Cost-effectiveness of intensive glycemic control, intensified hypertension control, and serum cholesterol level reduction for type 2 diabetes

CDC Diabetes Cost-effectiveness Group

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
Three interventions aimed at reducing the occurrence of Type 2 diabetes were considered:

- intensive glycaemic control (insulin or sulfonylurea therapy),
- intensified hypertension control (angiotensin-converting enzyme inhibitor or beta-blocker), and
- reduction in serum cholesterol levels (pravastatin).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients newly diagnosed as having Type 2 diabetes, who were aged 25 years or older. Patients in the intensified hypertension control had hypertension. This was defined as a systolic blood pressure of at least 160 mmHg, or a diastolic blood pressure of at least 95 mmHg. Patients in the reduction in serum cholesterol level model had a serum cholesterol level of at least 200 mg/dL.

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

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1990 and 1998. The price year was 1997.

Source of effectiveness data
The effectiveness evidence was derived from published studies, and was supported by the authors’ assumptions.

Modelling
A Markov decision model was used to simulate the disease progression of a hypothetical cohort of patients with Type 2 diabetes through several health states within various health conditions. The five health conditions were nephropathy, neuropathy, retinopathy, coronary heart disease (CHD) and stroke. The cohort of patients comprised 55% women in 10-year age groups. There were 8% aged 25 to 34 years, 8% aged 35 to 44 years, 26% aged 45 to 54 years, 18% aged...
55 to 64 years, 23% aged 65 to 74 years, 13% aged 75 to 84 years, and 4% aged 85 to 94 years. Patients could die from lower extremity amputation, end-stage renal disease, CHD, stroke, or from other causes unrelated to diabetes. All of the health state transition possibilities were shown.

**Outcomes assessed in the review**
The health outcomes assessed from the published studies were used as model inputs in the decision analysis.

For intensive glycaemic control, the outcomes assessed were the initial level of glycosylated haemoglobin (HbA1c), annual rate of change of HbA1c before treatment, treatment effect on HbA1c, annual rate of change of HbA1c after treatment, maximum level of HbA1c with and without treatment, and various hazard rates. The hazard rates for normal to microalbuminuria, microalbuminuria to clinical nephropathy, normal to neuropathy, and normal to photocoagulation, were assessed.

For intensive hypertension control, the outcomes assessed were risk reduction for CHD and stroke, and the hazard rates for normal to microalbuminuria, microalbuminuria to clinical nephropathy, and normal to photocoagulation.

For reduction in serum cholesterol level, the analysis assessed only the risk reduction of CHD for patients with or without CHD.

The health utility values associated with specific health states were also assessed.

**Study designs and other criteria for inclusion in the review**
Not stated. The authors only reported that one of the primary studies used in the analysis, the UKPDS, was a randomised controlled trial. However, the authors did refer to a technical report for more details (copy available from the authors).

**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**
The effectiveness evidence used in the decision model was mainly derived from 10 primary studies. Other studies were also used to derive effectiveness data.

**Methods of combining primary studies**
Not stated.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
For intensive glycaemic control:

the initial level of HbA1c was 6.8%;

the annual rate of change of HbA1c before treatment was 0.2%;

the treatment effect on HbA1c was -2% with conventional treatment and -2.9% with intensive treatment;

the annual rate of change of HbA1c after treatment was 0.2%;

the maximum level of HbA1c was 12% without treatment, 11% with conventional treatment, and 9 with intensive treatment;

the hazard rates were 2.62 for normal to microalbuminuria, 1.08 for microalbuminuria to clinical nephropathy, 1.67 for normal to neuropathy, and 2.74 for normal to photocoagulation.

For intensive hypertension control:

the risk reduction was 13% with moderate intervention relative to no treatment, 0% (or 21%) with intensive intervention relative to moderate intervention for CHD, 17% with moderate intervention relative to no treatment, and 44% with intensive intervention relative to moderate intervention for stroke;

with moderate intervention, the hazard rates were 0.05584 for normal to microalbuminuria, 0.15050 for microalbuminuria to clinical nephropathy, and 0.01660 for normal to photocoagulation; and

with intensive intervention, the hazard rates were 0.03773 for normal to microalbuminuria, 0.12810 for microalbuminuria to clinical nephropathy, and 0.01020 for normal to photocoagulation.

For reduction in serum cholesterol level, the risk reduction of CHD with pravastatin was 31% for patients without CHD and 25% for those with CHD, and 0% with no treatment.

The health utility values were 0.690 for blindness, 0.610 for end-stage renal disease, 0.8 for lower extremity amputation, 0.5 for stroke, 0.880 for cardiac arrest or myocardial infarction, and 0.947 for angina.

Methods used to derive estimates of effectiveness
The authors made some assumptions to support the data used in the decision model.

Estimates of effectiveness and key assumptions
The following assumptions were made:

all patients received conventional treatment to control blood glucose levels;

in the intensive hypertension control, the intervention had no effect on the CHD transition probabilities;

in the intensive hypertension control, all patients with a history of CHD or stroke received hypertension treatment and had faster rates of progression to microalbuminuria, clinical nephropathy, and photocoagulation than normotensive patients;

in the reduction in serum cholesterol level model, patients received pravastatin for the remaining lifetime.

Measure of benefits used in the economic analysis
The main benefit measure in the economic analysis was the QALYs. A 3% discount rate was used. The remaining (undiscounted) life-years were also assessed. Both benefit measures were derived using modelling.
Direct costs
A 3% discount rate was used since the lifetime costs were assessed. The unit costs and the quantities of resources used were not reported. In the intensive glycaemic control model, the economic analysis included the drugs, self-testing, outpatient visits and case management. In the other two models (intensified hypertension control and reduction in serum cholesterol levels), the analysis only considered the drug costs. The diabetes costs were derived from published studies. The cost/resource boundary adopted was that of the health care system. The drug costs were derived from acquisition costs. The resource use was derived from published studies. The overall costs of each intervention was estimated using modelling. The price year was 1997.

Statistical analysis of costs
No statistical analysis of the costs was carried out.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analyses were carried out to test the robustness of the estimated cost-effectiveness ratios to variations in some model inputs and study assumptions. For intensive glycaemic control, the assumptions about microalbuminuria, progression with hypertension, and probability of CHD were dropped. In addition, case management costs were excluded, and a different cost scenario with less physician visits, no case management costs and less self-testing, was used. For intensified hypertension control, the assumptions about characteristics of control patients, disease progression and probability of CHD were dropped. For reduction in serum cholesterol level, it was assumed that the intervention did not require additional visits. Finally, the discount rate was varied for all interventions.

Estimated benefits used in the economic analysis
The remaining life-years were 17.5240 with intensive glycaemic control and 17.2067 with the conventional intervention (difference: 0.3173). The QALYs were 12.0707 with intensive glycaemic control and 11.8791 with the conventional intervention (difference: 0.1915).

The remaining life-years were 14.9124 with intensive hypertension control and 14.4380 with the conventional intervention (difference: 0.4744). The QALYs were 10.7952 with intensive hypertension control and 10.3990 with the conventional intervention (difference: 0.3962).

The remaining life-years were 16.9909 for reduction in serum cholesterol level and 16.3187 with the conventional intervention (difference: 0.6722). The QALYs were 11.8165 for reduction in serum cholesterol and 11.4690 with the conventional intervention (difference: 0.3475).

Cost results
The total costs were $56,270 with intensive glycaemic control and $48,343 with the conventional intervention (difference: $7,927).

The total costs were $43,641 with intensive hypertension control and $44,417 with the conventional intervention (difference: $776).

The total costs were $63,204 for reduction in serum cholesterol level and $45,171 with the conventional intervention
Synthesis of costs and benefits
The costs and QALYs were combined using an incremental cost-utility analysis. The incremental cost per QALY gained with each intervention over standard care was $41,384 for intensive glycaemic control, -$1,959 for intensive hypertension control, and $51,889 for reduction in serum cholesterol level. Intensive hypertension control was dominant (more effective and less costly than the comparison).

Age at diagnosis had a strong impact for intensive glycaemic control. The cost per QALY started at $9,614 for patients aged 25 to 34 years and reached 2.1 million for patients aged 85 to 94 years. Age at diagnosis had little effect for intensified hypertension control and some effect for reduction in serum cholesterol level, with the lowest cost per QALY for patients aged 45 to 84 years.

All interventions reduced the cumulative incidence of complications. Dropping the assumptions did not result in substantial variations in the estimated cost-effectiveness ratios. For intensive glycaemic control, the cost-effectiveness ratios were mainly affected by a reduction in the CHD risk and the exclusion of case management costs. For reduction in serum cholesterol level, the cost-effectiveness ratios were mainly affected by the elimination of extra office visits. Intensified hypertension control remained generally associated with cost savings, with the exception of dropping the assumption of disease progression, which led to a higher cost per QALY.

Authors' conclusions
Intensified hypertension control was associated with cost savings, compared with a more moderate treatment based on drugs and diet. The costs of $40,881 per QALY for intensive glycaemic control and $51,889 per QALY for reduction in serum cholesterol level appear to have been comparable with the cost-effectiveness of other interventions funded in the health care system.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. There was evidence of effectiveness for each intervention, particularly from the UKPDS. You should assess whether the comparators represent interventions currently implemented in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis used data derived from several published studies. However, a formal review of the literature was not carried out. In addition, it was unclear whether the authors took into account possible differences among the primary studies when combining the effectiveness estimates. The authors also made some assumptions used in the decision model. Sensitivity analyses, in which the assumptions were changed, were carried out to test for the impact of these assumptions on the conclusions of the analysis.

Validity of estimate of measure of benefit
QALYs were used as the benefit measure in the economic analysis. These were derived from a model that simulated disease progression and was well described. The QALYs were appropriately discounted. The authors also referred to a technical report, which, by implication, should be available for appraisal. The use of QALYs enhances the comparability of the benefits assessed in the study with those from other interventions implemented in the health care system.

Validity of estimate of costs
The analysis of the costs was carried out from the perspective of the health system. All the relevant categories of costs were included in the analysis. The indirect costs were excluded. The authors stated that this omission could have affected the estimated costs, and their analysis may have underestimated the true social costs of the interventions. The
incremental analysis was correctly performed and appropriate sensitivity analyses were conducted.

**Other issues**
The authors did not compare their findings with those from other studies. The issue of the generalisability of the study results to other settings was not explicitly addressed, but the authors performed several sensitivity analyses. The results of the base-case and the sensitivity analysis results were reported in detail. The study referred to a population of patients newly diagnosed as having Type 2 diabetes, and this was reflected in the conclusions of the analysis. The authors acknowledged that there were some limitations of their study. First, extrapolation was required to assess long-term data from the short-term analyses. Second, the use of UK data for a population of US patients, which may have different treatment patterns.

**Implications of the study**
The authors noted that the study results may be used by decision-makers in terms of the possible adoption of the three technologies. They recommend the modelling approach generally in order to facilitate decision-making.

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