The evaluation of screening policies for diabetic retinopathy using simulation

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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 alternative screening policies for diabetic retinopathy (DR) were examined.

Under policy 1, a person was screened using the chosen screening method until background or more advanced DR was detected. The person was then assessed in an outpatient clinic by an ophthalmologist using mydriatic seven-field photography. If retinopathy was confirmed screening was stopped, and if not, it resumed. Patients with background DR were seen at more frequent intervals in the ophthalmic clinic, until they needed photocoagulation for treatable DR. The alternative methods of screening that were considered were:

- optometrist fundoscopy at screening intervals of 12 months and a 6-month interval between visits once DR had been detected;
- diabetologist ophthalmoscopy every 12 months, with an interval of 6 months between visits once DR had been detected; and
- general practitioner (GP) ophthalmoscopy every 12 months, with an interval of 6 months between visits once DR had been detected.

Under policy 2, the patients were screened using a mobile camera (1 photo, reviewed by a diabetologist) every 12 months, with visits every 6 months once background DR had been detected, until treatable DR was detected and confirmed by an ophthalmic clinic using a mydriatic method.

Under policy 1, patients who had been treated for either type of treatable DR continued to attend an ophthalmology outpatient clinic, while under policy 2 they continued to be screened until they had severe or central vision loss, required treatment for the other type of DR, or died.

Mydriatic seven-field photography reported by an ophthalmologist was assumed to be the 'gold' standard. This consisted of screening every 6 months, with visits every 3 months after DR had been detected.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised typical patients with Type 1 or Type 2 diabetes mellitus (DM) from England and Wales, who could develop DR.

Setting
There were several settings relating to the different alternatives of screening considered at analysis. These were primary...
care, secondary care or institution. The economic study was conducted in Southampton (UK).

**Dates to which data relate**
The effectiveness data were collected from primary studies published between 1975 and 2000. The cost data were collected from a website corresponding to 2001. The price year was not reported.

**Source of effectiveness data**
The effectiveness data were derived from a review of completed studies and some authors' assumptions.

**Modelling**
Discrete event simulation was used to model the progress of individual patients through simulated time. The model followed the prevalent and incident diabetic patients arising from a population of 500,000 patients with the demographic characteristics for England and Wales in order to run the model during a hypothetical period of 25 years.

**Outcomes assessed in the review**
All the effectiveness data used to run the model were shown on the website of the School of Management, University of Southampton [http://www.management.soton.ac.uk/retinopathy/model.htm](http://www.management.soton.ac.uk/retinopathy/model.htm). The outcomes found on this website were:

- the prevalence and incidence of insulin-dependent DM (IDDM) patients, according to age and gender;
- the prevalence and incidence of non-IDDM patients, according to age, gender and ethnic origin;
- the prevalence of DR in IDDM and non-IDDM patients, according to the stage of the disease (background DR, proliferative DR, diabetic macular oedema, or untreatable DR);
- the progression of eye disease for both IDDM and non-IDDM patients;
- mortality for IDDM and non-IDDM patients;
- screening and treatment data; and
- compliance.

The authors reported that the data were subdivided by gender and age in 10-year groups, where possible. The effectiveness data reported in the article were:

- the percentage of patients presenting DR at diagnosis;
- the percentage of patients with no DR progressing to any DR within 6 years (excluding deaths);
- the percentage of patients with no DR progressing to treatment in 6 years;
- the compliance rates for Type 1 DM patients, Type 2 DM patients and the patients overall;
- the rates of treatment efficacy for diabetic macular oedema and for proliferative DR; and
- the sensitivity and specificity of optometrist fundoscopy, diabetologist ophthalmoscopy, GP ophthalmoscopy, the mobile camera, and mydriatic seven-field photography (as reported by an ophthalmologist).

**Study designs and other criteria for inclusion in the review**
Not reported.
Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
The authors used the results of alternative studies performed in UK to validate the estimates of effectiveness obtained from the primary studies. These estimates were mainly based on the results from US studies. The sensitivities and specificities of the alternative modes included in the study were derived from several studies, including a systematic review.

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

Number of primary studies included
At least 38 published studies seem to have been included in the review. Of these, there was at least one systematic review and one randomised controlled trial.

Methods of combining primary studies
The authors derived estimates from the literature. They evaluated the comparability of the study designs to the policy scenarios under study in this article, and adjusted their estimates accordingly.

Investigation of differences between primary studies
The authors investigated the differences between some of the primary studies, and proposed explanations for some of these differences.

Results of the review
The results of the review, as reported in the study, were:

- The percentage of patients presenting DR at diagnosis was 15%.
- The percentage of patients with no DR progressing to any DR within 6 years (excluding deaths) was 38%.
- The percentage of patients with no DR progressing to treatment in 6 years was 2.2%.

- The compliance rates were 80% for Type 1 DM patients, 90% for Type 2 DM patients, and 82% for patients overall. Compliance with the ‘gold’ standard was assumed to be 95%.
- The rates of treatment efficacy were 0.62 for diabetic macular oedema and 0.80 for proliferative DR.
- The sensitivity of the screening methods was 73% for optometrist fundoscopy, 81% for diabetologist ophthalmoscopy, 52% for GP ophthalmoscopy, 61% for the mobile camera, and 98% for mydriatic seven-field photography (as reported by an ophthalmologist).
- The specificity of the screening methods was 93% for optometrist fundoscopy, 95% for diabetologist ophthalmoscopy, 84% for GP ophthalmoscopy, 85% for the mobile camera, and 100% for mydriatic seven-field photography (as reported by an ophthalmologist).

Methods used to derive estimates of effectiveness
The authors made assumptions to derive estimates of the effectiveness.
Estimates of effectiveness and key assumptions
The authors assumed that the incidence of Type 1 and Type 2 diabetes and the natural history of eye disease would remain stable for the following 25 years. Also, that Type 1 DM patients would have no eye disease before puberty or within the first 2 years after diagnosis, and would not suffer from treatable DR within the first 5 years after diagnosis.

Measure of benefits used in the economic analysis
The main summary measure of benefit used in the economic analysis was the average years of sight saved if the screening policy was implemented, compared with the alternative of no screening. The authors also reported the total number of years of sight lost due to DR in a hypothetical population of 500,000 individuals if none of the screening policies were implemented. Also, the number of patients saved from blindness under policy 1 (using an optometrist as the method for screening), under policy 2 (using the mobile camera as the method for screening), and with the 'gold' standard used at analysis. These measures were obtained from the model results.

Direct costs
Some, but not all, of the resource quantities were reported separately from the unit costs. The direct costs considered in the economic analysis were those of the health service. These included visits to the primary screener, ophthalmology outpatient visits, courses of treatment for clinically significant diabetic macular oedema and for proliferative DR, and use of the mobile camera when applicable (including set-up costs and quality assurance costs). The unit costs were obtained from the NHS Screening Committee 2001. Resource utilisation was derived from the model. Discounting was not performed, although it would have been relevant since the costs were incurred during 25 years. The authors reported the total cost per policy per year. The price year was not stated.

Statistical analysis of costs
No statistical analyses of the costs were reported.

Indirect Costs
No indirect costs were reported.

Currency
UK pounds sterling (€).

Sensitivity analysis
Sensitivity analyses were performed to assess the robustness of the results when different scenarios were considered. The screening intervals, the screening sensitivities and the population compliance with screening were varied under the different scenarios analysed.

Estimated benefits used in the economic analysis
Considering a hypothetical population of 500,000 individuals and a 25-year follow-up, the results obtained from the model were as follows.

The total number of years of sight lost due to DR would be 308 if none of the screening policies were implemented.

The total number of years of sight saved for diabetic patients overall, would be 168 if policy 1 was implemented by optometrist fundoscopy or by diabetologist ophthalmoscopy, 163 if policy 1 was implemented by GP ophthalmoscopy, and 158 if policy 2 was implemented by the mobile camera.
Compared with no screening, the total number of years of sight saved for Type 1 diabetic patients would be 43.1 if policy 1 was implemented by optometrist fundoscopy, 41.1 if policy 2 was implemented by the mobile camera, and 46.9 if the 'gold' standard was the screening method.

Compared with no screening, the number of years of sight saved for Type 2 diabetic patients would be 125.1 if policy 1 was implemented by optometrist fundoscopy, 116.9 if policy 2 was implemented by the mobile camera, and 138.2 if the 'gold' standard was the screening method.

The authors reported, as an incremental analysis, that policy 2 with the mobile camera saved 14.6% fewer years of sight than the 'gold' standard, and 6.0% fewer than optometrist fundoscopy.

Cost results
The total annual costs of the alternative policies for a hypothetical population of 500,000 individuals would be:

- For Type 1 diabetic patients, 92,000 for policy 1 implemented by optometrist fundoscopy, 58,000 for policy 2 implemented by the mobile camera, and 184,000 for the 'gold' standard; and
- For Type 2 diabetic patients, 588,000 for policy 1 implemented by optometrist fundoscopy, 392,000 for policy 2 implemented by the mobile camera, and 1,479,000 for the 'gold' standard.

Synthesis of costs and benefits
The costs and benefits were combined by calculating incremental cost-effectiveness ratios (ICERs) that compared the cost per year of sight saved with the alternative policies and the option of 'no screening'.

For Type 1 diabetic patients, the costs per year of sight saved were 2,143 if policy 1 was implemented by optometrist fundoscopy, 1,399 if policy 2 was implemented by the mobile camera, and 4,122 if the 'gold' standard was used as the screening strategy.

For Type 2 diabetic patients, the costs per year of sight saved were 4,700 if policy 2 was implemented by optometrist fundoscopy, 3,349 if policy 2 was implemented by the mobile camera, and 11,263 if the 'gold' standard was used as the screening strategy.

The results from the sensitive analyses showed that there was a trade-off between the intervals, screening sensitivity and compliance. The authors also acknowledged that to offer screening less than once a year would not be much more cost-effective.

Authors’ conclusions
Policy 2 was more cost-effective than policy 1 as long as the screening sensitivity and compliance were relatively high.

CRD COMMENTARY - Selection of comparators
To derive the costs and outcomes for each policy, the comparator was stated to be a 'no screening' alternative. Several policy options were compared. You should consider which screening strategy is widely used in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken, neither did they report the sources searched to identify the primary studies. The authors made assumptions about the effectiveness estimates, given the evidence of the literature and the study designs. They also reported that the estimates of effectiveness obtained from the primary studies may not have been directly comparable to those obtained from the studies used to validate the effectiveness results. The authors justified most of their assumptions by reference to the medical literature. They noted that there was considerable uncertainty surrounding the accuracy of the different screening tests, which was important as the preference of policy 2 generally depended on a high sensitivity.
Validity of estimate of measure of benefit
The estimation of benefits was modelled. The instrument used to derive the number of years of sight saved was a discrete event simulation model. This seems to have been appropriate since it allowed the authors to model the complex disease process in relation to the screening for DR.

Validity of estimate of costs
The costs of screening by a diabetologist or a GP were not included since, as the authors stated, it would have been difficult to estimate these costs. This may have been why the authors chose not to report the final costs for policy 1 when either diabetologist or GP ophthalmoscopy were the screening methods. All of the relevant costs for the other screening alternatives appear to have been included in the economic analysis. The generalisability of the results was hindered by the fact that not all the resource quantities were reported separately from the costs and the price year was not given. Discounting was not performed, although it would have been necessary since the hypothetical period considered was 25 years. When the ICERs were calculated, the screening strategies appear to have been compared to no screening. However, the authors did not calculate the ICERs comparing policies 1 and 2 or the different variants of policy 1, which would have been relevant for the economic analysis (since policy 1 presented higher costs but also higher benefits in terms of years of sight saved).

Other issues
The authors made some comparisons of their findings with those from other studies. The authors reported that the cost and benefit results were sensitive to the level of diabetes and diabetic retinopathy in the population.

Implications of the study
The authors recommended that further research should be performed on the total costs and benefits arising from a DR screening service, as these are very sensitive to the levels of diabetes and DR in the population. Moreover, they suggested further research to analyse the cost-effectiveness of the screening strategies when the benefits and costs are discounted.

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Other publications of related interest


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