UK National Screening Committee

Screening for Glaucoma

External review against programme appraisal criteria for the UK National Screening Committee

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The UK National Screening Committee secretariat is hosted by Public Health England.

About the UK National Screening Committee (UK NSC)

The UK NSC advises ministers and the NHS in the 4 UK countries about all aspects of population screening and supports implementation of screening programmes. Conditions are reviewed against evidence review criteria according to the UK NSC's evidence review process.

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Plain English summary

Glaucoma is a condition that can lead to blindness. This document looks at screening adults for one type of glaucoma (known as open angle glaucoma) which is found in 90% of people who have the condition. Older people are more likely to develop open angle glaucoma. This condition also runs in families and is more often found in people of black-African or black-Caribbean origin. Open angle glaucoma starts when one of the drainage channels of the eye becomes blocked, stopping the normal drainage of fluid. Pressure builds in the eye ball damaging the nerve at the back of the eye. Over a long time this nerve damage can cause blindness.

A national screening programme would aim to find people who had open angle glaucoma at an early stage so treatment could be started as soon as possible. In 2015 the UK NSC looked at the evidence for open angle glaucoma screening. At that time there was no agreed screening test that would accurately find people at the early stage of the disease before they developed symptoms. It was also not clear if a screening programme would be better at finding and treating people with open angle glaucoma, compared with people going through usual health care routes when they developed symptoms.

This document is an update of the 2015 UK NSC review. It considers new evidence published between October 2014 and March 2019. Two questions were considered:

- what is the accuracy of screening tests for open angle glaucoma?
- is there good quality evidence that a screening programme will find and treat people with open angle glaucoma better than their usual health care arrangements?

The UK NSC still cannot recommend population screening for open angle glaucoma in adults. There was not enough new evidence to change the conclusions of the previous UK NSC review. These areas are still uncertain:

- there was limited evidence about the accuracy of screening tests for open angle glaucoma
- a range of different tests have been proposed. These tests are difficult to compare with each other and it is not clear which test is the best one
- no high quality evidence was found that a screening programme will find and treat people with open angle glaucoma better than usual health care.

Executive summary

Purpose of the review

This document reviews the evidence on population screening for open angle glaucoma (OAG) in adults.

Background

OAG sometimes known as primary open angle glaucoma (POAG), or chronic open angle glaucoma (COAG), is the most common type of the disease accounting for at least 90% of all glaucoma cases. The condition runs in families and people of black-African or black-Caribbean origin are at an increased risk of developing OAG. Typically it affects both eyes, but there may be some asymmetry with more advanced disease in one eye.

In this type of glaucoma the drainage canal of the eye gradually becomes blocked allowing less fluid to leave the eye, causing an increase of pressure within the eyeball. Over time, the high pressure causes optic nerve damage which can lead to blindness. OAG is asymptomatic with a long latent phase over which time the condition increases in severity. Late diagnosis and advanced visual field loss at the time of diagnosis are among risk factors for progression to blindness. Optic nerve damage typically precedes visual functional impairment and between 25% and 40% of retinal ganglion cells may be lost before visual field loss is detected (via eye examination). The proportion of people who present early with OAG and progress to severe visual loss is not known.

Focus of the review

The aim of a screening programme for OAG would be to identify adults with the disease in order to initiate treatment prior to the condition becoming symptomatic. This review looks for evidence of whether there is a valid, accurate screening test for primary open angle glaucoma and if screening reduces morbidity of the condition compared to usual diagnosis and care.

Recommendation under review

The current UK NSC policy is that systematic population screening for OAG in adults is not recommended. The previous UK NSC external review of screening for OAG was published in 2015. The review concluded that it is not appropriate to implement a national screening programme for OAG as:

- studies assessing tests of structure and function were identified, but the sensitivity and specificity scores reported varied widely and no study reported acceptable sensitivity and specificity for use in general population screening
- various cut-off levels were used in the studies and it is not clear if the optimum cut-off levels for use in screening have been identified for any tests
- no randomised controlled trials assessing whether a screening programme for OAG would be effective in reducing morbidity were identified.

Findings and gaps in the evidence of this review

On the basis of the current evidence available about the 2 key questions important areas of uncertainty remain:

- the volume of evidence reporting results of tests for OAG in a general adult population was limited to 6 relatively small studies
- there was no agreed test, combination of tests or cut-off levels for the tests used for the screening examination
- screening performance statistics varied between studies and were not comparable
- no randomised controlled trials on the effectiveness of screening for OAG to reduce the morbidity of the condition were identified.

Recommendations on screening

On the basis of the current evidence available about the 2 key questions, of whether there is a valid, accurate screening test for OAG and if there are randomised controlled trials to investigate if screening is more effective in reducing morbidity from OAG, a national screening programme cannot be recommended. The current recommendation not to introduce a UK OAG screening programme should be retained.

Limitations

A limitation for this review is the lack of studies that meet all of the inclusion criteria for this review for 1 of the key questions.

This rapid review process was conducted over a condensed period of time (approximately 12 weeks). Searching was limited to 3 bibliographic databases and did not include grey literature sources. The review was guided by a protocol developed a priori. The literature search and first appraisal of search results were undertaken by 1 information scientist, and further appraisal and study selection by 1 reviewer. Any queries at both stages were resolved through discussion with a second reviewer. Studies not available in the English

language, abstracts, poster presentations, case series and case-control studies were not included. Studies that were not published in peer-reviewed journals were not reviewed.

Evidence uncertainties

The key area of uncertainty for OAG screening is agreement about which tests should be used and what the most effective cut-off should be for each of the screening tests carried out during the screening examination. Testing the visual field, measuring intraocular pressure, and examining images of the optic disc for abnormal findings are the 3 elements that comprised a screening examination in all the included prospective studies. Large, good quality prospective studies, using the same tests and cut-off levels that have been shown to produce the best statistical performance would be helpful in reducing gaps in the evidence base.

Introduction and approach

This evidence summary reviews screening for primary open angle glaucoma (OAG) against selected UK National Screening Committee criteria and updates the previous review in 2015[1].

Background

Glaucoma is the term used for a group of eye diseases in which progressive damage to the optic nerve leads, if untreated, to impaired vision and blindness. There are 2 forms of primary glaucoma (i.e. glaucoma that does not result from another eye disease or systemic disease): open angle glaucoma (OAG) and angle closure glaucoma (National Institute for Health and Care Excellence 2017)[2]. This review concerns screening for OAG.

OAG, sometimes known as primary open angle glaucoma (POAG), or chronic open angle glaucoma (COAG), is the most common type of the disease accounting for at least 90% of all glaucoma cases. Usually, the condition runs in families and people of black-African or black-Caribbean origin are at an increased risk of developing OAG. Typically it affects both eyes, but there may be some asymmetry with more advanced disease in one eye (NICE 2017)[2].

In OAG the drainage canal of the eye (called the trabecular meshwork) gradually becomes blocked allowing less fluid to leave the eye, causing an increase of pressure within the eyeball. Over time, the high pressure causes optic nerve damage which can lead to blindness. OAG is asymptomatic with a long latent phase over which time the condition increases in severity. Late diagnosis and advanced visual field loss at the time of diagnosis are among risk factors for progression to blindness (Abu-Hassan et al 2014)[3]. Optic nerve damage typically precedes visual functional impairment and between 25% and 40% of retinal ganglion cells may be lost before visual field loss is detected (via eye examination). The proportion of people who present early with OAG and progress to severe visual loss is not known (DeVience et al, 2018)[4].

The aim of a screening programme for OAG would be to identify adults with the disease in order to initiate treatment prior to the condition becoming symptomatic. This review looks for evidence of whether there is a valid, accurate screening test for glaucoma and if screening is more effective in reducing morbidity from OAG than usual diagnosis and care.

Current policy context and previous reviews

The current UK NSC policy is that systematic population screening for OAG in adults is not recommended. The previous UK NSC external review[1] of screening for OAG was published in 2015. The review concluded that it is not appropriate to implement a national screening programme for OAG as:

- studies assessing tests of structure and function were identified, but the sensitivity and specificity scores reported varied widely and no study reported acceptable sensitivity and specificity for use in general population screening
- various cut-off levels were used in the studies and it is not clear that optimum cut-off levels for use in screening have been identified for any tests
- no randomised controlled trials assessing whether a screening programme for OAG would be effective in reducing morbidity were identified.

In 2017 NICE[2] reviewed the evidence about case finding tools to identify people in the community at increased risk of developing OAG. No recommendation was issued on this. This was because the statistical data comparing the overall accuracy of the tools did not provided enough information to establish a recommendation, also there was no evidence on the cost effectiveness of such tools.

Objectives

The aim of the current review is to update the evidence in 2 key areas identified in the previous review. The key questions addressed in the current review were developed by the UK NSC with input from Solutions for Public Health.

The key questions and the UK NSC criteria that it relates to are presented in Table 1 below.

Table 1. Key questions for the evidence summary, and relationship to UK NSC screening criteria

	Criterion	Key questions	Studies Included
	THE TEST		
4	There should be a simple, safe, precise and validated screening test.	1. What is the diagnostic accuracy of screening tests for open angle glaucoma in adult population?	6
	THE SCREENING PROGRAMME		
11	There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity. Where screening is aimed solely at providing information to allow the person being screened to make an "informed choice" (eg. Down's syndrome, cystic fibrosis carrier screening), there must be evidence from high quality trials that the test accurately measures risk. The information that is provided about the test and its outcome must be of value and readily understood by the individual being screened.	2. Are there any RCTs assessing whether a screening programme for open angle glaucoma is effective in reducing morbidity?	0
13.	The benefit gained by individuals from the screening programme should outweigh any harms, for example from over diagnosis, overtreatment, false positives, false reassurance, uncertain findings and complications.		

Methods

The current review was conducted by Solutions for Public Health (SPH) in keeping with the UK National Screening Committee evidence review process. Database searches were undertaken up to 25th March 2019 to identify studies relevant to the questions detailed in

Table 1.

Eligibility for inclusion in the review

The following review process was followed:

1. Each abstract was reviewed against the inclusion/exclusion criteria by 1 reviewer. Where the applicability of the inclusion criteria was unclear, the article was included at this stage in order to ensure that all potentially relevant studies were captured.
2. Full-text articles required for the full-text review stage were acquired.
3. Each full-text article was reviewed against the inclusion/exclusion criteria by 1 reviewer, who determined whether the article was relevant to 1 or more of the review questions.
4. Any queries at the abstract or full-text stage were resolved through discussion with a second reviewer.
5. The review was quality assured by a second senior reviewer, not involved with the writing of the review in accordance with SPH's quality assurance process.

Eligibility criteria for the questions are presented in Table 2 below.

A total of 2056 references were identified by information scientists. These references were de-duplicated and an SPH reviewer assessed 513 titles and abstracts for appraisal and possible inclusion in the final review.

Overall, 15 studies were identified as possibly relevant during title and abstract sifting and further assessed at full text (see Appendix 2 for study flow).

Appraisal for quality/risk of bias tool

The following tools were used to assess the quality and risk of bias of each study included in the review:

- diagnostic accuracy studies: Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool

Databases/sources searched

A systematic search of 3 databases (Medline, Embase and Cochrane) was conducted to identify studies published up to 25th March 2019 relevant to the questions detailed in Table 2. The search strategy is presented in Appendix 1.

Table 2. Inclusion and exclusion criteria for the key questions

	Inclusion criteria							Exclusion criteria
Key question	**Population**	**Target condition**	**Intervention**	**Reference Standard**	**Comparator**	**Outcome**	**Study type**	
What is the diagnostic accuracy of screening tests for open angle glaucoma in the adult population?	Adult population	Open angle glaucoma	**Tests of Optic Nerve Structure** Heidelberg Retinal Tomography(HRT), Optical Coherence Tomography(OCT), Optic Disc Photography, Retinal Nerve Fiber Layer (RNFL) Photography, Scanning Laser Polarimetry (SLP) **Tests of Optic Nerve Function,** Frequency Doubling Technology (FDT), Goldmann Applanation, Tonometry (GAT) Noncontact Tonometry(NCT), Standard Automated Perimetry (SAP), Any testing tools for open angle glaucoma	Optic disc assessment and standard achromatic white on white perimetry		Measures of predictive validity of screening tests (eg, PPV, NPV, PLR, NLR, sensitivity, specificity)	Studies in randomly assigned or consecutively enrolled populations should be prioritised	Case control studies, case reports, case series, reviews, non-peer reviewed literature Non-English language Studies published before October 2014

Are there any RCTs assessing whether a screening programme for open angle glaucoma is effective in reducing morbidity?	Adult population	Open angle glaucoma	• screening programmes to identify individuals at high risk of OAG; • direct and indirect ophthalmoscopy; • fundus photography or computerized imaging of the posterior pole, optic disc, or retinal nerve (optical coherence tomography with the exception of OCT 1 and OCT 2), retinal tomography, scanning laser polarimetry; • pachymetry (corneal thickness measurement) when used in conjunction with another test to diagnose glaucoma; • perimetry (including short-wavelength, high-pass, motion, flicker perimetry, yellow and blue perimetry); • tonometry (contact and non contact tonometry).		Current diagnostic methods (e.g. NICE guidance), other combination methods or none Any treatment, no treatment or placebo	Chronic OAG eye damage (peripheral vision fade and tunnel vision) loss of vision blindness measurements of visual impairment as defined by included studies	Peer-reviewed evidence derived from the following types of study: Systematic reviews and (network) meta-analyses Randomised controlled trials (RCTs)	Non- English language publications Publications before October 2014

Question level synthesis

Criterion 4

There should be a simple, safe, precise and validated screening test.

Question 1 – What is the diagnostic accuracy of screening tests for open angle glaucoma in adult population?

Testing for OAG involves 3 elements: assessment of structural changes at the optic nerve head, measurement of intraocular pressure (IOP) and functional vision loss by visual field testing. Since most of the visual disability in OAG is related to visual field loss, testing for early visual field loss (i.e. using perimetry) are obvious choices of screening test. However, this does not rule out structural tests from OAG screening. A structural test such as changes to the optic nerve head or increases intraocular pressure might have a better diagnostic performance at the early stage of the condition when only minimal visual field loss has occurred (Burr et al 2007)[5].

This question was addressed by the previous NSC review in 2015[1]. One meta-analysis, one systematic review, 6 further studies assessing functional tests and 2 studies assessing structural tests were included. Generally, small sample sizes and outcomes of OAG tests for structure and function that varied widely in sensitivity and specificity precluded their suitability in general population screening. A further 12 case-control studies assessing tests to detect OAG were not included in the 2015 review as they did not consider performance in a screening population.

Eligibility for inclusion in the review

Population: Adult population.

Intervention:
Tests of Optic Nerve Structure
- Heidelberg Retinal Tomography(HRT),
- Optical Coherence Tomography(OCT),
- Optic Disc Photography,
- Retinal Nerve Fiber Layer (RNFL) Photography,
- Scanning Laser Polarimetry (SLP)

Tests of Optic Nerve Function,
- Frequency Doubling Technology (FDT),

- Goldmann Applanation, Tonometry (GAT),
- Noncontact Tonometry(NCT),
- Standard Automated Perimetry (SAP).
- Any testing tools for open angle glaucoma.

Reference standard: Optic disc assessment (monitors structural change) and standard achromatic white on white perimetry (monitors functional change).

Outcomes: Measures of predictive validity of screening tests (e.g. positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, sensitivity, specificity).

Study design: Studies in randomly assigned or consecutively enrolled populations should be prioritised. Study designs excluded: case-control studies, case reports, case series, reviews, non-peer reviewed literature.

Date and language: English language published since 1st October 2014.

Description of the evidence

Database searches yielded 507 results of which 15 were judged to be relevant to this question following abstract and title review. After review of the full texts, 6 studies met the key question criteria. The reasons for exclusion of the remaining 9 studies were:

- 1 systematic review and meta-analysis identified 45 publications of teleglaucoma screening from around the world but combined all types of measurements and examinations together to determine the accuracy of remote screening rather than a specific screening test (Thomas et al 2014)[6]
- 1 meta-analysis identified 81 small to medium (76-451 eyes) case-control studies and 6 screening studies (Fallon et al 2017)[7]. The case-control studies focussed on diagnosis in a clinical setting and the screening studies were all published prior to 2014.
- 1 systematic review identified 6 publications about screening for glaucoma using monoscopic disc photos of which 4 were published outside of the search dates (1976 to 2007) and 2 published in 2014 were case series (Newman-Casey et al 2014)[8]
- 2 publications were published prior to the specified search date (i.e. October 2014) for key question 1 (Blumberg et al 2014 and Charalel et al 2014) [9,10]
- 2 publications were case-control studies (Springelkamp et al 2014 and Schweitzer et al 2016)[11,12]
- 1 study was evaluating an eye check programme but not assessing the effectiveness of the tests used (Holdsworth et al 2017)[13]

- 1 study was determining costs of screening compared to costs of usual glaucoma detection (Anton et al 2017)[14]

One study was excluded at the initial sifting stage (Chan et al 2017)[15] as it was primarily examining prevalence and reported results for all cause glaucoma rather than OAG. The study is nevertheless an important recent UK publication of glaucoma and is mentioned in the discussion of findings below.

Discussion of findings

A study-level summary of data extracted from each included publication is presented in Appendix 3 'Summary and appraisal of individual studies' Tables 14 to19.

The 6 publications meeting the inclusion criteria reported screening test performance results from studies that invited a population (range n=221-4183) with unknown ocular history to be screened (Hark et al 2019, Song et al 2019, Zhao et al 2017, Boland et al 2016, Dabasia et al 2015, and Wahl et al 2016)[16,17,18,19,20,21]. Of the 6 studies 1 (Boland et al 2016)[19] was a retrospective cohort study and the remaining 5 were prospective cohort studies. Five of the studies targeted screening based on people with a higher risk of developing OAG due to ethnicity, age or family history. All studies used combinations of functional and structural types of screening test and employed a screening algorithm or model to determine who should be referred for a definitive eye examination (the reference standard). The results of the definitive eye examination were typically 'no glaucoma', 'suspected glaucoma' or 'definitive glaucoma'*. Test statistics† were sometimes reported separately for each test (Table 3) and then combined to determine overall screening performance (Table 4).

* People with 'suspected glaucoma' have one or more risk factors that may lead to glaucoma but do not yet have both optic nerve damage and vision loss due to the condition which is the case for people with definitive glaucoma(https://cks.nice.org.uk/glaucoma#!backgroundSub:2).

† Screening test performance statistics include: **sensitivity** — the ability of the test to correctly identify those who do have the condition solely from those who have tested positive by the reference standard; **specificity** — the ability of the test to correctly identify those who do not have the condition solely from those who have tested negative by the reference standard; **positive predictive value(PPV)** the proportion of the people who tested positive for the screening test of all those tested (who may or may not have the condition) who actually did have the condition; **negative predictive value (NPV)** — the proportion of the people who tested negative for the screening test of all those tested (who may or may not have the condition) who did not have the condition; **Positive likelihood ratio (PLR)** — likelihood that a positive test result would be expected in a patient with the condition compared to the likelihood that that same result would be expected in a patient without the condition; **Negative likelihood ratio (NLR)** — likelihood that a negative test result would be expected in a patient without the condition compared to the likelihood that that same result would be expected in a patient with the condition (Trevethan R sensitivity, specificity and predictive values, foundations, pliabilities and pitfalls in research and practice. Frontiers in Public Health 2017, 5;307, https://www.cebm.net/2014/02/likelihood-ratios/).

Functional screening tests

Visual field loss

Visual field loss using perimetry was measured by Frequency Doubling Technology (FDT) in 3 studies (Boland et al 2016, Dabasia et al 2015 and Wahl et al 2016)[19,20,21]. All 3 studies used different cut-off points to determine abnormal FDT findings resulting in referral.

Dabasia et al (2015)[20] calculated the screening test performance of FDT perimetry (with one or more missed locations at a probability[p] <1% level). Screening test performance varied with a sensitivity of 62.1% and specificity of 80.5% for suspected OAG and a sensitivity of 88.5% and specificity of 79.1% for definitive OAG. The other two studies[19,21] did not report FDT perimetry separately form the other tests carried out during the screening examination.

Dabasia (2015)[20] also used a prototype perimetry measure called the Moorfield Motion Displacement Test (MMDT) and used the developers recommended threshold of global probability of true damage (≥3.0). The screening test performance statistics varied somewhat with a reported a sensitivity of 51.7% and specificity of 82.8% for suspected OAG and a sensitivity of 65.4% and specificity of 81.2% for definitive OAG.

Intraocular pressure

Intraocular pressure (IOP) was measured by either non contact tonometry (NCT) (Song et al 2019, Dabasia et al 2015 and Wahl et al 2016)[17,20,21] or rebound tonometry (Hark et al 2019 and Zhao et al 2017)[16,18] in 5 out of 6 of the studies. The cut-off points for referral ranged from >21mmHg to >28mmHg.

Dabasia et al (2015)[20] and Wahl et al (2016)[21] both reported that IOP (>21mmHg) separately. IOP had a low sensitivity of detecting either definitive OAG (26.9%[20] to 61.54%[21]), suspected OAG (44.45%)[21] or combined suspected/definitive OAG (24.1%)[20]. Specificity was much higher with definitive OAG, ranging from 87.9%[20] to 91.57%[21] whilst suspected OAG was 92.68%**Error! Bookmark not defined.** and combined suspected/definitive OAG, was 88.6%[20].

The large(n=8401) UK cohort study examining all cause glaucoma prevalence (Chan et al 2017)[15] reported IOP mmHg in all people with newly diagnosed open angle glaucoma (n=107). In 76% of patients the mean IOP was under the threshold for ocular hypertension (21mmHg) and was not considered an adequate diagnostic measure for glaucoma.

Other studies did not report the screening performance of IOP alone.

Structural screening tests

Abnormalities of the optic nerve head and retina
Methods used to determine structural abnormalities in the back of the eye included non-mydriatic fundus imaging (Hark et al 2019, Song et al 2019, Zhao et al 2017, Boland et al 2016 and Wahl et al 2016)[16,17,18,19,21] and optical coherence tomography(OCT) (Dabasia et al 2015)[20].

These two methods of visualising the back of the eye enabled the following features to be determined: optic disc haemorrhage, excavation of the optic nerve head, the proportion of the optic cup that formed the optic disc (cup-disc ratio), optic nerve rim thickness (at the inferior, superior, nasal and temporal points – the ISNT rule‡ the nerve fibre layer thickness of the retina (RNFL), the ganglion cell complex (GCC) of the retina and asymmetry between the right and left eyes.

Five studies (Hark et al 2019, Song et al 2019, Zhao et al 2017, Boland et al 2016 and Wahl et al 2016)[16,17,18,19,21] reported cup-disc ratio (CDR) but the cut-offs were different in all studies ranging between >0.5 and >0.8. None of the five studies reported non-mydriatic fundus imaging alone as a screening test.

Dabasia et al (2015)[20] used OCT to measure the retinal nerve fibre layer (RNFL) thickness and the ganglion cell complex (GCC) of the retina. None of the measures alone resulted in satisfactory sensitivity as a screening tool to determine suspected or definitive OAG (sensitivity range from 24.1%, to 76.9% and specificity 90.3% to 98.2%).

Visual acuity
Visual acuity was used to screen people in one study (Zhao et al 2017)[18] who were referred for a definitive eye examination at a cut-off of acuity of 20/40 or worse (with glasses). Screening performance of visual acuity alone was not reported.

‡ The ISNT rule is used when evaluating the optic disc rim. Normal eyes show a characteristic configuration for disc rim thickness of Inferior ≥ Superior ≥ Nasal ≥ Temporal), it is widely used for clinical evaluation of the optic nerve head and can differentiate normal from glaucomatous eyes (Harizman et al The ISNT rule and differentiation of normal from glaucomatous eyes Arch Opthalmol 2006:124;1579-1583)

Table 3. Screening test performance for tests reported separately for suspected and definitive OAG

Screening test (cut-offs for referral)	Population	Indication	Sensitivity% (95% CI)	Specificity% (95% CI)	PPV%[§] (95% CI)	NPV% (95% CI)	PLR	NLR	Study
Functional test: Visual field loss									
FDT perimetry (≥1 missed location at p<1% level)	505 community screening participants aged ≥60 London UK Cohort study	Suspect and definitive OAG	62.1 (49.2 to 73.4)	80.5 (76.6 to 84.0)	NR	NR	NR	NR	Dabasia et al 2015[20]
		Definitive OAG	88.5 (71.0 to 96.0)	79.1 (75.2 to 82.5)	NR	NR	NR	NR	
MMDT perimetry (global probability of true damage≥3.0)	505 community screening participants aged ≥60 London UK Cohort study	Suspect and definitive OAG	51.7(39.2 to 64.1)	82.8(79.0 to 86.0)	NR	NR	NR	NR	Dabasia et al 2015[20]
		Definitive OAG	65.4(46.2 to 80.6)	81.2(77.5 to 84.5)	NR	NR	NR	NR	
Functional test: Intraocular pressure									
NCT using ORA – cornea compensated (IOP >21mmHg)	505 community screening participants aged ≥60 London UK Cohort study	Suspect and definitive OAG	24.1(15.0 to 36.5)	88.6(85.3 to 91.2)	NR	NR	NR	NR	Dabasia et al 2015[20]
		Definitive OAG	26.9(13.7 to 46.1)	87.9(84.7 to 90.5)	NR	NR	NR	NR	
Screening model 3: NCT (at least 1 eye IOP >21mmHg)	4183 Evonik employees aged ≥40 Germany Cohort study	Suspect OAG	44.45 (46.08 to 64.45)	92.68 (91.83 to 93.44)	17.04 (13.49 to 21.29)	98.71 (98.30 to 99.03)	7.57	0.48	Wahl et al 2016[21]
		Definitive OAG	61.54 (34.36 to 83.02)	91.57(90.69 to 92.38)	2.23 (1.12 to 4.40)	99.87 (99.68 to 99.95)	7.30	0.42	Wahl et al 2016[21]

[§] PPV was not reported in these papers and could not be calculated as although the overall number of people with a suspected or definitive POAG reference standard diagnosis was reported the number of people who screened positive for a particular test included as part of the screening examination and then who went on to receive a confirmed diagnosis was not reported.

Structural tests: Abnormalities of the optic nerve head and retina									
OCT - GCC – focal loss volume (>99% normal limit for this equipment)	505 community screening participants aged ≥60 London UK Cohort study	Suspect and definitive OAG	46.6(34.2 to 59.2)	91.4(88.4 to 93.7)	NR	NR	NR	NR	Dabasia et al 2015[20]
		Definitive OAG	73.1 (53.9 to 86.3)	90.3(87.3 to 92.6)	NR	NR	NR	NR	
OCT - GCC – global loss volume (>99% normal limit for this equipment)	505 community screening participants aged ≥60 London UK Cohort study	Suspect and definitive OAG	24.1(15.0 to 36.5)	98.2(96.5 to 99.71)	NR	NR	NR	NR	Dabasia et al 2015[20]
		Definitive OAG	46.2 (28.8 to 64.5)	97.9 (96.2 to 98.8)	NR	NR	NR	NR	
OCT - RNFL thickness – inferior quadrant (>99% normal limit for this equipment)	505 community screening participants aged ≥60 London UK Cohort study	Suspect and definitive OAG	46.6(34.3 to 59.2)	96.2(94.0 to 97.6)	NR	NR	NR	NR	Dabasia et al 2015[20]
		Definitive OAG	76.9(57.9 to 89.0)	95.0(92.6 to 96.6)	NR	NR	NR	NR	

OAG-open angle glaucoma, PPV- positive predictive value, NPV – negative predictive value, PLR- positive likelihood ratio, NLR- negative likelihood ratio, FDT – Frequency doubling technology, NR= Not reported, MMDT – Moorfield motion displacement test, NCT – non contact tonometry, ORA – ocular response analyser, IOP- intraocular pressure, OCT – optical coherence tomography, GCC- ganglion cell complex, RNFL- retinal nerve fibre layer

Combined performance of screening tests

All the studies combined the tests used at the screening examination to calculate screening performance statistics (Table 4). No studies combined the same screening tests with the same cut offs and all but one study (Wahl et al 2016[21]) reported only partial screening performance statistics. Wahl et al (2016)[21] reported the most complete set of screening test performance statistics from 4183 employees in a German company. People underwent a screening examination consisting of non-mydriatic fundus imaging combined with FDT perimetry and non-contact tonometry (Table 4). Wahl et al (2016)[21] reported very good screening test performance results for their screening algorithm however the method of producing the algorithm was not independent of the reference standard, compromising the validity of the results. In this study following the screening examination the results were sent to a glaucoma expert for grading (the reference standard) and then an algorithm based on a range of measures** was developed aiming to simulate the decision-making process of the glaucoma expert. The screening result was achieved by applying the resultant algorithm to the dataset.

The combination of tests used for the remaining 5 studies resulted in moderate to poor rates of sensitivity and specificity for suspected glaucoma and combined suspected and definitive glaucoma.

Song et al (2019)[17] and Hark et al (2019)[16] calculated positive predictive value (PPV) from their studies which combined CDR ratio (cut-offs ranged from >0.5 to >0.65), CDR difference between eyes (≥0.2), RNFL defect and IOP (>21mmHg). Song et al (2019) reported a PPV of 25.5% for definitive OAG and 61.4% for suspected OAG whilst Hark et al (2019)[16] reported a PPV of 78.1% for suspected/definitive OAG.

Zhao et al (2017)[18] did not report screening performance statistics separately for OAG from other ocular abnormalities and overall the combination of visual acuity test, CDR (>0.7) and IOP (≥23mmHg) resulted in a sensitivity of 97% and specificity of 92% for some form of ocular abnormality.

The retrospective analysis carried out by Boland et al (2016)[19] using CDR (≥0.6) and FDT perimetry (2 or more missed locations at the p<1% level) had a sensitivity of 66% and specificity of 70%.

** Algorithm - Points are given for the following criteria - IOP>28mmHg, IOP difference between eyes>2 mmHg, CDR(max) difference between eyes≥0.1, severity of excavation of optic nerve head, ISNT rule not respected, optic disc haemorrhage, CDR(max)>0.6 in small >0.7 in medium and >0.8 in large optic nerve head. A score of more than 1 point =possible glaucoma and score of >6 points is probable glaucoma. Wahl et al 2016

The UK study reported by Dabasia et al (2015)[20] combined inferior quadrant RNFL thickness and FDT perimetry and achieved sensitivities for both combined suspected/definitive OAG and definitive OAG alone of between 79.3% and 100% respectively. However, specificities were much lower for both combined suspected/definitive OAG and definitive OAG (range 63.3% to 65.2% respectively). From the data extracted the PPV was calculated for this screening examination. For combined definitive and suspect POAG the PPV was 22.5% and for definitive POAG only it was 14.8%.

Dabasia et al (2015)[20] also used Bayesian probabilistic reasoning†† to combine the best performing test parameters and cut-offs using highest positive likelihood ratios to determine post-test probabilities. For suspect/definitive OAG a post-test probability of >90% (compared with a pre-test probability of 11.5%) and for definitive OAG a post-test probability of >85% (compared with a pre-test probability of 5%) was achieved when the following tests were combined in series; FDT≥1missed location at p<1% level and RNFL inferior quadrant thickness or GCC global loss volume and corneal compensated IOP of >21mmHg. However, the tests for structural and functional abnormalities are not independent of one another which will lead to over estimation of Bayesian analysis post-test probability estimates.

†† In Bayesian probabilistic reasoning any unknown quantity of interest is assigned a ‘prior’ probability distribution which is mathematically updated to a ‘posterior’ probability distribution once data have been observed. The posterior distribution identifies the most likely values of the unknown quantity.

Table 4. Screening examination for combined tests to detect suspected or definitive glaucoma

Screening test (cut-offs for referral)	Population	Indication (n=reference standard result)	Sensitivity %(95% CI)	Specificity %(95% CI)	PPV %(95% CI)	NPV% (95% CI)	PLR	NLR	Study
Tests for intraocular pressure and abnormalities of the optic nerve head and retina									
Non-mydriatic fundus imaging (Vertical CDR >0.65 in average and large optic discs >0.5 in small optic discs, Vertical CDR diff between eyes ≥0.2, or rim width <0.2 any area or other defect) or **re-bound tonometry** (IOP≥21mmHg)	906 non-Caucasians aged ≥ 40 and Caucasians aged ≥ 65 or with family history and diabetes aged ≥ 40 USA Cohort study	Suspect (n=159) and definitive OAG(n=38)	NR	NR	78.1 (72.2 to 84.1)	NR	NR	NR	Hark et al 2019[16]
Non-mydriatic fundus imaging (Vertical CDR≥ 0.6 or Vertical CDR diff between eyes ≥0.2, or RNFL defect) or **NCT**(IOP>21mmHg)	221 people referred as part of OAG screening programme South Korea Cohort study	Definitive OAG(n=56)	NR	NR	25.5	NR	NR	NR	Song et al 2019[16]
		Suspect (n=79)and definitive OAG(n=56)	NR	NR	61.4	NR	NR	NR	
Tests for visual acuity, intraocular pressure and abnormalities of the optic nerve head									
Visual acuity (≤ 20/40) or **non-mydriatic fundus imaging** (CDR <0.7) or **re-bound tonometry** (IOP≥23mmHg)	901 African Americans aged ≥ 50 USA Cohort study	Accurate referral for abnormality (n=153 of which n=57 had suspect OAG and n=21 had definitive OAG)	97.0	92.0	NR	NR	NR	NR	Zhao et al 2017[18]
Tests for visual field loss and abnormalities of the optic nerve head									
FDT perimetry (2 or more missed locations at p<1% level x 2 reliable tests) and	548 people taking part in NHANES	CDR≤0.6 + FDT for definitive OAG(n=3)	33 (0 to 87)	77 (71 to 84)	NR	NR	NR	NR	Boland et al 2016[19]

non-mydriatic fundus imaging (CDR ≥0.6)	2005-2008 evaluation USA Retrospective cohort study	CDR ≥0.6 + FDT for definitive OAG (n=172)	66 (59 to 73)	70 (66 to 85)	NR	NR	NR	NR	
Tests for visual field loss and abnormalities of the retina									
OCT - RNFL thickness – inferior quadrant (>99% normal limit for this equipment) and **FDT** (≥1 missed location at p<1% level)	505 community screening participants aged ≥60 London UK Cohort study	Suspect(n=32) and definitive OAG (n=26)	79.3(67.2 to 87.7)	63.3(58.9 to 67.6)	22.5‡‡	NR	NR	NR	Dabasia et al 2015[20]
		Definitive OAG(n=26)	100 (87.1 to 100)	65.2(60.7 to 69.5)	14.8‡‡	NR	NR	NR	
Tests for visual field loss, intraocular pressure and detection of abnormalities of the optic nerve head and retina									
FDT perimetry and **non mydriatic fundus imaging** and **NCT** (Algorithm >1 point=possible glaucoma, >6 points= probable glaucoma)	4183 Evonik employees aged ≥40 Germany Cohort study	Suspect OAG algorithm score >1 point(n=111)	83.78 (75.72 to 89.54)	99.43 (99.15 to 99.62)	80.14 (71.92 to 86.45)	99.56 (99.30 to 99.72	147.8	0.16	Wahl et al 2016[21]
		Definitive OAG algorithm score >6 points(n=13)	84.62 (54.94 to 96.12)	99.98 (99.82 to 99.99)	91.67 (58.68 to 98.84)	99.95 (99.81 to 99.99)	3514.9	0.15	Wahl et al 2016[21]
Tests for visual field loss and intraocular pressure									
Screening model 1: **NCT**(1 eye IOP>21mmHg) or **FDT perimetry** (abnormal)	4183 Evonik employees aged ≥40 Germany Cohort study	Suspect OAG (n=111)	65.77 (56.58 to 73.98)	87.55 (86.50 to 88.53)	12.63 (10.16 to 15.59)	99.94 (98.55 to 99.23)	5.28	0.39	Wahl et al 2016[21]
		Definitive OAG (n=13)	100%	86.40 (85.32 to 87.41)	2.25 (1.31 to 3.83)	100%	7.35	0	Wahl et al 2016[21]
Screening model 2: **NCT** (at least 1 eye IOP >21mmHg) and **FDT** abnormal	4183 Evonik employees aged ≥40 Germany	Suspect OAG (n=111)	6.31 (3.04 to 12.64)	99.65 (99.42 to 99.80)	33.33 (16.79 to 55.33)	97.49 (96.97 to 97.93)	18.3	0.94	Wahl et al 2016[21]

‡‡ Calculated by reviewer

	Cohort study	Definitive OAG (n=13)	15.38 (3.87 to 45.06)	99.54 (99.28 to 99.71)	9.52 (2.39 to 31.13)	99.73 (96.52 to 99.85)	33.64	0.85	Wahl et al 2016[21]

CDR – cup-disc ratio, OAG-open angle glaucoma, PPV- positive predictive value, NPV – negative predictive value, PLR- positive likelihood ratio, NLR-negative likelihood ratio, FDT – Frequency doubling technology, NR= Not reported, NCT – non contact tonometry,ORA – ocular response analyser, IOP-intraocular pressure, OCT – optical coherence tomography, GCC- ganglion cell complex, RNFL- retinal nerve fibre layer.

The quality of the 6 individual studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) framework. The QUADAS-2 framework is used to assess the quality of primary test accuracy studies and includes 5 domains on patient selection, the index test, the reference standard, test strategy flow and timing and applicability. The questions included in these domains and the responses for the 6 studies are summarised in Table 5.

The main areas of concern across the studies came from the unclear risk of bias around the blinding used in the interpretation of the index test and reference standard and the interval between testing. Most studies did not report this information. The lack of independence of the screening algorithm based on the reference standard result compromised the validity of the screening performance statistics of one study**Error! Bookmark not defined.**. Another of limitation is the small sample size of some of the studies (n=221 to n=4183). Further details on the QUADAS-2 scores are provided in the Appendix 3 tables.

Table 5. QUADAS-2 scores summary.

	Hark et al 2019[16]	Song et al 2019[17]	Zhao et al 2017[18]	Boland et al 2016[19]	Dabasia et al 2015[20]	Wahl et al 2016[20]
Domain 1: Patient selection						
Consecutive or random sample of population enrolled?	Yes	Yes	Yes	Yes	Yes	Yes
Case-control design avoided?	Yes	Yes	Yes	Yes	Yes	Yes
Inappropriate exclusions avoided?	Yes	Yes	Yes	Yes	Yes	Yes
Domain II: Index test						
Index test results interpreted without knowledge of reference standard results?	Yes	Yes	No	U	Yes	U
Threshold pre-specified?	Yes	Yes	Yes	Yes	Yes	N
Domain III: Reference standard						
Reference standard likely to correctly classify condition?	Yes	Yes	U	No	Yes	Yes
Reference standard results interpreted without knowledge of index test results?	No	U	N	U	Yes	Yes
Domain IV: Test strategy flow and timing						
Appropriate interval between index test and reference standard?	U	U	U	U	Yes	U
Did all participants receive same reference standard?	Yes	Yes	U	Yes	Yes	Yes
All patients included in analysis?	No	Yes	N	Yes	Yes	Yes
Domain V: Applicability						
Applicable to UK screening population of interest?	Yes	U	Yes	Yes	Yes	Yes
Applicable to UK screening test of interest?	Yes	Yes	Yes	Yes	Yes	Yes
Target condition measured by reference test applicable to UK screening condition of interest?	Yes	U	Yes	Yes	Yes	Yes
Total number of 'yes' (out of 13)	**10**	**9**	**7**	**9**	**13**	**10**

Summary of Findings Relevant to Criterion 4: Criterion not met[§§]

One question about the diagnostic accuracy of screening tests for primary open angle glaucoma in the adult population was considered in this review. The previous UK NSC review about screening for glaucoma found that generally small sample sizes and outcomes of OAG tests for structure and function that varied widely in sensitivity and specificity precluded their suitability in general population screening.

This review identified 6 relatively small studies reporting results from populations that had been invited for screening for glaucoma (range n= 221 to n=4183). Of the 6 studies 5 targeted people at higher risk of developing OAG due to age, ethnicity, or family history.

The screening tests used within the studies are applicable to the general UK adult population.

There was no agreement about the most effective combination of tests or cut-off levels that should be used in a screening examination for OAG. The screening test performance statistics reported were variable and not comparable across studies.

The evidence base is therefore insufficient to conclude that there is a simple, safe, precise and validated screening test with known distribution of test values and agreed suitable cut-off levels.

This criterion is not met.

[§§] **Met** -for example, this should be applied in circumstances in which there is a sufficient volume of evidence of sufficient quality to judge an outcome or effect which is unlikely to be changed by further research or systematic review.
Not Met - for example, this should be applied in circumstances where there is insufficient evidence to clearly judge an outcome or effect or where there is sufficient evidence of poor performance.
Uncertain -for example, this should be applied in circumstances in which the constraints of an evidence summary prevent a reliable answer to the question. An example of this may be when the need for a systematic review and meta-analysis is identified by the rapid review.

Criterion 11 and 13

11 - There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity. Where screening is aimed solely at providing information to allow the person being screened to make an "informed choice" (eg. Down's syndrome, cystic fibrosis carrier screening), there must be evidence from high quality trials that the test accurately measures risk. The information that is provided about the test and its outcome must be of value and readily understood by the individual being screened.

13 – The benefit gained by individuals from the screening programme should outweigh any harms, for example from over diagnosis, overtreatment, false positives, false reassurance, uncertain findings and complications.

Question 2 – Are there any RCTs assessing whether a screening programme for open angle glaucoma is effective in reducing morbidity?

This question was addressed by the previous UK NSC review in 2015[1]. No RCTs of screening for OAG were identified by the literature search for the review.

The findings of most recent systematic review of glaucoma screening in the US (Ervin et al 2012 and Boland et al 2013)[22,23] led to the current recommendations of the United States Prevention Services Task Force (Moyer 2013) [24] and were reported in the previous UK NSC review (2015)[1].

The systematic review included 99 studies and 23 systematic reviews and concluded from their analysis that "the current evidence is insufficient to assess the balance of benefits and harms of screening for primary open-angle glaucoma (POAG) in adults" (Moyer 2013)[24]. In terms of benefits Moyer (2013)[24] reported that no studies directly examined whether screening prevents visual field loss, visual impairment or worsening quality of life. There were studies that showed that surgical treatment of early asymptomatic POAG reduced the number of patients whose visual field defects progress but not whether treatment reduced progression of visual impairment or improved quality of life.

Moyer et al (2013)[24] also reported that no studies had examined the harms of screening for POAG although some were reported in respect to treatment. Outcomes such as eye pain, burning, redness, dryness, cystoid macular edema and increased iris pigmentation due to topical eye medication were reported. Adverse outcomes due to surgery included infection, bleeding, hypotony, hyphemia, shallow anterior chambers, cataract development, choroidal detachment and synechia.

Ervin et al (2012)[23] concluded that there were no studies 'that provided evidence for direct or indirect links between glaucoma screening and visual field loss, visual impairment optic nerve damage, intraocular pressure or patient reported outcomes'.

Moyer (2013)[24] also reported concerns about over diagnosis and over treatment with glaucoma screening as not all people diagnosed with and treated for glaucoma go on to develop visual impairment and the magnitude or over diagnosis and overtreatment is unknown[24].

Burr et al (2014)[25] assessed the value of conducting an RCT for glaucoma screening in the UK. Four screening strategies were considered:

1. The population to be screened are invited to a primary care setting to receive tonometry and optic nerve photography by a technician or nurse who has received some training. Screen positives are referred to the hospital eye service.
2. The population to be screened are invited to a primary care setting to receive tonometry and optic nerve photography by a technician or nurse who has received some training. Screen positives are referred to the hospital eye service, but the tests used are tonometry and a visual field test (perimetry).
3. Screening with tonometry and optic nerve photography. Screen positives are examined by a specialised optometrist, who makes a diagnosis. Diagnostic test positives are referred to the hospital eye service.
4. Screening with tonometry and a visual field test (perimetry) with further diagnostic refinement and screen positives examined by a specialised optometrist who makes a diagnosis. Diagnostic test positives are referred to the hospital eye service.

Following their assessment, the authors concluded that glaucoma screening of a population selected on age is unlikely to be considered cost-effective and suggested that further research to understand and quantify the cost of sight impairment is a priority before proceeding to a large RCT evaluating a glaucoma screening or surveillance programme. Other particular areas of uncertainty were around test performance and uptake of either screening or current eye care.

Eligibility for inclusion in the review

Population: Adult population

Intervention:
Screening programmes to identify individuals at high risk of OAG

- direct and indirect ophthalmoscopy
- fundus photography or computerized imaging of the posterior pole, optic disc, or retinal nerve (OCT; with the exception of OCT 1 and OCT 2)

- retinal tomography, scanning laser polarimetry
- pachymetry (corneal thickness measurement) when used in conjunction with another test to diagnose glaucoma)
- perimetry (including short-wavelength, high-pass, motion, flicker perimetry, yellow and blue perimetry)
- tonometry (contact and non contact tonometry).

Comparator: Current diagnostic methods (e.g. NICE guidance), other combination methods or none.
Any treatment, no treatment or placebo

Outcomes:
- chronic OAG eye damage (peripheral vision fade and tunnel vision)
- loss of vision
- blindness
- measurements of visual impairment as defined by included studies

Study design: Peer-reviewed evidence derived from the following types of study
- systematic reviews and (network) meta-analyses
- randomised controlled trials (RCTs)

Date and language: English language published since 1st October 2014

Description of the evidence

Database searches yielded 513 results of which 8 were judged to be relevant to this question following abstract and title review. After review of the full texts, 5 studies were excluded. The reasons for exclusion of the 5 studies were:
- 1 systematic review and meta-analysis (Thomas et al 2014)[6] assessed teleglaucoma identified from studies using a variety of glaucoma detection tests. The review identified 45 cohort, economic and cost effectiveness studies but no RCTs. Clinical outcomes detailed in key question 2 eligibility criteria were not reported in the publication.
- 1 publication reported the modelling of possible outcomes of a screening programme for and African-American community (Blumberg et al 2014)[9]
- 1 publication was a mixed methods evaluation of a glaucoma check service for black-African and black-Caribbean people (Holdsworth et al 2017)[13]
- 1 study was a retrospective analysis of 2 cohorts of patients referred to secondary care from screening or primary care ophthalmology clinics (Song et al 2019)[17]
- 1 publication was a report of work based glaucoma screening in employees aged ≥40 (Wahl et al 2016)[21].

Discussion of findings

No RCTs assessing whether a screening programme for open angle glaucoma is effective in reducing morbidity were identified by the searches carried out for this review. There were 3 publications reporting results of glaucoma screening programmes (Anton et al 2017,Hark et al 2017 and Zhao et al 2017)[14,16,18].

Anton et al 2017[14] reported detection rates and costs of a screening programme in Spain but the screening performance statistics were beyond the scope of the study and the treatment outcomes and overall screening programme performance were not reported. Similarly the studies reported by Hark et al 2017[16] and Zhao et al 2017[18] focussed on the accuracy of screening test (see question 1 above) but did not report any data about treatment outcomes or the performance of the whole screening pathway.

Summary of Findings Relevant to Criterion 11 and 13: Criteria not met[***]

The 2015 UK NSC review did not identify any randomised controlled trials on screening for open angle glaucoma. This update review also did not find any RCTs on the effectiveness of screening for glaucoma to reduce the morbidity of the condition.

This criterion is not met.

[***] **Met** -for example, this should be applied in circumstances in which there is a sufficient volume of evidence of sufficient quality to judge an outcome or effect which is unlikely to be changed by further research or systematic review.
Not Met - for example, this should be applied in circumstances where there is insufficient evidence to clearly judge an outcome or effect or where there is sufficient evidence of poor performance.
Uncertain -for example, this should be applied in circumstances in which the constraints of an evidence summary prevent a reliable answer to the question. An example of this may be when the need for a systematic review and meta-analysis is identified by the rapid review.

Review summary

Conclusions and implications for policy

The aim of a national screening programme targeting OAG in the adult population would be to detect the early stages of the condition to reduce morbidity. This report is an update review on screening for OAG against select UK NSC criteria for appraising the viability, effectiveness and appropriateness of a screening programme. This review assessed 2 key questions to determine if new evidence published since 2014 suggests that reconsideration of the current recommendation for screening for OAG in the UK is required.

The 2 key questions in this review are concerned with the diagnostic accuracy of screening tests for OAG in the adult population and whether any high quality randomised controlled trials have been carried out that examine the effectiveness of an OAG screening programme in reducing morbidity from the condition.

On the basis of the current evidence available about the 2 key questions, a national screening programme cannot be recommended. Important areas of uncertainty remain:

- the volume of evidence reporting results of tests for OAG undertaken in a general adult population was limited to 6 relatively small studies
- there was no agreed test, combination of tests or cut-off levels for the tests used for the screening examination
- screening performance statistics varied between studies and were not comparable
- no randomised controlled trials on the effectiveness of screening for OAG to reduce the morbidity of the condition were identified. Results from glaucoma screening programmes focussed on accuracy of the screening test and not treatment outcomes or overall outcomes of the screening programme performance.

The current recommendation not to introduce a UK OAG screening programme should be retained.

Limitations

A limitation for this review is the lack of studies that meet all of the inclusion criteria for this review for 1 of the key questions.

This rapid review process was conducted over a condensed period of time (approximately 12 weeks). Searching was limited to 3 bibliographic databases and did not include grey literature sources. The review was guided by a protocol developed a priori. The literature

search and first appraisal of search results were undertaken by 1 information scientist, and further appraisal and study selection by 1 reviewer. Any queries at both stages were resolved through discussion with a second reviewer. Studies not available in the English language, abstracts, poster presentations, case series and case-control studies were not included. Studies that were not published in peer-reviewed journals were not reviewed.

Appendix 1 — Search strategy

Electronic databases

The search strategy included searches of the databases shown in Table 6. MEDLINE, MEDLINE In-Process, MEDLINE Daily, Epub Ahead of Print and Embase.

Table 6. Summary of electronic database searches and dates

Database	Platform	Searched on date	Date range of search
MEDLINE, MEDLINE In-Process, MEDLINE Daily, Epub Ahead of Print	Ovid SP	28th December 2018 25th March 2019	October 2014 to December 28th 2018 December 28th to 25th March 25th 2019
Embase	Ovid SP	28th December 2018 25th March 2019	October 2014 to December 28th 2018 December 28th to 25th March 25th 2019October 2014 to 25th March 2019
The Cochrane Library, including: - Cochrane Database of Systematic Reviews (CDSR) - Cochrane Central Register of Controlled Trials (CENTRAL) - Database of Abstracts of Reviews of Effects (DARE)	Wiley Online	28th December 2018 25th March 2019	CDSR: Issue 7 of 12, July 2016

Search Terms

Search terms included combinations of free text and subject headings (Medical Subject Headings [MeSH] for MEDLINE, and Emtree terms for Embase).

An initial search was conducted on 28th December 2018. A second search was performed on 25th March 2019 to correct an error in the original search terms and to search for additional studies published between 28th December 2018 and March 25th 2019.

The search terms used in the March 2019 search for MEDLINE, MEDLINE In-Process, MEDLINE Daily, Epub Ahead of Print Embase and for the Cochrane Library databases for each key question are shown in the tables below.

Table 7. Search strategy for key question 1 MEDLINE, MEDLINE In-Process, MEDLINE Daily, Epub Ahead of Print

# ▲	Searches	Results

1	Glaucoma, Open-Angle/	12681
2	glaucoma.ti.	31773
3	1 or 2	36172
4	Tomography, Optical Coherence/	28245
5	(optic$ adj (disc or nerve) adj photograp$).tw.	354
6	Visual Field Tests/	8361
7	screening mode perimetry.tw.	1
8	Manometry/	20216
9	tonometry.tw.	6217
10	Heidelberg retina tomography II.tw.	14
11	Frequency doubling technology.tw.	368
12	Standard automated perimetry.tw.	769
13	Goldmann applanation tonometry.tw.	801
14	Humphrey visual field analyser.tw.	24
15	tendency-orientated perimetry.tw.	1
16	(HRT or FDT or SAP or GAT).tw.	24633
17	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	83923
18	3 and 17	5078
19	Mass Screening/	96747
20	Vision Screening/	2089
21	Vision Tests/	9948
22	(screen$3 or test or tests or testing or detect$).tw.	4342662
23	19 or 20 or 21 or 22	4367988
24	Ocular Hypertension/	6169
25	Intraocular Pressure/	35380
26	((ocular or intraocular) adj3 (hypertension or pressure)).tw.	33872
27	(visual adj (field or function)).tw.	32458
28	(structure adj3 (optic nerve or retina$)).tw.	1718
29	24 or 25 or 26 or 27 or 28	78459
30	3 and 23 and 29	5194
31	18 or 30	8163
32	"Sensitivity and Specificity"/	334448
33	(sensitiv$ or specific$).tw.	3759677
34	Predictive Value of Tests/	189226
35	(PPV or positive predictive value$ or NPV or negative predictive value$).tw.	65936
36	((False or true) adj (negative$ or positive$)).tw.	74681
37	(test adj2 (accura$ or reliab$ or valid$)).tw.	36824
38	likelihood ratio$.tw.	14067
39	32 or 33 or 34 or 35 or 36 or 37 or 38	4099145
40	31 and 39	2188

41	("20181227" or "20181228" or "20181229" or "20181230" or "20181231" or "20190101" or "20190102" or "20190103" or "20190104" or "20190105" or "20190106" or "20190107" or "20190108" or "20190109" or "20190110" or "20190111" or "20190112" or "20190113" or "20190114" or "20190115" or "20190116" or "20190117" or "20190118" or "20190119" or "20190120" or "20190121" or "20190122" or "20190123" or "20190124" or "20190125" or "20190127" or "20190128" or "20190129" or "20190130" or "20190131" or "20190201" or "20190202" or "20190203" or "20190204" or "20190205" or "20190206" or "20190207" or "20190208" or "20190209" or "20190210" or "20190211" or "20190212" or "20190213" or "20190214" or "20190215" or "20190216" or "20190217" or "20190218" or "20190219" or "20190220" or "20190221" or "20190222" or "20190223" or "20190224" or "20190225" or "20190226" or "20190227" or "20190228" or "20190301" or "20190302" or "20190303" or "20190304" or "20190305" or "20190306" or "20190307" or "20190308" or "20190309" or "20190311" or "20190312" or "20190313" or "20190314" or "20190315" or "20190316" or "20190317" or "20190318" or "20190319" or "20190320" or "20190321" or "20190322").ez.	179044
42	("20181227" or "20181228" or "20181229" or "20181230" or "20181231" or "20190101" or "20190102" or "20190103" or "20190104" or "20190105" or "20190106" or "20190107" or "20190108" or "20190109" or "20190110" or "20190111" or "20190112" or "20190113" or "20190114" or "20190115" or "20190116" or "20190117" or "20190118" or "20190119" or "20190120" or "20190121" or "20190122" or "20190123" or "20190124" or "20190125" or "20190127" or "20190128" or "20190129" or "20190130" or "20190131" or "20190201" or "20190202" or "20190203" or "20190204" or "20190205" or "20190206" or "20190207" or "20190208" or "20190209" or "20190210" or "20190211" or "20190212" or "20190213" or "20190214" or "20190215" or "20190216" or "20190217" or "20190218" or "20190219" or "20190220" or "20190221" or "20190222" or "20190223" or "20190224" or "20190225" or "20190226" or "20190227" or "20190228" or "20190301" or "20190302" or "20190303" or "20190304" or "20190305" or "20190306" or "20190307" or "20190308" or "20190309" or "20190311" or "20190312" or "20190313" or "20190314" or "20190315" or "20190316" or "20190317" or "20190318" or "20190319" or "20190320" or "20190321" or "20190322").ed.	247214
43	"2019".yr.	380192
44	41 or 42 or 43	606814
45	40 and 44	50
46	31 and 38	56
47	limit 46 to yr="2014 -Current"	15
48	45 or 47	65
49	limit 48 to english language	64
50	from 49 keep 1-64	64

Table 8. Search strategy for key question 1 Embase

# ▲	Searches	Results
1	open angle glaucoma/	15681
2	glaucoma.ti.	33018
3	1 or 2	38688
4	optical coherence tomography/	42143
5	(optic$ adj (disc or nerve) adj photograp$).tw.	399
6	perimetry/	10212
7	screening mode perimetry.tw.	1
8	manometry/	16206
9	tonometry.tw.	9024
10	Heidelberg retina tomography II.tw.	17
11	Frequency doubling technology.tw.	424
12	Standard automated perimetry.tw.	951
13	Goldmann applanation tonometry.tw.	910
14	Humphrey visual field analyser.tw.	35
15	tendency-orientated perimetry.tw.	1
16	(HRT or FDT or SAP or GAT).tw.	32201
17	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	106185
18	3 and 17	5505
19	Mass Screening/	51376
20	Vision Test/	7897
21	(screen$3 or test or tests or testing or detect$).tw.	5664317
22	19 or 20 or 21	5680102
23	intraocular hypertension/	10676
24	Intraocular Pressure/	48493
25	((ocular or intraocular) adj3 (hypertension or pressure)).tw.	40191
26	(visual adj (field or function)).tw.	40620
27	(structure adj3 (optic nerve or retina$)).tw.	2340
28	23 or 24 or 25 or 26 or 27	99233
29	2 and 22 and 28	5163
30	18 or 29	8830
31	"Sensitivity and Specificity"/	317890
32	(sensitiv$ or specific$).tw.	4609260
33	predictive value/	143846
34	(PPV or positive predictive value$ or NPV or negative predictive value$).tw.	99117
35	((False or true) adj (negative$ or positive$)).tw.	100327
36	(test adj2 (accura$ or reliab$ or valid$)).tw.	45721
37	likelihood ratio$.tw.	18734
38	31 or 32 or 33 or 34 or 35 or 36 or 37	4868390
39	30 and 38	2279

40	("201901" or "201902" or "201903" or "201904" or "201905" or "201906" or "201907" or "201908" or "201909" or "201910" or "201911" or "201912" or "201913" or "201853").em.	922557
41	"2019".yr.	333566
42	40 or 41	932147
43	39 and 42	74
44	3 and 22 and 28 and 38	1644
45	44 not 39	93
46	limit 45 to yr="2014 -Current"	29
47	30 and 37	55
48	limit 47 to yr="2014 -Current"	15
49	43 or 46 or 48	118

Table 9. Search strategy for key question 1 using the Cochrane Library Databases (Searched via the Wiley Online platform)

ID	Search
#1	MeSH descriptor: [Glaucoma, Open-Angle] this term only
#2	(glaucoma):ti
#3	#1 or #2
#4	MeSH descriptor: [Mass Screening] this term only
#5	MeSH descriptor: [Vision Screening] this term only
#6	MeSH descriptor: [Vision Tests] this term only
#7	((screen* or test or tests or testing or detect*)):ti,ab,kw
#8	#4 or #5 or #6 or #7
#9	MeSH descriptor: [Ocular Hypertension] this term only
#10	MeSH descriptor: [Intraocular Pressure] this term only
#11	("ocular hypertension" or "intraocular hypertension" or "ocular pressure" or "intraocular pressure"):ti,ab,kw
#12	(("visual field" or "visual function")):ti,ab,kw
#13	((structure NEAR/3 (optic nerve or retina*))):ti,ab,kw
#14	#9 or #10 or #11 or #12 or #13
#15	#3 and #8 and #14
#16	MeSH descriptor: [Tomography, Optical Coherence] this term only
#17	(((optic* disc photograph*) or (optic* nerve photograph*))):ti,ab,kw
#18	MeSH descriptor: [Visual Field Tests] this term only
#19	("screening mode perimetry"):ti,ab,kw
#20	MeSH descriptor: [Manometry] this term only
#21	((tonometry or "Heidelberg retina tomography II" or "Frequency doubling technology" or "Standard automated perimetry" or "Goldmann applanation tonometry" or "Humphrey visual field analyser" or "tendency-orientated perimetry" or HRT or FDT or SAP or GAT)):ti,ab,kw
#22	#16 or #17 or #18 or #19 or #20 or #21
#23	#3 and #22
#24	#15 or #23

Table 10. Search strategy for Key question 2 MEDLINE, MEDLINE In-Process, MEDLINE Daily, Epub Ahead of Print

# ▲	Searches	Results
1	Glaucoma, Open-Angle/	12681
2	glaucoma.ti.	31773
3	1 or 2	36172
4	Mass Screening/	96747
5	Vision Screening/	2089
6	Vision Tests/	9948
7	(screen$3 or test or tests or testing or detect$).tw.	4342662
8	(early adj (diagnosis or identif$)).tw.	84947
9	4 or 5 or 6 or 7 or 8	4421658
10	3 and 9	7945
11	Meta-Analysis as Topic/	16820
12	meta analy$.tw.	143392
13	metaanaly$.tw.	1928
14	Meta-Analysis/	98727
15	(systematic adj (review$1 or overview$1)).tw.	138580
16	exp Review Literature as Topic/	12061
17	11 or 12 or 13 or 15 or 16	240225
18	cochrane.ab.	68657
19	embase.ab.	73848
20	(psychlit or psyclit).ab.	913
21	(psychinfo or psycinfo).ab.	27980
22	(cinahl or cinhal).ab.	23353
23	science citation index.ab.	2911
24	bids.ab.	478
25	cancerlit.ab.	623
26	18 or 19 or 20 or 21 or 22 or 23 or 24 or 25	121741
27	reference list$.ab.	16233
28	bibliograph$.ab.	16540
29	hand-search$.ab.	6252
30	relevant journals.ab.	1086
31	manual search$.ab.	3998
32	27 or 28 or 29 or 30 or 31	39512
33	selection criteria.ab.	28120
34	data extraction.ab.	17868
35	33 or 34	43825
36	Review/	2493237
37	35 and 36	28433
38	Comment/ or Letter/ or Editorial/	1707970
39	exp animals/ not humans.sh.	4561625

40	38 or 39	6206364
41	17 or 26 or 32 or 37	297961
42	41 not 40	282753
43	10 and 42	139
44	"systematic review"/	103286
45	10 and 44	48
46	43 or 45	140
47	Randomized Controlled Trials as Topic/	122173
48	randomized controlled trial/	478564
49	Random Allocation/	98192
50	Double Blind Method/	150280
51	Single Blind Method/	26469
52	clinical trial/	515289
53	clinical trial, phase i.pt.	18736
54	clinical trial, phase ii.pt.	30288
55	clinical trial, phase iii.pt.	14794
56	clinical trial, phase iv.pt.	1680
57	controlled clinical trial.pt.	92989
58	randomized controlled trial.pt.	478564
59	multicenter study.pt.	247407
60	clinical trial.pt.	515289
61	exp Clinical Trials as topic/	323433
62	(clinical adj trial$).tw.	328485
63	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	162507
64	PLACEBOS/	34281
65	placebo$.tw.	202744
66	randomly allocated.tw.	25912
67	(allocated adj2 random$).tw.	29045
68	47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67	1522304
69	letter/ or historical article/ or case report.tw.	1629527
70	exp animals/ not humans.sh.	4561625
71	69 or 70	6144862
72	68 not 71	1399879
73	10 and 72	876
74	46 or 73	986

75	("20181227" or "20181228" or "20181229" or "20181230" or "20181231" or "20190101" or "20190102" or "20190103" or "20190104" or "20190105" or "20190106" or "20190107" or "20190108" or "20190109" or "20190110" or "20190111" or "20190112" or "20190113" or "20190114" or "20190115" or "20190116" or "20190117" or "20190118" or "20190119" or "20190120" or "20190121" or "20190122" or "20190123" or "20190124" or "20190125" or "20190127" or "20190128" or "20190129" or "20190130" or "20190131" or "20190201" or "20190202" or "20190203" or "20190204" or "20190205" or "20190206" or "20190207" or "20190208" or "20190209" or "20190210" or "20190211" or "20190212" or "20190213" or "20190214" or "20190215" or "20190216" or "20190217" or "20190218" or "20190219" or "20190220" or "20190221" or "20190222" or "20190223" or "20190224" or "20190225" or "20190226" or "20190227" or "20190228" or "20190301" or "20190302" or "20190303" or "20190304" or "20190305" or "20190306" or "20190307" or "20190308" or "20190309" or "20190311" or "20190312" or "20190313" or "20190314" or "20190315" or "20190316" or "20190317" or "20190318" or "20190319" or "20190320" or "20190321" or "20190322").ez.	179044
76	("20181227" or "20181228" or "20181229" or "20181230" or "20181231" or "20190101" or "20190102" or "20190103" or "20190104" or "20190105" or "20190106" or "20190107" or "20190108" or "20190109" or "20190110" or "20190111" or "20190112" or "20190113" or "20190114" or "20190115" or "20190116" or "20190117" or "20190118" or "20190119" or "20190120" or "20190121" or "20190122" or "20190123" or "20190124" or "20190125" or "20190127" or "20190128" or "20190129" or "20190130" or "20190131" or "20190201" or "20190202" or "20190203" or "20190204" or "20190205" or "20190206" or "20190207" or "20190208" or "20190209" or "20190210" or "20190211" or "20190212" or "20190213" or "20190214" or "20190215" or "20190216" or "20190217" or "20190218" or "20190219" or "20190220" or "20190221" or "20190222" or "20190223" or "20190224" or "20190225" or "20190226" or "20190227" or "20190228" or "20190301" or "20190302" or "20190303" or "20190304" or "20190305" or "20190306" or "20190307" or "20190308" or "20190309" or "20190311" or "20190312" or "20190313" or "20190314" or "20190315" or "20190316" or "20190317" or "20190318" or "20190319" or "20190320" or "20190321" or "20190322").ed.	247214
77	"2019".yr.	380192
78	75 or 76 or 77	606814
79	74 and 78	14
80	limit 79 to english language	13

Table 11. Search strategy for key question 2 Embase

	Searches	Results
1	open angle glaucoma/	15681
2	glaucoma.ti.	33018
3	1 or 2	38688
4	Mass Screening/	51376

5	Vision Test/	7897
6	(screen$3 or test or tests or testing or detect$).tw.	5664317
7	(early adj (diagnosis or identif$)).tw.	121098
8	4 or 5 or 6 or 7	5752193
9	3 and 8	9283
10	exp Meta Analysis/	158260
11	meta analy$.tw.	184391
12	metaanaly$.tw.	8869
13	(systematic adj (review$1 or overview$1)).tw.	169636
14	10 or 11 or 12 or 13	321767
15	cochrane.ab.	88058
16	embase.ab.	92603
17	(psychlit or psyclit).ab.	989
18	(psychinfo or psycinfo).ab.	25304
19	(cinahl or cinhal).ab.	27021
20	science citation index.ab.	3322
21	bids.ab.	618
22	cancerlit.ab.	718
23	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22	145510
24	reference list$.ab.	18692
25	bibliograph$.ab.	20854
26	hand-search$.ab.	7539
27	relevant journals.ab.	1285
28	manual search$.ab.	4757
29	24 or 25 or 26 or 27 or 28	47753
30	selection criteria.ab.	33413
31	data extraction.ab.	21775
32	30 or 31	53160
33	review.pt.	2415069
34	32 and 33	26494
35	(letter or editorial).pt.	1645612
36	(exp animals/ or nonhuman/) not human/	6177451
37	35 or 36	7761030
38	14 or 23 or 29 or 34	383515
39	38 not 37	369518
40	9 and 39	153
41	Clinical Trial/	951658
42	Randomized Controlled Trial/	537282
43	controlled clinical trial/	458809
44	multicenter study/	208541
45	Phase 3 clinical trial/	38458
46	Phase 4 clinical trial/	3285
47	exp RANDOMIZATION/	81567

48	Single Blind Procedure/	34023
49	Double Blind Procedure/	158168
50	Crossover Procedure/	58342
51	PLACEBO/	330349
52	randomi?ed controlled trial$.tw.	196733
53	rct.tw.	31314
54	(random$ adj2 allocat$).tw.	39046
55	single blind$.tw.	22430
56	double blind$.tw.	195256
57	((treble or triple) adj blind$).tw.	929
58	placebo$.tw.	285204
59	Prospective Study/	503229
60	randomly allocated.tw.	31972
61	(allocated adj2 random$).tw.	35669
62	41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59	2092130
63	case study/ or case report.tw. or abstract report/ or letter/ or conference*.pt. or editorial.pt. or letter.pt. or note.pt.	6878445
64	(exp animals/ or nonhuman/) not human/	6177451
65	63 or 64	12416640
66	62 not 65	1466317
67	9 and 66	1240
68	40 or 67	1350
69	("201901" or "201902" or "201903" or "201904" or "201905" or "201906" or "201907" or "201908" or "201909" or "201910" or "201911" or "201912" or "201913" or "201853").em.	922557
70	"2019".yr.	333566
71	69 or 70	932147
72	68 and 71	43
73	limit 72 to english language	40

Table 12. Search strategy for key question 2 using the Cochrane Library Databases (Searched via the Wiley Online platform)

ID	Search
#1	MeSH descriptor: [Glaucoma, Open-Angle] this term only
#2	(glaucoma):ti
#3	#1 or #2
#4	MeSH descriptor: [Mass Screening] this term only
#5	MeSH descriptor: [Vision Screening] this term only
#6	MeSH descriptor: [Vision Tests] this term only
#7	((screen* or test or tests or testing or detect*)):ti,ab,kw
#8	(("early diagnosis" or "early identif*")):ti,ab,kw
#9	#4 or #5 or #6 or #7 or #8

#10	#3 and #9

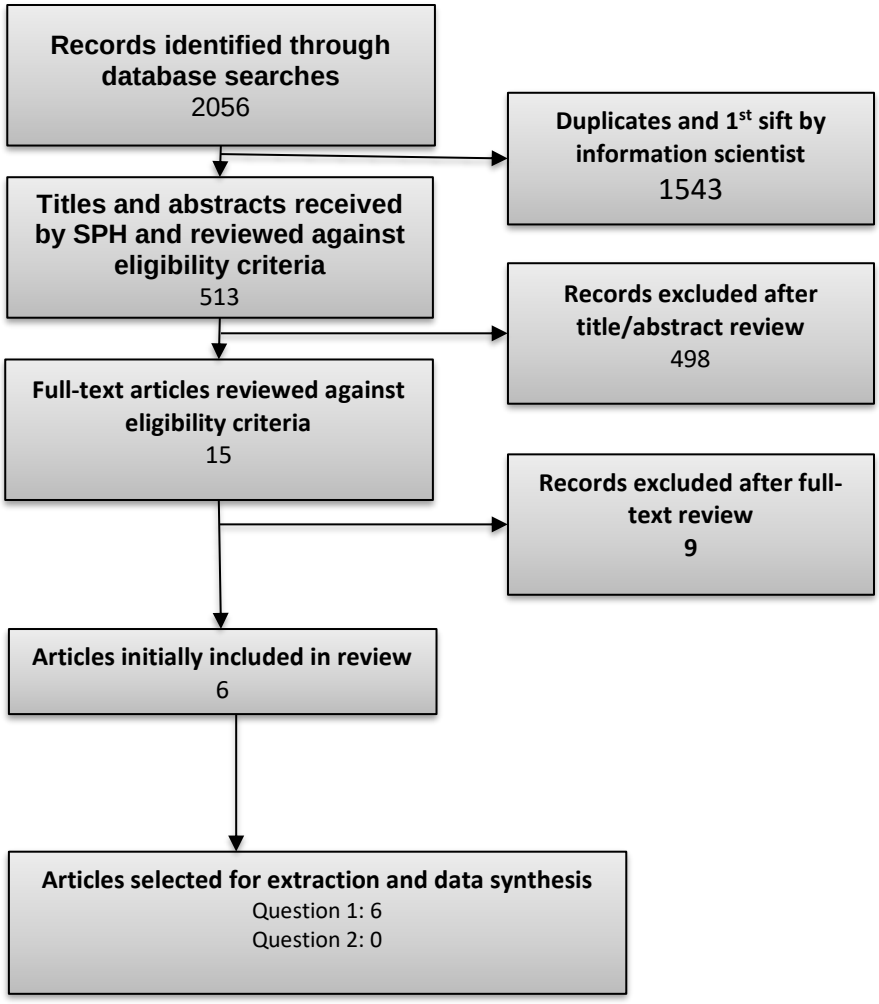
Results were imported into EndNote and de-duplicated. Results identified by either the December 2018 or March 2019 searches considered for inclusion in the review.

Appendix 2 — Included and excluded studies

PRISMA flowchart

Figure 1 summarises the volume of publications included and excluded at each stage of the review. In total 15 publications were judged to be relevant to 1 or more review questions and were considered for extraction. Publications that were included or excluded after the review of full-text articles are detailed below.

Figure 1. Summary of publications included and excluded at each stage of the review



Publications included after review of full-text articles

The 6 publications included after review of full-texts are summarised in Table 13 below.
Studies were prioritised for extraction and data synthesis. It was planned *a priori* that the following approach would be taken to prioritise studies for extraction:

1. Systematic reviews and meta-analyses would be considered the highest quality of evidence if any were found.
2. Prioritisation of studies with consecutively enrolled populations for key question 1
3. RCTs or systematic reviews and or meta analysis of RCTs only were included for key question 2

Table 13. Summary of publications included after review of full-text articles, and the question each publication was identified as being relevant to

Study	The condition	The test	The intervention	The screening programme	Implementation criteria
Hark et al 2019		Qu1			
Song et al 2019		Qu1			
Zhao et al 2017		Qu1			
Boland et al 2016		Qu1			
Dabasia et al 2015		Qu1			
Wahl et al 2016		Qu1			

Appendix 3 — Summary and appraisal of individual studies

Data Extraction

Studies relevant to criterion 4, key question 1: *What is the diagnostic accuracy of screening tests for open angle glaucoma in adult population?*

Table 14. Hark et al 2019

Publication	Hark L, Myers J, Ines A, Jiang A et al. Philadelphia Telemedicine Glaucoma Detection and Follow-Up Study: confirmation between eye screening and comprehensive eye examination diagnoses. Br J Opthalmol 2019; 0-7.
Study details	Results of a glaucoma screening programme in an underserved population in Philadelphia.
Study objectives	To implement glaucoma screening in an underserved population in Philadelphia. People with a positive screening test were randomised to different treatment interventions. This publication reports the results of people who were invited into the programme and outcomes of the screening test.
Inclusions	African-Americans, Hispanics/Latinos or Asians aged ≥ 40; Caucasians aged ≥ 65 and adults of any ethnicity with a family history of glaucoma and/or diabetes aged ≥ 40.
Exclusions	People seen in the past year by an ophthalmologist for a previous ocular diagnosis
Population	Between April 2015 and February 2017 906 people were screened from primary care practices and federally qualified health centres in areas of Philadelphia designated as federal Medically Undeserved Areas.
Intervention	• Visual acuity assessment using a digital acuity system (part of screening examination but not relevant to • Fundus imaging to check for abnormality - two monoscopic fundus photographs and one anterior segment photograph per eye were taken using a non-mydriatic, auto focus, hand held fundus camera (positive screen = vertical CDR >0.65 in average and large optic discs >0.5 in small optic discs, vertical CDR diff between eyes ≥0.2, or rim width <0.2 any area or other defect) • Intraocular pressure measured using re-bound tonometer (positive screen = IOP>21mmHg)
Comparator	• Visual acuity using a digital acuity system and white/white perimetry • Visual field test using a visual field analyser • Eye examination using slit lamp eye bi-microscopy

- Central corneal thickness using a pachymeter
- Intraocular pressure using Goldman applanation tonometer
- Gonioscopy and funduscopic examination

Outcomes

- 906 participants were screened of whom 334(36.9%) had an abnormal fundus image, 155(17.1%) fundus images were unreadable and 62(6.8%) had ocular hypertension
- 536 (59.2%) people were invited to attend visit 2
- 347 (64.7% of those invited) attended visit 2
- 280 (80.7%) participants who attended visit 2 were diagnosed with at least one ocular condition
- At screening 183 people were noted as having suspicious optic nerves, 143 (78.1%) were diagnosed as glaucoma or glaucoma suspects at visit 2
- People with a normal screening result were not seen for a definitive eye examination so of the screening performance measures only positive predictive value can be calculated.

Reported screening test performance statistics

Abnormal findings	Screening No.	Definitive eye examination No.	Positive predictive value (95% CI)
Suspicious optic nerve at screening leading to glaucoma or glaucoma suspect at definitive examination	183	143	78.1%(72.2 to 84.1)
Ocular hypertension	37	14	37.8%(22.2 to 53.5)
Abnormal photo or high IOP led to at least one ocular diagnosis	258	222	86.0%(81.8 to 90.3)

Quality appraisal

Question	**Assessment (Y, N, unclear)**	**Risk of Bias (low, high, unclear)**	**Supporting info**
Domain I: Patient selection			
Consecutive or random sample of population enrolled?	Y	L	Participants were recruited via community venues and specific inclusion and exclusion criteria were described.

	Case-control design avoided?	Y	L	
	Inappropriate exclusions avoided?	Y	L	Exclusions were to ensure a higher risk group of people were screened (by age, family history and ethnicity).
	Domain II: Index Test			
	Index test results interpreted without knowledge of reference standard results?	Y	L	Screeners and participants were unaware of reference standard results (screening test was carried out prior to reference standard).
	Threshold pre-specified?	Y	L	Thresholds for definitive and suspected glaucoma were pre-specified.
	Domain III: Reference standard			
	Reference standard likely to correctly classify condition?	Y	L	There were a range of tests to determine definitive glaucoma which are currently regarded as the gold standard.
	Reference standard results interpreted without knowledge of index test results?	N	H	Ophthalmologists carrying out the definitive eye examination knew the screening test results of participants.
	Domain IV: Test strategy flow and timing			
	Appropriate interval between index test and reference standard?	U	U	No information was reported on time between index test and reference standard.
	Did all participants receive same reference standard?	Y	L	All participants with a positive screen received the same reference standard. Participants with a negative screen did not receive a reference standard examination.
	All patients included in analysis?	N	H	A significant proportion of people referred for a definitive eye examination following screening did not attend (35%)
	Applicability			
	Applicable to UK screening population of interest?	Y	L	This is a targeted screening programme based on age, ethnicity and family history in inner city communities – a strategy which could be applied to a UK population. In this study by applying this strategy the participants in the screening

				programme were of African American origin. Applying this strategy in the UK is likely to result in a different screening population composition.	
	Applicable to UK screening test of interest?	Y	L	The tests are in use in the UK.	
	Target condition measured by reference test applicable to UK screening condition of interest?	Y	L	Yes the target condition and the reference test are both testing for open angle glaucoma which is the UK screening condition of interest.	

Table 15. Song et al 2019

Publication	Song YJ, Kim YW, Park KH, Kim YK, Choi HJ, Jeoung JW. Comparison of glaucoma patients referred by glaucoma screening versus referral from primary eye clinic. PLoS ONE [Electronic Resource]. 2019;14(1):e0210582.
Study details	Retrospective cohort study
Study objectives	To compare characteristics of people referred to a glaucoma outpatient clinic from mass glaucoma screening programme using IOP measurement and non-mydriatic fundus photography with those referred from primary eye clinics (using slit lamp and fundus examination plus IOP measurement).
Inclusions	People referred to a hospital glaucoma outpatient clinic between January 2013 and December 2014.
Exclusions	Subjects with a history of any retinal disease and intraocular surgery that could affect the visual field.
Population	221 people screened as part of the Gangnam eye study referred to the hospital glaucoma outpatient clinic (South Korea).
Intervention	Glaucoma screening examination comprising IOP measurement (positive screen= >21mmHg) and non-mydriatic fundus photography (positive screen =vertical CDR≥ 0.6 or vertical CDR diff between eyes ≥0.2, or RNFL defect).
Comparator	Slit lamp and fundus examination plus IOP measurement.
Reference standard	All referred subjects underwent the following tests at their first visit of the glaucoma clinic for definitive examination: • Best corrected visual acuity • Refraction • Goldman applanation tonometry • Goniscopy • Stereo optical disc photography • Red-free fundus photography • Standard automated perimetry

- Measure of corneal thickness
- Measure of axial length

Outcomes

Screening test statistics reported

	Positive predictive value	False positive rate
Definitive glaucoma screening programme referral	25.5%	
Screening programme referral for suspected or definitive glaucoma	61.4%	
Screening programme all referrals		38.6%

Quality appraisal

Question	**Assessment (Y, N, unclear)**	**Risk of Bias (Low, High, unclear)**	**Supporting info**
Domain I: Patient selection			
Consecutive or random sample of population enrolled?	Y	L	Populations were the screen positive participants in a screening programme seen within 2 dates. Clear exclusion criteria were reported and although not explicitly reported the assumption is that all other referrals were included (ie consecutive sample)
Case-control design avoided?	Y	L	
Inappropriate exclusions avoided?	Y	L	Only exclusions were previous history of any retinal disease and intraocular surgery that could affect the visual field.
Domain III: Index Test			
Index test results interpreted without knowledge of reference standard results?	Y	L	This was a retrospective comparison and the screening test/primary care clinic tests were carried out prior to the reference standard tests being undertaken.
Threshold pre-specified?	Y	L	Thresholds for definitive and suspected glaucoma were pre-specified.

Domain II: Reference standard			
Reference standard likely to correctly classify condition?	Y	L	There were a range of tests to determine definitive glaucoma which are currently regarded as the gold standard.
Reference standard results interpreted without knowledge of index test results?	U	U	It is likely that the screening test/primary care clinic test results were known to those undertaking the definitive clinical tests in the outpatient clinic.
Domain IV: Test strategy flow and timing			
Appropriate interval between index test and reference standard?	U	U	No information was reported on time between index test and reference standard
Did all participants receive same reference standard?	Y	L	All screen positive participants were referred to one hospital outpatient clinic where they all underwent the same set of tests.
All patients included in analysis?	Y	L	
Applicability			
Applicable to UK screening population of interest?	U	U	There is no description about who the Korean eye screening programme was targeting
Applicable to UK screening test of interest?	Y	L	Tests are in use in the UK
Target condition measured by reference test applicable to UK screening condition of interest?	Y	L	Yes the screening test and reference standard both aimed to test for open angle glaucoma which is the UK screening condition of interest.

Table 16. Zhao et al 2017

Publication	Zhao D, Guallar E, Gajwani P, Swenor B, Crews J, Saaddine J, et al. Optimizing Glaucoma Screening in High-Risk Population: Design and 1-Year Findings of the Screening to Prevent (SToP) Glaucoma Study. American Journal of Ophthalmology. 2017 August;180:18-28.
Study details	A prospective study to evaluate glaucoma screening and follow up in Baltimore in the US.
Study objectives	Evaluate glaucoma screening targeted at African Americans aged ≥50 in multiple inner city communities.

Inclusions	African- American men and women aged ≥50 living within inner city communities in Baltimore attending 'Screening to Prevent (SToP) Glaucoma study' community screening sessions.
Population	901 African- American men and women aged ≥50 living within inner city communities in Baltimore.
Intervention	Test for visual acuity (positive screen=≤ 20/40), non mydriatic fundus imaging of the macula and optic nerve (positive screen =CDR <0.7), and rebound tonometry to determine intraocular pressure (positive screen=IOP≥23mmHg).
Comparator/ reference standard	No details of 'definitive eye examination' were provided.
Outcomes	901 people between January 2015 and October 2015 were screened of whom 356 (39.5%) were referred for a definitive eye examination. Of the 356 people referred 153(43%) people attended the definitive eye examination. Of the 153 people attending for the definitive eye examination 57(37.3%) were diagnosed with suspected glaucoma and 21(13.7%) with definite glaucoma. Of those 78 people 29(37%) had been previously diagnosed and 49 (63%) were new cases. The funduscopic photos of the 901 people originally screened were reviewed by a glaucoma specialist and 10 further cases originally missed were called back whilst 43 people referred did not have any signs of eye abnormality. The sensitivity and specificity of an accurate referral based on photographic grading was 97.0% and 92.0% respectively. Of the 901 participants the overall yield of the programme for glaucoma was 8.7% and for and significant eye disease (Includes glaucoma, cataracts, diabetic retinopathy or age-related macular degeneration) 14.5%.

Quality appraisal

Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Domain I: Patient selection			
Consecutive or random sample of population enrolled?	Y	L	Participants were recruited via community venues and specific inclusion and exclusion criteria were described.
Case-control design avoided?	Y	L	
Inappropriate exclusions avoided?	Y	L	Exclusions were to ensure a higher risk group of people were screened (by age, family history and ethnicity).
Domain II: Index Test			

	Index test results interpreted without knowledge of reference standard results?	N	H	Screeners and participants were unaware of reference standard results (screening test was carried out prior to reference standard). However some people with previously known glaucoma (29(37%) of 78 cases diagnosed) were included in the study and this would have been known to the screeners.
	Threshold pre-specified?	Y	L	Thresholds for definitive and suspected glaucoma were pre-specified.
	Domain II: Reference standard			
	Reference standard likely to correctly classify condition?	U	U	The definitive eye examination was not described.
	Reference standard results interpreted without knowledge of index test results?	N	H	Ophthalmologists carrying out the definitive eye examination knew the screening test results of participants.
	Domain IV: Test strategy flow and timing			
	Appropriate interval between index test and reference standard?	U	U	No information was reported on time between index test and reference standard
	Did all participants receive same reference standard?	U	U	The reference standard is not described and there is no mention whether the same tests were used in each of the definitive eye examinations.
	All patients included in analysis?	N	H	A significant proportion of people referred for a definitive eye examination following screening did not attend (57%)
	Applicability			
	Applicable to UK screening population of interest?	Y	L	This is a targeted screening programme based on age, ethnicity and family history in inner city communities. It could be applied to any group within the adult population.
	Applicable to UK screening test of interest?	Y	L	These tests are in use in the UK
	Target condition measured by reference test applicable to UK screening condition of interest?	Y	L	Yes the screening test and reference standard both aimed to test for open angle glaucoma which is the UK screening condition of interest.

Table 17. Boland et al 2016

Publication	Boland MV, Gupta P, Ko F, Zhao D, Guallar E, Friedman DS. Evaluation of Frequency-Doubling Technology Perimetry as a Means of Screening for Glaucoma and Other Eye Diseases Using the National Health and Nutrition Examination Survey. JAMA Ophthalmology. 2016 Jan;134 (1):57-62.
Study details	Retrospective cohort study.
Study objectives	To understand the performance of frequency-doubling technology perimetry performed as part of the 2005 -2008 National Health and Nutrition Survey (NHANES) in respect of its use for screening for glaucoma.
Inclusions	Participants in the 2005 -2008 NHANES.
Population	548 participants (1073 eyes) with at least 1 eye with a cup disc ratio of 0.6 or greater and 360 eyes of 180 participants with CDR of less than 0.6 determined by fundus photography.
Intervention	FDT perimetry undertaken as part of the NHANES 2005-2008 evaluation (positive screen =at least 1 eye with a cup disc ratio of 0.6 or greater and 360 eyes of 180 participants with CDR of less than 0.6).
Comparator/ reference standard	Re-grading of fundus photographs (by a glaucoma expert) taken as part of the 2005-2008 NHANES evaluation.
Outcomes	Any FDT perimetry outcome that resulted in a referral (test results that were abnormal, unreliable or incomplete) was compared with the re-graded fundus images. Analysis assumed that the only cause of visual field defects was glaucoma. For participants with CDR ≤0.6 FDT had a sensitivity of 33% (95% CI 0% to 87%) and specificity of 77% (95% CI 71% to 84%) for identifying glaucoma. For participants with CDR ≥0.6 FDT had a sensitivity of 66% (95% CI 59% to 73%) and specificity of 70% (95%CI 66% to 85%) For all participants FDT had a sensitivity of 54.5% (95% CI 48% to 61%) and specificity of 76.8% (95%CI 76% to 78%) A significant proportion of those referred for further evaluation following FDT would be on the basis of the test not being done (14%), it being insufficient (1.5%) and unreliable (11%) compared to an abnormal test result (5.6%)
Quality appraisal	

Question	**Assessment (Y, N, unclear)**	**Risk of Bias (low, high, unclear)**	**Supporting info**
Domain I: Patient selection			

	Consecutive or random sample of population enrolled?	Y	L	The initial screening tests were carried out as part of the NHANES 2005-2008 evaluation that uses a stratified random sampling method to obtain a representative health data sample of the non-institutionalised US population. The fundus photographs of all those participating in the study were re-graded with the exception of people with no light perception vision or eye infection.
	Case-control design avoided?	Y	L	
	Inappropriate exclusions avoided?	Y	L	Only those with no light perception vision or eye infection were excluded.
	Domain II: Index Test			
	Index test results interpreted without knowledge of reference standard results?	U	U	It is not clear if the 3 glaucoma specialists knew the results of the FDT perimetry or vice versa when they regraded the fundus images.
	Threshold pre-specified?	Y	L	Thresholds for definitive and suspected glaucoma were pre-specified.
	Domain II: Reference standard			
	Reference standard likely to correctly classify condition?	N	H	The reference standard was the specialist evaluation of fundus images. This would not normally be the only method used to determine suspected or definitive glaucoma.
	Reference standard results interpreted without knowledge of index test results?	U	U	It is not clear if the 3 glaucoma specialists knew the results of the FDT perimetry or vice versa when they regraded the fundus images.
	Domain IV: Test strategy flow and timing			
	Appropriate interval between index test and reference standard?	U	U	The FDT perimetry and fundus imaging were likely to have been carried out during the same appointment. However the re-grading of the fundus images would not have taken place until some years later.
	Did all participants receive same reference standard?	Y	L	Yes – regrading of fundus images by the same group of glaucoma specialists.
	All patients included in analysis?	Y	L	

	Applicability			
	Applicable to UK screening population of interest?	Y	L	Yes – general population sample although a general population sample in the UK may have a different composition.
	Applicable to UK screening test of interest?	Y	L	These tests are in use in the UK.
	Target condition measured by reference test applicable to UK screening condition of interest?	Y	L	Yes the screening test and reference standard both aimed to test for open angle glaucoma which is the UK screening condition of interest.

Table 18. Dabasia et al 2015

Publication	Dabasia PL, Fidalgo BR, Edgar DF, Garway-Heath DF, Lawrenson JG. Diagnostic accuracy of technologies for glaucoma case-finding in a community setting. Ophthalmology. 2015 December;122(12):2407-15.
Study details	Prospective cross sectional study.
Study objectives	To assess performance of FDT perimetry, optical coherence tomography and ocular response analyser to detect glaucoma in a community in London.
Inclusions	People ≥60 years of age.
Population	505 members of a community local to a university-based eye clinic where the screening tests were carried out.
Intervention	• Frequency doubling technology(FDT) perimetry - visual field test • Moorfields Motion displacement test (MMDT) - visual function test • Optical coherence tomography (OCT) - retinal imaging • Ocular response analyser (ORA) - measure of IOP
Comparator	Standard ophthalmic eye examination using: • Humphrey field analyser - visual field test • Anterior segment assessment by biomicroscope/gonioscopy – examination of the front of the inside of the eye • Goldmann applanation tonometer (measure of IOP) • Posterior segment examination performed with dilated pupils using indirect ophthalmoscopy and fundus photography to image the retina

Outcomes

505 participants were screened with the index tests followed by the reference standard tests. The reference standard resulted in 26(5.1%) people classified as having definite glaucoma, 32(6.4%) classified as glaucoma suspects and 17(3.4%) classified as having ocular hypertension.

Screening test statistics for the best measure of each individual test for glaucoma suspect and definitive glaucoma

Test	Sensitivity (glaucoma suspect + glaucoma definitive) % (95%CI)	Specificity (glaucoma suspect + glaucoma definitive) % (95%CI)	Sensitivity (definitive glaucoma) % (95%CI)	Specificity (definitive glaucoma) % (95%CI)
FDT – 1 or more missed locations at p<1% level	62.1(49.2 to 73.4)	80.5(76.6 to 84.0)	88.5(71.0 to 96.0)	79.1(75.2 to 82.5)
MMDT(global probability of true damage≥3.0)	51.7(39.2 to 64.1)	82.8(79.0 to 86.0)	65.4(46.2 to 80.6)	81.2(77.5 to 84.5)
OCT - Ganglion cell complex – focal loss volume falling outside 99% normal limit of the manufacturers normal database for this equipment	46.6(34.2 to 59.2)	91.4(88.4 to 93.7)	73.1(53.9 to 86.3)	90.3(87.3 to 92.6)
OCT - Ganglion cell complex – global loss volume falling outside 99% normal limit of the manufacturers normal database for the equipment	24.1(15.0 to 36.5)	98.2(96.5 to 99.71	46.2(28.8 to 64.5)	97.9(96.2 to 98.8)
OCT - RNFL thickness – inferior quadrant falling outside 99% normal limit of the manufacturers normal database for the equipment	46.6(34.3 to 59.2)	96.2(94.0 to 97.6)	76.9(57.9 to 89.0)	95.0(92.6 to 96.6)
ORA – cornea compensated IOP	24.1(15.0 to 36.5)	88.6(85.3 to 91.2)	26.9(13.7 to 46.1)	87.9(84.7 to 90.5)

Combination of tests in the screening examination: test statistics for glaucoma suspect and definitive glaucoma

Screening examination and referral criteria	Number of suspect and definitive glaucoma cases identified by reference standard	Sensitivity% (95% CI)	Specificity% (95% CI)	PPV%	NPV
OCT - RNFL thickness – inferior quadrant (>99% normal limit for this equipment) and **FDT** (≥1 missed location at p<1% level)	Suspect(n=32) and definitive OAG (n=26)	79.3(67.2 to 87.7)	63.3(58.9 to 67.6)	22.5[10]	NR
	Definitive OAG(n=26)	100 (87.1 to 100)	65.2(60.7 to 69.5)	14.8‡‡	NR

PPV calculated by reviewer.

Using Bayesian analysis the authors combined the best performing test parameters and cut-offs to determine post –test probabilities.

For glaucoma suspect/definite glaucoma a post-test probability of >90% (compared with a pre-test probability of 11.5%) and for definitive glaucoma a post-test probability of >85% (compared with a pre-test probability of 5%) was achieved when the following tests were combined in series:

FDT≥1missed location at p<1% level OR MMDT global probability of true damage≥3.0 AND RNFL inferior quadrant thickness OR Ganglion cell complex global loss volume AND corneal compensated IOP of >21mmHg

The combination of tests for structural and functional abnormalities are not independent of one another which will lead to over estimation of Bayesian analysis post-test probability estimates.

Quality appraisal

Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Domain I: Patient selection			
Consecutive or random sample of population enrolled?	Y	L	Participants were invited to be screened by information distributed to community venues and local optometry practices.

[10] Calculated by reviewer

	Case-control design avoided?	Y	L	
	Inappropriate exclusions avoided?	Y	L	The only exclusion was people under the age of 60.
	Domain II: Index Test			
	Index test results interpreted without knowledge of reference standard results?	Y	L	Index test results were masked to findings of the reference standard and the person undertaking the index tests had no knowledge of previous ocular history or reference standard results.
	Threshold pre-specified?	Y	L	A range of cut-offs were pre-specified and applied to the results to determine the best combination of tests and thresholds.
	Domain II: Reference standard			
	Reference standard likely to correctly classify condition?	Y	L	Yes the definitive eye examination tests aimed to detect and classify OAG.
	Reference standard results interpreted without knowledge of index test results?	Y	L	The reference standard examination was carried out on the same day as the index tests. It is not clear from the methodology if personnel undertaking the reference standard were involved and knew the results of the index tests however the discussion states that clinicians undertaking the reference standard were masked to the outcome of the index test.
	Domain IV: Test strategy flow and timing			
	Appropriate interval between index test and reference standard?	Y	L	The reference standard examination was carried out on the same day as the index tests.
	Did all participants receive same reference standard?	Y	L	
	All patients included in analysis?	Y	L	
	Applicability			
	Applicable to UK screening population of interest?	Y	L	It was a UK population over the age of 60

	Applicable to UK screening test of interest?	Y	L	Tests are in use in the UK
	Target condition measured by reference test applicable to UK screening condition of interest?	Y	L	Yes they are testing for open angle glaucoma in the UK which is the UK screening condition of interest.

Table 19. Wahl et al 2016

Publication	Wahl J, Barleon L, Morfeld P, Deters C, Lichtmes A, et al The Evonik-Mainz Eye Care-Study (EMECS): Design and execution of the screening investigation. PLoS ONE 2014 ;9(6):e98538.
Study details	A prospective screening study.
Study objectives	To develop an expert system for glaucoma screening in a working population based on optic nerve images, FDT perimetry and non-contact tonometry.
Inclusions	Evonik industry emplyoyee aged ≥40.
Population	4183 of 13037 employees aged ≥40 examined at 13 sites of Evonik industries, Germany, between June 2007 and March 2008.
Intervention	• Non-mydriatic fundus photography – to evaluate the optic disc • Frequency doubling technology perimetry – to measure the visual field • Non- contact tonometry to measure IOP • Use of an algorithm and 3 screening models based on the results of the three tests to determine referral
Comparator/ reference standard	Clinical judgement based on the results of: • Non-mydriatic fundus photography – to evaluate the optic disc • Frequency doubling technology perimetry – to measure the visual field • Non- contact tonometry to measure IOP • Pachymetry to determine central corneal thickness • Visual acuity and objective refraction • Confocal laser scanning ophthalmoscopy All results collected each day, were sent to the Department of Ophthalmology at Mainz University Medical Center, where an evaluation was performed promptly by an experienced ophthalmologist Glaucoma suspects were identified on the basis of the evaluation of optic disc photography, IOP and FDT. The optic disc was categorised by size, cup-disc-ratio (CDR), ISNT-rule, morphology of excavation, disc haemorrhages and asymmetry between eyes.

Outcomes

The results as determined by the experienced ophthalmologist were compared with the use of the algorithm and three alternative screening models applied to the results of the FDT perimetry, non-contact tonometry and fundus photography.

Algorithm 1:Points are given for the following criteria - IOP>28mmHg, IOP difference between eyes>2 mmHg, CDR(max) difference between eyes≥0.1, severity of excavation of optic nerve head, ISNT rule not respected, optic disc haemorrhage, CDR(max)>0.6 in small >0.7 in medium and >0.8 in large optic nerve head. A score of more than 1 point =possible glaucoma and score of >6 points is probable glaucoma.

Screening model 1: At least 1 eye had IOP>21mmHg or FDT was abnormal

Screening model 2:At least 1 eye had IOP>21mmHg and FDT was abnormal

Screening model 3: At least 1 eye IOP>21mHg

Screening test performance statistics for suspected glaucoma

	No glaucoma suspect	Glaucoma suspect	Sensitivity %(95% CI)	Specificity % (95% CI)	PPV% (95% CI)	NPV% (95% CI)	PLR	NLR
Algorithm	4051 (97.22%)	116 (2.79%)	83.78 (75.72 to 89.54)	99.43 (99.15 to 99.62)	80.14 (71.92 to 86.45)	99.56 (99.30 to 99.72)	147.8	0.16
Screening model 1	3589 (86.13%)	578 (13.87%)	65.77 (56.58 to 73.98)	87.55 (86.50 to 88.53)	12.63 (10.16 to 15.59)	99.94 (98.55 to 99.23)	5.28	0.39
Screening model 2	4146 (99.5%)	21 (0.5%)	6.31 (3.04 to 12.64)	99.65 (99.42 to 99.80)	33.33 (16.79 to 55.33)	97.49 (96.97 to 97.93)	18.3	0.94
Screening model 3	3808 (91.38%)	358 (8.59%)	44.45 (46.08 to 64.45)	92.68 (91.83 to 93.44)	17.04 (13.49 to 21.29)	98.71 (98.30 to 99.03)	7.57	0.48

Screening test performance statistics for probable glaucoma

	No probable glaucoma	Probable Glaucoma	Sensitivity (95% CI)	Specificity (95% CI)	PPV% (95% CI)	NPV% (95% CI)	PLR	NLR
Algorithm	4155 (99.71%)	12 (0.29%)	84.62 (54.94 to 96.12)	99.98 (99.82 to 99.99)	91.67 (58.68 to 98.84)	99.95 (99.81 to 99.99)	3514.92	0.15
Screening model 1	3589 (86.13%)	578 (13.87%)	100%	86.40	2.25 (1.31 to 3.83)	100%	7.35	0

					(85.32 to 87.41)				
	Screening model 2	4146 (99.5%)	21 (0.5%)	15.38 (3.87 to 45.06)	99.54 (99.28 to 99.71)	9.52 (2.39 to 31.13)	99.73 (96.52 to 99.85)	33.64	0.85
	Screening model 3	3808 (91.38%)	358 (8.59%)	61.54 (34.36 to 83.02)	91.57(90.69 to 92.38)	2.23 (1.12 to 4.40)	99.87 (99.68 to 99.95)	7.30	0.42

CI – confidence interval, PPV – Positive predictive value, NPV – negative predictive value, PLR – positive likelihood ratio, NLR – negative likelihood ratio

Quality appraisal

Question	**Assessment (Y, N, unclear)**	**Risk of Bias (low, high, unclear)**	**Supporting info**
Domain I: Patient selection			
Consecutive or random sample of population enrolled?	Y	L	Participants were invited to be screened through workplace communications.
Case-control design avoided?	Y	L	
Inappropriate exclusions avoided?	Y	L	People aged >40 were invited.
Domain II: Index Test			
Index test results interpreted without knowledge of reference standard results?	U	U	The index test results were pseud anonymised but it isn't clear if the data set retained the reference standard result.
Threshold pre-specified?	N	H	No – the reference standard was based on the decision of a glaucoma expert on review of test results. A screening algorithm was designed based on how the expert made their decision. The algorithm was then applied to the pseudo anonymised test results. The reference test and screening test (algorithm) were not independent compromising the validity of the results.
Domain II: Reference standard			

Reference standard likely to correctly classify condition?	Y	N	A wide range of tests and images were gathered that were interpreted remotely by a glaucoma expert.
Reference standard results interpreted without knowledge of index test results?	Y	L	Yes the reference standard was undertaken first prior to an algorithm being developed to apply to screening examination results.
Domain IV: Test strategy flow and timing			
Appropriate interval between index test and reference standard?	U	U	No information was reported on time between index test and reference standard.
Did all participants receive same reference standard?	Y	L	Yes – all results were interpreted by the same ophthalmologist.
All patients included in analysis?	Y	L	All but 14(0.33%) patients where FDT perimetry result was not available.
Applicability			
Applicable to UK screening population of interest?	Y	L	Yes – all people invited over the age of 40 with in an occupational setting.
Applicable to UK screening test of interest?	Y	L	These tests are in use in the UK.
Target condition measured by reference test applicable to UK screening condition of interest?	Y	L	Yes the reference standard was testing for open angled glaucoma which is the UK screening condition of interest.

Appendix 4 – UK NSC reporting checklist for evidence summaries

All items on the UK NSC Reporting Checklist for Evidence Summaries have been addressed in this report. A summary of the checklist, along with the page or pages where each item can be found in this report, is presented in Table 20.

Table 20. UK NSC reporting checklist for evidence summaries

	Section	Item	Page no.
1.	TITLE AND SUMMARIES		
1.1	Title sheet	Identify the review as a UK NSC evidence summary.	Title page
1.2	Plain English summary	Plain English description of the executive summary.	4
1.3	Executive summary	Structured overview of the whole report. To include: the purpose/aim of the review; background; previous recommendations; findings and gaps in the evidence; recommendations on the screening that can or cannot be made on the basis of the review.	5
2.	INTRODUCTION AND APPROACH		
2.1	Background and objectives	Background – Current policy context and rationale for the current review – for example, reference to details of previous reviews, basis for current recommendation, recommendations made, gaps identified, drivers for new reviews Objectives – What are the questions the current evidence summary intends to answer? – statement of the key questions for the current evidence summary, criteria they address, and number of studies included per question, description of the overall results of the literature search. Method – briefly outline the rapid review methods used.	8
2.2	Eligibility for inclusion in the review	State all criteria for inclusion and exclusion of studies to the review clearly (PICO, dates, language, study type, publication type, publication status etc.) To be decided *a priori*.	14
2.3	Appraisal for quality/risk of bias tool	Details of tool/checklist used to assess quality, e.g. QUADAS 2, CASP, SIGN, AMSTAR.	14
3.	SEARCH STRATEGY AND STUDY SELECTION (FOR EACH KEY QUESTION)		
3.1	Databases/ sources searched	Give details of all databases searched (including platform/interface and coverage dates) and date of final search.	34

3.2	Search strategy and results	Present the full search strategy for at least one database (usually a version of Medline), including limits and search filters if used. Provide details of the total number of (results from each database searched), number of duplicates removed, and the final number of unique records to consider for inclusion.	33
3.3	Study selection	State the process for selecting studies – inclusion and exclusion criteria, number of studies screened by title/abstract and full text, number of reviewers, any cross checking carried out.	12,14,16,28, 44
4.	STUDY LEVEL REPORTING OF RESULTS (FOR EACH KEY QUESTION)		
4.1	Study level reporting, results and risk of bias assessment	For each study, produce a table that includes the full citation and a summary of the data relevant to the question (for example, study size, PICO, follow-up period, outcomes reported, statistical analyses etc.). Provide a simple summary of key measures, effect estimates and confidence intervals for each study where available. For each study, present the results of any assessment of quality/risk of bias.	Study level reporting: 46 Quality assessment: 26, 46
5.	QUESTION LEVEL SYNTHESIS		
5.1	Description of the evidence	For each question, give numbers of studies screened, assessed for eligibility, and included in the review, with summary reasons for exclusion.	16,29
5.2	Combining and presenting the findings	Provide a balanced discussion of the body of evidence which avoids over reliance on one study or set of studies. Consideration of four components should inform the reviewer's judgement on whether the criterion is 'met', 'not met' or 'uncertain': quantity; quality; applicability and consistency.	17,30
5.3	Summary of findings	Provide a description of the evidence reviewed and included for each question, with reference to their eligibility for inclusion. Summarise the main findings including the quality/risk of bias issues for each question. Have the criteria addressed been 'met', 'not met' or 'uncertain'?	27,30
6.	REVIEW SUMMARY		
6.1	Conclusions and implications for policy	Do findings indicate whether screening should be recommended? Is further work warranted? Are there gaps in the evidence highlighted by the review?	31
6.2	Limitations	Discuss limitations of the available evidence and of the review methodology if relevant.	32

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