BMJ Open Ophthalmology

Cost-effectiveness of monitoring ocular hypertension based on a risk prediction tool

Hangjian Wu ,[1] Gus Gazzard ,[2,3,4] Anthony King ,[5] James Morgan ,[6] David Wright ,[7] David P Crabb ,[8] Yemisi Takwoingi ,[9] Augusto Azuara-Blanco ,[7] Verity Watson ,[1] Rodolfo Hernández [1]

For numbered affiliations see end of article.

Correspondence to
Dr Rodolfo Hernández; r.a.hernandez@abdn.ac.uk

ABSTRACT

Background/Aims To assess the cost-effectiveness of making treatment decisions for patients with ocular hypertension (OHT) based on a risk prediction (RP) tool in the United Kingdom.

Methods A discrete event simulation model was constructed to compare the cost-effectiveness of an alternative care pathway in which the treatment decision was guided by a validated RP tool in secondary care against decision-making based on the standard care (SC). Individual patient sampling was used. Patients diagnosed with OHT and with an intraocular pressure of 24 mm Hg or over entered the model with a set of predefined individual characteristics related to their risk of conversion to glaucoma. These characteristics were retrieved from electronic medical records (n=5740). Different stages of glaucoma were modelled following conversion to glaucoma.

Results Almost all (99%) patients were treated using the RP strategy, and less than half (47%) of the patients were treated using the SC strategy. The RP strategy produced higher cost but also higher quality-adjusted life years (QALYs) than the SC strategy. The RP strategy was cost-effective compared with the SC strategy in the base-case analysis, with an incremental cost-effectiveness ratio value of £11 522. The RP strategy had a 96% probability of being cost-effective under a £20 000 per QALY threshold.

Conclusions The use of an RP tool for the management of patients with OHT is likely to be cost-effective. However, the generalisability of the result might be limited due to the high-risk nature of this cohort and the specific RP threshold used in the study.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Despite the development and continuing validation of the Ocular Hypertension Study–European Glaucoma Prevention Study tool, one of the most credible risk prediction models for developing glaucoma, the cost-effectiveness of implementing such risk prediction tool in the NHS has rarely been discussed. The recent National Institute for Health and Care Excellence guideline highlighted the need for further research on risk prediction tools.

WHAT THIS STUDY ADDS

⇒ We investigated the cost-effectiveness of making treatment decisions for ocular hypertensive patients based on a recently validated risk prediction tool using the electronic medical records of UK patients. We find that the risk prediction strategy produced higher costs and higher quality-adjusted life years (QALYs) than the standard care strategy. The risk prediction strategy was cost-effective in the base-case analysis under a £20 000 per QALY threshold and had a 96% probability of being cost-effective in probabilistic sensitivity analysis.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The results suggest that managing ocular hypertensive patients using a risk prediction tool can be cost-effective depending on patients' risk of conversion, the predictive power of the tool and the risk threshold used.

INTRODUCTION

Glaucoma is the second most common cause of irreversible registered blindness, affecting around 60 million of the world population and 10% of those aged 75 or above in the UK.[1 2] Ocular hypertension (OHT) and early glaucoma are mostly asymptomatic but can result in lifetime visual impairment and blindness without proper treatment. Intraocular pressure (IOP) is the only modifiable risk factor for conversion to glaucoma and disease progression. Therefore, long-term routine monitoring and treatment of

elevated IOP and visual field (VF) are key to controlling the disease and reducing the risk of visual impairment. OHT monitoring in the UK includes the assessment of IOP and signs of visual deterioration (eg, VF or optic nerve changes). Medical treatments such as prostaglandin analogues (PGAs) and/or beta-blockers (BB) lower IOP and help deter disease progression. If medical treatments fail, laser and surgery options exist for further management.

In the UK, patients with OHT are monitored either in primary care (eg, community

optometrists) or secondary care (eg, eye hospital doctors). The stratification of patients across settings is based on a patient's risk of developing lifetime visual impairment.[1] In England, over one million glaucoma-related outpatient visits take place in secondary care eye services each year.[3] Population ageing means that the number of OHT patients, suspected glaucoma patients and confirmed glaucoma patients can rise by 16%, 18% and 44% between 2015 and 2035, respectively.[4] However, unnecessary referrals can overburden the NHS. The Royal College of Ophthalmologists' Glaucoma Commissioning Guidance stated that many patients currently referred to secondary care can be discharged to primary care health professionals to free up secondary care NHS resources.[3]

An appropriate risk stratification tool using multiple clinical criteria to assign risk levels to individual patients can potentially release resource use in secondary care, yet there is no nationally agreed model for glaucoma management in the UK.[5] Simple risk stratification tools primarily based on VF measures can be misleading, while tools with multiple criteria can be complex to implement.[5] An RP model powered by multiple regression analysis is a promising candidate, as it incorporates multiple risk factors into the analysis and produces a simple risk estimate which facilitates its application. The glaucoma RP tool that has been developed and validated based on the results of the Ocular Hypertension Study (OHTS)[6] and the European Glaucoma Prevention Study (EGPS) is the most credible one so far,[7] yet it has not been recommended by clinical guidelines.[1] The tool estimates the individual's 5 year risk of conversion to glaucoma based on the following risk predictors: age, IOP, central corneal thickness (CCT), a measure of the VF test (pattern standard deviation [PSD]) and the optic nerve (the vertical cup to disc ratio; vCD ratio). The application of an RP tool with good predictive power could be used to identify patients who are most suitable to be monitored in primary care reducing demand on ophthalmology departments in secondary care and allowing health professionals in secondary care to focus on patients with a higher risk of vision loss.

Economic evaluations assess the relative efficiency of alternative healthcare technologies in terms of their cost and consequences.[8] In the literature, most economic evaluation studies of OHT or glaucoma monitoring examine the cost-effectiveness of different monitoring frequencies or delegating care to appropriately trained primary care healthcare professionals compared with the usual care in secondary care.[9–11] Only one study evaluated the cost-effectiveness of using a validated RP tool based on the OHTS–EGPS dataset to assist clinical decision-making.[12] The authors used two non-UK-based clinical trial datasets and two small observational datasets to validate the RP tool. However, the new National Institute for Health and Care Excellence (NICE) guideline highlights the need for further research on RP tools.[1] First, it has been 12 years since the publication of Burr *et al* (2012)'s work, during which time the NICE guidelines have been

updated significantly (eg, the treatment prioritised for OHT patients and suggested intervals of clinical tests). New evidence in modelling disease progression has also emerged based on recently published articles.[13] Second, new evidence shows that a new validated and calibrated RP tool using a large UK-based dataset from electronic medical records (EMRs) has a moderate improvement in predictive power compared with the previous RP tool based on the OHTS–EGPS dataset (information is available from the authors on request). In this study, we address these gaps by investigating the cost-effectiveness of this UK-based RP tool using a new decision analytic model.

METHODOLOGY

The model

A discrete event simulation (DES) model was developed to model OHT and glaucoma monitoring and treatment.[14] DES models offer flexibility and the ability to explicitly evaluate monitoring frequency.[15–17] Diagnosed OHT patients with IOP of ≥24 mm Hg entered the model with a set of predefined individual characteristics related to their risk of conversion to glaucoma (figures 1 and 2). An initial decision on the treatment was made by a secondary-care health professional (eg, a hospital ophthalmologist/optometrist). Patients without treatment were referred for annual check-ups in primary care. Patients who met the initial treatment rule in secondary care were treated with PGAs (80%) or selective laser trabeculoplasty (SLT) (20%).

Throughout the model, patients repeatedly faced three 'competing' events: check-ups (eye tests), conversion to glaucoma (or progression to more advanced glaucoma for open-angle glaucoma [OAG] patients) or death, whichever option had the shortest time-to-event would occur next. The likelihood of the occurrence of these events was governed by the time-to-event values, which were based on patients' characteristics and history of monitoring and treatment. Time-to-event was recalculated each time an event occurred. A schematic of the DES simulation is shown in figures 1 and 2.
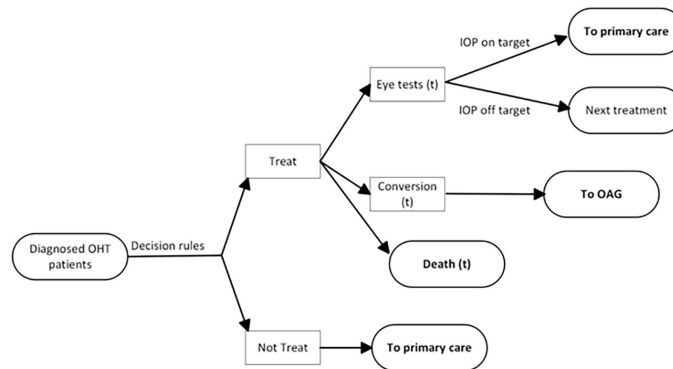
A population of newly diagnosed OHT patients with IOP of ≥24 mm Hg were simulated according to a set of predefined individual characteristics linked to their risk of conversion to glaucoma (ie, age, IOP, CCT, vCD ratio and PSD).[7] Additional risk factors (ie, whether an individual has hypertension, family history of glaucoma, diabetes and biological gender) relevant to the RP tool were also included. Sampling was based on individual patient data extracted from the EMR dataset of the UK OHT patients. The mortality rate of the UK general population is sourced from the UK life table.[18] Table 1 shows the detailed statistics of the individual characteristics.

Disease progression is modelled by considering the time it takes to reach each disease state. The time-to-conversion to glaucoma for OHT and time-to-progression for OAG patients were estimated following van Gestel,
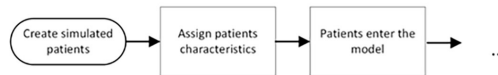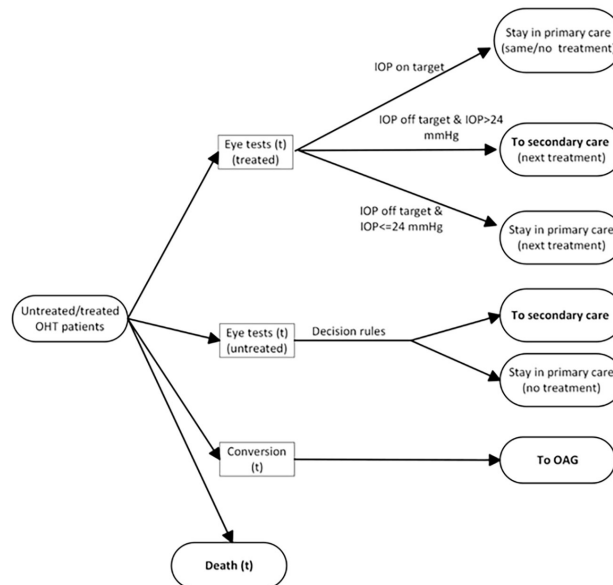
Figure 1 A schematic of the model structure. Diagnosed ocular hypertension (OHT) patients with intraocular pressure (IOP) of ≥24 mm Hg entered the model with a set of predefined individual characteristics related to their risk of conversion to glaucoma. An initial decision on treatment was made by a secondary-care health professional. Patients without treatment were referred for annual check-ups in primary care and can be referred back to secondary care following an unfavourable check-up. Patients who met the initial treatment rule in secondary care were treated with prostaglandin analogues (80% of them) or selective laser trabeculoplasty (20% of them). Treated patients with 'on target' IOP (ie, IOP reduced by 20% or more compared with the baseline IOP after treatment) were returned to primary care after one clinical visit for continued monitoring, while the treatment was escalated for 'off-target' patients following the treatment sequence. For treated or untreated patients monitored in the primary care settings, an observed conversion to glaucoma would trigger a referral to secondary care, and an immediate eye assessment was assumed to be conducted by the hospital ophthalmologists/optometrists to confirm the evidence of glaucoma. Patients with negative glaucoma assessment results would be referred back to primary care, and those with positive assessment results were remained in secondary care. In addition, treated OHT patients monitored in primary care with IOP measures deemed 'off-target' would be referred to secondary care. (t) means it's a time-to-event.

Severens and Webers *et al* (2010)'s approach.[13] Time-to-conversion was calculated based on patients' current IOP, age and other relevant risk factors. A key VF outcome, mean deviations (MD), was used to represent glaucoma progression, which was assumed to be positively associated with patients' IOP levels. The detailed calculation of time-to-conversion and time-to-progression can be found in online supplemental materials A1. A common glaucoma
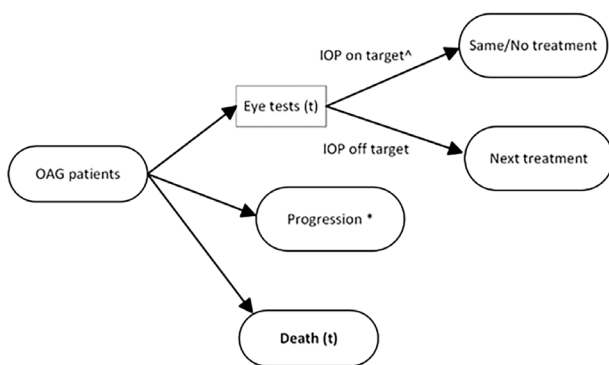
Stage 2: OAG route (secondary care)

Figure 2 A schematic of the model structure. Confirmed glaucoma patients would be maintained in secondary care for regular eye assessment by the hospital ophthalmologists/optometrists. Patients with 'on-target' IOP would be continuously treated with the current treatment (or no treatment), while the treatment was escalated for 'off-target' patients following the treatment sequence. *(t)* means a time-to-event. *Progression to the next level of glaucomatous stage, which can be moderate, severe or visual impairment. Patients cannot progress further on reaching visual impairment. ^'on-target' IOP means IOP reduced by 20% or more compared with the baseline IOP after treatment.

staging system was used to classify the VF outcome following Mills *et al* (2006).[19] Online supplemental table A5 in online supplemental materials A1 provides details of the glaucoma stages and corresponding MD values.

The clinical pathways, treatment sequence and eye test intervals for OHT and glaucoma monitoring were developed based on the 2022 NICE guidelines[1] and the advice of experts, consisting of four ophthalmologists, two health economists and two statisticians. Patients or the public were involved in the design, conduct, reporting or dissemination plans of our research. Two pathways were considered:

▶ OHT monitoring based on standard care (SC).
▶ OHT monitoring based on an RP tool.

All pathways are comprised of both primary care and secondary care monitoring and treatment but differ in the criteria for accepting patients for treatment. For the SC pathway (comparator), the criteria for accepting patients for treatment in secondary care were discussed in several meetings with the clinicians in the project management group, and a decision table was created based on the level of IOP, age and the patient's central corneal thickness (CCT) (see online supplemental table A2).

For the RP pathway (intervention), it was assumed that the RP tool was used by hospital ophthalmologists/optometrists to make clinical decisions regarding the treatment in secondary care. The RP tool was developed and validated using a large UK-based dataset retrieved from the EMRs (information is available from the authors on request). The RP tool provided risk estimates of the 5 year risk of conversion to glaucoma used to inform the treatment decision. Based on expert views, patients with a 5 year risk of conversion of ≥6% were initially treated in secondary care and remained in primary care without treatment otherwise. Additional explanations are provided in online supplemental material A1.

Table 1	Baseline characteristics of the extracted individual patients		
Baseline variables	**Mean**	**SD**	**Data source**
Number of individual patients in the extracted dataset	5740		
Age (years)	62.01	10.56	The EMR dataset (information is available from the authors on request)
CCT (µm)	558.66	35.83	
IOP (mmHg)	26.51	2.13	
PSD (dB)	1.63	0.34	
vCD ratio	0.46	0.17	
Hypertension (Y/N)	0.12	0.33	
Family history of glaucoma (Y/N)	0.26	0.44	
Diabetes (Y/N)	0.14	0.34	
Male (Y/N)	0.43	0.50	
Previously treated (Y/N)	0.36	0.48	
Mean deviation at conversion*	−2.94	2.67	
Life expectancy	Various		UK interim life tables 2018–2020 (gender average)[18]

*The mean deviations (MDs) at conversion were drawn from a gamma distribution with mean and SD extracted from the dataset. Individual patient sampling was not used due to missing data.
CCT, central corneal thickness; IOP, intraocular pressure; PSD, pattern standard deviation; vCD, vertical cup-to-disc.

A common treatment sequence was developed based on the NICE guidelines and expert views. Treatment effectiveness data were obtained from various sources in the literature.[11 20–24] The treatment sequence and effectiveness were detailed in online supplemental material A1.

The unit costs for monitoring were obtained from the NHS reference cost and Department of Health (NHS sight test fee).[25 26] Medications and surgical treatments were valued using national unit cost sources and validated trial studies.[25–27] We used the EQ-5D to value quality of life for each disease state in the model (ie, OHT, mild, moderate, severe glaucoma and visual impairment) based on a valuation study of an OAG population from the UK.[28 29] Clinical effectiveness, costs and utilities are reported in table 2. Additional explanations are provided in online supplemental material A1.

Table 2 Parameters and sources for the treatment effectiveness, costs and utilities

	Data input	Data source
Treatment		
PGAs (Latanoprost)*	Mean: 0.29 SD: 0.08	Valk et al (2005)[20] and van Gestel (2012)
PGAs and BB (Latanoprost and Timolol; additional effectiveness compared with Latanoprost)*	Mean: 0.14 SD:0.08	van Gestel (2012)[21] and Webers et al (2008)[22]
SLT	Mean: 0.312 SD: 0.08	Mean estimate: Chi et al (2020)[23]; SD: assumption
Trabeculectomy	Mean: 0.447 SD: 0.189	Kirwan et al (2013)[24] and Crabb et al (2014)[11]
Costs for monitoring†		
Secondary care: IOP only	£147	NHS reference costs (2021–2022)[25]; Ophthalmology outpatient attendance (service code: 130)
Secondary care: IOP and VF	£294	Assumption. Twice the unit cost for IOP only
Primary care: NHS sight test fee: IOP only	£11.57	Assumption. Half the unit cost for IOP and VF test fee
Primary care: NHS sight test fee: IOP and VF	£23.14	Department of Health (General Ophthalmic Services: NHS sight test fee, updated in April 2023)[26]
Costs for treatments†		
Latanoprost	£149.76 per year with 2.5 mL = £12.48	BNF 2023; Xalatan
Latanoprost and Timolol	£171.84 per year with 2.5 mL = £14.32	BNF 2023; Xalacom
SLT	£151 per patient	Gazzard et al (2019)[27]
Trabeculotomy	£1694 per patient	NHS reference costs (2021–2022); glaucoma surgical procedures (HRGs code: BZ92B; average of total cases)
Disease states		
Patients with OHT	0.8015	Assumption
Patients with mild OAG	0.8015	Burr, Kilonzo, et al (2007)[28]
Patients with moderate OAG	0.7471	Burr, Kilonzo, et al (2007)[28]
Patients with severe OAG	0.7133	Burr, Kilonzo, et al (2007)[28]
Visually impaired OAG patients	0.535	Burr, Mowatt, Hernández, et al (2007)[29]

*Assuming one bottle of the eyedrops per month per patient
†The cost for latanoprost and timolol were used to cost the PGAs and BB medical treatment, respectively. These unit costs were obtained from the British National Formulary (BNF), assuming one bottle of the eyedrops per month per patient. Unit cost for the Trabeculectomy was obtained from the NHS reference costs. The unit cost for the SLT was obtained from the LiGHT trial.
BB, beta-blockers; IOP, intraocular pressure; OAG, open-angle glaucoma; OHT, ocular hypertension; PGAs, prostaglandin analogues; SLT, selective laser trabeculoplasty; VF, visual field.

Data analysis

A cohort of 50 000 patients with diagnosed OHT were used in the simulation using Treeage (2023 R2.0) for the base-case analysis (the model is available from the authors on request). All analyses were based on the NHS perspective with all costs expressed in GBP and 2021/2022 UK prices. The adjustment was conducted using a web-based tool.[30] The time horizon of the model was lifetime with cost and utilities discounted at an annual rate of 3.5%.

To identify the key drivers of uncertainty around the costs and effectiveness, one-way and probabilistic sensitivity analyses (PSA) were conducted for (a) the threshold of treatment decision regarding the RP strategy, (b) medication and monitoring costs and (c) adherence rate to medication. The high number of simulated patients (eg, 50 000) increased the model running time but, on visual inspection, produced similar results to those obtained for 10 000 simulated patients. Therefore, 10 000 simulated patients with 1000 replications (second-order uncertainty) were used for sensitivity analyses.

Model validation and calibration

The model has been carefully validated based on the internal dataset used and several external data sources, with several calibrations being made. Details can be found in online supplemental material A2. A health analysis plan is available on request.

RESULTS

Base-case analysis

The simulated results for the base-case scenarios are shown in table 3. Almost all (99%) patients were treated in the RP strategy, while about 47% of patients were treated in the SC strategy. For the SC and RP strategies, 57% and 53% of the patients were estimated to have converted to glaucoma, respectively. In the SC strategy, more patients progressed to moderate (24%) and severe (11%) glaucoma and visual impairment (5%), which

implied quality-adjusted life year (QALY) losses due to VF defects. This was not surprising as more patients received treatment in the RP strategy. Regarding cost-effectiveness, the RP strategy incurred higher costs but gained higher QALYs than the SC strategy. The difference in QALYs between strategies was relatively small as the strategies differed mainly in the decision to treat determined at the start of the model. The RP strategy was cost-effective compared to the SC strategy with an incremental cost-effectiveness ratio (ICER) (£11 522) which was below the cost per QALY threshold of £20 000 used by NICE.

One-way sensitivity analysis

Overall, the RP remained cost-effective when the adherence rate was decreased to 75%, the cost of medication increased by up to 50% or the cost of monitoring increased by up to 50%. However, the change of the risk threshold for the RP tool had the largest impact on the ICER—the RP strategy became less cost-effective as the threshold increased, and ICER exceeded the cost-effective threshold of £20 000 when the risk threshold was more than 12%. The impact of medication costs is generally larger than the one for the monitoring costs. For example, increasing the cost of PGA up to 50% raise the ICER value from £12 100 up to £18 076 (ie, a 49% increase), while the cost of primary care full test up to 50% raise the ICER value from £12 100 up to £13 137 (ie, an 8.5% increase). The full sensitivity analysis results are presented in online supplemental material A3.

PSA

The cost-effectiveness scatterplots and cost-effectiveness acceptability curves can be found in online supplemental figures A2 and A3 in online supplemental material A3. The results showed that the RP strategy had a 98% probability of being cost-effective at the £20 000 per QALY threshold, which was consistent with the base-case results.

Table 3 Cost-effectiveness results for the base-case analysis

Pathway	Proportion of patients initially treated (%)	Proportion of patients in each state at the end of model run (%)				
		OHT	OAG mild	OAG moderate	OAG severe	Visual impairment
Standard care strategy	47%	43%	17%	24%	11%	5%
Risk prediction strategy	99%	47%	17%	22%	10%	4%
	Average total cost (£)	Incremental cost (£)	Average total QALYs	Incremental QALYs	ICER (£)	
Standard care strategy	4662		10.89			
Risk prediction strategy	4925	262	10.92	0.023	11 522	

Proportion of patients who were initially allocated to treatment based on the decision algorithm
ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

DISCUSSION

This study investigated the cost-effectiveness of an RP tool used in making clinical decisions in OHT monitoring. The costs and effectiveness of an RP tool used by health professionals were examined against the SC pathway using a DES model. Our results demonstrate that making treatment decisions based on our RP tool used in a secondary care setting can be cost-effective. This conclusion remains qualitatively unchanged against different scenarios and sensitivity analyses, except for a change in the risk threshold used to decide on treatment initiation. For a 5 year risk of conversion to glaucoma threshold of 12% or above, the RP strategy stopped being cost-effective.

A similar UK-based study concerning OHT monitoring was conducted by Burr *et al* (2012) in which the cost-effectiveness of two RP strategies were compared against a 'treat-all' strategy in which all patients were offered medication with no active monitoring of conversion.[12] The RP strategies in their study were not considered cost-effective using a £30 000 per QALY threshold. The discrepancy in findings is not surprising, as the model settings in our study have been tailored to reflect the current NICE guidelines and updated knowledge on modelling time to conversion and progression. We also had access to a comprehensive patient-level dataset extracted from EMRs, which allows us to perform individual patient sampling. In our study, the cohort had a higher 5 year risk of conversion compared with the simulated cohort in Burr *et al* (2012) (ie, 17% vs 10% patients converted to glaucoma in 5 years). Another notable difference is the use of a calibrated RP tool based on the patient records of UK OHT patients. Some US-based studies suggested that treating high-risk cohorts, such as those with advancing age, higher IOP, thinner CCT or with a 5 year risk of conversion of 10% or higher (based on the OHTS RP tool), against a 'treat-all' or 'treat-none' strategy, were likely to be cost-effective, which was inconsistent with our results.[31 32]

The strategies compared in this study differ only in the decision algorithm used to determine whether to offer treatment with the RP strategy under the current risk threshold, indicating a very high proportion of patients being initially treated with medications or SLT. The findings imply that medications and SLT are inexpensive, safe and effective treatment options that delay conversion to glaucoma and glaucoma progression, especially for a high-risk cohort such as the sample used in this study. This result is consistent with findings from the OHTS trial in which high-risk OHT patients benefited the most from the treatment.[33] However, the message cannot be simply interpreted as 'treating more people is always cost-effective' since several factors need to be considered in the implementation of clinical practice: (a) our sample includes a large proportion of patients with high risk profiles; in reality, more low-risk patients would need to be discharged to primary care for regular monitoring without treatment and (b)

patient-centred care has been an important aspect of OHT and glaucoma treatment in the UK. Treatment decisions must be tailored based on individual patient needs and take into account factors such as eyedrop tolerance and adverse effects.[34 35] Patients with intolerance to eyedrops and no immediate risk of conversion to glaucoma may not be offered treatment.

This study used a large-scale UK-based dataset extracted from the EMRs to model patient characteristics and adopted a comprehensive modelling approach, which reflects the current advances in disease progression modelling and updated NICE guidelines. This study also has three limitations. First, the RP tool used has limited predictive power with a concordance index (ie, c-index) of 0.69 in a recent validation study using UK OHT patients, while c-index of 1 represents a perfect prediction (information is available from the authors on request). Therefore, the cost-effective results of the RP strategy might be due to the particularly high-risk cohort defined in the model and the specific threshold used that result in almost all patients being treated in the RP strategy. The RP tool seems to fail to discriminate between those who need treatment and those who do not when the risk threshold for treatment is raised, which partly explains the inconsistency between the results of this and Kymes *et al* (2006)'s study.[32] Second, the risk stratification threshold (ie, 6%) used in this study is only based on one study (ie, Kass *et al* (2010)[33] and has not been widely discussed in the literature. However, our sensitivity analysis results show that the risk threshold can be a key factor affecting the cost-effective results. Third, we attached a zero R&D and production cost to the RP tool based on the assumption that these costs would be less important in the long run. However, little is known about the operating costs of using the risk calculator in clinical practice. Studies that investigate the monitoring of chronic conditions using digital technology suggest that operating costs such as integration and training costs may be nonnegligible.[36] Our results suggest that further studies are needed to confirm the observed cost-effectiveness analyses of monitoring strategies based on a more advanced RP algorithm, and the economic evaluation should incorporate fixed and running costs of applying the RP tool.

CONCLUSION

In conclusion, NICE has recommended the development of the RP algorithm for developing glaucoma in its recent guidance. Based on a recently validated RP tool using a UK-based dataset, we investigated the cost-effectiveness of using this tool to guide treatment decision in a secondary care setting compared with the SC. The results show that the RP tool is likely to be cost-effective, although this is subject to limitations regarding the characteristics of the sample used and the discriminatory power of the risk tool. Future research can extend the analysis to incorporate improved tools and different populations.

Author affiliations
[1]Health Economics Research Unit, Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, UK
[2]NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, UK
[3]Institute of Ophthalmology, University College London, London, UK
[4]NYU Langone Health, New York, New York, USA
[5]Department of Ophthalmology, Nottingham University Hospitals NHS Trust, Nottingham, UK
[6]Cardiff Centre for Vision Sciences, University of Wales College of Medicine, Cardiff, UK
[7]Centre for Public Health, Queen's University Belfast, Belfast, UK
[8]Division of Optometry & Visual Science, City University, London, UK
[9]Public Health, Epidemiology and Biostatistics, University of Birmingham, Birmingham, UK

X Augusto Azuara-Blanco @AAzuaraBlanco and Rodolfo Hernández @ rodolfoahernand

Patient and public involvement Patients and/or the public were involved in the design, conduct, reporting or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study involved human participants and was approved by the East of England Essex Research Ethics Committee, REC reference: 21/EE/0109. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data may be obtained from a third party and are not publicly available. Data are available upon reasonable request.

ORCID iDs
Hangjian Wu http://orcid.org/0000-0001-8377-3276
Gus Gazzard http://orcid.org/0000-0003-1982-5005
Anthony King http://orcid.org/0000-0002-3091-911X
James Morgan http://orcid.org/0000-0002-8920-1065
David Wright http://orcid.org/0000-0001-8948-3691
David P Crabb http://orcid.org/0000-0001-8754-3902
Yemisi Takwoingi http://orcid.org/0000-0002-5828-9746
Augusto Azuara-Blanco http://orcid.org/0000-0002-4805-9322
Verity Watson http://orcid.org/0000-0002-3824-5076
Rodolfo Hernández http://orcid.org/0000-0003-2619-8230

REFERENCES

1 National Institute for Health and Care Excellence. NICE: guidance on glaucoma: diagnosis and management of chronic open angle glaucoma and ocular hypertension. Available: https://www.nice.org.uk/guidance/NG81 [Accessed 20 Apr 2022].
2 Allison K, Patel D, Alabi O. Epidemiology of glaucoma: the past, present, and predictions for the future. *Cureus* 2020;12:e11686.
3 Khawaja AP, Sherratt M-A, Sparrow JM, *et al*. The Royal College of Ophthalmologists' glaucoma commissioning guidance: executive summary. *Eye (Lond)* 2017;31:818–22.
4 The Royal College of Ophthalmologists. The way forward. 2016. Available: https://www.rcophth.ac.uk/wp-content/uploads/2021/12/RCOphth-The-Way-Forward-Glaucoma-300117.pdf
5 Poostchi A, Kastner A, Konstantakopoulou E, *et al*. Clinical risk stratification in glaucoma. *Eye (Lond)* 2023;37:3121–7.
6 Kass MA, Heuer DK, Higginbotham EJ, *et al*. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002;120:701–13.
7 Ocular Hypertension Treatment Study Group, European Glaucoma Prevention Study Group, Gordon MO, *et al*. Validated prediction model for the development of primary open-angle glaucoma in individuals with ocular hypertension. *Ophthalmology* 2007;114:10–9.
8 Drummond MF, Sculpher MJ, Claxton K, *et al. Methods for the economic evaluation of health care programmes*. 4th edn. Oxford University Press, 2015. Available: https://pure.york.ac.uk/portal/en/publications/methods-for-the-economic-evaluation-of-health-care-programmes-3
9 Holtzer-Goor KM, van Sprundel E, Lemij HG, *et al*. Cost-effectiveness of monitoring glaucoma patients in shared care: an economic evaluation alongside a randomized controlled trial. *BMC Health Serv Res* 2010;10:312.
10 van Gestel A, Webers CAB, Beckers HJM, *et al*. The relationship between visual field loss in glaucoma and health-related quality-of-life. *Eye (Lond)* 2010;24:1759–69.
11 Crabb DP, Russell RA, Malik R, *et al*. Frequency of visual field testing when monitoring patients newly diagnosed with glaucoma: mixed methods and modelling. *Health Serv Deliv Res* 2014;2:1–102.
12 Burr JM, Botello-Pinzon P, Takwoingi Y, *et al*. Surveillance for ocular hypertension: an evidence synthesis and economic evaluation. *Health Technol Assess* 2012;16:1–271.
13 van Gestel A, Severens JL, Webers CAB, *et al*. Modeling complex treatment strategies: construction and validation of a discrete event simulation model for glaucoma. *Value Health* 2010;13:358–67.
14 TreeAge Software. TreeAge pro 2024, R1. 2024. Available: http://www.treeage.com [Accessed 22 Feb 2024].
15 Brennan A, Chick SE, Davies R. A taxonomy of model structures for economic evaluation of health technologies. *Health Econ* 2006;15:1295–310.
16 Caro JJ, Möller J, Getsios D. Discrete event simulation: the preferred technique for health economic evaluations? *Value Health* 2010;13:1056–60.
17 Karnon J, Stahl J, Brennan A, *et al*. Modeling using discrete event simulation: a report of the ISPOR-SMDM modeling good research practices task force--4. *Value Health* 2012;15:821–7.
18 Office for National Statistics. ONS website, statistical bulletin, national life tables – life expectancy in the UK: 2018 to 2020. 2021.
19 Mills RP, Budenz DL, Lee PP, *et al*. Categorizing the stage of glaucoma from pre-diagnosis to end-stage disease. *Am J Ophthalmol* 2006;141:24–30.
20 van der Valk R, Webers CAB, Schouten JSAG, *et al*. Intraocular pressure-lowering effects of all commonly used glaucoma drugs:

a meta-analysis of randomized clinical trials. *Ophthalmology* 2005;112:1177–85.

21 van GA. Glaucoma management: economic evaluations based on a patient level simulation model. Maastricht University, 2012

22 Webers CAB, Beckers HJM, Nuijts R, *et al*. Pharmacological management of primary open-angle glaucoma: second-line options and beyond. *Drugs Aging* 2008;25:729–59.

23 Chi SC, Kang YN, Hwang DK, *et al*. Selective laser trabeculoplasty versus medication for open-angle glaucoma: systematic review and meta-analysis of randomised clinical trials. *Br J Ophthalmol* 2020;104:1500–7.

24 Kirwan JF, Lockwood AJ, Shah P, *et al*. Trabeculectomy in the 21st century: a multicenter analysis. *Ophthalmology* 2013;120:2532–9.

25 Office for National Statistics. National cost collection for the NHS. n.d. Available: https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection

26 Department of Health. The NHS constitution for England. Available: www.gov.uk/government/publications/the-nhs-constitution-for-england [Accessed 24 Nov 2023].

27 Gazzard G, Konstantakopoulou E, Garway-Heath D, *et al*. Selective laser trabeculoplasty versus drops for newly diagnosed ocular hypertension and glaucoma: the LiGHT RCT. *Health Technol Assess* 2019;23:1–102.

28 Burr JM, Kilonzo M, Vale L, *et al*. Developing a preference-based Glaucoma Utility Index using a discrete choice experiment. *Optom Vis Sci* 2007;84:797–808.

29 Burr J, Mowatt G, Hernández 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.

30 Shemilt I, James T, Marcello M. A web-based tool for adjusting costs to a specific target currency and price year. *Evid Policy* 2010;6:51–9.

31 Stewart WC, Stewart JA, Nasser QJ, *et al*. Cost-effectiveness of treating ocular hypertension. *Ophthalmology* 2008;115:94–8.

32 Kymes SM, Kass MA, Anderson DR, *et al*. Management of ocular hypertension: a cost-effectiveness approach from the ocular hypertension treatment study. *Am J Ophthalmol* 2006;141:997–1008.

33 Kass MA, Gordon MO, Gao F, *et al*. Delaying treatment of ocular hypertension: the ocular hypertension treatment study. *Arch Ophthalmol* 2010;128:276–87.

34 Inoue K. Managing adverse effects of glaucoma medications. *Clin Ophthalmol* 2014;8:903–13.

35 Denis P, Lim KS, Alaghband P. Adverse Effects, Adherence and Cost–Benefits in Glaucoma Treatment. *Eur Ophthalmic Rev* 2011;05:116.

36 Gomes M, Murray E, Raftery J. Economic evaluation of digital health interventions: methodological issues and recommendations for practice. *Pharmacoeconomics* 2022;40:367–78.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open Ophth

Supplementary Material A1: additional description of model structure and data inputs

1. Discrete event simulation

A Discrete event simulation (DES) usually includes the following components: entities, attributes, events, relationships and outcomes. In this model, entities are simulated patients with diagnosed ocular hypertension (OHT) or open-angle glaucoma (OAG). Attributes are patients' characteristics, including age, intraocular pressure (IOP), and other risk factors of converting to glaucoma or progressing to more advanced glaucoma; events are eye tests (e.g., visual field (VF) and IOP tests), treatment, conversion to glaucoma (OHT only), progression to more advanced glaucoma states (OAG only), and death. Relationships are mathematical or logical relationships linking different elements together such as the mathematical expression linking the rate of disease progression with a patient's IOP level. Finally, outcomes include both clinical outcomes of interest (e.g., proportion of patients developing glaucoma) as well as economic outcomes (e.g., incremental cost, Quality-adjusted life years (QALYs) and Incremental Cost-Effectiveness Ratios (ICERs)).

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open Ophth

16 ## 2. Care pathways

17 *(1) Referral, monitoring and treatment criteria for each pathway*

Table A1: Referral, monitoring and treatment criteria for each pathway

Pathway	Referral criteria	Monitoring criteria	Treatment
SC	NICE guidelines and expert views (see the decision table A2 in supplementary material).\n\nPatients maintained in primary care would only be referred to secondary care if (a) conversion to OAG being observed, or (b) untreated patients met decision rules, or (c) observed "off-target" during the last checkup and IOP above 24mmHg for the treated patients	Based on NICE guidelines and expert views (see the frequency tables in Table A6, supplementary material).	Those who met the treatment criteria were treated and kept in secondary care. 80% were initially treated with PGAs and the rest (20%) were treated with SLT. Those who did not meet the treatment criteria were maintained in primary care without treatment.
RP	Those of low risk (5-year risk of conversion<6%) were NOT treated and maintained at the primary care, but those of intermediate risk (5-year risk of conversion between 6-13%) or high risk (5-year risk of conversion>13%) were treated at secondary care.	Same as above.	Those who were treated followed the same treatment sequence as those in the SC pathway.

18

19 *(2) Decision table for receiving treatment in the standard care pathway*

Table A2: Decision table for receiving treatment in the standard care pathway

	D1	D2	D3	D4	D5	D6
Conditions						
IOP (mmHg)	>30	27-29	27-29	24-26	24-26	24-26
Age (year)						<50
CCT (um)		<600		<500	500-600	>600
Family history (Y/N)			Y		Y	Y

Notes: D1 means decision rule 1; family history is also drawn from the same multinomial distribution as baseline risk factors such as IOP, age and CCT, with the parameters describing the mean, SD and correlations extracting from the EMRs dataset.

20

21 *(3) Risk stratification and calculation*

22   The RP tool was developed and validated using a large UK-based dataset retrieved from the EMRs,

23   comprising over 9,000 OHT patients from 11 hospital eye services in the UK with at least five years of

24   follow-up.[1] The RP tool provided risk estimates of the 5-year risk of conversion to glaucoma used to

25   inform the treatment decision; the calculation of the risk estimates is detailed below. Following Burr

26   et al. (2012)'s risk classification[1], patients were split into three groups based on the risk estimates: low

27   risk (<6%), intermediate risk (6-13%) and high risk (>13%). Based on expert views, the high and

28   intermediate risk groups were initially treated in secondary care and the low-risk group remained in

29   primary care for regular eye check-ups without treatment. However, low-risk patients could be referred

30   to secondary care when their risk of conversion exceeded the predefined threshold (6%).

31   The risk estimates for the RP tool can be calculated in Equation A.1-A.2:

32   Risk estimate $= 1 - 0.784 * e^{PI}$ (EQ A.1)

33
34   where $PI = 0.282 * (Age - 6.262) - 0.008 * (IOP - 24.731) + 0.058 * (CCT + 14.098) +$
35    $0.232 * (PSD - 8.379) + 0.099 * (vCD - 4.782) - 0.207 * hypertension - 0.026 *$
36    $family\ history + 0.239 * diabetes - 0.036 * sex$ (EQ A.2)
37

38   where updated age and IOP, and the baseline data were used for these variables. Hypertension, family

39   history, and diabetes are binary variables representing whether an individual has hypertension, family

40   history of glaucoma or diabetes, respectively. The inclusion of these variables represented the effects

41   of comorbidity on risk of conversion. Sex is a binary variable representing individual's biological gender

42   (i.e., male or female). For example, a patient X with the baseline characteristics shown in Table A3 is

43   estimated to have 10.1% of converting to glaucoma in the next 5 years.

Table A3: The profile of patient X

Age	Mean IOP	Mean CCT	Mean PSD	Mean vCDR	Sex	Family history	Diabetes	Hypertension
43.6	28	534	1.5	0.4	male	Yes	No	No

44

---

[1] Information is available from the authors upon request

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open Ophth

45   (4) Assumption of the time needed for patient discharge

46   In the model, we assumed that stable OHT patients were discharged to the primary care only after one

47   clinical visit. NICE guidelines suggested discharging patients 3-5 years after being stable in secondary

48   care. However, several clinicians confirmed that the most common clinical practice is to discharge

49   patients after one clinical visit due to capacity issues in UK hospitals.

50   ## 3. Modelling time-to-conversion and time-to-progression

51   (1) The calculation of time-to-conversion

52   The survival function to conversion can be calculated by as Equation A3:

53    $P = 1 - S = 1 - e^{-h_{it}*t}$ (EQ A3)

54   where $h_{it} = HR_{AGE}^{\frac{(AGE_{it} - \overline{AGE_{ref}})}{10}} * HR_{IOP}^{(IOP_{it} - \overline{IOP_{ref}})} * HR_{OTHER_i} * h$ (EQ A4)

55   In Equation A3, P is the cumulative probability of conversion; S is the survival function; h_{it} is the

56   current hazard rate of individual *i* at current event (time *t)*. In equation $A4$, HR_{AGE}, HR_{IOP}, HR_{OTHER}

57   are the hazard ratios of age (per 10 years older), IOP (per mmHg higher) and a combination of other

58   risk factors (i.e., CCT, vCD and PSD), respectively; AGE_{it} is the age of individual *i* at current event *t*;

59   IOP_{it} is the IOP of individual *i* at current event t; $\overline{AGE_{ref}}$ and $\overline{IOP_{ref}}$ are the average age and IOP of

60   the referenced population of the OHTS-EGPS study;[2] h_{ref} is the calibrated hazard rate of the

61   referenced population, which equals to 0.03.

62   Time-to-conversion estimates at event level can be derived from the equations above. A random draw

63   from a uniform distribution is then used to determine the time-to-conversion value from the

64   cumulative probability of conversion (i.e., only one probability was drawn for each patient at start of

65   the model). As we sampled individual patients from the EMRs dataset, the conversion time for those

66   who have been treated before the observation period may have been delayed compared with those

67   who haven't received any treatment. To ensure a consistent starting point, the time-to-conversion for

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open Ophth

68 the patients who have received treatment before was increased by an additional 2.7 years,

69 representing an average effect of medications on time-to-conversion, extracted from Kass et al.

70 (2010).[3]

71 (2) The calculation of time-to-progression

72 The current mean deviation (MD) score was modelled as the baseline MD plus the amount of MD

73 decreased since conversion (Equation A5). Note that the MD values theoretically cannot increase due

74 to the irreversible nature of glaucoma.

75 $$MD_{it} = MD\_Base_i - MDR_{it} * (T_t - T_{t-1}))$$ (EQ A5)

76 where MD_{it} is the MD for individual *i* at time *t* (current time), which is assumed to be smaller than 0;

77 MD_Base_i is the baseline MD; MDR_{it} is the progression rate of the MD; $T_t - T_{t-1}$ represents the

78 current time minus the last time when progression was internally checked. Following van Gestel,

79 Severens & Webers et al. (2010) approach,[4] progression rate was modelled as a function of current IOP.

80 The higher the IOP, the faster the disease would progress. The progression rate of MD was calculated

81 as Equation A6:

82 $$MDR_{it} = MDR_{ref} * HR_{it} = MDR_{ref} * HR_{IOP(OAG)}^{(IOP_{it} - \overline{IOP_{ref(OAG)}})} * HR_{OTHER}$$ (EQ A6)

83 where MDR_{ref} is the average progression rate of MD referenced to the OAG population in the EMGT

84 study;[5] $HR_{IOP(OAG)}$ is the hazard ratio of IOP (per 1 mmHg higher than average IOP in the referenced

85 OAG population in the EMGT study); $\overline{IOP_{ref(OAG)}}$ is the average IOP level referenced from the OAG

86 population in the EMGT study, which equals to 15.5 mmHg.[5]

87 Regarding the modelling of OAG progression, we mainly referenced the OAG population in the EMGT

88 study, as the EMRs dataset contains insufficient information about the characteristics of OHT patients

89 after converting to OAG. MDR_{ref} was drawn from a gamma distribution at patient level based on the

90 empirical results extracted from van Gestel (2012).[6] Hazard ratios and average value for the IOP were

91   also extracted from the EMGT study. Table A4 shows the parameters used to calculate time-to-

92   conversion and progression.

93   (3) Internal time-to-progression checks

94   OAG progression was checked internally with a fixed frequency (i.e., every 3 months) throughout the

95   model after patients converted to OAG. This avoided failure in the detection of disease progression in

96   time when time intervals between two clinical eye check-ups were large. Defined as a competing time

97   event against time-to-death and time-to eye checkup, the internal checkup calculated MD with no

98   implications on cost. The internal check-ups were not applicable to severe glaucoma patients, as the

99   actual eye check-ups for them were assumed to be sufficiently frequent to identify progression. Table

100   A4 shows the parameters used for the calculation of time-to-conversion and time-to-progression.

101   Table A5 shows the glaucoma staging system used in this study.

Table A4: Parameters used to calculate time-to-conversion and progression

	Parameters	Source
Hazard ratios		
Age (decade)	1.26	EMGT
IOP (OHT) (mmHG)	1.09	EMGT
IOP (OAG) (mmHG)	1.13	EMGT
HR_{OTHER}	Ln(Normal(0,0.7))	EMGT and van Gestel (2012)[6]
Average values of risk factors		
Age (years)	55	EMGT
IOP (OHT) (mmHg)	24	EMGT
IOP (OAG) (mmHg)	15.5	EMGT
Hazard rate in referenced OHT population		
h	0.03	Van Gestel (2012)[6] before calibration
Progression rate		
Progression rate of mean deviation (reference)	Gamma (2, 0.014)	Van Gestel (2012)[6]

102

Table A5: Glaucomatous staging system based on Mills et al. (2006)

Glaucoma severity	Mean deviation scores (dB)
Mild	−0.01 to −6.00
Moderate	−6.01 to −12.00
Severe	−12.01 to −20.00
Visual impairment	≤-20.01

103   (4) The IOP level at any time point

104   The level of IOP is a key risk factor affecting both conversion and progression. Generally, a lower level

105   of IOP compared with the baseline would delay the time-to-conversion and time-to-progression, and

106   vice versa. We adopted the approach detailed in van Gestel (2012),[6] in which the IOP level at any point

107   was modelled as the baseline IOP, plus an annual natural increase (i.e., 0.5%) and plus the IOP

108   reduction due to any effective treatment.

109   4. Treatment effects

110   4.1 Treatment sequence

111   80% of the OHT patients were initially treated with PGAs and 20% treated with Selective laser

112   trabeculoplasty (SLT). Recent development in the NICE guidelines suggests SLT being the initial

113   treatment for those with OHT who had risk of blindness in their lifetime. However, we assumed (based

114   on expert views) that only 20% of the OHT patients would go through SLT as a first treatment given the

115   capacity restrictions in many UK hospitals. We assumed that SLT would not be repeated within 2 years

116   based on the findings of the numbers of SLT from Gazzard et al. (2019).[7] SLT repeated more than 2

117   times during lifetime was possible only if the relative effectiveness of the SLT (compared with baseline

118   IOP) was over 20%.

119   The next treatment following PGAs was a combination of PGAs and BB, which was then followed by

120   SLT. Treatment escalation was triggered if a patient's IOP was "off target" (defined as a baseline IOP

121   reduction of less than 20%) or conversion to OAG was observed. A similar treatment sequence was

122   assumed for patients converting converted to glaucoma, except that trabeculectomy was considered

123   as a last resort if a patient did not meet the requirements for a SLT treatment. Patients were closely

124   monitored without treatment after a SLT or trabeculectomy had been conducted, until a treatment

125   escalation was triggered. The treatment sequence is visualised in Figure A1.
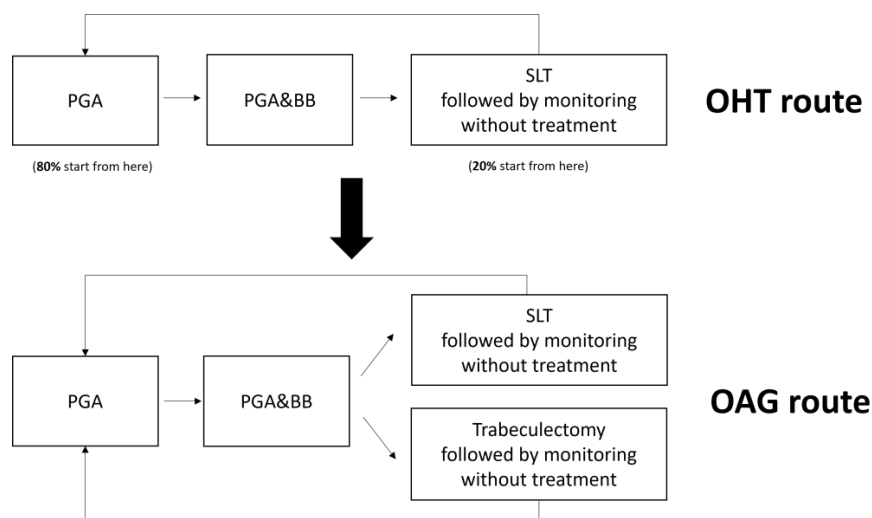
Figure A1: Treatment sequence for the ocular hypertension and open-angle glaucoma pathway.

126

127 4.2 Treatment effectiveness

128 (1) The effectiveness of SLT

129 The mean of the distribution describing the effectiveness of SLT was extracted from the results of a

130 meta-analysis conducted by Chi et al. (2020)[8], and the SD was based on the assumption.

131 (2) The effectiveness of trabeculectomy

132 Following several prospective studies on the effectiveness of trabeculectomy, the number of

133 trabeculectomies a patient can receive was restricted to one, and only a 9.4% of those who received

134 trabeculectomy before were allowed to have a second trabeculectomy in their lifetime if needed.[9,10]

135 The mean effectiveness of the trabeculotomy was initially extracted from the results of a literature

136 review conducted by Crabb et al. (2014).[11] We later fitted a PERT distribution so that about 13% of the

137 patients who received a trabeculotomy carried an effectiveness of less than 20% based on Kirwan et

138 al. (2013).[10]

139 (3) The effectiveness of medication

140 The effectiveness of the first-line medication, i.e., PGAs, was extracted from van Gestel (2012)[6] who

141 initially extracted the parameters from a meta-analysis study conducted by Valk et al. (2005),[12] and

142   then fine-tuned the effectiveness distribution based on views of clinical experts. The effectiveness of

143   PGAs & BB was expressed in addition to the first-line drug. The parameters for the effectiveness

144   distribution were extracted from van Gestel (2012)[6] who initially extracted the parameters from a

145   systematic review study conducted by Webers et al. (2008),[13] and then fine-tuned the distribution

146   based on views of clinical experts.

147   ## 5. Frequency of clinical visits and precision of the measurement of progression to

148   ## open-angle glaucoma

149   (1) precision of the measurement of progression to open-angle glaucoma

150   To reflect imperfect diagnostic accuracy of conversion from OHT to mild OAG in the community

151   optometrists setting, sensitivity and specificity were assumed to be less than 1 (0.76 and 0.93 for

152   sensitivity and specificity).[14] Perfect information for the diagnosis of glaucoma as well as the detection

153   of disease progression was assumed in the secondary care setting (sensitivity and specificity of both

154   conversion and progression equal to 1). It was further assumed that community optometrists would

155   detect conversion to OAG if the patient progressed to moderate or severe glaucoma, or visual

156   impairment.

157   (2) Frequency of clinical visits

158   The frequency of visits in the model depends on (a) disease status, (b) whether the last IOP

159   measurement is "on target" and (c) whether a patient has been treated (only for OHT patients). During

160   each visit, both IOP and VF were measured (Table A6). Visit frequency gradually decreased if there was

161   no sign of disease progression and remained unchanged at a certain point. For the OHT (treated) and

162   mild glaucoma patients, the required visit frequency was relatively low given the low risk of

163   progression to visual impairment. For moderate or more severe stages of glaucoma patients, time

164   interval between two visits became shorter. Untreated patients were recommended for an annual

165   check-up.

166   For a patient whose IOP measured during the last clinical visit was "on target", the next visit was timed

167   based on Table A6 below. If "off target", the length of time interval remained unchanged compared

168   with the last interval. For example, if an (treated) OHT patient's first visit occurred 3 months ago, and

169   the IOP was considered "on target", the next clinical visit would be 6 months after the first visit; if IOP

170   was "off target", the next clinical visit would still be 3 months.

Table A6: frequency of optometrists or ophthalmologist visits by treatment (in months)

Visit number	Monitoring intervals (treated patients)	Monitoring intervals (untreated patients)
OHT patients		
1	3	12
2	6	12
3 or more	12	12
OAG patients (mild glaucoma)		
1	3	
2	6	
3 or more	12	
OAG patients (moderate or severe glaucoma)		
1	1	
2	3	
3 or more	6	

171

172   ## 6. The unit cost and utility values

173   The unit cost for a visit to the NHS ophthalmology services was obtained from the NHS reference cost.

174   Following Burr et al. (2012),[1] this unit cost was assumed to include the IOP test only, whilst the unit

175   cost for both the IOP and VF tests was assumed to be twice the cost of IOP test given the time needed

176   to complete the visit. The unit cost for IOP and VF tests under community optometrist settings was

177   assumed to be equal to an NHS sight test fee.[1] Following the same logic, the fee for the IOP-only test

178   was halved. Medications and surgical treatments were valued using national unit cost sources (Table

179   2). We used the EQ-5D to value quality of life for each disease state in the model (i.e., OHT, mild,

180   moderate, severe glaucoma and visual impairment) based on a valuation study of an OAG population

181   from the UK.[15] Given small differences in visual damage between OHT and mild OAG, the utility scores

182   for these two states were assumed to be the same.[1] We assumed no reductions in quality of life due

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open Ophth

183   to treatment side effects based on the notion that side effects would either be mild for a very short

184   period of time, or would trigger a treatment change.

185   The unit cost for the SLT was extracted from the LiGHT trial, which compared the clinical and economic

186   effectiveness of using SLT as a first-line treatment for OHT and glaucoma patients with traditional

187   eyedrops as first line drugs.[7] The trial has led to a change in NICE guidelines, in which SLT is now

188   recommended as the first-line treatment for newly diagnosed OHT and OAG patients.[16]

189   Supplementary Material A2: model validation and calibration

190   The model has been carefully validated based on the internal (EMRs) dataset used and a number of

191   external data sources, and several calibrations have been made. The validation tasks conducted were:

192   (1) validating glaucoma progression rate and time-to-progression using the results from the EMGT

193   study;[5] (2) validating time-to-conversion using the EMRs and (3) validating the proportion of "on target"

194   patients in each medication using the results from the LiGHT trail.[7]

195   *(1) Task 1: validating progression rate and time-to-progression*

196   The EMGT study is a 6-year trial in which the effects of medication in reducing IOP in early untreated

197   OAG were investigated . The results suggest that the average progression rate for treated patients is

198   −0.03 dB per month (i.e., -0.36dB/year). To compare with this result, we aligned our model with the

199   baseline characteristics of patients in the EMGT study (i.e., baseline IOP=20.6 (SD=4.1) assuming a

200   gamma distribution; baseline MD = -5 (SD=3.7) assuming a gamma distribution; no trabeculotomy is

201   allowed). Our validation results suggested that the average progression rate is -0.27dB/year,

202   significantly lower than the one in the EMGT study.

203   **Relevant calibration conducted**: Given the slower glaucoma progression of the patients in this model

204   compared with the EMGT study, we changed the method to calculate the progression rate by dropping

205   the condition that the annual glaucoma progression rate (i.e., mean deviations) is allowed to be equal

206   to zero when IOP <13 mmHg, originally specified in van Gestel (2012)[6] . The model was rerun and the

207 results showed that the calibrated annual rate of progression is -0.33dB/year, similar to the one in

208 the EMGT study.

209 We further validated the model by comparing the time-to-progression estimates (closely linked to

210 the progression rate) in this model with the findings from a systematic review study in which time of

211 progressing to different stages of glaucoma were calculated from multiple sources.[17] Again, we align

212 the baseline setting of the testing model with the one in the systematic review study (i.e., baseline MD

213 = -4(SD=2) dB per year assuming a gamma distribution for comparing the time-to-progression

214 estimates of the two models from mild to moderate, MD = -6.02(SD=2) dB per year for comparing

215 time-to-progression from moderate to severe, and MD = -12.02(SD=2) dB per year for comparing time-

216 to-progression from severe to visual impairment. All the patients started with mild glaucoma when

217 comparing time-to-progression estimates from mild to glaucoma, and in a similar fashion, started with

218 moderate glaucoma when comparing time-to-progression from moderate to severe and started with

219 severe glaucoma when comparing time-to-progression from severe to visual impairment. The model

220 was run for lifetime). The results presented in Table A7 suggest that the progression in this model is

221 generally slightly slower than those reported in Burr et al. (2007),[17] but the differences are within a

222 acceptable range.

Table A7: Results for validation task 1

	Average progression rate (dB/year) – being calibration	Average progression rate (dB/year) – after calibration	Time-to-progression (mild to moderate)	Time-to-progression (moderate to severe)	Time-to-progression (severe to visual impairment)
EMGT study	-0.36	/	/	/	/
Burr et al. (2007)	-0.27	-0.33	5	14	16
This model	/	/	8	16	19

223

224

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open Ophth

225   (2) Task 2: validating the proportion of "on target" patients in each medication

226   The LiGHT study is a 3-year trial in which the clinical effectiveness of using SLT instead of eyedrops as

227   a first-line treatment for the newly diagnosed OHT and OAG patients was investigated.[7] The HTA report

228   (Table 11 in page 135) showed the proportion of "on-target" patients after first-line and second-line

229   medications, which can be used to verify the results in this study.[7] The first step of validation was

230   aligning our testing model with the baseline characteristics of patients in the LiGHT study (i.e., (a)

231   consistent baseline variables: baseline IOP = 24.4(SD=5); baseline MD = -3(SD=3.6); Baseline age = 62.7

232   (SD=11.6). (b) consistent initial proportion of patients in each state: 29.7% in OHT; 52.3% in mild OAG;

233   12.4% in moderate OAG; 5.6% in severe OAG. (c) all patients were treated at the beginning). The

234   validation results in Table A8 suggested that the proportions in first or second-line treatment at each

235   year were much smaller than those found in the LiGHT study.

236   **Relevant calibration conducted**: An adherence rate of 75% for the OHT patients had been considered

237   initially based on Burr et al. (2012),[1] yet later calibrated to 100% based on the LiGHT trial results. 100%

238   adherence rate was also a reasonable assumption as the distributions of medication effectiveness used

239   in the model already incorporated the low effectiveness because of non-adherence.

240   **Validation results after calibration:**

241   It can be seen from Table A8 that the proportions of patients who stayed on first or second-line drugs

242   after calibration were closer to those from the LiGHT trial. For example, the proportion of on-target

243   patients after first-line medication in the LiGHT trial is 89.6% and 86% in our model assuming a 100%

244   adherence rate. We also observed that the actual proportions in the LiGHT trial dropped faster than

245   those in our model. The gaps may be attributed to the following factors: (a) The distributions of

246   baseline IOP for different glaucomatous stages can be different in the trial, but the authors only

247   reported an overall distribution for the OAG patients; (b) the rules of treatment escalation were

248   different between the trial and this model. For example, the LiGHT trial allowed for re-adjustment of

249   IOP target depending on the control of IOP, which was not specified in this model; (c) the IOP targets

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open Ophth

250   used were different – the targets in the LiGHT were generally more stringent to achieve; (d) the results

251   reported in the LiGHT trial were at eye level instead of patient level. Given all the differences

252   mentioned above, the calibration for this task was only based on the results of first visit and at 12

253   months. However, results of longer time were reported for transparency.

Table A8: Results for validation task 2

	Firstline medication	Second-line or further medication	Source
First visit			
LiGHT trial	89.6%	/	Gazzard et al. (2019)[7]
This model (75% adherence rate)	65%		
This model (100% adherence rate)	86%		
At 12 months			
LiGHT trial	82.2%	13.1%	Gazzard et al. (2019)[7]
This model (75% adherence rate)	72%	25%	
This model (100% adherence rate)	87%	10%	
At 24 months			
LiGHT trial	71.5%	20.4%	Gazzard et al. (2019)[7]
This model (75% adherence rate)	69%	26.5%	
This model (100% adherence rate)	83%	13%	
At 36 months			
LiGHT trial	64.6%	25.6%	Gazzard et al. (2019)[7]
This model (75% adherence rate)	66%	27.5%	
This model (100% adherence rate)	79%	13.2%	
At 72 months			
LiGHT trial	42.6%	27.6%	Gazzard et al. (2023)[18]
This model (75% adherence rate)	56%	33%	
This model (100% adherence rate)	67%	19%	

254

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open Ophth

255   (3) Task 3: validating time-to-conversion

256   Using the original time-to-conversion equation from van Gestel (2012)[6] resulted in a 5-year conversion

257   rate of 10.9%, which differed from the observed conversion rate (i.e., 16.9%) from the EMRs sample

258   (i.e., the individual sampling dataset we used in this study), suggesting an overall higher risk profile of

259   this sample compared with the OHTS dataset referenced by van Gestel (2012).[6]

260   **Relevant calibration conducted**: In the calculation of time-to-conversion, hazard ratio for the

261   referenced population was increased from 0.02 to 0.03, proportional to the higher risk found in the

262   EMR sample vs the rate found in van Gestel (2012)'s study, to reflect the higher risk of the cohort

263   used in the model.

264   **Validation results after calibration:**

265   The estimated conversion rate after calibration was 15.3%, which was closer to the observed

266   conversion rate of the EMRs sample.

267   Supplementary Material A3: sensitivity analyses

268   (1) One-way sensitivity analysis

269   A number of parameter inputs were tested using one-way sensitivity analysis: (a) the threshold of

270   treatment decision regarding the RP strategy; (b) medication and monitoring costs; (c) adherence rate

271   to medication. We expect that a higher risk threshold for the RP strategy may change the CE results,

272   Therefore, we varied the value from 6% (base case) to 20%. Higher medication or monitoring cost

273   could increase the difference of total cost between the RP and SC strategies, which may change the CE

274   results. As the unit costs of the pharmaceutical brands used in the base-case analysis were already the

275   highest NHS indicative prices, we increased the unit costs of PGA and PGA&BB from +0% (base case)

276   to 50%. Similarly, we increased the unit costs of primary care and secondary care tests (IOP only and

277   full tests) by up to 50%, as no alternative source of unit costs can be used. Adherence rate can affect

278   the proportion of on-target IOPs, and subsequently affect the QALYs results. We decreased the

279   adherence rate from 100% (base case) to 75% (used in Burr et al. (2012)). The results of the one-way

280   sensitivity analysis can be found in Table A9.

Table A9: one-way sensitivity analysis results

Variable value	Strategy	Cost	Inc. cost	Eff	Inc. eff	ICER
Risk threshold						
0.06 (base case)	SC	£4,659		10.9006	0.0000	
0.06 (base case)	RP	£4,931	£272	10.9231	0.0225	£12,100
0.08	SC	£4,659		10.9006	0.0000	
0.08	RP	£4,918	£259	10.9211	0.0205	£12,632
0.1	SC	£4,659		10.9006	0.0000	
0.1	RP	£4,889	£230	10.9156	0.0150	£15,342
0.12	SC	£4,659		10.9006	0.0000	
0.12	RP	£4,838	£179	10.9088	0.0082	£21,896
0.14	SC	£4,659		10.9006	0.0000	
0.14	RP	£4,793	£134	10.9003	-0.0003	-£480,706
0.16	SC	£4,659		10.9006	0.0000	
0.16	RP	£4,747	£88	10.8913	-0.0092	-£9,483
0.18	SC	£4,659		10.9006	0.0000	
0.18	RP	£4,695	£36	10.8835	-0.0171	-£2,117
0.2	RP	£4,649		10.8766	0.0000	
0.2	SC	£4,659	£10	10.9006	0.0240	£414
Adherence						
0.75	SC	£4,851		10.8964	0.0000	
0.75	RP	£5,211	£360	10.9179	0.0215	£16,729
0.8	SC	£4,826		10.8970	0.0000	
0.8	RP	£5,159	£333	10.9187	0.0217	£15,348
0.85	SC	£4,773		10.8982	0.0000	
0.85	RP	£5,087	£314	10.9201	0.0219	£14,330
0.9	SC	£4,725		10.8989	0.0000	
0.9	RP	£5,027	£301	10.9210	0.0220	£13,673
0.95	SC	£4,686		10.8998	0.0000	
0.95	RP	£4,979	£292	10.9220	0.0222	£13,159
1 (base case)	SC	£4,659		10.9006	0.0000	
1 (base case)	RP	£4,931	£272	10.9231	0.0225	£12,100
Cost of PGA						
144.04 (base case)	SC	£4,659		10.9006	0.0000	
144.04 (base case)	RP	£4,931	£272	10.9231	0.0225	£12,100
158.444 (+ 10%)	SC	£4,728		10.9006	0.0000	
158.444 (+ 10%)	RP	£5,027	£299	10.9231	0.0225	£13,296
172.848 (+ 20%)	SC	£4,796		10.9006	0.0000	
172.848 (+ 20%)	RP	£5,123	£326	10.9231	0.0225	£14,491
187.252 (+ 30%)	SC	£4,865		10.9006	0.0000	

281

Table A9: continued

187.252 (+ 30%)	RP	£5,218	£353	10.9231	0.0225	£15,686
201.656 (+ 40%)	SC	£4,934		10.9006	0.0000	
201.656 (+ 40%)	RP	£5,314	£380	10.9231	0.0225	£16,881
216.06 (+ 50%)	SC	£5,002		10.9006	0.0000	
216.06 (+ 50%)	RP	£5,409	£407	10.9231	0.0225	£18,076

Cost of PGA and BB

165.27 (base case)	SC	£4,659		10.9006	0.0000	
165.27 (base case)	RP	£4,931	£272	10.9231	0.0225	£12,100
181.797 (+ 10%)	SC	£4,703		10.9006	0.0000	
181.797 (+ 10%)	RP	£4,992	£288	10.9231	0.0225	£12,793
198.324 (+ 20%)	SC	£4,748		10.9006	0.0000	
198.324 (+ 20%)	RP	£5,052	£304	10.9231	0.0225	£13,485
214.851 (+ 30%)	SC	£4,792		10.9006	0.0000	
214.851 (+ 30%)	RP	£5,112	£319	10.9231	0.0225	£14,177
231.378 (+ 40%)	SC	£4,837		10.9006	0.0000	
231.378 (+ 40%)	RP	£5,172	£335	10.9231	0.0225	£14,869
247.905 (+ 50%)	SC	£4,881		10.9006	0.0000	
247.905 (+ 50%)	RP	£5,232	£350	10.9231	0.0225	£15,561

Cost of secondary care full test

294 (base case)	SC	£4,659		10.9006	0.0000	
294 (base case)	RP	£4,931	£272	10.9231	0.0225	£12,100
323.4 (+ 10%)	SC	£4,937		10.9006	0.0000	
323.4 (+ 10%)	RP	£5,191	£253	10.9231	0.0225	£11,252
352.8 (+ 20%)	SC	£5,216		10.9006	0.0000	
352.8 (+ 20%)	RP	£5,450	£234	10.9231	0.0225	£10,404
382.2 (+ 30%)	SC	£5,494		10.9006	0.0000	
382.2 (+ 30%)	RP	£5,709	£215	10.9231	0.0225	£9,555
411.6 (+ 40%)	SC	£5,772		10.9006	0.0000	
411.6 (+ 40%)	RP	£5,968	£196	10.9231	0.0225	£8,707
441 (+ 50%)	SC	£6,051		10.9006	0.0000	
441 (+ 50%)	RP	£6,228	£177	10.9231	0.0225	£7,858

Cost of secondary care IOP-only test

147 (base case)	SC	£4,659		10.9006	0.0000	
147 (base case)	RP	£4,931	£272	10.9231	0.0225	£12,100
161.7 (+ 10%)	SC	£4,679		10.9006	0.0000	
161.7 (+ 10%)	RP	£4,949	£271	10.9231	0.0225	£12,014
176.4 (+ 20%)	SC	£4,699		10.9006	0.0000	
176.4 (+ 20%)	RP	£4,967	£269	10.9231	0.0225	£11,928
191.1 (+ 30%)	SC	£4,718		10.9006	0.0000	
191.1 (+ 30%)	RP	£4,985	£267	10.9231	0.0225	£11,842
205.8 (+ 40%)	SC	£4,738		10.9006	0.0000	
205.8 (+ 40%)	RP	£5,003	£265	10.9231	0.0225	£11,756
220.5 (+ 50%)	SC	£4,758		10.9006	0.0000	

282

Table A9: continued

220.5 (+ 50%)	RP	£5,021	£263	10.9231	0.0225	£11,670
Cost of primary care full test						
22.26 (base case)	SC	£4,659		10.9006	0.0000	
22.26 (base case)	RP	£4,931	£272	10.9231	0.0225	£12,100
24.486 (+ 10%)	SC	£4,685		10.9006	0.0000	
24.486 (+ 10%)	RP	£4,962	£277	10.9231	0.0225	£12,308
26.712 (+ 20%)	SC	£4,711		10.9006	0.0000	
26.712 (+ 20%)	RP	£4,992	£282	10.9231	0.0225	£12,515
28.938 (+ 30%)	SC	£4,736		10.9006	0.0000	
28.938 (+ 30%)	RP	£5,023	£286	10.9231	0.0225	£12,722
31.164 (+ 40%)	SC	£4,762		10.9006	0.0000	
31.164 (+ 40%)	RP	£5,053	£291	10.9231	0.0225	£12,930
33.39 (+ 50%)	SC	£4,788		10.9006	0.0000	
33.39 (+ 50%)	RP	£5,084	£296	10.9231	0.0225	£13,137
Cost of primary care IOP-only test						
11.13 (base case)	SC	£4,659		10.9006	0.0000	
11.13 (base case)	RP	£4,931	£272	10.9231	0.0225	£12,100
12.243 (+ 10%)	SC	£4,659		10.9006	0.0000	
12.243 (+ 10%)	RP	£4,932	£273	10.9231	0.0225	£12,104
13.356 (+ 20%)	SC	£4,660		10.9006	0.0000	
13.356 (+ 20%)	RP	£4,932	£273	10.9231	0.0225	£12,107
14.469 (+ 30%)	SC	£4,660		10.9006	0.0000	
14.469 (+ 30%)	RP	£4,933	£273	10.9231	0.0225	£12,110
15.582 (+ 40%)	SC	£4,660		10.9006	0.0000	
15.582 (+ 40%)	RP	£4,933	£273	10.9231	0.0225	£12,114
16.695 (+ 50%)	SC	£4,661		10.9006	0.0000	
16.695 (+ 50%)	RP	£4,934	£273	10.9231	0.0225	£12,117

283

284   (2) probabilistic sensitivity analysis

285   A number of distributions were generated to describe the second-order uncertainty around the mean

286   parameters for the utility, costs and treatment effectiveness. These distributions were then used in the

287   probabilistic sensitivity analysis. The parameter inputs are presented in Table A10.

288

Table A10: Parameters and sources for probabilistic sensitivity analysis

	Parameter	Distribution	Data source
Treatment effectiveness			
PGAs (Latanoprost)	Mean: 29.5% (base case) SD: 1%	Beta	SD Based on the 95% confidence interval in Valk et al. (2005)[12]
PGAs & BB (Latanoprost & Timolol) as second-line treatment (additional effectiveness compared with Latanoprost)	Mean: 14.1% (base case) SD: 3%	Beta	SD Based on the 95% confidence interval in Webers et al. (2008)[13]
SLT (additional effectiveness compared with PGAs)	Mean: 0.312 (base case) SD: 0.015	Beta	SD Based on the 95% confidence interval in Chi et al. (2020)[8]
Costs for treatments			
Latanoprost	Min=-10% Likeliest =mean (base case) Max=+10%	Triangular	Assumption
Latanoprost &Timolol	Min=-10% Likeliest =mean (base case) Max=+10%	Triangular	Assumption
SLT	From £96 to £151	Uniform distribution	LiGHT study (Gazzard et al, 2019)[7]
Trabeculotomy	Mean=£1,706 SD=£1,302	Empirical distribution from all types of cares (e.g., elective, non-elective)	NHS reference costs (2021-2022); Glaucoma surgical procedures (HRGs code: BZ92B)
Cost for monitoring			
The assumption between the price of IOP-only test and full test	Mean: 2 (times) SD: 0.5	Normal distribution	Assumption

289

Table A10: continued

Utility

|			
Utility for mild OAG	Mean=0.8015 (base case) SD=0.01	Beta	Burr, Kilonzo, et al. (2007)[15]
Utility for moderate OAG	Mean=0.7471 (base case) SD=0.01	Beta	Burr, Kilonzo, et al. (2007)[15]
Utility for severe OAG	Mean=0.7133 (base case) SD=0.01	Beta	Burr, Kilonzo, et al. (2007)[15]
Utility for visual impairment	Utility for severe OAG*multiplier distribution (u= -0.31029; σ= 0.16631)	Lognormal (multiplier distribution)	Burr, Mowatt, Hernández, et al. (2007)[19]

290
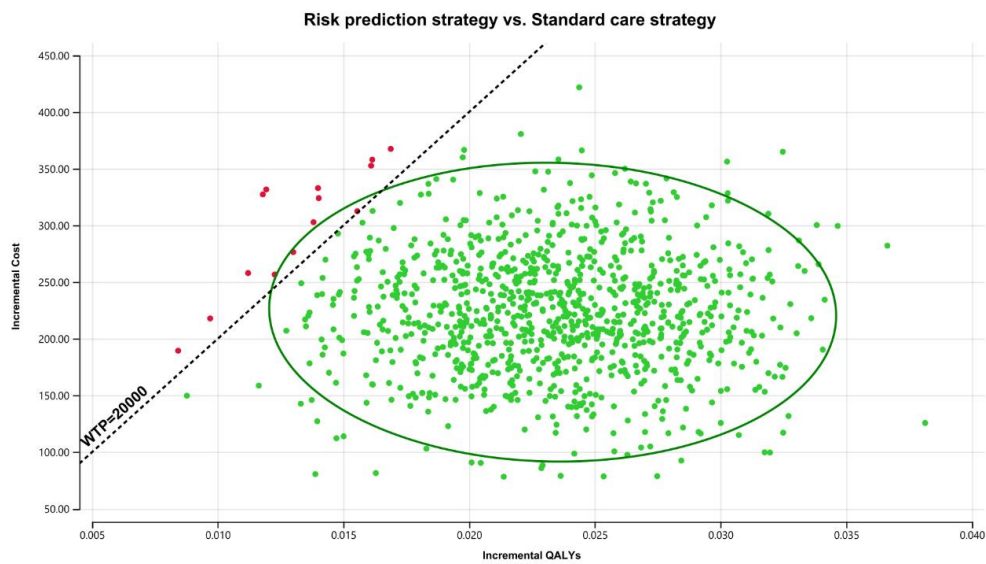
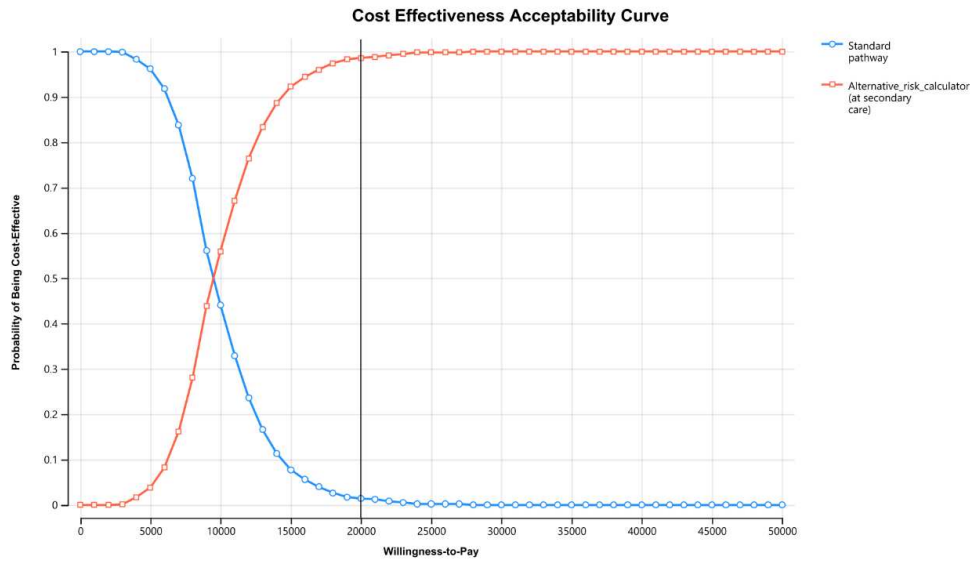**Figure A2**: Cost-effectiveness Scatterplots

291

Figure A3: Cost Effectiveness Acceptability Curve

292

293

References

294

295 1. Burr JM, Botello-Pinzon P, Takwoingi Y, et al. Surveillance for ocular hypertension: an evidence
296   synthesis and economic evaluation. *Health Technol Assess*. 2012;16(29):1-266.
297   doi:10.3310/HTA16290

298 2. Gordon MO, Torri V, Miglior S, et al. Validated prediction model for the development of
299   primary open-angle glaucoma in individuals with ocular hypertension. *Ophthalmology*.
300   2007;114(1):10-19.e2. doi:10.1016/J.OPHTHA.2006.08.031

301 3. Kass MA, Gordon MO, Gao F, et al. Delaying treatment of ocular hypertension: the ocular
302   hypertension treatment study. *Arch Ophthalmol*. 2010;128(3):276-287.
303   doi:10.1001/ARCHOPHTHALMOL.2010.20

304 4. Van Gestel A, Severens JL, Webers CAB, Beckers HJM, Jansonius NM, Schouten JSAG.
305   Modeling complex treatment strategies: construction and validation of a discrete event
306   simulation model for glaucoma. *Value Health*. 2010;13(4):358-367. doi:10.1111/J.1524-
307   4733.2009.00678.X

308 5. Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M. Reduction of Intraocular
309   Pressure and Glaucoma Progression: Results From the Early Manifest Glaucoma Trial. *Archives
310   of Ophthalmology*. 2002;120(10):1268-1279. doi:10.1001/ARCHOPHT.120.10.1268

311 6. Gestel A van. Glaucoma management : economic evaluations based on a patient level
312   simulation model. Published online January 1, 2012. doi:10.26481/DIS.20121005AG

313 7. Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. Selective laser trabeculoplasty versus
314   drops for newly diagnosed ocular hypertension and glaucoma: the LiGHT RCT. *Health Technol
315   Assess (Rockv)*. 2019;23(31):1-101. doi:10.3310/HTA23310

316 8. Chi SC, Kang YN, Hwang DK, Liu CJL. Selective laser trabeculoplasty versus medication for
317   open-angle glaucoma: systematic review and meta-analysis of randomised clinical trials. *Br J
318   Ophthalmol*. 2020;104(11):1500-1507. doi:10.1136/BJOPHTHALMOL-2019-315613

319 9. Landers J, Martin K, Sarkies N, Bourne R, Watson P. A twenty-year follow-up study of
320   trabeculectomy: risk factors and outcomes. *Ophthalmology*. 2012;119(4):694-702.
321   doi:10.1016/J.OPHTHA.2011.09.043

322 10. Kirwan JF, Lockwood AJ, Shah P, et al. Trabeculectomy in the 21st century: a multicenter
323   analysis. *Ophthalmology*. 2013;120(12):2532-2539. doi:10.1016/J.OPHTHA.2013.07.049

324 11. Crabb DP, Russell RA, Malik R, et al. Frequency of visual field testing when monitoring patients
325   newly diagnosed with glaucoma: mixed methods and modelling. *Health Services and Delivery
326   Research*. 2014;2(27):1-102. doi:10.3310/HSDR02270

327 12. Van Der Valk R, Webers CAB, Schouten JSAG, Zeegers MP, Hendrikse F, Prins MH. Intraocular
328   pressure-lowering effects of all commonly used glaucoma drugs: a meta-analysis of
329   randomized clinical trials. *Ophthalmology*. 2005;112(7):1177-1185.
330   doi:10.1016/J.OPHTHA.2005.01.042

331 13. Webers CAB, Beckers HJM, Nuijts RMMA, Schouten JSAG. Pharmacological management of
332   primary open-angle glaucoma: second-line options and beyond. *Drugs Aging*. 2008;25(9):729-
333   759. doi:10.2165/00002512-200825090-00002

334 14. Azuara-Blanco A, Burr J, Thomas R, Maclennan G, McPherson S. The accuracy of accredited
335   glaucoma optometrists in the diagnosis and treatment recommendation for glaucoma. *Br J*
336   *Ophthalmol*. 2007;91(12):1639-1643. doi:10.1136/BJO.2007.119628

337 15. Burr JM, Kilonzo M, Vale L, Ryan M. Developing a preference-based Glaucoma Utility Index
338   using a discrete choice experiment. *Optom Vis Sci*. 2007;84(8):797-808.
339   doi:10.1097/OPX.0B013E3181339F30

340 16. National Institute for Health and Care Excellence. NICE: Guidance on Glaucoma: Diagnosis and
341   Management of Chronic Open Angle Glaucoma and Ocular Hypertension.
342   https://www.nice.org.uk/guidance/NG81 (accessed 20 April 2022).

343 17. Burr JM, Mowatt G, Hernández R, et al. The clinical effectiveness and cost-effectiveness of
344   screening for open angle glaucoma: a systematic review and economic evaluation HTA Health
345   Technology Assessment NHS R&D HTA Programme www.hta.ac.uk. *Health Technol Assess*
346   *(Rockv)*. 2007;11(41). http://www.hta.ac.uk

347 18. Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. Laser in Glaucoma and Ocular
348   Hypertension (LiGHT) Trial: Six-Year Results of Primary Selective Laser Trabeculoplasty versus
349   Eye Drops for the Treatment of Glaucoma and Ocular Hypertension. *Ophthalmology*.
350   2023;130(2):139-151. doi:10.1016/J.OPHTHA.2022.09.009

351 19. Burr JM, Mowatt G, Hernández R, et al. The clinical effectiveness and cost-effectiveness of
352   screening for open angle glaucoma: a systematic review and economic evaluation. *Health*
353   *Technol Assess*. 2007;11(41). doi:10.3310/HTA11410

354

355