Survey of Ophthalmology xxx (xxxx) xxx

Contents lists available at ScienceDirect

Survey of Ophthalmology

journal homepage: www.elsevier.com/locate/survophthal

Review article

Review of smartphone funduscopy for diabetic retinopathy screening

Neil Vaughan, PhD, RFREng, FHEA, MSc, BSc [a,b,c,d,*]

[a] Exeter Centre of Excellence for Diabetes (ExCEeD), University of Exeter, Exeter, UK
[b] Faculty of Health and Life Sciences (HLS), University of Exeter, Exeter, UK
[c] Royal Academy of Engineering (RAEng), London, UK
[d] NIHR Exeter Biomedical Research Centre, Exeter, UK

ARTICLE INFO

Keywords:
Retinopathy
Funduscopy
Retinal imaging
Diabetic retinopathy
Smartphone funduscope

ABSTRACT

I detail advances in funduscopy diagnostic systems integrating smartphones. Smartphone funduscopy devices are comprised of lens devices connecting with smartphones and software applications to be used for mobile retinal image capturing and diagnosis of diabetic retinopathy. This is particularly beneficial to automate and mobilize retinopathy screening techniques and methods in remote and rural areas as those diabetes patients are often not meeting the required regular screening for diabetic retinopathy. Smartphone retinal image grading systems enable retinopathy to be screened remotely as teleophthalmology or as a stand-alone point-of-care-testing system. Smartphone funduscopy aims to avoid the need for patients to be seen by expert ophthalmologists, which can reduce patient travel, time taken for images to be processed, appointment backlog, health service overhead costs, and the workload burden for expert ophthalmologists.

1. Introduction

The WHO estimate that 552 million people will have diabetes by 2030.[31] One of the most common complications of diabetes is diabetic retinopathy (DR), which is the leading cause of blindness in working-aged people in developed countries.[5] To meet current screening requirements, all people with diabetes aged over 12 years should have retinal images screened annually. This produces over a billion retina images every year, which equates to 32 images per second needing to be analyzed and graded. Nearly half of diabetic adults in the United States of America do not receive recommended annual screening for DR, and other populations, particularly lower-middle income countries, have 10% screening rate or less.[20]

In addition to DR, retinal and fundus screening is also used to identify other conditions. Age-related macular degeneration is a disorder that affects central vision. Glaucoma is a group of eye diseases that can cause vision loss and blindness by damaging the optic nerve. There are also other retinal or optic nerve head pathologies that these portable fundus imaging devices can screen for.

1.1. Conventional funduscopy procedures

Conventional funduscope systems have been only based within hospitals, requiring patients to travel and with limited appointments based on ophthalmologist availability. Conventionally, a table-top camera such as the Zeiss Visucam$^{NM/FA}$ (Fig. 2A) is used for imaging. This device obtains the image of a patient's retina, which is then analyzed manually by an expert consultant ophthalmologist.

Funduscopy is a 4-step procedure to obtain clear imaging of the: (1) retinal blood vessels, (2) optic disc, (3) macula and (4) retinal periphery.

Usually pupil dilation is required for indirect ophthalmology because funduscopy with undilated pupils can be difficult. Temporary acting eye drops such as tropicamide 0.5–1.0% are often instilled in the eyes of the patient to enable attaining mydriatic photographs.[46] Dilation is also the recommended course when using smartphone lens-based retinal imaging devices; however, some models allow for good quality nonmydriatic imaging of the retina.

1.2. Advantages of smartphones for funduscopy

For over 10 years, smartphone use in ophthalmology has shown many advances, including in funduscopy imaging.[36] This technique is coined "smartphone funduscopy,"[5] or smartphone-based fundus imaging (SBFI). SBFI increases the chance of meeting annual screening needs for retinopathy of prematurity, particularly in developing parts of the world.[50]

* Corresponding author: Neil Vaughan, PhD, RFREng, FHEA, MSc, BSc, RILD Building, Royal Devon and Exeter Hospital, Barrack Rd, Exeter, EX2 5DW, UK.
E-mail address: n.vaughan@exeter.ac.uk.

https://doi.org/10.1016/j.survophthal.2023.10.006
Received 23 June 2023; Received in revised form 23 September 2023; Accepted 3 October 2023
Available online 6 October 2023

Advantages of smartphone funduscopy include: (1) avoiding the enormous financial burden of conventional digital fundus imaging systems. (2) SBFI could facilitate telemedicine-based fundus screening. (3) SBFI imaging technique has no contact with the corneal surface, which is less distressing particularly for children with retinopathy of prematurity. Point-of-care-testing for retinal examination has the potential to improve key health-care barriers for people with diabetes, including cost, access, and quality.[1] Smart funduscopy enables communities to more effectively and affordably screen population to identify patients at risk of losing vision from treatable conditions. There are millions who do not get regular eye examinations in the United States, other Western countries, and low-income countries who may benefit from mobile retina screening.[16] Smartphone retinal imaging devices could be used by patients themselves or their caregivers, rather than expert clinicians, which could enable nonophthalmic personnel to conduct ophthalmology examinations, pending verification of utility.[29]

Artificial intelligence (AI) and deep learning (DL) for screening retinopathy have the potential to further reduce the burden on expert ophthalmologists and may become the preferred strategy and cost-saving for the patient and family.[51] These AI retinopathy systems require safety, efficacy, and equity to secure clinical acceptance and payment. AI can be applied to images captured from a wide range of devices.

2. Smartphone devices for funduscopy image capture

This section presents a literature review, organizing the previously proposed smartphone based fundoscopy devices into various categories based on their functionality and methods.

2.1. Using a 20D or 28D lens with smartphone

Perhaps the simplest method for capturing retinal images was proposed by Lord and coworkers.[27] The method is similar to classical indirect ophthalmoscopy; by holding a 20D lens in front of the patient's eye and holding a smartphone at a distance using the other hand, the camera will autofocus onto the retinal image. When using this method with 20D lens, it is critical to have a light source - either external or the flashlight of the smartphone itself. Other similar systems have been proposed.[3,5] A set up using Samsung smartphones (Galaxy N9000) and a condensing lens of 20D was used to collect fundus images (Fig. 1A).[21] Diagnostic validation showed reasonable agreement to a slit lamp as gold standard by comparing classification accuracies. Diagnostics on the fundus images collected with the smartphone and the slit lamp examination were conducted by 2 independent specialists.

Condensing lenses of 28D have been used with a smartphone[23,24] to collect retinal images. A feature extraction system was proposed and implemented[23] using artificial neural networks with discrete wavelet transform. This AI system was able to identify stages of DR with a precision and recall of 63% and 57%, respectively; however, this AI algorithm was implemented on a PC and was not extended to run on a portable mobile phone platform. Histograms have been utilized[24] for comparison of retinal images with a database of healthy and affected eyes and were able to detect DR with 62% precision and 53% recall.

Various patients and clinicians[14,33,45] have contributed methods of using ophthalmology lenses with a smartphone for funduscopy imaging, which demonstrates the wide desire for a smart funduscope to be available for use. These devices for fundus images usually use a 20D or 28D lens.[14,45] The simple lens devices do not have many requirements, making them cheaper and easier to obtain. A disadvantage is increased difficulty in locating the correct distance from the eye, which requires anatomical knowledge and skill, alongside difficulties in stabilizing the hand held lens to avoid blur.

2.2. Ophthalmology devices using lenses with smartphone

The devices in this section hold a lens at the desired distance relative to the smartphone, which frees one hand of the operator and ensures the lens remains stationary to reduce blur.

The Paxos Scope adapter (Fig. 1B) has been used with iPod and 40D lens[50] as a noncontact indirect SBFI device to screen for retinopathy of prematurity. Fig. 1C shows a comparison between SBFI (front) and conventional fundus imaging (background). SBFI gave 56° field-of-view, and conventional fundus used a 130° field-of-view lens. Paxos Scope was also compared to clinical examinations[44] and found 91% sensitivity and 99% specificity.

The DIYretCAM[40] is a system that is intended for clinicians to build themselves from readily available parts. The parts needed to build a DIYretCAM, include a 20D lens, PVC pipes, and clips with a smartphone. The DIYretCAM device has been shown in clinical use to capture fan image of a macular hole.

The CellScope retina imaging device was designed[25] to be a speedy, easy to use, and cheap way to use a smartphone to collect fundus images. It contains at least 4 lenses, including a 54-diopter ophthalmic lens and other condenser and achromatic lenses. The initial prototype imaging device was called Ocular CellScope,[28] and it was further developed into the CellScope Retina.[25] The image is taken by a user holding the device in their hand and pointing it at the patient's retina. The smartphone's built-in light illuminates the retina. A green dot is the fixation target. Each image is approximately 50°. Five overlapping images are captured of the central, superior, nasal, temporal, and inferior retina. The smartphone app merges the 5 images into a single wide-field image of the retina spanning approximately 100°. Bluetooth is used from the phone to control the device's light and target.

The Fundus on Phone (FOP) device (Fig. 2B) is commercially available[41] from Remidio Ltd (Karnataka, India) for use with a smartphone camera. FOP is portable, consisting of an annular illumination design that eliminates corneal reflection, producing 45° field-of-view smartphone retinal photographs. FOP is designed to be used with the Medios DR, AI algorithm. Also, FOP device has been used in studies[18] with EyeArt AI software (EyeNuk Inc., Los Angeles, CA) and found 95.8% specificity. The FOP has been compared to a gold standard Zeiss

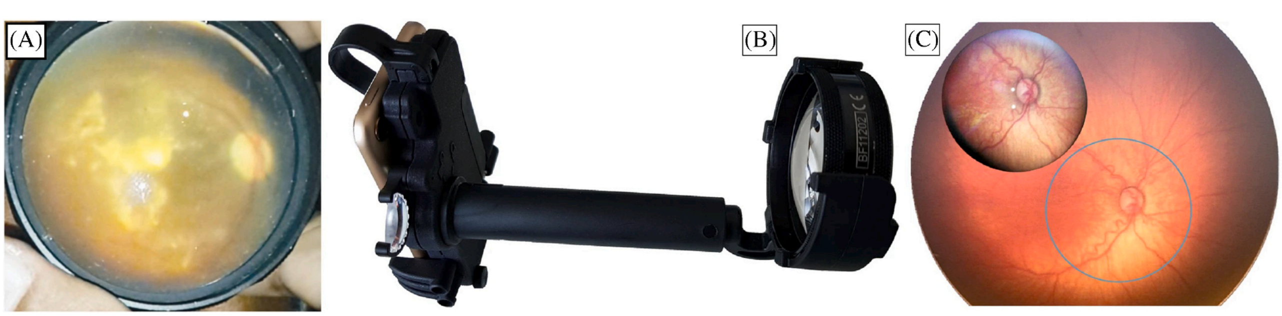

Fig. 1. *A:* Fundus image captured using a smartphone with 20 diopter condensing lens.[21] *B:* The Paxos Scope adapter.[50] *C:* Image taken with Paxos Scope, reproduced with licence (CC BY 4.0).

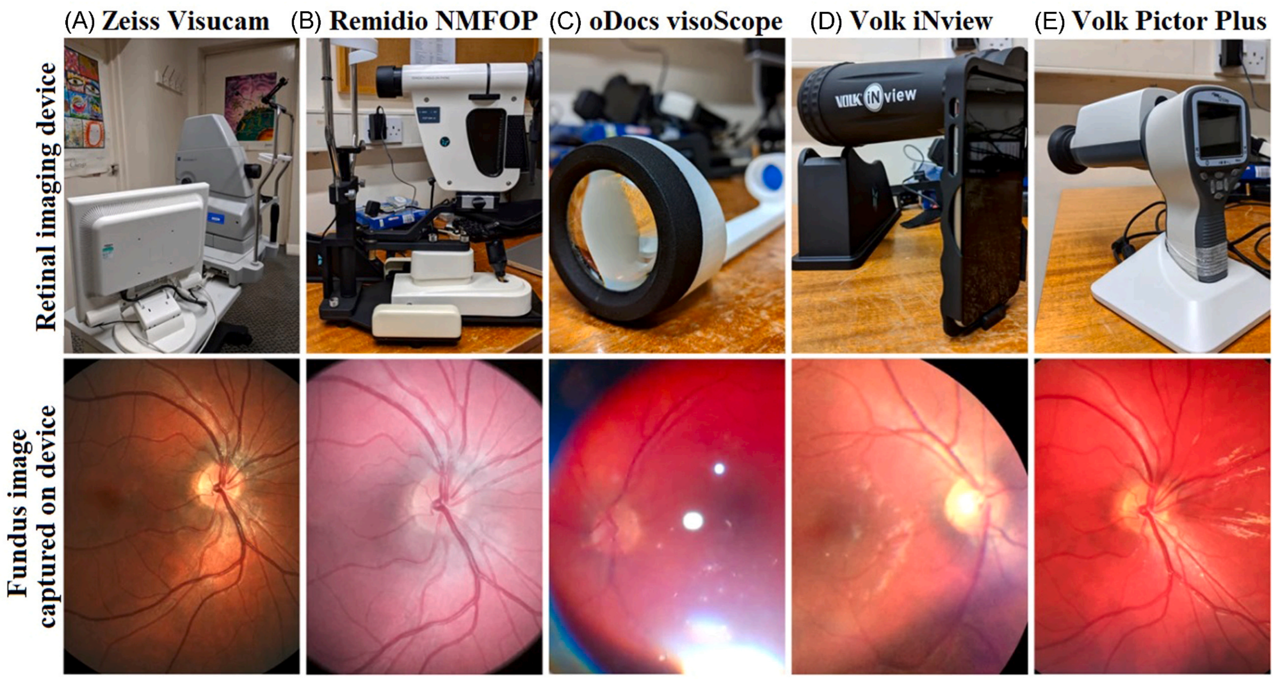

Fig. 2. *A:* Gold standard desktop Visucam image system and (B–E) 4 handheld imaging cameras,[9] reproduced with licence (CC BY 4.0).

Visucam (Fig. 2A), finding good comparable quality images in terms of acquisition rates, quality, and gradeability.[9]

Adapters have also been developed allowing slit lamp ocular anterior-segment imaging devices to connect to smartphones.[18] The Magnifi device (Arcturus labs) is a general purpose microscopy lens photoadapter fitting the iPhone 4, 4s and 5. The EyePhotoDoc fits iPhone 3 and 5 and is compatible is with Topcon SL-3E, Marco-2B, Haag-Streit BQ and Haag-Streit BM slit lamps. The Keeler portable iPhone adapter for slit lamp images fits an eyepiece 30 mm in diameter. Also the Zarf iPhone adapter for anterior-segment imaging (Zarf, Spokane, WA).

The visoScope 2.0 is a commercial device[48] (oDocs, Otago, NZ) that offers universal smartphone compatibility using open source 3D printed Nylon technology (Fig. 2C). Mydriasis of 4 mm+ is required for use. The visoScope has been evaluated by comparison to a gold standard Zeiss table-top fundus camera (Fig. 2A), and it performed less well in image acquisition rates, quality, and gradeability.[9] One advantage is that the visoScope is much more portable and costs less than the Zeiss table-top fundus camera.

The iNview retinal imaging device (Fig. 2D) and Pictor Plus (Fig. 2E) have both been commercialized (Volk Optical, Inc., OH). Both devices have been reviewed and compared to a gold standard desktop Zeiss camera.[9] This found that the Pictor is comparable to Zeiss table-top camera in image acquisition rates, quality, and gradeability, but the iNview performed less well.[9]

An alternative large desktop funduscopy device is the Topcon TRC

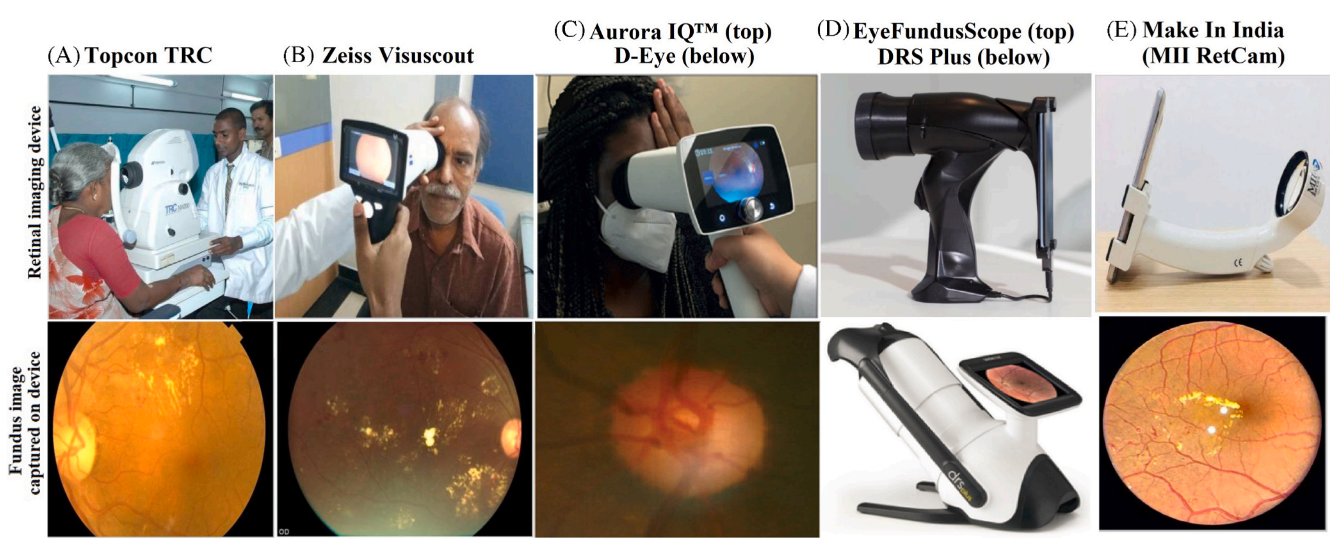

Fig. 3. *A:* Topcon TRC NW200 nonmydriatic desktop fundus camera in mobile telemedicine van in rural India,[39] reproduced with licence (CC BY 4.0). *B:* Zeiss Visuscout 100 handheld fundus camera with retinal image of sight-threatening diabetic retinopathy with post laser status center involving diabetic macular edema taken with,[39] reproduced with licence (CC BY 4.0). *C:* Aurora IQ (Optomed) handheld fundus photography device,[4] reproduced with licence (Elsevier RightsLink). *D, top:* EyeFundusScope smartphone fundus imaging device,[32] reproduced with licence (CC BY 4.0). *D, below:* DRS Plus Device,[43] reproduced with licence (CC BY 4.0). *E:* MII Retcam,[39] reproduced with licence (CC BY 4.0).

NW200 (Fig. 3A) that has been made more portable by fitting inside a telemedicine van for visiting rural villages in India.[39] The Zeiss Visuscout (Fig. 3B) is another portable fundus screening camera.[39]

The Aurora IQ (Optomed) (Fig. 3C) is a handheld fundus photography device that, without needing pharmacologic dilation of the pupils, provides a 50° field of view.[4]

The EyeFundusScope (Fraunhofer, Portugal) (Fig. 3D, top) is a teleophthalmology system with a dedicated mobile fundus camera optical system.[32] This includes spherical and aspherical lenses, polarizers, and beam splitters. This optical system enables the acquisition of 12MP images with 40° field of view for pupils ≥4 m, at a working distance (distance between lens closest to the eye and smartphone) of 30–40 mm.

DRS Plus (iCare, Finland) (Fig. 3D, below) is another excellent screening camera with confocal fundus imaging system, using LED light to produce TrueColour and detail-rich images for a variety of ocular disease or cataract.[43]

The Make In India Retinal Camera (MII RetCam) funduscopy device (Fig. 3E) holds a smartphone at a fixed distance from the lens and is a validated smartphone-based imaging system that is now commercially available.[39]

The SIGNAL Handheld Retinal Camera (Topcon Healthcare) is a mobile imaging solution for nonmydriatic retinal examination covering the macula and optic disc with 50° by 40° field of view and Wi-Fi compatibility for image transfer.

It has been proposed that patients could use fundus imaging devices on themselves,[26] termed "selfie fundus imaging."[47] Devices suitable for selfie imaging include existing commercial handheld fundus image capture devices such as the Volk InView (Fig. 2D) and Retinal Imaging camera (Bosch Eye Care Solutions, Germany).

2.3. Existing ophthalmoscopes combined with smartphones

The PanOptic + iExaminer (Fig. 4A) has been commercialized[49] by Welch Allyn Inc. (Skaneateles Falls, NY) and FDA approved in 2013. The iExaminer adapter is an interface between an iPhone and a PanOptic ophthalmoscope that allows retinal images with a 25° subtended angle to be captured using an iPhone, keeping all optical dimensions fixed and requiring less expertise to use. The +iExaminer has been used as part of a DR detection system for remote geographic areas.[35] An app using OpenCV for feature-based classification was used to differentiate DR from healthy images, and it was also proposed to use cloud computing to overcome mobile processing power limitations.[35] The iExaminer device can also work with the iExaminer App that takes and sends photos, but does not diagnose within the app. Images captured using the +iExaminer were used[52] to evaluate a DR grading application that implements a vessel segmentation method on fundus images. The DR app[52] is also compatible with fundus images taken on other commercially available specialized cameras, or downloaded from publicly available fundus datasets. The software developed in the DR app[52] was hosted in an independent android smartphone system (Fig. 4B), reaching an accuracy of 93.3% on a validation dataset of 40 color fundus images.

2.4. Using lenses from virtual reality headsets for smartphone funduscopy

In lower and middle income countries, there are many cases of retinopathy, and many patients are not examined as often as recommended. The 20D diopter lens usually costs over $75 USD, which can be prohibitive. An alternative to the 20D lens is to instead use other lenses available at lower cost, such as the 2 acrylic lenses used in virtual reality (VR) headsets such as the Google Cardboard. The lenses from VR headsets are usually about 22.2D diopter (4.5 cm), which is close enough to the standard 20D or 28D used in ophthalmoscopes. These VR lenses have been used for lower cost ophthalmoscopy.[12,17] We also propose a new prototype fundus imaging device which we have developed using a VR lens, as described later in Section 4.

2.5. Direct ophthalmoscopy smartphone devices

In another category are direct smartphone ophthalmoscopy devices. Direct devices attach a smaller lens or prism, directly onto the smartphone camera, removing the need for the lens to be held at a distance, making them even more compact. One such device is the D-eye, which uses a magnetic lens attachment which is magnetically attracted onto the back of the smartphone.[42] Fundus images taken with D-eye showed good agreement with slip lamp. The D-eye field of view is small without pharmacologic dilation of the pupils (less than 10°), but it is possible to evaluate the optic nerve appearance, especially when using the video function.

The Peek Retina device[34] (Peek Vision Ltd) used a small prism attached onto a Samsung smartphone. Peek Retina is no longer commercially available since 2020. There were also some preproduction prototypes of Peek Retina.[5]

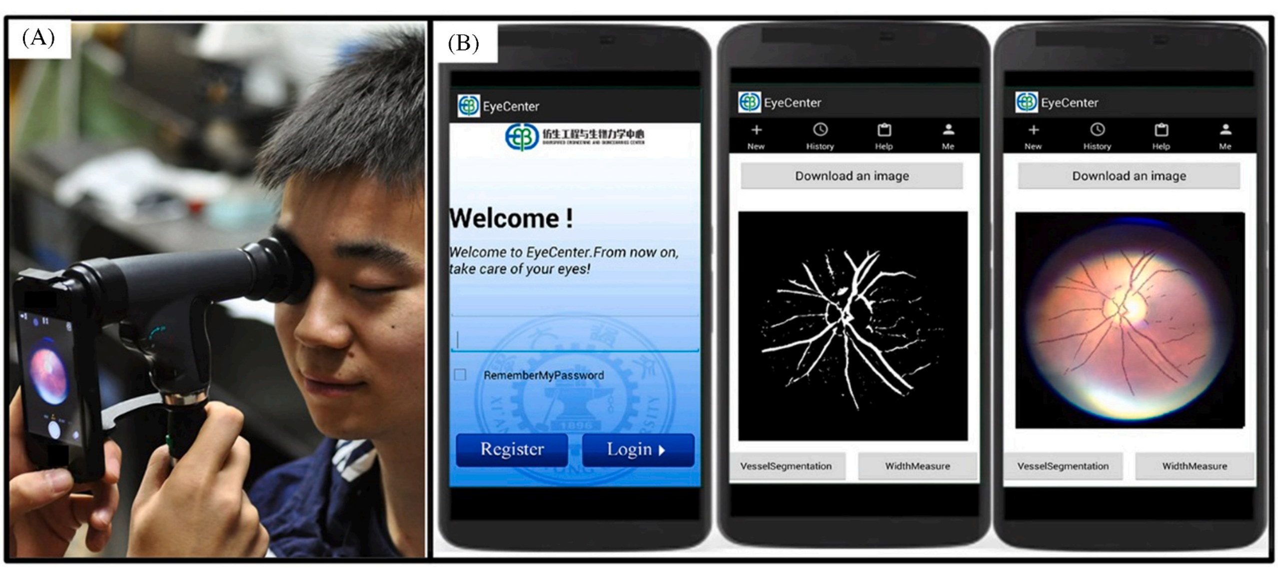

Fig. 4. *A:* PanOptic +iExaminer smart funduscopy[49] by Welch Allyn Inc. *B:* Smartphone app for diabetic retinopathy,[52] used with +iExaminer or other handheld ophthalmoscopes, reproduced with licence (CC BY 4.0).

2.6. Validations of smartphone retinal image quality compared to desktop cameras

Comparisons between grading of DR from images acquired by the FOP system (Fig. 2B) and traditional benchtop fundus photography show 92.7% sensitivity and 98.4% specificity.[37]

For grading DR, the D-Eye smartphone system images have been compared against slit-lamp. This found exact agreement when grading DR severity in 85% of cases and within one-\ step of agreement in 96.7%, with a sensitivity of 81% and a specificity of 98%.[42]

Images acquired by a smartphone with Paxos scope macrolens adapter (Fig. 1B) and external light source were compared with clinical examination for a DR grading task.[44] Smartphone-acquired photos demonstrated 91% sensitivity and 99% specificity in detection of moderate nonproliferative DR and worse.

The novel Volk iNview, Volk Pictor Plus, Remidio FOP and visoScope portable retinal imaging devices have been evaluated with good results[9] using comparison to the gold standard desktop Zeiss camera (Fig. 2A).

The studies identified in this section have demonstrated good potential for portable fundus imaging devices, with encouraging results for developing further smartphone based funduscopy innovation.

3. Fundus image analysis, diagnosis, and screening

After fundus images have been collected by imaging devices in Section 2, the fundus images next have to be analyzed or screened for DR. I shall discuss various fundus screening methods including (1) uploading images for expert review, (2) cloud-based Internet AI fundus screening, or (3) smartphone apps standalone AI fundus screening.

Some systems aim to be stand alone by taking the fundus image and analyzing the image on the same device. A summary of such systems is shown in Table 1, with further details in the subsections below.

3.1. Tele-ophthalmology - uploading retinal images from smartphones to hospitals

There have been various systems proposed for tele-ophthalmology that can take fundus images remotely[15] and send images either to the hospital or to a cloud-based Internet diagnostic service. Both of those, however, require an internet connection, which complicates use in rural communities.

Other research took fundus photographs by smartphone with 20D lens[21] and sent the retinal images by internet communication using existing software (WhatsApp) to a specialist for DR grading.

Tele-ophthalmology, which includes analysis of collected images, has also been implemented to provide DR diagnosis remotely.[30] The tele-retina screening program has been implemented to enable non-experts to capture retinal images from remote areas and transfer the images to ophthalmic centers for DR diagnosis.[6–8] Tele-retina needs a strong Internet connection between patients and health care centers.

3.2. AI cloud-based Internet screening

Cloud computing has been proposed and implemented for fundus image analysis.[35] This helps to overcome limitations in smartphone processing power because the computationally-intensive steps of analysis can be performed on a more powerful remote server. The cloud image analysis has been applied to fundus images captured through a smartphone camera combined with a PanOptic ophthalmoscope (Fig. 4A) and has potential to be applied to images from other lens-based ophthalmology imaging devices.[35]

The Remidio “FOP” system (Fig. 2B) employs smartphone cameras to collect fundus images of diabetic participants and diagnoses the images with the help of AI on a cloud-based diagnostic service.[38] The smartphone and cloud-service joint automatic diagnosis of DR resulted in 95.8% sensitivity and 80.2% specificity for detecting any DR, including moderate DR and clinically significant macular edema, and 99.1% sensitivity and 80.4% specificity in detecting vision-threatening diabetic retinopathy, which includes severe and proliferative stages of DR.

Several major companies are actively developing efforts in the field of funduscopy and AI to diagnose DR and systemic eye conditions. Kaggle, the world’s largest data science community, has contributed several publically available datasets for fundus images, ophthalmology, and DR detection. Kaggle’s DR detection competition in 2015 had 6993 entries worldwide.[22]

Although not directly related to smartphones, it is worth mentioning briefly Google’s efforts, as well as other companies, for example, DeepMind, in the field of funduscopy and AI to diagnose DR as well as systemic conditions.

Google Deepmind[11] is using AI to predict retinal disease progression, including macular degeneration,[53] collaborating with Moorfields Eye Hospital and Google Health. This demonstrates the potential of using AI to predict eye disease progression. In addition to fundus images, 3-dimensional (3D) optical coherence tomography images have been used. Although not currently focused on smartphones, Deepmind’s technology may later be suitable for adaptation onto portable platforms.

Google Lens is a vision- and AI-based app based on neural networks available on most Android smartphones. Google Lens has been proposed and evaluated for classifying retinal disorders from fundus images.[47] Using MESSIDOR retinopathy image dataset,[10] it was found that Google Lens could correctly classify retinal or fundus image type, but for identification of DR or DME, the response lacked specificity, but may have future potential.

3.3. Commercial AI smartphone apps for fundus analysis

This section describes available AI apps that can run on smartphones which are commercially available to purchase for the analysis, diagnosis or screening of fundus images, taken with either a smartphone or ophthalmoscope.

Fundus images taken on a smartphone by using a lens or fundus device can be analyzed within commercial fundus analysis applications, including: ProCamera for iOS (Cocologics), or FiLMiC Pro for Android and iOS (FiLMiC Inc).

An alternative system[19] has uses DL fundus analysis and proposed integrating the AI screening system into a smartphone app; however the AI app did not integrate with a fundus camera for capturing retinal images. Smartphone DR screening results could be produced for existing retinal images captured from other ophthalmoscopes.[19]

Table 1
Summary of validated smartphone based DR screening systems.

Reference	Features	Device	Camera	Performance
35	Feature extraction classification	Smartphone	Ophthalmoscope	Unspecified
52	Vessel segmentation	Android Phone	Not specified	Accuracy 93.3%
24	Discrete wavelet transform AI classification	Smartphone	Light emitting diode with condensing lens and smartphone	Precision 63% Recall 57%
38	AI cloud diagnostic service	Smartphone and cloud diagnostics	Smartphone camera	Sensitivity 95.8%, Specificity 80.2%
21	Validate accuracy of smartphone diagnosis	Samsung Galaxy N9000	Samsung Galaxy N9000 camera with 20 diopter lens	Unspecified
24	Histogram comparison	Smartphone	28D condensing lens and smart phone	Precision 62%, Recall 53%

DR = diabetic retinopathy.

A DL classifier has been developed for classifying fundus images[2] and has been evaluated using 14,327 fundus images from the MESSIDOR dataset[10] with a reported 94.6% correct identification.

The EyeArt AI DR screening software has been used,[38] with images from the Remidio "FOP" device (Fig. 2B), in a task of grading fundus images and obtained 95.8% specificity, validated with ophthalmologists. EyeArt achieves DR analysis using image enhancement, interest region identification, descriptor computation, deep neural network ensembles for classification, and detection of clinically significant macular edema surrogate markers. FOP is clinically AI trained and validated. A large, publically-available dataset of retinal images[13] was used, with a training database of 78,685 patients taken using desktop mydriatic fundus cameras.

4. Proposed smartphone retinal imaging funduscopy with application

We present our newly developed novel smartphone fundoscope (Smart-Fundoscope) prototype which we have recently developed (Fig. 5A). The lens is attached into a sterile plastic tube which securely holds the lens at the correct fixed distance from the smartphone. The tube is attached onto a smartphone case which enables it to fit tightly onto the phone. The camera is set to record video, and LED flash torch is switched on (Fig. 5B). A second prototype has a screw cap that can extend or retract the lens for fine tuning the image focus (Fig. 5C). The prototype 1 was tested and produces suitably high resolution microscopic zoom images (Fig. 5D).

4.1. Application for analyzing retinal images on a smartphone

A smartphone app prototype was developed (Fig. 6A) that can obtain fundus images either by interfacing with a developed lens attachment (Figs. 5A–C) or from existing retinal image datasets such as EyePACS.[13] This app could be extended in future to apply a pretrained machine learning model (neural network) within the smartphone to give stand-alone diagnosis. It may require additional CPU power to process high resolution fundus images with full feature detection and classification, to identify retinopathy grading in fundus images with reasonable accuracy and duration. If the smartphone app is unable to classify the fundus image, a flow process was defined (Fig. 6B) whereby images can be uploaded onto a cloud based classification system, and the third stage is to forward the fundus image to the ophthalmology expert for manual viewing and diagnosis.

5. Conclusion

Stand-alone DR screening systems with no external dependencies are beginning to be developed and evaluated. These systems aim to provide a superior method particularly by enabling point-of-care testing, so the patient can obtain a diagnosis without requiring a hospital visit and appointment, which can free up health resources and expert ophthalmologists' time.

Evaluation of stand-alone DR grading systems can have 2 main phases: (1) compare fundus images between novel smartphone devices and the gold standard conventional digital fundus systems such as the Zeiss Visucam (Fig. 2A) to identify quality assurance and practicalities. (The comparison is necessary to both current conventional nonportable telemedicine strategies and clinical fundus examination devices to validate smartphone retina imaging techniques and potentially to achieve compliance for DR screening[29] and (2) compare the diagnosis accuracy between smartphone AI app and expert ophthalmologist. This would need to be completed with a large number of fundus images to ensure that a comparison of classification accuracy takes into account variations in image properties depending on which imaging device has been used to image the retina.

There are 2 main components for stand-alone point-of-care-testing DR screening: (1) image capture using a lens-based attachment device interfacing with a smartphone camera, (2) image processing and analysis for grading retinopathy, which can be achieved using a smartphone app that contains a trained ML model uploaded to a cloud-based diagnosis service. For image capture, the proposed handheld imaging devices that connect to any universal smartphone can provide capability to take reasonable quality fundus images. The developed ophthalmoscope prototypes integrate with smart phones and are independent of the host smartphone device because, over time, smartphones are rapidly changing, and older smartphones become quickly obsolete and are discontinued, which has previous prevented smartphone ophthalmoscopes from working a few years after being developed. Also, a wide range of users would have a wide variety of different smartphones. A challenge of capturing diagnostic fundus images on a smartphone is the quality of the retinal images captured compared to a conventional digital fundus ophthalmoscope system. For deploying automatic image screening and diagnosis for DR, the proposed smartphone retinopathy devices are becoming capable of running DL or neural networks for image analysis. Cloud-based AI retinal diagnosis is also proposed to address the limited processing power and memory on smartphones. In future, there may gradually be diminished reliance on uploading smartphone funduscopy

Fig. 5. A developed prototype smart funduscope. *A,B:* Case attached with sterile plastic tube containing lenses. *C:* Screw prototype with adjustable lens height for focusing image. *D:* Example of the high magnification capabilities of proposed smart funduscope.

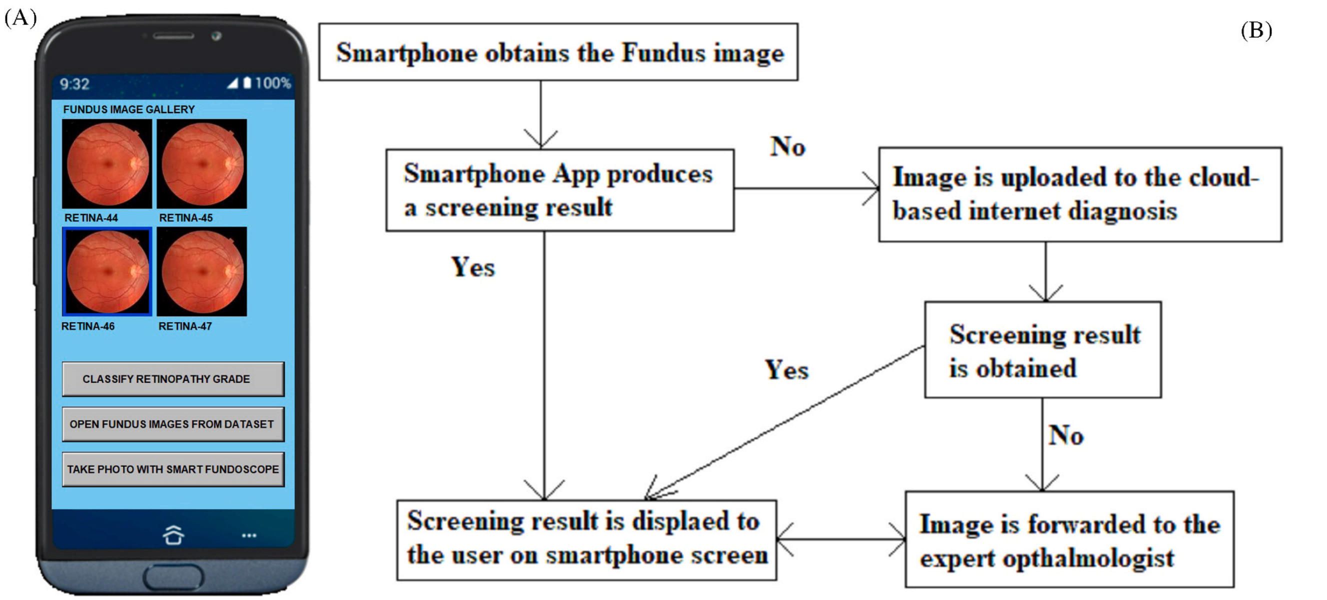

Fig. 6. *A:* Developed Smart-Fundoscope app screen. *B:* Proposed flowchart for image screening.

images to AI cloud-based DR grading systems as higher powered processing becomes possible on smart devices and DL efficiency and efficacy progresses.

5.1. Methods of literature search

The literature search was conducted using the major search databases include Scopus, PubMed, IEEE Xplore, ASME Digital Collection and Google scholar. Additional references were identified from related citations within the articles found. Two sets of keywords were used for literature search. The first set of keywords for imaging devices included: “fundoscopy devices,” “ophthalmoscopy devices,” “Ophthalmology devices,” “fundus camera.” The second set of keywords for image analysis algorithms included: “fundus image analysis,” “fundoscopy imaging,” “smartphone retinal image analysis.”

Declaration of Competing Interest

The authors have no conflict of interest to declare.

References

1 Abràmoff MD. Chapter 12. The Autonomous Point-of-care Diabetic Retinopathy Examination. In: Klonoff DC, Kerr D, Mulvaney SA, eds. *Diabetes Digital Health*. UK: Elsevier Oxford; 2020:159–178. https://doi.org/10.1016/B978-0-12-817485-2.00012-2, 978-0-12-817485-2.

2 Baget-Bernaldiz M, Pedro RA, Santos-Blanco E, Navarro-Gil R, Valls A, Moreno A, et al. Testing a deep learning algorithm for detection of diabetic retinopathy in a Spanish diabetic population and with MESSIDOR database. *Diagnostics*. 2021;11(8):1385.

3 Bastawrous A. Smartphone fundoscopy. *Ophthalmology*. 2012;119(2):432–433. https://doi.org/10.1016/j.ophtha.2011.11.014.

4 Biousse Valérie, Danesh-Meyer Helen V, Saindane Amit M, Lamirel Cédric, Newman Nancy J. Imaging of the optic nerve: technological advances and future prospects. *Lancet Neurol*. 2022;21(12):1135–1150. https://doi.org/10.1016/S1474-4422(22)00173-9.

5 Bolster NM, Giardini ME, Bastawrous A. The diabetic retinopathy screening workflow: potential for smartphone imaging. *J Diabetes Sci Technol*. 2016;10:318–324.

6 Bursell SE, Brazionis L, Jenkins A. Telemedicine and ocular health in diabetes mellitus. *Clin Exp Optom*. 2012;95(3):311–327. https://doi.org/10.1111/j.1444-0938.2012.00746.x.

7 Cavallerano J, Lawrence MG, Zimmer-Galler I, Bauman W, Bursell S, Gardner WK, Horton M, Hildebrand L, Federman J, Carnahan L, Kuzmak P. Telehealth practice recommendations for diabetic retinopathy. *Telemed J e-health Off J Am Telemed Assoc*. 2004;10(4):469–482.

8 Coronado, A.C. (2014). Diagnostic accuracy of tele-ophthalmology for diabetic retinopathy assessment: a meta-analysis and economic analysis.

9 Das S, Kuht HJ, De Silva I, et al. Feasibility and clinical utility of handheld fundus cameras for retinal imaging. *Eye*. 2023;37(2):274–279. https://doi.org/10.1038/s41433-021-01926-y.

10 Decencière E, Zhang X, Cazuguel G, Lay B, Cochener B, Trone C, Klein JC. Feedback on a publicly distributed image database: the Messidor database. *Image Anal Stereol*. 2014;33(3):231–234.

11 Deepmind. Using AI to predict retinal disease progression; 2020. https://www.deepmind.com/blog/using-ai-to-predict-retinal-disease-progression. Accessed 22/10/03.

12 Eghrari AO, Wang A, Brady CJ. Google cardboard indirect ophthalmoscopy. *Retina*. 2017;37(8):1617.

13 EyePACS. Retinal image database comprised of over 5 million retinal images; 2021. ⟨http://www.eyepacs.com/data-analysis⟩. Accessed 22/10/03.

14 Eyewiki. How to Use Smartphone to Take Fundus Photograph; 2022. ⟨https://eyewiki.aao.org/Smartphone_Funduscopy_-_How_to_Use_Smartphone_to_Take_Fundus_Photographs⟩. Accessed 22/10/03.

15 Foster A, Resnikoff S. The impact of Vision 2020 on global blindness. *Eye*. 2005;19(10):1133. https://doi.org/10.1038/sj.eye.6701973.

16 Garg SJ. Applicability of smartphone-based screening programs. *JAMA Ophthalmol*. 2016;134:158–159. https://doi.org/10.1177/1932296815617969.

17 Ghofrani S, Rezaei M, Wang A, Eghrari AO, Brady CJ. Google Cardboard anterior and posterior segment imaging: a valuable tool for limited-resource settings. *Investig Ophthalmol Vis Sci*. 2015;56(7), 4101–4101.

18 Haddock LJ, Qian C. Smartphone technology for fundus photography. *Retin Phys*. 2015;12(6):51–58.

19 Hagos, M.T. (2020). Point-of-Care Diabetic Retinopathy Diagnosis: A Standalone Mobile Application Approach. arXiv preprint arXiv:2002.04066. ⟨https://doi.org/10.48550/arXiv.2002.04066⟩.

20 Harris MI, Klein R, Cowie CC, Rowland M, Byrd-Holt DD. Is the risk of diabetic retinopathy greater in non-Hispanic blacks and Mexican Americans than in non-Hispanic whites with type 2 diabetes? A U.S. population study. *Diabetes Care*. 1998;21:1230–1235.

21 Jamil AZ, Ali L, Tahir MY, Shiraz FS. Smart phone: a smart technology for fundus photography in diabetic retinopathy screening. *Pak J Ophthalmol*. 2018;34(4):225–230. https://doi.org/10.36351/pjo.v34i4.259.

22 Kaggle. Diabetic Retinopathy Detection; 2015. ⟨https://www.kaggle.com/c/diabetic-retinopathy-detection⟩. Accessed 2023-08-30.

23 Kashyap, N., Singh, D.K. and Singh, G.K., (2017). Mobile Phone Based Diabetic Retinopathy Detection System Using ANN-DWT. In: 2017 4th IEEE Uttar Pradesh Section International Conference on Electrical, Computer and Electronics (UPCON). IEEE, pp. 463–467.

24 Kashyap N, Singh DK, Singh GK. Color Histogram- and Smartphone-Based Diabetic Retinopathy Detection System. In: Ray K, Sharan SN, Rawat S, Jain SK, Srivastava S, Bandyopadhyay A, eds. *Engineering Vibration, Communication and Information Processing*. Singapore: Springer; 2019:669–678.

25 Kim TN, Myers F, Reber C, Loury PJ, Loumou P, Webster D, et al. A smartphone-based tool for rapid, portable, and automated wide-field retinal imaging. *Transl Vis Sci Technol*. 2018;7(5):21. https://doi.org/10.1167/tvst.7.5.21.

26 Kumari S, Venkatesh P, Tandon N, Chawla R, Takkar B, Kumar A. Selfie fundus imaging for diabetic retinopathy screening. *Eye*. 2022;36(10):1988–1993.

27 Lord RK, Shah VA, San Filippo AN, Krishna R. Novel uses of smartphones in ophthalmology. *Ophthalmology*. 2010;117(6):1274.

28 Maamari RN, Keenan JD, Fletcher DA, Margolis TP. A mobile phone-based retinal camera for portable wide field imaging. *Br J Ophthalmol*. 2014;98:438–441.

29 Micheletti JM, Hendrick AM, Khan FN, Ziemer DC, Pasquel FJ. Current and next generation portable screening devices for diabetic retinopathy. *J Diabetes Sci Technol*. 2016;10(2):295–300.
30 Mohammadpour M, Heidari Z, Mirghorbani M, Hashemi H. Smartphones, tele-ophthalmology, and VISION 2020. *Int J Ophthalmol*. 2017;10(12):1909.
31 National Eye Institute. *Facts About Diabetic Eye Disease*. National Eye Institute; 2017. Accessed 22/10/03 ⟨https://nei.nih.gov/health/diabetic/retinopathy⟩.
32 Nunes F, Madureira P, Rêgo S, Braga C, Moutinho R, Oliveira T, Soares F. A mobile tele-ophthalmology system for planned and opportunistic screening of diabetic retinopathy in primary care. *IEEE Access*. 2021;9:83740–83750.
33 Palacios E. (2014) How to Do Your Own Fundus Exam, YouTube, ⟨https://www.youtube.com/watch?v=OiiobuS9neA⟩. Accessed 22/10/03.
34 Peek Vision. Peek Retina, YouTube; 2019. ⟨https://www.youtube.com/watch?v=SJO9QQWg8BU⟩. Accessed 22/10/03.
35 Prasanna, P., Jain, S., Bhagat, N., & Madabhushi, A. (2013) Decision Support System for Detection of Diabetic Retinopathy Using Smartphones. In: 2013 7th International Conference on Pervasive Computing Technologies for Healthcare and Workshops. IEEE, pp. 176–179. ⟨https://doi.org/10.4108/icst.pervasivehealth.2013.252093⟩.
36 Pujari A, Saluja G, Agarwal D, Selvan H, Sharma N. Clinically useful smartphone ophthalmic imaging techniques. *Graefe's Arch Clin Exp Ophthalmol*. 2021;259(2):279–287.
37 Rajalakshmi R, Arulmalar S, Usha M, et al. Validation of smartphone based retinal photography for diabetic retinopathy screening. *PLoS One*. 2015;10, e0138285.
38 Rajalakshmi R, Subashini R, Anjana RM, Mohan V. Automated diabetic retinopathy detection in smartphone-based fundus photography using artificial intelligence. *Eye*. 2018;32(6):1138.
39 Rajalakshmi R, Prathiba V, Arulmalar S, Usha M. Review of retinal cameras for global coverage of diabetic retinopathy screening. *Eye*. 2021;35(1):162–172.
40 Raju B, Raju NSD, Akkara JD, Pathengay A. Do it yourself smartphone fundus camera–DIYretCAM. *Indian J Ophthalmol*. 2016;64(9):663.
41 Remidio. Fundus on Phone (FOP); 2022. ⟨https://www.remidio.com/products/fop⟩. Accessed 22/10/03.
42 Russo A, Morescalchi F, Costagliola C, Delcassi L, Semeraro F. Comparison of smartphone ophthalmoscopy with slit-lamp biomicroscopy for grading diabetic retinopathy. *Am J Ophthalmol*. 2015;159(2):360–364. https://doi.org/10.1016/j.ajo.2014.11.008.
43 Skevas C, de Olaguer NP, Lleó A, Thiwa D, Schroeter U, Lopes IV, Xiao D. Implementing and evaluating a fully-functional AI-enabled model for chronic eye disease screening in a real clinical environment. *Research Square*. 2023. https://doi.org/10.21203/rs.3.rs-3132440/v1.
44 Toy BC, Myung DJ, He L, Pan CK, Chang RT, Polkinhorne A, Blumenkranz MS. Smartphone-based dilated fundus photography and near visual acuity testing as inexpensive screening tools to detect referral warranted diabetic eye disease. *Retina*. 2016;36(5):1000–1008.
45 Tran T.M. (2018) Tips on smartphone funduscopy, YouTube, ⟨https://www.youtube.com/watch?v=KxcynnkgnPQ⟩. Accessed 22/10/03.
46 Venkatesh P. Google Lens: a potential cost-effective screening tool for diabetic retinopathy. *Med Hypothesis Discov Innov Optom*. 2022;3(1):34–38.
47 Venkatesh P, Kumar S, Tandon N, Takkar B, Praveen PA. Selfie fundus imaging: innovative approach to retinopathy screening. *Natl Med J India*. 2018;31(6):345–346.
48 visoScope, 2022. ⟨www.odocs-tech.com⟩, ⟨https://www.youtube.com/watch?v=oV53ccDs0rI⟩. Accessed 22/10/03.
49 Welch Allyn Inc. PanOptic + iExaminer, Skaneateles Falls, NY, USA; 2022. ⟨https://www.welchallyn.com/en/microsites/iexaminer.html⟩. Accessed 22/10/03.
50 Wintergerst MW, Petrak M, Li JQ, Larsen PP, Berger M, Holz FG, Krohne TU. Non-contact smartphone-based fundus imaging compared to conventional fundus imaging: a low-cost alternative for retinopathy of prematurity screening and documentation. *Sci Rep*. 2019;9(1):1–8. https://doi.org/10.1038/s41598-019-56155-x.
51 Wolf RM, Channa R, Abramoff MD, Lehmann HP. Cost-effectiveness of autonomous point-of-care diabetic retinopathy screening for pediatric patients with diabetes. *JAMA Ophthalmol*. 2020;138(10):1063–1069. ⟨https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2770183⟩.
52 Xu X, Ding W, Wang X, Cao R, Zhang M, Lv P, Xu F. Smartphone-based accurate analysis of retinal vasculature towards point-of-care diagnostics. *Sci Rep*. 2016;6:34603. https://doi.org/10.1038/srep34603.
53 Yim J, Chopra R, Spitz T, Winkens J, Obika A, Kelly C, De Fauw J. Predicting conversion to wet age-related macular degeneration using deep learning. *Nat Med*. 2020;26(6):892–899.