Clinical Ophthalmology

Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

Accuracy of Low-Cost, Smartphone-Based Retinal Photography for Diabetic Retinopathy Screening: A Systematic Review

Mohammad Eko Prayogo[1,2], Alfia Fatma Zaharo[1], Novandriati Nur Rizky Damayanti[1], Felicia Widyaputri[1], Jarir At Thobari[3,4], Vina Yanti Susanti[5], Muhammad Bayu Sasongko[1]

[1]Department of Ophthalmology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada – Sardjito Eye Center, Dr. Sardjito General Hospital, Yogyakarta, Indonesia; [2]Department of Ophthalmology, Universitas Gadjah Mada Academic Hospital, Universitas Gadjah Mada, Yogyakarta, Indonesia; [3]Department of Pharmacology and Therapy, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia; [4]Clinical Epidemiology and Biostatistics Unit (CE&BU), Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia; [5]Department of Internal Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia

Correspondence: Muhammad Bayu Sasongko, Department of Ophthalmology, Faculty of Medicine, Universitas Gadjah Mada/Prof. Dr. Sardjito General Hospital, Jalan Farmako Sekip Utara, Yogyakarta, Indonesia, Tel/Fax +62 274 552850, Email mb.sasongko@ugm.ac.id

Purpose: Diabetic retinopathy (DR) is a leading cause of blindness. Early DR screening is essential, but the infrastructure can be less affordable in low resource countries. This study aims to review the accuracy of low-cost smartphone-based fundus cameras for DR screening in adult patients with diabetes.

Methods: We performed a systematic literature search to find studies that reported the sensitivity and specificity of low-cost smartphone-based devices for fundus photography in adult patients with diabetes. We searched three databases (MEDLINE, Google Scholar, Scopus) and one register (Cochrane CENTRAL). We presented the accuracy values by grouping the diagnosis into three: any DR, referrable DR, and diabetic macular oedema (DMO). Risk of bias and applicability of the studies were assessed using QUADAS-2.

Results: Five out of 294 retrieved records were included with a total of six smartphone-based devices reviewed. All of the reference diagnostic methods used in the included studies were either indirect ophthalmoscopy or slit-lamp examinations and all smartphone-based devices' imaging protocols used mydriatic drops. The reported sensitivity and specificity for any DR were 52–92.2% and 73.3–99%; for referral DR were 21–91.4% and 64.9–100%; and for DMO were 29.4–81% and 95–100%, respectively.

Conclusion: Sensitivity available low-cost smartphone-based devices for DR screening were acceptable and their specificity particularly for detecting referrable DR and DMO were considerably good. These findings support their potential utilization for DR screening in a low resources setting.

Keywords: diabetic retinopathy screening, smartphone-based funduscopy, low-cost retinal photography, tele-screening

Introduction

Diabetic retinopathy (DR) is a common diabetic retinal microvascular complication found in approximately one in every three individuals with diabetes,[1,2] which potentially leads to irreversible blindness if left untreated. Evidence has suggested that 3.7 million people are blind or visually impaired due to DR. More importantly, this number has increased nearly 1.5-fold from 1990 to 2010.[3]

Routine screening and timely treatment are key for successful management of DR to avoid visual loss.[4,5] Once identified early, timely treatment for DR may reduce the risk of DR progression and visual loss by 50% in a year,[6] emphasizing the importance of early DR screening in diabetic patients despite any symptoms. Both the International Council of Ophthalmology (ICO) and the American Diabetes Association (ADA) recommended at least annual screening of visual acuity and retinal examination for every person with diabetes to avoid delayed treatment.[7,8] Retinal photography

Received: 3 May 2023
Accepted: 21 July 2023
Published: 18 August 2023

for diagnostic purposes of DR can be done either as a stereoscopic or two-dimensional photograph, with a ≥30° field, with or without mydriatic drugs, with or without optical coherence topography (OCT). However, retinal photography for community DR screening is still not adequately available in many countries, particularly in countries with lower health financial resources.[9,10]

In the last two decades, rapid advancement of digital fundus photography has resulted not only in picture quality but also increased portability of the devices.[11,12] At the same time, there is also advancement of a smartphone camera system that aligns with this, allowing researchers and industries to create smaller and more affordable devices fitted to a smartphone camera system that captures retinal images.[13,14] While the quality may not be as good as a standard, table-top fundus camera, these systems may improve the cost-effectiveness of DR screening and will potentially change the outlook of DR screening strategies in low resource settings in the near future.

Recent reviews and meta-analyses have provided extensive discussion and comparisons of various imaging modalities in DR grading, including portable, smartphone-based fundus imaging in DR grading, and some have also reported their sensitivity and specificity values.[15–17] However, none of these articles specifically focused on low-cost devices. In this paper, we will systematically review all available low-cost, smartphone-based fundus camera systems and reported their accuracy for DR screening in patients with diabetes. This review will complement previous reviews and provide additional evidence and understanding about the potential role and importance of low-cost, smartphone-based devices for DR screening, particularly in low resource settings.

Materials and Methods

Search Strategies

The protocol for this review was registered in PROSPERO in June 2021 under the registration number CRD42021249746.[18] We implemented our search strategy that has been developed for MEDLINE through PubMed and adapted it to search literature from other electronic databases and registers including Scopus, Google Scholar, and Cochrane Central Register of Controlled Trials (CENTRAL). We used the following combinations of keywords: "diabetes mellitus", "smartphone fundus photograph", and "diabetic retinopathy". Only studies published in English and studies of human subjects were filtered. There were no restrictions for date of publication. We also manually searched from the reference list of all primary studies to see if there were any relevant studies to be included. Further details regarding our keywords and search strategy are included in Supplementary Table 1–4.

Study Selection

We included studies involving smartphone-based device(s) that: 1) assessed diagnostic test accuracy of the device for detecting DR in diabetic adult older than 18 years; 2) compared one or more devices with a reference standard that has been widely accepted to diagnose DR such as: all types fundus photography, slit-lamp bio-microscopy, direct ophthalmoscopy, indirect ophthalmoscopy; 3) using low-cost smartphone-based devices with either a direct or indirect ophthalmoscopy concept that has a retail price range less than $700 (approximately equivalent to IDR 10,000,000); and 4) reported sensitivity and specificity or had sufficient data to develop a 2×2 table. There were no limitations regarding whether health professionals or trained examiners operated the smartphone-based device, the use of mydriatic drugs, the grading process, the materials of the device, and the smartphone details (brand, series, manufacturers). Studies were excluded if they used sophisticated LED illumination externally attached to the smartphone.

Title and abstracts of studies that met the inclusion criteria were reviewed by four personnel (MEP, MBS, AFZ, or RMI) independently. Disagreements were resolved through discussion by MEP, MBS, and AFZ, followed by selecting the included full texts and consolidation of disagreements. We extracted the following data from included studies: 1) author; 2) year of publication; 3) participant characteristics (eg, sample size, country setting, mean age, mean duration of diabetes); 4) index test characteristics (eg, type of compatible smartphone, illumination source, type of lens, ophthalmoscopy method); 5) imaging protocol for index test (eg, the use of mydriatic drugs, retinal field of view, working distance, image format, and resolution); 6) reference test; and 7) test outcomes of sensitivity and specificity. We further contacted the corresponding author to request additional data (ie, sensitivity and specificity) when these were not available from the

text. We also performed searches in various marketplaces to obtain the average price for each device. An Excel database was created to facilitate our reviewer in selecting eligible studies and recording extracted data.

Risk of Bias and Analysis

We used the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool to assess the risk of bias and applicability of all included studies. Two reviewers performed the assessment independently (MEP and AFZ) and any disagreements were resolved through discussion with all the authors.

The unit of assessment we used to calculate the sensitivity and specificity of a smartphone-based device was the proportion of participants. For the purpose of our analysis, we categorised the outcomes into three groups to analyse the accuracy of smartphone-based devices to diagnose any DR, diabetic macular oedema (DMO), and referrable DR (moderate non-proliferative DR [NPDR] with DMO or severe NPDR or worse, with or without DMO) based on clinical grading using retinal photographs without any OCT examination.[7] Studies that did not include sensitivity and specificity of these groups of interest but reported other detailed test outcomes such as true positive (TP), false positive (FP), true negative (TN), and false negative (FN) numbers were included and analysed using a 2×2 table to acquire the sensitivity and specificity values. These data were presented in a forest plot created using RevMan 5.4.

Results

Search Results

Our keywords search strategy resulted in 294 records. After title and abstract screening, 17 articles were considered relevant for the full text retrieval. One study article was a conference abstract, thus only 16 full text articles were further assessed. From full text screening, one study used synthetic eyes as test subjects, nine were embedded with high-cost /sophisticated devices and assessed other interventions' accuracy (AI, tablet, camera, portable fundus camera device called EyeScan and high-cost smartphone-based fundus camera called Remidio Fundus on Phone [FOP]), and two studies did not include any accuracy values, leaving only five studies that met our inclusion criteria. This selection process is detailed in Figure 1.

Characteristics of Included Studies and Assessment of Biases

Studies included in this review were conducted in the United States of America (USA),[14,19] Cameroon,[13] Italy,[20] and India,[21] with a sample size ranging from 50 to 220 participants. Participants' mean age ranged from 56.7 to 60.5 years and diabetes duration ranged from 7.0 to 11.9 years. Four studies used the International Classification of DR (ICDR) whereas only one used the Modified Early Treatment of Diabetic Retinopathy Study (ETDRS) grading system (Table 1).

Figure 2 illustrates the risk of bias assessment of included studies. All included studies had potential biases from an unclear patient selection due to inadequate reporting of the recruitment strategy (ie, failure to report exclusion criteria or sampling method). There was one study by Kim et al[14] that had potential biases from insufficient documentation of patient selection, index test, reference standard, and flow and timing of the examinations. The number of participants included in the analysis were not reported in two studies.[14,21]

Diagnostic Accuracy for DR, Referrable DR, and DMO

Detailed characteristics and image protocol of the smartphone-based devices reported in this review are presented in Table 2. There were six different smartphone-based devices reported in included studies (Peek Retina,[21] D-EYE,[20,21] Do-it-yourself solution by Sankara,[21] Paxos Scope,[19,21] MII RetCam,[13] and CellScope Retina[14]). All devices were compared with indirect ophthalmoscopy examination as the reference standard, except for the D-EYE[20] that also used slit-lamp examination and CellScope Retina[14] that only used slit-lamp examination for the reference. The principal work of three devices (Peek Retina, D-EYE, and DIY) were similar to direct ophthalmoscopy while the others (Paxos Scope, MII Ret Cam, and CellScope Retina) were similar to indirect ophthalmoscopy. All devices required fully dilated pupils for the examinations. Some of the studies did not include the observed field of view, so the review authors made assumptions based on the retinal photographs taken by those devices that were included in the studies.

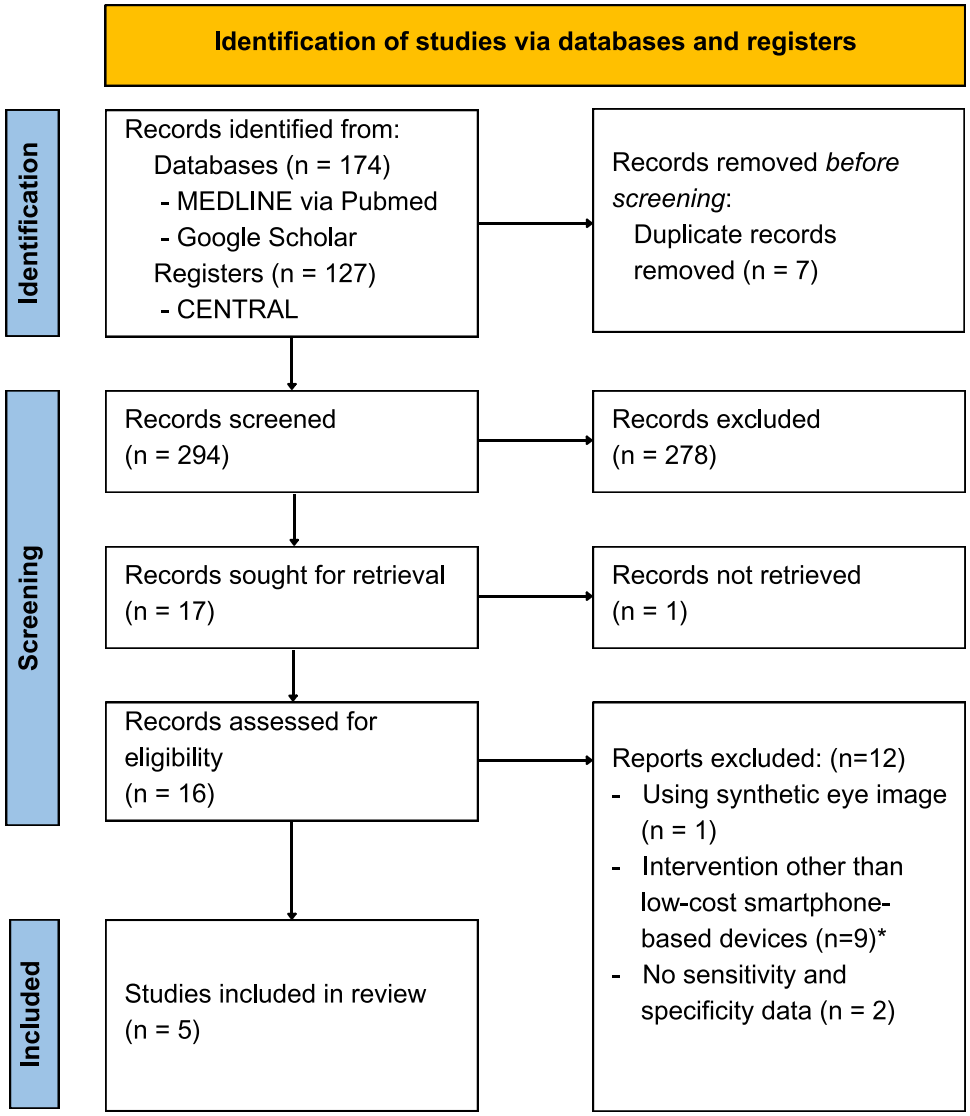

Figure 1 Prisma flow diagram regarding study selection process.
Note: *Other interventions including artificial intelligence (3 studies), tablet (1 study), DSLR camera (1 study), hand-held fundus camera (1 study), and high-cost smartphone-based device (3 studies).

The diagnostic accuracy of the six devices is summarized in Table 2. We found that the sensitivity for detecting any DR, referrable DR, and DMO ranged between 52–92.2%; 21–91.4%; and 29.4–81%, respectively, with the highest sensitivity acquired using the CellScope Retina, except for detecting DMO (the highest sensitivity was achieved using the D-EYE). Meanwhile, the specificity for detecting any DR, referrable DR and DMO ranged between 73.3–99%; 64.9–100%; and 95–100%, respectively. The accuracy in diagnosing referrable DR was not assessed for the MII Ret Cam device.

Four of five articles included in this study presented their original data following five DR severity levels: no DR, mild NPDR, moderate NPDR, severe NPDR, and PDR, and also presented data for DMO, with the exception of the study by Toy et al.[19] Two of these articles further re-categorized these severity levels into simplified DR classification for clinical purpose: any DR or non-referrable DR, and referrable DR.[14,19] Calculated sensitivity and specificity values of these devices were based on this classification. Wintergerst et al[21] is the only exception, as they only presented concise classification of any DR, referrable DR, and DMO.

Mii Ret Cam showed wide variation of sensitivities in diagnosing five DR severity level. The lowest sensitivity was reported in the diagnosis of moderate NPDR (43%) and the highest in PDR (100%).[13] D-EYE sensitivities also varied between 55–96%, but the lowest sensitivity was for diagnosing severe NPDR and the highest was for normal

Table 1 Characteristics of Included Studies

Authors, Year	Country	Study Design	Study Setting	Sample Size (n, Patients / Eyes)	Age of Participants (Mean ± SD, Years)	Diabetes Duration (Mean ± SD, Years)	DR Severity Scale
Bilong et al, 2019[13]	Cameroon	Cross-sectional	National Obesity Centre of Yaounde Central Hospital, Cameroon	220 / 440	57.7 ± 10.2	7.9 ± 6.9	ICDR severity scale
Kim et al, 2018[14]	USA	Cross-sectional	Michigan Kellogg Eye Center Retina Clinic at University of Michigan, Michigan	71 / 142	56.7 ± 16.9	NR	Modified ETDRS grading system
Russo et al, 2015[20]	Italy	Prospective clinic-based comparative study	Ophthalmic Diabetic Center of "Spedali Civili di Brescia", Brescia	120 / 240	58.8 ± 16.4	11.6 ± 9.7	ICDR severity scale
Toy et al, 2016[19]	USA	Prospective, single institutional comparative study	Santa Clara Valley Medical Center, California	50 / 100	60.5 ± 10.6	11.9 ± 8.4	ICDR severity scale
Wintergerst et al, 2020[21]	India	Cross-sectional	Thirteen Diabetic Retinopathy Outreach Eye Clinics in and around Bangalore	193 / 381	56.64 ± 10.85	6.96 ± 6.59	ICDR severity scale, referral criteria based on ICO and ADA

Abbreviations: ADA, American Diabetes Association; DR, diabetic retinopathy; ETDRS, Early Treatment of Diabetic Retinopathy Study; ICDR, International Classification of Diabetic Retinopathy; ICO, International Council of Ophthalmology; NR, not reported.

fundus without DR. On the other hand, sensitivities for diagnosing moderate NPDR and PDR were both good, which were 82% and 89%, respectively.[20] Similar results were demonstrated by CellScope Retina, in which the lowest sensitivity was for diagnosing any DR (94%) and PDR

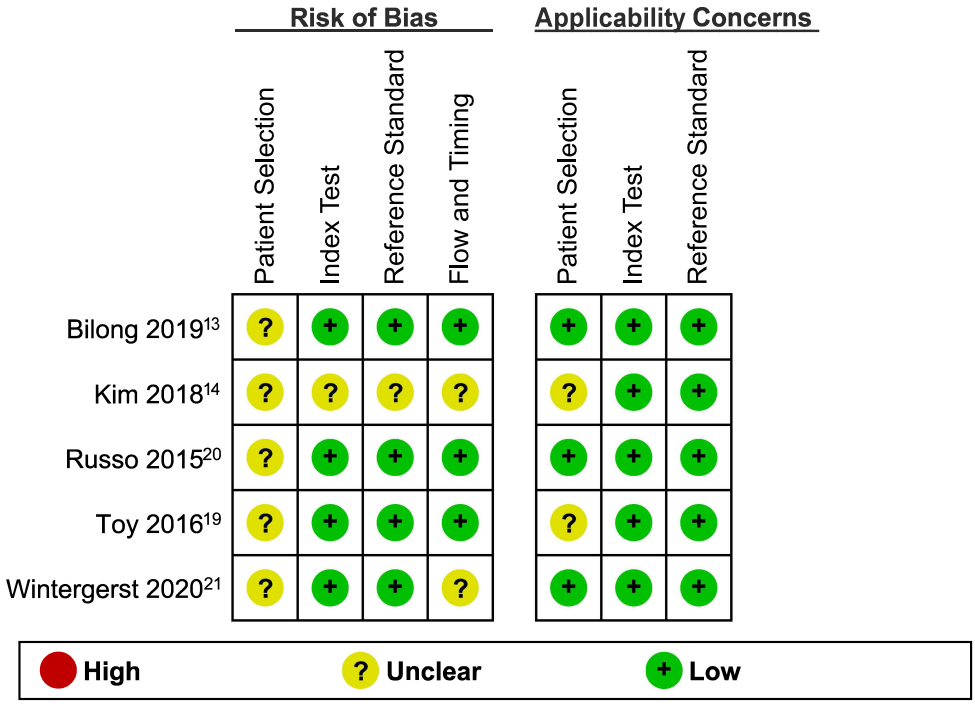

Figure 2 Risk of bias assessment using QUADAS 2 tools.

Table 2 Smartphone-Based Devices' Accuracy, Characteristics, Image Protocol, and Retail Price Range

	Peek Retina[21]	D-EYE[20,21]	DIY Solution by Sankara[21]	Paxos Scope[19,21]	MII Ret Cam[13]	CellScope Retina[14]
Device characteristics						
Compatible with	Samsung Galaxy S4	iPhone 5 and Samsung Galaxy S4	Samsung Galaxy S4	iPhone 5s and iPod Touch	iPhone 5s	iPhone 5s
Principle of work	Direct ophthalmoscopy method	Direct ophthalmoscopy method	Direct ophthalmoscopy method	Indirect ophthalmoscopy method	Indirect ophthalmoscopy method	Indirect ophthalmoscopy method
Illumination source	NR	NR	Single LED with external battery attached to the smartphone	Simple external LED	Built-in smartphone's flash	Single white LED
Lens type	NR	NR	NR	Volk Digital ClearField lens[19] and pan retinal 2.2 lens from Volk Optical[21]	20 D lens	54 D ophthalmic lens
Image protocol						
Mydriatic	Yes	Yes	Yes	Yes	Yes	Yes
Field of view	20–40*	20;[20] 20–40*[21]	20–40*	45;[19] 20–40*[21]	20–40*	50° (individual image) and 100° (wide-field montage)
Working distance	NR	100 mm	NR	50.8 mm	NR	NR
File resolution	Video: 1,280×720 with 15 fps rendered into 400×400 up to 600×600 image	Photo: 3,264×2,448 (using iPhone 5); Video: 1,280×720 with 15 fps rendered into 400×400 up to 600×600 image (using Samsung Galaxy S4)	Video: 1,280×720 with 15 fps rendered into 400×400 up to 600×600 image	Photo: taken with 8 megapixel camera (using iPhone 5s); Video: 1,920×1,080 with 30 fps rendered into 550×550 image (using iPod Touch)	NR	Photos (5 in total): each with resolution of 1,600x1,200, could be rendered using a software into a 5-image montages with 52.3 pixels/retinal degree resolution
Sensitivity (%)						
Any DR	52	86;[20] 59[21]	73	79[21]	73.3	92.2
Referrable	21	84;[20] 41[21]	57	91;[19] 76[21]	N/A	91.4
DMO	60	81;[20] 58[21]	64	79[21]	77.8	29.4
Specificity (%)						
Any DR	96	96;[20] 96[21]	94	99[21]	90.5	73.3
Referrable	100	100;[20] 99[21]	98	99;[19] 99[21]	N/A	64.9
DMO	97	98[20,21]	98	100[21]	95	98.0

(*Continued*)

Table 2 (Continued).

	Peek Retina[21]	D-EYE[20,21]	DIY Solution by Sankara[21]	Paxos Scope[19,21]	MII Ret Cam[13]	CellScope Retina[14]
Reference standard	Indirect ophthalmoscopy	Slit-lamp examination[20] and indirect ophthalmoscopy[21]	Indirect ophthalmoscopy	Indirect ophthalmoscopy	Indirect ophthalmoscopy	Slit-lamp examination
Retail price range	$134–$200†	$400–435	N/A	$299†	$245–380	N/A

Notes: *Field of view assumed by authors based on fundus photographs included in the article. †Product has been discontinued and only existed in limited marketplace.
Abbreviations: DIY, do-it-yourself; DR, diabetic retinopathy; DMO, diabetic macular oedema; fps, frame per second; LED, light emitting diode; N/A, not available; NR, not reported.

(72%).[14] Paxos Scope has the lowest sensitivity among other devices in diagnosing mild NPDR (0%) and the highest sensitivity for severe NPDR and PDR (100%).[19]

Specificities for diagnosing DR in all four articles were more comparable, except for CellScope Retina. Paxos Scope has a specificity ranging between 99–100%, with the highest for severe NPDR and PDR.[19] Both Mii Ret Cam and D-Eye had their lowest specificity for mild NPDR (90% and 93%, respectively) and the highest for PDR (both 100%).[13,20] CellScope Retina showed substantial variation in specificity: 40% for any DR and 94% for PDR.[14]

Four out of six devices had retail price ranges less than $700, with the exception of DIY by Sankara, which is a modification to the smartphone that can be assembled by ourselves, and CellScope Retina, which is not commercially available at this time.

Meta-Analyses

Any DR

Four out of five studies (679 participants) presented data for any DR[13,14,19,20] and were evaluated using a Forest plot, as shown in Figure 3. The sensitivity ranged from 72–94%, and specificity from 40–99%. The most extreme values from

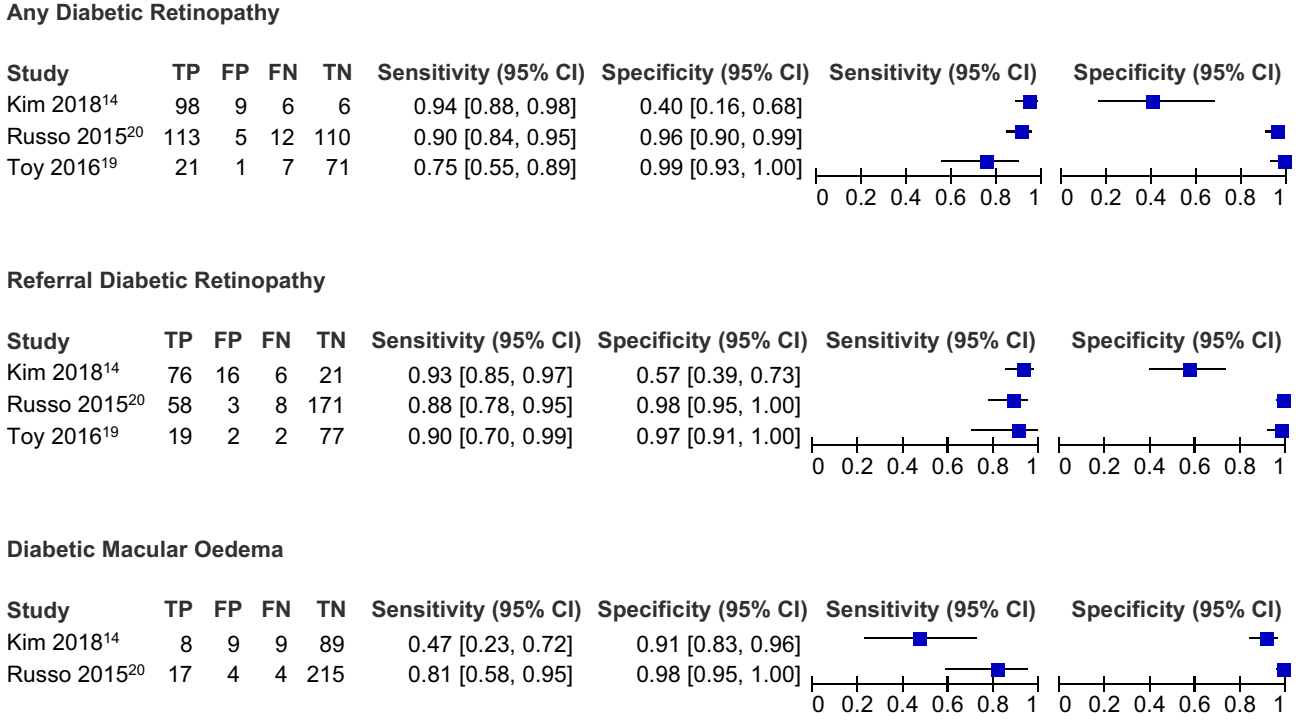

Figure 3 Forest plot for sensitivity and specificity of any DR, referral DR, and DMO.

studies with smaller sample sizes and wide 95% CIs was found in CellScope Retina.[14] One study did not contribute data to the meta-analysis because sensitivity was not estimable.[21]

Referral DR

Three out of five studies presented data for referral DR from a total of 459 participants.[14,19,20] Sensitivities for referral DR ranged from 88–93%, and specificities from 57–98% from a total 459 participants of the three studies (Figure 3).

DMO

In DMO groups, three out of five studies with a total of 573 participants[13,14,20] contributed to the estimation of sensitivity, which ranged between 47% and 81%. The most extreme values were from CellScope Retina which had smaller sample sizes and wide 95% CIs.[14] Specificity was more homogenous, ranging from 91–100% (Figure 3).

Discussion

In this systematic review, we reported the sensitivity and specificity of six low-cost, smartphone-based devices in detecting DR, referrable DR, and DMO when compared with indirect ophthalmoscopy and slit-lamp bio-microscopy as the reference standard. These devices showed considerably good sensitivity (52–92%) and specificity (73–99%) when detecting the presence of any DR. However, a wider range of sensitivity was reported when detecting referrable DR (21–91%) and DMO (29–81%), as opposed to their high specificity for referrable DR (65–100%) and DMO (95–100%). This suggests that the use of low-cost, smartphone-based devices for DR screening in the community should be acceptable, particularly for countries or areas with a lack of facilities, difficult geographical features, or health financing constraints.

There were a very limited number of previously published studies for comparison. A recent systematic review and meta-analysis by Tan et al[17] also analysed six different smartphone-based devices from nine articles, but only three of those devices met our inclusion criteria. Three articles featured a high-cost device (more than $700) called Remidio FOP; one of them featured a handheld 20D lens that does not use an adaptor; and one article featured a device called Ocular CellScope that was an early design of CellScope Retina.[14]

The accuracy of these low-cost devices were nearly comparable to the recommended retinal examination for DR screening using either direct/indirect ophthalmoscopy, slit-lamp examination, or traditional table-top fundus cameras with a ≥30° field of view.[7] The study by Baeza et al[22] compared dilated 45° single-field photographs using a table-top fundus camera with gold standard of seven standard stereoscopic 30° field photographs as proposed by ETDRS[23] and found sensitivity and specificity for detecting any DR of 77% and 98%, respectively, and for detecting referrable DR of 82% and 99%, respectively. A similar study by Murgatroyd et al[24] using a slit-lamp examination as reference standard shows sensitivity and specificity for detecting any DR of 86% and 91%, respectively, and for detecting referrable DR of 81% and 92%, respectively. A Veteran Affairs Diabetes Trial (VADT) study compared clinical examination using both direct and indirect ophthalmoscopy with standard 7-field ETDRS fundus photographs and found that the sensitivity and specificity for detecting any DR were 51% and 91%, respectively. In addition to any DR, the sensitivity and specificity for detecting PDR were 61% and 98%, respectively. However, the sensitivity for detecting DMO was low (24%), in contrast to its high specificity (98%).[25]

Rapid technological advances in retinal imaging have improved the accuracy and time consumption of DR detection.[26] Moreover, with the presence of artificial intelligence (AI), efforts or personnel needs to perform the screening have reduced. Landmarks studies have documented that machine learning system could detect referrable DR from retinal photographs with sensitivity and specificity of more than 90% when compared with expert decision.[27,28] For example, one of the latest technologies in AI for DR detection was the development of an active deep learning (ADL) method using an artificial bee colony (ABC) algorithm. This method has been shown to have enhanced ability to detect five levels of DR severity whilst an earlier AI method was only able to detect two DR levels: referrable and non-referrable DR.[29] These results indicated its potential in clinical scenario to enhance efficiency in DR screening coverage. However, much attention has mostly focused on the development of a DR screening system which involved the use of sophisticated or expensive equipment that are less portable and less affordable for low resource countries.

In this review, we found only five out of hundreds available studies in the literature have attempted to use low-cost devices to screen DR. Unlike currently established DR screening systems that use a table-top fundus camera, low-cost smartphone devices have not gained much interest possibly due to a priori assumption that the accuracy would be low.[13,21] This review clearly suggested otherwise, that accuracy of the available low-cost devices was not far behind the table-top camera system and was suitable in the context of DR screening.[30] Relatively lower sensitivity may indicate that these smartphone-based devices may have missed included early or no DR cases into referrable DR group or recognized cases without DMO as having DMO. However, high specificity in detecting referrable DR and DMO has strongly emphasized that once a case is not detected as referrable DR or DMO, that case is less likely to have referrable DR or DMO needing further treatment.

It is noteworthy that small field of view could be one prominent limitation of smartphone-based devices when compared with table-top fundus camera. Four out of five devices we included in this review have a field of view ranging from 20–40°, barely in accordance to recommended ICO screening guidelines.[7] Prior review had shown that most studies regarding DR screening using a table-top fundus camera capture at least a single 45° field of view and others had claimed the importance of a wider field of view to identify DR characteristics that may occur in the peripheral retina.[30,31] A single 60° field of view was found to improve the screening process because it can still detect microaneurysm lesions and referral DR with a lower number of capture. Remidio Vistaro was reported to provide a 65° field of view and the montage of two fundus photographs could exceed the standard 7-field ETDRS view.[32,33] The latest technology of ultra-wide field (UWF) imaging with a ≥100° field of view was found to be very effective in detecting peripheral DR lesions because it can capture around 82% of the retinal surface.[34] A study compared UWF retinal imaging with a 200° field of view and standard 7-field ETDRS and found 51% of the DR lesion was found within the standard ETDRS view, 15% found in the peripheral outside the standard ETDRS view, and 34% were distributed evenly.[35] In order to overcome this problem, there are alternative imaging protocols than can be done to capture a wider field of view beyond the initial capabilities of these devices, such as using a montage of several photographs (eg, CellScope Retina) or using video mode (eg, Peek Retina, D-EYE, Paxos Scope).

There are some important implications of this review. To date, nationwide systematic DR screening has been fully implemented only in very few countries, such as the UK and Ireland.[31,36] Other high resource countries, for example the USA, Singapore, and European countries, are progressing substantially but have not yet established the same system as the UK.[9] On the other hand, developing countries or countries with low health resources are mostly struggling with the provision of equally accessible screening and treatment facilities in each area in the country due to financial barriers.[9,37] In the context of Indonesia as an example, Indonesia is one of the developing countries having a growing burden of diabetes but multiple problems related to DR screening: 1) difficult geographical features; 2) inadequate health infrastructures and access in rural areas; 3) uneven distribution of eyecare personnel; and 4) a low government budget for eye healthcare. Devices included in this study have a market price below $700 (ranged between $134–$435), which are more affordable compared to a standard table-top fundus camera such as Zeiss Visucam Pro NM that has the average market price range of $10,000. This review may propound that low-cost, smartphone-based devices can significantly reduce the financial burden of DR screening which is heavily related to providing a large amount of fundus cameras and frequent retinal imaging.[38] Several devices we included in this study had been trialled in developing countries that have similar problems with ours: Peek Retina was used for screening in Uganda and Mii Ret Cam in India.[13,39] More importantly, these devices are simple and should not be difficult to manufacture. Therefore, with the current state of advancement in smartphone technology, researchers and industries working in this area should be more encouraged to develop similar devices.

There were several studies which were excluded because it features smartphone-based devices that has retail prices over $700. Remidio FOP was one of the excluded devices, which is a product manufactured in India that employs an indirect ophthalmoscopy method, can be used without mydriatic, has a 45° field of view and lens adjustment between −20 D to +20 D.[40] This device had gone through clinical validation to diagnose DR and, compared to standard 7-field fundus photography, it has a high sensitivity and specificity for any DR (93% and 98%, respectively), referral DR (88% and 95%, respectively), and DMO (87% and 95%, respectively).[41] Unfortunately, we found that the retail price for Remidio FOP far exceeds our definition of low cost, which is between $5,000-$8,000. Another device we excluded was

Eyer, which was a smartphone-based device produced in the United States. Similar to Remidio FOP, Eyer also employs an indirect ophthalmoscopy method, hasa 45° field of view and autofocus range from −20 to +20 D. This device also went through clinical validation and has sensitivity of 91% and specificity of 81% when compared to single-field table-top fundus photography for referrable DR. It also showed a relatively good agreement (73%) for diagnosing all six levels of DR severity. However, the retail price also exceeded our definition of low cost, which is around $4,500.[42] Out of the six smartphone-based devices we included in this review, Peek Retina is the only device that had gone through clinical validation to diagnose DR. Compared to a standard ophthalmic fundus camera, it has good sensitivity and specificity for diagnosing any DR (84% and 79.9%, respectively).[39] Peek Retina also had validation studies for optic disc imaging, which shows excellent agreement (kappa coefficient of 0.69) between the smartphone-based device and the standard ophthalmic fundus camera.[43] These findings are similar to another validation study done in Brazil to evaluate smartphone-based devices in measuring cup-to-disc ratio, which also shows excellent agreement.[44]

The strength of our study is the use of a detailed search strategy pre-defined in our study protocol. However, limitations are noted. First, because not all studies presented detailed data needed for our calculations, we were only able to perform simple meta-analyses using a Forest plot. Second, we did not redefine the definition of referrable DR used in included studies. However, there were only slightly different definitions of referral-warranted DR which all were referred to definitions used in prominent studies.[7] Finally, there were also potential biases associated with the reference standards being clinical examinations instead of retinal photography using a table-top fundus camera and the process of capturing retinal images that were influenced by image qualities and smartphone camera specifications.

Conclusion

In conclusion, this review found that currently available low-cost, smartphone-based devices showed a relatively wide range of overall sensitivity but more consistent specificity for detecting any DR, referrable DR, and DMO. The accuracy of these devices was not far behind the high-cost DR screening systems, suggesting the potential use of low-cost, smartphone-based devices for DR screening in countries that struggle to provide a high-cost DR screening system. More importantly, this review may enlighten researchers in this area that there are opportunities to develop more affordable smartphone-based devices with better accuracy to increase the availability of affordable DR screening equipment.

Acknowledgments

The authors thank Roihan Muhamad Iqbal (RMI) for providing valuable input in developing the systematic search strategy and involved in the article screening process.

Funding

This study was partially supported by the National Endowment Fund (LPDP) (contract no. PRJ-73/LPDP/2019).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Yau JWY, Rogers SL, Kawasaki R, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care*. 2012;35(3):556–564. doi:10.2337/dc11-1909
2. Sasongko MB, Widyaputri F, Agni AN, et al. Prevalence of diabetic retinopathy and blindness in Indonesian adults with type 2 diabetes. *Am J Ophthalmol*. 2017;181:79–87.
3. Leasher JL, Bourne RR, Flaxman SR, et al. Global estimates on the number of people blind or visually impaired by diabetic retinopathy: a meta-analysis from 1990 to 2010. *Diabetes Care*. 2016;39(9):1643–1649.
4. Royle P, Mistry H, Auguste P, et al. Pan-retinal photocoagulation and other forms of laser treatment and drug therapies for non-proliferative diabetic retinopathy: systematic review and economic evaluation. *Health Technol Assess*. 2015;19(51):v–xxviii, 1–247.
5. El Rami H, Barham R, Sun JK, Silva PS. Evidence-based treatment of diabetic retinopathy. *Semin Ophthalmol*. 2017;32(1):67–74.
6. The Diabetic Retinopathy Study Research Group. Photocoagulation treatment of proliferative diabetic retinopathy. Clinical application of Diabetic Retinopathy Study (DRS) findings, DRS report number 8. *Ophthalmology*. 1981;88(7):583–600.
7. Wong TY, Sun J, Kawasaki R, et al. Guidelines on diabetic eye care: the international council of ophthalmology recommendations for screening, follow-up, referral, and treatment based on resource settings. *Ophthalmology*. 2018;125(10):1608–1622.

8. American Diabetes Association. Microvascular complications and foot care: standards of medical care in diabetes-2021. *Diabetes Care*. 2021;44 (Suppl 1):S151–S167.
9. Vujosevic S, Aldington SJ, Silva P, et al. Screening for diabetic retinopathy: new perspectives and challenges. *Lancet Diabetes Endocrinol*. 2020;8 (4):337–347.
10. Murthy KR, Murthy PR, Kapur A, Owens DR. Mobile diabetes eye care: experience in developing countries. *Diabetes Res Clin Pract*. 2012;97 (3):343–349.
11. Natarajan S, Jain A, Krishnan R, Rogye A, Sivaprasad S. Diagnostic accuracy of community-based diabetic retinopathy screening with an offline artificial intelligence system on a smartphone. *JAMA Ophthalmol*. 2019;137(10):1182–1188.
12. Rajalakshmi R, Subashini R, Anjana RM, Mohan V. Automated diabetic retinopathy detection in smartphone-based fundus photography using artificial intelligence. *Eye*. 2018;32(6):1138–1144.
13. Bilong Y, Katte JC, Koki G, et al. Validation of smartphone-based retinal photography for diabetic retinopathy screening. *Ophthalmic Surg Lasers Imaging Retina*. 2019;50(5):S18–S22.
14. Kim TN, Myers F, Reber C, et al. A smartphone-based tool for rapid, portable, and automated wide-field retinal imaging. *Transl Vis Sci Technol*. 2018;7(5):21.
15. Kanclerz P, Tuuminen R, Khoramnia R. Imaging modalities employed in diabetic retinopathy screening: a review and meta-analysis. *Diagnostics*. 2021;11(10):154.
16. Piyasena M, Murthy GVS, Yip JLY, et al. Systematic review and meta-analysis of diagnostic accuracy of detection of any level of diabetic retinopathy using digital retinal imaging. *Syst Rev*. 2018;7(1):182.
17. Tan CH, Kyaw BM, Smith H, Tan CS, Tudor Car L. Use of smartphones to detect diabetic retinopathy: scoping review and meta-analysis of diagnostic test accuracy studies. *J Med Internet Res*. 2020;22(5):e16658.
18. Prayogo M, Sasongko M, At Thobari J, et al. Accuracy of low-cost smartphone-based screening test for diabetic retinopathy - a systematic review; 2021. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021249746. Accessed July 25, 2023.
19. Toy BC, Myung DJ, He L, et al. 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.
20. 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 e361.
21. Wintergerst MWM, Mishra DK, Hartmann L, et al. Diabetic retinopathy screening using smartphone-based fundus imaging in India. *Ophthalmology*. 2020;127(11):1529–1538.
22. Baeza M, Orozco-Beltran D, Gil-Guillen VF, et al. Screening for sight threatening diabetic retinopathy using non-mydriatic retinal camera in a primary care setting: to dilate or not to dilate? *Int J Clin Pract*. 2009;63(3):433–438.
23. Early Treatment Diabetic Retinopathy Study Research Group. Grading diabetic retinopathy from stereoscopic color fundus photographs--an extension of the modified Airlie House classification. ETDRS report number 10. *Ophthalmology*. 1991;98(5 Suppl):786–806.
24. Murgatroyd H, Ellingford A, Cox A, et al. Effect of mydriasis and different field strategies on digital image screening of diabetic eye disease. *Br J Ophthalmol*. 2004;88(7):920–924.
25. Emanuele N, Klein R, Moritz T, et al. Comparison of dilated fundus examinations with seven-field stereo fundus photographs in the Veterans Affairs Diabetes Trial. *J Diabetes Complications*. 2009;23(5):323–329.
26. Gulshan V, Rajan RP, Widner K, et al. Performance of a deep-learning algorithm vs manual grading for detecting diabetic retinopathy in India. *JAMA Ophthalmol*. 2019;137(9):987–993.
27. Gulshan V, Peng L, Coram M, et al. Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs. *JAMA*. 2016;316(22):2402–2410.
28. Ting DSW, Cheung CY, Lim G, et al. Development and validation of a deep learning system for diabetic retinopathy and related eye diseases using retinal images from multiethnic populations with diabetes. *JAMA*. 2017;318(22):2211–2223.
29. Özbay E. An active deep learning method for diabetic retinopathy detection in segmented fundus images using artificial bee colony algorithm. *Artif Intell Rev*. 2023;56(4):3291–3318.
30. Fenner BJ, Wong RLM, Lam WC, Tan GSW, Cheung GCM. Advances in retinal imaging and applications in diabetic retinopathy screening: a review. *Ophthalmol Ther*. 2018;7(2):333–346.
31. Scanlon PH. The English National Screening Programme for diabetic retinopathy 2003–2016. *Acta Diabetol*. 2017;54(6):515–525.
32. von Wendt G, Ronnholm P, Heikkila K, Summanen P. A comparison between one- and two-field 60 degree fundus photography when screening for diabetic retinopathy. *Acta Ophthalmol Scand*. 2000;78(1):14–20.
33. Sivaraman A, Nagarajan S, Vadivel S, et al. A novel, smartphone-based, teleophthalmology-enabled, widefield fundus imaging device with an autocapture algorithm. *Transl Vis Sci Technol*. 2021;10(12):21.
34. Ghasemi Falavarjani K, Tsui I, Sadda SR. Ultra-wide-field imaging in diabetic retinopathy. *Vision Res*. 2017;139:187–190.
35. Aiello LP, Odia I, Glassman AR, et al. Comparison of early treatment diabetic retinopathy study standard 7-field imaging with ultrawide-field imaging for determining severity of diabetic retinopathy. *JAMA Ophthalmol*. 2019;137(1):65–73.
36. Pandey R, Morgan MM, Murphy C, et al. Irish National Diabetic RetinaScreen Programme: report on five rounds of retinopathy screening and screen-positive referrals. (INDEAR study report no. 1). *Br J Ophthalmol*. 2022;106(3):409–414.
37. Sasongko MB, Indrayanti SR, Wardhana FS, et al. Low utility of diabetic eye care services and perceived barriers to optimal diabetic retinopathy management in Indonesian adults with vision-threatening diabetic retinopathy. *Diabetes Res Clin Pract*. 2021;171:108540.
38. Sasongko MB, Wardhana FS, Febryanto GA, et al. The estimated healthcare cost of diabetic retinopathy in Indonesia and its projection for 2025. *Br J Ophthalmol*. 2020;104(4):487–492.
39. Yusuf AM, Lusobya RC, Mukisa J, Batte C, Nakanjako D, Juliet-Sengeri O. Validity of smartphone-based retinal photography (PEEK-retina) compared to the standard ophthalmic fundus camera in diagnosing diabetic retinopathy in Uganda: a cross-sectional study. *PLoS One*. 2022;17(9): e0273633.
40. Prathiba V, Rajalakshmi R, Arulmalar S, et al. Accuracy of the smartphone-based nonmydriatic retinal camera in the detection of sight-threatening diabetic retinopathy. *Indian J Ophthalmol*. 2020;68(Suppl 1):S42–S46.

41. Rajalakshmi R, Arulmalar S, Usha M, et al. Validation of smartphone based retinal photography for diabetic retinopathy screening. *PLoS One*. 2015;10(9):e0138285.
42. de Oliveira JAE, Nakayama LF, Zago Ribeiro L, et al. Clinical validation of a smartphone-based retinal camera for diabetic retinopathy screening. *Acta Diabetol*. 2023;2023:1–7.
43. Bastawrous A, Giardini ME, Bolster NM, et al. Clinical validation of a smartphone-based adapter for optic disc imaging in Kenya. *JAMA Ophthalmol*. 2016;134(2):151–158.
44. Titoneli CC, Filho MS, Lencione D, Vieira FP, Stuchi JA, Paula JS. Clinical validation of a smartphone-based handheld fundus camera for the evaluation of optic nerve head. *Arq Bras Oftalmol*. 2021;84(6):531–537.