 0.70 for men and 0.66 for women with MET, and 0.70 and 0.66, respectively, with placebo.

For nephropathy, the hazard rates were 0.0202 at baseline and for hypertension with moderate control from normal to microalbuminuria; 0.0284 at baseline and for hypertension with moderate control from microalbuminuria to nephropathy; and 0.02327 at baseline and for hypertension with moderate control from nephropathy to end-stage renal disease.

For neuropathy, the hazard rates were 0.036 from normal to peripheral neuropathy, and 0.0067 from peripheral neuropathy to low-extremity amputation. The probability of additional amputation was 11%, the probability of diabetes foot ulcer was 4%, and the probability of death from amputation was 10.5%.

For retinopathy, the hazard rates from normal to photocoagulation were 0.011 at baseline and 0.0166 for hypertensive with moderate control, and 0.1065 for photocoagulation both at baseline and for hypertensive with moderate control.

The hazard rates for stroke to death were 0.142 at the time of the event and 0.092 after one year.

The relative risk reduction of CHD with treatment was 13%, while the relative risk reduction of stroke with treatment was 17%.

Methods used to derive estimates of effectiveness

The authors made some assumptions that were used in the decision model.

Estimates of effectiveness and key assumptions

It was assumed that ILM and MET would be applied until diabetes onset, and that health and quality of life benefits associated with the interventions persisted until diabetes onset. In the pre-diabetes period, there was no risk for microalbuminuria and peripheral neuropathy. After the first 3 years of treatment, the diabetes, hypertension and high cholesterol onset risk reductions were assumed to have been equal to those observed in the first 3 years. No CHD hazard rates were considered.

Measure of benefits used in the economic analysis

The summary benefit measure was the expected number of quality-adjusted life-years (QALYs). This was derived by combining survival and quality of life data, either derived from the literature or based on authors' assumptions, using the decision model. The utility values were obtained using the Quality of Well-Being Index. An annual discount rate of 3% was used.

Direct costs

Discounting was relevant since the lifetime costs were estimated. An annual discount rate of 3% was applied. The unit costs were not presented separately from the quantities of resources used, as the costs were reported using macro-categories. The health services included in the economic evaluation were those related to ILM, MET, placebo (including identifying participants, implementing and maintaining the interventions, and monitoring and treating the side effects of the interventions), as well as the services outside of the DPP. The cost/resource boundary of the health care system appears to have been adopted as only direct medical costs were included in the analysis. The total costs over the lifetime

horizon were estimated using a modelling approach that considered the impact of the patients' characteristics and co-morbidities. Both the costs and resource use data appears to have been estimated on the basis of a prior 3-year economic evaluation of DPP interventions. The price year was 2000.

Statistical analysis of costs
The costs were treated deterministically in the base-case, but probabilistic distributions were assigned to each category of costs in the stochastic sensitivity analysis.

Indirect Costs
The indirect costs (i.e. productivity losses) were not included.

Currency
US dollars ($).

Sensitivity analysis
Deterministic sensitivity analyses were carried out to examine the robustness of the estimated cost-utility ratios in the following scenarios:

different age groups;

reduced costs of MET and ILM;

reduced effectiveness of MET and ILM;

both reduced costs and reduced effectiveness of MET and ILM;

higher and lower discount rates; and

the inclusion of direct non-medical costs.

The ranges of values used in the sensitivity analyses were based on authors' assumptions or were derived from the literature. A probabilistic sensitivity analysis was also carried out, where all model inputs were assigned distributions of probability.

Estimated benefits used in the economic analysis
The estimated lifetime QALYs were 10.89 with ILM, 10.45 with MET, and 10.32 with placebo.

Cost results
The total lifetime costs were $51,974 with ILM, $55,261 with MET, and $51,339 with placebo.

Synthesis of costs and benefits
An incremental cost-utility ratio was calculated to combine the costs and benefits of the DPP interventions. The incremental cost per QALY was $1,124 with ILM over placebo, $31,286 with MET over placebo, while ILM dominated (more effective and less costly) MET.

The sensitivity analysis showed that ILM was generally cost-effective or cost-saving in comparison with placebo. The cost per QALY increased in old age groups, or with reduced effectiveness, but ILM remained cost-effective (always lower than $11,700 per QALY). Compared with placebo, MET resulted in very high cost per QALY in old patients or with reduced effectiveness. When non-medical direct costs were also considered, the incremental cost per QALY was

raised to $8,790 per QALY for ILM over placebo and $29,900 for MET over placebo.

The probabilistic sensitivity analyses showed that among participants of 50 years of age, the median cost of ILM was $4,137 per QALY (95% of the cost-utility ratios were between -$587 and $9,456). The median cost of the MET intervention was $36,327 per QALY (95% of the cost-utility ratios were between $16,509 and $84,583).

Authors' conclusions

Both intensive lifestyle modification (ILM) and metformin (MET) provided substantial health benefits at an attractive cost in the prevention of Type 2 diabetes in adults with impaired glucose tolerance. From the perspective of the health care system, ILM should represent the intervention of choice because it was cost-saving.

CRD COMMENTARY - Selection of comparators

The selection of the comparators was appropriate since it reflected the possible interventions for preventing Type 2 diabetes in adults with impaired glucose tolerance. Placebo was also considered for comparative purposes. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness

The effectiveness evidence came mainly from published studies, but it was not stated whether a systematic review of the literature had been undertaken to identify the primary studies. Most of the evidence came from a clinical trial and the other studies appear to have been identified selectively. The issue of comparability of the sources used was not addressed, and it was unclear whether the primary estimates were combined using a narrative approach. Some assumptions were also made. The impact of changes in model inputs was extensively investigated in the sensitivity analysis.

Validity of estimate of measure of benefit

The use of QALYs as the summary benefit measure was appropriate as they incorporate the impact of the intervention on life expectancy and quality of life, which are relevant aspects of care for the patients considered in the study. The source of the utility values was reported. Discounting was applied, as recommended in US guidelines. QALYs are comparable with the benefits of other health care interventions.

Validity of estimate of costs

The definition of the perspective adopted in the study was unclear. The authors stated that both the health system and societal perspectives were adopted, but in the societal perspective the indirect costs were not considered. The assumption that indirect costs are captured in the assessment of QALYs appears inappropriate. A detailed breakdown of the cost items was not provided, and it was unclear which categories of costs were included in the economic evaluation. This reduces the possibility of replicating the study. The costs and the resource use data came from a published economic evaluation of the DPP intervention within the trial follow-up period (3 years). The unit costs and the quantities of resources used were not reported. A multiplicative model was used to assess the impact of different patients' characteristics and the presence of co-morbidities.

Other issues

The authors reported the results of other interventions in diabetic patients and stated that, in general, few interventions were cost-saving. However, no comparisons with the findings of other studies were carried out. The issue of the generalisability of the study results to other settings was implicitly addressed in the sensitivity analysis, where alternative scenarios were considered. The study referred to adults with impaired glucose tolerance.

Implications of the study

The study results suggested that policy makers should promote diabetes prevention interventions, in particular ILM, in

high-risk individuals.

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Other publications of related interest
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