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## Cost-effectiveness and diagnostic accuracy of telemedicine in macular disease and diabetic retinopathy: A systematic review and meta-analysis.

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# Cost-effectiveness and diagnostic accuracy of telemedicine in macular disease and diabetic retinopathy

## A systematic review and meta-analysis

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### Abstract

**Objective:** To determine cost-effectiveness and the diagnostic accuracy of teleophthalmology (TO) in the detection of macular edema (ME) and various grades of diabetic retinopathy (DR).

**Methods:** MEDLINE, EMBASE, and Cochrane databases were searched for TO, ME, and DR on May 25, 2016. The search was updated on April 2, 2019. Pooled sensitivity and specificity for ME and various grades of DR were determined using Meta-Disc software. A systematic review of the articles discussing the cost-effectiveness of TO screening was also performed.

**Results:** Thirty-three articles on the diagnostic accuracy and 28 articles on the cost-effectiveness were selected.

**Conclusions:** Telescreening is moderately sensitive but very specific for the diagnosis of diabetic retinopathy. Non-mydratric Teleretinal screening services are cost-effective, decrease clinics workload, and increase patient compliance if provided free of cost in remote low socioeconomic regions.

**Abbreviations:** CSME = clinically significant macular edema, DME = diabetic macular edema, DoD = Department of Defense, DR = diabetic retinopathy, ETDRS = Early Treatment Diabetic Retinopathy Screening, IHS = Indian Health Service, JVN = Joslin Vision Network, ME = macular edema, NPDR = non-diabetic proliferative diabetic retinopathy, PDR = proliferative diabetic retinopathy, QALY = quality-adjusted life-year, TO = teleophthalmology, VA = Department of Veterans Affairs.

**Keywords:** diabetic retinopathy, macular edema, teleophthalmology

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## 1. Introduction

Recent surveys indicate that approximately 382 million of the world population and 29.1 million of the US population has diabetes mellitus.<sup>[1,2]</sup> If no action has been taken, this number will double by 2035.<sup>[1]</sup> With such a significant portion of the population affected by diabetes, managing complications of this disease are paramount. The most common complication of diabetes is diabetic retinopathy (DR), affecting about 28% of the diabetic population.<sup>[3]</sup> According to WHO, DR accounts for almost 17% of all cases of blindness in the USA and Europe, and the number of Americans with DR will nearly double from 7.7 million to 14.6 million by the end of 2050.<sup>[4]</sup> Good glycemic control, early diagnosis, and prompt management of DR can delay the progression of DR into blindness.<sup>[5]</sup> Despite this knowledge, only about 55% of the diabetic patients in the United States receive retinopathy screening.<sup>[6]</sup> Similarly, the systematic implementation of DR testing is not common in many low and middle-income countries.<sup>[5,7]</sup> The main reasons responsible for the poor compliance to the DR screening are high testing expenses, inadequate health care facilities, and limited access to conventional screening strategies.<sup>[8]</sup> Teleophthalmology recently has gained particular importance as an alternative screening method to overcome the barriers in the face of DR screening.<sup>[9]</sup>

Teleretinal technology is believed to improve access and reduce the cost of the DR and ME screening. However, the diagnostic accuracy and cost of this screening modality depend on many variables including the use of pupillary mydriasis, an instrument

used, the qualifications of the photographer, number of photographic fields, and the image interpreter. Many studies have been done to discuss the utility of this technology, but the literature on the cost-effectiveness and diagnostic accuracy of Teleretinal screening are yet limited. We present the results of a systematic review and meta-analysis of studies evaluating the cost-effectiveness and pooled sensitivity and specificity of TO in DR and ME screening.

## 2. Methods

### 2.1. Search strategy and selection criteria

The initial literature search for relevant articles was performed on May 25, 2016, using MEDLINE (PubMed, Ovid), Embase, and Cochrane databases. The search was updated on April 2, 2019. There was no language or time restriction placed on the search. The search strategies included various combinations of text-words and medical subject headings (MeSH) to generate 2 subsets of citations: one for ME or DR, using the MeSH and terms like “macular edema,” “diabetic retinopathy,” “diabetic maculopathy,” “diabetic macular edema,” “diabetic ophthalmopathy,” “diabetic eye disease,” and “diabetic ocular disease” and the other for teleophthalmology using terms and MeSH like “telemedicine,” “telehealth,” “mhealth,” “ehealth,” “medical informatics,” “clinical decision support system,” “computer-assisted decision making,” “information system,” “teleophthalmology diabetes,” “tele maculopathy diabetes,” “tele health-care,” “mobile health,” “health information technology,” “software-assisted analysis.” The terms from the 2 subsets were combined in 1:1 combination and finally results from all the possible combinations were downloaded into an EndNote library. Based on our research question, we also manually searched the references in all known articles to identify studies that were missed by the initial search. An ethics approval was obtained from the institutional review board (IRB) for this study.

The selection criteria for the included studies were: recruited subjects with macular edema or diabetes mellitus either type 1 or type 2, discussed the cost-effectiveness or cost-utility of teleophthalmology screening, provided data on the sensitivity or specificity of Teleretinal screening. Studies with insufficient data, discussing only the prevalence of diabetes, case reports, and conference papers were excluded, as studies with no enough description of its subjects.

### 2.2. Study selection

The titles and abstracts of the selected articles were reviewed independently by 3 authors and the articles which met the inclusion criteria were reviewed by the fourth author. Full-text articles that were potentially relevant to the study were also reviewed by all the 4 authors to confirm the eligibility. Disagreements were resolved by mutual consensus and after a detailed group discussion.

### 2.3. Data abstraction and analysis

Two reviewers extracted data on the study characteristics, cost-effectiveness, and sensitivity and specificity of Teleretinal screening. Disagreements were resolved by consensus and by a discussion with a third reviewer. After carefully assessing the extracted data, pooled sensitivity and specificity were calculated

using the Meta-Disc software, RevMan Version 5.3, London, United Kingdom.

### 2.4. Quality assessment

The quality assessment of all the included articles studies was performed using the RevMan 5.3. Selection, detection, attrition, and reporting bias for all studies was assessed.

## 3. Results

The combined systematic search strategy identified a total of 3814 articles. After excluding 1201 duplicate items, the remaining 2613 pieces of literature were screened for relevance based on their titles and abstracts, and 2183 articles were further excluded. A total of 430 were deemed potentially eligible and retrieved for a full review. After a detailed review, a total of 369 articles were further excluded for the following reasons: screening strategies other than teleophthalmology (n=145), telemedicine services of diabetic care (n=27), cost of diabetic care (n=26), telemedicine for treatment of DR (n=48), diabetes prevalence and management (n=62), telerehabilitation of diabetics (n=18), telemedicine on visual acuity and retinitis pigmentosa (n=9), and articles on Teleretinal diabetic prevalence (31). Thirty-three articles on the diagnostic accuracy and 28 articles on the cost-effectiveness were included.

Figure 1 presents a Preferred Reporting Item for Systematic Reviews and Meta-analysis (PRISMA) flowchart of the study selection process along with reasons for study exclusion.

### 3.1. Summary characteristics of the included studies for diagnostic accuracy

A total of 33 studies were selected for the analysis. All these studies used Teleretinal screening either alone or in comparison to other screening modalities like ophthalmoscopy, slit-lamp examination, or 7-field Early Treatment Diabetic Retinopathy Screening (ETDRS). Both men and women with either type 1 or type 2 studies were included in the recruited studies, except Hubbard et al<sup>[10]</sup> study which included patients with type 1 DM only. More than 10,000 people from 8 different countries were screened in all the studies. Almost 80% of the total studies were conducted in the UK, Canada, and at various states of the United States. In >50% of the included studies, digital imaging was carried out with mydriasis except for Hansen et al<sup>[11]</sup> and Lawrence<sup>[12]</sup> study in which both mydriatic and non-mydriatic images were obtained. Images were transferred through a secure web browser, telemetrically, or via an online network.<sup>[13–16]</sup> A description of the included studies for diagnostic accuracy is presented in Table 1.

## 4. Discussion

### 4.1. Diagnostic accuracy

The cumulative diagnostic accuracy of teleophthalmology for diabetic macular edema (DME) showed a mean sensitivity of 59% with a range as <30% and a maximum value of 88%. While specificity ranged from 82% to 98% with a mean of 93% and a standard deviation of about 6%. While for clinically significant macular edema (CSME) these values were 38% and 100%, respectively. The mean for CSME was 66%, the standard

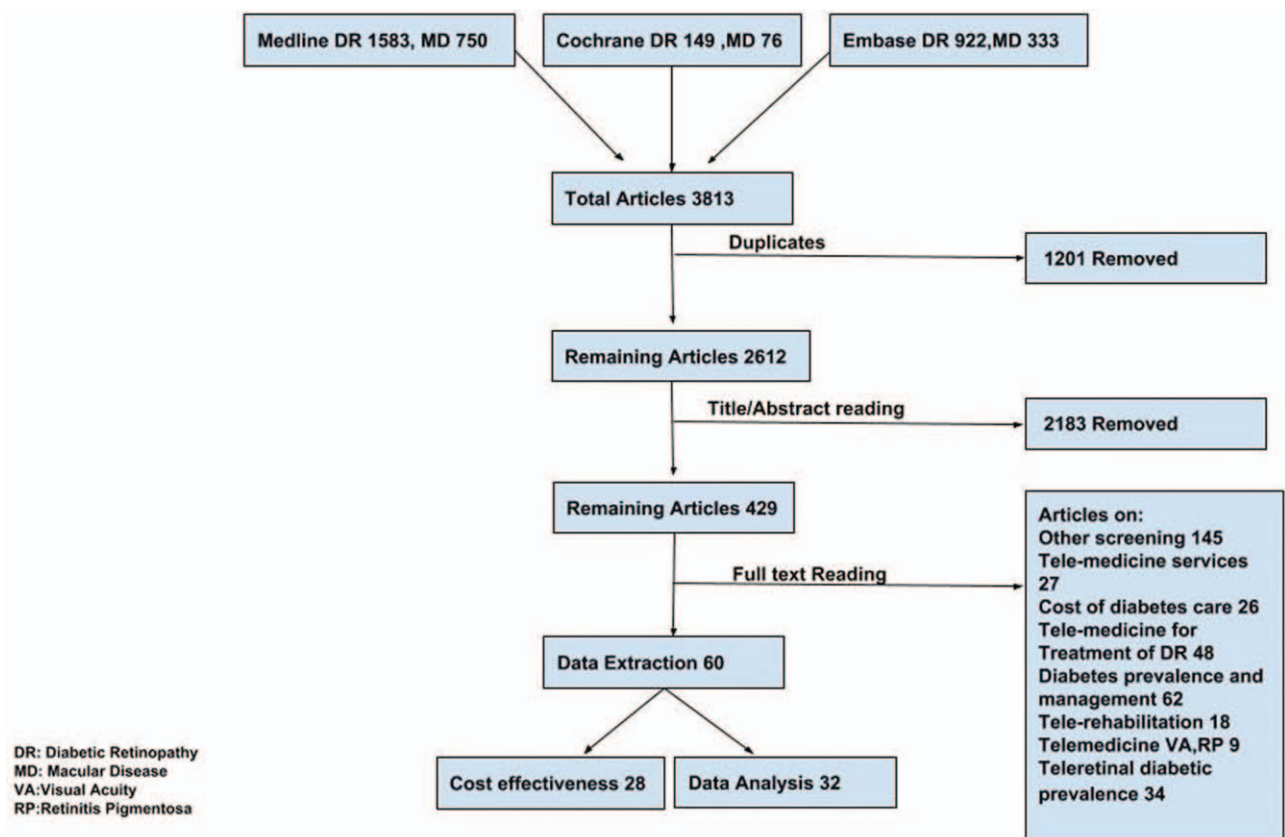


Figure 1. PRISMA flow sheet of the selected studies.

deviations for both were 26% and 22%, respectively. The specificity ranged from 75% to 100% with a mean of 94% and a standard deviation of about 8%.

Teleophthalmology was found to be 87% sensitive and 91% specific for the absence of retinopathy. For mild non-diabetic proliferative diabetic retinopathy (NPDR), the total number of articles was 16, with a minimum value of sensitivity 35% and a maximum value of 93% with a mean of 74% and the standard deviation was 0.16481. The mean specificity ranged from none to 98% with a mean of 50% and the standard deviation was 44%. The sensitivity of moderate NPDR was reported in 15 articles having a minimum to maximum range 32% to 100% with a mean and standard deviation of 71% and 19% respectively. These values for specificity ranged from none to 98% with a mean and standard deviation of only 48% and 47% respectively. For severe NPDR, the mean sensitivity was 42% with a standard deviation of 27% and a range from none to 79%. Surprisingly the specificity of telemedicine was very high ranging from 94% to 100% and a mean of 94% having only 1% of standard deviation. As far as individuals with low risk proliferative diabetic retinopathy (PDR) were concerned, the teleophthalmology was found to 75% sensitive with respect to the gold standard ophthalmoscopy with a range from 0% to 100% among different studies. These values were ironically high for mean specificity that was 98% ranging from 94% to 100% among individual studies having a negligible standard deviation of only 2%. Lastly, for high-risk PDR, the minimum sensitivity value of 0.00 and a maximum value of 100% were found among studies while the mean sensitivity was 76% and the standard deviation was 31%.

The specificity ranged from 69% to 100% and the mean and the standard deviation was 94% and 9% respectively. The individual sensitivities and specificities of the included studies are tabulated in supplementary table S1, <http://links.lww.com/MD/E387>.

#### 4.2. Quality assessment of included studies

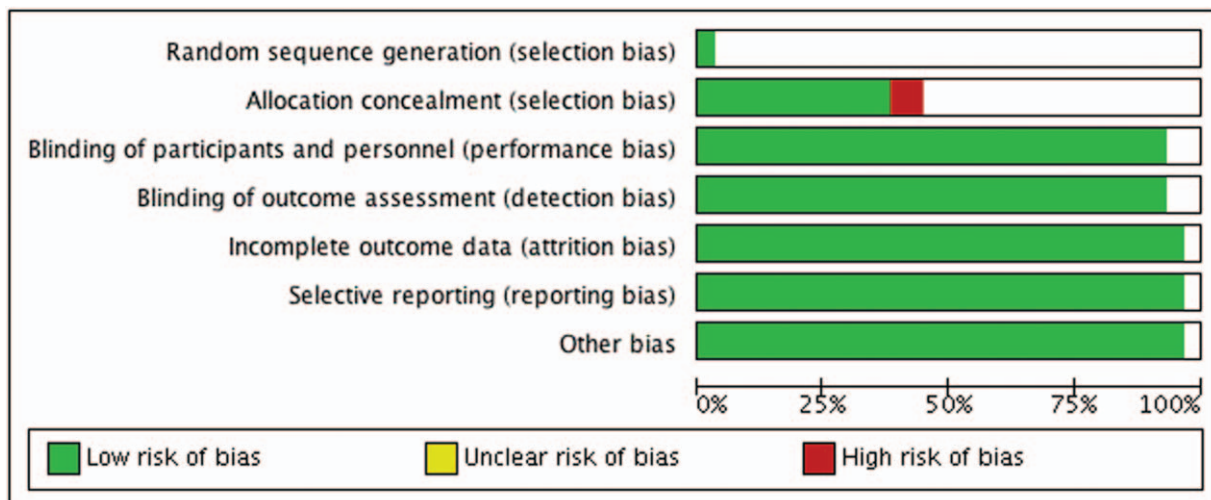
The detailed quality assessment and risk of bias assessment of the included studies are summarized in supplementary table S2, <http://links.lww.com/MD/E388> and shown in Fig. 2 below. The detailed summary of bias assessment is shown in supplementary figure S1, <http://links.lww.com/MD/E384>. Overall the quality of the studies included in our meta-analysis was high. The allocation concealment might have introduced a high risk of selection bias in the Hansen study.<sup>[11]</sup> Silva performed 2 similar studies in 2012 and the risk of bias assessment could be done only on one study while the second study had insufficient information. Selection criteria were well defined in almost all studies. Chances for detection bias and attrition bias were low as there not enough unblinded studies or studies reporting incomplete data respectively. Due to complete reporting of outcomes in all studies, the reporting bias was minimal in all studies.

#### 4.3. Cost-effectiveness

Cost-effective Teleretinal screening programs have been reported in many clinical settings, including Canada, India, United States, Norway, and the United Kingdom.<sup>[42-60]</sup> A total of 28 studies were identified assessing the cost-effectiveness of teleophthalmol-

**Table 1**  
**Characteristics of the included studies for the diagnostic accuracy.**

SNo.	Author	Sample size (patients/ no of eyes)	Mean age/ range, y	Mean duration of diabetes, y	No of fields, degree, scope (stereo/mono), mydriatic use (yes/no)	Image resolution (pixels)
1	Massin et al, 2005, France [17]	74/147	52/25–74	8/0–23	5, 45, non-stereoscopic, color, No	1490 × 960
2	Hansen et al, 2004 [11]	83/165	47/25–70	22/1–53	5, 45, non-stereoscopic, color, both	1450 × 1026
3	Schiffman et al, 2005 [18]	111/222	57/18–99	19/1–49	15, 55–60, non-stereoscopic, color, no	N/A
4	Gangaputra et al, 2011 [19]	96/157	62/37–86	19/NA	4–7, 30–60, stereoscopic, color, yes	N/A
5	Hubbard et al, 2011 [10]	319/628	48/NA	27.2/NA	7, 30, stereoscopic, color, yes	N/A
6	Kernt et al, 2011 [13]	34/66	62/NA	14.3/NA	1200, non-stereoscopic, color, yes	N/A
7	Maker et al, 2012 [20]	106/211	49/19–78	23.7/NA	7, 30, stereoscopic, color, yes	1280 × 1024
8	Silva et al, 2012 [21]	3864/7728	53/NA	12–13/NA	1100 and 200, stereoscopic, color, no	1000 × 1000
9	Kernt et al, 2012 [14]	141/212	64/25–78	12/3–39	1180–200, non-stereoscopic, color, no	3900 × 3072
10	Tennant et al, 2000, Canada [22]	121/241	57/9.0–83	8.5/NA	7, 30, stereoscopic, yes	2008 × 3040
11	Gomez-Ulla et al, 2002, Spain [23]	70/126	N/A/NA	NA	N/A, 35–45, N/A, no	N/A
12	Harding et al, 1995, UK [24]	395/NA	60.2/NA	NA	3, 45, non-stereoscopic, yes	NA
13	Li et al, 2010, US [25]	85/152	59/33–83	NA	9, 45, monoscopic, color, yes	2400/3000 × 2000
14	Silva et al, 2012, US [26]	126/67	49/24–83	21.1/(1–51)	3 field 45°, 2 field 30°, stereoscopic, no	1200 × 1600
15	Cavallerano et al, 2012, US [27]	158 /316	56/22–86	7.0/(0.1–42)	NA, 35, stereoscopic, no	N/A
16	Torok et al, 2015, Hungary [28]	52/104	65.2/NA	16.4/NA	7, N/A, N/A, No	N/A
17	Ting et al, 2012, Aus [29]	136/272	53.9/NA	13.9 /NA	3, 35, non-stereoscopic, yes	N/A
18	Usher et al, 2004, UK [30]	1273/NA	N/A/NA	N/A	NA, 45, N/A, N/A, yes	570 × 570
19	Bursell et al, 2001, US [31]	54/108	48/20–75	17.7/3–42	3, 45°, stereoscopic, no	640 × 480.
20	Russo, et al, 2015, Italy [32]	120/240	58.8/NA	11.6/6–9.7	N/A, 20, NA, N/A, yes	N/A
21	Pirbhai et al, 2005, UK [33]	118/223	79.2/NA	N/A	N/A, N/A, N/A, yes	1024 × 1024
22	Peter et al, 2006, Aus [34]	N/A/NA	N/A/NA	N/A	Four different fields, 60/45/30, N/A, yes	N/A
23	Rudnisky et al, 2007, Canada [15]	102/204	57/18–99	1 m–35 yr	7, 30, stereoscopic (field1, 3) non-stereoscopic (field3, 7), color, yes	3040 × 2008
24	Cook et al, 2014, UK [35]	N/A/NA	N/A/NA	N/A	N/A, N/A, N/A, N/A	N/A
25	Lin et al, 2002, US [16]	197/NA	NA/21–80	N/A	1, 45°, stereoscopic, no	640 × 480
26	Rajalakshmi et al, 2015, India [36]	301/602	53/43–63	12.5 ± 7.3	4, 45, N/A, N/A, yes	N/A
27	Boucher et al, 2003, Canada [37]	98/196	59/26–92	N/A	2, 45, non stereoscopic, color, no	1024 × 768
28	Andonegui et al, 2010, Spain [38]	1223	N/A	N/A	N/A	N/A
29	Lawrence, 2004, US [12]	N/A	67.5	12.4/0–58	N/A, 45, non-stereoscopic, color, both	640 × 480
30	Alessandro [39]	1281	65.69 ± 12.64 years	1	3, 30, N/A, yes	N/A
31	Rodríguez [40]	394	N/A	5	N/A	N/A
32	Pritam [41]	564/1128	53 (20–85)	5	7, N/A, stereoscopic, color, yes	N/A
33	Sasso FC [72]	1907/3814	66/57–72	8	N/A	N/A



**Figure 2.** Quality assessment of the included studies shows inclusion of well conducted studies.

**Table 2****Cost effectiveness of teleretinal screening and characteristics of the included studies.**

SNo.	Author, year, country	Population characteristics	Screening modalities	Screening outcomes	Economic outcomes
1	Bjorvig et al, 2002, Norway <sup>[42]</sup>	250,42 diabetic patients	Conventional evaluation by ophthalmologist vs digital images transmitted via email	Cost comparisons depending on volume of screening	At higher workloads, telemedicine led to lower costs; at 200 patients per year, telemedicine cost \$164 per patient and conventional examinations cost \$243.5 per patient
2	Maberley et al, 2003, Canada <sup>[43]</sup>	650	Visits every 6 months by retina specialists vs photographic screening with a digital camera	Costs per sight-year saved and costs per QALY	The camera program was more cost-effective, and had the best cost-per-QALY ratio, at \$15,000; the camera program would cost <\$5000 per year of vision saved if 65% or more of the population was screened
3	Aoki et al, 2004, US <sup>[44]</sup>	10,000	Non Mydriatic retinal camera TO vs conventional evaluation by eye care provider	QALYs gained and costs generated	Average CE was \$882 per QALY for TO and \$947 for non-TO; in the TO strategy, 12.4% of patients reached blindness versus 20.5% in non-TO; ARR for blindness: 8.1%, NNS by TO to prevent a blindness case: 12.4%
4	Whited et al, 2005, US <sup>[45]</sup>	Large cohort from IHS, VA, and DoD data	Clinic based ophthalmoscopy with pupil dilation vs JVN digital TO system (JVN)	Number of true positive cases of proliferative DR detected	Number of additional cases and savings with JVN: IHS: 148 cases and \$525 690; VA: 96 PDR cases and \$2 966 111; DoD: 165 and \$129,046; JVN provides better outcomes at lower costs than clinic-based ophthalmoscopy in most scenarios
5	Li et al, 2012, US <sup>[46]</sup>	611 diabetic patients	Non-Mydriatic fundus camera vs conventional retinal examination	Prevalence of DR/cost comparison	Telemedicine-based DR screening cost less than conventional examinations (\$49.95 vs \$77.80)
6	Rachapelle et al, 2013, India <sup>[47]</sup>	1000	Mobile van, optometrist takes 4 dilated stereoscopic 45° fields digital retinal photographs with non mydriatic camera	QALY gained from TO vs no screening, CU at different intervals	Rural TO was cost-effective (\$1320 per QALY) compared with no screening; screening intervals of up to every 2 years also were cost-effective, but annual screening was not (\$3183 per QALY)
7	Kirkizlar et al, 2013, US <sup>[48]</sup>	900, T1D and T2D	TO vs regular office visits and evaluation by ophthalmologist	DR, ME, blindness, and associated QALYs	TO is CE in most conditions; telemedicine screening is not CE in patients aged older than 80 years or in populations with >3500 patients
8	Phan et al, 2014, US <sup>[49]</sup>	1793 diabetic patients	Topcon digital retinal cameras, non mydriatic imaging	Cost of teleretinal screening	Teleretinal screening was associated with cost reduction to health plan payers (average cost reduction per screen of \$24.38) and a decrease in eye clinic physician workload but failed to match the investment cost (53% gained back by study end)
9	Brady et al, 2014, US <sup>[50]</sup>	99 (base case), 100,000 trials (Monte Carlo simulation)	3-field non mydriatic fundus photography; images were transmitted to a remote expert reader	Estimation of costs of screening for PDR	TO screening for PDR resulted in savings of \$36 per patient (base case), and a median of \$48 in the simulation model
10	Maamari et al 2013 <sup>[51]</sup>	N/A	55°, non mydriatic image	Cost of the camera	Ocular CellScope \$883.22
11	Taylor et al 1999 <sup>[52]</sup>	*197**534	45°, mydriatic image vs 7 field stereo photography	Cost of the number of images	For this reason, although multiple photography is a good idea, it is costly with 35 mm photos approximately £0.30 each and Polaroids £1 each; costs which are increasing.

(continued)

**Table 2**  
(continued).

SNo.	Author, year, country	Population characteristics	Screening modalities	Screening outcomes	Economic outcomes
12	Taylor et al 2000 <sup>[53]</sup>	64,905 people screened	TO vs no screening program	Number of true positive cases of proliferative DR detected	The average cost of screening was f13.1 1 per patient and the average cost of identifying a person requiring laser therapy was f1110.
13	Davis et al <sup>[54]</sup>	165; 85	TO vs no screening program	Usual care, transportation and equipment costs	Usual care; staff time and fringe benefits \$12. Transportation \$19, supplies and incentives \$1: total \$32 DTC intervention; staff time and fringe benefits \$802. Transportation \$217 telemedicine equipment \$225 teaching aids \$45 supplies and incentives \$99 mailing and shipping \$25 total \$1413 screening eye exam; staff time and fringe benefits \$20 equipment and supplies \$266 total \$286
14	Invernizzi et al 2015, Italy <sup>[55]</sup>	1281	3-field, 30° images vs slit-lamp fundusoscopic examination	Cost of image generation	For the remote reading of images, the cost was calculated at €2.50 per reading. The cost of image generation plus reading was therefore €4.45 per patient.
15	Lawrenson et al 1995 <sup>[56]</sup>	396	50 degree mydriatic images	Usual care and equipment costs	Nurse \$3 photographer \$5 travel and accommodation \$3 film \$5 ophthalmologist \$3 administration \$2 total \$21 camera cost \$22,200 carrying case \$1100 frame for station wagon \$1350 total 24,650 \$ depreciated over 5 years at \$5000 per annum
16	Rein et al, 2011 <sup>[57]</sup>	N/A	TO vs Annual, Biennial and Self-referral	Cost comparisons depending on referral duration	Self-referral resulted in average per person ophthalmologic-related costs of US \$7,368, telemedicine increased costs by US \$3,343, biennial evaluation by US \$3636, and annual evaluation by US \$4809
17	Leese et al, 1993, UK <sup>[58]</sup>	2,984/5,968	TO vs no screening program	Cost per patient screened	The screening programme in Tayside cost £10 per patient screened
18	Bjørvig et al, 2002 <sup>[59]</sup>	20–200	TO vs no screening program	Cost comparisons depending on volume of screening	The total cost of examination by conventional methods was Nkr8555 at a workload of 20 patients per annum and Nkr288,040 at 200 patients per annum. In comparison, the total cost of telemedicine examination was Nkr171,102 and Nkr194,169 at the same respective workloads
19	Müller et al, 2006, AUS <sup>[60]</sup>	1695	TO vs no screening program	Usual care and equipment costs	Total study expenditure, including costs of personnel (AU\$131,300), transportation (AU\$16,400), consumables (AU\$20,900) and equipment (AU\$80,100), was approximately AU\$248,500. Screening cost per participant was only about AU\$145, compared with AU\$433 in the VIP.

(continued)



**Table 2**  
(continued).

SNo.	Author, year, country	Population characteristics	Screening modalities	Screening outcomes	Economic outcomes
20	Thompson et al 1995, UK <sup>[61]</sup>	4312 eyes	TO vs no screening program	Cost comparisons depending on clinical screening settings	The cost of diagnosis per true positive case of sight-threatening retinopathy ranged from £633 to £ 1079 for general practitioners, £497 for a mobile community-based retinal camera, £1546 for a hospital based retinal camera, £1028 for opticians and £1033 for hospital physicians.
21	Brown-Connolly et al 2014 <sup>[62]</sup>	5219*, 6426**	*Non-mydratric images vs **Biometric Screening		Vision screening for adults >65 years old 650,17 vs \$1,202,906
22	Sculpher et al, 1992, UK <sup>[63]</sup>	3423 diabetic patients	Evaluation of 13 screening options	Cost of different modalities, expected cost per true positive case detected	Cost savings can result with systematic screening during the same appointment as other routine health checks, compared to screening requiring additional visits
23	James et al, 2000, England (64)	1363 diabetic patients	Systematic: 3-field, non-stereoscopic photography using mydriasis; opportunistic: direct ophthalmoscopy	Sight-threatening eye disease	The CE was £209 and £289 for systematic and opportunistic screening, respectively, and incremental CE was £32 for each additional case; systematic screening remained more cost-effective than opportunistic screening
24	Facey et al, 2002, Scotland <sup>[65]</sup>	2000 iterations through Crystal Ball	Conducted by optometrists, hospitals and GPs at any opportunity vs a systematic health authority program, primarily by digital camera (mydratric and non mydratric screening)	Cost per QALY for the move from one screening program to another	The most cost-effective modality: combination of single staffed hospital units and mobile vans using non mydratric digital photography
25	Tu et al, 2004, England <sup>[66]</sup>	769 optometric screen and 874 digital photography	Topcon non mydratric model (professional medical photographer) vs slit-lamp biomicroscopy (optometrists)	Detection of sight-threatening DR	CE for optometry=total cost/true positives=£18,454/22=£839; cost per patient screened=£25,599.30/874=£29.29; CE for digital photography=£25,599/30=£853; CE was poor in both models
26	Khan et al, 2013, South Africa <sup>[67]</sup>	14,541, primary care, T2D	Mobile non mydratric digital camera (photographs taken by a trained technician with supervision by an ophthalmic nurse)	Cost per blindness case averted	Non Mydratric fundus photography is cost-effective; the cost of DR screening was \$22 per person; ICER was \$1206 per blindness case averted
27	Lian et al, 2013, Hong Kong <sup>[68]</sup>	2766 diabetic patients	Non Mydratric fundus camera (optometrist); subsequently graded by optometrist and ophthalmologists	Uptake of screening and severity of DR detected	Lower screening (OR, 0.59; CI, 0.47–0.74) and a lower detection rate of DR (OR, 0.73; CI, 0.60–0.90) in the pay group
28	Kawasaki et al, 2014, Japan <sup>[69]</sup>	50,000 hypothetical cohort	Incidental diagnosis, non mydratric 45° photograph in high risk people, annual fundus examinations; systematic screening by ophthalmologists using dilated fundus examination	Rate of detecting DR, preventing blindness, and costs of DR management	DR screening program in Japan is cost-effective compared to the no systematic screening; blindness reduction of ~16%; incremental cost of \$64.6, and incremental effectiveness of 0.0054 QALYs per person screened; ICER was \$11,857 per QALY

AA = African American, ARR = absolute risk reduction, CE = cost effectiveness, CI = confidence interval, CU = cost-utility, DoD = Department of Defense, DR = diabetic retinopathy, GP = general practitioner, ICER = incremental cost-effectiveness ratio, IHS = Indian Health Service, JVN = Joslin Vision Network, ME = macular edema, Nkr = Norwegian Krone, NNS = number needed to screen, NP = nurse practitioner, OCT = optical coherence tomography, OR = odds ratio, PA = physician assistant, PDR = proliferative diabetic retinopathy, QALY = quality-adjusted life-year, T1D = type 1 diabetes, T2D = type 2 diabetes, TO = teleophthalmology, VA = Department of Veterans Affairs.

ogy screening of DR and ME in these clinical settings. The cost analysis was done based on delivery modalities (e.g., telemedicine, clinic camera), screening models like systematic screening versus opportunistic and screening outcomes such as Quality-Adjusted Life-Year (QALY), cost per true positive case detection, DR severity, screening intervals, population, and referral duration (Table 2).

Populations screened at a younger age, higher HbA1c, using insulin, or with high transportation costs derive most of the benefit from Teleretinal screening.<sup>[44,48]</sup> Besides, disease burden and population size determine the cost-effectiveness of a Teleretinal screening program. Compared with conventional screening, Teleretinal screening was cost-effective at a high workload. A saving of 74\$ and NKr 28,7186 per patient was noticed in a population of 200 patients per year.<sup>[42,59]</sup> At lower workload of 20 patients, the cost-saving for Teleretinal screening was only about NKr 8384 with respect to the conventional screening.<sup>[59]</sup> However, teleophthalmology (TO) was not economic in patients >80 years of age and in population >3500 patients, similarly multiple photographs with 35 mm photos cost approximately £0.30 extra for each image.<sup>[48,52]</sup> Furthermore, in many studies, non-mydratic screening approaches perform well and were cost-effective compared with mydratic use.<sup>[43,65,45,46,67]</sup>

Subjects with a high socioeconomic condition or those living in better areas were screened more often but were less likely to have DR detected, suggesting the importance of access to screening.<sup>[68]</sup> Free screening was associated with a higher compliance rate, higher chances of DR detection, and a decreased workload on clinic physicians. Multiple studies discussed the approximate cost of the usual care like supplies and incentives, transportation charges, staff time, and fringe benefits (19\$–32\$).<sup>[54,56,60]</sup> The per-patient cost of screening was estimated to be 24\$ to 36 \$.<sup>[49,50]</sup> If telemedicine equipment and teaching aids were added the approximate screening cost per participant was about AUS \$145 per visit and about 5000 US \$ per annum.<sup>[54,56,60]</sup> The systematic screening model was more cost-effective than the opportunistic screening model in many studies. James et al<sup>[64]</sup> showed that the cost was £209 and £289 for systematic and opportunistic screening, respectively.

Screening interval is also an important factor in determining the cost-effectiveness of Teleretinal screening in asymptomatic patients screening every 2 years can save 900 to 1863 US \$ than annual screening.<sup>[47,57]</sup> Whited et al<sup>[45]</sup> compared clinic-based ophthalmoscopy to teleretinal screening at Joslin Vision Network (JVN) to determine the true positive case detection cost. In Indian Health Service (IHS) 148 cases saved \$525,690, in the Department of Veterans Affairs (VA) 96 PDR cases saved \$2,966,111 while in the Department of Defense (DoD) 165 cases saved \$129,046, concluding that JVN provides better outcomes at lower costs than clinic-based ophthalmoscopy in most scenarios. Tu et al<sup>[66]</sup> in his study showed that true positive detection cost of DR on digital photography by TO was significantly lower (£839) than slit-lamp detection cost of DR (£853) and cost per patient screened was as little as £29.29 per patient.

## 5. Limitations

Our study did not focus on the prevalence of telemedicine and telescreening in developing countries.

Teleretinal screening would offer more benefits in developing and underdeveloped countries. A population-based survey in Nakuru, Kenya revealed that the prevalence of any type of DR was 35.9% and of severe non-proliferative DR was 13.9%.<sup>[70]</sup> Similarly, within Asia-Pacific India has a 10% prevalence of DR while Indonesia has a prevalence of 43% for DR. We believe that such developing countries would benefit more from a teleretinal screening program.<sup>[71,72]</sup>

## 6. Conclusion

Teleophthalmology is very sensitive and specific for the absence of retinopathy but for the diseased retina, these values have widespread variations. It is highly specific for DME, CSME, PDR, and severe NPDR but non-specific for mild or moderate NPDR. The sensitivity of all kind of retinopathies was not impressive. However, the relatively small cost of Teleretinal screening makes for an attractive platform for both image acquisition, storage, interpretation, and transmission. In contrast to clinical examination and conventional screening, Teleretinal screening reduces the burden in the eye clinic and improves access in remote environments. Moreover, screening a small number of individuals is not economically sound, and a larger population screening with the omission of pupillary mydriasis can be more cost-effective. Telescreening also increases screening compliance and prevent blindness in a high number of a population if the services are offered free of cost.

## Author contributions

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