Non-contact tests for the diagnosis of Angle Closure glaucoma: an economic evaluation protocol

Introduction

Angle closure glaucoma (ACG) is responsible for approximately 1 in 6 glaucoma cases in the UK(1). Risk of primary angle closure glaucoma (PACG) is higher among females, the elderly and the farsighted, and more prevalent among Asians(2).

PACG diagnosis requires the anterior chamber angles to be carefully examined to identify angle closure. Gonioscopy is the gold standard technique to do this(3). However, it has several drawbacks, such as the need for a high level of competence from the practitioner that often requires it to be performed in a hospital setting, patient cooperation and eye contact, moreover it has been shown to exhibit only fair repeatability(4). Therefore, there is a need for alternative mechanisms and/or use of combination of screening tools to improve detection rates of angle closure. A computerised imaging technique called anterior segment optical coherence tomography (AS-OCT) produces optical cross-sectional images of ocular structures. Another non-contact technique is Limbal anterior chamber depth (LACD). Both may serve as alternative methods for the identification of suspected PACG for further investigation.

This paper describes the statistical and health economic analysis plans for a study - Technologies for the Diagnosis of Angle Closure glaucoma (ACE)(5). The primary aim of the study is to determine the sensitivity and specificity of AS-OCT and LACD to detect angle-closure compared with the reference standard of gonioscopy (by an ophthalmologist with glaucoma expertise). The secondary aims of the study are: to determine positive predictive values, negative predictive values, positive and negative likelihood ratios of AS-OCT and LACD to detect angle-closure compared with the reference standard of gonioscopy; to determine the concordance of AS-OCT and LACD with the reference standard of gonioscopy; to explore the diagnostic accuracy of AS-OCT and LACD compared with the reference standard of gonioscopy by ethnicity, and gender and healthcare profession of interpreter (for AS-

OCTs); to explore different sensitivity and specificity cut offs of LACD and AS-OCT compared with the reference standard of gonioscopy, to explore combining LACD and AS-OCT compared with the reference standard of gonioscopy and; to evaluate cost-effectiveness of AS-OCT and LACD for patients referred to hospital with SAC compared to gonioscopy.

Methods

The details of the ACE study are reported in the protocol registered and published(5).

Study design: In brief, a prospective, cross-sectional, multi-centre, study of people referred to Hospital eye services (HES) with suspected angle closure (SAC) will be conducted.

Sample size: Previous studies have shown that using a cut off to capture 90% sensitivity corresponds to a specificity of around 75% with AS-OCT or with LACD(6, 7). The study will have a 95% probability of detecting the true sensitivity of either test to within ±3.5% (i.e. the confidence interval for the true sensitivity would be approximately 7 percentage points in width), based upon a sensitivity of 90%. The study will also have a 95% probability of detecting the true specificity of either test to within ±5% (i.e., the confidence interval for the true specificity would be 10% in width), assuming a true specificity of 75%. These sample size estimates are conservative because they are based on using only one eye per person, while in practice, information from both eyes will be used. Based these figures the sample size calculation indicates that 600 participants will need to be recruited over 12 months from 12 sites involved in the study across UK.

Data collection: Consecutive eligible patients referred to HES by optometrists with SAC will be approached to take part in the study. Recruited patients referred to HES by optometrists with SAC will be approached and those who consent will undergo testing with the two non-contact technologies as well as gonioscopy (reference standard) on the same day. Non-contact tests will produce an outcome of 'Yes', 'No' or 'indeterminate' for comparison against gonioscopy outcomes: a definitive PACG or no PACG. Patients will undergo AS-OCT and the image will be sent to a reading centre. The LACD will be

performed by a hospital optometrist who does not have specialized glaucoma training or expertise, to match the skills of community optometrists. Each participant will subsequently be examined by a consultant ophthalmologist with glaucoma expertise who will perform a gonioscopy examination to provide the reference standard. Those performing tests will be masked to the outcomes of other tests ASOCT will be performed by photographer, imaging technician. The ASOCT to be interpreted by photographer, imaging technician, optometrist and ophthalmologist. LACD will be performed by an optometrist. Gonioscopy will be performed by an ophthalmologist. Analyses will be based on the individual assumed to read the test in practice.

Exclusion and inclusion criteria: Eligibility will be confirmed by an ophthalmologist and documented on the case report form (CRF). Those recruited will be adults (≥18 years) referred from community optometry to HES with SAC. Patients not willing to participate or unable to give consent will be excluded from the study.

*Ethics approval and consent of the patients***:** Ethics approval of the study taken.

As the study involves one research visit, it is not envisaged that patients will withdraw consent. If they were to withdraw consent once the images had been obtained and/or questionnaires completed, then the images/questionnaires will not be used for the study. A withdrawal of consent will be recorded on CRF.

Economic evaluation

The economic evaluation will adopt an approach in which AS-OCT, LACD, AS-OCT and LACD are compared relative to each other and against gonioscopy in an examination of relative cost-effectiveness for the identification of PACG. A within trial analysis will be undertaken in which results are confined to concordance with gonioscopy and modelled beyond the trial over a typical patient's life time for longer term costs and effects.

Perspective: NHS health

Time horizon: 40 years

Health system costs in the ACE trial:

Time and grade of the staff involved in the delivery of gonioscopy, LACD and AS-OCT will be reported by providers on the CRF. These will be used in a base case within trial analysis to estimate the labour costs associated with performance of tests. The labour costs will be based on self-reported time taken to complete the test and interpret results. Fixed costs associated with equipment costs or overheads will not be examined. Given the longevity of the equipment and its routine use with other users of HES any additional fixed cost or difference in this would be negligible per patient across study arms.

In the base case beyond trial analysis, treatment costs related to health states associated with disease progression (glaucoma related states i.e., mild, moderate, severe) will be estimated using the GATE study (8) with adjustment of costs for inflation based on PSSRU(9). Data collected during the ACE trial in respect of health-related quality of life (HRQoL) at baseline will also be examined to explore if it can be used in sensitivity analysis to estimate differences in HRQoL for SAC, PACG and visual impairment in addition to data from GATE.

Comparator: Three comparison groups will be created based on data collected: (A) comparison of gonioscopy versus LACD only; (B) comparison of gonioscopy versus AS-OCT only; and (C) comparison of gonioscopy versus LACD and AS-OCT concordant responses. We will also compare LACD with AS-OCT. “Success” and “failure” are as detailed in Table 1 for non-contact tests undertaken either in isolation or as a composite test against gonioscopy.

Table1: “Success” and “failure” for non-contact tests undertaken either in isolation or as a composite test w.r.t gonioscopy

Gonioscopy	LACD	LACD/G Result	AS-OCT	AS-OCT/G Result	Composite Result
Positive	Positive/Yes	Success	Positive/Yes	Success	Success
Positive	Negative/No	Fail	Negative/No	Fail	Fail
Positive	Positive/Yes	Success	Negative/No	Fail	Success
Positive	Negative/No	Fail	Positive/Yes	Success	Success
Negative	Negative/No	Success	Negative/No	Success	Success
Negative	Positive/Yes	Fail	Positive/Yes	Fail	Fail
Negative	Negative/No	Success	Positive/Yes	Fail	Fail
Negative	Positive/Yes	Fail	Negative/No	Success	Fail

Indeterminate results from non-contact tests will be recorded and examined to ascertain variations across tests, reading errors by staff and patient compliance or corneal damage issues. A sensitivity analysis will be performed in which the indeterminate results are treated as requiring further investigation with gonioscopy and as an alternative as normal, in a separate analysis The implications for cost-effectiveness of the treatment of indeterminate results will be explored.

Within trial analysis: To determine cost-effectiveness, we will examine within trial results by calculating incremental cost-effectiveness ratios using non-parametric bootstrapping with 1000 samples (to allow for the possible joint distribution of costs and outcomes) to estimate confidence intervals(10). The intervention will assume triage of patients with suspected cases – as determined through non-contact test(s) proceeded to gonioscopy compared with all referrals proceeding directly

to gonioscopy. The exercise will be repeated for each of the non-contact tests separately and when run in combination. We will examine uncertainty around the willingness to pay threshold for a "success" – i.e. an unnecessary referral to HES - using cost-effectiveness acceptability curves. A range of thresholds will be used, informed by the cost charged for tests in the private sector e.g., mean reimbursed price levied by private insurers.

In sensitivity analyses gonioscopy and non-contact test costs will be varied based on dispersion observed within the trial in the time taken to undertake tests. Gonioscopy costs will also be estimated based on a first consultant outpatient episode at HES.

To examine longer term effects, a Markov model of costs and effects across alternate tests over an expected lifetime horizon will be constructed using MS excel. The model will be developed based on that used in a previously published study(8). The model will comprise 6 states – normal vision, suspected glaucoma, glaucoma without blindness, glaucoma-related unilateral blindness, glaucoma-related bilateral blindness and dead. Here the possibility that inaccurate testing may delay identification and permit progression, through delayed treatment will be examined. This model will examine the cost-utility of the non-contact screening tests.

Model parameters: Transition probabilities, mean costs and outcomes associated with the various states will be taken from the literature, supplemented where appropriate from the trial and if necessary expert opinion will be sought (Appendix-1).

Prevalence data and proportion of glaucoma patients by severity of disease will be based on the GATE study(8). Data regarding incidence, progression, and the relative rate of progression of treated and untreated patients will be based on the previous published models of glaucoma management and

surveillance(11). The annual probabilities in different age groups (40-59, 60-75 years) of having an eye test by a community optometrist will be taken from the published literature(8). The mean staff time (minutes) for performing the tests and baseline QoI by age and by glaucoma status will be collected from the ACE study and used to inform parameters of the Markov model related to cost. The proportion of agreements and disagreements of the tests individually as well as in the combination will be taken from the ACE study

The trajectory of Health related quality of life (HRQOL) after "normal vision" will be based on estimates from GATE(8) and from data collected as part of the trial should sufficient numbers be collected. The base-case analysis will use a cohort of 40-year-old patients recruited in the study for a 40-year time horizon. As HRQOL will vary based on age and time spent in a given state, adjustments for these will be made to reflect changes associated with cohort aging over repeated cycles of the model up to termination (death) for all members.

EQ-5D-5L data will be gathered at baseline as an alternative to estimates used in GATE. A mean, reflecting the EQ5D health of those with suspected ACG will be estimated at the baseline. Any differences in EQ5D between those with and without ACG as confirmed by gonioscopy will be used to help populate the model to understand the impact of suspected ACG, and PACG but not yet visually impaired by glaucoma.

A similar approach will be adopted with respect to costs. It is anticipated that cycle length will be 12 months, half-cycle corrections will be applied.

While we anticipate false negatives/positives will be identified quickly without adverse health effects, the model will allow us to examine differential costs over a hypothetical lifetime for the cohort as well as to explore scenarios in which delayed identification does result in adverse effects.

Effectiveness: The proportion of accurate diagnoses across modalities using gonioscopy as reference standard will provide a measure of effect and the differences in these will provide a measure of the incremental effect for the within trial study.

While NICE do not currently recommend use of the EQ-5D-5L preference weights work is currently underway in the UK to estimate new weights(12). Should the new weights be available at the time of the analysis they will be used. Should they not be available we will use a cross-walk to convert 5L descriptions to 3L values before applying the 3L weights(12).

Discounting: Costs and outcomes will be discounted at 3.5% per annum as per current NICE guidance(13).

Uncertainty analysis

A threshold of £20,000-£30,000 per quality adjusted life year (QALY) will be assumed based on NICE methods guide(14). Uncertainty around the threshold willingness to pay for a QALY will be explored using cost-effectiveness acceptability curves. Uncertainty will be explored using a series of sensitivity analyses including a probabilistic sensitivity analysis. Sub-group analyses will examine potential difference in ICERs across groups differentiated by ethnicity (white versus non-white) and age at diagnosis.

Missing data will be handled in a fashion consistent with that set out in the statistical analysis plan and for economic data in a manner consistent with good practice as set out in Faria et al 2014(15).

In the probabilistic sensitivity analysis, a beta distribution will be assigned to prevalence and transition probabilities, a gamma distribution to cost parameters and a log-normal distribution to odds ratios. The LogNormal and Gamma distributions are strictly positive and can deal with cost data. The Beta

distribution is intuitively attractive for the use with utility data because it also has a maximum value of 1.0(16).We will perfom1000 iterations of the bootstrapping procedure to create a sample of bootstrapped means for costs and QALYs with distributions for each. The means and other parametric statistics to be calculated for the bootstrap distribution. The contribution to the uncertainty will be presented in a tornado diagram.

Results will be reported in a fashion consistent with the revised-CHEERS checklist and ISPOR modelling good practice(17).

Statistical analysis

Tables of characteristics of individuals included in the study will be produced. These will include means and standard deviations (or medians and interquartile ranges) for quantitative variables and frequencies and relative frequencies for categorical variables. The time interval between the LACD, AS-OCT and gonioscopy tests will also be calculated and included in this table.

A flow chart of patients through the study will be produced highlighting the numbers undergoing each test and reasons for exclusions. Adverse events in either group will be documented.

A cross tabulation of AS-OCT compared with gonioscopy will be produced. The sensitivity and specificity of AS-OCT compared with gonioscopy will then be calculated using data from both eyes, confidence intervals will be determined using variance inflation factors to account for the lack of independence of each eye in the same person (using the svy function in STATA) [Genders]. This analysis will be repeated for LACD.

A sensitivity analysis will be conducted calculating sensitivity and specificity using a multi-level logistic regression model, with eyes nested within person, and person as a random effect. We will extend this model to include site and operator of the various tests to explore any impact these have on the width

of the confidence intervals for sensitivity and specificity. The diagnostic accuracy of AS-OCT and LACD will be compared by ethnicity, gender and interpreter (optometrists, photographers/imaging technicians and ophthalmologists).

Similar methods will be used to calculate other measures of diagnostic performance (including positive and negative predictive values, and positive and negative likelihood ratios) for LACD and AS-OCT compared with gonioscopy. Concordance between LACD and AS-OCT compared with gonioscopy will be calculated based upon proportion agreement and kappa.

Exploratory analyses will be conducted to investigate the predictive ability of different cut-offs of LACD compared with gonioscopy. The sensitivity and specificity of LACD will be calculated for each cut off of temporal LACD (0%, 5%, 15%, 25%, 40%, 75%, 100%) and nasal LACD (0%, 5%, 15%, 25%, 40%, 75%, 100%) and based upon the worst of the two values. A cut-off will be selected to obtain a sensitivity of 90% and the resulting specificity will be determined, because it is a high sensitivity it is important to capture true positives and even a lower specificity could result in reductions in large numbers of face-to-face examinations. Similar analysis will be repeated for different cut-offs of AS-OCT.

Exploratory analysis will investigate the predictive ability of using both tests. First, we will fit a logistic regression with gonioscopy result as the outcome and including both tests as exploratory variables (LACD and AS-OCT) to calculate a combined risk score based upon the predicted probability from the model. Next, a ROC curve will be plotted of this risk score against the gonioscopy result and a cut-off will be selected to obtain a sensitivity of 90% and the resulting specificity will be determined. Finally, the predictive accuracy of the two tests used in sequence will be determined based upon first using the LACD result and then using the AS-OCT result only in the LACD positive individuals. The final result

based upon this sequential strategy will be compared with gonioscopy as previously. This analysis will be repeated using the AS-OCT cut-off of <10% or the cut-off which is closer to 90% specificity.

A complete case analysis will be conducted as we expect limited missing data and we expect missing tests results to be random, for instance caused by blurred images or camera failure. The reason for missing data will be recorded in the CRF. If necessary, we will conduct a sensitivity analysis using multiple imputation methods to impute missing test results based upon available characteristics of included patients.

References:

1. Azuara-Blanco A, Burr J, Ramsay C, Cooper D, Foster PJ, Friedman DS, et al. Effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE): a randomised controlled trial. The Lancet. 2016;388(10052):1389-97.
2. Wright C, Tawfik MA, Waisbourd M, Katz LJ. Primary angle-closure glaucoma: an update. Acta Ophthalmologica. 2016;94(3):217-25.
3. Riva I, Micheletti E, Oddone F, Bruttini C, Montescani S, De Angelis G, et al. Anterior Chamber Angle Assessment Techniques: A Review. J Clin Med. 2020;9(12).
4. Desmond T, Tran V, Maharaj M, Carnt N, White A. Diagnostic accuracy of AS-OCT vs gonioscopy for detecting angle closure: a systematic review and meta-analysis. Graefes Arch Clin Exp Ophthalmol. 2022;260(1):1-23.
5. Azuara-Blanco A, Lawrenson JG, King AJ, Foster PJ, Virgili G, Guiney M, et al. Technologies for the diagnosis of angle closure glaucoma (ACE): protocol of a prospective, multicentre, cross-sectional diagnostic study. BMJ Open. 2023;13(10):e073975.
6. Baskaran M, Iyer JV, Narayanaswamy AK, He Y, Sakata LM, Wu R, et al. Anterior Segment Imaging Predicts Incident Gonioscopic Angle Closure. Ophthalmology. 2015;122(12):2380-4.
7. Dabasia PL, Edgar DF, Murdoch IE, Lawrenson JG. Noncontact Screening Methods for the Detection of Narrow Anterior Chamber Angles. Investigative Ophthalmology & Visual Science. 2015;56(6):3929-35.
8. Azuara-Blanco A, Banister K, Boachie C, McMeekin P, Gray J, Burr J, et al. Automated imaging technologies for the diagnosis of glaucoma: a comparative diagnostic study for the evaluation of the diagnostic accuracy, performance as triage tests and cost-effectiveness (GATE study). Health Technol Assess. 2016;20(8):1-168.
9. Unit Costs of Health and Social Care | PSSRU 2024 [Available from: https://www.pssru.ac.uk/project-pages/unit-costs/.
10. Briggs AH, Wonderling DE, Mooney CZ. Pulling cost-effectiveness analysis up by its bootstraps: a non-parametric approach to confidence interval estimation. Health Econ. 1997;6(4):327-40.
11. Tang J, Liang Y, O'Neill C, Kee F, Jiang J, Congdon N. Cost-effectiveness and cost-utility of population-based glaucoma screening in China: a decision-analytic Markov model. Lancet Glob Health. 2019;7(7):e968-e78.
12. Nicecomms. Position statement on use of the EQ-5D-5L value set for England (updated October 2019) | Technology appraisal guidance | NICE guidance | Our programmes | What we do | About | NICE. CorporatePage. 2018 2018-11-26.

13. Economic evaluation | NICE health technology evaluations: the manual | Guidance | NICE. 2024.
14. NICE. NICE health technology evaluations:the manual 2023.
15. Faria R, Gomes M, Epstein D, White IR. A guide to handling missing data in cost-effectiveness analysis conducted within randomised controlled trials. Pharmacoeconomics. 2014;32(12):1157-70.
16. Edlin R, McCabe C, Hulme C, Hall P, Wright J. Probability Distributions for Cost and Utility Parameters. In: Edlin R, McCabe C, Hulme C, Hall P, Wright J, editors. Cost Effectiveness Modelling for Health Technology Assessment: A Practical Course. Cham: Springer International Publishing; 2015. p. 105-18.
17. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. Value Health. 2022;25(1):10-31.

Appendix- 1

A. Input parameters for the model

Table 1: Costs (£) associated with current practice of gonioscopy to detect angle-closure by an ophthalmologist.

Name	**Description**	**Value (£)**	**Source**
hc_OPHGON	Ophthalmologist led gonioscopy		Time from CRF and NHS grade salary
hc_FOPD	Ophthalmology first outpatient appointment	166.64	NHS Reference Cost (HRG WF01B)

* cost per use estimate

Table 2: Costs (£) associated with LACD and ASOCT to detect angle-closure by optometrist, imaging technician and ophthalmologist.

Name	**Description**	**Value (£)**	**Source**
hc_OPTLACD	Optometrist led LACD		Time from CRF and NHS grade salary
hc_OPTASOCT	Optometrist led ASOCT		Time from CRF and NHS grade salary
hc_OPHASOCT	Ophthalmologist led ASOCT		Time from CRF and NHS grade salary
hc_TECHASOCT	Trained photographer/imaging technician led ASOCT		Time from CRF and NHS grade salary
Hc_nurse	Additional staff/nurse performing or assisting LACD/ASOCT		Time from CRF and NHS grade salary

Table 3: Annual treatment costs* (£) associated with various stages of Glaucoma

Name	Description	Value ($)	Standard Error	Source
hc_GMI	Annual healthcare cost _Glaucoma mild treatment			
hc_GMO	Annual healthcare cost – Glaucoma moderate treatment			
hc_GS	Annual healthcare cost - Glaucoma severe treatment			
hc_SI	Annual healthcare cost - Sight impaired			
hc_ATRISK	Annual healthcare cost - At risk of glaucoma state- Multiprofessional follow-up ophthalmology outpatient appointment			

****Cost from GATE study will be considered and inflator based on PSSRU*** . https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2018/

Table 4: Utility weights for the model

Name	Description	Value	Standard Error	Source
u_N	Annual utility – Normal	1		Assumption
u_GMI	Annual utility – mild glaucoma			
u_ GMO	Annual utility – Moderate glaucoma			
u_GS	Annual utility -Severe glaucoma			
u_SI	Annual utility – Sight impaired			
u_ATRISK	Annual utility – At risk of glaucoma			
u_Dead	Annual utility - Dead			

Table 5: Sensitivity and specificity values of the Gonioscopy, LACD and ASOCT*

Name	Description	Value	Standard Error	Source
sen_LACD				
spec_LACD				
sen_ASOCT				

spec_ASOCT				

* Baskaran M, Iyer JV, Narayanaswamy AK, He Y, Sakata LM, Wu R, et al. Anterior Segment Imaging Predicts Incident Gonioscopic Angle Closure. Ophthalmology. 2015;122(12):2380-4
Dabasia PL, Edgar DF, Murdoch IE, Lawrenson JG. Noncontact Screening Methods for the Detection of Narrow Anterior Chamber Angles. Investigative Ophthalmology & Visual Science. 2015;56(6):3929-35.

Table 6: Prevalence and progression probabilities

Name	**Description**	**Source**
Age	Cohort age(years)	Base case assumption
Prev_glau	Prevalence of Angle closure glaucoma	ACE trial ?/ GATE
Prop_norm	Proportion of normal	ACE trial ?/GATE
Prop_atrisk	Prevalence of 'at risk of glaucoma'	ACE trial?/GATE
Prop_mild	Proportion of mild glaucoma	ACE trial?/GATE
Prop_moder	Propotion of moderate glaucoma	ACE trial?/GATE
Prop_severe	Proportion of severe glaucoma	ACE trial?/GATE
Prog_mild	Progression to mild glaucoma from at risk/suspect	GATE study or experts from the ACE study
Prog_moder	Progression to moderate glaucoma	Burr et al. 2014
Prog_Sever	Progression to severe glaucoma	Burr et al. 2014
Prog_impai	Progression to sight impaired	Burr et al. 2014
Reduc_treat	Reduction on risk of progression from any medical treatment of glaucoma	Burr et al. 2014
Mortality	Mortality	Life tables
Incid_40 **Incid_50** **Incid_60**	Incidence of glaucoma 40 year old 50 year old 60 year old	 Burr et al 2007 Burr et al 2007

Incid_70	70 year old	Burr et al 2007
Incid_80	80 year old	Burr et al 2007

B. Dummy tables

Table 1: Healthcare costs of the non-contact tests undertaken either in isolation or as a composite test.

Tests	**Mean time(minutes) (SD)**	**Cost(£) Mean (SD)**	**Mean difference in cost w.r.t reference standard**
LACD* only			
ASOCT only**			
LACD + ASOCT			
Gonioscopy***			

***Time of optometrist*
*****Time for performing test by technician time in addition to time for interpretation of technician/optometrist/ophthalmologist*
*****Time of ophthalmologist *only*
NB: ASOCT performed by photographer, imaging technician. ASOCT interpreted by photographer, imaging technician, optometrist and ophthalmologist.

Table 2: Proportion of success and uncertain/indeterminate w.r.t to gonioscopy in the ACE trial

	LACD 95%CI	**ASOCT 95%CI**	**LACD+ASOCT 95%CI**
Success (S)			
Indeterminate			

Table 3: Incremental cost effectiveness ratios: base case

Intervention	**Proportion success (S)**	**Difference in success (δS)**	**Mean Cost (£)**	**δCost (£)**	**QALYS**	**δQALYS**	**ICER 95%CI (PS)**	**ICER 95%CI (QALYs)**
LACD								
ASOCT								

LACD+OSCT								
Gonioscopy								

Table 4: Incremental cost effectiveness ratios for an increase to the unit costs of the non contact tests based on upper bound of confidence intervals

Intervention	**Proportion success (S)**	**Mean Cost (£)**	**δCost (£)**	**QALYS**	**δQALYS**	**ICER 95%CI (PS)**	**ICER 95%CI (QALYS)**
Upper bound 95%CI							
LACD							
ASOCT							
LACD+OSCT							
Gonioscopy							
Lower bound 95%CI							
LACD							
ASOCT							
LACD+OSCT							
Gonioscopy							

Table 5: Incremental cost effectiveness ratios for changes in the age of the suspected angle closure (SAC) at referral to hospital eye services

Start age (years)	**Test**	**Proportion Success (PS)**	**Diff PS 95%CI**	**Mean cost(£)**	**δ Cost(£)**	**QALYs**	**δQALYS**	**ICER 95%CI (PS)**	**ICER 95%CI (QALYs)**
40	LACD								
	ASOCT								
	LACD+AOSCT								
	Gonioscopy								
50	LACD								
	ASOCT								
	LACD+OSCT								
	Gonioscopy								
60	LACD								
	ASOCT								

	LACD+OSCT								
	Gonioscopy								
70	LACD								
	ASOCT								
	LACD+OSCT								
	Gonioscopy								

Table6: Incremental cost effectiveness ratios for ethnicity of the suspected angle closure (SAC) at referral to hospital eye among whites

Ethnicity	**Test**	**Proportion Success (PS)**	**Diff PS 95%CI**	**Mean cost(£)**	**δ Cost(£)**	**QALYs**	**δQALYS**	**ICER 95%CI (PS)**	**ICER 95%CI (QALYs)**
White	LACD								
	ASOCT								
	LACD+AOSCT								
	Gonioscopy								
Non-white	LACD								
	ASOCT								
	LACD+OSCT								
	Gonioscopy								

Table 7: Incremental cost effectiveness ratios for treating mild , moderate, severe glaucoma patients

Intervention	**Cost(£)**			**QALYs**			**ICER,95%CI**		
	Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe
LACD									
ASOCT									
LACD+OSCT									
Gonioscopy									

Table 8: Incremental cost effectiveness ratios for changes in sensitivity of ophthalmologists

Sensitivity	Test	**Proportion success (S)**	**Diff PS 95%CI**	**Mean cost(£)**	**δ Cost (£)**	**QALYs**	**δQALYS**	**ICER 95%CI (PS)**	**ICER 95%CI (QALYs)**
Upper	LACD								
	ASOCT								
	LACD+OSCT								
	Gonioscopy								
Point estimate	LACD								
	ASOCT								
	LACD+OSCT								
	Gonioscopy								
Lower	LACD								
	ASOCT								
	LACD+OSCT								
	Gonioscopy								

Table 9: Incremental cost effectiveness ratios of varying the prevalence in literature for Angle Closure glaucoma and 'suspected angle closure'(SAC) with the referred cohort of the trial

Intervention	**Mean cost(£)**	**δ Cost(£)**	**QALYs**	**δQALYS**	**ICER 95%CI**
LACD					
ASOCT					
LACD+OSCT					
Gonioscopy					

Table 10: Incremental cost effectiveness ratios of varying the quality of life of the 'suspected angle closure' (SAC) health state of the referred cohort w.r.t to Gate study

Intervention	Mean cost(£)	δ Cost(£)	QALYs	Δ QALYS	ICER 95%CI
LACD					
ASOCT					
LACD+OSCT					
Gonioscopy					

Figures

1. CEAC for different willingness to pay thresholds.
2. Sensitivity analysis around cost and outcomes influenced by wait times.
3. Tornado diagram**:** *Sources of uncertainty* i.e., *time* for gonioscopy, LACD, ASOCT*, Skillset:* Optometrist/ technician for LACD