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 interventions examined in the study were guideline recommendations for the prevention of nephropathy in diabetes mellitus type 1 and 2. The key-points of the guidelines implemented in 1998 in The Netherlands were intensive insulin treatment and complication-specific care. The recommendations focused on annual screening of urine for micro-albuminuria, ACE inhibitors in advanced micro-albuminuria, treatment of hypertension, and reinforcement of healthy lifestyle.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised type 1 and 2 diabetic patients without renal complications.

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

Dates to which data relate
Data on effectiveness were derived from studies published between 1988 and 1998. No dates for resource use were reported. No price year was reported.

Source of effectiveness data
Effectiveness data were based on a review of the literature and authors' assumptions.

Modelling
A semi-Markov compartment model was constructed to simulate the course of diabetes in a hypothetical cohort of 100 diabetic patients in cycles of one year. The average age of disease incidence was 15 years for type 1 diabetes and 55 years for type 2 diabetes. The average age of the prevalence cohort entering the model was 21 years for type 1 diabetes and 62 years for type 2 diabetes. After each year, patients could progress to the next health state, die, or remain in the same health state. The health states included in the model were normo-albuminuria, micro-albuminuria, macro-albuminuria, end-stage renal disease (ESRD), and death. Two separate analyses were conducted for types 1 and 2 diabetes.
Outcomes assessed in the review
The outcomes estimated from the literature were the following transition probabilities used in the two decision models (for type 1 and 2 diabetes):

- from normo- to micro-albuminuria;
- from micro- to macro-albuminuria;
- from macro-albuminuria to ESRD;
- annual mortality rate for normo-albuminuria patients;
- annual mortality rate for micro-albuminuria patients;
- annual mortality rate for macro-albuminuria patients; and
- annual mortality rate for ESRD patients.

Utility weights were also derived from a published study.

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
Six primary studies were used to derive the effectiveness evidence.

Methods of combining primary studies
Primary studies were combined using narrative methods.

Investigation of differences between primary studies
Not stated.

Results of the review
In the case of type 1 diabetes and with current care (cc) and guideline care (gc), the transition probabilities were as follows:

From normo- to micro-albuminuria:

0.0198 (cc) and 0.0126 (gc) in years 0-2;
0.0327 (cc) and 0.0289 (gc) in years 3-5;
0.0436 (cc) and 0.0278 (gc) in years 6-9;
0.0510 (cc) and 0.0325 (gc) in years 9-10; and
0.0368 (cc) and 0.0234 (gc) after 10 years.

From micro- to macro-albuminuria:
0.0306 (cc) and 0.0102 (gc) in all years.

From macro-albuminuria to ESRD:
0.0200 (cc) and 0.0097 (gc) in the first year;
0.0750 (cc) and 0.0195 (gc) in the second year;
0.0281 (cc) and 0.0453 in the third year;
0.0627 (cc) and 0.0005 (gc) in the forth year; and
0.0119 (cc) and 0.0047 (gc) after the forth year.

The annual mortality rates for type 1 diabetes ranged from 0.0042 to 0.200 with current care, while there was no change with guideline care.

In the case of type 2 diabetes and with current care and guideline care, the transition probabilities were as follows:

From normo- to micro-albuminuria:
0.0232 (cc) and 0.0232 (gc) in years 0-1;
0.0155 (cc) and 0.0119 (gc) in years 2-4;
0.0226 (cc) and 0.0173 (gc) in years 5-8;
0.0518 (cc) and 0.0397 (gc) in years 9-13; and
0.0109 (cc) and 0.0084 after 14 years.

From micro- to macro-albuminuria:
0.0474 (cc) and 0.0474 (gc) in the first year; and
0.0177 (cc) and 0.0092 (gc) in later years.

From macro-albuminuria to ESRD:
0.0042 (cc) and 0.0021 (gc) in years 0-11;
0.0385 (cc) and 0.0193 (gc) in years 12-19; and
0.0740 (cc) and 0.0370 (gc) after 20 years.

The annual mortality rates for type 2 diabetes ranged from 0.0305 to 0.3000 with current care, while there was no change with guideline care.
The utility weight for ESRD was 0.61.

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

**Estimates of effectiveness and key assumptions**
The main assumption made in the analysis was that no ACE-inhibitors were used in the current care scenario. The utility weight for diabetes patients following current treatment strategies or intensive treatment was set at 1 and was assumed to be the same for all treatment strategies.

**Measure of benefits used in the economic analysis**
The benefit measures used in the economic analysis were quality-adjusted life-years (QALYs) saved and complication-free life years gained. Both were discounted at a rate of 3%. Utility weights were derived from a published study, as reported earlier.

**Direct costs**
A 3% discount rate was used, as the time horizon of the model was 15 years. Unit costs were reported separately from quantities of resources for some of the cost items. The health services included in the economic evaluation were general practitioner visits, specialist visits, laboratory, OPD running costs, nurses, overhead costs, insulin, materials and self-control for current treatments and general practitioner visits, telephone consultation, laboratory, OPD running costs nurses, OPD running costs in later years, insulin, materials and self-control, and ACE inhibitors for guidelines treatments. Costs of renal replacement, such as dialysis and transplantation, were also included. The cost/resource boundary adopted in the study was that of the health system. The estimation of costs and resource use was based on actual expenditures and was derived from a Dutch survey and other published studies. Total costs were calculated using modelling. No price year was reported.

**Statistical analysis of costs**
Costs were treated deterministically.

**Indirect Costs**
Indirect costs were not included in the analysis.

**Currency**
Dutch guilders (Dfl).

**Sensitivity analysis**
No sensitivity analyses were conducted, but the model was validated using diabetes and dialysis prevalence data from national statistics.

**Estimated benefits used in the economic analysis**
In the cohort of patients with type 1 diabetes, the undiscounted (and discounted) complication-free life-years gained were 2.9 (and 1.1) with intensive blood glucose control, 0.4 (and 0.1) with ACE-inhibitors, and 4.2 (and 1.4) with both treatment measures; and

the undiscounted (and discounted) QALYs saved were 1.1 (and 0.7) with intensive blood glucose control, 0.2 (and 0.04) with ACE-inhibitors, and 1.6 (and 0.6) with both treatment measures.
In the cohort of patients with type 2 diabetes, the undiscounted (and discounted) complication-free life-years gained were 0.2 (and 0.1) with intensive blood glucose control, 0 (and 0) with ACE-inhibitors, and 0.2 (and 0.1) with both treatment measures; and the undiscounted (and discounted) QALYs saved were 0.08 (and 0.04) with intensive blood glucose control, 0 (and 0) with ACE-inhibitors, and 0.08 (and 0.4) with both treatment measures.

Cost results
In the cohort of patients with type 1 diabetes, the undiscounted (and discounted) yearly extra cost per patient was Dfl 555 (and Dfl 365) with intensive blood glucose control, Dfl -350 (and Dfl -175) with ACE-inhibitors, and Dfl 430 (and Dfl 310) with both treatment measures.

In the cohort of patients with type 2 diabetes, the undiscounted (and discounted) yearly extra cost per patient was Dfl -10 (and Dfl -5) with ACE-inhibitors and Dfl 82 (and Dfl 66) with both treatment measures.

Synthesis of costs and benefits
A cost-effectiveness analysis was conducted to combine costs and benefits of guideline care. It appears that an incremental analysis was performed as cost and benefit data of guideline care were compared with those of current care.

In the cohort of patients with type 1 diabetes, the undiscounted (and discounted) cost per complication-free life-year was Dfl 9,500 (and Dfl 17,000) with intensive blood glucose control, cost-saving with ACE-inhibitors, and Dfl 5,000 (and Dfl 11,000) with both treatment measures.

The discounted (and undiscounted) extra cost per QALY was Dfl 25,000 (and Dfl 26,000) with intensive blood glucose control and Dfl 13,500 (and Dfl 26,000) with both treatment measures.

In the cohort of patients with type 2 diabetes, the undiscounted (and discounted) cost per complication-free life-year was Dfl 12,500 (and Dfl 17,500) with intensive blood glucose control, cost-saving with ACE-inhibitors, and Dfl 11,500 (and Dfl 16,500) with both treatment measures.

The discounted (and undiscounted) extra cost per QALY was Dfl 33,000 (and Dfl 52,000) with intensive blood glucose control and Dfl 31,000 (and Dfl 50,000) with both treatment measures.

The process of model validation led to reassuring results.

Authors’ conclusions
The authors concluded that their study confirmed the cost-effectiveness of the new guidelines for prevention of diabetic nephropathy. Such guidelines made explicit costs and outcomes of the treatments and enhanced “appropriate clinical decision making and better informed priority setting in resource allocation at various levels in health care management”. Intensive blood glucose control was cost-effective and the use of ACE-inhibitors was cost-saving from the perspective of the health system.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. Current care was selected as it represented the actual management for patients with type 1 or 2 diabetes. You, as a user of this database, should decide whether it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on published studies, but a systematic review of the literature was not undertaken. Search methods and design of the primary studies were not reported. The authors did not state whether
differences across primary studies were considered when estimating effectiveness. Several assumptions were made in the analysis, and sensitivity analyses were not conducted to investigate such assumptions. These issues may affect the internal validity of the analysis.

Validity of estimate of measure of benefit
QALYs were used as the summary benefit measure in the economic analysis and were obtained from a decision model. The use of QALYs allows the study results to be compared across interventions.

Validity of estimate of costs
The analysis of costs was conducted from the perspective of the health system and it appears that all relevant categories of costs were included in the study. A detailed breakdown of costs was given and the sources of cost data were stated. Unit costs were reported separately from quantities of resources for some cost items, but no price year was given, thus hindering any later reflation exercises. Costs were treated deterministically and no sensitivity analysis was performed. Cost estimates were quite specific to the study setting. These factors may limit the external validity of the study results.

Other issues
The authors did not compare their findings with those from other studies and did not address the issue of the generalisability of the study results to other settings. Two distinct analyses were conducted for patients with type 1 or 2 diabetes and this was reflected in the conclusions of the study.

Implications of the study
The study proved the cost-effectiveness of the guidelines implemented in The Netherlands for the prevention of diabetic nephropathy.

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None stated.

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