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Predictive Value of Screening Tests for Visually Significant Eye Disease

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Abstract

Purpose—To determine the predictive value of ophthalmic screening tests with visually significant eye disease in a cohort of American Indian/Alaskan Natives from the Pacific Northwest.

Design—Validity assessment of a possible screening protocol.

Methods—Ophthalmic technicians performed a screening examination including medical and ocular history, best-corrected visual acuity, limbal anterior chamber depth assessment, frequency doubling technology perimetry (FDT, C-20-5), confocal scanning laser ophthalmoscopy, nonmydriatic digital photography, and tonometry on 429 participants. An ophthalmologist performed a comprehensive eye exam on subjects with one or more abnormal screening tests and a random selection of those with normal screening tests. We used univariate and multivariate logistic regression to determine the association between abnormal screening test results and visually significant eye disease. We also determined the predictive value of screening tests with ocular disease.

Results—Univariate analysis identified history of eye disease or diabetes mellitus ($p<.001$), visual acuity <20/40 ($p<.001$), abnormal/poor quality confocal scanning laser ophthalmoscopy ($p<.001$), abnormal FDT ($p<.001$), and abnormal/poor quality non-mydriatic imaging ($p<.001$) as associated with visually significant eye disease. A multivariate analysis found visually significant eye disease to be associated ($p<.001$; receiver operating curve area= .827, negative predictive value=84%) with four screening tests: visual acuity <20/40, abnormal/poor quality non-mydriatic imaging, abnormal FDT and abnormal/poor quality confocal scanning laser ophthalmoscopy.

Conclusions—Ophthalmic technicians performing a subset of screening tests may provide an accurate and efficient means of screening for eye disease in an American Indian/Alaskan Native population. Confirmation of these results in other populations, particularly those with a different profile of disease prevalence is needed.

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Keywords

Community-based screening; American Indian; Alaskan Native; age-related macular; degeneration; glaucoma; cataract; diabetic retinopathy

Introduction

Studies[1–3] frequently use visual acuity assessment or questionnaires to screen for eye disease. Often these tests in isolation are inadequate to accurately and reliably detect eye disease.[2,4,5] Other screening studies report results for a single condition such as diabetic eye disease or glaucoma.[6–9] These approaches are limited in their comprehensive ability to identify those with other asymptomatic eye disease in a community-based screening.

Only limited work examines screening modalities for multiple ocular diseases. One such study in an adult, primarily black, internal medicine primary care population suggested a two step approach, first using a questionnaire to identify those at risk followed by referral for dilated examination.[10] The prevalence of asymptomatic ocular disease within a population would be expected to vary the usefulness of a questionnaire as an initial screening tool. Another study found presenting visual acuity less than 20/40 was highly sensitive for eye disease, but was unable to identify an individual vision screening test that was both highly sensitive and specific for disease and they did not evaluate a combination of screening tests.[11]

Early identification and therapeutic intervention reduces the morbidity associated with ocular disease, particularly those without clinical symptoms in their early stages, such as glaucoma and diabetic retinopathy. Clinical studies, however, have yet to identify screening methods with high predictive values for identifying ocular disease in the general population. We assess the utility of employing a panel of ophthalmic screening techniques administered by an ophthalmic technician to identify participants with ocular disease and compare these results to a comprehensive eye examination by an onsite ophthalmologist. This study provides an opportunity to evaluate the predictive value of a panel of ophthalmic screening tests in a community-based study. Health care providers could use this testing paradigm to identify persons most likely to have eye disease and who would benefit from referral for comprehensive eye examination and treatment.

Methods

Study population

This study includes data from the previously published Tribal Vision Project[12–15], a cross-sectional eye disease prevalence study in American Indian and Alaskan Native participants. The current study is a validity assessment of a possible screening protocol. Briefly, we randomly selected American Indian and Alaskan Native participants from 3 tribes from the Northwest United States who were 40 years of age or older. All subjects had access to onsite medical care with ophthalmic care based on referral. We excluded participants with dementia or serious illness preventing travel to the clinic. We provided free transportation if

needed. The Portland Area Indian Health Service Institutional Review Board approved this study. All participants signed an informed consent prior to enrollment in the study.

Screening testing

Ophthalmic technicians performed an interview and examination consisting of a medical and ocular history, random finger stick blood glucose and glycosolated hemoglobin, automated refraction, tonometry (Tono-Pen XL, Medtronic Solan, Jacksonville, FL), slit lamp assessment of limbal anterior chamber depth[16], frequency doubling technology perimetry (FDT, program C-20-5), confocal scanning laser ophthalmoscopy of the optic disc and peripapillary retina, and non-mydriatic digital imaging of the fundus and optic disc. Participants had normal FDT testing if results had no areas of abnormal sensitivity and the test was reliable (less than 33% fixation losses or false positives). Subjects underwent repeat FDT perimetry if the initial result for an eye was abnormal (at least one area of abnormal sensitivity) or unreliable (defined as over 33% fixation losses or false positives). If abnormal or unreliable results persisted on repeat testing, subjects were considered screening failures.[17,18]

Comprehensive eye examination by an ophthalmologist

Technicians referred subjects for a dilated, comprehensive exam by an onsite ophthalmologist if they had a personal history of glaucoma, retinopathy, macular degeneration, other eye abnormality or diabetes, a blood glucose >127 mg/dL or an A1C>5.7%. Subjects were also referred if one or both eyes had a best corrected visual acuity <20/40, intraocular pressure >21 mmHg, temporal limbal anterior chamber depth <25% of corneal thickness[16], abnormal or unreliable FDT perimetry on initial and repeat testing[18], borderline or abnormal Moorfield's regression or poor quality confocal scanning laser ophthalmoscopy[19], or the presence of optic nerve, retinal or other eye disease on non-mydriatic imaging or poor quality non-mydriatic digital imaging. If participants met the referral criteria in at least one eye, they were encouraged to have an exam. We also randomly selected 30% of subjects with normal screening results to have a dilated eye examination by an ophthalmologist to determine the predictive ability of passing all of the screening tests. The ophthalmologist was masked to the screening test results. The examination included slit lamp biomicroscopy of the anterior segment, gonioscopy, Lens Opacity Classification System III grading of the lens[20], dilated fundus examination and perimetry testing (24-2 Swedish interactive threshold algorithm standard, Humphrey Field Analyzer II, Carl Zeiss Meditech, Dublin, CA). The ophthalmologist used standard criteria for classification of ocular disease (Table 1). A separate ophthalmologist independently confirmed any abnormality found during the comprehensive eye exam by chart review of the patient history, testing results, and photographs of the optic disc and macula, and this result was used to define the presence or absence of eye disease.

Statistical testing

We calculated summary statistics, cross tabulations and binomial univariate logistic regression using R version 2.15.1. We compared the demographic characteristics using chi-square or t-tests as applicable for those that did and did not complete the follow up examination.

We used statistical weighting in R to determine the prevalence of eye diseases because not all of the participants completed the comprehensive exam with an ophthalmologist. We created weights by dividing the total number of normal screening exam results by the number of participants with normal screening exam results who completed the follow-up examination (120/20=6.0); and by dividing the total number of abnormal screening exam results by the number of participants with abnormal screening exam results who completed the follow-up examination (309/210=1.471).[21]

In contrast to the above analysis, we only used data from participants that completed the comprehensive eye exam for the predictive value of the screening tests. We used the logistic procedure in SAS 9.3 to determine the screening tests with significant univariate associations (p value <.05). Those with univariate associations were used as possible covariates for a multivariate model using a stepwise logistic regression procedure with a chi-square significance level of .05 for entering and retaining a covariate in the final model. We calculated sensitivity, specificity, positive and negative predictive values using 2×2 tables for each individual screening test with the different eye diseases as well as for the comprehensive screening panel and those tests found associated with visually significant eye disease with any eye disease.

We used IBM SPSS statistics (version 21.0.0.0, Armonk, NY) to create a receiver operator curve to assess the diagnostic precision of detecting eye disease with the final multivariate subset of screening tests associated with eye disease. For this graph, we used the predictive values of a logistic regression equation with eye disease as the outcome of interest (1=yes, 0=no eye disease) with 4 independent variables from the final multivariate model: visual acuity worse than 20/40, abnormal/poor quality non-mydriatic imaging, abnormal FDT perimetry and abnormal/poor quality confocal scanning laser ophthalmoscopy as the screening tests.

Results

Demographic characteristics

Table 2 describes the demographic characteristics of the 429 participants. A significant proportion of the population was diabetic (20.0%) or had hypertension (31.9%). A prior history of eye disease was reported by 22.8% of subjects.

Table 3 shows the percentage of participants failing the individual screening parameters. Of the 429 participants, only 120 (28.0%) passed all of the screening tests. The most commonly failed screening test was FDT perimetry (195/429, 45.5%) making this the largest source of referral for further ophthalmic examination. Abnormal or poor quality confocal scanning laser ophthalmoscopy was also common in our cohort (146/429, 34.0%). As may be expected, subjects with a best corrected visual acuity <20/40 frequently had abnormal FDT (40/51, 78.4%). Only 36.3% (4/11) of subjects with an intraocular pressure > 21 mm Hg had an abnormal FDT.

Of the 309 subjects with abnormal screening tests, 210 (68.3%) completed the comprehensive follow up examination. The participants completing follow up examination

and those that did not were similar in gender, age, diabetes, hypertension or history of eye disease. However, subjects with a follow up examination were more likely to have failed confocal scanning laser ophthalmoscopy screening than their counterparts that did not follow up (52% vs. 38%, $p<.05$); there were no other differences in demographic characteristics or proportion of failed screening tests between the two groups. We also examined 20 out of 36 (20/36, 55.6%) subjects with normal screening results to provide a measure of specificity.

Table 4 displays the prevalence of eye disease. The most common diseases included age-related macular degeneration, glaucoma, diabetic retinopathy, and other retinal disease. The ophthalmologists considered one participant with normal screening tests to have early age-related macular degeneration based on drusen of the macula but had a best-corrected visual acuity of 20/20 in both eyes. We defined visually significant cataract only if their visual acuity was less than 20/40 and the cataract was felt to be the primary cause of the reduced acuity.

Association analysis

Table 5 shows the univariate logistic regression results of the screening tests for eye disease. Abnormal or poor quality non-mydriatic imaging was significantly associated with all eye diseases. As expected, diabetic retinopathy was associated with a personal history of diabetes and abnormal blood sugar or hemoglobin A1C. Intraocular pressure greater than 21 mm Hg was uncommon. Age-related macular degeneration, the most common ocular disease in our cohort, was associated with visual acuity less than 20/40, abnormal or poor quality confocal scanning laser ophthalmoscopy, abnormal FDT and abnormal or poor quality non-mydriatic photography.

We used those screening tests significant ($p <.05$) in univariate analysis (Table 5) as candidate covariates for the multivariate model. Table 6 shows the results of the stepwise logistic regression to identify the best combination of screening tests to be associated with individual eye diseases and ‘any eye disease’. The multivariate analysis identified visual acuity worse than 20/40, abnormal or poor quality non-mydriatic photography, abnormal FDT, and abnormal or poor quality confocal scanning laser ophthalmoscopy to be associated with any eye disease (last column).

We calculated the sensitivity and specificity of the comprehensive screening panel as 99 and 16% respectively. We found the positive predictive value of our comprehensive screening panel to be 53.3%. The negative predictive value was 95% because the ophthalmologist identified small drusen fitting the criteria for age-related macular degeneration in one subject with all normal screening tests. This participant demonstrated a best-corrected visual acuity of 20/20 in both eyes.

We were interested in how the subset of screening tests associated with any eye disease in multivariate analysis would perform, and re-classified subjects using only this subset of screening tests (visual acuity worse than 20/40, abnormal or poor quality non-mydriatic photography, abnormal FDT, and abnormal or poor quality confocal scanning laser ophthalmoscopy). Of the original 309 subjects failing at least one of the screening tests, 271

continued to be classified as screening failures using only the 4 screening tests listed above (63.2% of the original cohort, 271/429). For the 210 subjects with abnormal screening using the complete testing panel who then underwent a comprehensive exam, 186 continued to be classified as screening failures. Our analysis considered the remaining 24 (out of 210 subjects) as passing screening, and only 7 of these subjects had eye disease on clinical examination (three with diabetic retinopathy, two with macular degeneration, and one with glaucoma). However, the three subjects with diabetic retinopathy had bilateral best-corrected visual acuities of 20/20 and only background diabetic retinopathy; and the two subjects with macular degeneration also had best corrected visual acuities of 20/20 in both eyes and only small retinal pigmented epithelial changes or small drusen in at least one eye. The subject designated as having glaucoma passed FDT screening and had normal intraocular pressure during the screening. However, the comprehensive eye exam demonstrated small peripheral defects with white-on-white standard automated perimetry and glaucomatous rim thinning in the left eye only. Overall, this suggests that the screening tests may have missed early stage diabetic retinopathy, glaucoma, and macular degeneration.

Table 7 describes the diagnostic precision of the comprehensive screening panel, comprehensive screening panel excluding FDT, and of the 4 screening tests (visual acuity worse than 20/40, abnormal or poor quality non-mydriatic photography, abnormal FDT, and abnormal or poor quality confocal scanning laser ophthalmoscopy) in the final multivariate model. The 4 screening tests had a sensitivity of 94%, and a specificity of 32%. The positive predictive value was 57%, and the negative predictive value was 84.1%. A receiver operating characteristic curve (Figure 1) had an area under the curve of .827 (.772, .882, 95% CI).

We also determined the sensitivity and specificity for the individual screening tests with eye disease (Supplemental material available at AJO.com). We did not find a single screening test to provide much diagnostic precision with the sensitivity of the individual screening tests ranging from 4% (intraocular pressure >21) to 74% (abnormal FDT), and similarly poor specificity. Overall, this suggests no single screening test has enough diagnostic precision to screen for eye disease. However, a subset of screening tests (visual acuity worse than 20/40, abnormal or poor quality non-mydriatic photography, abnormal FDT, and abnormal or poor quality confocal scanning laser ophthalmoscopy) may be useful.

Discussion

We examined a panel of screening tests for their utility in identifying subjects with ocular disease in a population of American Indians/Alaskan Natives. We determined that visual acuity less than 20/40, abnormal or poor quality non-mydriatic photography, abnormal FDT, and abnormal or poor quality confocal scanning laser ophthalmoscopy were predictive of visually significant eye disease. These tests showed high negative predictive value with rare misclassification of participants with early macular degeneration, glaucoma, or background diabetic retinopathy. It also showed a high proportion of eye disease in those with an abnormal test. This suggests that a subset of screening tests could provide a basis for community based ophthalmic screening.

Our subset of screening tests associated with visually significant eye disease had a sensitivity of 94%, a specificity of 32%, a positive predictive value of 57%, a negative predictive value of 84% and a ROC curve of 82.7%. These results leave room for improvement. However, in identifying subjects with ocular disease, the screening tests missed only those with early macular degeneration or diabetic retinopathy with 20/20 vision and glaucoma with only early perimetric changes. One may argue that these missed diseases would not require treatment at this early stage and could be discovered at a later time. While the negative predictive value of our screening design was high, the lower positive predictive value of our screening exams may result in over referral of patients for further ophthalmology exams.

Prior community based eye disease screening programs have similar findings. A community-based screening program conducted by trained lay person screeners found 57% of those screened met one or more referral criteria.[3] In another study of subjects recruited from an internal medicine clinic, 66.7% met at least one referral criteria during screening for a comprehensive eye examination[10], similar to our findings here. As our screening paradigm was not tested in an independent validation sample, the predictive performance of our identified subset of screening tests may be less in other populations. Similarly, the predictive value of screening tests vary with the prevalence of disease within a population and alternative combinations of screening tests than those identified here may be more beneficial in communities with different disease burdens.

An advantage of our screening approach is the administration of tests by eye care paraprofessional (e.g. ophthalmic technicians), thus decreasing the burden of eye disease case finding by eye care providers. This approach also allowed for the utilization of ophthalmic technologies such as confocal scanning laser ophthalmoscopy and non-mydriatic fundus photos for screening; both tests proved useful in identifying eye disease in our population. Future studies need to examine methods to reduce false positive results to make the positive predictive value higher and decrease the burden of referral. Despite the possibility for over referral, our study identified a limited panel of ophthalmic screening tests that could be adapted for use in medically underserved communities without routine access to ophthalmic care to increase recognition of at risk members within the population.

A high rate of abnormal FDT screening contributed to our lower positive predictive value; a third of the patients with an abnormal screening test but no eye disease on comprehensive examination were those with an abnormal FDT. Others have identified a low positive predictive value with population based screening for glaucoma using FDT[9,22,23]; however, the potential greater sensitivity to early glaucomatous defects with FDT[8] makes it appealing for screening. Additionally, FDT has shown utility in identifying diseases other than glaucoma[24]. Abnormal FDT testing has also been reported in diabetics.[25] FDT normative databases did not include Native Americans and development of a normative database specific to this population may have improved performance.[26] We used the C-20-5 FDT algorithm for screening, which presents stimuli at a contrast level that 95% of healthy age-matched controls would be expected to detect; this screening algorithm is designed to have a higher sensitivity to detect early field defects at the expense of specificity. The use of an alternative screening algorithm, such as the C-20-1 program which uses stimuli at a contrast

level 99% of healthy age-matched controls should detect, could improve specificity, although the trade off in identifying patients with disease would need to be assessed.

The use of confocal scanning laser ophthalmoscopy in community based glaucoma screening is uncommon[27–29]; in these studies, confocal scanning laser ophthalmoscopy is moderately sensitive (61-85%) with a higher specificity (86-96%). In our population, we found confocal scanning laser ophthalmoscopy to have a similar sensitivity (75.7%) for glaucoma, with a slightly lower specificity (56.5%) to previous studies. To our knowledge, the current study is the first to incorporate screening with confocal scanning laser ophthalmoscopy with a combination of community based screening tests.

More than 20% of our study population was diabetic, a known risk factor for visual impairment.[30] Our analysis identified a history of diabetes, abnormal blood sugar or hemoglobin A1C and abnormal non-mydriatic photos as associated with diabetic retinopathy, which re-emphasizes the usefulness of these screening modalities in monitoring for diabetic eye disease.[31,32] Sensitivity and specificity estimates for diabetic retinopathy fundus photography range from 38-100% and 75-100% when compared with dilated ophthalmoscopy[32], similar to the observed sensitivity of 65.2% and specificity of 76.5% in our cohort.

We offered participants a free, on-site comprehensive ophthalmology exam if they had an abnormal screening exam and random selection of those with normal testing. We provided gift cards, free transportation, childcare, and a work release with paid-time off to complete the examination. Despite this, some participants did not return for the full eye examination, including both those with abnormal screening results and those invited back who had normal screening results. However, the overall 60% rate of follow-up is very similar to results in prior community screening programs.[3,33,34] Reasons for not returning were similar to previous studies[3,33,34] and included lack of time for additional examination, a desire to avoid dilation, a second opinion from their local eye care provider, and not believing the results of screening.

Our study demonstrates the feasibility of identifying patients with visually significant eye disease in an American Indian/Alaskan Native population using commonly available screening techniques administered by ophthalmic technicians and suggests a combination of screening tests that may be most useful. The current U.S. Preventive Task Force recommendation on screening for primary open angle glaucoma in asymptomatic patients in the primary care setting concludes that there is currently insufficient evidence to assess the balance of benefits versus harms to screening.[35] Perhaps screening studies to detect all eye disease (similar to the current study) would show benefits in limiting ocular morbidity. Future studies will need to be completed to assess the feasibility of implementation of such a program and its effects on visual health care outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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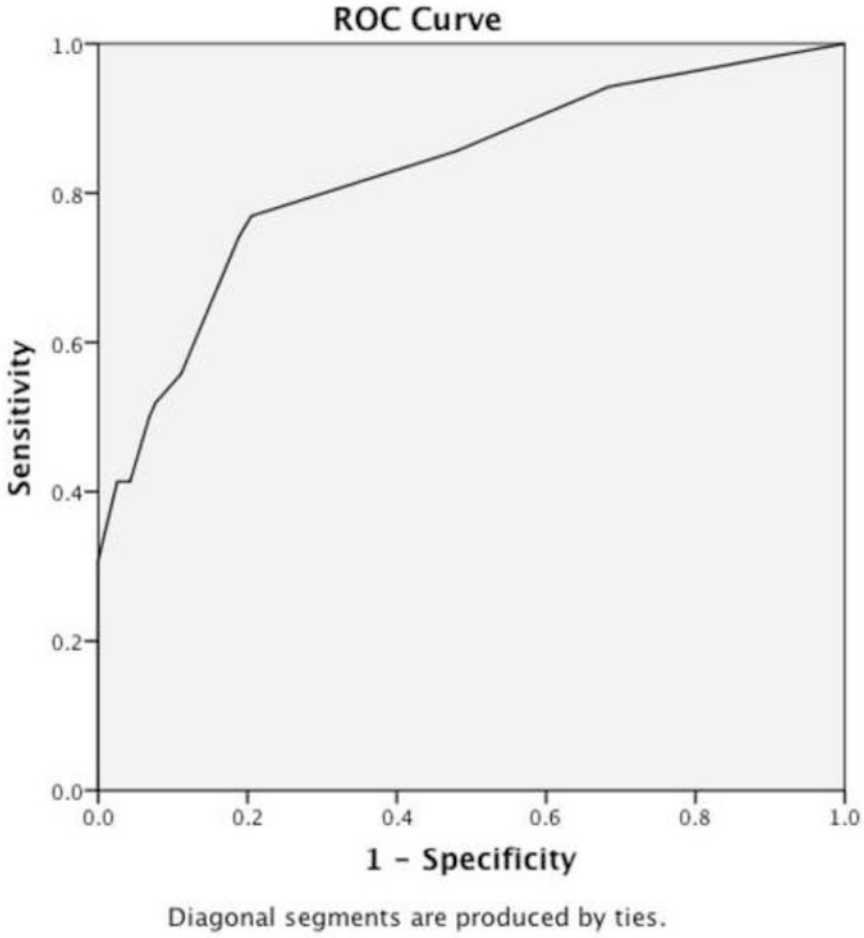

Figure 1.

Receiver operating characteristic curve relating the multivariate subset of screening tests (visual acuity < 20/40, abnormal or poor quality non-mydriatic imaging, abnormal frequency doubling technology perimetry, abnormal or poor quality confocal scanning laser ophthalmoscopy) to eye disease.

Table 1

Case definitions of ocular diseases: Screening tests for visually significant eye disease.

Eye Disease	Definition
Visually significant cataract	Visual acuity ≤20/40 with lens opacities (LOCSIII score ≥2.0 for cortex, posterior subcapsular, nuclear or hypermature cataract) without another ocular explanation[19]
Glaucoma	Presence of: **1** Cup-to-disc ratio ≥ 0.8 or glaucomatous features (rim thinning, excavation, nerve fiber defect) and glaucomatous visual field loss **2** Cup-to-disc ratio ≥ 0.8 or glaucomatous features (rim thinning, excavation, nerve fiber defect) and an inability to satisfactorily complete visual field testing **3** Subjects unable to complete visual field testing with optic discs unable to be viewed and IOP >22[36]
Diabetic retinopathy	Presence of any non-proliferative retinopathy (microaneurysms, dot blot hemorrhages or intraretinal microvascular angiopathy), proliferative retinopathy (neovascularization with or without high risk characterization) or clinically significant macular edema[37–39]
Age-related macular degeneration	Presence of soft drusen >125 microns, macular pigmentary changes, geographic atrophy or macular neovascularization not associated with other retinal disease[40]
Other retinal disease	Additional retinal disease, such as prior retinal artery or vein occlusion or uveitic disease
Narrow angles	No visible angle structures in two or more quadrants on gonioscopy[36]
Corneal disease	Presence of any corneal disease, such as edema, scarring or neovascularization

Table 2

Demographic characteristics: Screening tests for visually significant eye disease. Data are presented as number (%) unless otherwise specified.

Characteristics	**N=429**
Female gender	271 (63.2)
Age (Mean (SD), range in years)	55.7 (11.6), 40-88
Diabetic (history of diabetes, hemoglobin A1C > 5.7 or fasting blood glucose > 127)	86 (20.0)
Hypertensive (systolic blood pressure > 135 or diastolic blood pressure > 80)	137 (31.9)
Personal history of eye disease[a]	98 (22.8)

[a]Glaucoma, retinopathy, macular degeneration, other eye abnormality SD; standard deviation

Table 3

Participants with abnormal results on initial screening tests administered by an ophthalmic technician: Screening tests for visually significant eye disease.

Ophthalmic Screening Test	N=429[a] N (%)
Screening pass on all tests	120 (28.0)
History of eye disease or diabetes	98 (22.8)
Blood glucose >127 or HgbA1C >5.7	63 (14.7)
Visual acuity <20/40	51 (11.9)
Narrow limbal anterior chamber depth	49 (11.4)
Abnormal or poor quality CSLO	146 (34.0)
Abnormal FDT	195 (45.5)
Abnormal or poor quality non-mydriatic photo	92 (21.4)
Intraocular pressure > 21 mm Hg	11 (2.6)

[a]Total numbers do not add to 429 because participants could be abnormal on multiple screening tests.

Table 4

Prevalence of ocular disease with a comprehensive eye exam by an onsite ophthalmologist: Screening tests for visually significant eye disease.

Ocular Disease[a]	**Number (%) N=230**[b]
Corneal disease	8 (2.7)
Narrow angles	2 (0.7)
Visually significant cataract	11 (3.8)
Glaucoma	36 (12.5)
Diabetic retinopathy	23 (7.9)
Age-related macular disease	54 (19.6)
Other retinal disease	22 (8.5)
Any eye disease	113 (39.8)
Normal eye examination	117 (60.2)

[a] Case definitions listed in Table 1

[b] Numbers do not add to 230 because a participant could have more than one ocular disease. We used statistical weights of 1.471 for those with screening abnormal results and 6.0 for those with screening normal results (See Methods, Statistical analysis section) to calculate weighted prevalence percentages.[20]

Table 5

Univariate association testing of abnormal screening results with ocular disease using logistic regression: Screening tests for visually significant eye disease.

	Corneal Disease		**Visually Significant Cataract**		**Glaucoma**		**Diabetic Retinopathy**	
	OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
History of eye disease or diabetes	-	-	-	-	-	-	20.9 (5.8, 115.6)	<.001
Abnormal blood glucose	-	-	-	-	-	-	9.8 (3.8, 25.4)	<.001
Visual acuity <20/40	32.1 (3.7, 1503.9)	<.001	**	**	3.3 (1.5, 7.4)	.004	-	-
Narrow anterior chamber depth	-	-	-	-	0.1 (0.003, 0.9)	.04	-	-
Abnormal/poor quality CSLO	-	-	-	-	4.1 (1.7, 9.5)	.001	3.1 (1.2, 8.3)	.02
Abnormal FDT	-	-	8.5 (1.2, 372.9)	.02	4.5 (1.7, 13.9)	<.001	-	-
Abnormal/poor quality non-mydriatic photo	6.8 (1.1, 72.6)	.02	8.1 (1.8, 49.0)	.002	2.8 (1.3, 5.8)	.008	6.1 (2.4, 15.2)	<.001
Intraocular pressure > 21 mm Hg	-	-	-	-	-	-	-	-

	Age-related Macular Degeneration		Other Retinal Disease		Any Eye Disease	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
History of eye disease or diabetes	-	-	4.3 (1.7, 10.8)	.002	3.6 (1.9, 6.6)	<.001
Abnormal blood glucose	-	-	-	-	-	-
Visual acuity <20/40	3.4 (1.6, 7.1)	.001	5.9 (2.3, 15.1)	<.001	18.8 (5.6, 98.8)	<.001
Narrow anterior chamber depth	-	-	-	-	-	-
Abnormal/poor quality CSLO	2.6 (1.3, 4.0)	.006	-	-	3.1 (1.8, 5.4)	<.001
Abnormal FDT	2.7 (1.4, 5.2)	.005	-	-	4.3 (2.4, 7.5)	<.001
Abnormal/poor quality non-mydriatic Photo	2.6 (1.4, 5.0)	.004	5.1 (2.0, 12.7)	<.001	8.0 (4.0, 16.2)	<.001
Intraocular pressure > 21 mm Hg	-	-	-	-	-	-

Associations significant at the p≤0.05 level are reported. '-' indicates nonsignificant results. N=230.

OR; odds ratio, CI; confidence interval; CSLO; confocal scanning laser ophthalmoscopy; FDT; frequency doubling technology perimetry; Case definitions of ocular diseases listed in Table 1.

** Visual acuity was omitted from association testing with visually significant cataract as vision <20/40 was required for the diagnosis of visually significant cataract

Table 6

Multivariate stepwise logistic regression analysis including screening tests found significantly associated with each disease in univariate testing: Screening tests for visually significant eye disease.

	Visually Significant Cataract	Glaucoma	Diabetic Retinopathy	Age-related Macular Degeneration	Other Retinal Disease	Any Eye Disease
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
History of eye disease or diabetes			9.9 (2.6, 38.1)			
Abnormal blood glucose			5.2 (1.7, 15.5)			
Visual acuity <20/40	**			2.5 (1.1, 5.6)	3.9 (1.4, 10.6)	13.8 (3.7, 51.5)
Narrow anterior chamber depth		0.1 (0.02, 0.9)				
Abnormal/poor quality CSLO		4.6 (1.9, 11.3)		2.3 (1.1, 4.6)		2.8 (1.5, 5.5)
Abnormal FDT		4.8 (1.8, 12.7)		2.3 (1.1, 4.7)		3.7 (1.9, 7.2)
Abnormal/poor quality non-mydriatic Photo	8.2 (2.1, 31.9)		3.9 (1.3, 11.5)		3.4 (1.2, 9.0)	4.8 (2.1, 10.7)
Intraocular pressure > 21 mm Hg						

Listed values have a p-value <.05 in the final model from the Wald test. N=230.

OR; odds ratio, CI; confidence interval; CSLO; confocal scanning laser ophthalmoscopy; FDT; frequency doubling technology perimetry; Case definitions of ocular diseases listed in Table 1.

** Visual acuity was omitted from association testing with visually significant cataract as vision <20/40 was required for the diagnosis of visually significant cataract

Table 7

Performance measures of screening tests in identifying eye disease: Screening tests for visually significant eye disease

	Sensitivity	Specificity	PPV	NPV
Comprehensive screening panel	99%	16%	53%	95%
Comprehensive screening panel excluding FDT	93%	35%	58%	84%
Screening tests associated with eye disease in the final multivariate model[a]	94%	32%	57%	84%

N=230. PPV; positive predictive value; NPV; negative predictive value; FDT; frequency doubling technology perimetry

[a]Visual acuity worse than 20/40, abnormal or poor quality non-mydriatic photography, abnormal frequency doubling technology perimetry, and abnormal or poor quality confocal scanning laser ophthalmoscopy