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REVIEW ARTICLE

The Truth About Diabetic Eye Screening: A Deep Dive into Diagnostic Accuracy

Ragni Kumari[1,*]

[1] *Assistant Professor, Department of Optometry, UPUMS, Saifai, Etawaha, U.P., India*

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* *Corresponding author*.
Ragni Kumari
ragnimishraa@gmail.com

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ABSTRACT

Diabetic retinopathy (DR) is a leading cause of preventable blindness worldwide, emphasizing the importance of early detection through effective screening methods. The diagnostic accuracy of various DR screening techniques, including direct ophthalmoscopy, retinal photography, and telemedicine, remains a critical factor in improving clinical outcomes. This review aims to evaluate and compare the sensitivity, specificity, and overall diagnostic performance of different DR screening methods. Objective of the study is to assess the diagnostic accuracy of DR screening methods, including retinal photography, telemedicine, direct ophthalmoscopy, and other emerging technologies. A comprehensive literature search was conducted across databases including PubMed, Scopus, and Google Scholar up to May 2025. Studies involving adult diabetic populations and evaluating screening methods such as direct ophthalmoscopy, retinal photography, slit-lamp examination, and tele-retinal screening were included. Data on sensitivity, specificity, and other diagnostic metrics were extracted by an independent reviewer. The quality of included studies was assessed using the QUADAS-2 tool. Due to heterogeneity among studies, a narrative synthesis was performed without meta-analysis. Various screening methods showed differing diagnostic accuracies influenced by technology, examiner expertise, and population characteristics. Retinal photography, especially with mydriasis, demonstrated higher sensitivity and specificity compared to direct ophthalmoscopy. Tele-retinal screening showed promise in improving access in remote cohorts. However, variability in study designs and outcome reporting limited direct comparison. This review highlights that retinal photography, particularly when combined with telemedicine, offers the most reliable screening method for DR in terms of diagnostic accuracy. However, emerging technologies such as AI-based systems may improve detection rates in the future. Further high-quality, large-scale studies are needed to validate these findings and optimize screening protocols, especially in resource-limited settings.

Keywords: Diabetic retinopathy; Screening; Diagnostic accuracy; Retinal photography; Telemedicine

INTRODUCTION

Diabetic retinopathy (DR) is one of the most common complications of diabetes, leading to blindness if left untreated. It is the result of prolonged hyperglycemia causing damage to the blood vessels in the retina. As the global prevalence of diabetes increases, DR has become a major cause of visual impairment worldwide. Early detection and timely intervention are essential to prevent vision loss, making regular screening for DR crucial. Various screening methods, ranging from ophthalmoscopy to retinal photography and telemedicine-based technologies, have been employed to identify DR at its earliest stages. These methods are evaluated based on their sensitivity and specificity to determine how effectively they can detect DR and distinguish it from non-affected individuals. This paper provides a detailed review of the different screening techniques used for DR, along with their associated sensitivity and specificity, as well as the classification systems used for managing DR.

Diabetes mellitus (DM) is among the fastest-growing chronic diseases globally and remains a leading cause of acquired vision loss[1]. According to the World Health Organization (WHO), the number of people living with diabetes is expected to rise dramatically, from 171 million in 2000 to 366 million by 2030[2]. One of the most significant microvascular complications of DM is diabetic retinopathy (DR), which continues to be the primary cause of vision impairment in middle-aged, economically active populations[3]. As the global burden of diabetes increases,

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the number of individuals affected by DR and vision-threatening diabetic retinopathy (VTDR)—which includes severe non-proliferative DR, proliferative DR (PDR), and diabetic macular edema (DME)—is projected to reach 191.0 million and 56.3 million, respectively, by 2030[3].

Over the past few decades, there have been significant advancements in understanding the epidemiology of DR, improving systemic control of diabetes to delay DR onset and progression, and enhancing the clinical assessment, diagnosis, and management of DR and Vision-Threatening Diabetic Retinopathy (VTDR). It is well-established that timely screening, early detection, and appropriate treatment can prevent visual impairment due to diabetes[4]. Randomized controlled trials have demonstrated that early intervention can reduce the risk of severe vision loss by 57%[5]. Despite this, DR screening remains inconsistent in both developing and developed countries. Efforts are often hindered by ambiguous screening guidelines (e.g., clinical examination vs. fundus photography), and the high resource demands of comprehensive DR screening programs[6]. As a result, DR is a growing public health concern, particularly in low- and middle-income countries where access to trained eye care professionals and advanced eye-care services (e.g., laser treatment or intravitreal injections) is limited. It is essential for stakeholders—both public and private—to pursue innovative strategies to improve DM management, expand access to DR screening, and develop cost-effective, community-based screening initiatives.

This review aims to examine the global prevalence and incidence of DR, its major risk factors, current screening practices, and the public health challenges involved in implementing effective DR screening and management programs.

METHODOLOGY

This systematic review was conducted over a period of three months by a single author based in Lucknow, India, with the primary aim of evaluating the diagnostic accuracy of various screening methods for diabetic retinopathy (DR), particularly focusing on sensitivity and specificity as key outcome measures. The review was structured in accordance with the PRISMA-DTA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Diagnostic Test Accuracy) guidelines to ensure methodological rigor, transparency, and reproducibility.

A comprehensive literature search was carried out using multiple databases, including PubMed, Scopus, ScienceDirect, and Google Scholar, to identify relevant peer-reviewed articles published until May 2025. The search employed a combination of keywords and Medical Subject Headings (MeSH) terms such as "diabetic retinopathy," "screening," "sensitivity," "specificity," "diagnostic accuracy," "retinal photography," "ophthalmoscopy," and "telemedicine." Manual searches of reference lists from identified articles and previously published systematic reviews were also conducted to ensure the inclusion of all pertinent studies.

Studies were included in the review if they involved adult participants with either type 1 or type 2 diabetes mellitus, and if they assessed the diagnostic performance of any DR screening method—such as direct ophthalmoscopy, slit-lamp biomicroscopy, mydriatic or non-mydriatic fundus photography, and tele-retinal imaging. Eligible studies had to report diagnostic accuracy metrics, including sensitivity and specificity. Both primary research articles (cohort and cross-sectional studies) and review articles were considered. Exclusion criteria included studies that focused exclusively on treatment without discussing screening, lacked sufficient diagnostic accuracy data, or were conducted in non-diabetic populations. Editorials, letters, and conference abstracts without full-text data were also excluded.

Data extraction was performed independently using a standardized format. Information extracted included study characteristics (author, year, country, sample size, and demographics), screening method details (type, equipment, need for mydriasis, and personnel involved), reference standards used for DR confirmation (e.g., dilated fundus examination by a retinal specialist or ETDRS grading), and diagnostic performance metrics (sensitivity, specificity, confidence intervals, PPV, NPV). Additional contextual findings, such as cost, accessibility, and patient compliance, were also noted where available. Any discrepancies or unclear data points were resolved by reviewing supplementary materials or contacting authors when feasible.

To assess the methodological quality and risk of bias of included studies, the QUADAS-2 tool was utilized, which examines four key domains: patient selection, index test, reference standard, and flow/timing. Each domain was rated as low, high, or unclear risk of bias. As the review was conducted by a single author, extra caution was taken to ensure internal consistency, and efforts were made to minimize subjective interpretation during study selection and data synthesis.

Due to significant heterogeneity across studies—particularly in the screening methods, population characteristics, and outcome measures—a quantitative meta-analysis was not feasible. Therefore, a narrative synthesis was employed. Studies were grouped by the screening modality, and their diagnostic accuracy metrics were compared descriptively. Major trends, strengths, limitations, and implications of each screening approach were summarized to provide a comprehensive understanding of their performance and practical utility in real-world settings.

RESULTS

Global Epidemiology of DR

Global Prevalence:

WHO estimates, DR accounts for approximately 4.8% of the 37 million global cases of blindness[7]. A pooled analysis involving 22,896 individuals with diabetes from 35 population-based studies conducted in the U.S., Australia, Europe, and Asia revealed that the global prevalence of any DR (across both T1DM and T2DM) was 34.6% (95% CI 34.5–34.8), with 7% (6.9–7.0) affected by VTDR[8].

Type 1 Diabetes (T1DM):

DR prevalence among T1DM patients varies widely (10%–50%), depending on geographic region, screening methodology, and diabetes duration[9]. Due to differences in health care systems and disease management, comparisons across populations must be interpreted cautiously. The EURODIAB study, involving 31 clinics across 16 European countries, reported DR prevalence ranging from 25% in Austria to 60% in Portugal[10]. A pooled analysis from two U.S. studies (WESDR and the New Jersey 725 study) found that 82% of T1DM patients had some form of DR, and 32% had VTDR[11]. Prevalence is generally lower in Asia, with rates of 13.4% in India[12] and 14% in China[13]. In Australia and New Zealand, DR prevalence ranges between 25% and 42%[14]. The prevalence of DME increases with diabetes duration from low levels within five years of diagnosis to as high as 29% after 20 years[15]. Temporal variation in prevalence likely reflects improved healthcare over time, suggesting that incidence studies may offer more accurate insights.

Type 2 Diabetes (T2DM):

Internationally, the prevalence of DR and VTDR among T2DM patients is estimated at 25.2% and 6.9%, respectively[8]. In the UK, studies such as the Liverpool Diabetic Eye Study[16] and the UKPDS report DR prevalence ranging from 25% to 27%. In Sweden, Denmark, and Italy, prevalence is slightly higher at 30%–40%[17]. U.S.-based studies—including the San Luis Valley Study, LALES, MESA, and VADT[18]—report prevalence rates between 30% and 50%, with Hispanic populations experiencing the highest rates[19].

Australian studies (AusDiab, BMES, MVIP, and the Newcastle study)[20] report DR prevalence between 22% and 35%, with VTDR affecting 1.2%–7.1% of T2DM patients. Historically, DR prevalence in Asia has been relatively low[21]. In China, estimates range from 28% to 43%, with rural areas exhibiting higher rates due to limited access to screening services[22]. In contrast, urban Indian populations show higher diabetes (28.2% vs. 10.4%) and DR (18% vs. 10.3%) prevalence than rural counterparts[23]. A multi-ethnic Asian study by Chiang et al. found racial disparities in diabetes prevalence but not DR, with the highest rates among Indians (28.9%), followed by Malays (24.8%) and Chinese (20.1%)[24].

The Singapore Indian Eye Study revealed a 33% DR prevalence among Indian migrants to Singapore—higher than that of Indians living in urban India[25]. Researchers suggest that this disparity may stem from abrupt changes in diet and lifestyle, stress, financial hardship, or other socio-environmental factors.

Incidence and Progression of DR

Type 1 Diabetes (T1DM):

In Europe, 50% of T1DM patients without DR at baseline developed retinopathy within 5–7 years, and 9% with mild NPDR progressed to PDR within five years. The U.S.-based WESDR found a 10-year DR incidence of 74%, rising to 97% at 25 years. Among those with baseline DR, the incidence of progression ($\geq$2 steps on the ETDRS scale) was 64% at 10 years and 83% at 25 years. Long-term WESDR data also show a decline in PDR and DME incidence during the latter half of the 25-year study[26].

Type 2 Diabetes (T2DM):

In the UK, the 5-year cumulative incidence of DR in T2DM patients was 4%, rising to 16.4% at 10 years[26]. Annual DR incidence in the U.S. (LALES) was 7.1%, comparable to WESDR (8.6%) and the Barbados Eye Study (7.5%)[27]. These rates were higher than those reported in predominantly white, non-U.S. cohorts. In Australia, the BMES reported 5-year cumulative DR incidence and progression rates of 22.2% and 25.9%, respectively. In Hong Kong, 4-year cumulative incidence, progression, and VTDR rates were 15.2%, 45.5%, and 0.03%[28].

Declining DR Trends in Developed Countries

With greater awareness of DR risk factors, improved glycemic control, and broader access to community screening, DR prevalence and incidence have declined in developed nations like the U.S., Australia, and many parts of Europe. A systematic review and meta-analysis (1975–2008) revealed significantly lower DR prevalence and severe visual loss rates post-1985. The 10-year incidence of PDR and SVL dropped from 11.5% and 6.0%, respectively, to 6.6% and 2.6%. In WESDR, the annual incidence of PDR declined from 3.4% to 1.4%, and CSME incidence fell from 1.0% to 0.4% among T1DM patients[29].

Despite these improvements, more recent rural studies show higher DR prevalence compared to metropolitan areas, reflecting disparities in healthcare access[30]. Although a clear decline in DR incidence among T1DM patients is documented, trends among T2DM populations remain less certain and require further study.

Hyperglycemia

The Diabetes Control and Complications Trial (DCCT) and the UK Prospective Diabetes Study (UKPDS) were landmark studies demonstrating that tight glycemic control (HbA1c of 7% or lower) can reduce the risk of DR development and progression in both Type 1 (T1DM) and Type 2 Diabetes (T2DM) patients[31]. In the DCCT for T1DM, intensive treatment (median HbA1c of 7.2%) led to a 76% reduction in DR incidence and a 54% reduction in DR progression compared to conventional treatment (median HbA1c of 9.1%)[31]. In the UKPDS, intensive glycemic control resulted in a 25% reduction in DR risk, including the need for laser photocoagulation[32]. For every 1% decrease in HbA1c, there is a 40% reduction in DR development, a 25% reduction in progression to vision-threatening DR (VTDR), a 25% reduction in the need for laser therapy, and a 15% reduction in blindness[33].

Intensive glycemic control also reduces the 4-year incidence of DME by 58%[34]. The benefits of early intensive glycemic control are long-lasting, with a sustained impact over many years, a phenomenon known as "legacy effect" or metabolic memory. This suggests that early normalization of glycemia can stop the pathological processes caused by hyperglycemia, such as oxidative stress and glycation of proteins and lipids . However, tight control can lead to early worsening of DR and an increased risk of hypoglycemic episodes. The DCCT noted a higher incidence of DR worsening in the intensive treatment group compared to the conventional group (13.1% vs. 7.6%) but this was reversed by 18 months. Additionally, intensive treatment increases the risk of hypoglycemia three-fold[35].

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) study showed that targeting an HbA1c level of less than 6% led to increased mortality and more hypoglycemic events compared to standard treatment[36]. However, the ADVANCE trial did not show an increase in death with intensive treatment. It found that an HbA1c target between 6.5% and 7% reduces macrovascular and microvascular events and deaths[36].

Hypertension

While some epidemiological studies did not consistently identify blood pressure as a risk factor for DR, several randomized controlled trials (RCTs) have demonstrated the benefits of tight blood pressure control in reducing DR incidence and progression. The UKPDS, the first RCT to examine this, showed that patients with tight blood pressure control had a 34% reduction in DR progression and a 47% reduction in visual acuity deterioration[37]. A 10 mmHg increase in systolic blood pressure corresponds to a 10% increased risk of early DR and a 15% risk of proliferative DR (PDR) or DME[38].

Additionally, medications targeting the renin–angiotensin system, such as angiotensin II receptor blockers (e.g., candesartan and losartan) and angiotensin-converting enzyme inhibitors (e.g., enalapril), have shown additional benefits in slowing DR progression, independent of their blood pressure-lowering effects[39]. The Diabetic Retinopathy Candesartan Trials (DIRECT) found that candesartan reduced the incidence of DR by 18% in T1DM and 13% in T2DM, although the results did not reach statistical significance for the primary endpoint in T2DM[39].

Hyperlipidemia

The relationship between lipid levels and DR is still unclear. Some studies have shown that increased triglycerides are associated with DR severity, while higher LDL cholesterol and non-HDL cholesterol are associated with DME[39]. The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study demonstrated that fenofibrate (a triglyceride-lowering agent) reduced the need for laser treatment in patients with DR, particularly those with pre-existing retinopathy[40].

Body Mass Index (BMI)

Recent studies have shown that obesity, particularly a high waist-to-hip ratio and BMI above 31 kg/m^2 in men and 32 kg/m^2 in women, is associated with a higher risk of DR[40]. However, evidence linking BMI directly with DR is still inconsistent. Some studies have found no significant association between obesity and DR progression, while others have linked a high BMI with more severe DR[40].

Puberty and Pregnancy

Puberty increases the risk of DR development, particularly in T1DM. The period post-menarche has been shown to carry a 30% higher risk of DR compared to the prepubertal period[40]. Pregnancy, particularly in women with T1DM, increases the risk of DR progression by 2.3 times[33]. Early stages of pregnancy with no DR or mild non-proliferative DR show low progression, but among those with NPDR, 47% progress to more severe forms, and 50% of these require laser treatment. Postpartum, 29% of women experience regression of DR[33].

Cataract Surgery

Cataract surgery can lead to DR progression, particularly when preoperative glycemic control is poor[14]. The shift to phacoemulsification surgeries has reduced the risk of DR progression post-surgery compared to older cataract extraction techniques. For those with severe DR (PDR), panretinal photocoagulation should ideally be performed before cataract surgery to reduce the risk of postoperative DME[15].

Inflammatory Biomarkers

Chronic inflammation plays a role in the pathogenesis of DR. Elevated levels of inflammatory markers such as C-reactive protein (CRP), intercellular adhesion molecule 1 (ICAM-1), and vascular cell adhesion molecule 1 (VCAM-1) have been linked to DR progression[41]. Elevated ICAM-1 levels, for example, have been associated with retinal hard exudates, a hallmark of DR[41].

Genetic Risk Factors

Genetic factors contribute to DR development, although research is still in the early stages. Twin studies and family studies suggest that individuals with a family history of DR are at a significantly higher risk of developing DR themselves. Several genetic markers have been proposed, including genes related to aldose reductase (ALR2), vascular endothelial growth factor (VEGF), and the receptor for advanced glycation end products (RAGE)[41]. However, many of these associations have been weak or inconsistent, and the field requires further study.

Major Risk Factors for Diabetic Retinopathy (DR)

The risk factors for DR can be categorized into modifiable and non-modifiable factors (Table 1). Modifiable factors include hyperglycemia, hypertension, hyperlipidemia, and obesity (F 1), while non-modifiable factors include the duration of diabetes, puberty, and pregnancy, all of which contribute to the development and progression of DR.

Table 1: Risk Factors for Diabetic Retinopathy

Risk Factor Type	Risk Factors	Details
Modifiable Factors	HbA1c	A decrease of 1% in HbA1c can reduce DR risk by 40%, need for laser treatment by 25%, and blindness risk by 15%[31].
	Systolic Blood Pressure	A 10-mmHg reduction in systolic BP reduces DR risk by 35%, laser treatment by 35%, and blindness by 50%[31].
	Hyperlipidemia	High triglyceride and LDL levels are linked to DR and diabetic macular edema (DME)[33].
	Body Mass Index (BMI)	Higher BMI (men >31, women >32) increases DR risk[38].
Non-Modifiable Factors	Puberty	Post-pubertal individuals (higher risk of DR, 30% more than prepubertal individuals)[38].
	Pregnancy	Pregnancy increases DR progression by 2.3 times, especially for pre-existing DR[38].

Modifiable Factors

- **HbA1c**

A decrease of 1% in HbA1c can lead to a 40% reduction in retinopathy, a 25% reduction in the need for retinal laser treatment, and a 15% reduction in blindness risk for individuals with diabetes[41].

- **Systolic Blood Pressure**

A 10-mmHg reduction in systolic blood pressure can decrease the risk of retinopathy by 35%, the need for retinal laser treatment by 35%, and the risk of blindness by 50%[42]. However, two Asian clinic-based studies did not find a significant relationship between blood pressure and the incidence or progression of DR.

- **Hyperlipidemia**

DR is associated with elevated triglyceride levels, while diabetic macular edema (DME) is linked to higher LDL cholesterol, non-HDL cholesterol, and an unfavorable HDL/LDL ratio[42].

- Body Mass Index (BMI)

Increased waist–hip ratio and BMI greater than 31 kg/m^2 for men and 32 kg/m^2 for women are associated with a higher risk of DR development. In contrast, BMI below 20 kg/m^2 also increases the risk of DR[42].

Non-Modifiable Factors

- **Puberty**

Post-pubertal individuals have a 30% higher risk of DR development. Furthermore, the onset of DR is typically faster (2 years earlier) compared to those in the prepubertal stage[42].

- **Pregnancy**

Pregnancy increases the risk of DR progression by 2.3 times . During the postpartum period, 29% of pregnant women experience DR regression. However, pregnant women with pre-existing DR are at a significantly higher risk of progression, with 47% experiencing progression and 50% requiring laser treatment[42].

DR Screening Programs

Early detection and timely intervention can prevent up to 98% of diabetes-related visual impairment[6]. Various screening methods are used for DR, including retinal photography, direct ophthalmoscopy, and tele-retinal screening. The International Council of Ophthalmology recommends that eye care providers evaluate visual acuity, HbA1c levels, blood pressure, and other diabetes-related complications to determine the urgency of referral to ophthalmologists[7].

Screening Methods for Diabetic Retinopathy

Different methods for screening diabetic retinopathy have been developed to cater to various settings, including primary care, specialized clinics, and telemedicine platforms. These methods differ in terms of the technology used, the need for pupil dilation, and the level of training required for professionals interpreting the results.

These methods aim to identify different stages of diabetic retinopathy, from early non-proliferative diabetic retinopathy (NPDR) to advanced proliferative diabetic retinopathy (PDR). Table 2 highlights the sensitivity (the ability to correctly identify individuals with DR) and specificity (the ability to correctly identify individuals without DR) of various screening methods. Higher sensitivity and specificity are ideal as they reduce both false-negative and false-positive results, ensuring effective detection and management of DR.

Screening Programs and Technologies

In many countries, including the United Kingdom, the United States, and Australia, national screening programs have been developed to detect DR early. For example, the National Health Service (NHS) in the UK recommends using two-field mydriatic retinal photography for screening, aiming for a sensitivity of at least 80% and specificity above 95%.

In contrast, telemedicine-based screening programs have proven effective, especially in rural and underserved areas. Tele-retinal screening involves digital retinal imaging and remote interpretation, increasing access to screening while minimizing costs. For example, in the United States, telemedicine programs have expanded DR screening to veterans and military personnel, reducing the need for in-person visits.

Non-mydriatic retinal photography, which doesn't require pupil dilation, is becoming more common in primary care settings. However, while it provides a convenient and accessible option, its higher failure rate and inability to provide stereoscopic views may limit its effectiveness in detecting advanced DR stages.

Classification Systems for Diabetic Retinopathy

Classifying the severity of DR is critical for determining the appropriate management and treatment. Several classification systems have been developed to help practitioners identify the extent of the disease, ranging from simple grading systems for primary care to more detailed systems for research settings.

One widely used classification system is the Airlie House seven standard 30° stereoscopic fields with the ETDRS (Early Treatment Diabetic Retinopathy Study) grading scale, which assigns severity levels for DR based on clinical findings. For primary care settings, simpler systems are often preferred, such as the World Health Organization (WHO) classification, which categorizes DR into three levels based on clinical findings that indicate the need for referral:

1. Lesions that require monitoring in a few months
2. Lesions requiring referral for treatment as soon as possible
3. Sight-threatening lesions requiring immediate referral

Another commonly used classification system is the International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scale, which helps in diagnosing the severity of DR based on fundus findings such as microaneurysms, hemorrhages, and retinal vascular changes (Table 3).

Retinal Photography and Screening Programs

The UK National Institute for Clinical Excellence (NICE) guidelines recommend DR screening tests to have a sensitivity of at least 80% and specificity of 95%, with a technical failure rate under 5%. The Public Health England has introduced guidelines for the National Health Service (NHS) diabetic eye screening programs, emphasizing the importance of two-field mydriatic retinal photography.

Mydriatic retinal photography, when combined with ophthalmoscopy for ungradable cases, is considered the most effective DR screening strategy. It ensures better-quality retinal images with a minimum sensitivity of 80% in detecting any grade of DR.

However, pupil dilation remains a concern for some healthcare providers, due to the risk of acute angle-closure attacks in certain populations, particularly those of Asian descent.

Non-mydriatic retinal photography is popular in primary care since it doesn't require pupil dilation. While it offers a cost-effective option, it comes with challenges such as higher technical failure rates and difficulties in obtaining stereoscopic views.

Tele-Retinal and Mobile Eye Screening

Tele-retinal and mobile eye screening have proven to be cost-effective methods for DR screening in many countries, including Australia, the United States, the United Kingdom, and India. Tele-retinal screening uses digital retinal imaging combined with remote interpretation, which significantly enhances access to DR screening, especially in rural and remote areas.

For instance, in the United States, a national tele-retinal imaging program has been implemented, providing services to veterans and military personnel. Similarly, the National Health Service in the United Kingdom has developed a National Diabetic Retinopathy Screening Program, aiming for a 100% screening rate for patients with diabetes.

Table 2: Sensitivity and Specificity of Various DR Screening Methods

Screening Method	Practitioners	Outcome Measure	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)
1. Direct Ophthalmoscopy	GPs	Any DR	63 (56–69)	75 (70–80)
	Optometrists	Any DR	74 (67–81)	80 (75–85)
	GPs	Referrable DR	66 (54–77)	94 (91–96)
	Optometrists	Referrable DR	82 (68–92)	90 (87–93)
2. Dilated Slit Lamp Examination	Ophthalmologists	Referrable DR	87 (84–92)	95 (92–98)
	Optometrists	Referrable DR	73 (52–88)	90 (87–93)
3. Retinal Still Photography				
i. **Mydriatic**				
Single field (35°) – Colour	GPs	Any DR	79 (74–85)	73 (68–79)
	Optometrists	Any DR	88 (83–93)	68 (62–74)
	Diabetologists	Any DR	73 (67–79)	93 (90–96)
Two fields (50°) – Colour	Retinal photographers	Referrable DR	96 (87–100)	89 (86–91)
Two fields (50°) – Red Free	Retinal photographers	Referrable DR	93 (82–98)	87 (84–90)
Three fields (30°) – Colour	Ophthalmologist	Any DR	95 (87–98)	99 (95–99)
	Medical Officers	Any DR	92 (83–96)	96 (92–98)
ii. **Non-mydriatic**				
Single field (35°) – Colour	Trained Grader 1	Any DR	72 (66–79)	96 (92–99)
	Trained Grader 2	Any DR	64 (57–71)	99 (95–100)
Single field (35°) – Red Free	Trained Grader	Referrable DR	78	86
4. Retinal Video Recording – Colour	Ophthalmologist 1	Any DR	94 (84–98)	99 (95–99)
	Ophthalmologist 2	Any DR	93 (83–98)	95 (89–98)

- **DR:** Diabetic Retinopathy
- **GPs:** General Practitioners

In Singapore, the national Singapore Diabetic Retinopathy Program utilizes telemedicine with centralized reading at the Singapore Eye Research Institute to efficiently process images and return results within an hour.

Public Health Challenges and the Importance of DR Screening

Diabetes continues to place a significant strain on public health systems globally. With an estimated 387 million people affected by diabetes worldwide in 2015, this number is expected to rise to 592 million by 2035.

The economic burden is substantial, with direct costs for treating diabetes in the United States totalling $245 billion in 2012. If everyone with diabetes received regular DR screening and appropriate treatment, significant savings in medical costs and sight preservation could be achieved annually.

Despite efforts to implement screening programs, DR remains a leading cause of blindness, particularly in working-age adults. Early detection and timely treatment are crucial to preventing permanent visual impairment due to DR.

DISCUSSION

This systematic review highlights the significant global burden of diabetic retinopathy (DR), affecting approximately 34.6% of individuals with diabetes worldwide, with 7% developing vision-threatening diabetic retinopathy (VTDR)[10]. These figures, however, vary widely based on geography, diabetes type, healthcare infrastructure, and socioeconomic conditions. For instance, prevalence among patients with type 1 diabetes (T1DM) ranges from 10% to 50%, with higher rates typically observed in Western populations. In the EURODIAB study, prevalence varied from 25% in Austria to 60% in Portugal[12], while U.S. data show rates as high as 82% for any DR and 32% for VTDR in T1DM patients[13]. Comparatively, prevalence in Asia remains lower, such as 13.4% in India[14] and 14% in China[15].

Among individuals with type 2 diabetes (T2DM), global DR and VTDR prevalence is estimated at 25.2% and 6.9%, respectively[10]. Studies from the UK report DR prevalence between 25% and 27%[21,22], while Scandinavian countries and Italy show slightly higher figures of 30% to 40%[23–25]. U.S.-based studies show even higher prevalence, especially in Hispanic populations[30]. In Asia, DR rates are climbing, with rural China reaching 43%[38,39] and urban India showing higher rates than rural counterparts, likely due to disparities in access to healthcare and lifestyle differences[37,40].

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Table 3: International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scales

Proposed Disease Severity Level	Clinical Findings	ETDRS Levels	Management Options
No Apparent Retinopathy	No abnormalities	Level 10: DR absent	Optimize vascular risk factors
Mild NPDR	Microaneurysms (MAs) only	Level 20: Very mild NPDR	Optimize vascular risk factors
Moderate NPDR	More than MAs, less than severe NPDR	Levels 35, 43, 47: Moderate NPDR	Optimize vascular risk factors and refer to an ophthalmologist
Severe NPDR	Extensive intraretinal hemorrhages, venous beading, or prominent IRMA in 2+ quadrants	Levels 53A-E: Severe to very severe NPDR	Optimize vascular risk factors and refer for scatter laser treatment
Proliferative Diabetic Retinopathy (PDR)	Neovascularization or vitreous/preretinal hemorrhage	Levels 61-85: PDR	Optimize vascular risk factors and refer for scatter laser treatment
Diabetic Macular Edema (DME)	Retinal thickening or hard exudates in posterior pole	-	Review in 1-2 years, and optimize vascular risk factors
Mild DME	Retinal thickening or hard exudates near but not involving the macula center	Non-CSME	Optimize vascular risk factors and refer to an ophthalmologist
Moderate DME	Retinal thickening or hard exudates approaching the macula center	Non-CSME	Optimize vascular risk factors and refer for laser treatment if necessary
Severe DME (CSME)	Retinal thickening or hard exudates involving the macula center	CSME	Optimize vascular risk factors and refer for anti-VEGF or laser treatment

- **CSME:** Clinically Significant Macular Edema
- **DME:** Diabetic Macular Edema
- **IRMA:** Intraretinal Microvascular Abnormalities
- **MA:** Microaneurysms
- **NPDR:** Non-Proliferative Diabetic Retinopathy
- **PDR:** Proliferative Diabetic Retinopathy

Among Indian migrants to Singapore, the DR prevalence reached 33%, higher than their counterparts in India, possibly due to rapid environmental and dietary changes, stress, and financial challenges[42].

Longitudinal studies indicate a high incidence and progression of DR, particularly among T1DM patients. In Europe, 50% of those without DR at baseline developed it within 5–7 years, and 9% with mild non-proliferative DR (NPDR) progressed to proliferative DR (PDR) within five years[33]. In the U.S., the WESDR found a 10-year DR incidence of 74%, rising to 97% at 25 years, with progression occurring in 64% and 83% of patients at 10 and 25 years, respectively[43]. In contrast, T2DM patients show a slower progression. The UKPDS reported a 5-year cumulative incidence of 4%, increasing to 16.4% at 10 years[26], while studies like LALES and the Barbados Eye Study reported annual incidence rates of 7.1% and 7.5%, respectively[27].

Encouragingly, several developed countries have seen a decline in DR prevalence and incidence due to improved glycemic control, better hypertension and lipid management, and the implementation of national screening programs. A meta-analysis revealed a significant drop in DR and severe vision loss (SVL) after 1985, with the 10-year incidence of PDR and SVL decreasing from 11.5% and 6.0% to 6.6% and 2.6%, respectively. In the WESDR cohort, annual PDR incidence declined from 3.4% to 1.4%, and clinically significant macular edema (CSME) incidence dropped from 1.0% to 0.4%[44]. However, these trends are not universal; rural populations in both high- and low-income countries still report disproportionately high DR rates, emphasizing persistent inequalities in healthcare access[37,40].

This review also affirms the importance of managing both modifiable and non-modifiable risk factors. Hyperglycemia remains the most critical modifiable factor, with landmark studies such as the DCCT and UKPDS demonstrating that every 1% reduction in HbA1c reduces the risk of DR by 40%, the need for laser therapy by 25%, and the risk of blindness by 15%[35]. The DCCT showed that intensive glycemic control reduced DR incidence by 76% and progression by 54% among T1DM patients[36]. The long-term benefits of early glycemic control, known as the "legacy effect," suggest that metabolic memory may preserve retinal integrity years after intervention[44]. However, intensive treatment is not without risks; it increases the incidence of hypoglycemia and may initially worsen DR. The ACCORD trial even associated very tight control (HbA1c <6%) with increased mortality, highlighting the need for individualized treatment goals[44].

Hypertension and hyperlipidemia are also key contributors. A 10-mmHg reduction in systolic blood pressure lowers the risk of DR progression by 35% and blindness by 50%[44].

Although some Asian studies failed to show a strong link, randomized controlled trials like the UKPDS and DIRECT trials have confirmed that blood pressure control and the use of angiotensin receptor blockers such as candesartan and enalapril help slow DR progression[22]. Similarly, lipid control plays a role in managing diabetic macular edema (DME). Elevated LDL and triglyceride levels correlate with DR severity, and studies such as the FIELD trial showed that fenofibrate reduces the need for laser treatment in patients with DR[41].

Body mass index (BMI) and waist-hip ratio are additional modifiable risk factors, with both low (<20 kg/m^2) and high BMI (>31 kg/m^2 in men, >32 kg/m^2 in women) linked to increased DR risk[42]. Non-modifiable factors like puberty and pregnancy also significantly impact DR progression. Puberty increases DR risk by 30%, likely due to hormonal changes, and pregnancy, especially in women with pre-existing DR, increases progression risk by 2.3 times, with up to 50% requiring laser treatment[35].

Screening remains the cornerstone of DR prevention. Various methods offer differing accuracy levels. Mydriatic retinal photography, especially two-field imaging, is among the most accurate, with sensitivity and specificity often exceeding 90% (Table 2). In contrast, non-mydriatic methods, while more accessible and preferred in primary care, have higher failure rates and lower sensitivity, particularly in detecting VTDR. The success of national programs, such as the NHS Diabetic Eye Screening Program in the UK, demonstrates that combining mydriatic photography with central grading can yield high detection rates and cost-effectiveness[18].

Tele-retinal and mobile screening programs are increasingly used to extend services to underserved areas. These systems are particularly valuable in regions where access to ophthalmologists is limited. For instance, the U.S. Veterans Health Administration has implemented a national tele-retinal imaging initiative, and Singapore's centralized telemedicine system ensures rapid image processing and referral[42]. However, challenges remain. Non-mydriatic methods often miss advanced disease stages, and pupil dilation is avoided in some populations due to the risk of angle-closure glaucoma, especially among Asians.

Classification systems such as the International Clinical DR and DME Disease Severity Scale and the ETDRS scale provide standardized criteria for staging and referral. These systems are critical for ensuring timely and appropriate treatment, especially when screening programs are scaled to national levels.

Ultimately, early detection and timely intervention can prevent nearly all cases of diabetes-related vision loss[6]. As diabetes prevalence rises globally, projected to reach 592 million by 2035, DR screening must be integrated into routine diabetes care. Technological advancements, particularly in retinal imaging and telemedicine, offer promising avenues to scale up screening, especially in resource-limited settings. However, these must be paired with robust health system planning, workforce training, and public health policies to ensure equitable access.

In conclusion, while notable progress has been made in reducing DR-related vision loss in high-income countries, disparities persist globally. A multi-pronged approach—combining early risk factor control, technological innovation in screening, and systemic policy-level interventions—is essential to curb the burden of diabetic retinopathy and safeguard vision worldwide.

Strengths and Limitations

A major strength of this review lies in its comprehensive and global perspective, covering diverse geographic regions and populations. By integrating data from both high- and low-income countries, the review offers a nuanced understanding of diabetic retinopathy (DR) prevalence, risk factors, progression, and screening strategies across different healthcare systems. Another strength is the inclusion of both type 1 and type 2 diabetes, highlighting key differences in epidemiology and disease progression, which is crucial for tailoring prevention and management strategies. The review also synthesizes findings from large, landmark studies such as the DCCT, UKPDS, WESDR, and newer telemedicine-based screening programs, providing robust evidence for clinical decision-making and policy formulation.

However, several limitations must be acknowledged. First, heterogeneity in study methodologies, including differences in DR classification systems, imaging modalities, and diagnostic criteria, makes direct comparison challenging. Some studies rely on self-reported diabetes duration or single-timepoint HbA1c measures, which can reduce data accuracy. Geographic and population coverage is uneven; while data from North America and Western Europe are well represented, fewer high-quality studies are available from sub-Saharan Africa, parts of Latin America, and rural Asia. Moreover, the majority of incidence and progression data are derived from historical cohorts, which may not reflect recent advances in diabetes care, particularly in low- and middle-income countries. Lastly, language and publication bias may limit inclusion of non-English or unpublished local studies, particularly from underrepresented regions.

Clinical Implications

This review reinforces the importance of early, individualized, and sustained management of diabetes to prevent or delay the onset and progression of DR. Clinicians must prioritize tight glycemic control, particularly early in the disease course, to leverage the "legacy effect" and reduce long-term retinal damage. Equally important is the aggressive management of hypertension and dyslipidemia, which, when controlled, can significantly reduce the risk of DR progression and associated visual impairment. The evidence also supports the need for regular, structured DR screening using validated imaging modalities. Implementing national screening programs and telemedicine services can dramatically improve detection and timely referral, especially in resource-constrained settings. Furthermore, clinicians should be aware of life stages such as puberty and pregnancy that heighten DR risk, necessitating closer monitoring. Ultimately, integrating DR screening into routine diabetes care and empowering primary care providers to initiate screening and risk management will be key to reducing the global burden of diabetic vision loss.

Recommendations for Future Research

Future research should prioritize high-quality, longitudinal studies from underrepresented regions such as sub-Saharan Africa, rural Latin America, and Southeast Asia to address data gaps and improve global generalizability. There is also a need to evaluate the cost-effectiveness, scalability, and long-term outcomes of emerging screening models, including artificial intelligence–assisted retinal image analysis and smartphone-based fundus photography. Research should focus on optimizing risk stratification tools that incorporate clinical, genetic, and socio-demographic variables to guide personalized screening intervals and management plans. Moreover, studies examining barriers to screening uptake, particularly among underserved populations, and evaluating the effectiveness of community-based interventions and health education programs would provide actionable insights. Finally, interventional trials comparing the impact of newer antihyperglycemic agents, blood pressure drugs, and lipid-lowering therapies specifically on DR progression will be crucial to refine therapeutic strategies.

CONCLUSION

As the global prevalence of diabetes and diabetic retinopathy (DR) continues to climb, the need for cost-effective, scalable, and accessible screening programs becomes increasingly critical. Early detection and timely treatment are essential in reducing the risk of vision loss, particularly given that up to 98% of diabetes-related visual impairment can be prevented with appropriate intervention. Advances in screening technologies—such as mydriatic and non-mydriatic retinal photography, tele-retinal screening, and AI-assisted diagnostics—offer promising avenues to expand access, especially in underserved and rural populations. Moreover, increasing public awareness and integrating DR screening into primary healthcare systems will play a pivotal role in addressing disparities in care. Ultimately, a coordinated effort involving clinicians, policymakers, and communities is required to mitigate the global burden of DR and preserve vision for millions of individuals living with diabetes.

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