Clinical impact and health economic consequences of post-transplant type 2 diabetes mellitus
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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 health intervention examined in the study was renal transplantation.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised both diabetic and nondiabetic patients, who were aged 15 to 55 years and underwent renal transplantation.

Setting
The setting was a hospital. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness evidence and resource use data were gathered from data published from 1988 to 1998. The price year was 2000.

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

Modelling
A probabilistic decision model was used to simulate the natural history of PTDM and to estimate the long-term medical and economic outcomes. A hypothetical cohort of 10,000 patients was followed for 10 years in which three groups of patients, with initial ages of 15, 35 and 55 years, were considered. The model simulated the progression of patients to five co-morbidities of diabetes: retinopathy, nephropathy, neuropathy, coronary heart disease (CHD), and cerebrovascular disease (CVD). These corresponded to five time-varying Markov submodels, which were run in parallel, allowing the cohort to develop more than one complication simultaneously. Each model cycle lasted one year. Each submodel comprised different health states.

There were five states in the retinopathy model: no retinopathy (state 1), background retinopathy (state 2), proliferative retinopathy (state 3), macular oedema (state 4), and severe loss of vision (state 5).

There were four states in the nephropathy model: no nephropathy (state 1), haemodialysis (state 2), peritoneal dialysis (state 3), and graft failure and death from end-stage renal disease (ESRD) (state 4).
There were four states in the neuropathy model: no history of peripheral vascular disease (PVD) (state 1), PVD (state 2), first amputation (state 3), and second amputation (state 4).

There were three states in the CHD model: no history of CHD (state 1), CHD (state 2), and death from CHD (state 3).

There were three states in the CVD model: no CVD (state 1), stroke or transient ischaemic attack (state 2), and death from stroke (state 3).

Outcomes assessed in the review
The outcomes assessed from the literature and used as model inputs were the initial prevalence rates of diseases, and the transition probabilities across health states in each submodel.

Study designs and other criteria for inclusion in the review
Not stated.

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 was mainly obtained from sixteen primary studies.

Methods of combining primary studies
A narrative method was used to combine the primary studies.

Investigation of differences between primary studies
Not carried out.

Results of the review
In the retinopathy model, the initial prevalence of no retinopathy was 100%. The transition rates were:

0.073, 0.12, and 0.113 (three estimates for the three age cohorts) from state 1 to state 2;

0.0025, 0.00925, and 0.026 from state 2 to state 3;

0.047, 0.0935, and 0.08 from state 2 to state 3;

0.088 (single estimate for all age classes) from state 3 to state 4; and

0.05 from state 4 to state 5.

In the nephropathy model, the initial prevalence of no nephropathy was 100%. The transition rates were:
0.0364, 0.0358, 0.0425, and 0.0419 (four rates apply to periods 1, 2, 3, and 4+ years after transplant) from state 1 to state 2;

0.0246, 0.0242, 0.0286 and 0.0283 from state 1 to state 3;

0.0479, 0.0275, 0.0165, and 0.00468 from state 1 to state 4;

0.09 and 0.099 (two rates apply to periods 1 and 2+ years after transplant) from state 2 to state 1;

0.17 and 0.09 from state 2 to state 4;

0.11 and 0.101 from state 3 to state 1; and

0.09 and 0.0769 from state 3 to state 4.

In the CHD model, the initial prevalence of no CHD was 100% at age 15 years and 77.33% at 35 and 55 years. The initial prevalence of state 2 was 22.67% at 35 and 55 years. The transition rates depended on the patients' characteristics.

In the CVD model, the initial prevalence of no CVD was 100% at age 15 years and 83% at 35 and 55 years. The initial prevalence of state 2 was 17% at 35 and 55 years. The transition rates depended on the patients' characteristics.

In the neuropathy model, the initial prevalence of no PVD was 100% at age 15 years and 96.5% at 35 and 55 years. The initial prevalence of state 2 was 3.5% at 35 and 55 years. The transition rates were:

0.0144 (single rate applies to all periods after transplant) from state 1 to state 2;

0.028, 0.03337, and 0.0467 (three estimates for the three age cohorts) from state 2 to state 3; and

0.1386 from state 3 to state 4.

Methods used to derive estimates of effectiveness

The authors made some assumptions to support the data obtained from published studies.

Estimates of effectiveness and key assumptions

The authors made the following assumptions:

that time since onset of diabetes was the same as time since transplant, and that the time of diabetes onset coincided with the time of diagnosis;

the initial prevalence of retinopathy and nephropathy was 0 in both diabetic and nondiabetic patients;

the graft loss rate for patients without PTDM was 50% of the rate for diabetic patients;

the basic level of peripheral vascular disease was 3.5% in the 35- and 55-year-old cohorts and 0 in the 15-year-old cohort;

the initial prevalence of CVD was 17% in the 35- and 55-year-old cohorts and 0 in the 15-year-old cohort;

the initial prevalence of CHD was 22.7% in the 35- and 55-year-old cohorts and 0 in the 15-year-old cohort; and

the ratio of probability of CVD death to probability of developing CVD was equal to the ratio of probability of stroke mortality to stroke.
Measure of benefits used in the economic analysis
Several benefit measures over the 10-year period were assessed from the decision model. These included: patient and graft survival; average life expectancy; mortality; the probabilities of CHD events, stroke, PVD, proliferative retinopathy or macular oedema, severe vision loss; and the expected number of amputations. The main benefit measures were patient and graft survival, and the average life expectancy.

Direct costs
The use of a discount rate was not reported, although discounting would have been relevant given that the costs were assessed over a time horizon of 10 years. The unit costs were reported but the quantities of resource were not. The cost items included in the analysis were those associated with the treatment of the disease. These included inpatient and outpatient care (dialysis and transplantation for example), medication, medical equipment, supplies, and laboratory tests. Direct non-medical costs, such as transportation, caregivers and lodging, were excluded. The costs and resources were estimated from published studies. All of the costs were adjusted to 2000 prices.

Statistical analysis of costs
No statistical analysis of the costs was performed.

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

Currency
UK pounds sterling (€).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
Reductions in patient survival due to the presence of PTDM, compared with absence of PTDM, were 7.2% (from 83 to 76%) in the age class 15 years, 7.3% (from 83 to 75%) in the age class 35 years, and 9.6% (from 73 to 63%) in the age class 55 years.

Reductions in graft survival were 18% (from 61 to 43%) in the age class 15 years, 19% (from 63 to 4%) in the age class 35 years, and 18% (from 65 to 48%) in the age class 55 years.

Average life expectancy was reduced by 0.32 years (from 9 to 8.6 years) in the age class 15 years, 0.34 years (from 9 to 8.6 years) in the age class 35 years, and 0.47 years (from 8.5 to 8 years) in the age class 55 years.

For the remaining benefit measures, the presence of PTDM increased the probabilities of occurrence of co-morbidities.

Cost results
The total costs were increased by 13,794 (from 98,531 to 112,325) in the age class 15 years, 14,575 (from 97,737 to 112,312) in the age class 35 years, and 12,383 (from 92,353 to 104,736) in the age class 55 years.

Synthesis of costs and benefits
No synthesis of the costs and the benefits was carried out.
Authors' conclusions
The clinical and economic impact of post-transplant diabetes mellitus (PTDM) was negative, since it compromised the long-term prognosis for patients after successful renal transplantation. It also led to reduced patient and graft survival, and increased treatment costs.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The intervention under examination was not the technology (renal transplantation) but the disease (PTDM), and thus patients who did not develop PTDM were used for comparison since the aim of the study was to assess the active implications of PTDM on clinical and economic outcomes. You should assess which patient groups are considered in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis used data derived from published studies. A formal review of the literature was not undertaken and it was unclear whether the authors considered the impact of differences in the primary studies when estimating the effectiveness. In addition, the effectiveness estimates were combined using narrative methods. Several assumptions were made in the decision model, but no sensitivity analysis was subsequently conducted to test the robustness of the conclusions. These issues may reduce the internal validity of the analysis.

Validity of estimate of measure of benefit
Several model outcomes were obtained from the decision model, which appears to have been appropriate to simulate the natural history of PTDM co-morbidities. However, no summary benefit measure was used in the economic analysis, and the costs and the benefits were not combined.

Validity of estimate of costs
The analysis of the costs was carried out from the perspective of the health care system. All direct medical costs related to the treatment of the disease and its co-morbidities were included in the study. Direct non-medical costs and indirect costs were not included in the analysis. The price year was reported and the unit costs were given. However, the costs were treated deterministically and sensitivity analyses were not carried out. The cost data were generally estimated using published studies. No discounting was reported, although it would have been relevant as the costs were assessed over a time horizon of 10 years.

Other issues
The authors made few comparisons of their findings with those from other studies. The external validity of the analysis was quite low due to the lack of sensitivity analyses. The authors stated that the assumptions made in the model were likely to underestimate the morbidity in patients with PTDM. Consequently, "the model-predicted burden differential of PTDM represents a minimum, with the real difference probably being greater".

Implications of the study
The authors suggest that their results could help develop a profile of transplant patients in whom prevention and control of PTDM may provide greater economic benefits. Further research should focus on patients who receive renal transplantation at 35 years, for whom conservative estimates were used in the effectiveness analysis.

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