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Gaps in Glaucoma care: A systematic review of monoscopic disc photos to screen for glaucoma

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Introduction

Glaucoma continues to be the third leading cause of blindness in the United States[1] despite proven treatments that can minimize vision loss,[2–4] indicating that our medical interventions are not impacting disease burden for many Americans in a meaningful way. Glaucoma is also the second leading cause of blindness worldwide.[5] In order to address this gap in glaucoma care, there is a need to develop and implement improved methods for glaucoma screening. is one important arena in which our system for delivering glaucoma care is limiting our impact on the societal burden of vision-threatening disease.

In terms of screening, 50% of those who have glaucoma remain undiagnosed in the US.[21,22] Estimates for undiagnosed glaucoma are much higher in low-income countries, and one study estimated that undiagnosed glaucoma may be as high as 96% in Nepal.[23] A recent study found that among those US glaucoma patients who are undiagnosed, one-third have mild disease, one-third have moderate disease, one-third have severe disease and 3.4% of newly diagnosed subjects were blind in one eye.[24] Though the US Preventive Task Force issued a statement in 2013 stating that current evidence is insufficient to recommend screening for primary open-angle glaucoma in adults, there is clearly a need to develop a population-based screening protocol that is effective in identifying those at risk for vision loss from glaucoma.[25]

Glaucoma progression poses a serious economic burden. Not only is there a 4-fold increase in direct costs as glaucoma severity increases from early to end-stage disease,[26] but glaucoma-related blindness also leads to a 30-fold increase in indirect costs to society due to lost productivity and additional burdens on families.[27] Any intervention that identifies people with glaucoma earlier in the disease state to start treatment before occurrence of significant visual loss will both slow disease progression and limit the functional and economic costs that glaucoma places on individuals and society.

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A more efficient, sensitive and specific screening process is necessary to facilitate the early diagnosis and treatment of primary open angle glaucoma. A study conducted by the Glaucoma Screening Platform Study Group in the United Kingdom found that the majority of practitioners in the eye care community would prefer if screening for eye disease was conducted through primary care providers where medical assistants who had received training in optic nerve photography and screening perimetry would carry out the testing.[47] Obtaining stereoscopic disc images and standard reliable perimetry requires a higher level of skill to provide quality data, and often requires more expensive equipment and a longer patient visit. In contrast, screening modalities using non-mydriatic single field (monoscopic) photography may provide a more efficient screening method with or without screening perimetry. This technique may provide a cost-effective modality in which screening for glaucoma could take place in primary care providers' offices. In this systematic review, we will gather and analyze the effectiveness of screening for glaucoma using non-stereoscopic disc photos.

Materials and Methods

This study used a systematic approach to searching the published literature using Pubmed and Embase. Final searches were conducted on June 27, 2014. Two searches were run on each database, the first including terms and medical subject headlines (MeSH) mapping to "telemedicine" and "glaucoma," and the second search including terms mapping to "non-stereoscopic" and "glaucoma." The specific searches that were generated to account for synonyms of the keywords and MeSH headings are available in Appendix 1. Articles chosen were restricted to the English language and only included published articles; abstracts were excluded.

The searches generated 221 titles. Once duplicate titles were removed, the searches revealed 147 unique references regarding telemedicine and glaucoma and 31 titles regarding glaucoma and monoscopic photographs. Two independent researchers (PANC and AJV) evaluated the titles and agreed upon reading 77 abstracts of these references to determine their eligibility based on pre-determined inclusion criteria. Inclusion criteria: evaluation of single-field, monoscopic photographs for the screening and diagnosis of glaucoma in comparison to standard diagnosis via stereoscopic disc photographs or clinical exam. Exclusion criteria: any study in which all patients were not screened with both an imaging protocol and a gold standard exam. The gold standard was defined as either a clinical exam by an ophthalmologist or stereoscopic disc photographs evaluated by an ophthalmologist.

After the criteria were applied, the two researchers screened the abstracts and determined that 29 full-length papers should be screened further. The references of the 29 papers were screened to ensure that the original search criteria had not missed any relevant citations, and no new relevant citations were found. After further review and discussion of these articles, the two researchers (PANC and AJV) came to consensus agreement that 6 of the 29 articles met the inclusion criteria for this study. Of the 29 papers, 14 were excluded because not all subjects underwent a gold-standard exam, 2 were excluded as they discussed only diabetic retinopathy or macular degeneration, and 7 were excluded because all images taken were

stereoscopic. Thus, only six studies remained. We will describe these six studies but we will not aggregate their data as all outcome variables were not the same.

Each researcher abstracted information from each study onto a standard data abstraction form and the data abstracted was compared for agreement. Consensus was reached for all data abstracted through discussion. Given the lack of well-known quality assessment tools for case series, data quality was assessed using the Modified Delphi Technique.[48] This model includes a series of questions regarding: clear statement of objectives; participant/recruitment characteristics; well defined outcome measures; statistical analysis; description of random variability; competing interests. The Modified Delphi Technique recommends a process of utilizing the questions from their 18-question checklist that apply to a specific type of study. We found that 10/18 questions applied to this type of case series assessment (Appendix 2). The questions that were excluded were questions regarding the nature of the intervention, follow-up and adverse events as none of these were relevant to these screening studies.

Results

Six studies were identified that met all of the inclusion and exclusion criteria (Table 1). Though the studies were of varying quality, they were all included because of the few total number of studies on the effectiveness of non-stereoscopic disc photos to screen for glaucoma. The six studies will be summarized below.

1. Mydriatic photographs with standard fundus camera and telemedicine protocol versus standard clinical exam.

   Maa and colleagues[49] conducted a prospective consecutive case series comparing screening for glaucoma suspect status based on a telemedicine protocol versus a standard clinical examination in 104 eyes of 52 subjects presenting to the Veterans Affairs eye clinic in Atlanta, Georgia. They enrolled all new patients presenting to the comprehensive clinic who consented to participate. Participants received a standard eye exam from an ophthalmologist along with fundus photos. The fundus photos included three 45° non-stereoscopic mydriatic photos of the 1) optic nerve and macula, 2) superotemporal arcade, 3) nasal field. The type of fundus camera used was not specified. A second ophthalmologist was given each participant's visual acuity, refractive error (via autorefraction), central corneal thickness, intraocular pressure, pupil exam and fundus photographs. This tele-ophthalmologist was asked to determine whether or not the participant was a glaucoma suspect and warranted further evaluation. There was 87% agreement between the ophthalmologist evaluating the participant in-person and the tele-ophthalmologist for making the diagnosis of glaucoma suspect. The tele-ophthalmology protocol was 64% sensitive and 95% specific for the diagnosis of glaucoma suspect (Table 2). This study received a quality score of 8/10 as there was not an adequate description of the study participants' socio-demographic characteristics and the variability of their point estimates for sensitivity and specificity (e.g. standard deviation or standard error) was not reported.

2. Mydriatic photographs with direct ophthalmoscope with custom digital video camera versus clinical exam.

   Marcus and colleagues[50] conducted a prospective pilot study of a novel fundus imaging technology compared to a standard clinical examination by an ophthalmologist that included 39 eyes of 20 diabetic patients. The fundus camera was a digital micro-video camera (Cohu Model #8282-1; Cohu Inc., San Diego, CA) attached to a Welch Allyn direct ophthalmoscope. This study took place in Atlanta, Georgia and the participants were 50% black, 50% white, 75% male, 25% female and their mean age was 48 (range 32–66). A non-ophthalmologist obtained the photographs with this camera after dilating the pupils. The non-ophthalmologist was video-conferencing with an ophthalmologist in real time so that the ophthalmologist could give directions on how to best obtain the images. After the photos were taken, the ophthalmologist examined the patient through complete dilated fundus exam. A third ophthalmologist who was masked to the patient's diagnoses but knew the patient's vision and intraocular pressure graded the video fundus images to classify glaucoma suspect status. The images from 18/39 eyes (46%) were deemed un-gradable and clinical findings were not reported for these eyes. Of the 21 gradable images, the sensitivity for correctly identifying glaucoma suspects was 50% and the specificity was 100% compared to clinical exam (Table 2). The quality score for this study was an 8/10 as they had non-consecutive recruitment and the variability of their point estimates for sensitivity and specificity (e.g. standard deviation or standard error) was not reported.

3. Non-mydriatic photographs with a portable fundus camera versus clinical exam.

   Kumar and colleagues[51] conducted a prospective screening study of 399 eyes of 201 patients which compared the diagnosis of glaucoma made by standard dilated fundus examination by a glaucoma specialist utilizing Humphrey visual field testing versus a diagnosis of glaucoma made by a glaucoma specialist only reading non-stereoscopic, non-mydriatic disc photos. This study took place in Australia, and 55% of subjects were female, 46% were male and the average age was 61 years. 50/201 subjects (25%) had a positive family history of glaucoma but no subject had been diagnosed with glaucoma before this study. The grader was a glaucoma specialist who was masked to the clinical examination status but knew the patient's age, sex and whether or not there was a family history of glaucoma. An ophthalmic photographer took the fundus photos with a portable, non-mydriatic fundus camera (Nidek NM-200D, Nidek, Tokyo, Japan) and took as many photographs as needed to obtain a good quality image. The mean number of images necessary or amount of time necessary to obtain a good quality image was not reported. The sensitivity to detect glaucoma based on age, sex, family history status and vertical cup-to-disc ratio >0.5 as identified by non-mydriatic, non-stereoscopic fundus photos was 67.4%, and the specificity to correctly identify disease was 93.6% compared to full examination by a glaucoma specialist (Table 2). The test characteristics were essentially unchanged (sensitivity 69.8%, specificity 94.2%) when glaucoma status was determined by dilated fundus examination by a glaucoma specialist along with age, sex and family history of glaucoma. The

glaucoma specialist reading the fundus images correctly classified 87.9% of those with glaucoma using monoscopic photos compared to full examination. When the grader was also given results from Humphrey Frequency Doubling Technology (FDT) testing, the correctly classified images increased to 93.9%, the sensitivity to detect glaucoma increased to 83.7%, and the specificity increased to 96.8%. This study received a quality score of 9/10 as the variability of their point estimates for sensitivity and specificity (e.g. standard deviation or standard error) was not reported.

4. Mydriatic photographs with a portable fundus camera versus standard stereoscopic disc photos.

   Yogesan and colleagues[52] compared three ophthalmologists' ability to detect a cup-to-disc ratio >0.6 on non-stereoscopic disc photos taken with a portable camera (Nidek NM-100, Nidek, Tokyo, Japan) versus disc photos taken with a standard stereoscopic fundus camera (Zeiss FF, Carl Zeiss, Oberkochen, Germany). To establish a gold standard, a fourth ophthalmologist measured the vertical cup-to-disc ratio directly from photographic slides on a light table using a x10 loupe and a 0.1mm graticule. This prospective study was conducted in Australia and included consecutive patients from the glaucoma clinic at the Lions Eye Institute. The participants' glaucoma status (normal vs glaucoma suspect vs glaucoma) was not reported. An ophthalmic photographer took all fundus photographs. The three ophthalmologists who were grading the photographs had a mean sensitivity of 73.7% (range 67%–87%) and specificity to correctly identify disease of 74.7% (range 68%–79%) (Table 2). Whether or not the ophthalmologists grading the images were masked to the patients' clinical status was not reported. The quality score for this study was a 6/10 as the characteristics of the participants were not described, the exclusion criteria was not defined, competing interests and funding sources were not provided and the variability of their point estimates for sensitivity and specificity (e.g. standard deviation or standard error) was not reported.

5. Stereoscopic versus monoscopic disc photographs compared to clinical exam.

   Lichter[53] compared 16 ophthalmologists' ability to correctly classify 16 disc photos from 8 patients for the presence of glaucomatous optic nerve damage. The ophthalmologists had expertise in glaucoma and were from 16 different institutions in the United States. Mydriatic disc photos were taken (Zeiss Fundus Camera, Germany) by an ophthalmic photographer with or without the Allen separator to generate a set of 16 monoscopic images and a set of 16 stereoscopic image pairs. The gold standard was a clinical exam by a glaucoma specialist. The outcome of interest from this study was the number of photographs that were classified correctly for the presence of glaucoma in the monoscopic condition compared to the stereoscopic condition. Under monoscopic viewing, 57% (146/256) of images were classified correctly whereas under stereoscopic viewing, 73% (186/256) of images were classified correctly (Table 2). Though the statistical significance of this difference between the two viewing modalities was not reported, the author notes that this difference is clinically relevant. The quality score for this study was

a 5/10 as the characteristics of the participants were not described, and though the eligibility criteria are stated, they are not replicable as the author chose participants to try to include a wide variety of optic disc phenotypes, additionally, recruitment was not consecutive, there was no statistical evaluation given for the outcome of interest for this review and the variability of their estimates for correctly classifying disease (e.g. standard deviation or standard error) was not reported.

6. Stereoscopic versus monoscopic disc photographs compared to clinical exam.

   Chan and colleagues[54] compared 14 glaucoma specialists' (including 2 glaucoma fellows) ability to correctly classify the presence of glaucomatous optic neuropathy. The presence of glaucoma was determined through a panel of 5 glaucoma specialists who came to consensus on the diagnosis after reviewing the clinical examination data, including intraocular pressure and visual fields as well as dilated stereoscopic disc photos. The study took place in Melbourne, Australia and mydriatic disc photos were taken by an ophthalmic photographer both monoscopically (Kowa VX-10, Kowa, Tokyo, Japan) and stereoscopically (Nidek 3-DX, Nidek, Gamagori, Japan). Chan and colleagues began with a convenience sample of 197 eyes from 197 patients, selected 67 high-quality disc photos, separated the disc photos into categories based on glaucoma disease status (normal, mild glaucoma, moderate glaucoma and severe glaucoma based on modified Hodapp-Anderson-Parrish guidelines), and then randomly chose 5 disc photos to include for evaluation from each category, for a total of 20 pairs of stereoscopic and monoscopic disc photos. Of photos of discs with known glaucoma, 81%±8% of stereoscopic photos were correctly classified and 76%±10% of monoscopic photos were correctly classified (p=0.37). Of photos of discs known not to have glaucoma, 83%±4% of stereoscopic photos were correctly classified and 78%±8% of monoscopic photos were correctly classified (p=0.44) (Table 2). There was no statistically significant difference between monoscopic and stereoscopic viewing conditions and the ability of the glaucoma specialist to correctly classify glaucomatous status based on disc photos. The quality score for this study was an 8/10 as there was no description of the socio-demographics of the study population and subject recruitment was not consecutive.

Discussion

The specificity of monoscopic photos to detect glaucoma compared to clinical exam was excellent in these studies (93.6%–100% specificity), but the sensitivity of this method was much lower (50%–67.4%). A highly specific test will give a true negative test result for those without disease, and will give very few false positive results. It is important to have high specificity in a screening test so that there are not too many people who falsely test positive who then require further follow-up to determine whether or not they truly have disease, which is costly both in terms of health care dollars and the patient's time and anxiety. It is particularly important to have reasonable specificity in a screening test when the disease being screened for has a low prevalence in the population, such as glaucoma. Vaahtoranta and colleagues determined that a population-based screening program that

evaluated all Finnish adults age 50–79 for glaucoma every five years would be cost effective only if the specificity of the testing was ≥96%.[55] It is also important for a screening test to have reasonable sensitivity. From this review, it appears that monoscopic disc photos have the potential to meet this criterion. A highly sensitive test will give a true positive test result to those who have disease, and give very few false negative results. A highly sensitive screening test will not miss anyone who truly has glaucoma by designating them as "normal."

The sensitivity plays an important role in determining the positive predictive value (PPV) of a screening test. The PPV is calculated by multiplying the sensitivity of the test by the prevalence of disease in a population and dividing by the probability of a positive test.[56] Therefore, the pre-test probability of developing a disease is important in determining the utility of a screening test. Because the prevalence of glaucoma among the general population is about 2%, if monoscopic photos performed as well, on average, in a screening setting as they did in these case series, the positive predictive value would be 24.5%. That means that about 75% of those who screen positive for glaucoma would actually be false positives. If monoscopic photos were used to screen only high risk individuals, such as African-Americans age 65 and older who have a 6% prevalence of glaucoma,[57] the positive predictive value would increase to 50.4%. If the photos were used to screen even higher risk individuals such as African-Americans who have a family history of glaucoma, and a 10% prevalence of glaucoma was assumed, the positive predictive value would increase to 63.9%. One caveat is that case-control studies, and likely case series as well, are known to overestimate the power of a screening test by about three-fold compared to an evaluation of the screening test in the population in which the test will be used.[58] This is a major shortfall in all of the literature that we have identified to date describing the utility of monoscopic disc photos in screening for glaucoma. Further research evaluating the sensitivity and specificity of monoscopic disc photos to detect glaucoma in a community-based setting will be important for further validation of this technique.

The monoscopic photos in this review had a lower sensitivity to detect glaucoma than would be optimal, as one wants to ensure that a screening test does not miss people with true disease. However, the sensitivities and specificities for monoscopic photos were not very different from one report of the ability of an ophthalmologist to detect glaucoma with a dilated fundus exam and direct ophthalmoscopy. In one study cited by the US Preventive Services Task Force in their 2005 review of the effectiveness of screening for glaucoma, they noted that a dilated exam by an ophthalmologist is 59% sensitive and 73% specific in detecting glaucoma.[59] A meta-analysis of screening tests for detecting open-angle glaucoma included 6 studies that evaluated the test characteristics of stereoscopic optic disc photography, and they found that the 3 high quality studies had a sensitivity of 74% (95% Credible Interval, 30%–95%) and a specificity of 82% (95% Credible Interval, 45%–97%). All of the six studies combined had a sensitivity of 73% (95% Credible Interval, 61%–83%) and a specificity of 89% (50%–99%).[60] In this review of monoscopic photographs, the sensitivity was slightly lower and the specificity was similar to detect glaucoma. We are not able to estimate whether these differences would be statistically significant because the majority of the studies of monoscopic photos identified (5/6) did not give measures of variability to their estimates (e.g. standard deviation or standard error). In the future, it will

be important for studies evaluating novel screening techniques to provide measures of variability so that the results can be more easily compared between studies and clinicians can have a better understanding of the limits of the screening techniques.

Kumar and colleagues[51] found that the sensitivity to detect glaucoma could be increased dramatically by combining demographic characteristics (age>45, family history of glaucoma), monoscopic fundus photos judged to have a vertical cup-to-disc ratio >0.5 and any abnormalities on a reliable FDT. This combination of variables increased the sensitivity to detect disease from 67.4% to 83.7% and increased the specificity from 93.6% to 96.8% by including FDT results. Interestingly, they also found that including intraocular pressure did not change the sensitivity to detect disease. FDT has been tested on its own in population-based studies. In the Beijing Eye Study in China, FDT was 64.3% sensitive in detecting disease among subjects 40 years and older compared to the diagnosis of glaucoma by clinical exam by an ophthalmologist with glaucoma training. [61] In the Tajimi Study in Japan, FDT was 55.6% sensitive and 92.7% specific in detecting glaucoma among a population of subjects over the age of 40 where glaucoma was defined after clinical examination data was reviewed by a panel of six ophthalmologists.[62] Combining socio-demographic data (age >45, family history of glaucoma), monoscopic fundus photos and FDT results has the potential to improve the effectiveness of community-based screening for glaucoma.

Kumar and colleagues[51] used a portable, non-mydriatic fundus camera to take the monoscopic photographs. A portable, non-mydriatic fundus camera and FDT perimetry are potentially technologies that could be deployed in primary care settings, both in the US and abroad. A survey study in the UK found that health care providers would prefer if glaucoma screening could occur in the primary care setting.[47] Glaucoma screening could be deployed in a primary care setting if a telemedicine structure was utilized. A medical assistant in a primary care provider's office could be trained to take non-mydriatic disc photos and administer a screening perimetry test if the perimetry test was deemed necessary. It is easier to train non-ophthalmic personnel to take high-quality monoscopic disc photos than stereoscopic photos, and the length of the examination with monoscopic photos compared to stereoscopic photos is also decreased, therefore decreasing the burden on the patient. The images could then be sent via secured servers to reading centers where trained ophthalmolgists graded the images and determined whether or not they would like the patient to have a screening perimetry test. The perimetry test would then take place in the local primary care doctor's office, and the results would be sent to the reading center where the ophthalmologist would determine whether the patient needed to come for full ophthalmic evaluation. This process would be very similar to what is already in place in the United Kingdom for diabetic retinopathy screening. Ultimately, the grading of disc photos will likely be done by automated software, and only discs that the software cannot accurately grade (such as a tilted disc or a myopic disc) would be adjudicated by an ophthalmologist. This type of software is already in development for screening for diabetic retinopathy.

In some low-income countries such as in India, there is already a model for providing eye care to those in remote areas through eye camps. A team of eye care professionals, including

ophthalmologists, ophthalmic technicians, medical assistants and camp managers bring ophthalmic equipment to a remote village far from the central eye hospital. The eye care professionals screen everyone who comes to the eye camp, mainly for refractive error and cataract, provide glasses at the eye camp, and then facilitate transportation back to the main eye hospital for further treatment for cataract. Due to the large volume of patients seen in an eye camp, it is difficult to complete a dilated fundus exam to screen for pathology in the posterior pole in this setting. If it can be shown that monoscopic disc photos taken with a portable fundus camera are reasonably sensitive and specific for identifying those at risk for glaucoma, an ophthalmic photographer could come to the eye camp and take non-mydriatic fundus photos with a portable fundus camera. An ophthalmologist would read them during the eye camp and specify which patients had a cup to disc ratio ≥0.7 who would then go on to get screening perimetry. Those who had a cup to disc ratio ≥0.7 and an abnormal screening perimetry exam would be transported back to the main eye hospital for glaucoma treatment in the same way that patients are transported back for cataract surgery.

Some feel that OCT may provide a more sensitive and specific tool for glaucoma screening than fundus photos, and it is also a test that could be provided in a primary care setting and then interpreted by ophthalmologists in a reading center to determine appropriate follow-up. Blumberg and colleagues recently conducted a Monte-Carlo microsimulation to model the efficacy of SD-OCT screening on visual field outcomes for African-Americans over the age of 50.[63] They found that the program, along with the costs for treating individuals who have glaucoma, would cost between $46,416-$67,814 per quality-adjusted life-year (QALY), which is an acceptable cost/QALY in the US healthcare system. They also found that strategies that would maximize the effectiveness of treatment, such as improved adherence to physician recommendations for treatment and follow-up would significantly reduce the cost/QALY. One important assumption made in this model was that the sensitivity of SD-OCT to detect disease was 85% and the specificity was 95%, though these numbers were not derived from population based studies as that data was not available. When additional population-based data becomes available to better gauge the effectiveness of SD-OCT, monoscopic fundus photos and FDT to screen for glaucoma, it will be necessary to compare the cost-effectiveness between these different modalities. SD-OCT would likely require a much more significant initial capital investment than either a portable, non-mydriatic fundus camera or FDT. In terms of establishing screening programs in low-income countries, cost will be an even more significant hurdle than in higher-income countries. Less expensive screening modalities will be even more imperative in low-income countries than they are in the US in order to work to reduce the burden of global blindness from glaucoma.

Conclusion

In order to reduce the burden of vision loss from glaucoma at a population level, improved tools for population-based screening and improved systems for ensuring adherence to treatment and follow-up recommendations once disease is detected are needed. Monoscopic disc photos, potentially taken by portable fundus cameras, could be an important component of this assessment. The development of improved cameras that can capture adequate quality images without mydriasis may help enable glaucoma screening to occur in a primary care setting. The ability to instantly and simultaneously transmit these images via wireless

internet is also a desired feature that would enable improved communication between primary care providers and ophthalmologists. FDT, or perhaps other perimetric tests, all measures of optic nerve function, combined with monoscopic disc images, a measure of optic nerve structure, may be a cost-effective way to screen for glaucoma at the primary care providers' office. Once it is known that portable fundus cameras take good enough quality images that their sensitivity and specificity for detecting disease are reasonable, it will be important to test these cameras in population-based studies to more accurately assess the parameters of the screening test in the population in which it would be utilized.

Expert Commentary

Further research is needed to evaluate the sensitivity and specificity of monoscopic disc photos to aid in identifying patients at risk for glaucoma. It is helpful when studies evaluate test parameters comparing monoscopic photos both to standard stereoscopic photos and to clinical exam. Having both outcomes aids in analyzing whether or not a more simple test is comparable to a more labor-intensive test as well as in analyzing whether or not this more simple test could be used instead of the gold standard of a clinical exam as a screening tool. Future studies should include reports of the standard deviation and standard error of their estimates in order to better compare results between studies. Additional studies are needed both in controlled environments such as in an ophthalmology clinic and in population-based settings, such as in an eye-camp or primary care provider's office, to determine whether monoscopic photos could be used as a reasonable first-line screening tool for identifying those at high-risk for glaucoma.

Five year view

The development of improved portable non-mydriatic fundus cameras that are easier to use will enable para-professional staff in a primary care setting to take monoscopic disc photos. The development of automated software to help grade the optic nerve will also facilitate more wide-spread implementation of a glaucoma screening program. As technology evolves and these screening tools become easier to use, the ophthalmology community may be better able to develop a more cost-effective way to screen for glaucoma through primary care provider's offices close to patients' homes or through eye camps in low-income countries where a team of eye care providers comes to the patients' village.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol. Mar; 2006 90(3):262–267. [PubMed: 16488940]

2. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. The AGIS Investigators. Am J Ophthalmol. Oct; 2000 130(4):429–440. [PubMed: 11024415]

3. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol. Jun; 2002 120(6):701–713. [PubMed: 12049574]

4. Leske MC, Heijl A, Hussein M, Bengtsson B, Hyman L, Komaroff E. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. Arch Ophthalmol. Jan; 2003 121(1):48–56. [PubMed: 12523884]

5. Mariotti SP, Pascolini D. Global estimates of visual impairment. Br J Ophthalmol. 2012; 96:614–618. [PubMed: 22133988]

6. Quigley HA, West SK, Rodriguez J, Munoz B, Klein R, Snyder R. The prevalence of glaucoma in a population-based study of Hispanic subjects: Proyecto VER. Arch Ophthalmol. 2001 Dec; 119(12): 1819–26. [PubMed: 11735794]

7. Tielsch JM, Katz J, Singh K, Quigley HA, et al. A Population-based Evaluation of Glaucoma Screening: The Baltimore Eye Survey. Am J Epidemiol. 1991; 134(10):1102–1110. [PubMed: 1746520]

8. Thapa SS, Paudyal I, Khanal S, et al. A population-based survey of the prevalence and types of glaucoma in Nepal: The Bhaktapur Glaucma Study. Ophthalmology. 2012; 119(4):759–764. [PubMed: 22305097]

9. Heijl A, Bengtsson B, Oskarsdottir SE. Prevalence and severity of undetected manifest glaucoma: results from the early manifest glaucoma trial screening. Ophthalmology. 2013 Aug; 120(8):1541–5. [PubMed: 23631945]

10. Screening for Glaucoma: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2013; 159:I-28.

11. Lee PP, Walt JG, Doyle JJ, et al. A multicenter, retrospective pilot study of resource use and costs associated with severity of disease in glaucoma. Arch Ophthalmol. Jan; 2006 124(1):12–19. [PubMed: 16401779]

12. Poulsen PB, Buchholz P, Walt JG, Christensen TL, Thygesen J. Cost analysis of glaucoma-related blindness in Europe. Int Congr Ser. 2005; 1282:262–266.

13. Burr JM, Campbell MK, Campbell SE, Francis JJ, Greene A, Hernandez R, Hopkins D, McCann SK, Vale LD. Developing the clinical components of a complex intervention for a glaucoma screening trial: a mixed methods study. BMC Med Res Methodol. 2011; 11:1–10. [PubMed: 21208427]

14. Moga C, Guo B, Schopflocher D, Harstall C. Development of a quality appraisal tool for case series studies using the modified Delphi Technique. Institute of Health Economics. 2012:1–71.

15**. Maa AY, Evans C, DeLaune WR, Patel PS, Lynch MG. A novel tele-eye protocol for ocular disease detection and access to eye care services. Telemedicine and e-Health. 2014; 20(4):318–323. Prospective case series comparing screening for glaucoma suspect status based on a telemedicine protocol using monoscopic fundus photos to standard clinical exam. [PubMed: 24527668]

16**. Marcus DM, Brooks SE, Ulrich LD, et al. Telemedicine diagnosis of eye disorders by direct ophthalmoscopy: A pilot study. Ophthalmology. 1998; 105:1907–1914. Prospective study of a micro-video camera attached to a direct ophthalmoscope compared to clinical exam. [PubMed: 9787363]

17**. Kumar S, Giubilato A, Morgan W, et al. Glaucoma screening: analysis of conventional and telemedicine-friendly devices. Clin and Exp Ophthalmol. 2007; 35:237–243. a. Prospective case series comparing the diagnosis of glaucoma made by clinical exam versus the diagnosis of glaucoma made from monoscopic, non-mydriatic disc photos.

18**. Yogesan K, Constable IJ, Barry CJ, et al. Evaluation of a portable fundus camera for use in the teleophthalmologic diagnosis of glaucoma. Journal of Glauocma. 1999; 8:297–301. a. Prospective case series comparing the diagnosis of glaucoma made by evaluating monoscopic

images taken with a portable fundus camera versus stereoscopic images taken with a standard fundus camera.

19**. Lichter PR. Variability of expert observers in evaluating the optic disc. Trans Am Ophthalmol Soc. 1976; 74:532–72. a. Case series comparing ophthalmologists' ability to correctly classify glaucomatous nerves based on monoscopic versus stereoscopic disc photos. [PubMed: 867638]

20**. Chan HHL, Ong DN, Xiang Y, et al. Glaucomatous Optic Neuropathy Evaluation (GONE) project: The effect of monoscopic versus stereoscopic viewing conditions on optic nerve evaluation. Am J Ophthalmol. 2014; 157:936–944. Case series comparing ophthalmologists' ability to correctly classify glaucomatous nerves based on monoscopic versus stereoscopic disc photos. [PubMed: 24508161]

21. Vaahtoranta-Lehtonen H, Tuulonen A, Aronen P, et al. Cost effectiveness and cost utility of an organized screening programme for glaucoma. Acta Ophthalmol Scand. 2007; 85:508–518. [PubMed: 17655612]

22**. Momont AC, Mills RP. Glaucoma screening: Current perspectives and future directions. Seminars in Ophthalmology. 2013; 28(3):185–190. a. Review of screening tests for glaucoma with detailed discussion of Bayes Theorem and the probability of having the disease given a positive screening test result and the implications for glaucoma screening. [PubMed: 23697622]

23. National Eye Institute. [Accessed June 27, 2014] US Age-Specific Prevalence Rates for Glaucoma by Age and Race/Ethnicity. 2010. http://www.nei.nih.gov/eyedata/glaucoma.asp#1

24. Medeiros FA. How should diagnostic tests be evaluated in glaucoma? British Journal of Ophthalmology. 2007; 91(3):273–274. [PubMed: 17322462]

25. Fleming C, Whitlock E, Beil T, et al. Screening for primary open-angle glaucoma in the primary care setting; an update for the US Preventive Services Task Force. Ann Fam Med. 2005; 3:167–70. [PubMed: 15798044]

26. 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(12):5373–5385. [PubMed: 18614810]

27. Wang YX, Xu L, Zhang RX, Jonas JB. Frequency-doubling threshold perimetry in predicting glaucoma in a population-based study: The Beijing Eye Study. Arch Ophthalmol. 2007; 125(10): 1402–1406. [PubMed: 17923550]

28. Iwase A, Tomidokoro A, Araie M, Shirato S, Shimizu H, Kitazawa Y. Tajimi Study Group. Performance of frequency-doubling technology perimetry in a population-based prevalence survey of glaucoma: The Tajimi Study. Ophthalmology. 2007; 114:27–32. [PubMed: 17070580]

29. Blumberg DM, Vaswani R, Nong E, et al. A comparative effectiveness analysis of visual field outcomes after projected glaucoma screening using SD-OCT in African American communities. Invest Ophthalmol Vis Sci. 2014; 55:3491–3500. [PubMed: 24787570]

Key issues

- In this systematic review, the specificity of monoscopic photos to detect glaucoma compared to clinical exam was excellent (93.6%–100% specificity) and the sensitivity to detect disease was lower (50%–67.4%).
- A population-based glaucoma screening program evaluating adults aged 50–79 estimated that the program would be cost-effective if testing was ≥96%,[55] and from this review, it appears that monoscopic disc photos have the potential to meet this criterion.
- This area of study is limited by the few number of studies that have been carried out and by the lack of reporting of standard deviation or standard error in estimates of sensitivity and specificity, making it difficult to compare results between studies.
- Further research is needed to validate the use of monoscopic non-mydriatic photos taken with portable fundus cameras in identifying individuals at high-risk for glaucoma, both in the controlled setting of an eye clinic and in the real-world setting of a population-based study.

Table 1

Study Descriptions

Author	Year	Location	# of Eyes Screened	Study Methodology
Lichter	1976	Michigan, USA	16	Zeiss fundus camera monoscopic vs. stereoscopic photos compared to clinical exam
Marcus et al.	1998	Georgia, USA	39	Custom direct ophthalmoscopy with digital microcamera vs. Clinical exam
Yogesan et al.	1999	Australia	51	Handheld Nidek NM-100 camera vs. Carl Zeiss FF Retinal Camera
Kumar et al.	2007	Australia	399	Handheld Nidek NM-200D camera vs. Clinical exam
Maa et al.	2014	Georgia, USA	104	Three 45° images (camera not specified) vs. Clinical exam
Chan et al.	2014	Australia	20	Kowa VX-10 monoscopic vs. Nidek 3DX stereoscopic photos compared to clinical exam

Table 2

Outcomes for Detecting Glaucoma

Method	**Outcome Measures**				
1. Camera vs. Clinical Exam	**Sensitivity**	**Specificity**	**% of stereoscopic photos correctly classified with glaucoma**	**% of monoscopic photos correctly classified with glaucoma**	**P value**
Marcus et al. 1998	50%	100%			
Kumar et al. 2007	67.4%	93.6%			
Maa et al. 2014	64%	95%			
Lichter 1976			73%	57%	
Chan et al. 2014			81% ± 8%	76% ± 10%	0.37
2. Camera vs. camera	**Sensitivity**	**Specificity**	**% of stereoscopic photos correctly classified with glaucoma**	**% of monoscopic photos correctly classified with glaucoma**	**P value**
Yogesan et al. 1999	73.7%	74.7%			