Cost-utility analysis of screening intervals for diabetic retinopathy in patients with 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
Screening intervals for diabetic retinopathy in patients with Type 2 diabetes mellitus.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
Hypothetical patients based on the US population of diabetic patients older than 40 years from the Third National Health and Nutrition Examination Survey.

Setting
Community. The study was carried out at the University of Michigan, Ann Arbor, USA.

Dates to which data relate
Effectiveness estimates were derived from studies published between 1977 and 1998. Resource use and cost data estimates were derived from studies published between 1991 and 1996. The price year was not reported.

Source of effectiveness data
Effectiveness data were derived from a review of the literature.

Modelling
A non-stationary Markov model was used to simulate progression of diabetic retinopathy and macular edema. An ordinal logistic regression was used to smooth the predictions of levels of eye disease based on age and glycemic control.

Outcomes assessed in the review
The review assessed characteristics of the diabetic population older than 40 years, annual disease progression rates, mortality multipliers, and the characteristics of retinopathy screening tests.

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
Summary statistics from individual studies were included.

Number of primary studies included
At least 19 primary studies were included.

Methods of combining primary studies
Narrative method.

Investigation of differences between primary studies
Not stated.

Results of the review
Values in parenthesis show the range tested in the sensitivity analysis.

Annual progression rate from retinopathy (state 3) to high-risk PDR was 0.08 (0.06-0.1). Annual progression rates from retinopathy (state 1 or 2) to macular edema were 0.006 (0.001-0.01) and from retinopathy (state 3) to macular edema 0.03 (0.01-0.05). Annual progression rates from high-risk PDR to blindness with photocoagulation were 0.02 (0.002-0.03) and without photocoagulation were 0.09 (0.07-0.11). Annual progression rates from macular edema to blindness with photocoagulation were 0.03 (0.01-0.05) and without photocoagulation were 0.05 (0.03-0.07).

The mortality multiplier was 1.8 (1.6-2) for diabetes mellitus, 1.23 (1.09-1.35) for retinopathy levels less than 35, 1.49 (1.37-1.61) for retinopathy 43-53e, 1.76 (1.64-1.88) for PDR or macular edema, and 2.34 (2.22-2.46) for blindness.

5% (4-6%) of patients with no retinopathy would be diagnosed as having non-proliferative retinopathy. 0.3% (0.02-0.6%) of patients with no retinopathy would be diagnosed as having PDR. 2.2% (2.1-2.3%) of patients with non-proliferative retinopathy would be diagnosed as having no retinopathy. 0.2% (0.1-0.3%) of patients with non-proliferative retinopathy would be diagnosed as having PDR. 2.2% (2.1-2.3%) of patients with PDR would be diagnosed as having no retinopathy. 0.3% (0.2-0.4%) of patients with PDR would be diagnosed as having non-proliferative retinopathy.

The sensitivity and specificity of the screening test for macular edema were 0.82 (0.7-0.94) and 0.79 (0.67-0.91), respectively. The remaining test characteristics are given in the paper (table 1).

The proportion of the population with early retinopathy varied between 0.085 for 40-49 year old patients with haemoglobin level of 7% and 0.251 for 70-79 year old patients with haemoglobin level of 13%. The proportion of the population with different levels of glycemic control varied between 0.005 for 70-79 year old patients with haemoglobin level of 13% and 0.188 for 60-69 year old patients with haemoglobin level of 7%.

These data formed the principal input parameters to the Markov model.

Measure of benefits used in the economic analysis
NHS Economic Evaluation Database (NHS EED)
Produced by the Centre for Reviews and Dissemination
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Patient time spent blind, and quality adjusted life years (QALYs) were used as the measures of benefit. QALYs were calculated by using the time spent blind and the utility of blindness. The utility of blindness was derived from published studies and taken to be 0.69. Years of life were discounted at an annual discount rate of 3%.

Direct costs
Direct costs were discounted at an annual rate of 3%. Quantities and costs were reported separately. Direct costs related to those costs of an ophthalmology visit with dilated eye examination, laser photocoagulation, and fluorescein angiogram. Other costs such as government provision of disability compensation and Medicare payments were also included. The quantity/cost boundary adopted was that of the third-party payer although a governmental and societal perspective was assessed in the sensitivity analysis. The estimation of quantities and costs was based on actual data. Resource use and cost estimates were derived from published studies. The price year was not reported.

Statistical analysis of costs
Not reported.

Indirect Costs
The costs associated with blindness were included in the sensitivity analysis for those who became blind at age 65 or over, and those who become blind before 65.

Currency
US dollars ($).

Sensitivity analysis
One-way and multivariate (Monte Carlo simulation) sensitivity analyses were performed on each variable included in the model.

Estimated benefits used in the economic analysis
45 year old patients with haemoglobin level of 11% had a 86.1% risk of any retinopathy, 22.4% risk of blindness with no screening and 10.1% risk of blindness with annual screening, and spent 8.1 years blind with no screening and 7.7 years with annual screening.

65 year old patients with haemoglobin level of 9% had a 49.4% risk of any retinopathy, 2.7% risk of blindness with no screening and 1.2% risk of blindness with annual screening, and spent 4.3 years blind with no screening and 4.2 years with annual screening.

75 year old patients with haemoglobin level of 7% had a 35.6% risk of any retinopathy, 0.8% risk of blindness with no screening and 0.3% risk of blindness with annual screening, and spent 3.0 years blind with no screening and 2.7 years with annual screening.

Risk of blindness varied by age and haemoglobin level. More frequent screening was more effective. For a 45 year old patient with haemoglobin level of 11%, screening every 5 years decreased time spent blind by 164 days. Screening every 3 years reduced time spent blind by 24 days and annual screening further reduced time spent blind by 21 days. For most groups, the marginal return on increasing screening frequency is small.

5.3 million people have been diagnosed as having type 2 diabetes. This population will accumulate 50,081,384 QALYs without any retinopathy screening and 50,216,915 QALYs with screening at 5-year intervals.

Cost results
Screening the population with type 2 diabetes at 5-year intervals would cost approximately $2.3 billion.

**Synthesis of costs and benefits**
Annual screening usually cost more per QALY gained than less frequent screening intervals. The patients for whom screening is most cost-effective are those who have particularly poor glycemic control. Screening the population with type 2 diabetes at 5-year intervals would cost $16,790 per QALY gained. The marginal cost-effectiveness of increasing the screening frequency to every year costs more than $107,000 per QALY gained. For high-risk populations, the inclusion of the social cost of blindness makes annual screening money saving compared with no screening. However, inclusion of these costs has minimal impact on the marginal cost-effectiveness of increasing screening frequency. The results were not sensitive to changes in the cost of the screening examination, but were sensitive to changes in the utility of blindness.

**Authors’ conclusions**
Annual retinal screening for all patients with type 2 diabetes without previously detected retinopathy may not be warranted on the basis of cost-effectiveness, and tailoring recommendations to individual circumstances may be preferable.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was clear. You, as a user of this database, should verify whether these health technologies are relevant to your own setting.

**Validity of estimate of measure of benefit**
Relevant measures of benefits were used. However, the effectiveness data may have been derived from a non-systematic review of the literature. The internal validity of the effectiveness estimates cannot, therefore, be fully assessed given the limited information provided about the literature review and the quality assessment of the primary studies. Some effectiveness estimates were derived from single studies although this limitation was minimised in the sensitivity analyses. Estimates of the utility of blindness derived from studies varied widely and only limited information was available on the impact of states of visual impairment less than blindness.

**Validity of estimate of costs**
All relevant direct costs were included. Baseline cost analysis covered the third-party payer but the authors introduced additional social costs to explore other perspectives in the sensitivity analyses, though these had minimal impact on the baseline results. Although this was a strong point of the analysis the costs were based on Medicare reimbursement and, hence, do not reflect true opportunity costs.

**Other issues**
It should be remembered that ophthalmologists and not primary care physicians carried out screening. The authors noted that hypertension control might further reduce the efficacy of screening. Hence, the benefits of screening for those with excellent blood pressure control may have been overestimated. The authors did not consider that an annual screening programme could allow other conditions, such as glaucoma and cataracts, to come to earlier medical attention. The study was limited in its ability to address potential variations in retinopathy risk in ethnic minority populations. The reported estimates were population-specific, and not patient-specific. Adequate comparisons with other relevant studies were made and the generalisability of the results was discussed. The authors do not appear to have presented their results selectively. The study enrolled patients older than 40 years with type 2 diabetes and this was reflected in the authors’ conclusions.

**Implications of the study**
More empirical data are needed on the efficacy of varying screening frequencies.
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