REVIEW

A Systematic Review of Digital Ophthalmoscopes in Medicine

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Purpose: Recent advances in telemedicine have led to increased use of digital ophthalmoscopes (DO) in clinical settings. This review aims to assess commercially available DOs, including smartphone (SP), desktop, and handheld ophthalmoscopes, and evaluate their applications.
Methods: A literature review was performed by searching PubMed (pubmed.ncbi.nlm.nih.gov), Web of Science (webofknowledge.com), and Science Direct (sciencedirect.com). All English-language papers that resulted from the search terms "digital ophthalmoscope", "screening tool", "glaucoma screening", "diabetic retinopathy screening", "cataract screening", and "papilledema screening" were reviewed. Studies that contained randomized clinical trials with human participants between January 2010 and December 2020 were included. The Risk of Bias in Systematic Reviews (ROBIS) tool was used to assess the methodological quality of each included paper.
Results: Of the 1307 studies identified, 35 met inclusion and exclusion criteria. The ROBIS tool determined that 29/35 studies (82.8%) had a low risk of bias, 3/35 (8.5%) had a moderate risk of bias, and 3/35 (8.5%) had a high risk of bias.
Conclusion: The continued adoption of DOs remains uncertain because of concerns about the image quality for non-mydriatic eyes and the confidence in data captured from the device. Likewise, there is a lack of guidelines for the use of DOs, which makes it difficult for providers to determine the best device for their practice and to ensure appropriate use. Even so, DOs continue to gain acceptance as technology and practice integration improve, especially in underserved areas with limited access to ophthalmologists.
Keywords: fundoscopy, teleophthalmology, diagnostics, screening, referral

Introduction

Three of the leading causes of preventable vision loss worldwide are glaucoma, cataracts, and diabetic retinopathy (DR). A major contributing factor to vision loss due to these conditions is inadequate access to care, leading to late diagnosis and treatment. As of October 2019, it was estimated that more than half of the 3 million Americans with glaucoma were unaware of their condition.[1] Cataracts account for one in three cases of blindness and one in six cases of visual impairment, highlighting the need for treatment.[2] The increasing prevalence of systemic risk factors in the aging US population is expected to accelerate onset of these ocular manifestations.[3,4]

Limited access due to geographic barriers, high costs, lack of patient education, and transportation create additional challenges.[5–7] Pervasive barriers in urban populations including transportation and physical disability have contributed to a 25% prevalence of undiagnosed diabetic retinopathy.[7] Movement of screening and follow-up appointments to teleophthalmology may mitigate these obstacles.[5]

The limited cadre trained to operate traditional direct ophthalmoscopes and biomicroscopy precludes their use as a screening tool universally. These systems are restricted to ophthalmology clinics and emergency departments. A digital solution can decentralize this, allowing remote providers to monitor screening and refer patients to ophthalmologists when necessary. This article categorizes and reviews the current progress of digital ophthalmoscopy, referred to as computer-aided, handheld-, and smartphone-based devices which digitize available systems of direct ophthalmoscopy.

Materials and Methods

Inclusion Criteria

The eligibility criteria for this review included a systematic search using PubMed, Web of Science, and Science Direct. The included studies estimate the size and direction of the effect of interventions presented as numerical data on an individual study-level basis and with quantitative synthesis (meta-analysis). Additionally, the classification of the type of DO subdivided the category into three groups: desktop-based digital ophthalmic devices, handheld digital ophthalmic devices, and smartphone-based retinal imaging DO in either a mydriatic or non-mydriatic fashion. Ophthalmology patients were defined as those who were diagnosed and treated for an ophthalmic condition at the beginning of the study. Further, we included studies involving participants who had glaucoma, diabetic retinopathy, and cataracts.

Search Strategy and Screening

PubMed, Web of Science, and Science Direct were searched from 2010 to 2020. The search keywords for each database included: "digital ophthalmoscope", "screening tool", "glaucoma screening", "diabetic retinopathy screening", "cataract screening", and "papilledema screening." Studies were limited to randomized clinical trials published between January 2010-December 2020 involving human subjects and written in English (Figure 1).

In addition to the literature review database search, relevant studies were reviewed by the coauthors for relevance to the area of focus of the paper. Assessments of the study design, population, intervention, and methodology were completed during the review process.

Outcomes

The reported outcomes included comparing manufacturing companies, price, field of view (FOV), and size among the different DOs. Furthermore, the DOs were compared using cup-to-disc (c/d) ratios, kappa (κ) coefficient for interrater image quality, accuracy, and ophthalmic disease detection sensitivity. When more than one review included the same studies, the review that reported the most complete presentation of the results was selected for inclusion in the overview.

Assessment of Methodological Quality

We assessed the methodological quality of each included study using the Risk of Bias In Systematic Reviews (ROBIS) tool. Two review authors (AM and NP) independently performed quality assessments. Disagreements regarding the overall assessments were resolved through discussion, with a third reviewer as the final arbitrator (RR). The rationale behind assessments was documented. We calculated the measures of agreement and reliability between raters for each ROBIS domain.

Data Synthesis

We stratified the included systematic reviews by type of pathology assessed (glaucoma, diabetic retinopathy, cataracts), type of DO, and type of analysis (with or without meta-analysis). When a meta-analysis was performed, we reported pooled estimates using the models and measures of effect reported by systematic review authors with 95% confidence intervals (CIs). These measures included the sensitivity and specificity of each device for detecting various outcomes. Further, a κ-coefficient statistical analysis, which measures the degree of interrater agreement between variables, was recorded from the studies identified for this review and was included when possible. No additional statistical analyses were performed.

Results

Results of the Literature Search

We obtained a total of 1307 citations through database searches. Following the application of the inclusion and exclusion criteria, 35 published studies were included in the analysis. They contained data on diabetic retinopathy, glaucoma, cataracts, functionality, and comparison reports related to digital ophthalmoscopes.
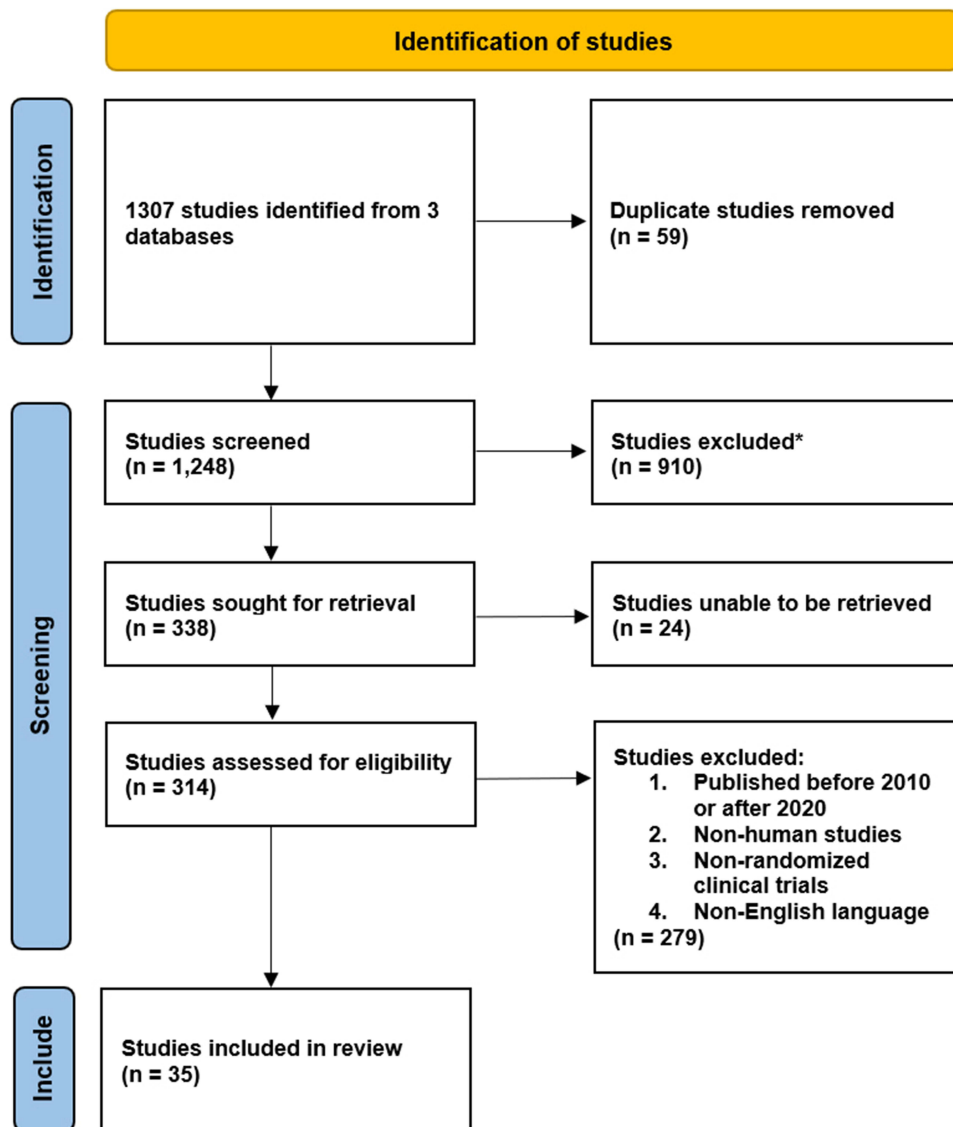
Figure 1 PRISMA flow diagram illustrating the study selection process for the systematic review. *Records excluded after manual review by authors determined that studies were not relevant to the current review.
Notes: PRISMA figure adapted from Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow et al The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. Creative Commons.

Methodological Quality

Using the ROBIS tool, 29/35 studies (82.8%) had a low risk of bias, 3/35 (8.5%) had a moderate risk of bias, and 3/35 (8.5%) had a high risk of bias across all the ROBIS domains. These include study eligibility criteria, identification and selection of studies, data collection and appraisal, and synthesis and findings.

Digital Ophthalmoscope Use in Screening for Ophthalmic Disease
Smartphone-Based Retinal Imaging in Diabetic Retinopathy

With respect to diabetic retinopathy, Karakaya et al[8] compared the ability of various smartphone-based retinal cameras, including iExaminer (Welch Allyn; Skaneateles Falls, NY, USA), D-EYE (D-EYE Srl; Padova, Italy), Peek Retina (Nesta, London, UK), and iNview (Volk Optical Inc.; Mentor, OH, USA) (Table 1). Data on the sensitivity and specificity of each device for detecting DR were used as comparative metrics (Table 2). Russo et al[9] utilized the International Clinical Diabetic Retinopathy Disease Severity scale[10] to compare DR grading agreement between a slit-lamp

Table 1 Comparison of Digital Ophthalmoscopes and Classification

Device Classification	Device	Company	Estimated Price (USD)	Field of View (°)	Size of Device
Gold standard	Direct Ophthalmoscope	Various	$400	5°	Standard
Computer-aided digital ophthalmoscope	3nethra	Forus	$8000	45°	Large
	Topcon TRC-NW8FPLUS	Topcon	$20,000+	30°- 45°	Large
	Icam	Optovue	$14,000-$17,000	45°	Large
	Visucam	Carl Zeiss	$13,000+	30°- 45°	Large
	Canon CR-2	Canon Medical Systems	$15,000+	45°	Large
	Optos Daytona[a]	Optos PLC	$85,000+	45°-200°	Large
	Pictor	Volk Optical Inc	$6500	40°	Medium
	Smartscope PRO	Optomed Oy	$7000	40°	Medium
	Versacam	Nidek	$4000	45°	Medium
	FOP NM- 10	Remedio Innovative Solutions	$8000	40°	Medium
Smartphone based digital ophthalmoscope	D-Eye	D-EYE Srl	$435	5°-20°	Small
	iExaminer kit[b]	Welch Allyn	$700-$1000	26°	Small
	Paxos	Digisight Technologies	$299	56°	Small
	Peek Retina	Peek Vision	$225	20°	Small
	20D Volk lens	Volk Optical Inc	$348	46°- 60°	Small
	iNview	Volk Optical Inc	$799	50°	Small

Notes: [a]FOV model dependent; [b]Used in conjunction with PanOptic ophthalmoscope.

biomicroscope and D-EYE, a digital retinal camera magnetically attached to an iPhone 5 (Apple Inc.; Cupertino, CA, USA). The latter showed greater sensitivity to lens transparency and pupil diameter with a higher portion of images deemed ungradeable. However, the D-Eye's 8 megapixel camera, offers approximately 150 pixels per retinal degree which exceeds the standard benchmark resolution set by the United Kingdom's National Health Service for effective detection of retinopathy (6 megapixels and 30 pixels per degree).[11] Prathiba et al[12] tested the ability of a non-mydriatic fundus on phone (FOP) smartphone-based nonmydriatic retinal imaging camera (FOP NM-10; Remedio Innovative Solutions Pvt. Ltd, Bangalore, India) to detect sight-threatening diabetic retinopathy (STDR). A sensitivity of 88% and 82% was determined by two graders, respectively, with a high specificity of 99% to detect STDR when compared with a Zeiss FF450 desktop mydriatic fundus camera (Zeiss; Jena, Germany). Several studies used the κ-coefficient between graders to assess overall image quality (Table 2).

Computer-Aided & Handheld Non-Mydriatic Imaging in Diabetic Retinopathy

Malerbi et al[13] revealed agreement as a screening tool regarding the classification of diabetic retinopathy for observation or referral when comparing binocular indirect ophthalmoscopy (BIO) to telemedicine protocols using a Canon CR-s Digital Retinal Camera (Canon Medical Systems; Amstelveen, Netherlands) for DR screening. However, there was poor

Table 2 Comparison of Digital Ophthalmoscope in Various Ocular Pathologies

Pathology	Device Type	Study Title	Digital Ophthalmoscope	Comparison Device	VCDR	Sensitivity	Specificity	k-Coefficient	P-value
Diabetic Retinopathy	**Smartphone based**	Karakaya[8]	iExaminer	n/a	n/a	61.0%	n/a	n/a	n/a
			D-EYE			62.0%			
			Peek-Retina			69.0%			
			iNview			75.00%			
		Russo[9]	D-Eye	Slit lamp	n/a	81.00%	98.0%	0.780	<0.0001
	Desktop-based and handheld non-mydriatic	Prathiba[12]	FOP NM-10	Desktop mydriatic camera	n/a	75.20%	95.20%	0. 850	<0.0001
		Malerib[13]	Canon CR	BIO	n/a	n/a	n/a	0.670–0.740	n/a
Glaucoma	**Smartphone based**	Russo[14]	D-Eye	Slit lamp	0.1–0.9	38.0–100%	84.0–100%	0.630	<0.0001
		Bastawrous[15]	iExaminer kit	Desktop retinal camera	0.7–1.0	n/a	n/a	0.690	n/a
		Giardini[16]	Ophthalmoscope adapter on Samsung S3	n/a	0.1–1.0	n/a	n/a	n/a	n/a
	Desktop-based and handheld non-mydriatic	Issac[17]	PanOptic	n/a	n/a	100%	90.0%	n/a	n/a
Cataracts	**Smartphone based**	Dickson[18]	D-Eye	Indirect ophthalmoscope	n/a	73.2%	97.0%	n/a	n/a
		Furdova[19]	Lenovo Smartphone with Volk Lens 20D	n/a	n/a	n/a	n/a	n/a	n/a

Abbreviation: VCDR = vertical cup to disc ratio

agreement in terms of actual classifiation of DR. This disagreement was thought to be due to the limitations of BIO in detecting minor changes, like microaneurysms,neovascularization, or macular edema.

Smartphone-Based Retinal Imaging in Glaucoma

Russo et al[14] compared smartphone ophthalmoscopy using a D-EYE adapter on an iPhone 5s (Apple Inc.; Cupertino, CA, USA) with slit-lamp indirect biomicroscopy to assess undilated vertical cup-to-disc ratio (VCDR) (Figure 2). D-EYE identification of optic nerve was feasible in 104 of 107 eyes, and two masked glaucoma specialists deemed the modalities to have significant grading agreement in 73.4% of cases (κ = 0.63, p < 0.001). A low-cost molded plastic adapter was manufactured and clipped over a Samsung Galaxy SIII smartphone (Samsung Electronics Co.; Seoul, South Korea) in the 2014 Giardini et al[16] glaucoma screening cohort, which yielded no significant difference in VCDR between dilated Digital Retinal Camera (DRS+, Haag Streit CenterVue, Italy) footage and smartphone-acquired footage (p = 0.98). In a follow-up assessment of the Nakuru Eye Disease Cohort study of primary open-angle glaucoma incidence, amongst other diseases, Bastawrous et al[15] used Peak Retina, a prism adapter, over a Samsung SIII GT-I9300 smartphone (Samsung Electronics Co.; Seoul, South Korea) to image optic nerve heads. No discernable difference was noted between mydriatic photographs taken with a lay photographer using Peek Retina when compared to an experienced retinal photographer. The results showed that the image quality obtained with the smartphone adapter allowed for effective glaucomatous disc grading[17] (Table 2).

Computer-Aided Imaging in Glaucoma

Issac et al[17] reported the application of adaptive threshold-based fundus processing for glaucoma screening. This threshold-based method functions in lieu of cumbersome manual segmentation of optic disc and cup with color intensity discernment to generate a binary image. After initial fundus imaging with a Welch Allyn PanOptic Ophthalmoscope (Welch Allyn; Skaneateles Falls, NY, USA), optic cup segmentation was done by green channel histogram, followed by "ISNT" feature selection[20] including c/d ratio, neuroretinal rim (NRR) area, and blood vessel area. Sixty-seven images rendered with Artificial Neural Network and Support Vector Machine classifiers obtained a diagnostic accuracy of 94.1%, specificity of 90%, and sensitivity of 100%. Alternative computer aided diagnostics include superpixel segmentation and vessel kinking for optic cup boundary detection are also becoming implemented for detection of glaucomatous discs.[21]
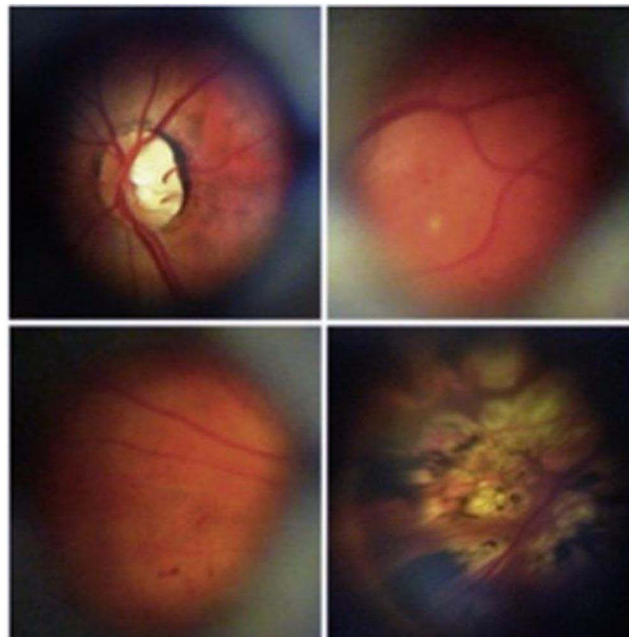

Figure 2 Representative retinal images of no apparent diabetic retinopathy (top left), mild nonproliferative diabetic retinopathy (top right), moderate nonproliferative diabetic retinopathy (bottom left), and panretinal photocoagulation scars in proliferative diabetic retinopathy (bottom right).
Notes: Reprinted from *AmJ Ophthalmol,* volume 159(2), Russo A, Morescalchi F, Costagliola C, Delcassi L, Semeraro F. Comparison of smartphone ophthalmoscopy with slit-lamp biomicroscopy for grading diabetic retinopathy. 360–364.e1, Copyright 2015, with permission from Elsevier.[9]

Smartphone-Based Retinal Imaging in Cataracts

A study by Dickson et al[18] utilized a D-EYE DO to analyze the presence of abnormalities, VCDR, and optic nerve size and color compared to the results of BIO. Three D-EYE examiners reviewed the videos for fundus abnormalities, optic-disc characteristics and c/d ratios. The results showed no statistical difference between the D-EYE and BIO mean c/d ratios. The study concluded that the D-EYE could reliably be used clinically to detect abnormalities and measure the c/d ratio, including in some patients with cataracts. Also, a study from 2017 used a 20D Volk Spherical lens (Volk Optical Inc.; Mentor, OH, USA) and a smartphone to examine the anterior segment and fundus. The results showed that the diagnostic technique was suitable for photo documentation and could successfully identify various diseases, including cataracts, in the patient populations[19] (Table 2).

Discussion

Limitations of Digital Ophthalmoscopes

As of yet, there are limited repositories available to compare commercially available DO systems. The standard of retinal imaging involves using a desktop mydriatic fundus camera. However, these desktop-based DOs have drawbacks such as being cumbersome, confined to office settings, technician-dependent, and costly.[12,22] The 3nethra device (Forus, Bangalore) is the most affordable option within this category, whereas Optos Daytona (Optos PLC; Dunfermline, UK) provides the best FOV (45°–200°) (Table 1). Although not considered the standard of care, handheld non-mydriatic DOs offer certain advantages, such as being lightweight, portable, and suitable for dilated and non-dilated patients.[23]

Numerous studies have evaluated handheld cameras for detecting diabetic retinopathy with relatively high sensitivities and specificities.[24–26] Nevertheless, these devices have their own sets of limitations, such as the need for consistent manual alignment to maintain focus, and issues with light reflexes on the condensing lens.[12,27] The most affordable option among direct ophthalmoscopes is the handheld PanOptic, while the Versacam provides the best FOV (45°) (Table 1 and 2).

Emerging smartphone-based DOs present another viable alternative. Their compact size makes them lightweight, ergonomically friendly, and easily transportable.[14] They do not require dilation and necessitate minimal training, making them ideal for non-specialists and telemedicine in rural areas.[12,22,24] Multiple aforementioned studies have found the D-EYE smartphone reliable in examining DR, glaucoma, cataracts, and even hypertensive emergencies. The Peek Retina is the most inexpensive in this group, while the 20D Volk lens paired with a smartphone offers the best FOV (60°). Among smartphone-based DO options, we recommend using a 20D Volk lens paired with a smartphone for fundus photography, given its wide FOV, affordability, and versatility (Table 1).

Overall, DOs are portable, cost-effective, facilitate collaboration, and are user-friendly.[28,29] Still, some existing fundus cameras have a limited FOV, necessitate frequent pupillary dilation, and require skilled operators to produce montage images.[30] Enhancements in optical designs are needed to expand the FOV further and improve image quality. Encouragingly, research has demonstrated that DOs offer an improved FOV compared with traditional ophthalmoscopes without mydriasis. This could be further enhanced by utilizing 3D imaging or software that intelligently stitches multiple images together, enabling the capture of different regions of the peripheral retina.[31]

Device Training & Ophthalmologist Workload

Many studies have emphasized the significance of proper training and the time required to acquire the skills necessary to capture high-quality retinal images or videos effectively. Despite sufficient practice, challenges with focusing and dealing with bothersome lens reflections may arise.[27] Consequently, the quality of the captured images and the accuracy of the test results could potentially fail to identify underlying pathologies.

As more areas facing eye specialist shortages begin to employ DOs, specialists may be inundated with images for review. Integrating artificial intelligence and machine learning to analyze captured images is a viable solution to alleviate this burden.[32] Further research is required to develop effective training guidelines for user-friendly ophthalmoscopes to ensure the capture and analysis of high-quality data that can be accurately assessed efficiently with machine learning algorithms.

Privacy Concerns

Some of the significant concerns regarding the use of DOs are privacy and security risks related to online storage and transfer of captured images or videos.[33,34] One study on health information technology demonstrated that some patients refused to participate because of perceived privacy and security risks.[33] Similarly, another study highlighted how clinicians fear data loss and confidentiality risks.[34] DO developers should follow HIPAA guidelines, remove any protected health information, and encrypt their data on secure applications, private networks, or third-party management software.[35]

Limitations of the Review Process

The search was limited to articles written between 2010 and 2020 and written in English, possibly introducing bias and concerns of applicability in non-English populations. Our search included three databases, potentially overlooking the pertinent studies available in other databases. Our inclusion criteria focused on predetermined ophthalmic conditions which excludes other relevant DO analyses. Future research should address these limitations to provide a more robust understanding of the effectiveness of digital ophthalmoscopy in various ophthalmic conditions.

Conclusion

Digital ophthalmoscopy methods offer novel algorithms to optimize anterior and posterior segment evaluation. Such systems may augment current access to care by providing more affordable and accessible diagnostic tools for remote communities with limited specialists. This systematic review suggests effectiveness of DOs in evaluating diabetic retinopathy, glaucoma, and cataracts with respect to traditional ophthalmoscopy. Integrating this imaging with geo-tagging could also enable further database creation that can help improve resource allocation in worldwide screening programs. With ongoing development, the ability for DOs to handle non- mydriatic photography and media opacities will likely continue to improve. Given the challenges inherent in providing high quality ophthalmic care in rural or otherwise underserved communities, the ongoing improvement of DO technologies should be a priority.

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Disclosure

The authors declare that they have no conflicts of interest in this work.

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