



# City Research Online

## City, University of London Institutional Repository

---

**Citation:** Fidalgo, B. R., Dabasia, P., Jindal, A., Edgar, D. F. ORCID: 0000-0001-9004-264X, Ctori, I. ORCID: 0000-0003-1523-4996, Peto, T. and Lawrenson, J. ORCID: 0000-0002-2031-6390 (2019). Role of advanced technology in the detection of sight-threatening eye disease in a UK community setting.. *BMJ Open Ophthalmology*, 4(1), e000347.. doi: 10.1136/bmjophth-2019-000347

This is the accepted version of the paper.

This version of the publication may differ from the final published version.

---

**Permanent repository link:** <https://openaccess.city.ac.uk/id/eprint/23827/>

**Link to published version:** <http://dx.doi.org/10.1136/bmjophth-2019-000347>

**Copyright and reuse:** City Research Online aims to make research outputs of City, University of London available to a wider audience. Copyright and Moral Rights remain with the author(s) and/or copyright holders. URLs from City Research Online may be freely distributed and linked to.

---

City Research Online:

<http://openaccess.city.ac.uk/>

[publications@city.ac.uk](mailto:publications@city.ac.uk)

---

# Role of advanced technology in the detection of sight-threatening eye disease in a UK community setting

Bruno R Fidalgo ,<sup>1</sup> Priya Dabasia,<sup>1</sup> Anish Jindal ,<sup>1</sup> David F Edgar,<sup>1</sup> Irene Ctori ,<sup>1</sup> Tunde Peto,<sup>2</sup> John G Lawrenson <sup>1</sup>

**To cite:** Fidalgo BR, Dabasia P, Jindal A, *et al*. Role of advanced technology in the detection of sight-threatening eye disease in a UK community setting. *BMJ Open Ophthalmology* 2019;**4**:e000347. doi:10.1136/bmjophth-2019-000347

► Additional material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/bmjophth-2019-000347>).

Received 27 May 2019  
Revised 23 September 2019  
Accepted 31 October 2019



© Author(s) (or their employer(s)) 2019. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

<sup>1</sup>Applied Vision Research Centre, School of Health Sciences, City, University of London, London, UK

<sup>2</sup>School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Belfast, UK

## Correspondence to

Professor John G Lawrenson; [j.g.lawrenson@city.ac.uk](mailto:j.g.lawrenson@city.ac.uk)

## ABSTRACT

**Background/aims** To determine the performance of combinations of structural and functional screening tests in detecting sight-threatening eye disease in a cohort of elderly subjects recruited from primary care.

**Methods** 505 subjects aged ≥60 years underwent frequency doubling technology (FDT) perimetry, iVue optical coherence tomography (iWellness and peripapillary retinal nerve fibre layer (RNFL) scans) and intraocular pressure with the Ocular Response Analyzer, all performed by an ophthalmic technician. The reference standard was a full ophthalmic examination by an experienced clinician who was masked to the index test results. Subjects were classified as presence or absence of sight-threatening eye disease (clinically significant cataract, primary open-angle glaucoma, intermediate or advanced age-related macular degeneration and significant diabetic retinopathy). Univariate and multivariate logistic regression analyses were used to determine the association between abnormal screening test results and the presence of sight-threatening eye disease.

**Results** 171 subjects (33.8%) had one or more sight-threatening eye diseases. The multivariate analysis found significant associations with any of the target conditions for visual acuity of <6/12, an abnormal FDT and peripapillary RNFL thickness outside the 99% normal limit. The sensitivity of this optimised screening panel was 61.3% (95% CI 53.5 to 68.7), with a specificity of 78.8% (95% CI 74.0 to 83.1), a positive predictive value of 59.5% (95% CI 53.7 to 65.2) and an overall diagnostic accuracy of 72.9% (95% CI 68.8 to 76.8).

**Conclusions** A subset of screening tests may provide an accurate and efficient means of population screening for significant eye disease in the elderly. This study provides useful preliminary data to inform the development of further larger, multicentre screening studies to validate this screening panel.

## INTRODUCTION

Population ageing is leading to substantial increases in visual impairment.<sup>1</sup> Sight loss from cataract, age-related macular degeneration (AMD), diabetic retinopathy and uncorrected refractive error affects approximately two million of the UK population.<sup>1</sup> The burden of sight loss disproportionately affects the elderly,<sup>2</sup> with one in five people

## Key messages

### What is already known about this subject?

► Previous studies have found that no single test has sufficient predictive power to detect sight-threatening eye disease. Consequently, population screening for single sight-threatening disorders has not been shown to be cost effective.

### What are the new findings?

► This study found that a subset of screening tests that evaluate ocular structure and function had good discriminatory power for detecting sight-threatening eye disease in a cohort of elderly participants recruited from primary care.

### How might these results change the focus of research or clinical practice?

► The results provide useful data to inform the development of larger, multicentre population studies to evaluate the effectiveness and cost-effectiveness of screening for eye disease in the elderly.

aged 75 years or over, and one in two people aged 90 years and over living with sight loss.<sup>3</sup> Poor access to routine NHS sight testing in ‘at-risk’ populations, coupled with the absence of symptoms in the early stages of many of these diseases, can lead to delayed or late presentation.<sup>4 5</sup> Given that a significant proportion of sight loss can be prevented through early detection and timely therapeutic interventions, it is likely that investment in prevention and screening for sight-threatening eye disease would lead to improved socioeconomic outcomes.<sup>6</sup>

Previous studies have examined the predictive power of individual screening tests to detect eye disease in both clinic-based and general populations and have found that no single test has sufficient predictive power to detect sight-threatening eye disease.<sup>7–10</sup> By contrast, the performance of combining screening tests has shown greater promise. For example, Kopplin and Mansberger evaluated a test battery performed by ophthalmic

technicians for the detection of visually significant eye disease in a population of American Indian and Alaskan Native participants.<sup>11</sup> The authors identified that visual acuity worse than 6/12 (20/40), abnormal or poor-quality non-mydratric photography, abnormal frequency doubling technology (FDT) perimetry, and abnormal or poor-quality confocal scanning laser ophthalmoscopy had the greatest predictive value.

We have previously demonstrated that combining structural and visual-function tests improves case detection of primary open-angle glaucoma (POAG) in a representative population of elderly subjects in the community.<sup>12</sup> The aim of the current study was to extend this analysis to determine the performance of screening test combinations in detecting sight-threatening eye disease in the same population.

## METHODS

### Study population

This prospective diagnostic accuracy study was conducted in an urban community eye clinic in London, UK, between September 2012 and September 2013. Men and women aged  $\geq 60$  years were invited to participate via a written invitation sent to community groups and local optometry practices. There were no exclusion criteria, and participants with prediagnosed ocular disease were included. Participants underwent a series of technology-based index tests followed by a reference standard ophthalmic examination (detailed further), conducted on the same day, to establish ocular health status. [Figure 1](#) shows the study flow diagram.

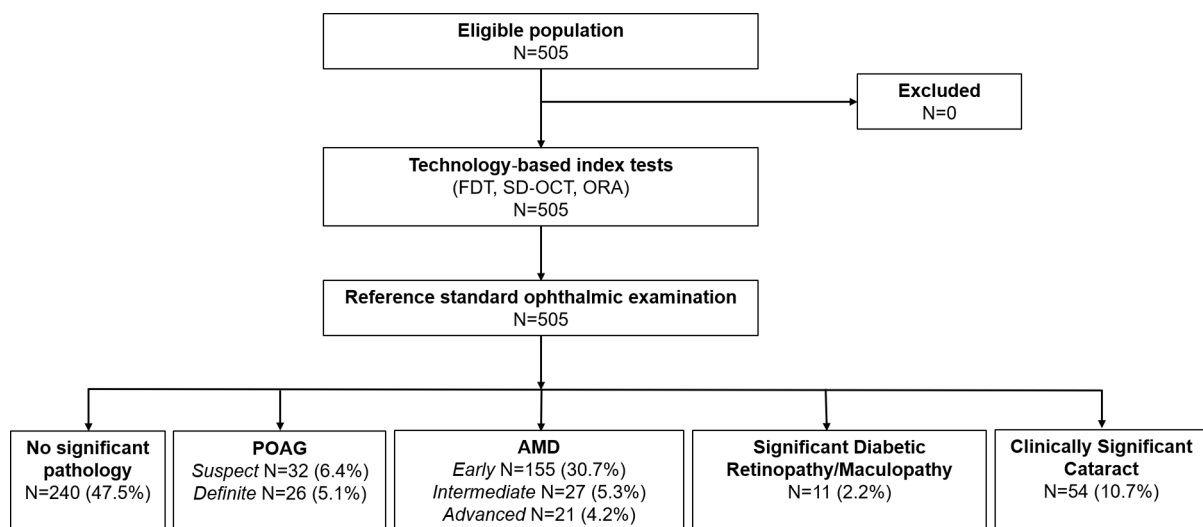
### Index tests

The technology-based assessment comprised the measurement of intraocular pressure (IOP) using the Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments, Depew, NY, USA), assessment of visual fields with

first-generation FDT perimetry (FDT; Carl Zeiss Meditec, Dublin, CA, USA) in C-20-5 suprathreshold mode and measurement of structural parameters of the macula and optic nerve head by spectral domain optical coherence tomography (SD-OCT) (iVue SD-OCT; Optovue, Fremont, CA, USA). Two optical coherence tomography (OCT) scans were performed: the proprietary iWellness protocol, which reports full retinal thickness and ganglion cell complex (GCC) thickness with normative comparisons, and a peripapillary retinal nerve fibre layer (RNFL) scan. An experienced ophthalmic technician performed all index tests with no prior knowledge of the subjects' ocular status or findings from the reference standard ophthalmic examination. Thresholds of abnormality for the index tests were prespecified and were based on commonly used cut-offs reported in the literature or manufacturers' suggested thresholds, based on comparisons with the instruments' internal normative database. For the FDT, an abnormal result was defined using two thresholds:  $\geq 1$  location missed at either the  $p < 5\%$  or the  $p < 1\%$  significance level. The test was repeated once if one or more locations were missed or if the result was unreliable. For the SD-OCT, the defined cut-off for abnormality was any parameter falling outside the 99% normal limit based on the manufacturer's integrated normal database; IOP  $> 21$  mm Hg was used as the threshold for the ORA.

### Reference standard ophthalmic examination

All participants underwent a standard ophthalmological examination conducted by an experienced clinician who was trained and validated in glaucoma according to standard UK practice and also completed grader accreditation in diabetic retinopathy and AMD at the Reading Centre, Moorfield's Eye Hospital, London, UK. The reference standard examination was conducted on the same day as the index tests, and the clinician was masked to the



**Figure 1** Study flow diagram. The number of eye conditions exceeds the number of participants due to ocular comorbidity. AMD, age-related macular degeneration; FDT, frequency doubling technology; ORA, Ocular Response Analyzer; POAG, primary open-angle glaucoma; SD-OCT, spectral domain optical coherence tomography.

**Table 1** Diagnostic criteria used for classifying the most prevalent eye diseases<sup>n</sup>
**Definitions of eye diseases**

Eye condition	Classification	Description
POAG	Definite	1. Open anterior chamber angle 2. Localised absence of neuroretinal rim, cup:disc ratio $\geq$ 0.7, or interocular asymmetry in vertical cup:disc ratio $\geq$ 0.2 in similar-sized discs 3. Presence of a concordant glaucomatous field defect based on criteria amended from Hodapp <i>et al</i> <sup>15</sup>
	Suspect	Features of glaucomatous optic neuropathy but with normal or equivocal fields or subjects with glaucomatous visual field defects but without concordant disc damage
Diabetic retinopathy*	Background retinopathy (R1)	Microaneurysms, dot and blot haemorrhages, venous loops and cotton wool spots
	Preproliferative retinopathy (R2)	Venous beading, venous reduplication, multiple blot haemorrhages, intraretinal microvascular abnormality
	Proliferative retinopathy (R3)	Active proliferative retinopathy
	Maculopathy (M1)	Groups of exudates, clinically significant macular oedema
AMD	Early AMD (AREDS category 2) <sup>34</sup>	Several small drusen or a few medium-sized drusen in one or both eyes
	Intermediate AMD (AREDS category 3) <sup>34</sup>	Many medium-sized drusen or one or more large drusen ( $\geq$ 125 $\mu$ m) in one or both eyes
	Advanced AMD (AREDS category 4) <sup>34</sup>	Geographical atrophy of the RPE involving the foveal centre or any features of neovascular AMD
Clinically significant cataract	LOCS II grading <sup>35</sup>	LOCS II score of $\geq$ 2 for cortex, posterior subcapsular, nuclear or hypermature cataract

\*The grading system for diabetic retinopathy was based on that used by the UK NHS Diabetic Eye Screening Programme (<https://www.gov.uk/government/publications/diabetic-eye-screening-retinal-image-grading-criteria>). AMD, age-related macular degeneration; AREDS, Age-Related Eye Disease Study; LOCS II, Lens Opacities Classification System II; POAG, primary open-angle glaucoma.

index test results. The reference examination consisted of LogMAR best-corrected visual acuities, full anterior segment assessment by slit-lamp biomicroscopy, assessment of limbal anterior chamber depth (with potentially occludable angles examined using gonioscopy), measurement of IOP using the Goldmann applanation tonometer, posterior segment examination through dilated pupils using indirect ophthalmoscopy and threshold visual field testing with a Humphrey field analyzer using Swedish Interactive Thresholding Algorithm (SITA) standard 24-2 pattern. The diagnostic criteria classifying the most commonly identified eye diseases are given in [table 1](#).

### Sample size calculation

The sample size was originally determined based on an anticipated sensitivity of 0.75 to detect POAG<sup>13</sup> with a minimal acceptable precision of  $\pm$ 0.25 with 0.95 probability. This would require approximately 50 cases, and based on an anticipated prevalence of POAG in an elderly population of 8%–10%,<sup>14</sup> it was therefore estimated that at least 500 participants would be needed. For this secondary analysis, we prospectively determined that a similar number of cases of intermediate and advanced AMDs would be required, based on a disease prevalence of 8% in the target population,<sup>14</sup> an anticipated index

test sensitivity of 0.75 and an equivalent level of precision.<sup>11</sup>

### Statistical analysis

Summary statistics were tabulated and standard measurements of diagnostic accuracy (sensitivity, specificity, and positive and negative predictive values) were calculated to determine the ability of each index test to detect sight-threatening eye disease. We defined sight-threatening eye disease as a clinically significant cataract, definite or suspect POAG, intermediate or advanced AMD and significant diabetic retinopathy (proliferative or preproliferative) or diabetic maculopathy.

The unit of analysis was the individual participant and a comparison was made between the most abnormal index test from either eye and the overall reference standard classification. Unreliable results from the FDT and data from repeatedly poor-quality ORA and SD-OCT acquisitions were removed from the analysis.

Binomial logistic regression was used to identify the index tests with significant univariate associations ( $p < 0.05$ ) with individual eye diseases. Those with significant univariate associations were included as potential covariates in a multivariate model using stepwise logistic regression. A significance level of  $p < 0.05$  was set for

**Table 2** Eye disease identified by the reference standard examination

Condition	n (%)
<b>AMD</b>	
Early	155 (30.7)
Intermediate	27 (5.3)
Advanced	21 (4.2)
<b>Diabetic retinopathy</b>	
Background	26 (5.1)
Preproliferative	4 (0.8)
Proliferative	2 (0.4)
Maculopathy	5 (1.0)
<b>POAG</b>	
Suspect	32 (6.4)
Definite	26 (5.1)
Cataract (clinically significant)	54 (10.7)

AMD, age-related macular degeneration; POAG, primary open-angle glaucoma.

entering and retaining the covariate in the final model. The impact of adding best-corrected visual acuity of <6/12 to the model was also evaluated post hoc, and the diagnostic performance of the final multivariate subset of screening tests was calculated.

All statistical analyses were performed using SPSS software V.21.0 ([www.ibm.com/SPSS\\_Statistics](http://www.ibm.com/SPSS_Statistics)) and MedCalc V.18.0 ([www.medcalc.org](http://www.medcalc.org)).

### Patient and public involvement

There was no patient involvement in the development of the research question or the study design; however, patient networks were used in study recruitment.

### RESULTS

The study recruited a total of 505 subjects with a median age of 68 years (range 60–92). Fifty-nine per cent were female. Self-reported ethnicities were white (88%), South Asian (8%), black (2%), Chinese (1%) and ‘other’ (1%). Approximately 12% of the population had diabetes and 16% reported a family history of glaucoma.

The eye diseases most commonly identified by the reference standard ophthalmic examination were AMD (n=203, 40%), definitive or suspect POAG (n=58, 12%) and clinically significant cataract (n=54, 11%). Based on the criteria from Hodapp *et al.*,<sup>15</sup> the 26 definitive cases of POAG were classified as follows: early n=11 (42%), moderate n=6 (23%) and advanced n=9 (35%).

Table 2 provides a summary of the prevalence of eye disease in our sample based on the previously described diagnostic criteria.

On repeat examination, 97% of the index tests were reliable and of sufficient quality for analysis. A total of 195 (38.6%) participants passed all three screening tests; 186 (36.8%) participants had one abnormal test result;

112 (22.2%) had two abnormal results; and 12 (2.4%) showed an abnormality on all three tests.

The test most commonly failed was the FDT, with 193 (38%) participants missing  $\geq 1$  location(s) at the 5% level.

### Logistic regression analysis

Tables 3 and 4 show the results of the univariate and multivariate logistic regression analyses for the association between abnormal screening test results and the presence of sight-threatening eye disease. An abnormal FDT (based on one or more points missed at the  $p < 5\%$  or  $p < 1\%$  levels) was significantly associated with all target diseases. Visual acuity of <6/12 similarly showed univariate associations with all diseases, with the exception of significant diabetic retinopathy/maculopathy.

An abnormal SD-OCT (one or more parameters outside the 99% normal limit) was associated with POAG, AMD and diabetic retinopathy. The strongest association was observed between peripapillary RNFL thickness and POAG. An IOP of >21 mm Hg (determined by the ORA) was uncommon (14%) and showed no significant association with any of the target conditions. The sensitivity and specificity of the individual tests can be found in the online supplementary table.

The tests that were significant ( $p < 0.05$ ) in the univariate analysis were used as candidate covariates in a stepwise multivariate logistic regression model (table 4). In the multivariate analysis, visual acuity of <6/12 was significantly associated with a clinically significant cataract and AMD. An abnormal FDT at either the 5% or 1% level was associated with cataract and POAG, and an abnormal SD-OCT was predictive of POAG, AMD and diabetic retinopathy. The multivariate analysis identified that visual acuity of <6/12, one or more locations missed at the 5% level on the FDT and the peripapillary RNFL thickness outside the 99% normal limit were predictive of sight-threatening eye diseases. The diagnostic performance of this optimised screening panel for any of the target conditions is summarised in table 5. The sensitivity and specificity of the panel were 61.3% and 78.8%, respectively, with a positive predictive value of 59.5% and an overall diagnostic accuracy of 72.9%. Of the subjects with a potentially sight-threatening eye disease that would not have been detected using the optimised subset of tests, the majority were classified as either having a clinically significant cataract, suspect glaucoma or intermediate AMD. Only five participants with the most severe disease, definitive glaucoma (n=1), significant diabetic retinopathy (n=1) or advanced AMD (n=3), would have been missed.

### DISCUSSION

The current study evaluated the predictive value of a panel of standard screening tests in identifying sight-threatening eye disease in an elderly, predominantly white population. We established that reduced visual acuity, abnormal FDT and peripapillary RNFL thickness outside the 99% normal limit were predictive of any


**Table 3** Univariate association testing of abnormal screening results with significant ocular disease using logistic regression

	Clinically significant cataract		POAG (definite)		POAG (definite and suspect)		Significant diabetic retinopathy/maculopathy		Age related macular degeneration		Any sight-threatening eye disease	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Visual acuity <6/12	6.69 (3.57 to 12.46)	NS	4.54 (1.97 to 10.47)	2.06 (1.04 to 4.06)	NS	4.88 (2.54 to 9.40)	4.99 (2.90 to 8.60)					
Family history of glaucoma	NS	NS	4.93 (2.19 to 11.09)	2.92 (1.59 to 5.36)	NS	NS	NS					
IOP >21 mm Hg	NS	NS	NS	NS	NS	NS	NS					
FDT ≥ 1 point missed at 1% level	3.07 (1.72 to 5.47)	28.69 (8.45 to 97.48)	6.68 (3.74 to 11.92)	5.29 (1.25 to 22.48)	2.95 (1.60 to 5.41)	5.48 (3.55 to 8.46)						
FDT ≥ 1 point missed at 5% level	3.45 (1.91 to 6.23)	22.21 (5.19 to 95.15)	5.20 (2.83 to 9.55)	5.02 (1.00 to 25.11)	2.75 (1.50 to 5.06)	4.60 (3.10 to 6.83)						
SD-OCT (GCC thickness)	NS	28.64 (10.41 to 78.77)	7.40 (4.10 to 13.33)	NS	3.67 (1.93 to 6.96)	3.77 (2.31 to 6.15)						
SD-OCT (full retinal thickness)	NS	5.14 (2.23 to 11.81)	3.32 (1.90 to 5.81)	18.06 (2.20 to 148.13)	2.75 (1.51 to 5.03)	2.57 (1.72 to 3.84)						
SD-OCT (peripapillary RNFL thickness)	NS	39.03 (15.52 to 98.12)	19.27 (9.57 to 38.82)	NS	4.41 (2.09 to 9.29)	7.20 (3.54 to 14.66)						

FDT, frequency-doubling technology; GCC, ganglion cell complex; IOP, intraocular pressure; NS, not significant; POAG, primary open-angle glaucoma; RNFL, retinal nerve fibre layer; SD-OCT, spectral domain optical coherence tomography.

sight-threatening eye disease. These tests showed high positive and negative predictive values for the detection of POAG, AMD, significant diabetic retinopathy and clinically significant cataract, suggesting that a subset of screening tests could provide a basis for ophthalmic screening in the community. A trained technician could easily conduct these tests, and screen-positive individuals could then be referred for a full ophthalmic assessment.

Kopplin and Mansberger<sup>11</sup> have similarly shown that ophthalmic technicians could effectively identify visually significant eye disease in a cohort of American Indian and Alaskan Native participants using a similar battery of screening tests. The test combination used in this study had a sensitivity of 94% and a specificity of 32%. By contrast, the sensitivity and specificity of the screening panel used in the current study were 61% and 79%, respectively, with similar positive and negative predictive values (60% and 80%). Although the screening panel failed to identify approximately a third of subjects with cataract, suspect glaucoma and intermediate AMD, over 90% of those with the most severe disease were detected.

An earlier UK study investigated the cost-effectiveness of a similar 'technician screening' model for POAG in a population aged >40 years, compared with the current opportunistic case finding strategy.<sup>16</sup> The authors concluded that screening was unlikely to be cost-effective, based on a comparison of the incremental cost-effectiveness ratio to a standard threshold of a societal willingness to pay of £30 000 per quality-adjusted life year. However, a sensitivity analysis showed that the cost-effectiveness of screening for POAG was highly dependent on disease prevalence. For example, at a prevalence of 5%, the technician screening model became more cost-effective than current practice. The cost-effectiveness of population screening for eye disease could be increased by either screening a group with a higher prevalence of a target condition or extending the screening programme to encompass several diseases. In the current study, the prevalence of sight-threatening eye disease in our elderly participants was in the region of 30%, and therefore, technician screening for significant eye disease in this population is highly likely to be cost-effective. Furthermore, our model could provide a screening template for the detection of significant eye disease in underserved populations. Although at a higher risk of eye disease, people from minority ethnic groups and those from lower socioeconomic groups are less likely to access eye care services and consequently are at a greater risk of late presentation with associated poorer outcomes.<sup>17–20</sup>

The index tests used were designed to detect structural and/or functional defects. The first-generation FDT perimeter in the C-20–5 suprathreshold mode was used to evaluate visual function and determines contrast thresholds at 17 locations within the central 20 degrees of the visual field. Stimuli are initially presented at a contrast level that should be detected by 95% of age-matched normal subjects. This test was originally developed for glaucoma screening; however, the FDT has

**Table 4** Multivariate stepwise logistic regression analysis of abnormal screening results with significant ocular disease

	Clinically significant cataract	POAG (definite)	POAG (definite and suspect)	Age related macular degeneration (AMD)	Significant diabetic retinopathy/maculopathy	Any sight-threatening eye disease
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Visual acuity<6/12	5.53 (2.91 to 10.54)	NS	NS	4.49 (2.40 to 8.41)	NS	4.12 (2.26 to 7.52)
Family history of glaucoma	NS	4.75 (1.51 to 14.92)	2.50 (1.20 to 5.20)	NS	NS	NS
IOP>21 mm Hg	NS	NS	NS	NS	NS	NS
FDT≥1 point missed at 1% level	NS	8.55 (2.22 to 32.96)	3.93 (2.05 to 7.53)	NS	NS	NS
FDT≥1 point missed at 5% level	2.60 (1.40 to 4.84)	NS	NS	NS	NS	3.62 (2.38 to 5.51)
SD-OCT (GCC thickness)	NS	5.52 (1.57 to 19.41)	NS	NS	NS	NS
SD-OCT (full retinal thickness)	NS	NS	NS	NS	17.86 (2.18 to 146.47)	NS
SD-OCT (peripapillary RNFL thickness)	NS	9.10 (2.85 to 28.96)	11.98 (5.61 to 25.60)	3.81 (1.74 to 8.35)	NS	5.24 (2.45 to 11.24)

FDT, frequency-doubling technology; GCC, ganglion cell complex; IOP, intraocular pressure; NS, not significant; POAG, primary open-angle glaucoma; RNFL, retinal nerve fibre layer; SD-OCT, spectral domain optical coherence tomography.

also been shown to be effective for the detection other eye diseases.<sup>21</sup> An abnormal FDT result showed a univariate association with all target conditions and a threshold of ≥1 point missed at the 5% level was retained in the final multivariate model. Similarly, an abnormality in one or more SD-OCT parameters showed a univariate association with POAG, AMD and diabetic retinopathy. The OCT parameters selected for the analysis and the associated pass/fail criteria (value outside the 99% CI based on the iVue SD-OCT normative database) were established a priori. Thinning of the peripapillary RNFL showed the strongest association, and this parameter was retained in the final model. Predictably, the association was strongest for POAG, but a statistically significant association was also found for AMD. While the OCT is widely used as a diagnostic tool for neovascular AMD, where it is particularly effective in detecting subretinal fluid,<sup>22</sup> more

recently, morphological changes in the inner retina have been documented in eyes with AMD. Changes in the thickness of the GCC and RNFL have been reported in both atrophic and neovascular forms of AMD.<sup>23 24</sup>

In the UK and internationally, there has been a shift towards integrating advanced imaging technologies, particularly OCT, into routine case finding.<sup>25–28</sup> Global interest in the value of SD-OCT for detecting retinal disease has recently been fuelled further by the application of artificial intelligence (AI) based on deep learning algorithms.<sup>29 30</sup> Applying AI to a set of real-world OCT scans, taken from patients referred into a large tertiary referral centre, showed a diagnostic performance that was comparable and, in some cases, better than clinical experts for a range of sight-threatening retinal diseases.

### Strengths and limitations

To our knowledge, this is the first UK study that has evaluated the performance of a combination of screening tests to detect clinically significant eye diseases in a primary care setting. The study has a number of strengths. The design, analysis and reporting complied with the principles of the Standards for Reporting of Diagnostic Accuracy statement.<sup>31</sup> To reduce spectrum bias, the target population included consecutive subjects who met the inclusion criteria, and there were no exclusions. Although it is possible that higher numbers of those with a personal or family history of eye disease were more likely to agree to participate in the study, the prevalence of sight-threatening eye disease in our population (30%) was similar to a London-based cross-sectional study that used random sampling.<sup>14</sup> Therefore, we believe that the study sample is likely to be broadly representative of the

**Table 5** Diagnostic performance of the optimised panel of screening tests (SD-OCT, FDT and measurement of visual acuity) in identifying sight-threatening eye disease

	Value (95% CI)
Sensitivity (%)	61.3 (53.5 to 68.7)
Specificity (%)	78.8 (74 to 83.1)
Positive likelihood ratio	2.9 (2.3 to 3.7)
Negative likelihood ratio	0.5 (0.40 to 0.60)
Disease prevalence (%)	33.7 (29.6 to 39.1)
Positive predictive value (%)	59.5 (53.7 to 65.2)
Negative predictive value (%)	80.0 (76.6 to 83.0)
Overall accuracy (%)	72.9 (68.8 to 76.8)

local population. The reference standard used to classify the participants' ocular status corresponded to that used in a typical hospital eye clinic and was based on the results of a standard ophthalmic examination by a validated clinician. All index tests and the reference standard examination were undertaken on the same day, and the clinician performing the reference examination and the ophthalmic technician undertaking the index tests were masked to the results.

The study also has some limitations. Although a large sample of the population was examined, the prevalence of the individual target conditions was low, and consequently, the reported measures of index test performance were associated with wide confidence intervals. Furthermore, since the identified panel of screening tests was not tested on an independent validation sample, it is possible that the predicative value of these tests may be lower in other populations. Approximately 90% of our study population was of white European origin, and therefore, our findings may not be generalisable to other ethnic groups.

The current study did not include a formal cost-effectiveness analysis. One of the tenets of Wilson and Jungner's widely implemented 'Principles and Practice of Screening for Disease'<sup>32</sup> states that 'the cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.' An economic evaluation of any proposed screening programme is therefore essential to assess the full costs of implementing, operating and sustaining the programme. Recent studies in ophthalmology have recognised the efficiencies gained in screening for more than one eye condition. For example, AMD screening carried out simultaneously with digital screening for diabetic retinopathy is cost-effective in the context of a public healthcare system in Hong Kong.<sup>33</sup>

## CONCLUSIONS

Our study has demonstrated the feasibility of using a panel of standard screening tests performed by an ophthalmic technician to detect sight-threatening eye disease in a representative sample of the elderly population. The results provide useful data to inform the development of larger, multicentre population studies to evaluate the effectiveness and cost-effectiveness of screening for eye disease in the elderly.

**Acknowledgements** The authors thank Optovue for the loan of the iVue optical coherence tomographer.

**Contributors** BRF: study design and conception, collection of data, data analysis and interpretation, writing of the manuscript and approval; PD: study design and conception, collection of data, data analysis and approval; AJ, IC and TP: data analysis and interpretation and approval; DFE: study design and conception, data analysis and interpretation, and approval; JGL: study design and conception, data analysis and interpretation, writing of the manuscript and approval.

**Funding** The study was funded by the College of Optometrists UK.

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Ethics approval** The study was approved by the research and ethical committee of the Division of Optometry and Visual Science, City, University of London (reference number 189A.4b) and adhered to the tenets of the Declaration of Helsinki. Informed written consent was obtained prior to participation.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

## ORCID iDs

Bruno R Fidalgo <https://orcid.org/0000-0003-1134-2148>

Anish Jindal <https://orcid.org/0000-0002-1200-9438>

Irene Ctori <http://orcid.org/0000-0003-1523-4996>

John G Lawrenson <http://orcid.org/0000-0002-2031-6390>

## REFERENCES

- 1 Pezzullo L, Streatfeild J, Simkiss P, *et al*. The economic impact of sight loss and blindness in the UK adult population. *BMC Health Serv Res* 2018;18:63.
- 2 Evans BJW, Rowlands G. Correctable visual impairment in older people: a major unmet need. *Oph Phys Optics* 2004;24:161–80.
- 3 RNIB. Future sight loss UK (1): the economic impact of partial sight and blindness in the UK adult population, 2009. Available: [https://www.rnib.org.uk/sites/default/files/FUSUK\\_Report.pdf](https://www.rnib.org.uk/sites/default/files/FUSUK_Report.pdf) [Accessed 8 May 2019].
- 4 Boodhna T, Crabb DP. Disease severity in newly diagnosed glaucoma patients with visual field loss: trends from more than a decade of data. *Ophthalmic Physiol Opt* 2015;35:225–30.
- 5 Lane M, Mathewson PA, Sharma HE, *et al*. Social deprivation as a risk factor for late presentation of proliferative diabetic retinopathy. *Clin Ophthalmol* 2015;9:347–52.
- 6 WHO. Towards universal eye health: a global action plan 2014–2019 (WHA66.4), 2013. Available: [http://apps.who.int/gb/ebwha/pdf\\_files/WHA66-REC1/A66\\_REC1-en.pdf?ua=1](http://apps.who.int/gb/ebwha/pdf_files/WHA66-REC1/A66_REC1-en.pdf?ua=1) [Accessed 8 May 2019].
- 7 Ariyasu RG, Lee PP, Linton KP, *et al*. Sensitivity, specificity, and predictive values of screening tests for eye conditions in a clinic-based population. *Ophthalmology* 1996;103:1751–60.
- 8 Wang F, Tielsch JM, Ford DE, *et al*. Evaluation of screening schemes for eye disease in a primary care setting. *Ophthalmic Epidemiol* 1998;5:69–82.
- 9 Ivers RQ, Macaskill P, Cumming RG, *et al*. Sensitivity and specificity of tests to detect eye disease in an older population. *Ophthalmology* 2001;108:968–75.
- 10 Boland MV, Gupta P, Ko F, *et al*. 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 Ophthalmol* 2016;134:57–62.
- 11 Kopplin LJ, Mansberger SL. Predictive value of screening tests for visually significant eye disease. *Am J Ophthalmol* 2015;160:538–46.
- 12 Dabasia PL, Fidalgo BR, Edgar DF, *et al*. Diagnostic accuracy of technologies for glaucoma case-finding in a community setting. *Ophthalmology* 2015;122:2407–15.
- 13 Mowatt G, Burr JM, Cook JA, *et al*. Screening tests for detecting open-angle glaucoma: systematic review and meta-analysis. *Invest Ophthalmol Vis Sci* 2008;49:5373–85.
- 14 Reidy A, Minassian DC, Vafidis G, *et al*. Prevalence of serious eye disease and visual impairment in a North London population: population based, cross sectional study. *BMJ* 1998;316:1643–6.
- 15 Hodapp E, Parrish RK, Anderson DR. *Clinical decisions in glaucoma*. St. Louis, MO: The CV Mosby Co, 1993: 52–61.
- 16 Hernández RA, Burr JM, Vale LD, *et al*. Economic evaluation of screening for open-angle glaucoma. *Int J Technol Assess Health Care* 2008;24:203–11.
- 17 Dickey H, Ikenwilo D, Norwood P, *et al*. Utilisation of eye-care services: the effect of Scotland's free eye examination policy. *Health Policy* 2012;108:286–93.
- 18 Gulliford MC, Dodhia H, Chamley M, *et al*. Socio-Economic and ethnic inequalities in diabetes retinal screening. *Diabet Med* 2010;27:282–8.





- 19 Fraser Set *et al.* Deprivation and late presentation of glaucoma: case-control study. *BMJ* 2001;322:639–43.
- 20 Ng WS, Agarwal PK, Sidiki S, *et al.* The effect of socio-economic deprivation on severity of glaucoma at presentation. *Br J Ophthalmol* 2010;94:85–7.
- 21 Cioffi GA, Mansberger S, Spry P, *et al.* Frequency doubling perimetry and the detection of eye disease in the community. *Trans Am Ophthalmol Soc* 2000;98:195–9.
- 22 Ouyang Y, Heussen FM, Keane PA, *et al.* The retinal disease screening study: prospective comparison of nonmydriatic fundus photography and optical coherence tomography for detection of retinal irregularities. *Invest Ophthalmol Vis Sci* 2013;54:1460–8.
- 23 Zucchiatti I, Parodi MB, Pierro L, *et al.* Macular ganglion cell complex and retinal nerve fiber layer comparison in different stages of age-related macular degeneration. *Am J Ophthalmol* 2015;160:602–7.
- 24 Lee EK, Yu HG. Ganglion Cell-Inner plexiform layer and peripapillary retinal nerve fiber layer thicknesses in age-related macular degeneration. *Invest Ophthalmol Vis Sci* 2015;56:3976–83.
- 25 Jamous KF, Kalloniatis M, Hayen A, *et al.* Application of clinical techniques relevant for glaucoma assessment by optometrists: concordance with guidelines. *Ophthalmic Physiol Opt* 2014;34:580–91.
- 26 Dabasia PL, Edgar DF, Garway-Heath DF, *et al.* A survey of current and anticipated use of standard and specialist equipment by UK optometrists. *Ophthalmic Physiol Opt* 2014;34:592–613.
- 27 Ly A, Nivison-Smith L, Zangerl B, *et al.* Self-Reported optometric practise patterns in age-related macular degeneration. *Clin Exp Optom* 2017;100:718–28.
- 28 Kiely PM, Cappuccio S, McIntyre E. Optometry Australia scope of practice survey 2015. *Clin Exp Optom* 2017;100:260–9.
- 29 Ting DSW, Pasquale LR, Peng L, *et al.* Artificial intelligence and deep learning in ophthalmology. *Br J Ophthalmol* 2019;103:167–75.
- 30 De Fauw J, Ledsam JR, Romera-Paredes B, *et al.* Clinically applicable deep learning for diagnosis and referral in retinal disease. *Nat Med* 2018;24:1342–50.
- 31 Bossuyt PM, Reitsma JB, Bruns DE, *et al.* The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. *Ann Intern Med* 2003;138:W1–12.
- 32 Wilson JMG, Jungner G. *Principles and practice of screening for disease*. Geneva: World Health Organization, 1968. <https://apps.who.int/iris/handle/10665/37650>
- 33 Chan CKW, Gangwani RA, McGhee SM, *et al.* Cost-effectiveness of screening for intermediate age-related macular degeneration during diabetic retinopathy screening. *Ophthalmology* 2015;122:2278–85.
- 34 Ferris FL, Davis MD, Clemons TE, *et al.* A simplified severity scale for age-related macular degeneration: AREDS report No. 18. *Arch Ophthalmol* 2005;123:1570–4.
- 35 Chylack LT *et al.* Lens opacities classification system II (LOCS II). *Arch Ophthalmol* 1989;107:991–7.