

This article has been published in the International Journal of Technology Assessment
in Health Care 2008;24:203-11 and is available at:

<http://journals.cambridge.org/action/displayFulltext?type=6&fid=1824612&jid=&volumeId=&issueId=&aid=1824608>

Economic evaluation of screening for open angle glaucoma

Authors: Hernández R.¹, Burr J.M.², Vale L.^{1,2}, for the OAG screening project group.

1. Health Economics Research Unit. Institute of Applied Health Sciences, College of Life Sciences and Medicine, University of Aberdeen. Aberdeen, Scotland, UK.

2. Health Services Research Unit. Institute of Applied Health Sciences, College of Life Sciences and Medicine, University of Aberdeen. Aberdeen, Scotland, UK.

Correspondence to:

Rodolfo Hernández, Research Fellow, Health Economics Research Unit, University of Aberdeen, Polwarth Building, Foresterhill, Aberdeen, AB25 2ZD.

e-mail: r.a.hernandez@abdn.ac.uk

Tel.: +44-1224-558992

Fax: +44-1224-550926

ABSTRACT

Objectives

To assess the cost-effectiveness of screening for open-angle glaucoma (OAG) in the UK; OAG is an important cause of blindness worldwide.

Methods

A Markov Model was developed to estimate lifetime costs and benefits of a cohort of patients facing, alternatively, screening or current opportunistic case finding strategies. Strategies, varying in how screening would be organised, (e.g. invitation for assessment by a glaucoma-trained optometrist (GO) or for simple test assessment by a technician) were developed, and allowed for the progression of OAG and treatment effects. Data inputs were obtained from systematic reviews. Deterministic and probabilistic sensitivity analyses were performed.

Results

Screening was more likely to be cost-effective as prevalence increased, for 40 year olds compared with 60 or 75 year olds, when the re-screening interval was greater (10 years), and for the technician strategy compared with the GO strategy. For each age cohort and at prevalence levels of $\leq 1\%$, the likelihood that either screening strategy would be more cost-effective than current practice was small. For those aged 40 'technician screening' compared with current practice has an Incremental Cost Effectiveness Ratio (ICER) that society might be willing to pay when prevalence is 6% to 10% and at over 10% for 60 year olds. In the UK the age specific prevalence of OAG is much lower. Screening by GO, at any age or prevalence level, was not associated with an ICER $<£30,000$.

Conclusions

Population screening for OAG is unlikely to be cost-effective but could be for specific sub-groups at higher risk.

KEYWORDS

Economic evaluation, Glaucoma, Screening, cost effectiveness analysis, cost utility analysis.

Conflicts of interest

None

Source of funding

The paper was developed from a Health Technology Assessment on the clinical and cost effectiveness of screening for OAG, funded by the National Institute for Health Research Health Technology Assessment programme (project number 04/08/02).

Acknowledgements

The authors are grateful for the comments from independent reviewers of the Health Technology Assessment Programme on which this paper is based.

We thank members of the OAG project group, G. Mowatt, M.A. Rehman Siddiqui, J. Cook, T. Lourenco, C. Ramsay, C. Fraser, A. Azuara-Blanco, J. Deeks, J. Cairns, R. Wormald, S. McPherson, D. Wright, K. Rabindranath, and A. Grant., for guidance on all aspects of the project.

The Health Services Research Unit and the Health Economics Research Unit are both core funded by the Chief Scientist Office of the Scottish Government's Health Directorates. The views expressed in this report are those of the authors and not necessarily those of the funders.

1 Introduction

Glaucoma is a progressive optic neuropathy leading to blindness if untreated. Worldwide, glaucoma is the leading cause of irreversible blindness and open-angle glaucoma (OAG) accounts for about 50% of glaucoma blindness (18). In a developed country setting the majority of OAG cases will remain undiagnosed by current case finding strategies (9).

Risk factors for developing OAG are raised intraocular pressure (IOP), increasing age, black ethnicity, family history of glaucoma, myopia and diabetes (9). A key criterion for a screening programme is that early detection leads to a better outcome than late detection. A systematic review (two trials, 500 patients) of treatment effectiveness, demonstrated that treatment reduces the risk of progression in early disease (16). Population screening for OAG might allow the early treatment and hence reduce the incidence of visual impairment and blindness. However, it is important to know if the screening for OAG is cost-effective but existing economic evaluations are insufficient for evidence-based recommendations (13). The aim of this study was to model the cost-effectiveness of screening for OAG compared with current practice, in the UK, of opportunistic case finding.

2 Methods

The Model

We developed a Markov Model (MM)(Figure 1) (7;20). Health state definitions (see website, Box 1) were based on the severity of binocular visual field loss,

adapted from a scoring system of the integrated visual field, reported by Crabb and colleagues (10).

The model structure allows individuals to enter as healthy (no OAG), and at varying degrees of OAG severity. Over time, healthy individuals can develop OAG (i.e. new incident cases), while those with OAG can develop more severe disease and eventual visual impairment. The treatment states refer to treated disease at each stage. The absorbing state in the model is death and individuals can move into this state from any other state within the model.

The model allows for a cohort of the population, some with OAG, to pass through different strategies. The model identifies that strategy which leads to the largest proportion of individuals with OAG "crossing the bridge" into treatment (Figure 1). A complete version of the model can be obtained from the authors.

Model strategies

We considered three strategies within the model: current practice and two alternative screening strategies. Current UK practice involves the opportunistic identification of cases by community optometrists as part of a routine eye test. There are many tests and configurations of testing arrangements that are potentially suitable for an OAG screening programme; the modelled pathways were determined by consensus by an expert panel. The two alternative screening strategies vary in how screening would be organised. In one, individuals are invited for a screening examination by a glaucoma trained optometrist and undergo a complete glaucoma assessment involving a measure of IOP, an assessment of the optic nerve and a visual field test. In the second strategy, individuals are invited for an automated test quantifying functional visual field

loss or structural damage of the optic nerve, together with a measurement of IOP, by a technician and individuals identified as at risk are then referred for a full glaucoma assessment by a glaucoma optometrist. In all three strategies any individual identified as positive at the end of screening or case finding would be referred to an ophthalmologist for definitive diagnosis and, if necessary, treatment.

Glaucoma treatments

Once OAG is diagnosed, we have assumed that treatment would be initiated. There is a cascade of eye drop treatment options for each disease stage as well as their combination with laser or surgical treatment. Evidence on their effectiveness suggested that these could be approximated by a single effect size but treatment might vary by OAG severity and progression rate. We assumed initial medical treatment by a beta blocker or prostaglandin analogue, followed by an additional drop of another class of medications if initial treatment was ineffective. For those for whom this fails, argon trabeculoplasty or surgery (trabeculectomy) is the next treatment step. In addition to medications, treatment involves visits to the ophthalmologist every six weeks at the beginning of treatment and a full assessment every six months. After surgery the patient would be seen at an ophthalmology outpatient clinic at one, two, four, eight, 12, and 26 weeks post surgery.

Parameter estimates used in the model

We obtained the model parameter estimates (Table 1) from a series of systematic reviews of test accuracy, epidemiology, treatment effectiveness and cost-

effectiveness as well as other systematic, focused searches. Detailed description of the parameters estimates can be found in Burr and colleagues (9).

Probabilities

Table 1a reports the prevalence, incidence and progression of glaucoma parameters used. As there were many potential target groups, each with different risk levels, we ran the model for a range of prevalence values, aiming to identify a prevalence where screening might be considered worthwhile, and thus the population most likely to benefit from screening.

Data on the annual probabilities of having an eye test, by sex and age came from the British Household Panel Survey (BHPS) (4). We obtained screening acceptance data from the epidemiology review (9).

We did not identify any studies reporting the diagnostic accuracy of current practice, thus we derived sensitivity and specificity estimates from Tuck and colleagues (23), the most appropriate, in terms of geographical coverage, number of patients seen and number of participating optometrists.

The accuracy of the glaucoma optometrist testing was taken from a recent study by Azuara-Blanco and colleagues (6), a Scottish comparative, masked, performance study. Data from the Baltimore Eye Survey (19) were used for the estimation of the proportion of normal or OAG patients with one of the main risk factors for OAG, IOP \geq 26mmHg (19). Estimation of the proportion of people able to perform the test (rate of indeterminacy) required for the 'technician' screening strategy came from the systematic review of screening tests (9). The model used sensitivity and specificity values for the technician further test equal

to or greater than 0.8. As the systematic review showed that no one test or test combination was clearly more accurate and acceptable, we included a range of sensitivity and specificity values in the model, rather than modelling the performance of one test or combination thereof. Finally, ophthalmologist assessment was assumed as the reference standard. For probabilistic sensitivity analysis we assumed beta distributions for all parameters except for: technician further test indeterminacy, sensitivity and specificity and the proportion of people referred for observation as glaucoma suspects by an ophthalmologist's diagnostic assessment (uniform distributions).

Costs

Table 1b shows the cost data used (2006 pounds sterling). We used a 2% inflation rate for adjustments into a common price year, where no inflation rate indices were available. Where no information on ranges was obtainable we assumed a triangular distribution and rates of 0.5 and 1.5 times the likeliest value were used as lower and upper limits. We obtained the cost for the optometrist test from the NHS 'sight' test fees (3). For the purposes of costing we assumed that the IOP testing used Goldmann applanation tonometry (GAT) with disposable tips, and that the glaucoma optometrist assessment used the same test combination as ophthalmologist diagnosis (a combination of IOP measurement by GAT, slit lamp examination, funduscopy, and a visual field test). The cost of ophthalmologist diagnosis was based on the cost of two standard ophthalmology outpatient consultations (5) and for the observation state cost where patients judged at risk would be seen yearly for up to five years or until OAG was diagnosed.

We estimated the treatment costs from a European study including data from 194 patients, containing data for the UK by severity of glaucoma (22). The likeliest value for the cost of visual impairment was taken to be the mean value of the last two disease stages (22) as these corresponded to the visual impairment category used in this study. We assumed a triangular distribution for probabilistic sensitivity analysis.

We used the NHS fees for optometrists in Scotland for the glaucoma optometrist assessment (2), and costs for the 'technical screening strategy' from the Scottish Diabetic Retinopathy Screening study (1), and the screening invitation costs (Table 1.b) from the same study.

Quality of life and Utilities

We used EQ-5D utility estimates from a recent UK study involving almost 300 participants (8), including a subjective and objective assessment of glaucoma severity. We used the objective scores for each health state for the base case and subjective scores in the sensitivity analysis (Table 1b). We developed the utility state for visual impairment using weight data for the glaucoma severe state and the relative difference from Gupta and colleagues (12). We attached Beta distributions to these glaucoma utility weights parameters. (web site Briggs 2006)

We assumed that there were no differences in the utility between undiagnosed OAG and treated OAG at each level of severity.

Base case analysis

We ran the base case analysis for cohorts of 40, 60 and 75 year old males, for a range of prevalence values, for a lifetime horizon with screening occurring every

three years, and conducted from the UK National Health Service (NHS) perspective. The cycle length was set at one year and a 3.5% discount rate was used. (web site NICE 2004) The results are presented in incremental cost-effectiveness ratios (ICERs). We undertook probabilistic analyses for ranges of OAG prevalence from 0.1% to 10%.

Sensitivity analysis

One way, two-way and multiway sensitivity analyses for the main parameters within the model were conducted, almost all of which were combined with probabilistic sensitivity analysis.

In these analyses we explored the effects of longer screening intervals (e.g. five and ten years) and varying the annual probability of a community optometrist eye test (2%, 13%, 37%) uptake rates using one-way sensitivity analysis. We varied the sensitivity and specificity of the technician test within plausible ranges of 0.5 to 1.0 for sensitivity and 0.8 to 1.0 for specificity.

Additionally, we performed several targeted sensitivity analyses on a 40 year old cohort, at a 5% (except where otherwise stated) OAG prevalence rate and a ten year screening interval (a combination which seemed most likely to be cost-effective). As the group of individuals with higher OAG prevalence rate would have a higher chance of visiting the optometrist, we conducted an analysis assuming 1.5 times and twice the probability of having an eye test for current practice strategy. We used alternative triangular probability distributions for progression and incidence using lower and upper base case limits as more likely values. We also explored the impact of using subjective glaucoma severity based health state utilities (8). We also conducted high and low cost scenario analyses.

Finally, we used one-way sensitivity analysis to identify threshold values for the annual cost of visual impairment to explore the effect of widening the perspective of the analysis. This final analysis was conducted for 1% and 5% prevalence rate of OAG.

3 Results

Table 2 reports the estimated relative cost-effectiveness by screening strategy at different levels of prevalence of OAG for cohorts aged 40, 60 and 75 years respectively. In each analysis as prevalence increases, costs increase and QALYs fall for all three strategies and all age cohorts. In each analysis at each prevalence level and age group considered, current practice is the least costly but also the least effective of the three strategies. Adopting a 'technician' strategy is more effective but more costly than current practice and screening by a glaucoma optometrist is more effective but more costly than the 'technician' screening strategy.

For each age group considered the ICER from adopting 'technician' screening compared with current practice falls as prevalence increases. Similarly, for each age group considered, the ICER gained from adopting 'glaucoma optometrist' screening compared with 'technician' screening also falls as prevalence increases.

In the base case analysis for a 40 year-olds cohort a 'technician' screening strategy compared with current practice has an ICER that society might be willing to pay when prevalence is approximately 6% to 10% (Table 2) and over 10% for a 60 year-olds. For a 75 year-olds cohort, current practice strategy has an ICER that might be considered worthwhile (Table 2) even when prevalence level is 20%

(not shown). Furthermore, for no age cohort and no prevalence level is screening by the glaucoma optometrist instead of screening by the technician associated with an ICER less than £30,000.

Sensitivity analysis performed around the base case

The probabilistic sensitivity analysis (Table 3) indicates for every cohort group and at prevalence levels of 1% or less, the likelihood that any screening strategy would be more cost-effective than current practice is small. At 5% prevalence for the 40 year-olds cohort level there is less than 50% likelihood that 'technician' screening might be considered cost-effective at a willingness to pay for a QALY of £30,000. Glaucoma optometrist screening is unlikely to be considered cost-effective.

Increasing the screening interval reduces the ICER for each age group and each prevalence level, as OAG on average, progresses relatively slowly and QALY reduction is more than compensated for by costs reduction. Varying the annual uptake rates for community optometrist testing led to both cost and QALYs rising as uptake increased. The higher the uptake, the better the current practice strategy performs. The results of the sensitivity analysis on sensitivity and specificity of the test following the measurement of IOP in the 'technician' strategy indicate that the ICER is relatively insensitive to changes in these variables.

Targeted sensitivity analyses

Further sensitivity analysis for a 40 year old cohort, ten year screening interval and a 5% OAG prevalence indicated that screening with the 'technician' strategy

might be considered worthwhile (see web site Table 4a). Probabilistic sensitivity analysis demonstrates that the uncertainty around model parameter estimates was important, e.g. even though the ICER for the comparison of the 'technician' with the current practice strategy is £20,571 there is only 42% likelihood that the cost per QALY would be less than £20,000.

Furthermore, sensitivity analyses on uptake of community optometrist testing demonstrated that the QALY gain for the current practice strategy more than compensates for its' higher cost. The ICER of the 'technician' strategy compared with current practice increased, as did the ICER for the comparison of the 'glaucoma optometrist' strategy compared with the 'technician' strategy. Changes to the rate of OAG incidence did not greatly alter cost-effectiveness, however, as the rate of progression increased (See web site Table 4.b 'high') then, the likelihood that either screening strategies could be considered cost-effective increased, as screening is likely to detect more cases and hence delay progression. Using alternative valuations for health utilities, varying the cost of diagnosis by the ophthalmologist, the costs of treatment, inviting people to be screened or their subsequent tests had little effect on cost-effectiveness.

The threshold analysis for the cost of visual impairment and 1% OAG prevalence shows the 'technician' strategy dominates the current practice strategy when the annual cost for visual impairment is around £16,000; moreover, the ICER is less than £30,000 if the cost of visual impairment is greater than £8,800. For the 'glaucoma optometrist' strategy to be considered cost-effective compared with the 'technician' strategy would require the annual cost of visual impairment to be greater than £40,000. (see web site, Figure 2)

4 Discussion

We conducted a model based cost-utility analysis of the screening for OAG that compared technician or glaucoma optometrist based screening with current practice (e.g. opportunistic case finding). Data to populate this model came from a series of systematic reviews of the literature and incorporated extensive sensitivity analyses to the imprecision surrounding parameter estimates and other forms of uncertainty. The distributions used to characterise the statistical imprecision varied by parameter but were consistent with prior experience about which type of distribution would be appropriate for the type and nature of the data available. (web site Iverson 1984, Philips 2004) Although, the best use was made of, in some cases, limited data, further information on the value of almost all parameter estimates would be useful.

Our study suggests that general population screening is unlikely to be cost-effective as the prevalence of OAG in the younger cohorts (estimated 0.9% at aged 50), most likely to enjoy the benefits of screening for longer, is too low. However, screening might be cost-effective for selected 'at risk' sub-groups. Targeted screening of 40 to 50 year-olds with a risk factor, (e.g. black ethnicity or those with a family history of glaucoma), is more likely to be cost-effective assuming a prevalence of OAG between 3% to 4% and a screening interval of ten years. These groups account for about 6% of the UK population.

In our model costs increase as prevalence increases because a larger proportion of individuals in the cohort incur the costs of diagnosis and the continuing costs of treating the OAG. The mean cost per person and estimated QALYs are higher

for the 40 year-old cohort than the older cohorts because they are less likely to die during the time horizon of the model. Estimated mean QALYs fall as prevalence increases because a greater proportion of the cohort experiences the adverse health effects of OAG.

The model was sensitive to the annual costs for visual impairment (VI). The higher the annual cost of VI the more likely screening to become cost-effective. The thresholds for this to happen are not dissimilar to the costs estimated by Meads and Hyde(17) (e.g. annual cost of VI of approximately £7900 for the first year and £7700 for subsequent years).

The more likely people are to have an eye test in the current practice strategy (i.e. the comparator), the less likely screening is cost-effective. A relative high attendance for eye tests in the current practice setting might explain the somewhat counterintuitive results.

A review of other cost effectiveness evaluations of screening for OAG (13) identified only one previous study that attempted to compare an active screening strategy with current practice (11). This study also concluded that screening for OAG was not cost-effective. However, a recently published cost-utility analysis of OAG screening in Finland (24) concluded that a screening programme could be cost-effective, especially in older groups where prevalence rates are higher. In contrast to the Finnish analysis our model assumes that no one in the cohorts was receiving treatment prior to screening or opportunistic case detection. The net effect of relaxing this assumption is unclear. Stopping inappropriate glaucoma treatment could make screening more cost-effective. However, care should be taken to consider cost and consequences of those individuals identified as

inappropriately treated (e.g. raised IOP but no glaucomatous visual field loss). Furthermore, if individuals were treated appropriately, there would be no benefit from screening and its cost-effectiveness would be lower. A further factor driving the difference between the conclusions of the Finnish study and our work was the inclusion by the Finnish study of the costs of visual impairment. Our results were also sensitive to the inclusion of these higher costs.

One limitation of our study was that the utility associated with treated and untreated glaucoma was assumed to be the same. This ignores any utility loss associated with adverse effects of treatment. Adverse treatment effects are estimated to reduce quality of life by between 7 and 11% depending upon severity of these effects, as estimated by Burr and colleagues (8). Future studies should consider using a measure appropriate for use within an economic evaluation in people whose glaucoma has not progressed, both before and after treatment has started.

The systematic review identified insufficient evidence to meaningfully distinguish between the variety of tests that might be used in practice. This led to the simplification of the care pathways where the battery of tests used by a glaucoma optometrist was represented by a single value for sensitivity and specificity of a test. This and other simplifications (such as the small number of stages to represent disease progression) were made following consultation with experts. Further research to develop the model structure and the associated parameter values is required.

Overall, although the evidence on cost-effectiveness should be treated cautiously, the results indicate some patient groups where the organisation of targeted

screening, i.e. a surveillance programme, might be given further consideration. However care pathways would need to be in place for those not eligible for screening. In situations where it might be feasible to organise a service for the target population further primary research on the effectiveness and cost-effectiveness of such a programme is required. A randomised controlled trial is the optimal study design but prior to such a study being undertaken further research is needed to develop feasible strategies to identify individuals in 'at risk' groups and the optimal configuration of screening strategies to maximise screening attendance.

5 Conclusion

General population screening is unlikely to be considered cost effective. However, screening for OAG is associated with an ICER that society might be willing to pay for particular cohorts of patients, namely, targeted screening for 50 year-olds at high risk (e.g family history and/or black ethnicity) may be worthwhile. Results are sensitive to the assumed annual cost of visual impairment.

Further data related to both improving the estimates available for some of the parameters in the model but also from a well designed controlled study comparing viable screening strategies in the cohorts of patients for whom this research has indicated that screening might be potentially cost-effective, are required to confirm the findings.

References

- 1 *Organisation of services for diabetic retinopathy screening. HTA Report 1.* Glasgow: NHS Quality Improvement Scotland (Health Technology Board for Scotland (HTBS)), 2002.
- 2 *General ophthalmic services. Primary Care Circular PCA 2005(0)03* [document on the Internet]. Scottish Executive; 2005 [accessed October 2007] .
- 3 *General ophthalmic services. Primary Care Circular 2005 PCA(0)1* [document on the Internet]. Scottish Executive; 2005 [accessed October 2007] .
- 4 *British Household Panel Survey (BHPS)* [website on the Internet]. Institute for Social & Economic Research, University of Essex; 2006 [accessed October 2007].
- 5 *General Ophthalmic Services* [webpage on the Internet]. ISD Scotland ; 2007 [accessed October 2007] .
- 6 Azuara-Blanco A, Burr J, Thomas R, MacLennan G, McPherson S. The accuracy of accredited glaucoma optometrists in the diagnosis and treatment recommendation for glaucoma. *Br J Ophthalmol* 2007; 91:1639-1643.
- 7 Briggs AH, Sculpher MJ. An introduction to Markov modelling for economic evaluation. *Pharmacoeconomics* 1998; 13:397-409.
- 8 Burr JM, Kilonzo M, Vale L, Ryan M. Developing a preference-based Glaucoma Utility Index using a discrete choice experiment. *Optom Vis Sci* 2007; 84:797-808.
- 9 Burr JM, Mowatt G, Hernandez R et al. The clinical effectiveness and cost-effectiveness of screening for open angle glaucoma: a systematic review and economic evaluation. *Health Technol Assess* 2007; 11(41).
- 10 Crabb DP, Fitzke FW, Hitchings RA, Viswanathan AC. A practical approach to measuring the visual field component of fitness to drive. *Br J Ophthalmol* 2004; 88:1191-1196.
- 11 Gooder P. *Screening for glaucoma. Development and Evaluation Committee (DEC) Report No 38.* Bristol: Research & Development Directorate South and West, 1995.

- 12 Gupta V, Srinivasan G, Mei SS et al. Utility values among glaucoma patients: an impact on the quality of life. *Br J Ophthalmol* 2005; 89:1241-1244.
- 13 Hernandez R, Rabindranath K, Fraser C et al. Screening for open angle glaucoma: systematic review of cost-effectiveness studies. *J Glaucoma* 2008 In press.
- 14 Hollows FC, Graham PA. Intra-ocular pressure glaucoma and glaucoma suspects in a defined population. *Br J Ophthalmol* 1966; 50:570-586.
- 15 Lee AJ, Wang JJ, Rochtchina E et al. Patterns of glaucomatous visual field defects in an older population: the Blue Mountains Eye Study. *Clin Experiment Ophthalmol* 2003; 31:331-335.
- 16 Maier PC, Funk J, Schwarzer G, Antes G, Falck-Ytter YT. Treatment of ocular hypertension and open angle glaucoma: meta-analysis of randomised controlled trials. *Br Med J* 2005; 331:134-136.
- 17 Meads C, Hyde C. How much is the cost of visual impairment: caveat emptor. *Pharmacoeconomics* 2006; 24:207-209.
- 18 Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol* 2006; 90:262-267.
- 19 Sommer A, Tielsch JM, Katz J et al. Relationship between intraocular pressure and primary open angle glaucoma among white and black Americans: The Baltimore Eye Survey. *Arch Ophthalmol* 1991; 109:1090-1095.
- 20 Sonnenberg FA, Beck JR. Markov models in medical decision making: a practical guide. *Med Decis Making* 1993; 13:322-336.
- 21 Tielsch JM, Katz J, Singh K et al. A population-based evaluation of glaucoma screening: the Baltimore Eye Survey. *Am J Epidemiol* 1991; 134:1102-1110.
- 22 Traverso CE, Walt JG, Kelly SP et al. Direct costs of glaucoma and severity of the disease: a multinational long term study of resource utilisation in Europe. *Br J Ophthalmol* 2005; 89:1245-1249.
- 23 Tuck MW. Referrals for suspected glaucoma: an International Glaucoma Association survey. *Ophthalmic Physiol Opt* 1991; 11:22-26.
- 24 Vaahtoranta-Lehtonen H, Tuulonen A, Aronen P et al. Cost effectiveness and cost utility of an organized screening programme for glaucoma. *Acta Ophthalmol Scand* 2007; 85:508-518.

- 25 Wolfs RC, Ramrattan RS, Hofman A, de Jong PT. Cup-to-disc ratio: ophthalmoscopy versus automated measurement in a general population: The Rotterdam Study. *Ophthalmology* 1999; 106:1597-1601.

Web-only References

Guide to the methods of technology appraisal [document on the Internet]. London: National Institute for Clinical Excellence; 2004. [accessed October 2007]. Available from: URL: <http://www.nice.org.uk/page.aspx?o=201974>.

Briggs A, Sculpher M, Claxton K. Decision modelling for health economic evaluation. Oxford: Oxford University Press; 2006.

Iversen GR. Bayesian statistical inference. Thousand Oaks, CA: Sage Publications; 1984.

Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, Woolacot N, Glanville J. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technol Assess* 2004;8(36).

TABLES**WEB SITE Box 1** **Definitions of glaucoma health states**

<i>No glaucomatous impairment</i>	Under observation as suspect glaucoma but not on medication and no glaucoma visual field defect in either eye
<i>Mild glaucoma</i>	On treatment, no binocular visual field loss, unilateral glaucoma visual field defect present
<i>Moderate glaucoma</i>	Up to five missed points (< 10decibels[dB]) in the binocular central 20 degrees of visual field
<i>Severe glaucoma</i>	Binocular visual field loss below UK driving standard**
<i>Visual Impairment (includes partial sight and blind)</i>	As per criteria for 'Severe' except binocular visual field loss includes both the upper and lower fields of vision

** 6 or more adjoining missed points (< 10dB), and any additional separate missed point(s) OR a cluster of 4 or more adjoining missed points (<10dB); either of which is either wholly or partly within the central 20 degree superior or inferior hemispheric field.

Table 1.a **Model parameter inputs**

Probability	Value	Source	Distribution, and values used to define the distribution
Cohort start age	40	Base case assumption	60 and 75 years old
Prevalence of Glaucoma	0 to 0.2		
Proportion of glaucoma mild	0.50	Lee 2003(15) Tielsch 1991(21)	0.475 and 0.45 for 60 and 75 years old, respectively
Proportion of glaucoma moderate	0.30	Tielsch 1991(21)	
Proportion of glaucoma severe	0.15	Tielsch 1991(21)	
Proportion of visual impaired	0.05	Burr 2007(9)	0.075 and 0.10 for 60 and 75 years old, respectively
Incidence of glaucoma:		Burr 2007(9)	
40 years old	0.0003	Burr 2007(9)	Triangular: min=0.0001; likeliest=0.0003; max= 0.0008
50 years old	0.0003	Burr 2007(9)	Triangular: min=0.0001; likeliest=0.0003; max= 0.0008
60 years old	0.0008	Burr 2007(9)	Triangular: min=0.0002; likeliest=0.0008; max= 0.0022
70 years old	0.00181	Burr 2007(9)	Triangular: min=0.00068; likeliest=0.00181; max= 0.0044
80 years old	0.00141	Burr 2007(9)	Triangular: min=0.00097; likeliest=0.00141; max= 0.01

Progression of glaucoma to:			
glaucoma moderate	0.25	Burr 2007(9)	Triangular: min=0.125; likeliest=0.25; max= 0.75
glaucoma severe	0.11	Burr 2007(9)	Triangular: min=0.055; likeliest=0.11; max= 0.33
visual impaired	0.1	Burr 2007(9)	Triangular: min=0.05; likeliest=0.1; max= 0.30
RR treated-non treated	0.65	Burr 2007(9)	Lognormal. (Mean=-0.43; sd=0.148)
Mortality	Various	Burr 2007(9)	
Probabilities of having an eye test in current practice:			
40 to 59	0.248	Regression analysis on BHPS data(9)	Normal. Mean 0.248; s.e.:0.0019142
60 to 75	0.3769	Regression analysis on BHPS data(9)	Normal. Mean 0.3769; s.e.:0.0046524
75 and over	0.42	Regression analysis on BHPS data(9)	Normal. Mean 0.42; s.e.:0.0051359
Screening Acceptance. All groups	0.78	Range: min from Rotterdam Study(25); Max from Rhondda Valley Study(14)	Triangular: min=0.66; likeliest=0.78; max= 0.918
Optometrist test sensitivity	0.32	Tuck 1991(23)	Beta: n=1378; r=436
Optometrist test specificity	0.99	Tuck 1991(23)	Beta: n=274,228; r=273,614
Glaucoma Optometrist test sensitivity	0.73	Azuara Blanco 2007 (6)	Beta: n=33, r=24
Glaucoma Optometrist test specificity	0.96	Azuara Blanco 2007(6)	Beta: n=67, r=64
Proportion of normal with IOP < 26	0.96	Burr 2007(9)	Beta: n=5682, r=5455
Proportion of glaucoma with IOP ≥ 26	0.35	Burr 2007(9)	Beta: n=20, r=7
Technician further test indeterminacy	0.1	Burr 2007(9)	Uniform: 0.06-0.20
Technician further test sensitivity	0.8	Assumption	Uniform: 0.8 - 1
Technician further test specificity	0.8	Assumption	Uniform: 0.8 - 1
Ophthalmologist test sensitivity	1	Assumption	None defined
Ophthalmologist test specificity	1	Assumption	None defined
Ophthalmologist observation proportion	0.43	Henson. Manchester Glaucoma Optometry scheme 2005 data (personal communication D Henson. 2006)	Uniform: 0.39 - 0.47

Table 1.b Model parameter inputs: costs and utilities

Costs	Value (£)	Source	Distribution, and values used to define the distribution
Optometrist test	18.39	Department of Health(3)	Triangular: min=9.20; likeliest=18.39; max=27.59
Ophthalmologist diagnosis tests	133	Scotland National Statistics(5)	Triangular: min=77; likeliest=133; max=397
Glaucoma Mild Treatment	420	Traverso 2005(22)	Triangular: min=210; likeliest=420; max=630
Glaucoma Moderate Treatment	473	Traverso 2005(22)	Triangular: min=236.5; likeliest=473; max=709.5
Glaucoma Severe Treatment	376	Traverso 2005(22)	Triangular: min=188; likeliest=376; max=564
Visual Impairment annual cost	669	Traverso 2005(22)	Triangular: min=585.41; likeliest=669; max=752.06
Screening Invitation Glaucoma	10.45	NHS Quality Improvement Scotland(1)*	Triangular: min=5.23; likeliest=10.45; max=15.68
Optometrist test	46.5	Scottish Executive(3)**	Triangular: min=23.25; likeliest=46.50; max=69.75
Technician IOP tests	10.63	NHS Quality Improvement Scotland(1)	Triangular: min=5.32; likeliest=10.63; max=15.95
Technician 2 nd test	10.63	NHS Quality Improvement Scotland(1)	Triangular: min=5.32; likeliest=10.63; max=15.95
Quality of Life	Utility weight	Source	Distribution, and values used to define the distribution
Normal	1	Assumption	None
Glaucoma Mild	0.8015	Burr 2007(8)	Beta, (alpha = 8.2, beta = 2)
Glaucoma Moderate	0.7471	Burr 2007(8)	Beta, (alpha = 11.4, beta = 3.5)
Glaucoma Severe	0.7133	Burr 2007(8)	Beta, (alpha = 1.2, beta = 0.4)
Visual Impaired	0.5350	Developed using data from Gupta 2005(12)	Log-Normal, u = -0.31029, sigma = 0.16631

* Take into account the cost for national coordination, local health board coordination, screening offices and call and recall, development and maintenance of call and recall software, and development and maintenance of image capture software.

** The Scottish eye examination includes a full eye examination, visual field, and IOP (e.g. with non-contact tonometry), and supplementary exams if clinically indicated (e.g. applanation pressures and threshold fields).

Table 2 Base Case results: Incremental cost-effectiveness for the selected start age cohorts by prevalence rate

Prevalence	Strategy	40 year old cohort			60 year old cohort			75 year old cohort		
		Cost (£)	QALYs	ICER	Cost (£)	QALYs	ICER	Cost (£)	QALYs	ICER
1.0%	Current practice	257.40	19.231		187.10	12.477		103.47	6.905	
	Technician	520.36	19.233	107,938	364.37	12.479	134,060	210.76	6.905	200,028
	GO	617.34	19.234	398,881	430.42	12.479	409,416	250.74	6.905	521,062
2.0%	Current practice	333.89	19.166		232.42	12.438		125.01	6.884	
	Technician	608.76	19.170	65,924	418.47	12.440	88,094	238.87	6.885	137,032
	GO	705.86	19.171	240,717	484.79	12.440	264,869	279.22	6.885	350,449
4.0%	Current practice	486.85	19.036		323.06	12.360		168.11	6.843	
	Technician	785.57	19.044	39,118	526.67	12.363	55,160	295.11	6.845	89,440
	GO	882.89	19.045	134,460	593.52	12.364	156,016	336.17	6.845	213,985
6.0%	Current practice	639.82	18.906		413.71	12.281		211.20	6.802	
	Technician	962.38	18.918	29,051	634.87	12.286	41,963	351.35	6.804	69,757
	GO	1,059.93	18.919	93,416	702.25	12.287	111,083	393.12	6.804	155,507
8.0%	Current practice	792.79	18.777		504.35	12.203		254.30	6.761	
	Technician	1,139.19	18.791	23,775	743.07	12.209	34,851	407.58	6.764	58,999
	GO	1,236.97	18.793	71,648	810.98	12.210	86,547	450.08	6.764	123,022
10.0%	Current practice	945.76	18.647		594.99	12.124		297.39	6.720	
	Technician	1,316.00	18.665	20,527	851.27	12.132	30,405	463.82	6.723	52,218
	GO	1,414.00	18.667	58,158	919.71	12.133	71,088	507.03	6.723	102,350

ICER = Incremental cost-effectiveness ratio; GO = 'glaucoma optometrist' strategy

Table 3 Likelihood of a strategy being cost-effective for selected age cohorts start age and screening intervals

Cohort start age	Screening Interval	Strategy	Probabilistic cost-effectives for different threshold values for Society's willingness to pay for a QALY (%)							
			1% prevalence of OAG				5% prevalence of OAG			
			10,000	20,000	30,000	50,000	10,000	20,000	30,000	50,000
40	3 years (Base Case)	Current practice	100.0%	98.8%	93.9%	78.5%	94.4%	71.5%	50.8%	34.9%
		Technician	0.0%	1.2%	5.9%	21.0%	5.4%	27.9%	48.0%	61.3%
		GO	0.0%	0.0%	0.2%	0.5%	0.2%	0.6%	1.2%	3.8%
	5 years	Current practice	100.0%	97.1%	88.2%	69.2%	87.6%	58.6%	43.2%	29.2%
		Technician	0.0%	2.7%	11.5%	30.1%	12.2%	40.2%	53.3%	60.4%
		GO	0.0%	0.2%	0.3%	0.7%	0.2%	1.2%	3.5%	10.4%
10 years	Current practice	99.8%	92.1%	79.1%	56.2%	82.5%	54.3%	40.2%	29.6%	
	Technician	0.2%	7.7%	20.3%	42.5%	16.7%	42.3%	51.4%	51.1%	
		GO	0.0%	0.2%	0.6%	1.3%	0.8%	3.4%	8.4%	19.3%
60	3 years (Base Case)	Current practice	100.0%	98.4%	92.9%	79.2%	96.4%	79.3%	64.0%	46.1%
		Technician	0.0%	1.5%	6.9%	20.2%	3.5%	20.1%	34.7%	50.5%
		GO	0.0%	0.1%	0.2%	0.6%	0.1%	0.6%	1.3%	3.4%
	5 years	Current practice	100.0%	97.2%	90.0%	74.4%	93.1%	73.3%	56.7%	40.3%
		Technician	0.0%	2.7%	9.6%	24.7%	6.7%	25.7%	40.5%	50.8%
		GO	0.0%	0.1%	0.4%	0.9%	0.2%	1.0%	2.8%	8.9%
10 years	Current practice	100.0%	95.1%	86.9%	69.3%	88.1%	63.9%	49.3%	34.9%	
	Technician	0.0%	4.8%	12.7%	29.5%	11.5%	33.6%	44.0%	48.4%	
		GO	0.0%	0.1%	0.4%	1.2%	0.4%	2.5%	6.7%	16.7%
75	3 years (Base Case)	Current practice	100.0%	99.6%	96.1%	88.1%	99.1%	89.8%	78.7%	64.0%
		Technician	0.0%	0.4%	3.7%	11.5%	0.9%	9.9%	20.4%	33.8%
		GO	0.0%	0.0%	0.2%	0.4%	0.0%	0.3%	0.9%	2.2%
	5 years	Current practice	100.0%	99.6%	96.5%	88.1%	98.2%	86.9%	74.5%	59.9%
		Technician	0.0%	0.4%	3.5%	11.9%	1.7%	12.4%	24.2%	34.9%
		GO	0.0%	0.0%	0.0%	0.0%	0.1%	0.7%	1.3%	5.2%
10 years	Current practice	100.0%	99.1%	94.6%	84.3%	96.1%	82.2%	69.7%	53.8%	
	Technician	0.0%	0.9%	5.2%	15.1%	3.8%	16.9%	27.9%	37.5%	
		GO	0.0%	0.0%	0.2%	0.6%	0.1%	0.9%	2.4%	8.7%

GO = 'glaucoma optometrist' strategy

WEB SITE Table 4.a Deterministic and probabilistic analysis results. Analyses for a 40 year old cohort with a 10 year screening interval and 5% prevalence of OAG

Strategy	Cost (£)	QALYs	ICER	10,000	20,000	30,000	50,000
Current practice	563.34	18.971		82.5%	54.3%	40.2%	29.6%
Technician	703.24	18.978	20,571	16.7%	42.3%	51.4%	51.1%
GO	744.38	18.979	42,188	0.8%	3.4%	8.4%	19.3%

ICER = Incremental cost-effectiveness ratio; GO = 'glaucoma optometrist' strategy

WEB SITE Table 4.b Likelihood of a strategy being cost-effective for different incidence and progression parameter values. Analyses for a 40 year old cohort with a 10 year screening interval and 5% prevalence of OAG

Model parameter	PDs Parameters*	Strategy	Probabilistic cost-effectives for different threshold values for Society's willingness to pay for a QALY (%)			
			10,000	20,000	30,000	50,000
Incidence	High	Current practice	82.0%	53.9%	40.0%	29.6%
		Technician	17.0%	42.4%	50.7%	50.0%
		GO	1.0%	3.7%	9.3%	20.4%
	Low	Current practice	83.6%	55.7%	42.6%	30.6%
		Technician	15.5%	40.6%	48.2%	49.3%
		GO	0.9%	3.7%	9.2%	20.1%
Progression: Mild to Moderate	High	Current practice	78.8%	48.0%	35.2%	23.8%
		Technician	20.5%	48.3%	55.3%	54.8%
		GO	0.7%	3.7%	9.5%	21.4%
	Low	Current practice	82.2%	54.6%	39.2%	27.8%
		Technician	16.9%	42.4%	51.3%	53.2%
		GO	0.9%	3.0%	9.5%	19.0%
Progression: Moderate to Severe	High	Current practice	77.4%	41.2%	28.2%	18.1%
		Technician	21.9%	55.2%	62.2%	59.2%
		GO	0.7%	3.6%	9.6%	22.7%
	Low	Current practice	89.6%	68.2%	52.3%	36.2%
		Technician	10.1%	30.2%	42.0%	50.8%
		GO	0.3%	1.6%	5.7%	13.0%
Progression: Severe to VI	High	Current practice	75.8%	46.2%	32.8%	22.3%
		Technician	23.2%	49.8%	57.4%	55.4%
		GO	1.0%	4.0%	9.8%	22.3%
	Low	Current practice	86.9%	66.2%	53.1%	41.6%
		Technician	12.5%	31.4%	39.9%	42.6%
		GO	0.6%	2.4%	7.0%	15.8%

GO = 'glaucoma optometrist' strategy; VI = visual impairment

* High SA: the likeliest parameter value for the triangular distribution equal to maximum value from base case analysis; maximum value was assumed to be twice the maximum used in the base case (truncated if necessary at 1) and the minimum value was assumed to be equal to the likeliest value from the base case.

Low SA: likeliest parameter value for the triangular distribution equal to the minimum value from base case analysis; the maximum was assumed to be the likeliest value from the base case (truncated if necessary at 1) and the minimum value was assumed to be equal to zero.

Figure 1 Markov model for OAG

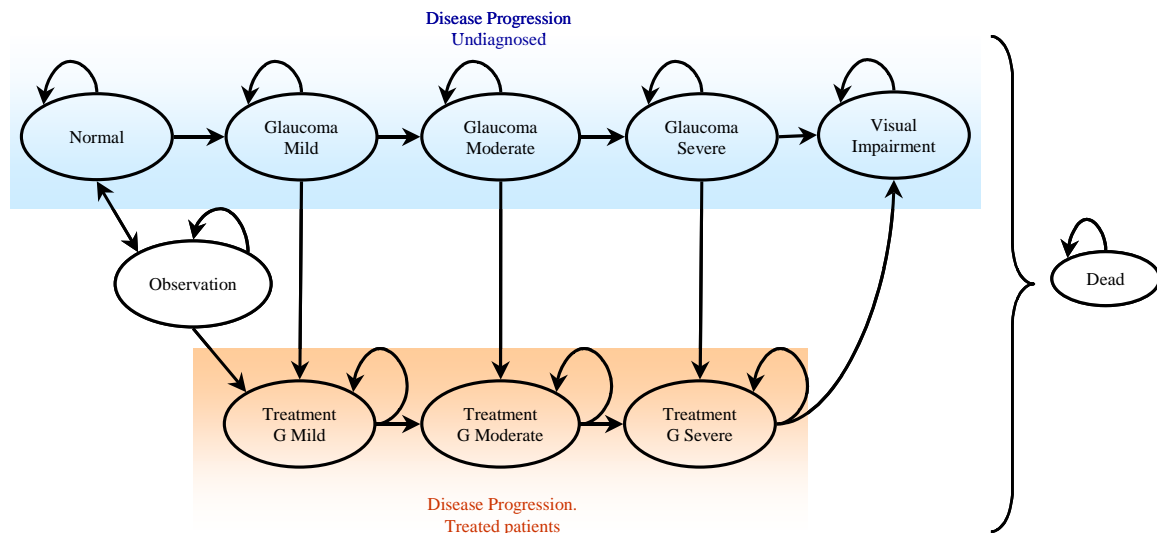
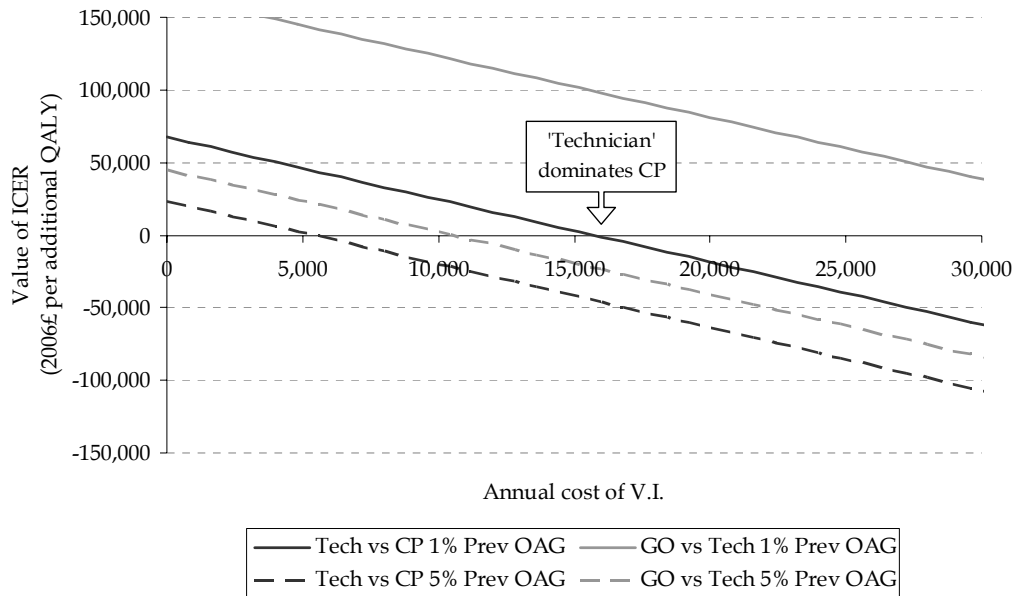


Figure 1 Markov model for OAG

Circles represent health states while the arrows show the possible directions in which individuals could move at the end of each cycle, depending on the transition probabilities. The states considered in the model were those thought to reflect care pathways for people with and without glaucoma. The first line represents the pathway for undiagnosed individuals while the bottom section of the figure reflects glaucoma progression for treated patients. The observation state includes individuals considered suspect but without a definite diagnosis.

WEB SITE Figure 2 Value of ICERs for alternative visually impaired annual costs. Analyses for a 40 year old cohort, 10 year screening interval



WEB SITE Figure 2 Value of ICERs for alternative visually impaired annual costs. Analyses for a 40 year old cohort, 10 year screening interval

At 1% OAG prevalence rate, 'technician' strategy dominates NS (e.g. ICER ≤ 0) for an annual cost of VI of £16,000. 'Technician' strategy looks cost effective (e.g. ICER \leq £30,000) for an annual cost of VI of £8,800. At 5% OAG prevalence rate 'technician' strategy dominates NS for an annual cost of VI of £6,000; and G.O. dominates 'technician' strategy at an annual cost of VI of £11,000.

Tech = Technician strategy; CP = Current practice; GO = Glaucoma trained optometrist; VI = visual impairment