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Nonmydriatic Fundus Photography in a High-Risk Population of Samoans with Diabetes: The Soifua Manuia Eye Screening Program

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Master of Public Health Candidate 2019

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Original Article—Clinical Science

Nonmydriatic Fundus Photography in a High-Risk Population of Samoans with Diabetes: The Soifua Manuia Eye Screening Program

Short Title: The Soifua Manuia Eye Screening Program

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COMPETING INTERESTS None declared.

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ABSTRACT

IMPORTANCE Novel methods of detecting eye disease are needed due to the challenges associated with service delivery in resource-limited settings.

BACKGROUND The objective of this study is to determine whether clinically gradable fundus images can be obtained using a low-cost, handheld non-mydriatic fundus camera by a non-ophthalmic provider in a remote setting.

DESIGN Cross-sectional study

PARTICIPANTS Two-hundred and six individuals (412 eyes) in the Pacific Island nation of Samoa with pre-diabetes and diabetes (HbA1c ≥5.7% or FBG ≥110 mg/dl).

METHODS Participants underwent non-mydriatic fundus photography with the PanOptic iExaminer System, along with an assessment of near vision, medical, and ophthalmic histories. Images were remotely graded by an ophthalmologist and optometrist, who were blinded to participants' demographic and biometric data.

MAIN OUTCOME MEASURES The percentage of clinically gradable images, positive findings, and degree of inter-rater reliability and agreeability among graders were measured.

RESULTS Clinically gradable images were obtained from 337 eyes (81.8%). Positive findings were identified in 29.1% of participants: 7 participants (3.4%) had non-proliferative diabetic retinopathy, 19 participants (9.2%) had evidence of background retinopathy, 33 participants (16.0%) had features of glaucoma, and 10 participants (4.9%) had other lesions, tumors, or structural abnormalities. Those with positive findings were referred for expedited review by a local ophthalmologist.

CONCLUSION AND RELEVANCE Positive ophthalmic findings, including features of diabetic retinopathy and glaucoma, were readily identified in individuals at risk for undiagnosed eye disease screened with the PanOptic iExaminer. Use of smartphone-based remote screening holds promise as a cost-effective public health intervention in resource-constrained settings.

KEY WORDS: Chronic Disease Epidemiology, Retinal-Imaging, Telemedicine, Epidemiology, Diabetic Retinopathy, Glaucoma

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INTRODUCTION

Screening for vision-threatening conditions represents a significant challenge to improving eye care in resource-constrained settings. Low- to middle-income countries (LMICs) are disproportionately burdened by several chronic conditions, including diabetes,[1] placing these populations at significant risk for microvascular and macrovascular complications.[2] The number of individuals with visual impairment and blindness due to diabetic retinopathy continues to rise worldwide,[3] even though timely detection and treatment has the potential to reduce permanent vision loss[4] or even restore central vision in many cases.[5] Despite international guidelines and recommended best practices that promote an annual ophthalmic examination for patients with diabetes mellitus,[6] only 50-60% of people in high-income countries complete such screening.[7] Globally, only 7.4-13% of people in LMICs undergo screening due to cost, knowledge, and access issues.[8] Novel methods that address the challenges of limited personnel and lack of expensive ophthalmic equipment may reduce avoidable vision loss, but their ability to identify visually significant eye disease remains poorly defined.

The advent of smartphone-based non-mydriatic fundus cameras allows for highly mobile, cost-effective screening programs capable of reaching remote and underserved areas.[9-14] Screening with ophthalmoscopes and other portable devices can be performed quickly and inexpensively by trained providers.[15,16] Recent advances in imaging and communication technologies have expanded the use of ocular telehealth programs,[17,18] and handheld, battery-operated devices have ameliorated challenges associated with fundus photography outside of the traditional clinic.[19] For example, diabetic retinopathy screening camps in rural India have identified sight-threatening retinopathy in nearly 7% of the population and referred patients for further treatment.[20] Unfortunately, access to trained providers to staff such outreach efforts remains in short supply.

While ocular telehealth programs have revealed that digital images can be procured by non-ophthalmic providers with reasonable specificity and sensitivity,[19, 20-23] few studies have explored the potential for remote diagnosis using more portable, lower-cost instruments.[24] Furthermore, no study to date has undertaken a diabetic screening program in the Pacific, a region facing some of the highest rates of diabetes globally.[25] To address these knowledge gaps, we piloted a low-cost, smartphone-based remote retinal diagnosis system to screen for ocular complications in Samoa, a LMIC population with a high prevalence of diabetes and low access to ophthalmology services. Our objective was to determine the percentage of gradable images that could be obtained using the PanOptic iExaminer System (Welch Allyn Inc., NY) and to determine whether this device could be used to successfully screen for diabetic retinopathy and other eye conditions in a high-risk population of Samoans with diabetes and elevated blood glucose levels.

METHODS

Study Design and Setting

The study took place in the independent Pacific Island nation of Samoa. As a result of recent epidemiologic transition, nearly 47% of Samoan adults have diabetes and >80% are overweight/obese.[26-29] Individual control of diabetes and management of retinal complications is a challenge for the Pacific Islands, where limited equipment and uncertain supply chains for diagnostics make glucose monitoring difficult.[30] Geographic isolation from Hawaii and New Zealand (each more than 2000 miles away) requires that most residents receive care in Samoa, where only one full-time ophthalmologist serves a population of nearly 200,000 people.[31]

The present study was undertaken alongside an ongoing longitudinal study of the genetics of obesity and diabetes among Samoans: the Samoan Obesity, Lifestyle, and

Genetic Adaptation Group's *Soifua Manuia* ("Good Health") study. A village-based screening of a convenience sample of approximately 700 Samoan adults (Samoan ethnicity based on four Samoan grandparents) was conducted in 12 urban and peri-urban villages between June and August 2018, focusing on individuals between the ages of 30.5 and 50 years. Exclusion criteria included pregnancy, use of weight loss medication, prior weight loss surgery, participation in a major diet or physical activity program, or a weight loss of >5% of total body weight in the past 12 months. Only one individual per family was selected to minimize relatedness among the samples.

All participants were screened for glycosylated hemoglobin (HbA1c; A1c Now point-of-care System [PTS Diagnostics, IN]), body mass index (BMI), and blood pressure (Omron HEM 907XL, Omron Healthcare, IL). Individuals >50 years of age who were ineligible for the larger study based on their age were also offered health screening, including a random finger-prick fasting blood glucose (Bayer Contour, NJ). All participants with pre-diabetes and diabetes (HbA1c ≥5.7% or FBG ≥110 mg/dl) were offered eye screening with the PanOptic iExaminer.

Eye Examinations and Image Grading

Participants underwent a non-mydriatic, bilateral eye examination using the PanOptic iExaminer attached to an iPhone 6S (Apple, Inc., CA). Similar to a direct ophthalmoscope, the device is a handheld instrument, but provides a five-fold larger view of the fundus than a standard ophthalmoscope (approximately 25° versus 5°). A 3.5V re-chargeable power handle was used to power the device in the field. The iExaminer is the only smartphone-based imaging device with U.S. Food and Drug Administration (FDA) approval to date.[32]

All examinations were performed outside of a traditional clinic in a village-based location by a health worker trained in the basics of eye examination, as well as in the use of

the PanOptic iExaminer (L.C.L.). Images were de-identified and submitted for remote review by an ophthalmologist trained in retina (D.J.R.) and an optometrist (M.K.B.) at Lahey Hospital & Medical Center in Peabody, MA. Graders were blinded to participants' demographic and biometric data and evaluated each pair of eyes independently. The best available image for each eye was used to grade the overall quality of the field examination according to a 5-point scale based on the Feasibility of Non-mydriatic Ocular Fundus Photography (FOTO-ED) Studies.[33-35] Any features likely related to diabetic retinopathy, e.g. retinal hemorrhages, or other abnormalities of the vasculature that could be attributed to diabetes and/or hypertension were defined broadly as "retinopathy." Other lesions and abnormalities were identified based on clinical judgment. Due to the requirement of a clear view of the optic disc, only images with a grade of 3 or higher were considered adequate to grade the cup-to-disc ratio (CDR).[24] Glaucoma suspect status was defined by a CDR in one or both eyes $\geq$0.6 or a difference in CDR between the two eyes $\geq$0.2.

Visual Acuity Assessment

Near visual acuity exams were conducted by a single lay examiner (LCL) with a Rosenbaum Pocket Vision Screener held at approximately 14 inches from the eye with and without correction as previous described.[36,37] A visual acuity limitation was defined as an inability to achieve vision ≥20/40. As a part of the ophthalmic focused history, participants communicated any visual acuity or anatomic complaints.

Informed Consent and Referral System

The majority of encounters were performed in English (nearly 90%), one of the two official languages of the Independent State of Samoa. All participants were offered the use of an interpreter, a Samoan research assistant fully versed in study procedures. No formal record of language preference was recorded for the purposes of this study. Participants

were provided detailed information about the study and the data collection protocols and gave additional informed consent for participation. Research protocols and the informed consent procedures were approved both by the Yale University Institutional Review Board and the Health Research Committee of the Samoan Ministry of Health.

All participants were informed about the importance of obtaining an annual comprehensive eye exam regardless of their screening results. An expedited referral to a local ophthalmologist was provided to any participant when any of the following conditions were met: (1) presence of a positive finding upon telemedicine screening; (2) an inability to obtain images; (3) a near visual acuity limitation of $\leq$20/40, and/or (4) a subjective report of a functional or anatomic impairment beyond the scope of the eye screening. Research assistants from the *Soifua Manuia* study provided letters to all participants in need of an expedited referral.

Statistical Analysis

Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., NC). Data were analyzed independently by eye and subsequently by participant. For analysis of variance and chi-square analyses, a two-sided $p<0.05$ was considered to be the threshold of statistical significance. Cohen's Kappa (κ) statistic was used to assess the interobserver agreement for glaucoma suspect status by participant. Cronbach's alpha coefficient and the intraclass correlation coefficient (ICC) estimates and their 95% confidence intervals were calculated based on a single-measures, absolute-agreement, two-way mixed effects model.

RESULTS

User Experience

Several environmental factors impacted the use of the PanOptic iExaminer System: (1) electrical charging and battery-life of the device; (2) lighting; (3) stabilization of viewing distance; and (4) examination time and participant compliance. Fundus imaging was performed in traditional Samoan *fales* (open-sided houses). Electricity was unavailable at these examination sites, requiring overnight charging of the lithium-ion batteries to permit intermittent operation of the device for 10-12 hours in the field each day. Examining an undilated eye in outdoor daytime illumination leads to constriction of the pupil. To overcome this, curtains were hung to construct a “tent” to block light. By reducing ambient illumination, participants did not have to cover their fellow eye while being imaged. Additionally, the eye-cup of the PanOptic iExaminer System is compressible, providing a flexible viewing distance, but makes it challenging to for examiners with limited direct ophthalmoscopy experience. Lastly, light from the device itself may be uncomfortable for many participants. The more experienced the examiner, the shorter the total time required for image capture, significantly enhancing participant comfort and compliance. Fewer than 1% of eligible participants declined eye screening.

Clinical Characteristics

The mean age of participants was 45.4 ± 9.1 years, and 61.27% (n=125) were female (Table 1). Mean A1c was 7.48 ± 2.16%, and mean fasting blood glucose was 315.78 ± 116.31 mg/dl. Within our sample, 48 (23.41%) participants had a prior diabetes diagnosis, and the mean years since diagnosis was 4.2 ± 4.6. Thirty-nine percent of participants had measured blood pressure in the hypertensive range (systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg). Fewer than 1% of all participants had undergone any eye examination in the past year with a local ophthalmologist. No participants reported a prior history of laser, eye injections or surgery.

Table 1. Description of the study population

Sample Characteristics[†]	
Age (years), mean (SD)	45.4 (9.1)
Female, n (%)	125 (61.27)
Weight (kg), mean (SD)	100.90 (23.93)
HbA1c[†] (%), mean (SD)	7.48 (2.16)
FBG[†] (mg/dl), mean (SD)	315.78 (116.31)
BMI (kg/m^2), mean (SD)	37.20 (11.56)
Uncorrected visual acuity (logMAR), mean (SD)	0.27 (0.28)
Corrected visual acuity (logMAR), mean (SD)	0.07 (0.15)
Systolic BP (mm Hg), mean (SD)	131.01 (20.50)
Diastolic BP (mm Hg), mean (SD)	85.65 (12.85)
Hypertension, n (%)[§]	77 (39.09)
Previous hypertension diagnosis, n (%)	17 (8.72)
Previous diabetes diagnosis, n (%)	48 (23.41)
Years since diabetes diagnosis, [¶] mean (SD)	4.2 (4.6)

[†] HbA1c, hemoglobin A1c (%); FBG, fasting blood glucose (mg/dl); SD, standard deviation; BMI, body mass index (kg/m^2); BP, blood pressure (millimeters mercury); LogMAR, log minimum angle of resolution.

[‡] HbA1c: Participants 30.5 to 50 years of age (n=180). FBG: Participants more than 50 years of age (n=23).

[§] Hypertension = systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg.

[¶] Years since the diagnosis of diabetes (n=22); a majority of participants were diagnosed at the time of screening.

Clinical Imaging

A total of 393 eyes (95.4%) from 206 participants were successfully imaged using the PanOptic iExaminer. Nineteen eyes (4.6%) from 16 participants (7.8%) could not be imaged by the device. A total of 2,758 images were collected and submitted for remote diagnostic review, an average of 6.96 ± 2.94 images per eye (range: 1-18 images). All available images for each eye were used for clinical grading.

Twenty-six percent (106/412) of eyes had at least one image graded as excellent overall quality, 56.1% (231/412) as good, 11.4% (47/412) as fair, and 0.2% (1/419) as inadequate with no structures identifiable (Figure 1). Overall, 337 eyes (81.8%) had clinically gradable images taken by the device. Only 54 eyes (13.1%) had a field of view that fully captured the macula. As expected due to the importance of image quality in successfully identifying pathology, there was a significant association between image quality and positive findings (χ^2=14.22 *P*=0.014). Of note, there was also a significant association between image quality and study date ($F_{5,392}$=3.50, *P*=0.004), indicating an improvement in image capture by the lay examiner (L.C.L.) over time.

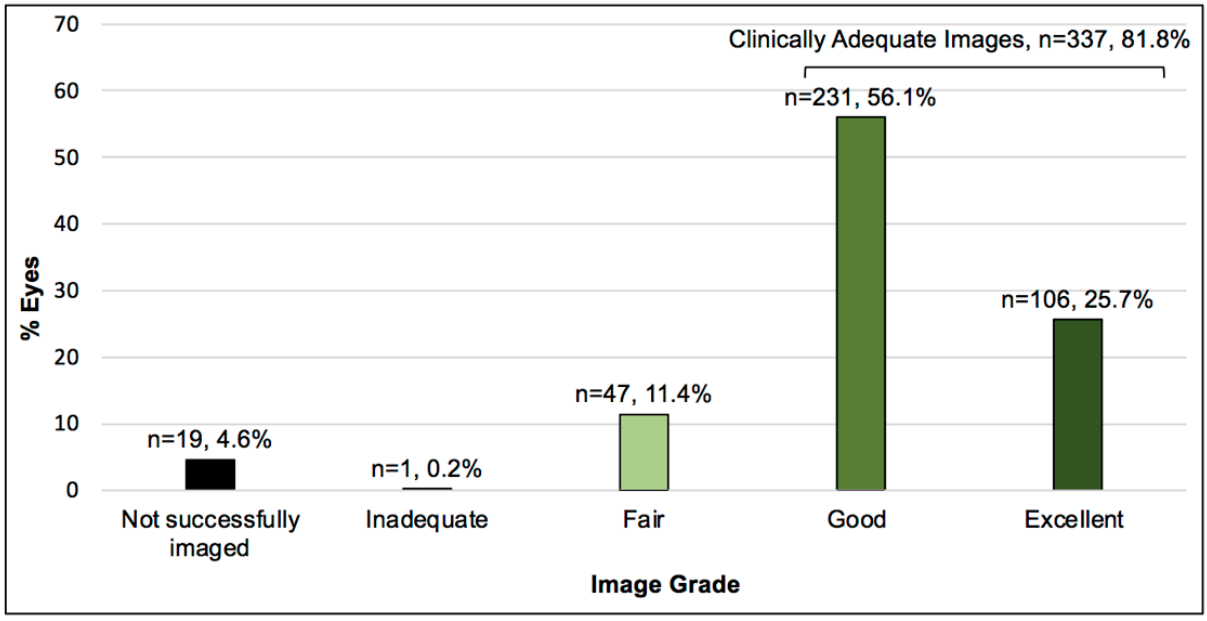

Figure 1. Image quality using the PanOptic iExaminer System Percent of eyes (n=412) with at least one fundus photo obtained within each image category: Grade 1=inadequate; Grade 2=fair; Grade 3=good; Grades 4 and 5=excellent. Grade 1 was assigned to images where the fundus was not visualized, Grade 2 images had a view of the fundus that did not include a full or clear view of the optic disc, Grade 3 images had a full and sharp view of the optic disc, Grade 4 images had a full, clear view of the optic disc in addition to some surrounding structures, and Grade 5 images had a full view of the optic disc in addition to extensive choroidal detail and views of the both the superior and inferior vascular arcades.

Findings

Positive findings upon screening with the PanOptic iExaminer were identified in 29.1% of participants (60/206) (Table 2). Features of moderate non-proliferative diabetic retinopathy were detected in 7 participants (3.4%), and other vascular changes related to diabetes and/or hypertension were found in 19 participants (9.2%). In total, 24 participants (11.7%) had evidence of background retinopathy (Figure 2), which was significantly associated with level of HbA1c ($F_{1,176}$=10.48, P=0.001), corrected visual acuity ($F_{1,190}$=13.50, P=0.0003), and BMI category (i.e. normal, overweight, obese) (χ^2=10.48, P=0.005) (Table

3). There was no association between mean systolic and diastolic blood pressure and background retinopathy (*P*=0.299 and *P*=0.871, respectively), suggesting that the observed changes were likely attributable to diabetes. Additionally, there was no association between reported ophthalmic complaints and background retinopathy (χ^2=0.50, *P*=0.478), as expected due to the frequently asymptomatic nature of diabetic eye disease. No cases of proliferative diabetic retinopathy or clinically significant diabetic macular edema were identified. Importantly, the device detected additional findings in 37 participants (18.0%), including 33 participants (16.0%) with features suggestive of glaucoma, and 10 participants (4.9%) with other findings, including lesions, tumors, or other structural abnormalities (Table 2).

Table 2. Frequency of positive findings following image review

Findings[†]	**Eyes (%)**	**Participants (%)**
Glaucoma suspect[‡]	39 (9.5)	33 (16.0)
Retinopathy	30 (7.3)	24 (11.7)
Background retinopathy/hypertensive changes	24 (5.8)	19 (9.2)
Moderate non-proliferative retinopathy	7 (1.7)	7 (3.4)
Other	11 (2.7)	10 (4.9)
Myelination of nerve fiber layer	4 (1.0)	4 (1.9)
Choroidal lesion	1 (0.24)	1 (0.49)
Congenital coloboma	1 (0.24)	1 (0.49)
Chorioretinal degeneration	2 (0.49)	1 (0.49)
Lesion on optic disc	1 (0.24)	1 (0.49)
Morning glory disc anomaly	1 (0.24)	1 (0.49)
Disc tumor (e.g. angioma/meningioma)	1 (0.24)	1 (0.49)
Total unique positive findings	**75 (18.2)**	**60 (29.1)**

[†] Findings are presented as a number and percentage of total eyes (n=412) and participants (n=206).

[‡] No drance hemorrhages were noted in any participant.

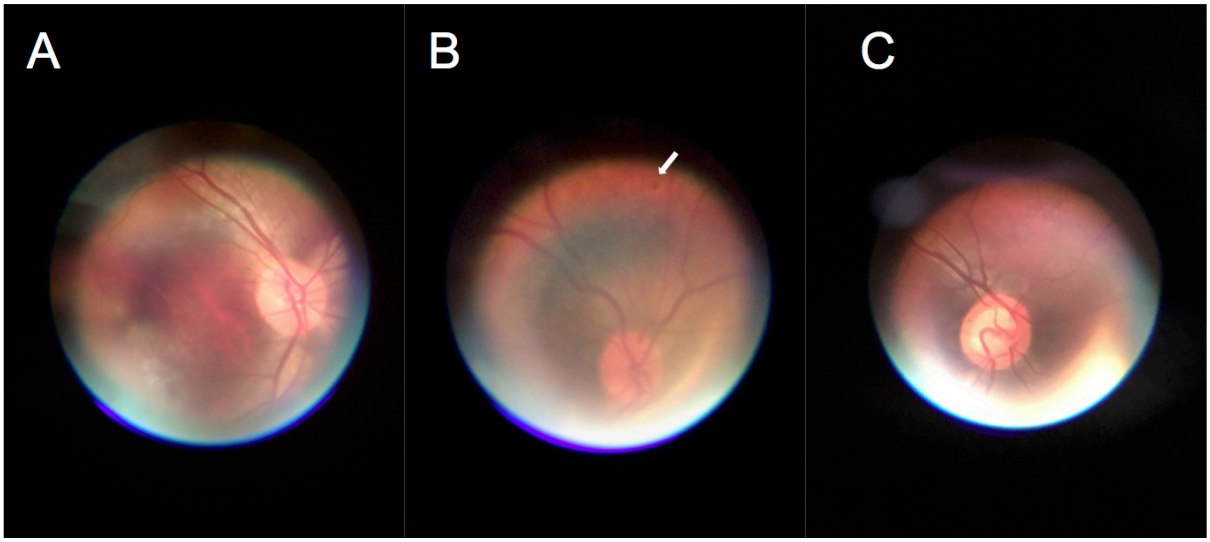

Figure 2. Representative fundus photographs in three participants with positive findings upon PanOptic iExaminer screening (A) Healthy fundus with foveal detail in a 35-year old participant. (B) Nonproliferative diabetic retinopathy in a 65-year old participant. (C) Example of a glaucoma suspect (based on enlarged CDR) in a 45-year old participant. Lens reflexes and shadows due to camera alignment are commonly present at the edges of even higher quality images.

Table 3. Associations of study population characteristics with background retinopathy

Characteristic[†]	Participants	Background Retinopathy (%)	Significance *P*[‡]
Age (years)			0.741
31.5-50	169	11.24	
50+	30	13.33	
Sex			0.350
Female	120	13.33	
Male	78	8.97	
HbA1c (%)			0.001*
Systolic BP (mm Hg)			0.299
Diastolic BP (mm Hg)			0.871
Hypertension referral given[§]			0.994
Yes	75	12.00	
No	117	11.97	
Body mass index (kg/m^2)			0.005*
<26	14	35.71	
26 to 32	43	13.95	
32+	121	7.44	
Uncorrected near vision (logMAR)			0.091
Corrected near vision (logMAR)			<0.001*
Eye complaint[¶]			0.478
Yes	128	13.28	
No	71	9.86	

[†] HbA1c, hemoglobin A1c (%); BP, blood pressure (millimeters mercury); LogMAR, log minimum angle of resolution

[‡] *P*-value represents one-way ANOVA F-test for continuous variables and χ^2 test for categorical variables.

[§] Hypertension referral given to participants presenting with either systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg.

[¶] Patients were asked if they were experiencing any limitations with their vision or problems related to their eyes.

* Statistically significant

There was agreement between graders for all cases of diabetic retinopathy and for all structural lesions identified. Formal assessment of inter-rater agreement for the features of the optic disc, i.e., CDR, also showed a high degree of accordance at 93.0% (Table 4). Subsequently, there was a moderately strong agreement for glaucoma suspect status (90.3% agreement) with κ = 0.53 (95% CI=0.33 - 0.73), a rate of agreement similar to previously published studies evaluating disc photos.[38] Finally, the intra-class correlation coefficients (ICCs) for the CDR and its difference were 0.841 (95% CI=0.81-0.87) and 0.68 (95%CI=0.59-0.75), respectively.

Table 4. Inter-rater reliability and agreement of image grading: optometrist versus ophthalmologist

CDR† Agreement (%)	CDR α ICC (95% CI)	CDR Absolute Difference (±SD)	CDR Difference α ICC (95% CI)	Glaucoma Suspect Agreement (%)	Glaucoma Suspect Agreement Kappa (95% CI)
93.0%	0.91 0.84 (0.81-0.87)	0.01 (± 0.06)	0.81 0.68 (0.59- 0.75)	90.3%	0.53 (0.33-0.73)

† CDR, cup-to-disc ratio; α: Cronbach's alpha; ICC: intra-class correlation coefficient; CI: confidence interval; SD: standard deviation.

Participants presented with an average CDR of 0.39 $\pm$ 0.11 and CDR asymmetry of -0.01 $\pm$ 0.09, and showed no significant association with image quality ($F_{4,174}$=1.05, *P*=0.382). Likewise, there was no significant association between image quality and glaucoma suspect status agreement ($F_{4,378}$=0.85, *P*=0.496), or between image quality and

the CDR absolute difference ($F_{4,371}$=0.37, *P*=0.830), indicating that our observed inter-rater agreeability was not limited by variability in image quality captured by the device.

Referrals

Nearly half of all participants, 100 of the 206 studied (48.5%) were referred for an expedited consult with a local ophthalmologist as a result of the screening program. A positive finding on ophthalmic imaging was the reason for 61% of referrals. An additional 19% were referred due to a participant reporting an anatomic or functional abnormality (e.g. prior eye trauma, floaters, visual field changes, teary or itchy eyes). A further 14% of participants were referred due to an inability to obtain images, likely due to cataracts, small pupils, or other media opacities. Finally, 6% of participants were referred due to a visual acuity limitation (≤20/40).

DISCUSSION

Our study is the first to field-test the PanOptic iExaminer System as a method of screening for retinal complications stemming from diabetes in a remote, resource-constrained LMIC setting. The study screened 0.1% (206 individuals) of the total population of Samoa (196,440).[39] We found that fundus images could be successfully obtained in 95.4% of participants, with 81.8% of eyes having images of clinical diagnostic quality. Given the study was performed on participants with undilated eyes in an outdoor setting remote to the traditional ophthalmic clinic with limited-to-no electricity, the device performed remarkably well. Although more advanced non-mydriatic cameras are available, the durability and maintainability of the PanOptic iExaminer System in the field proved promising. In comparison to other fundus cameras that cost at or above $10,000, the

PanOptic iExaminer can be acquired for well under $1,000, making this device highly accessible and cost-effective for use in LMICs.

Although we found that 11.7% of participants presented with background retinopathy changes, non-proliferative diabetic retinopathy was definitively detected in only 7 participants (3.4%), despite their risk status. Studies have demonstrated that diabetic retinopathy screening by non-ophthalmic providers achieves a lower rate of detection compared to retina specialists and general ophthalmologists.[38] Although it is possible that the relatively low prevalence of diabetic retinopathy identified was a function of the device, it is also likely a function of the duration and severity of diabetes in the relatively young cohort of adults in the study.[40] For example, a demographically similar study of adults between the ages of 35 to 44 years and a diabetes duration of fewer than 10 years identified a retinopathy prevalence of 3%.[41] Importantly, the findings from the handheld non-mydriatic fundus camera used in this study are validated, at least in part, by clinical A1c and other biomarkers that would be expected to predict retinopathy (Table 3). Our study sample also proved strategic in many ways due to the lower prevalence of cataracts and other media opacities in this segment of the population, allowing for a high image capture rate (95.4%).[42,43]

Our screening program additionally identified 16.0% of participants with glaucoma suspect status based solely on features identified from imaging the optic disc. Cupping of the optic nerve head is a hallmark for glaucomatous optic neuropathy. However, there is wide variation within the human population,[44] and no normative data for the Samoan population exists. CDR asymmetry is another well-known hallmark of glaucoma and is by itself predictive of glaucoma prevalence.[45] However, optic disc structural changes do not imply that a person has glaucoma, and structural features by themselves are not appropriate to screen for glaucoma. Furthermore, although there was a high level of grader agreement, allowing a glaucoma specialist to adjudicate the results could further enhance the validation of the instrument in comparison to a gold standard. A formal glaucoma screening program

should also incorporate the use of a handheld tonometer and assess for other risk factors associated with the disease.[15]

The present study benefited from the use of an iPhone 6S in comparison to prior studies' that employed an iPhone 3G, yielding a nearly six-fold increase in resolution.[33,35] As smartphone technology advances, the ability to capture images in lower light with better detail is likely to improve.[46] Furthermore, studies have illustrated the advantage of using fundus imaging over traditional ophthalmoscopy alone to identify retinal lesions.[47] Automated detection and analysis of images using artificial intelligence and point-of-care decision support is also likely to play a role in future screening programs.[9]

One of the most significant limitations of our study stems from the fact that the PanOptic iExaminer is limited to a 25° field of view, leaving unexamined the vast majority of the retina. Diabetic retinopathy is peripheral more than 50% of the time.[48] Although the device likely underestimates the true burden of eye disease in Samoa and risks providing false assurance to patients for whom an abnormal finding was not identified, the program approved by the Samoan Ministry of Health exceeds the prevailing standard of care. The vast majority of diabetic participants screened have been unable to access eye care for a variety of reasons. Furthermore, the device detected the presence of many other ocular abnormalities in nearly one-third of our study participants, many of whom did not otherwise present with visual acuity limitations or other symptoms. Although we do not have access to the results of the ophthalmic examinations provided to participants following our screening program, our study successfully established a referral system. Extending the approach presented by building the infrastructure to allow local eye care providers to receive and grade images would also be a significant process improvement. Furthermore, the subset of individuals in our sample who are in the larger genetic and metabolic Samoan study may also yield useful information in directing future eye screening interventions.

In conclusion, it is not only the ability to screen patients for eye disease, but also the ability to facilitate the connection to eye care that is of paramount importance for those with diabetes and other conditions that pose a risk to vision.[44] The present study demonstrates that a portable, smartphone-based non-mydriatic fundus camera can successfully be integrated into an eye screening program, facilitating the detection of ocular disease.

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CONTRIBUTORS LCL: Research design, collection of data, analysis and interpretation of data, manuscript preparation and revision; NLH: research design, analysis and interpretation of data, manuscript preparation and revision; MKB: image grading, analysis and interpretation of data, manuscript revision; TK & MSR: administrative and technical support, manuscript revision; DJR: research design, image grading, analysis and interpretation of data, manuscript preparation and revision.

ETHICS APPROVAL The study was approved by the Yale University International Review Board (HIC Protocol: #2000021910) and the Health Research Committee of the Samoan Ministry of Health.

Figure 1. Image quality using the PanOptic iExaminer System Percent of eyes (n=412) with at least one fundus photo obtained within each image category: Grade 1=inadequate; Grade 2=fair; Grade 3=good; Grades 4 and 5=excellent. Grade 1 was assigned to images

where the fundus was not visualized, Grade 2 images had a view of the fundus that did not include a full or clear view of the optic disc, Grade 3 images had a full and sharp view of the optic disc, Grade 4 images had a full, clear view of the optic disc in addition to some surrounding structures, and Grade 5 images had a full view of the optic disc in addition to extensive choroidal detail and views of the both the superior and inferior vascular arcades.

Figure 2. Representative fundus photographs in three participants with positive findings upon PanOptic iExaminer screening (A) Healthy fundus with foveal detail in a 35-year old participant. (B) Nonproliferative diabetic retinopathy in a 65-year old participant. (C) Example of a glaucoma suspect (based on enlarged CDR) in a 45-year old participant. Lens reflexes and shadows due to camera alignment are commonly present at the edges of even higher quality images.

Table 1. Description of the study population

Table 2. Frequency of positive findings following image review

Table 3. Associations of study population characteristics with background retinopathy

Table 4. Inter-rater reliability and agreement of image grading: optometrist versus ophthalmologist

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