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AI-Enabled Devices for Autonomous Detection of Diabetic Retinopathy

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List of Abbreviations

ADA	American Diabetes Association
AI	Artificial intelligence
Center	Center for Evidence-based Policy
CI	Confidence interval
CMS	Centers for Medicare & Medicaid Services
CoE	Certainty of evidence
FDA	US Food and Drug Administration

Executive Summary

Background

Diabetic retinopathy is the most common cause of vision loss for people with diabetes,[1,2] and occurs when chronic high blood sugar damages the blood vessels that nourish the retina.[3] Over time, diabetic retinopathy can lead to blindness or serious eye conditions, including diabetic macular edema, neovascular glaucoma, or retinal detachment.[3] According to the Centers for Disease Control and Prevention's Vision and Eye Health Surveillance System, the age-adjusted prevalence of diabetic retinopathy in New York State is 25.5% among people with diabetes.[4]

The American Diabetes Association (ADA) recommends an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist at the time of diabetes diagnosis for patients with type 2 diabetes, or within 5 years of onset for patients with type 1 diabetes.[1] The ADA recommends repeated dilated retinal exams at least every other year for individuals with no signs of retinopathy, but more frequently for those with signs of retinopathy.[1] Early detection of diabetic retinopathy leads to better outcomes,[1,3] but rising rates of diabetes in the US have led to increased demand for screening for diabetic retinopathy by a limited pool of qualified ophthalmologists and optometrists.[5,6]

Artificial intelligence (AI)-based screening systems have been proposed as a means of increasing access to screening and decreasing screening-associated costs.[7] Trained through deep learning by convolutional neural networks (a type of computer network architecture designed to process image data), AI-enabled diagnostic screening tools use machine-learning algorithms to automatically interpret retinal photographs.[7-9] AI-enabled systems provide diagnostic screening to identify individuals with more-than-mild diabetic retinopathy.[1,7,10] In theory, autonomous AI-enabled diagnostic screening tools would allow primary care providers to refer patients to eye care specialists only if needed, rather than referring all patients with diabetes for a dilated screening eye exam.[1,7,10]

As of April 1, 2026, the US Food and Drug Administration (FDA) had cleared 3 fully autonomous AI systems for detecting diabetic retinopathy without human oversight, all through the 510(k) pathway (Table ES1): AEYE-DS,[11] EyeArt,[12] and a product from Digital Diagnostics that was recently renamed LumineticsCore.[13] Because all research related to the Digital Diagnostics device references IDx-DR,[13] the product name prior to the change to LumineticsCore, this device is referred to as IDx-DR throughout this report. All 3 devices follow a similar process for capturing and processing retinal images: a fundus camera is attached to a computer with the client software installed; the client software guides users through acquisition of the required number and type of images, which are transferred to a server hosted at a secure data center; AI algorithms proprietary to each device are used to analyze the fundus images, and results are transferred to the client software that then displays them to the user with an assessment of: negative, positive, or ungradable.[11,12,14] AEYE-DS, EyeArt, and IDx-DR are all FDA-cleared for identification of more-than-mild diabetic retinopathy, which requires referral to an ophthalmologist (and is thus described as referrable retinopathy).[11-13] Patients without more-than-mild retinopathy do not require a referral and are advised to repeat screening in the following 1 to 2 years.[1]

Table ES1. FDA-Cleared AI Devices for Diabetic Retinopathy Diagnostic Screening

Device (Manufacturer) Initial FDA Decision Latest Version	FDA-Specified Fundal Camera(s)	Indication	Output
AEYE-DS (AEYE Health) AKA Aurora Eye Nov 10, 2022 No version number	Topcon NW400, Optomed Aurora	Detection of more-than-mild DR in adults with diabetes not previously diagnosed with DR	More-than-mild DR • Detected • Not detected • Insufficient quality
EyeArt (Eyenuk) Aug 3, 2020 v 2.2.0	Canon CR-2 AF, Canon CR-2 Plus AF, and Topcon NW400	Detection of more-than-mild DR and vision-threatening DR (severe non-proliferative DR or proliferative DR and/or diabetic macular edema) in the eyes of adults with diabetes not previously diagnosed with DR	More-than-mild DR • Negative • Positive • Ungradable Vision-threatening DR • Negative • Positive • Ungradable
LumineticsCore (Digital Diagnostics) AKA IDx-DR Apr 11, 2018 v. 2.3	Topcon NW400	Detection of more-than-mild DR in adults with diabetes not previously diagnosed with DR	More-than-mild DR • Detected • Not detected • Insufficient quality

Abbreviations. AI: artificial intelligence; DR: diabetic retinopathy; FDA: US Food and Drug Administration.

Output for all 3 FDA-cleared screening tools includes an ungradable category—cases that could not be analyzed because of insufficient image quality (Table ES1).[11,12,14] Poor image quality can result from factors related to camera operators (i.e., camera positioning or out-of-focus images)[10,15] and patient factors (i.e., cataracts, retinal lesions, or other artifacts that obscure images).[10,15-17] Both EyeArt and IDx-DR incorporate processes in the image-capture protocol to reduce the number of ungradable images (less information is available regarding AEYE's protocols).[10,18] The screening tools provide real-time feedback to camera operators, alerting them of the need to retake images that the algorithm deems to be of insufficient quality.[18,19] In practice, however, primary care staff may not have time in their workflow to take multiple pictures, which can lead to higher numbers of ungradable cases.[20] Additionally, all 3 systems incorporate reflex dilation protocols, which instruct staff capturing the fundus images to use dilation after a preset number of unsuccessful attempts to capture readable images without dilation.[10,18] While dilation is routine in ophthalmology and optometry offices, it may not be practical in many primary care practices.[21]

Studies assessing the diagnostic accuracy of these autonomous AI-enabled diabetic retinopathy screening systems used a variety of different dilation protocols, including dilating all patients, no patients, or some patients. Diagnostic efficacy studies also used varied approaches for handling ungradable cases. In primary care practice, however cases that are marked as ungradable by the AI-enabled diagnostic screening tool would require a referral to an ophthalmologist or retinal specialist for a full exam.[1] To assess the diagnostic accuracy and clinical utility of utilizing AI-enabled diagnostic screening tools in primary care practices or diabetes care clinics, where time per patient is limited and staff often do not have the time or training to dilate patients' pupils, the

most directly relevant studies would assess undilated eyes and treat ungradable images as referable in diagnostic accuracy assessments. Additional issues in evaluating autonomous AI-enabled diabetic retinopathy screening tools include FDA-prescribed processes for locking and unlocking of algorithms[22] and the opacity of algorithmic processes in AI-based software, which can hamper the identification and evaluation of error patterns.[23]

Autonomous AI-enabled diabetic retinopathy screening systems are billed under Category 1 current procedural terminology (CPT) code 92229, which first became effective in 2021 and is included as part of a Healthcare Effectiveness Data and Information Set quality metric maintained by the National Committee for Quality Assurance that measures receipt of eye exams among adult patients with diabetes.[24-32] The New York State fee-for-service Medicaid program does not currently provide coverage for the service code.[33] Following the FDA's De Novo pathway clearance of the IDx-DR system in 2018, the service was initially covered under Medicare's Outpatient Prospective Payment System (OPPS) through a bridge payment before eventually receiving separate, standalone reimbursement through the OPPS starting in 2021, when the CPT code became active.[29] After initially being carrier priced by Medicare Administrative Contractors, the CPT code received a separate national payment rate through the Medicare Physician Fee Schedule starting in 2022.[29,34] Recorded utilization of the service based on health care claims data has grown quickly since that time.[35,36]

Methods

The aim of this report is to evaluate the evidence related to the accuracy, clinical utility, and potential harms of autonomous AI-enabled diagnostic screening tools for identification of diabetic retinopathy, while providing contextual information from clinical practice guidelines, cost-effectiveness studies, and coverage policy reviews. The specific key questions (KQs) for this report are in the full report.

Researchers from the Center for Evidence-based Policy (Center) searched Ovid MEDLINE and other clinical evidence sources for studies evaluating test accuracy, clinical utility, safety, cost and cost-effectiveness studies, and clinical practice guidelines. Inclusion and exclusion decisions were made by consensus of 2 screeners. We applied the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach to rate the certainty of evidence for primary outcomes. To identify relevant coverage policies, we searched 9 state Medicaid program websites, 8 private payer websites, and the Centers for Medicare & Medicaid Services (CMS) for local and national coverage determinations and broader coverage policy documentation of autonomous AI-enabled diagnostic screening tools for identification of diabetic retinopathy.

Summary of Clinical Evidence and Recommendations

We identified 26 diagnostic accuracy studies (reported in 28 publications), 3 ongoing clinical trials, 3 cohort studies, 4 clinical practice guidelines (together with 1 professional statement on use of AI in diabetic retinopathy screening), and 2 cost-effectiveness studies that addressed 1 or more of the KQs. We did not identify any published diagnostic accuracy studies for the AEYE device, which was FDA-cleared for screening of more-than-mild diabetic retinopathy on November 10, 2022. In the absence of any peer-reviewed publications related to AEYE, we

included results of a study posted in the ClinicalTrials.gov record in analyses for KQs 1 and 2, although detail is limited and the study protocol is heavily redacted.[37]

Diagnostic Accuracy

Methods varied across studies for dilation protocols and handling of images that the AI tool deemed ungradable. Patients were imaged without any dilation in 8 EyeArt studies[16,21,38-43] and 6 IDx-DR studies.[20,44-48] Reflex dilation was used in 2 EyeArt studies (including 1 that provided results for both no dilation and reflex dilation),[38,49] 4 IDx-DR studies,[18,49-51] and the sole AEYE study.[37] All patients had their pupils dilated prior to image capture in 6 EyeArt studies[10,15,19,52-54] and 1 IDx study.[55] One IDx-DR study did not report on the dilation status of participants' pupils.[17] Eight EyeArt studies omitted patients with any image the AI screener judged ungradable,[15,16,21,38,40,42,43,49] 6 EyeArt studies included ungradable images as referable in diagnostic accuracy calculations,[10,19,39,41,52,54] and 1 EyeArt study reported diagnostic accuracy when ungradable images were included and excluded.[53] Ten IDx-DR studies omitted patients with any image the AI screener judged ungradable,[17,18,20,45-50] 1 included patients with ungradable images as referrable, and 2 IDx-DR studies reported diagnostic accuracy when ungradable images were included and excluded.[44,51] All studies provided results on a per-patient basis, except for a single EyeArt study that presented results only on a per-eye basis and thus had limited ability to demonstrate diagnostic accuracy because in practice patients are referred for follow up based on their worst eye (i.e., patients are referred, not individual eyes).[15]

Sensitivity and specificity are measures that describe how well a clinical test performs.[56] Sensitivity indicates the proportion of patients with diabetic retinopathy (either more-than-mild or vision threatening, depending on the study) who have true-positive test results, while specificity indicates the proportion of patients without diabetic retinopathy who have true-negative test results.[56]

EyeArt for Identification of More-Than-Mild Diabetic Retinopathy

When patients with 1 or more images rejected by the algorithm as ungradable were omitted from analysis, sensitivity for EyeArt ranged from 75% (Wintergerst 2022) to 100% (Mokhashi 2022) in studies in which patients' eyes were not dilated,[21,40] compared with 95.5% (Ipp 2021) and 100% (Musetti 2025) in studies that used reflex dilation and 92% in a study in which all patients' eyes were dilated (Ibanez-Bruron 2024).[38,49,53] Specificity ranged from 78% to 98% in studies without dilation[16,21,38,40,42] and from 73% to 88% in studies that included dilation.[38,49,53] When ungradable cases were considered referrals, sensitivity and specificity were 74% and 87% (Vought 2023) and 100% and 66% (Liu 2021), respectively, in the 2 studies that did not include dilation.[39,41] When all patients received pupil dilation prior to fundus imaging, sensitivity ranged from 91% (Tufail 2016) to 96% (Olvera-Barrios 2021 and Heydon 2021),[10,19,54] while specificity ranged from 37% (Tufail 2016) to 74% (Ibanez-Bruron 2024).[10,53] In a study by Bhaskaranand and colleagues (2019) that combined retrospective data from patients who were dilated, undilated, or dilation unknown, both sensitivity and specificity were 91%.[52]

EyeArt for Identification of Vision-Threatening Diabetic Retinopathy

Seven EyeArt studies reported diagnostic accuracy results for prediction of vision-threatening diabetic retinopathy.[10,16,38,39,42,53,54] When cases rejected by the algorithm as ungradable were omitted from analysis, sensitivity ranged from 50% to 100% in studies in which no patients had

pupil dilation.[16,42] Sensitivity was 100% in a study in which all patients were dilated.[53] Specificity was >90% in all studies where ungradable images were omitted.[16,38,42,53] In 4 EyeArt studies where ungradable results were categorized as referrals, sensitivity ranged from 67% in a study where no patients had pupils dilated to 100% in 2 studies where all patients were dilated.[10,39,53] Specificity ranged from 16% in a study where all patients were dilated to 89% in a study in which no patients were dilated.[10,39]

IDx-DR for Identification of More-Than-Mild Diabetic Retinopathy

When cases rejected by the algorithm as ungradable were omitted from analysis, sensitivity for IDx-DR ranged from 68.5% to 100% for patients without dilation, and specificity ranged from 47% to 98%.[20,44,48] In the 4 studies that used reflex dilation, sensitivity ranged from 79% to 100%, while specificity ranged from 66% to 94%.[50,51] In the single study in which all patients had their pupils dilated, sensitivity was 100% and specificity was 82%.[55] Only 2 studies of IDx-DR reported diagnostic accuracy results when ungradable cases were considered referrals.[44,51] A study that assessed patients without dilation reported sensitivity of 95% and specificity of 93%, while a study utilizing reflex dilation reported sensitivity of 82% and specificity of 85%.[44,51]

AEYE-DS for Identification of More-Than-Mild Diabetic Retinopathy

While no published diagnostic accuracy results were available for AEYE, the ClinicalTrials.gov record for NCT04612868 included results for 462 of 531 enrolled participants (87.0%) who had both AEYE-DS results and results from a professional reading center, where retinal specialists assessed images remotely.[37] Any patient with an ungradable image as judged by AEYE was omitted from analysis.[37] The AEYE-DS protocol accepted by the FDA allows for submission of either 1 image per eye or 2 images per eye.[37] With 2 images (1 per eye) submitted to AEYE, sensitivity was 92.98% and specificity was 91.36%.[37] With 4 images (2 per eye) submitted to AEYE, sensitivity was 94.74% and specificity was 88.64%.[37]

Subgroup Analyses

Only 1 publication, an observational study by Tufail and colleagues (2016), provided diagnostic accuracy calculations for population subgroups.[10] The study explored AI-based retinal image screening systems for pre-screening or as a replacement for first-level human graders in the United Kingdom's National Health Service diabetic eye screening program.[10] While EyeArt is not FDA-cleared for use in pediatric populations, the study included a consecutive series of patients aged 12 and older who attended an annual London-based diabetic eye screening program and had macular- and disc-centered retinal images taken.[10] All patients received pharmacologic dilation and ungradable images were included in analysis as referrable.[10] The study compared a number of AI-based screening tools that were commercially available in Britain, 1 of which was EyeArt.[10] Neither sensitivity nor specificity for EyeArt differed significantly between men and women.[10] When analyzed by age group, sensitivity and specificity did not differ significantly between patients under 50 and those aged 50 to < 65 years.[10] However, sensitivity was significantly lower in patients in the higher age group (65 to 98 years) compared with those under age 50, suggesting a higher likelihood for false negatives in older individuals screened by EyeArt.[10]

Ongoing Studies

We did not identify any ongoing studies related to AEYE-DS. We identified 1 ongoing trial for EyeArt[57] and 2 for IDx-DR.[58,59] The ongoing EyeArt study is evaluating the screening tool in a primary care practice, randomizing patients aged ≥ 22 years of age with diabetes to EyeArt screening or usual care (referral to an eye care provider for screening).[57] One ongoing study (currently recruiting) is testing IDx-DR in a pediatric population (aged 8 to 21) with type 1 or type 2 diabetes, which may indicate the company intends to file for an expanded indication for the AI-enabled device in the future.[58] Another ongoing trial (NCT05808699) is testing performance of IDx-DR with a handheld fundus camera.[58]

Clinical Utility

Most diagnostic accuracy studies focused on providing sensitivity and specificity estimates against results obtained from professional reading centers where retinal specialists viewed and rated images remotely, or the gold standard of a comprehensive dilated eye exam by an ophthalmologist or retinal specialist, and do not track how those determinations would translate into action. For example, diagnostic accuracy studies do not report how many more patients would be screened because of the use of the AI-enabled tools in primary care or diabetes care settings, or how many patients identified with referable diabetic retinopathy would go on to have a full exam with an ophthalmologist or retinal specialist.[17,44,60]

We identified 1 cohort study that compared patient follow up on ophthalmologist referral for patients who attended primary care and endocrinology clinics that implemented undilated IDx-DR screening with those who attended practices that used asynchronous teleophthalmology screening.[61] Rates of follow up were significantly higher for patients who received a finding of more-than-mild retinopathy in the AI-workflow compared to the human screener workflow ($P < .001$), although there were no significant differences for patients with ungradable results ($P = .26$).[61] In a second cohort study, Huang and colleagues (2024) conducted a retrospective cross-sectional survey to compare the likelihood of having an annual diabetic retinopathy screening exam for 5,580 patients at primary care sites that implemented IDx-DR with 29,684 patients at sites that did not implement IDx-DR.[62] Patients at sites where IDx-DR was available were more likely to adhere to screening recommendations, although we do not know whether patients who were screened from sites where AI screening was available actually had screening with IDx or whether they accepted a referral to an ophthalmologist for screening.[62] Patients enrolled in Medicare, Medicare Advantage, or Medicaid were all more likely to adhere to screening recommendations when they were treated at a site where IDx-DR was available.[62] A third cohort study, which was conducted by the IDx-DR research team (2023), reported results of a model used to estimate the impact on vision loss of screening with IDx-DR compared to referral of all patients by a primary care provider to an ophthalmologist or optometrist for dilated diabetic eye exams.[63] The authors estimated that the proportion of adults with diabetes who would develop any vision loss at 5 years was significantly lower for AI-based screening strategies compared with traditional eye care provider-based screening.[63]

Of the 8 prospective diagnostic accuracy studies that took place in primary care settings or diabetes care clinics,[18,20,21,39,40,44,47,49] only 2 provided any details on the practicality of using these autonomous AI-enabled diagnostic screening tools in clinical practice.[20,21] A study by Wintergerst and colleagues (2022) conducted in primary care practices in Germany reported that image

acquisition with EyeArt took an average of 7.5 minutes for both eyes, with the majority of imaging sessions completed in less than 10 minutes.[21] A study by van der Heijden and colleagues (2018) describe results of screening with IDx-DR in a diabetes care center in the Netherlands.[20] The authors do not report mean image acquisition time or mean number of imaging attempts per patient, but they note that staff operating the fundus cameras were prompted by the software to take a new photograph if image quality was low, but "the scheduled time per patient most often did not allow this."[20(p64)]

AI-enabled diabetic retinopathy screening tools are promoted as a practical means of screening without dilation, which would increase clinical utility for primary care practices and endocrinology practices in which dilation of patient pupils may not be practical.[64] Among the 8 EyeArt studies that did not use dilation, the proportion of patients that the AI tool flagged as ungradable ranged from < 1% to 36%.[16,21,38-43] Excluding an outlier study that reported that only 1 of 499 patients was excluded due to poor image quality[43] and 2 studies that did not report the number of ungradable patients,[38,42] the mean percentage of patients that were considered ungradable by the AI-enabled diagnostic screening tools was 19%. Only 3 IDx-DR studies reported on gradability for studies that did not use dilation, with percentages of patients with ungradable images ranging from 25% to 36.5%.[20,44,47]

GRADE Summary

Because we did not identify any publications related to AEYE, we did not include AEYE in the GRADE tables and we are unable to estimate certainty of evidence for the clinical effectiveness or clinical utility of this tool.[37] Table ES2 provides GRADE ratings for all studies of EyeArt and IDx-DR that included enough detail to allow for pooling of results, regardless of the dilation protocol used or handling of ungradable cases. Three of the included studies used approaches that best reflect potential real-world use of these AI-enabled diagnostic screening tools in primary care practice: analyzing eyes without dilation and considering ungradable results as referrals.[39,41,44] Summary of GRADE ratings for these 3 studies are included in Table ES3.[39,41,44]

Table ES2. Summary of Findings (GRADE)[a] for Detection of More-Than-Mild Diabetic Retinopathy

Metric	Number of Participants (Studies)	Pooled Estimate (95% CI), Range	CoE	Rationale for CoE Rating
EyeArt				
Sensitivity	156,883 (10)	94.97% (92.42 to 97.52)	●●○○ Low	Downgraded 1 level for moderate risk of bias across majority of studies and 1 level for consistency due to variation in outcomes across studies, even when approach to study design and analysis were similar (i.e., all eyes dilated and ungradable tests omitted)
Specificity		71.03% (57.83 to 84.23)	●●○○ Low	
PPV		39.90 (23.70 to 56.09)	●●○○ Low	
NPV		98.70% (97.87 to 99.53)	●●●○ Moderate	Downgraded 1 level for moderate risk of bias across majority of studies
Ungradable rate	102,907 (7)	Mean 12.34% (12.28 to 12.41) Range 1% to 29.4%	●○○○ Very low	Downgraded 1 level for moderate risk of bias in the majority of studies, 1 level for consistency due to wide variation in reported results, and 1 level for imprecision due to the small number of studies reporting this outcome and subsequent lack of clarity on how close this figure is to the true rate
IDx-DR				
Sensitivity	8,857 (9)	88.63 (75.13 to 100)	●○○○ Very low	Downgraded 2 levels for high risk of bias across majority of studies and 1 level for consistency due to variation in outcomes across studies, even when approach to study design and analysis were similar (i.e., all eyes dilated and ungradable tests omitted)
Specificity		78.05 (66.98 to 89.12)	●○○○ Very low	
PPV		41.95 (26.42 to 57.48)	●○○○ Very low	
NPV		97.90 (96.17 to 99.63)	●●○○ Low	Downgraded 2 levels for high risk of bias across majority of studies
Ungradable rate	10,302 (6)	Mean 21.35% (21.12 to 21.58) Range 8.3 to 36.5	●○○○ Very low	Downgraded 2 levels for high risk of bias in the majority of studies and 1 level for imprecision due to the small number of studies reporting this outcome and subsequent lack of clarity on how close this figure is to the true rate

Note. [a] For methods and interpretation of GRADE ratings, see Appendix C.
Abbreviations. CI: confidence interval; CoE: certainty of evidence; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; NPV: negative predictive value; PPV: positive predictive value; RoB: risk of bias.

Table ES3. Summary of Findings (GRADE)[a] for Detection of More-Than-Mild Diabetic Retinopathy Without Pupillary Dilation and Counting Ungradable Images as Referrals

Outcome	Study	Results, % (95% CI)	CoE	Rationale for CoE Rating
EyeArt				
Sensitivity	Liu 2021 Vought 2023	100% (90.51 to 100) 74% (no CI)	●●○○ Low	The larger study (Liu) had moderate RoB (the other was high). Degree of consistency is unknown because 1 study lacked confidence intervals. No downgrade for precision because that issue is already addressed in consistency.
Specificity	Liu 2021 Vought 2023	65.67% (56.98 to 73.65) 87% (no CI)	●●○○ Low	
PPV	Liu 2021 Vought 2023	44.58% (38.89 to 50.41) 72% (no CI)	●●○○ Low	
NPV	Liu 2021 Vought 2023	100% (95.89 to 100) 88% (no CI)	●●○○ Low	
Ungradable rate	Liu 2021 Vought 2023	29.4% EyeArt 16.1% human in Liu 11% EyeArt 2% single grader 15% retina specialist in Vought	●●○○ Low	The larger study (Liu) had moderate RoB (the other was high). Downgraded 1 level for consistency for large outcome differences between studies.
IDx-DR				
Sensitivity	Dow 2023	95.45% (77.16 to 99.88)	●○○○ Very low	In each case, downgraded 2 levels for high RoB and 1 level for imprecision related to a single study with small sample size.
Specificity	Dow 2023	93.10% (83.27 to 98.09)	●○○○ Very low	
PPV	Dow 2023	84% (67 to 93.14)	●○○○ Very low	
NPV	Dow 2023	98.18% (88.82 to 99.73)	●○○○ Very low	
Ungradable rate	Dow 2023	36.5% IDx-DR, 6.9% human	●○○○ Very low	

Note. [a] *For methods and interpretation of GRADE ratings, see Appendix C.*
Abbreviations. CI: confidence interval; CoE: certainty of evidence; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; NPV: negative predictive value; PPV: positive predictive value; RoB: risk of bias.

Harms

Among the 3 cohort studies that explored clinical utility of AI-enabled devices for diabetic retinopathy screening, none reported on adverse events or addressed the possibility of harms.[61-63] Diagnostic accuracy studies of autonomous AI-enabled diabetic retinopathy screening tools did not reference or report on adverse events. The clinical trial record for AEYE-DS rationalized that the study could not result in any harms to participants because it was using previously acquired retinal images and researchers were not interacting directly with participants.[37]

Cost and Cost-Effectiveness

We identified 2 economic evaluations that met inclusion criteria.[65,66] Both studies modeled use of autonomous AI-enabled diagnostic screening using data from EyeArt studies of undilated screening in primary care practices and found that AI-enabled diabetic retinopathy screening was cost effective compared with the standard method of referring all patients with diabetes to an

ophthalmologist or retinal specialist for a dilated screening exam.[65,66] However, one of these studies found that cost-effectiveness in the model was highly dependent on specificity, illustrating how excessive false positives could neutralize cost savings through unnecessary referrals and diagnostics.[65]

Clinical Practice Guideline Recommendations

Our searches identified 4 clinical practice guidelines that addressed the use of AI-enabled tools for routine screening for diabetic retinopathy in adult patients with diabetes; all 4 were published, revised, or reaffirmed within the past 5 years.[64,67-69] All 4 guidelines described the use of AI-enabled diagnostic screening tools as a promising approach to increase access to routine diabetic retinopathy screening, but only one, the American Diabetes Association's 2026 Preferred Practice Pattern, recommend FDA-cleared autonomous AI-enabled diagnostic screening tools as an appropriate strategy for screening.[64] A 2020 statement from the American Academy of Ophthalmology, which was not an official clinical practice guideline, noted that use of AI-enabled diagnostic screening devices carries some risk of medicolegal liability of harm to the patient from a missed diagnosis or a breach of protected health information.[70]

Coverage Policies

Autonomous AI-enabled diabetic retinopathy screening systems are covered under CPT Category 1 code 92229, which became effective in 2021.[27-30]

Medicare has covered AI-enabled diabetic retinopathy screening through its OPPS since 2018, initially under a bridge payment (packaged into payment with separately payable services during same visit) before eventually setting a separate, standalone reimbursement rate starting in 2021.[29,71] The service is also paid under the Medicare Physician Fee Schedule, first as a carrier-priced service before receiving a national payment rate in 2022.[29] In 2026, the CPT code 92229 was listed on the physician fee schedule with a $46.76 reimbursement rate,[34] and on the OPPS with a $60.27 reimbursement rate.[71] CMS has not issued a Medicare national coverage determination for the AI-enabled diabetic retinopathy screening service, and does not currently have any local coverage determinations from Medicare Administrative Contractors (MACs).[72] One MAC (Noridian) previously issued a billing and coding article on remote retinal screening that included CPT code 92229, but the article was retired in 2023.[73,74]

Only 2 of the 8 reviewed commercial health plans maintain specific coverage policy information for AI-enabled diabetic retinopathy analysis (Aetna,[75] Anthem BlueCross BlueShield[76]), and both insurers cover CPT code 92229 for screening of diabetic retinopathy. We did not identify specific coverage policies for the other 6 insurers (Cigna, Fidelis Care, Healthfirst, MetroPlusHealth, Molina, UnitedHealthcare). Among the 6 reviewed insurers that offer New York Medicaid managed care organization (MCO) plans, the prior authorization look-up tools for Anthem[77] and Fidelis Care[78] listed CPT code 92229 as a service that did *not* require precertification for the Medicaid line of business—indicating possible Medicaid MCO coverage for those 2 plans.

Of the 9 comparator Medicaid agencies, 7 appear to cover AI-enabled diabetic retinopathy analysis, based on their coverage of CPT code 92229 (California,[79-81] Florida,[82,83] Massachusetts,[84,85] New Jersey,[86] North Carolina,[87] Pennsylvania,[88] Texas[89,90]). Two Medicaid

agencies (Oregon,[91] Washington[92]) do not include CPT code 92229 on the state fee schedule, and Oregon's clinical policy (maintained by its Health Evidence Review Commission) includes the code on a list of explicitly excluded services.[93,94] None of the 7 Medicaid agencies providing coverage appear to have public clinical criteria or other guidance documentation around service use.

Conclusions

Autonomous AI-enabled systems have the potential to increase access to diabetic retinopathy screening and improve early detection of diabetic retinopathy.[18] One of the major advantages of AI-based diabetic retinopathy screening is the ability to implement point-of-care testing in primary and community health care settings without the need for specialized equipment or training in ophthalmology.[43] In this context, the performance of the AI-enabled diagnostic screening tools in patients without any dilation is the most important measure of diagnostic accuracy and clinical utility. Studies that estimate diagnostic accuracy based on exclusion of patients with any images the AI tools considered to be of insufficient quality risk inflating estimates of device accuracy. In real-world situations, patients with ungradable images would need to be referred to an ophthalmologist or retinal specialist for further review.[17]

Only 1 study related to IDx-DR for detection of more-than-mild diabetic retinopathy included patients who were assessed without dilation and considered ungradable cases as referrals; it reported a sensitivity of 95% and specificity of 93%.[44] Only 2 diagnostic accuracy studies of EyeArt for detection of more-than-mild diabetic retinopathy met these criteria, reporting a sensitivity of 74% to 100% and specificity of 66% to 87%.[39,41] Variations in outcomes for the 2 EyeArt studies may have been due to differences in the study populations; one study took place in a primary care practice with a predominantly African American population[39] and the other incorporated data from both a primary care practice and a community screening event (where image quality might be expected to be lower than images captured in an office setting) with a primarily Caucasian and Hispanic population.[41]

The balance of sensitivity and specificity across diagnostic accuracy studies, regardless of the use of dilation or the handling of AI-ungradable cases, suggests that the software is unlikely to miss cases of referable diabetic retinopathy but may refer patients unnecessarily.[40] However, given that all patients with diabetes who meet the ADA screening guidelines would be referred from primary care or their diabetes management practice for a comprehensive dilated exam with an ophthalmologist or retinal specialist in the absence of the screening tool, the high false-positive rates found in many diagnostic accuracy studies would not represent a heightened workload for specialists in practice.

The 2 economic evaluations we identified both used data from EyeArt studies, considered ungradable cases to be referrable, and concluded that AI-enabled diabetic retinopathy was cost effective compared with usual practice, without any difference in quality-adjusted life years.[65,66] All 4 clinical practice guidelines we identified recognized the potential of FDA-cleared autonomous AI-enabled diabetic retinopathy screening tools to increase access to routine diabetic retinopathy screening,[64,67-69] but only a guideline from the American Academy of Ophthalmology (2026) specifically refers to FDA-cleared AI-enabled diagnostic screening tools as appropriate strategies for screening.[67]

Medicare has provided some level of coverage for AI-enabled diabetic retinopathy screening since 2018,[29] and utilization has increased quickly since the service CPT code came online in 2021.[35,36] The service appears to be covered widely among comparator state Medicaid agencies and by the 2 reviewed health plans that maintain specific policies.

Background

Description of the Condition

Diabetic retinopathy is the most common cause of vision loss for people with diabetes,[1,2] and occurs when chronic hyperglycemia, or high blood glucose, causes damage to the blood vessels that nourish the retina.[3] There are 2 forms of diabetic retinopathy—proliferative and nonproliferative.[3] In the more common nonproliferative version of diabetic retinopathy, chemical and structural changes in the retinal capillaries and arterioles, such as microaneurysms and microthrombosis, disrupt normal vascular function, increasing vascular permeability and ultimately leading to retinal edema with possible ischemia.[3] Progressive ischemia can lead to proliferative diabetic retinopathy, in which new blood vessels grow to counter the damage; however, the fragile new vessels leak or bleed easily and progressively damage vision.[3] Over time, diabetic retinopathy can lead to blindness or serious eye conditions, including diabetic macular edema (fluid leak into the macular portion of the retina, creating blurry vision), neovascular glaucoma (blood vessel growth that blocks fluid from draining out of the eye), or retinal detachment (caused by scars forming on the back of the eye).[3]

Duration of diabetes is the greatest risk factor for diabetic retinopathy, followed by poorly managed blood sugar levels, high blood pressure, and high cholesterol.[1,3] African Americans and Hispanic Americans have significantly higher rates of diabetic retinopathy than non-Hispanic White individuals,[4,95] and minorities often present at a more advanced stage of disease, in part because of disparities in screening rates.[96] Intensive diabetes management is the most effective means of preventing diabetic retinopathy or slowing its progression, although treatment with laser photocoagulation or intravitreous injections of anti-vascular endothelial growth factor may be required for individuals with more advanced disease.[1]

Screening for Diabetic Retinopathy

The American Diabetes Association (ADA) recommends retinopathy screening for adults with type 1 diabetes within 5 years of onset of diabetes.[64] The ADA recommends an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist at the time of the diabetes diagnosis for patients with type 2 diabetes, with repeated dilated retinal exams every year for individuals who have no sign of retinopathy (with the option of every other year after 1 or more normal eye exams), but more frequently for those who have signs of retinopathy.[64] The ADA advises that retinal photography is not a substitute for a comprehensive eye exam but may help to increase access to screening in areas where qualified eye care professionals are not readily available.[64]

Prevalence of Diabetic Retinopathy in New York State

Age-adjusted prevalence of diabetes in New York State was 9.3% in 2023, higher than the national prevalence of 8.6%.[97] According to the Centers for Disease Control and Prevention's Vision and Eye Health Surveillance System, adjusted prevalence of diabetic retinopathy in New York State is 25.5% among people with diabetes.[4] As shown in Table 1, the prevalence of diabetic retinopathy is higher among men, Black individuals, and people ≥ 40 years of age.[4] New York counties with ≥ 30% prevalence of diabetic retinopathy among people with diabetes are listed in Table 2 (a full list of New York counties is available in Appendix J).[4]

Table 1. Prevalence of Diabetic Retinopathy in New York (2021) Among People With Diabetes*

Population	Prevalence*	95% Confidence Interval
Statewide	25.51%	21.22 to 30.49
0 to 17 years	9.32%	3.81 to 32.48
18 to 39 years	17.7%	13.33 to 23.21
40 to 64 years	26.01%	20.67 to 32.32
65 to 84 years	27.88%	21.69 to 35.43
Male	27.12%	21.69 to 33.47
Female	23.59%	19.12 to 28.92
Black, non-Hispanic	33.93%	25.80 to 43.31
Hispanic, any race	28.28%	21.38 to 37.11
White, non-Hispanic	23.33%	17.60 to 30.19
Non-vision threatening	20.81%	16.44 to 26.06
Vision threatening	4.7%	3.61 to 6.13

**Adjusted for age, race/ethnicity, and sex.*
Source: Centers for Disease Control and Prevention Vision & Eye Health Surveillance System.[4]

Table 2. New York Counties with Highest Diabetic Retinopathy Prevalence

Counties With Prevalence ≥ 30% in People With Diabetes	Prevalence*	95% Confidence Interval
Greene	35.53%	29.43 to 42.50
Schoharie	35.12%	28.94 to 42.00
Tompkins	34.55%	28.48 to 41.24
Jefferson	34.37%	28.53 to 41.11
Rensselaer	33.41%	27.73 to 40.07
Cayuga	31.2%	25.89 to 37.31
Rockland	30.65%	25.44 to 36.51

**Adjusted for age, race/ethnicity, and sex.*
Source: Centers for Disease Control and Prevention Vision & Eye Health Surveillance System.[4]

Description of the Intervention

Rising rates of diabetes in the US and around the world have led to increased demand for screening for diabetic retinopathy, despite limited availability of qualified ophthalmologists.[5,6] While early detection of diabetic retinopathy leads to better outcomes,[1,3] a recent study found that more than half of people with diabetes in the US do not receive recommended annual dilated eye exams.[98] Screening rates are somewhat higher in New York State, with an average of 61% of adults with commercial health maintenance organization coverage, 51% with commercial preferred or exclusive provider organization coverage, and 63% of those with Medicaid managed care plans receiving an eye exam in 2024.[99] Artificial intelligence (AI)-based screening systems are proposed as means of increasing access to screening and decreasing costs associated with screening.[7] Trained through deep learning by convolutional neural networks (a type of network

architecture designed to process image data), machine-learning algorithms automatically interpret retinal photographs, and patients are referred to eye care specialists only if needed.[7-9]

As of April 1, 2026, the US Food and Drug Administration (FDA) had cleared 3 fully autonomous AI systems for detecting diabetic retinopathy without human oversight, all of which were cleared through the 510(k) pathway (Table 3). These devices are AEYE-DS,[11] EyeArt,[12] and a product from Digital Diagnostics that was recently renamed LumineticsCore.[13] Because all research related to the Digital Diagnostics device references IDx-DR,[13] the product name prior to the change to LumineticsCore, this device is referred to as IDx-DR throughout this report.

The FDA-cleared devices all require a camera operator to obtain point-of-care fundus images, although there is ongoing research into smartphone-based systems.[8,100,101] AI-based screening systems are designed to work with specific cameras (Table 3) and while high-quality images are integral to successful screening, no minimum amount of training for camera operators is specified in any of the FDA-cleared systems.[11,12,14] All systems are indicated for use only in the populations in which they have been studied in diagnostic accuracy studies, which results in contraindications or warnings related to their use in other populations, such as pregnant women or patients with a history of ocular injections or laser treatment of the retina.[102,103] None of the FDA-cleared devices are cleared for use in pediatric populations.

All 3 FDA-cleared devices follow a similar process for capturing and processing images.[11,12,14] The fundus camera is attached to a computer where the client software is installed.[11,12,14] The number and type of retinal fundus images required per eye in each system is described in Table 3.[11,12,14] The client software guides users through acquiring images which are transferred to a server hosted at a secure data center.[11,12,14] AI algorithms proprietary to each device are used to analyze the fundus images and return results.[11,12,14] Results are transferred to the client software that then displays them to the user in less than 60 seconds: negative, positive, or ungradable.[11,12,14]

The ADA recommends that individuals with any level of more-than-mild diabetic retinopathy detected in screening be referred to an ophthalmologist for follow up.[1] Those with no diabetic retinopathy or only mild nonproliferative diabetic retinopathy are recommended for standard yearly screening, with no immediate follow up required.[1] More-than-mild diabetic retinopathy is thus also referred to as 'referrable diabetic retinopathy.'[1] Both AEYE-DS and IDx-DR are FDA-cleared solely for detection of more-than-mild diabetic retinopathy (Table 3).[11,12,14] EyeArt is cleared for detection of both more-than-mild and vision-threatening diabetic retinopathy (Table 3).[11,12,14]

Table 3. FDA-Cleared AI Devices for Diabetic Retinopathy Diagnostic Screening

Device (Manufacturer) Initial FDA Decision Latest Version	FDA-Specified Fundal Camera(s)	Indication	Input	Output
AEYE-DS (AEYE Health) AKA Aurora Eye Nov 10, 2022 No version number	Topcon NW400, Optomed Aurora	Detect more-than-mild DR in adults with diabetes not previously diagnosed with DR	Macula and disc-centered color fundus images with at least 45° field of view, 2 images per eye; Or Macula-centered color fundus images with at least 45° field of view, 1 image per eye	More-than-mild DR • Detected • Not detected • Insufficient quality
EyeArt (Eyenuk) Aug 3, 2020 v 2.2.0	Canon CR-2 AF, Canon CR-2 Plus AF, and Topcon NW400	Detect more-than-mild DR and vision-threatening DR (severe non-proliferative DR or proliferative DR and/or diabetic macular edema) in the eyes of adults with diabetes not previously diagnosed with DR	Macula and disc-centered retinal fundus images with 45° field of view, 2 images per eye	More-than-mild DR • Negative • Positive • Ungradable vision-threatening DR • Negative • Positive • Ungradable
LumineticsCore (Digital Diagnostics) AKA IDx-DR Apr 11, 2018 v. 2.3	Topcon NW400	Detect more-than-mild DR in adults with diabetes not previously diagnosed with DR	Macula- and disc-centered color fundus images with 45° field of view, 2 images per eye	More-than-mild • Detected • Not detected • Insufficient images quality

Abbreviations. AI: artificial intelligence; DR: diabetic retinopathy; FDA: US Food and Drug Administration.

Place of Autonomous AI-Enabled Diagnostic Screening Tools in the Care Pathway

The American Academy of Ophthalmology recommends that primary care providers either refer patients with diabetes to an ophthalmologist for a dilated eye exam or use photographic screening to determine who needs a referral to an ophthalmologist for follow up.[67] These guidelines identify autonomous AI systems as one option for primary care screening.[67] These AI-enabled tools are diagnostic screening systems, designed to identify individuals with more-than-mild diabetic retinopathy for referral to an ophthalmologist or eye care provider for a full dilated exam, definitive diagnosis, and treatment planning.[10] In theory, limiting ophthalmology referrals to those patients who are most likely to need it, rather than referring all patients who meet screening guidelines, would increase access and lower costs.[18,43] AI-based diabetic retinopathy screening is promoted as a means of reducing reliance on a scarce pool of human diabetic retinopathy screeners who manually assess digital fundus photographs, while providing a

practical and accessible means for implementing point-of-care testing in primary and community health care settings.[43] The AI-based screeners do not require dilation of pupils for all patients, which removes a hurdle to implementation of standard screening in the primary care pathway.[104] However, implementation of AI-based diagnostic screening in primary care requires practices to invest in fundus cameras and software licenses, as well as staff training for operating the cameras and working with the AI software.[43,105] Initial studies have demonstrated that non-mydriatic cameras (i.e., cameras that do not require pupil dilation) paired with AI algorithms can be operated effectively by general health care staff, facilitating diabetic retinopathy screening in primary care practices.[105]

Screening Versus Diagnosis

Each of the 3 systems is classified by the FDA as a "Retinal Diagnostic Software Device" (21 CFR 886.110).[11-13] Both AEYE-DS and EyeArt describe the purpose of their systems as 'diagnostic screening' in their FDA filings,[11,12] while IDx-DR describes its goal as automated detection of more-than-mild diabetic retinopathy.[13] The terms 'screening' and 'diagnosis' are often conflated in publications of these AI-enabled tools. For example, the study by Ipp and colleagues (2021) refers to EyeArt's ability to diagnose more-than-mild diabetic retinopathy, while also concluding that EyeArt "may increase adherence to recommended annual screenings and allow for accelerated referral of patients."[38(p2)] Studies co-authored by Michael Abràmoff, the founder of IDx-DR, describe the tool as an autonomous diagnostic system,[18,51] while also arguing for its place in the screening pathway.[18,20,51] The heart of discussion in publications for all 3 systems focuses on the ability of these tools to detect referrable diabetic retinopathy to reduce the number of patients who require referral to an ophthalmologist or retinal specialist for a full dilated exam.

As this report focuses on studies exploring the role of the 3 AI-enabled systems in the primary care pathway (where screening is conducted), we use the term 'AI-enabled diagnostic screening system' throughout.

Minimizing the Occurrence of Ungradable Images

All 3 FDA-cleared screening tools include an ungradable category as a potential output. Ungradable cases include those that could not be analyzed due to insufficient image quality (Table 3).[11,12,14] Poor image quality can result from factors related to camera operators (i.e., camera positioning or out-of-focus images)[10,15] and patient factors (i.e., cataracts, retinal lesions, or other artifacts that obscure images).[10,15-17] Both EyeArt and IDx-DR incorporate processes in the image-capture protocol to reduce the number of ungradable images (less information is available regarding AEYE's protocols).[10,18] Both screening tools provide real-time feedback to camera operators, alerting them of the need to re-take images that the algorithm deems to be of insufficient quality.[18,19] In practice, however, primary care staff have reported not having time in their workflow for taking multiple pictures, which can lead to a higher number of ungradable cases.[20]

FDA documentation for all 3 AI-enabled diagnostic screening tools describes reflex pharmacological dilation protocols.[10,18] The EyeArt protocol specifies that if the second imaging attempt is still ungradable, the patient may be dilated with medicated eye drops (e.g., tropicamide 1.0%) and re-imaged.[10] The IDx and AEYE-DS protocols suggests dilation after 3

unsuccessful attempts to capture readable images.[18] While dilation is routine in optometry and ophthalmology offices, it is not practical in many primary care practices.[21] Patients must have a dark area to rest for approximately 15 to 30 minutes after administration of mydriatic eye drops before eyes are fully dilated, which can present time and space challenges for busy practices.[21,106] Additionally, patients may decline to have their eyes dilated due to side effects, like blurry vision and light sensitivity, that can prevent them from driving and interfere with work and daily life in the hours immediately after dilation.[106]

Handling of Ungradable Images in Diagnostic Accuracy Studies

Diagnostic accuracy studies take different approaches to handling ungradable images. Some studies exclude any patients with ungradable images from analysis,[15-18,20,21,38,42,43,45,46,48-51,55] while others treat patients without results as automatic referrals and include them in analysis as referable retinopathy.[10,19,39,41,44,47,53,54] When analysis excludes patients with unreadable images, it risks inflating estimates of the device's accuracy.[17,107] Omitting patients that had images of insufficient quality also excludes people who would need additional clinical review in a real-life situation, which carries a real cost of time and resources for both patients and health care providers.[17]

Measuring Clinical Utility in Diagnostic Accuracy Studies

Key question (KQ) 2 focused on clinical utility. Most diagnostic accuracy studies focused on providing sensitivity and specificity estimates against a gold standard.[108] In the case of diabetic retinopathy, that standard is a dilated eye exam performed by an ophthalmologist or retinal specialist or grading of retinal photographs remotely by retinal specialists.[10] Few diagnostic accuracy studies addressed clinical impact or utility.[108] The National Cancer Institute defines clinical utility as the likelihood that a test will result in an improved health outcome by prompting an intervention.[109] The information generated by a screening or diagnostic test does not by itself create any health benefit.[60] If test results are used to guide decision making, then study authors should be able to demonstrate that testing led to a change in clinical recommendations or interventions.[60] In the case of screening for diabetic retinopathy, that change would be referral to an ophthalmologist or retinal specialist for a comprehensive dilated eye exam for those screening positive for more-than-mild diabetic retinopathy or vision-threatening retinopathy, and studies would include a measure of how many patients followed through on referrals.[17,44]

However, many studies focused on diagnostic accuracy do not report on actual referrals, dealing only in hypothetical referrals, and do not provide information on the number of patients who go on to have full dilated exams by an ophthalmologist or retinal specialist. We incorporate other measures of clinical utility into analysis for KQ2, such as rates of referral for follow up for AI-enabled systems compared to human graders, likelihood of patient follow up with an ophthalmologist or retinal specialist after referral, clinical staff's perceptions of AI-enabled diagnostic screening systems usability, and the proportion of patients with images deemed ungradable by the AI-enabled screener.

Additional Challenges in Evaluation of AI Models

Locking and Unlocking of Algorithms

As of 2025, the FDA has only cleared AI and machine-learning tools with locked algorithms, which the FDA defines as, "an algorithm that provides the same result each time the same input is applied to it and does not change with use."[110] When an FDA-cleared AI or machine-learning device is put on the market, manufacturers have been required to lock the algorithm to limit any future training of the AI on new data, which means algorithms can no longer learn on their own and adapt once the software as a medical device receives FDA approval.[110,111] However, as part of the FDA premarket submission, applicants are required to submit a Predetermined Change Control Plan as part of a Total Product Lifecycle framework that includes an Algorithm Change Protocol that describes how the algorithm will learn and change, and how the applicant will implement algorithmic changes in a controlled manner that manages patient risk.[22] The Predetermined Change Control Plan includes the types of changes that can be implemented without the need for additional regulatory review, along with the processes for evaluating and documenting those changes.[112,113] Thus, FDA-cleared software as a medical device can periodically unlock the algorithm and provide additional training and enhancement, without the need for additional regulatory review.[22,112]

The FDA stresses the importance of transparency to allow users and patients to understand how the devices function and to recognize the benefits, risks, and limitations of software as a medical device.[22] While this is a valid goal, in practice AI-enabled medical devices lack transparency around their algorithms.[22,112] Because of the proprietary nature and complexity of deep-learning algorithms, it is not easy for users, patients, or regulators to understand the decision-making process, which "raises serious concerns about accountability, bias mitigation, and the potential for misuse."[112(p7)]

Black Box Algorithms

The opacity of algorithms in AI-based software as a medical device reflects more than just protection of intellectual property.[23] The term 'black box' refers to an AI system in which even the developers are unaware of the details of the actual decision-making process.[23] Developers and users can see inputs and outputs, but the details of how the system operates, makes decisions, and generates results are ultimately a mystery.[23] Black box AI systems, like the ones being reviewed in this report, are powered by deep learning and multilayered neural networks that create processes that are so complex that even their developers cannot trace the exact path from input to output.[23]

Potential for Screening Error

While human screening by ophthalmologists or retinal experts is considered the gold standard in diabetic retinopathy screening,[10] the use of autonomous AI-enabled screeners raises additional questions about the ultimate arbiter of the 'true' presence of disease and the potential for screening error.[111] If a human ophthalmologist in a diagnostic accuracy study misses an abnormality that is detected by AI, for example, the case is counted as a false positive, even if its finding is actually correct.[111] Without follow up to track results of any additional testing or subsequent changes to the patient's diagnosis, the case will continue to be incorrectly categorized as a false positive.[111] At the opposite extreme, the existence of most AI algorithms as

proprietary black boxes means that there is no transparency when the algorithm generates unexpected or incorrect outputs, hampering the identification and evaluation of error patterns.[111]

Systematic Reviews

Systematic reviews related to FDA-cleared AI-based diabetic retinopathy screening tools have combined disparate studies in meta-analyses, without any subgroup analyses related to dilation or classification of ungradable cases. Wang and colleagues (2026) provided meta-analysis of 17 studies related to EyeArt, but included studies testing EyeArt with smartphone cameras, which are not FDA-cleared for use with autonomous AI-enabled diagnostic screening tools.[114] They noted the challenges of comparing studies with different protocols related to pupillary dilation, repeat imaging, and hybrid AI-human approaches, but did not include any subanalyses despite noting large differences in specificity based on study design.[114] Khan and colleagues (2025) included 13 studies related to IDx-DR and provide pooled sensitivity and specificity estimates for any diabetic retinopathy, rather than referable diabetic retinopathy (the indication for which IDx-DR is FDA-cleared); the authors did not provide any subanalyses for different screening approaches or mention the challenges related to differences in dilation protocols or handling of ungradable images.[115] A number of other systematic reviews combined data from studies of any machine-learning approach to diabetic retinopathy detection, without any subanalyses for individual screening tools.[116-118]

Policy and Regulatory Context

AI-enabled diabetic retinopathy analysis is billed under a specific CPT code, 92229, described as: "*Imaging of retina for detection or monitoring of disease; point-of-care autonomous analysis and report, unilateral or bilateral*" (Appendix I).[27] The current CPT code became effective at the start of 2021 (the first Category 1 code issued for an autonomous AI tool).[28-30,119,120] The code's description originally referred to "automated" analysis, but was subsequently amended to specify "autonomous" analysis.[28]

New York State Medicaid Coverage

New York fee-for-service Medicaid does not currently cover AI-enabled diabetic retinopathy analysis (CPT code 92229).[33]

Inclusion of AI-Enabled Diabetic Retinopathy Analysis Within HEDIS Quality Measure

The National Committee for Quality Assurance (NCQA) maintains a set of quality measures known as the Healthcare Effectiveness Data and Information Set (HEDIS).[25,26] These metrics are used by many health insurance plans, including Medicaid MCOs, to measure performance, including patient access to services and receipt of high-quality care.[25,26]

HEDIS currently includes a care effectiveness measure titled "Eye Exam for Patients with Diabetes" (also known as EED), that measures the percentage of people between ages 18 and 75 with type 1 or type 2 diabetes who had a retinal eye exam during the measurement year.[24,26,31,32,121] The CPT code for AI-enabled diabetic retinopathy analysis,[32i]retinopathy analysis, 92229, is one of the service codes that meets the measure criteria (billed by any provider type).[24,26,31,32,121] The inclusion of autonomous analysis tools within the measure criteria was first announced in a 2020 measure update by NCQA, prior to the activation of the Category

1 CPT code, when the eye exam measure was one component within a broader metric titled "Comprehensive Diabetes Care" (the eye exam portion was subsequently split into its own standalone measure).[26,122,123]

The New York State Department of Health maintains a set of quality assurance reporting requirements measures that health plans collect and report in the domains of adult health, behavioral health, child and adolescent health, experience with care, provider network, and women's health.[99,124] Reporting plan types include commercial plans (both health maintenance organizations, HMOs; and preferred or exclusive provider organizations, PPOs or EPOs); Medicaid managed care plans; specialized Medicaid managed care plans called HIV Special Needs plans; Medicaid managed care plans for individuals with behavioral health conditions called Health and Recovery plans; Child Health Plus plans; and Essential plans.[99,124] The diabetic eye exam HEDIS measure (EED, which includes CPT 92229 in its criteria) is one of the measures reported by plans to the Department of Health each year.[99,124]

In 2024, the adult diabetic eye exam statewide average rates for the different plan types, along with the range reported across individual insurers, were[99]:

- **Commercial (HMO):** 61% statewide (56% to 79% across plans)
- **Commercial (PPO/EPO):** 51% statewide (41% to 65%)
- **Essential:** 63% statewide (57% to 72%)
- **Medicaid Managed Care:** 63% statewide (56% to 71%)
- **Health and Recovery:** 58% statewide (49% to 73%)
- **HIV Special Needs:** 59% statewide (49% to 68%)

Regulation of AI-Enabled Medical Devices

Artificial intelligence-powered tools such as AI-enabled diabetic retinopathy analysis typically are authorized and regulated by the FDA under a category classification termed, "software as a medical device."[29,125,126] Such tools can be authorized for use as devices by the FDA through 3 different pathways[29,127]:

- **510(k) clearance,** for low- or moderate-risk devices that demonstrate "substantial equivalence" in safety and efficacy to another device already on the market (known as a "predicate device")
- **De Novo classification**, another type of FDA clearance for low- or moderate-risk devices without a comparator predicate device; this pathway results in FDA *authorization* of the device
- **Premarket approval (PMA)**, an FDA regulatory classification requiring a higher level of evidence and review that determines the device is both safe and effective; this pathway results in FDA *approval of the* device

Tools like AI-enabled diabetic retinopathy analysis can be further described as "software as a service" (SaaS) applications (not a regulatory classification), which use algorithm-powered software to help health care providers make clinical assessments (in the of case of this technology review, helping to screen and diagnose diabetic retinopathy).[29] The FDA maintains an ongoing list of authorized Artificial Intelligence-Enabled Medical Devices, now more than 1,400 entries.[128] Research has shown that the vast majority of these products are cleared through the 510(k) pathway.[129] Once approved, authorized, or cleared by the FDA, the companies marketing

such technologies often contract with health care providers to supply them with the technology for a certain fee (e.g., subscription or single use-based); providers then submit billing claims to insurers each time the AI-enabled service or product is used for patient care.[119,125,130,131]

Medicare Coverage of AI-Enabled Diabetic Retinopathy Analysis

Medicare's coverage of AI-enabled diabetic retinopathy analysis offers an early example of large-scale coverage decisions and considerations for these types of tools. Once approved, authorized, or cleared by the FDA, SaaS applications can receive Medicare coverage if they fit into a Medicare benefit category and meet other statutory requirements including "being reasonable and necessary for the treatment of illness and injury."[29,125] Medicare, like other payers, also has to determine the appropriate payment methodology for software products such as AI-enabled diabetic retinopathy analysis, which are typically separate from a medical device (often working on top of or augmenting the products of other devices and technologies, like image files)—for example, if the payment should be bundled as part of a larger episode of care alongside other related services, or paid separately.[29,125,130-132]

In 2018, after the FDA's original authorization of the IDx-DR system through the De Novo pathway, the service started to receive Medicare reimbursement under the Outpatient Prospective Payment (OPPS) system, initially as part of a "bridge payment" with status indicator "Q1," meaning that it was that packaged into payment with separately payable services provided during the same visit.[29,133,134] This was done through temporary bridge coding with 92250-TC, the technical component of the CPT code for fundus photography.[29,135]

During the next several years, AI-enabled diabetic retinopathy analysis received more explicit attention through its initial reference within the American Diabetes Association's Standard of Diabetes Care guidelines in 2019,[136] its inclusion in the HEDIS quality measure for diabetic eye exams in 2020,[122] and the creation of Category 1 CPT code 92229 specifically for AI-enabled autonomous analysis and report of retinal imaging that became active in January 2021.[27,30,120] Starting in 2021, Medicare provided separate payment for the service under the OPPS system.[71] The service also receives separate reimbursement under the Medicare Physician Fee Schedule, first through carrier pricing by Medicare Administrative Contractors, until a national payment rate with set relative value units was established in 2022.[29,34]

Reported Utilization of AI-Enabled Diabetic Retinopathy Analysis

Because AI-enabled diabetic retinopathy services have received reimbursement under a specific CPT code since 2021, claims-based utilization data on the service is now emerging. A 2025 analysis of Medicare claims by Manatt Health showed that CPT code 92229 was the second-most heavily used AI-enabled device code between 2018 and 2023.[36] The number of Medicare beneficiaries receiving the service jumped from 1,327 in 2021 (the first year that the separate Category 1 CPT code was active) to 16,085 members in 2023[36] (there are currently ~70 million Medicare beneficiaries[137]). A 2023 study analyzed a large commercial payer database of more than 210 million unique people with more than 11 billion CPT claims between January 2018 and June 2023 and identified more than 15,000 total claims for CPT code 92229 starting in 2021, with monthly claims jumping from less than 100 at the start of 2022 to around 300 per month in 2023.[35] Another analysis of both Medicare and commercial claims data from 2019 to 2023

showed similar trends,[130] while an analysis of patient health records showed more consistent use from 2019 to 2023.[138]

Methods

This review is based on KQs identified by the New York State Department of Health. Search parameters, KQs, and methodologies for identifying, assessing, and reporting evidence are described in the following sections. While we typically limit inclusion to studies conducted in countries rated as *very high* on the United Nations Human Development Index, we included diagnostic accuracy studies conducted in any country to ensure that we captured evidence related to performance of these AI-enabled diagnostic screening tools across the full diversity of the populations that have been studied. Additional details are available in the Evidence Based Benefit Review Advisory Committee Methods Manual online and Appendix C.

Key Questions

The aim of this report is to evaluate the evidence related to diagnostic accuracy, clinical utility, and potential harms of autonomous AI-enabled diagnostic screening tools for identification of diabetic retinopathy, while providing contextual information from clinical practice guidelines, cost-effectiveness studies, and coverage policy reviews. Our research was guided by the following KQs.

KQ1. What is the diagnostic accuracy of AI-enabled, FDA-cleared devices for autonomous detection of diabetic retinopathy in individuals with type 1 or type 2 diabetes?

- a. Does diagnostic accuracy vary by patient characteristics (e.g., age, sex) or condition characteristics (e.g., type of diabetes, duration of diabetes)?
- b. Does diagnostic accuracy vary by characteristics of the images obtained (e.g., quality of fundus images)?

KQ2. What is the clinical utility of AI-enabled, FDA-cleared devices for autonomous screening for diabetic retinopathy in individuals with type 1 or type 2 diabetes?

- a. Does clinical utility vary by patient characteristics (e.g., age, sex) or condition characteristics (e.g., type of diabetes, duration of diabetes)?

KQ3. What are the harms of using AI-enabled, FDA-cleared devices to autonomously diagnose diabetic retinopathy in individuals with type 1 or type 2 diabetes?

- a. Do harms vary by patient characteristics (e.g., age, sex) or condition characteristics (e.g., type of diabetes, duration of diabetes)?
- b. Do harms vary by characteristics of images obtained (e.g., quality of fundus images)?

KQ4. What are the results of relevant US-based cost analyses of AI-enabled FDA-cleared devices used to autonomously diagnose diabetic retinopathy in individuals with type 1 or type 2 diabetes?

KQ5. What do clinical practice guidelines recommend regarding the use of AI-enabled, FDA-cleared devices to autonomously diagnose diabetic retinopathy in individuals with type 1 or type 2 diabetes?

KQ6. What are relevant Medicaid, Medicare and private health plan coverage policies for screening for diabetic retinopathy among individuals with type 1 or type 2 diabetes?

Study Eligibility Criteria

As AI-enabled diagnostic screening systems are only FDA-cleared for use in adults with diabetes, we focused our analysis on this population (Table 4).

Table 4. Key Study Inclusion Criteria

Study Component	Inclusion Criteria
Populations	Adults who meet American Diabetes Association criteria for diabetic retinopathy screening: Diagnosis of Type 1 diabetes for ≥ 5 years Diagnosis of Type 2 diabetes
Interventions	AI-enabled devices FDA-cleared on or before April 1, 2026, for autonomous screening for diabetic retinopathy, including: AEYE-DS (AEYE Health) EyeArt (Eyenuk) LumineticsCore, formerly IDx-DR (Digital Diagnostics)
Comparators	Usual care (retinal screening by an optometrist or ophthalmologist) Clinical reference standard grading of fundus photographs based on ICDR or ETDRS classification criteria Another FDA-cleared device for screening for diabetic retinopathy
Outcomes	Critical (will be presented in GRADE tables) Measures of diagnostic accuracy (i.e., sensitivity, specificity, positive predictive value, negative predictive value, area under the curve, positive likelihood ratio, negative likelihood ratio) Diagnosis and classification of diabetic retinopathy (i.e., proportion of patients with a finding of more-than-mild diabetic retinopathy or vision-threating diabetic retinopathy) Adverse events Important (will not be presented in GRADE tables) Proportion of ungradable results (non-readable images and inconclusive results) Specialist referral rate compared to reference standard of human grading
Timing and follow up	No minimum follow up (KQs 1–2) Cost-effectiveness analyses published within 5 years (KQ4) Guidelines published, reviewed and reaffirmed, or updated within 5 years (KQ5)
Setting	Studies conducted in any country, regardless of Human Development Index (KQ1) Studies conducted in countries categorized as very high on the Human Development Index (KQs 2–3) Studies conducted in US, or using US-based health systems data (KQ4) Guidelines developed by organizations in countries categorized as very high on the Human Development Index (KQ5)
Study design	KQ1 (diagnostic accuracy) Randomized controlled trials Controlled prospective observational studies Diagnostic accuracy studies KQ2 (clinical utility) Randomized controlled trials Controlled prospective observational studies KQ3 (harms)

Study Component	Inclusion Criteria
	Randomized controlled trials Observational studies (prospective or retrospective) KQ4 (cost-effectiveness) Evidence-based clinical practice guidelines that provide specific treatment recommendations KQ5 (clinical practice guidelines) Evidence-based clinical practice guidelines that provide specific treatment recommendations
Sample size	Minimum of 20 participants per study arm
Publication type	Peer-reviewed publication of primary study results Published in the English language Ancillary publications with additional comparative follow up or prespecified subgroup analysis

Abbreviations. ETDRS: Early Treatment Diabetic Retinopathy Study; FDA: US Food and Drug Administration; GRADE: Grading of Recommendations Assessment, Development, and Evaluation; ICDR: International Clinical Diabetic Retinopathy; KQ: key question; US: United States.

Evidence and Policy Searches

An information specialist from the Center for Evidence-based Policy (Center) searched Ovid MEDLINE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and other information sources for studies evaluating test accuracy, cohort studies, cost and cost-effectiveness studies, and clinical practice guidelines. A Center information specialist also searched trial registries for relevant ongoing trials. Searches were conducted January 9, 2026, through January 14, 2026, and March 4, 2026 (clinical trial registries). A full list of searched sources and search strategies is provided in Appendix A.

A Center policy analyst searched 9 state Medicaid program websites, 8 health plan websites, the Medicaid State Waivers List, and the Centers for Medicare & Medicaid Services (CMS) for local and national coverage determinations and broader coverage policy documentation of AI-enabled diabetic retinopathy analysis. Appendix A lists the search terms we used to identify relevant policies, as well as the sources we searched.

Screening and Inclusion

Two Center researchers used the DistillerSR systematic review software platform to screen publications identified in the searches using the detailed inclusion and exclusion criteria listed in Appendix B. Disagreement about inclusion was resolved through discussion. Appendix D lists included studies, and Appendix G lists studies excluded during full text screening along with the primary reason each study was excluded. Figure 1 shows the numbers of studies screened and included or excluded at each step.

Risk of Bias Assessment

Two Center researchers assessed each included study for risk of bias using standard forms. Appendix E has detailed tables with criteria considered for assessing risk of bias or methodological quality. Disagreement between the researchers was resolved through discussion.

Data Abstraction

One Center researcher used a standard form to extract all data presented in tables, and a second researcher verified each data point against the original publication for a random selection of 25% of included studies. One Center researcher assessed the suitability of outcome data for meta-analysis, and a second researcher reviewed outcome data and confirmed final decisions regarding meta-analysis.

Synthesis

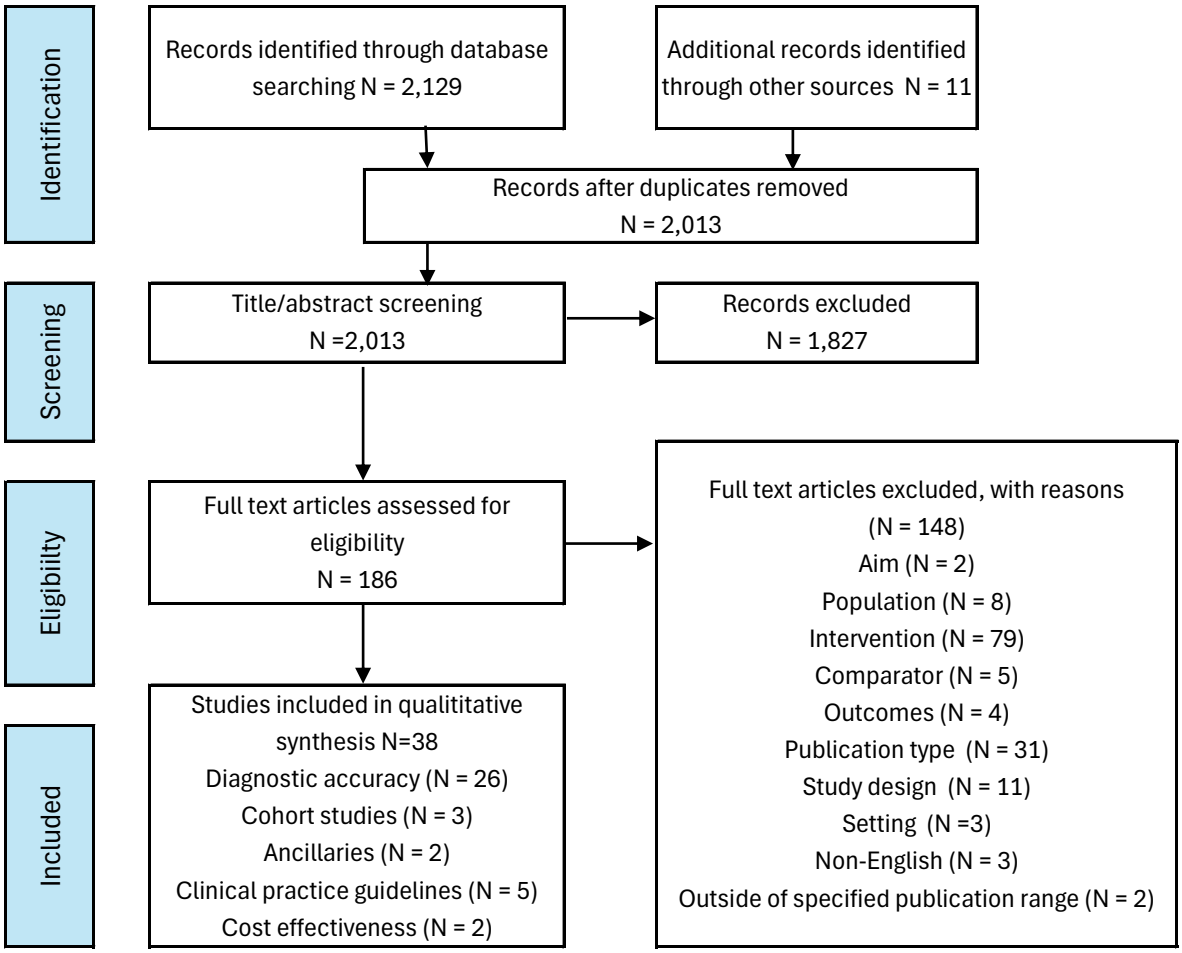
Due to the heterogeneity of included studies arising from differences in dilation protocols and handling of ungradable images in analysis, we did not conduct any meta-analysis for this topic. We provide a qualitative synthesis of data from the included studies, together with tables to summarize study characteristics and outcomes. We applied the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach to rate the certainty of evidence prespecified key outcomes (Appendix F).[139] The GRADE system defines the overall quality of a body of evidence for an outcome in the following manner[139]:

- **High (randomized controlled trials [RCTs] start here):** Raters are very confident that the estimate of the effect of the intervention on the outcome lies close to the true effect. Typical sets of studies are RCTs with few or no limitations, and the effect estimate is likely stable.
- **Moderate:** Raters are moderately confident in the estimate of the effect of the intervention on the outcome. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is different. Typical sets of studies include RCTs with some limitations or well-performed nonrandomized studies with additional strengths that guard against potential bias and have large estimates of effects.
- **Low (nonrandomized studies start here):** Raters have little confidence in the estimate of the effect of the intervention on the outcome. The true effect may be substantially different from the estimate of the effect. Typical sets of studies include RCTs with serious limitations or nonrandomized studies without special strengths.
- **Very low:** Raters have no confidence in the estimate of the effect of the intervention on the outcome. The true effect is likely to be substantially different from the estimate of the effect. Typical sets of studies include nonrandomized studies with serious limitations or inconsistent results across studies.
- **Not applicable:** Researchers did not identify any eligible studies.

Evidence Review

The initial evidence search identified 2,013 potentially relevant publications (Figure 1). Following full text review, we identified 26 diagnostic accuracy studies reported in 28 publications, 3 cohort studies, 5 clinical practice guidelines, and 2 cost-effectiveness studies that addressed 1 or more of the KQs. Additionally, we identified 3 ongoing clinical trials.

Figure 1. Prisma Diagram of the Study Selection Process



KQ1. Diagnostic Accuracy

EyeArt and IDx-DR

We identified 26 diagnostic accuracy studies reported in 28 publications. Of these, 14 studies (16 publications) assessed EyeArt,[7,10,15,16,19,21,38-43,52-54,140] 11 studies (11 publications) assessed IDx-DR,[17,18,20,44-48,50,51,55] and 1 study included EyeArt and IDx-DR.[49]

AEYE-DS

We did not identify any published diagnostic accuracy studies for AEYE, which was FDA-cleared for identification of more-than-mild diabetic retinopathy on November 10, 2022. The AEYE Health team has several publications related to development and validation of different AI models (Table 5), but none were related to the FDA-cleared diagnostic screening tool for detection of diabetic retionopathy.[141-146] The company's FDA 510(k) applications refer to 2 different studies—1 enrolling 317 subjects and the other enrolling 362 subjects—but do not provide citations for any published studies or clinical trial identification numbers.[11,147] Published work by the AEYE Health research team related to other AI products references the company's FDA applications as the only source of information for diagnostic accuracy information related to the AEYE diabetic retinopathy screening tool.[141,144] There were 3 records in ClinicalTrials.gov for

the AEYE diabetic retinopathy screening tool,[37,148,149] only 1 of which included study results (NCT04612868).[37] While the study protocol did include a section for previous clinical studies with the investigational device, the entirety of the section is redacted,[37] which would indicate prior work related to algorithm development, rather than testing of the AEYE screening tool. In the absence of any peer-reviewed publications related to AEYE, we included results of this study from the ClinicalTrials.gov record in analysis for KQs 1 and 2.[37]

Table 5. Published Studies From the AEYE Research Team

Author Year	Focus
Bressler 2024[143]	Training AI to discern laser patterns in patients who have received laser photocoagulation, for disease management and follow up
Bressler 2025[141]	Development and validation of an autonomous screening tool for detection of diabetic macular edema (a complication of diabetic retinopathy)
Bressler 2026[142]	Development of a deep learning model for non-contact optimal blood pressure biometry
Dvey-Aharon 2026[146]	Development of a machine-learning algorithm for glaucoma detection
Rom 2022[145]	Training of a tool to predict future development of DR, not to identify current DR
Rom 2024[144]	Training a machine-learning algorithm for diabetes detection from non-diabetic retinopathy fundus images

Abbreviations. AI: artificial intelligence; DR: diabetic retinopathy.

Reporting of Diagnostic Accuracy Results

Table 6 summarizes characteristics for the 26 published studies related to EyeArt and IDx-DR and the unpublished study related to AEYE. Methods varied across studies for dilation protocols and handling of images that the AI tool deemed ungradable. Standard protocols for all 3 AI-based screening tools stipulate reflex dilation—where camera operators make a preset number of attempts to capture images readable by the AI system, after which pupils are pharmacologically dilated if time allows.[11-13] Patients were imaged without any dilation in 8 EyeArt studies[16,21,38-43] and 6 IDx-DR studies.[20,44-48] Reflex dilation was used in 2 EyeArt studies (including 1 that provided results for both no dilation and reflex dilation),[38,49] 4 IDx-DR studies,[18,49-51] and the sole AEYE study.[37] All patients had their pupils dilated prior to image capture in 6 EyeArt studies[10,15,19,52-54] and 1 IDx study.[55] One IDx-DR study did not report on dilation of participants' pupils.[17] Eight EyeArt studies omitted patients with any image the AI screener judged ungradable (Appendix Table H1),[15,16,21,38,40,42,43,49] 6 EyeArt studies included ungradable images as referable in diagnostic accuracy calculations (Appendix Table H2),[10,19,39,41,52,54] and 1 EyeArt study reported diagnostic accuracy when ungradable images were included and when they were excluded.[53] Ten IDx-DR studies omitted patients with any image the AI screener judged ungradable (Appendix Table H1),[17,18,20,45-50] 1 included patients with ungradable images as referrable (Appendix Table H2), and 2 IDx-DR study reported diagnostic accuracy when ungradable images were included and when they were excluded.[44,51]

Both IDx-DR and AEYE are FDA-cleared solely for identification of more-than-mild diabetic retinopathy,[11,13] while EyeArt is cleared for identification of both more-than-mild and vision-threatening diabetic retinopathy.[12] Our ratings of certainty of evidence focus solely on identification of more-than-mild diabetic retinopathy and exclude results from 3 studies that did not address this question. One EyeArt study and 1 IDx-DR study reported results only for identification of any diabetic retinopathy and do not provide information on the AI-based screeners' ability to identify more-than-mild diabetic retinopathy (Appendix Table H3).[17,43] While flagging any indication of retinopathy (including mild and non-referrable cases) is unlikely to miss any potential cases of diabetic retinopathy, the algorithms were not trained for this purpose and the indiscriminate approach to screening leads to exceedingly low positive predictive values (Appendix Table H3). All studies provided results on a per-patient basis, with the exception of a single EyeArt study (Sarao et al., 2020) that presented results on a per-eye basis and thus had limited ability to demonstrate diagnostic accuracy, as patients were referred for follow up on the basis of their worst eye (i.e., patients were diagnosed, not individual eyes) (Appendix Table H3).[15]

Table 6. Characteristics of Included Diagnostic Accuracy Studies

Author, Year Version Study Design Location RoB	Participant Demographics	Dilation Protocol	Handling of AI-Ungradable Images
AEYE			
Unpublished clinical trial data NCT04612868 Prospective cohort US NA	N = 468 Mean age (range): 55 y (21 to 28) Female, n (%): 246 (52.6) • Race, n (%): • White, 323 (69.0) • Asian, 9 (1.9) • Black, 132 (28.2) • American Indian or Alaska Native, 1 (0.2) • Mixed, 2 (0.4) • Unspecified, 1 (0.2) Children included: No	Reflex dilation (after 3 attempts)	Excluded
EyeArt			
Bhaskaranand, 2019 v2.0 Retrospective cohort US and International Moderate	N = 101,710 patients Mean age (SD): NR Female, n (%): NR Race: NR Children included: NR	Combines dilated, undilated, and unknown	Ungradable = referable
Guedes, 2025 Version 2.1.0 Prospective cohort Canary Islands (Spain) Moderate	N = 499 Mean age (SD): 65.1 (11) Female, n (%): 232 (46.5) Race, n (%): NR Children included: No	None dilated	Excluded

Author, Year Version Study Design Location RoB	Participant Demographics	Dilation Protocol	Handling of AI-Ungradable Images
Heydon, 2021 Version 2.1 Prospective cohort UK Moderate	N = 30,405 Mean age (range): Mean from 60 to 66 y across 3 sites (range 12 to 107) Female, %: 43 to 46 across 3 sites Race, % range across 3 sites: • White European, 35.8 to 66.9 • Asian, 2.5 to 43.0 • Black, 1 to 26.3 • Mixed, 0.5 to 2.1 • Unspecified, 4.6 to 29.3 Children included: 12 and older	All dilated	Ungradable = referable
Ibanez-Bruron, 2024 Version NR Retrospective cross sectional Chile High	N = 366 Mean age (SD): 61 y (14) Female, n (%): 223 (61) Race, n (%): NR Children included: NR	All dilated	Analyses with and without inclusion of ungradable
Ipp, 2021 v 2.1.0 Prospective cohort US High	N = 235 Mean age (SD): 51.9 y (10.0) in 45 patients from primary care sites, 60.5 y (11.0) in 190 patients from eye care sites Female, n (%): 137 (58.3) Race, n (%): • White, 137 (73.6) • Asian, 9 (3.8) • Black, 40 (17.0) • Native Hawaiian or Pacific Islander, 1 (0.4) • Other, 12 (5.1) Children included: No	Analyses for those without any dilation and those with reflex dilation	Excluded
Karabeg, 2025 Version 2.1.0 Prospective cohort Norway Moderate	N = 128 Median age (IQR): 52.5 y (44.5 to 64.5) Female, n (%): 51 (39.8) Race, n (%): NR Children included: No	None dilated	Excluded
Liu, 2021 v 2.0 Prospective cohort US Moderate	N = 185 Mean age (SD): 57.4 y (11.4) Female, n (%): 97 (53.9) Race, n (%): • White, 27 (15.0) • Black, 141 (78.3) • Other, 10 (5.6) • Unspecified, 2 (1.1) Children included: No	None dilated	Ungradable = referable

Author, Year Version Study Design Location RoB	Participant Demographics	Dilation Protocol	Handling of AI-Ungradable Images
Mokhashi, 2022 Version NR Retrospective cohort US Moderate	N = 260 Mean age (SD): 60.7 y (11.7) Female, n (%): 158 (60.8) Race, n (%): • Black, 205 (78.8) • Caucasian, 12 (4.6) • Hispanic White, 37 (14.2) • Asian or Pacific Islander 3 (1.2) • Other 3 (1.2) Children included: No	None dilated	Excluded
Olvera-Barrios, 2021 v 2.1.0 Retrospective cohort UK High	N = 1257 Mean age (SD): NR Female, n (%): NR Race, n (%): NR Children included: None	All dilated	Ungradable = referable
Sarao, 2020 v 2.1 Prospective observational Italy High	N = 165 Mean age (SD): 64.7 y (14) Female, n (%): 77 (47) Race, n (%): NR Children included: No	All dilated	Excluded
Tufail, 2016 Version NR Retrospective cohort England Moderate	N = 20,258 patients Median age: 60.0 y (IQR 50.4 to 70.4) Female, n (%): 9319 (46) Race, %: • White European, 41.4 • Asian, 34.7 • Black, 19.6 • Mixed, 0.7 • Other, 3.7 Children included: 12 and up	All dilated	Ungradable = referable
Van, 2024 v 2.0 Retrospective cohort Vietnam Moderate	N = 583 Mean age (SD): 61.8 y (10.5) Female, n (%): 346 (59.3) Race, n (%): NR Children included: No	None dilated	Excluded
Vought, 2023 Version NR Retrospective observational US High	N = 62 Mean age (SD): 64 y (NR) Female, n (%): 34 (56) Race, %: • Caucasian (Portuguese), 69% • Hispanic, 21% • African American, 10% Children included: No	None dilated	Ungradable = referable

Author, Year Version Study Design Location RoB	Participant Demographics	Dilation Protocol	Handling of AI-Ungradable Images
Wintergerst, 2022 v 2.1 Prospective cohort Germany High	N = 72 Mean age (SD): 68.95 y (11.41), range 32 to 86 Female, n (%): 38 (50.75) Race, n (%): NR Children included: No	None dilated	Excluded
IDx-DR			
Abramoff, 2018 Version NR Prospective observational US Moderate	N = 819 Median age (range): 59 y (22 to 84) Female, %: 52.5% Race, %: • Hispanic, 16.1% • Not Hispanic, 83.3% • White, 63.4% • Black, 28.6% • Asian, 1.6% Children included: No	Reflex dilation	Excluded
Dow, 2023 Version NR Prospective cohort and retrospective analysis US High	N = 1222 Mean age (range): 58.4 y (21 to 98) Female, n (%): 540 (44.2) Race, %: • Asian, 33.1% • Black, 7.4% • Hispanic or Latino, 21.2% • Native American or Pacific Islander, 2.5% • White, 25% • Non-Hispanic other, 10.8% Children included: No	None dilated	Analyses with and without inclusion of ungradable
Grzybowski, 2025 Version NR Retrospective cohort Poland Moderate	N = 758 Mean age (SD): NR Female, n (%): NR Race, n (%): NR Children included: NR	None dilated	Excluded
Grzybowski, 2023 Version NR Retrospective cohort Poland High	N = 807 Mean age (SD): NR Female, n (%): NR Race, n (%): NR Children included: NR	None dilated	Excluded

Author, Year Version Study Design Location RoB	Participant Demographics	Dilation Protocol	Handling of AI-Ungradable Images
Mehra, 2022 Version NR Retrospective cohort US Moderate	N = 1,052 Mean age (SD): NR Female, n (%): 421 (40) Race, n (%): • White, 815 (78) • Hispanic, 18 (2) • Black, 72 (7) • Other, 118 (11) Children included: No	Reflex dilation	Excluded
Poschkamp, 2025 Version NR Prospective cohort Germany Moderate	N = 1,716 patients Mean age (SD): 50.4 y (18.5) Female, n (%): 729 (72.5) Race, n (%): NR Children included: age 6 and up	None dilated	Excluded
Riotto, 2024 Version NR Retrospective cohort Switzerland High	N = 1,141 Mean age (SD): NR Female, n (%): NR Race, n (%): NR Children included: NR	Not reported	Excluded
Sedova, 2022 v. 2.2 Prospective cohort Austria High	N = 54 Mean age (SD): 55 y (15.5) Female, n (%): 21 (39) Race, n (%): NR Children included: No	None dilated	Excluded
Shah, 2021 v. 2.0 Retrospective cohort Spain High	N = 2,680 Median age: 74 y Female, n (%): 1,942 (55) Race, n (%): NR Children included: NR	All dilated	Excluded
van der Heijde, 2018 v. 2.0 Retrospective cohort Netherlands High	N = 898 Mean age (SD): 65.0 y (11.9) Female, n (%): 311 (43.9) Race, n (%): NR Children included: NR	None dilated	Excluded
Verbraak, 2019 v. 2.1 Retrospective cohort Netherlands Moderate	N = 1,293 Mean age (SD): 63 y (11.3) Female, %: 47 Race, n (%): NR Children included: NR	Reflex dilation	Analyses with and without inclusion of ungradable
Tested clinical effectiveness of both EyeArt and IDx			
Musetti, 2025 EyeArt v 2.0, IDx-DR NR Prospective cohort Switzerland High	N = 201 Mean age (SD): 65.03 y (13.1) Female, n (%): 93 (46.3) Race, n (%): NR Children included: No	Reflex dilation	Excluded

Abbreviations. NR: not reported; RoB: risk of bias; SD: standard deviation; y: years.

Diagnostic Accuracy Results

The following pages summarize key diagnostic accuracy information for the different study protocols: when cases considered ungradable by the AI-based screening tools were omitted (Appendix Table H1) or when ungradable cases were considered referable (Appendix Table H2). Tables are further categorized by pupil dilation protocol (all patients dilated, no patients dilated, or the reflex dilation protocol used). We report sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios if they were presented in the publications or could be derived from outcome tables (confusion matrices) provided by the authors.

Sensitivity and specificity are measures that describe how well a clinical test performs.[56] Sensitivity describes the proportion of true positive tests out of all patients with diabetic retinopathy, while specificity denotes the percentage of true negatives out of all subjects who do not have diabetic retinopathy.[56] A test's predictive value is directly related to prevalence of the disease in the population (i.e., as prevalence increases, positive predictive value will increase but negative predictive value will decrease).[150] Positive predictive value describes the probability that a person has the disease if they test positive; conversely, negative predictive values denote the probability that a person is disease-free if they test negative.[150,151] In the absence of data from a confusion matrix, calculation of positive and negative predictive values requires assumptions about disease prevalence, which can vary by population included in the study.[56] For this reason, we did not calculate positive or negative predictive values if they were not provided by the authors, unless a confusion matrix was included in the publication or could be constructed from provided information.

While predictive values relate broadly to populations, likelihood ratios are more applicable to decision making about individual patients.[152,153] The positive likelihood ratio is a measure of how much more likely a positive test result is in someone with the condition compared to someone without it, while the negative likelihood ratio is a measure of how much less likely a negative test result is in someone with the condition compared to someone without it.[152-154] The ideal value for a positive likelihood ratio to rule in a diagnosis is ≥ 10, while the ideal value for a negative likelihood ratio to rule out a diagnosis is < 0.1.[153,154] When the values of likelihood ratios, whether positive or negative, are close to 1, it indicates that the test has little clinical utility.[153,154]

EyeArt for Identification of More-Than-Mild Diabetic Retinopathy

Figures 2 through 6 illustrate the range of sensitivity and specificity values in reported in different studies, grouped by study design. Studies that did not include confusion matrices, or did not provide enough information for us to construct one, are represented by zero values in the forest plots because we do not know the confidence intervals of their estimates. When cases rejected by the algorithm as ungradable were omitted from analysis (Table H1), sensitivity for EyeArt ranged from a low of 75% (Wintergerst 2022) to a high of 100% (Mokhashi 2022) in studies where patients' eyes were not dilated,[21,40] but were 95.5% (Ipp 2021) and 100% (Musetti 2025) in studies that used reflex dilation and 92% in a study in which all patients' eyes were dilated (Ibanez-Bruron 2024).[38,49,53] Specificity ranged from 78% to 98% in studies without dilation[16,21,38,40,42] and from 73% to 88% in studies that included dilation.[38,49,53]

When ungradable cases were considered referrals (Appendix Table H2), sensitivity and specificity were 74% and 87% (Vought 2023) and 100% and 66% (Liu 2021) in the 2 studies that did not include dilation.[39,41] Data from the study by Vought and colleagues (2023) could not be incorporated into Figure 2, however, because data is limited to sensitivity and specificity figures without confidence intervals.[41] When all patients had pupil dilation prior to fundus imaging, sensitivity ranged from 91% (Tufail 2016) to 96% (Olvera-Barrios 2021 and Heydon 2021),[10,19,54] while specificity ranged from 37% (Tufail 2016) to 74% (Ibanez-Bruron 2024).[10,53] In a study by Bhaskaranand and colleagues (2019) that combined retrospective data from patients who were dilated, undilated, or dilation unknown, both sensitivity and specificity were 91%.[52]

Figure 2: EyeArt Sensitivity and Specificity in Non-Dilated Eyes, With Ungradable Images Treated as Referrals

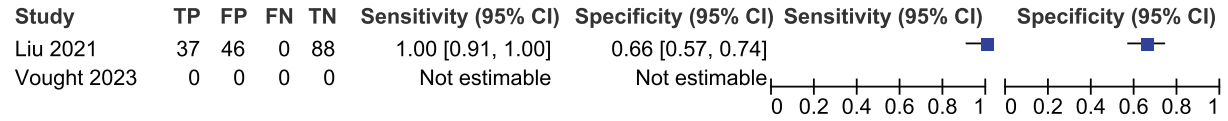


Figure 3. EyeArt Sensitivity and Specificity in Non-Dilated Eyes, With Ungradable Images Omitted From Analysis

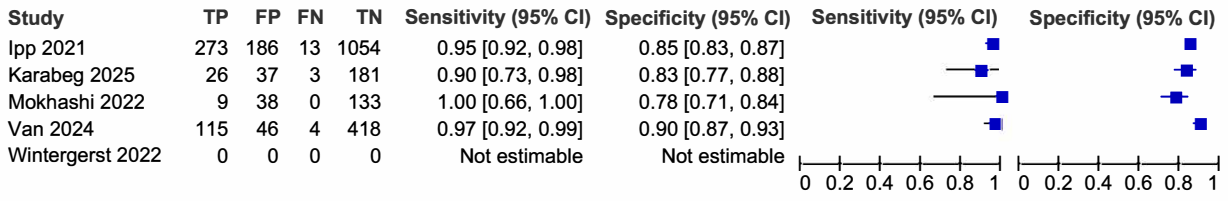


Figure 4. EyeArt Sensitivity and Specificity With Reflex Dilation, With Ungradable Images Omitted From Analysis

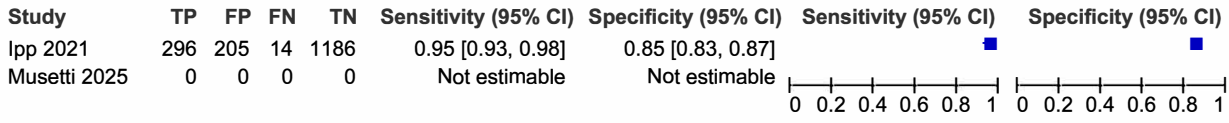


Figure 5. EyeArt Sensitivity and Specificity in Dilated Eyes, With Ungradable Images Treated as Referrals

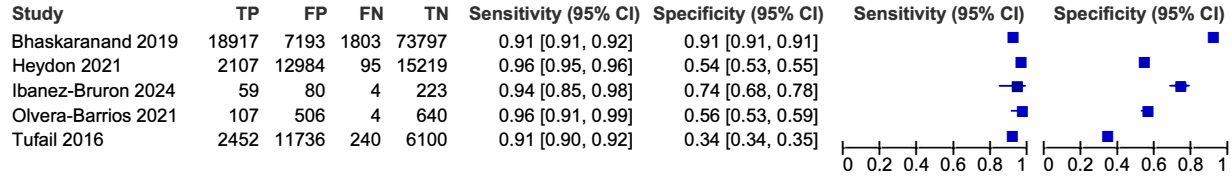
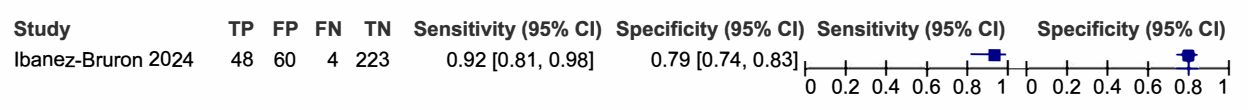


Figure 6. EyeArt Sensitivity and Specificity in Dilated Eyes, With Ungradable Images Omitted From Analysis



IDx-DR for Identification of More-Than-Mild Diabetic Retinopathy

Figures 7 through 11 illustrate the range of sensitivity and specificity values in reported in different studies, grouped by study design. As in the EyeArt section, studies that did not include confusion matrices, or did not provide enough information for us to construct one, were represented by zero values in the forest plots because we did not know the confidence intervals of their estimates. When cases rejected by the algorithm as ungradable were omitted from analysis (Appendix Table H1), sensitivity for IDx-DR ranged from 68.5% (van der Heijden 2018) to 100% (Sedova 2022) for patients without dilation and specificity ranged from 47% (Sedova 2022) to 98% (Dow 2023) (Figure 9).[20,44,48] In the 4 studies that used reflex dilation, sensitivity ranged from 79% (Verbraak 2019) to 100% (Mehra 2022), while specificity ranged from 66% (Musetti 2025) to 94% (Verbraak 2019) (Figure 10).[50,51] In the single study in which all patients had their pupils dilated (Shah 2021), sensitivity was 100% and specificity was 82% (Figure 11).[55]

Only 2 studies of IDx-DR reported diagnostic accuracy results when ungradable cases were considered referrals.[44,51] The study by Dow and colleagues reported a sensitivity of 95% and specificity of 93% in patients without dilation (Figure 7).[44] The study by Verbraak and colleagues (2019), used a reflex dilation protocol, reported a sensitivity and specificity of 82% and 85% (Figure 8).[51]

Figure 7: IDx-DR Sensitivity and Specificity in Non-Dilated Eyes, With Ungradable Images Treated as Referrals

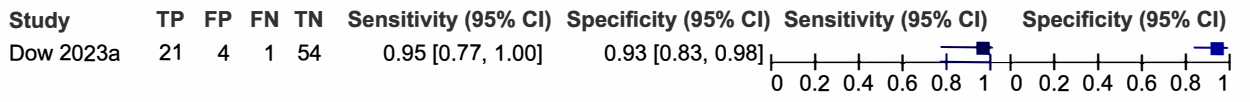


Figure 8. IDx-DR Sensitivity and Specificity With Reflex Dilation, With Ungradable Images Treated as Referrals

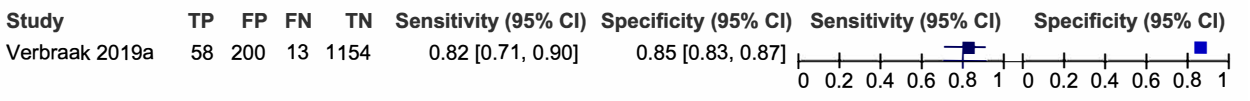


Figure 9. IDx-DR Sensitivity and Specificity in Non-Dilated Eyes, With Ungradable Images Omitted From Analysis

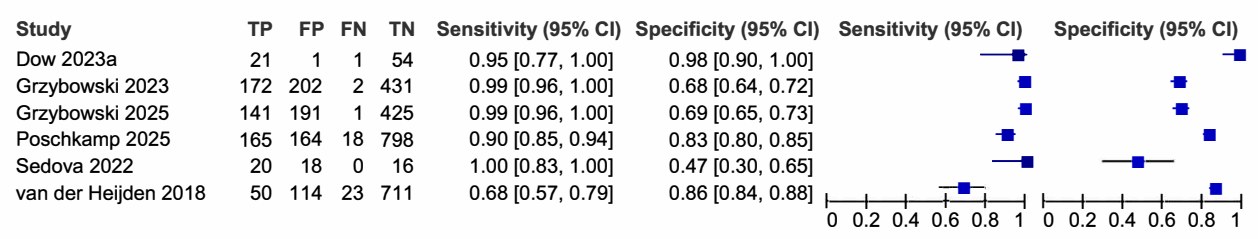


Figure 10. IDx-DR Sensitivity and Specificity With Reflex Dilation, With Ungradable Images Omitted From Analysis

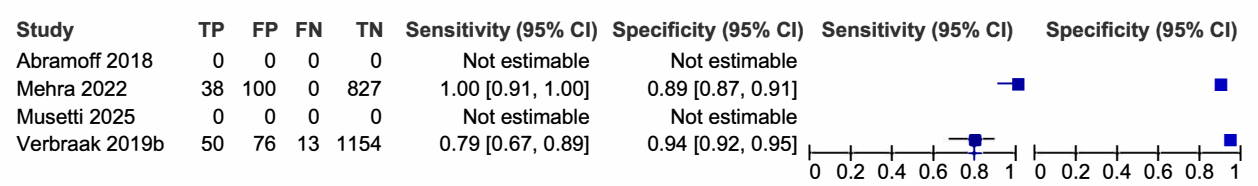
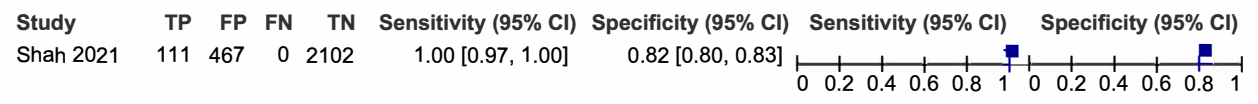


Figure 11. IDx-DR Sensitivity and Specificity in Dilated Eyes, With Ungradable Images Omitted From Analysis



AEYE-DS for Identification of More-Than-Mild Diabetic Retinopathy

While no published diagnostic accuracy results were available for AEYE, the ClinicalTrials.gov record for NCT04612868 included results for 462 individuals who had fully analyzable data with results from a professional reading center (based on worst eye analysis) and AEYE-DS results (87% of 531 enrolled patients).[37] The study was designed to validate the safety and efficacy of the AEYE-DS device at primary care and other point-of-care sites in the Louisville, Kentucky area.[37] A novice camera operator at each study site captured fundus images with the TopCon NW400 device.[37] The study protocol describes a reflex dilation approach, with pharmacologic dilation following 3 imaging attempts by a novice operator if AEYE still indicated that at least 1 image was of insufficient quality.[37] Images captured by the novice camera operator were uploaded to AEYE for analysis, providing 1 of 3 possible outputs: insufficient image quality, positive for more-than-mild diabetic retinopathy, or negative for more-than-mild diabetic retinopathy.[37] Following the AEYE portion of the protocol, all study subjects underwent pharmacologic dilation (if not already completed) and had images captured by a trained ophthalmic photographer.[37] All images captured—both dilated and undilated—were submitted to a professional grading service for assessment, with their findings serving as the reference standard.[37] Any patient with an ungradable image as judged by AEYE was omitted from analysis (Table H1).[37] The device protocol called for macula and disc-centered color fundus images with at least a 45° field of view and 2 images per eye or, alternately, macula-centered color fundus images with at least a 45° field of view, 1 image per eye.[37] With 2 images (1 per eye) submitted to AEYE, sensitivity was reported as 92.98% (95% confidence interval [CI], 83.3 to 97.24) and

specificity as 91.36% (95% CI, 88.22 to 93.72).[37] With 4 images (2 per eye) submitted to AEYE, sensitivity was 94.74% (95% CI, 85.63 to 98.19) and specificity was 88.64% (95% CI, 85.18 to 91.38).[37] No predictive values (positive or negative) were provided and data was not sufficient for constructing a confusion matrix to calculate these outcomes.[37]

EyeArt for Identification of Vision-Threatening Diabetic Retinopathy

Seven EyeArt studies reported diagnostic accuracy results for prediction of vision-threatening diabetic retinopathy (Appendix Table H3).[10,16,38,39,42,53,54] When cases rejected by the algorithm as ungradable were omitted from analysis, sensitivity ranged from 50% in a study in which no patients had pupil dilation (Karabeg) to 100% in a study in which all patients were dilated (Ibanez-Bruron 2024) and a study in which no patients were dilated (Van 2024).[16,42,53] Specificity was > 90% in all studies where ungradable images were omitted.[16,38,42,53]

Four EyeArt studies reported diagnostic accuracy results for prediction of vision-threatening diabetic retinopathy where ungradable results were categorized as referrals.[10,39,53,54] Sensitivity ranged from 67% in 1 study where no patients had pupils dilated (Liu 2022) to 100% in 2 studies where all patients were dilated (Ibanez-Bruron 2024; Olvera-Barrios 2021).[10,39,53] Specificity ranged from 16% in a study where all patients were dilated (Tufail 2016) to 89% in a study where no patients were dilated (Liu 2021).[10,39]

Subgroup Analyses for EyeArt Data

Only 1 publication, a British study described by Tufail and colleagues (2016), provided diagnostic accuracy calculations for population subgroups.[10] The study was designed to determine the screening performance of AI-based retinal image screening systems to replace first-level human graders or provide pre-screening in the United Kingdom's National Health Service's (NHS) diabetic eye screening program.[10] The study included a consecutive series of patients aged 12 and older who attended an annual London-based diabetic eye screening program and had macular- and disc-centered retinal images taken in accordance with NHS imaging standards.[10] The study compared a number of AI-based screening tools that were commercially available in Britain.[10] While IDx-DR was originally included in the study, the company withdrew from the study after processing the test set, citing commercial reasons; no results for IDx-DR were provided.[10] EyeArt had not initially been involved but asked to join the study in 2013.[10] The reference standard was consensus grading based on 2 human graders, with arbitration by a third-party screening service in cases of disagreement between the human reader and the AI-based screening tool.[10]

EyeArt is not FDA-cleared for use in pediatric populations.[10] The proportion of patients in the study sample who were below the age of 21 is not reported, but the median age was 60 years (interquartile range, 50.4 to 70.4) and results were provided by age group.[10] The sample was ethnically diverse, with 41% of patients of White European ancestry, 34.7% Asian, and 19.6% Black.[10] The Asian category included Asian British, Indian, Pakistani, Bangladeshi, and any other Asian background.[10] All patients received pharmacologic dilation, and ungradable images were included in analysis as referrable.[10] Results by age group, sex, and ethnicity are provided in Appendix Table H4.[10] Neither sensitivity nor specificity differed significantly between men and women.[10] When analyzed by age group, sensitivity and specificity did not differ significantly between patients under 50 and those aged 50 to < 65 years.[10] However, sensitivity was

significantly lower in patients in the higher age group (65 to 98 years) compared with those under age 50, which suggests there may be a higher likelihood of false negatives in older individuals screened by EyeArt.[10]

Diagnostic Accuracy in Studies Differing From FDA Indications

Two of the included studies (one EyeArt,[43] one IDx-DR[17]) reported diagnostic accuracy of the AI-enabled tools for identifying any diabetic retinopathy, rather than more-than-mild diabetic retinopathy. Additionally, although patients are referred for follow up based on the findings in their worst eye, one EyeArt study calculated accuracy on a per-eye basis, rather than a per-patient basis.[15] Diagnostic accuracy results for these 3 studies are presented in Appendix Table H5.

Ongoing Studies

We did not identify any ongoing studies related to AEYE-DS. We identified 1 ongoing trial for EyeArt[57] and 2 for IDx-DR[58,59]; both are described in Table 7.

An ongoing study from EyeArt is designed to demonstrate the value of the AI technology in a diverse, real-world setting. Patients aged ≥ 22 years with diabetes being treated at a primary care practice were randomized to EyeArt screening or usual care (referral to an eye care provider for screening).[57] The study, which has an estimated completion date in 2026, will evaluate the implementation and effectiveness of the AI intervention on diabetic screenings rate, early stages of diabetic retinopathy detection, and referrals to the specialist for follow up on abnormal results.[57]

An ongoing study (NCT05463289) is testing IDx-DR in a pediatric population (aged 8 to 21) with type 1 or type 2 diabetes.[59] While the device is not FDA-cleared for use in children or adolescents, the study may indicate the company's plans to file for an expanded indication for the AI-enabled device.[59] Another ongoing trial (NCT05808699) is testing performance of IDx-DR with a handheld fundus camera.[58] While the study has an estimated completion date of more than a year ago (January 30, 2025), it is listed in ClinicalTrials.gov as 'active, not recruiting.'[58]

Table 7. Ongoing Trials

Study ID Study Name Location Status Enrollment Estimated Completion Date	Study Design Description	Primary Outcome(s)
EyeArt		
NCT06721351[57] Diabetic Retinopathy Screening Point-of-Care Artificial Intelligence (DRES POCAI) US Active, not recruiting N = 548 (actual) April 30, 2026	Randomized trial Participants will be randomized into two groups: usual care (receive a retinal screening by an optometrist) or intervention group (receive a retinal screening using a special camera and FDA-cleared EyeArt system, an autonomous AI-based DR screening).	• Completion of DR screening • Results of DR screening • DR screening efficiency (number of orders submitted, screenings completed, number of ungradable and time of attempts, time (minutes) the participant spent in front of the camera

Study ID Study Name Location Status Enrollment Estimated Completion Date	Study Design Description	Primary Outcome(s)
IDx-DR		
NCT05808699[58] Camera Qualification of an Additional Fundus Camera Paired With An Autonomous AI for Detecting Diabetic Retinopathy US Active, not recruiting N = 626 (actual) January 30, 2025	Observational A multi-center study to demonstrate non-inferiority of the automated device detecting diabetic retinopathy using a handheld fundus camera with IDx-DR	• Sensitivity and specificity
NCT05463289[59] ACCESS 2: AI for pediatriC diabetiC Eye examS Study 2 (ACCESS2) US Recruiting N = 500 (estimated) June 30, 2026	Single arm interventional Determine if use of a nonmydriatic fundus camera using autonomous artificial intelligence software at the point of care increases the proportion of underserved youth with diabetes screened for diabetic retinopathy, and to determine the diagnostic accuracy of the autonomous AI system in detecting diabetic retinopathy from retinal images of youth with diabetes.	• Equivalence in proportion screened for diabetic retinopathy of white and non-white youth with autonomous AI

Abbreviations. AI: artificial intelligence; DR: diabetic retinopathy; FDA: US Food and Drug Administration.

KQ2. Clinical Utility

Most diagnostic accuracy studies focus on providing sensitivity and specificity estimates against the gold standard of a comprehensive dilated eye exam by an ophthalmologist or retinal specialist.[10,108] Many diagnostic accuracy studies, particularly those using retrospective data, focus on identification of cases where the AI-based screening tool would identify patients with referable (i.e., more-than-mild) diabetic retinopathy and comparison of those estimates with specialist determinations of the presence or absence of referable disease. These studies are solely concerned with the accuracy of the AI algorithms and do not track how those determinations would translate into action—for example, how many more patients would be screened with the AI-enabled tools in primary care or diabetes care settings or how many patients identified with referable diabetic retinopathy would go on to have a full exam with an ophthalmologist or retinal specialist.[17,44,60] Our literature searches identified 4 cohort studies that addressed any aspect of clinical utility for these AI-enabled diagnostic screening tools. We also used data from the clinical accuracy studies to provide information on other markers of clinical utility when they were reported: 1) the number of cases that were rejected by the AI algorithm for having one or more unreadable images compared with the number of patients that human

graders would have scored as unreadable and 2) the number of patients that required pupil dilation in order to obtain gradable images. The unpublished clinical trial record for AEYE-DS included general references to imageability, which could be considered a proxy measure of clinical utility.[37]

Measures of Clinical Utility for AEYE-DS

There were no published studies—either diagnostic accuracy studies or cohort studies—related to AEYE-DS and all information regarding the system came from the ClinicalTrials.gov record.[37] The trial included imageability as a secondary outcome, defined as the percentage of participants who received a diagnostic output (positive for more-than-mild diabetic retinopathy or negative for more-than-mild diabetic retinopathy) from the AEYE-DS device.[37] Results were provided in tables, with very little context or description.[37] The record indicated that 531 participants were enrolled, but only 468 were considered to be analyzable.[37] The reasons for exclusion for the other 63 participants were not reported.[37] Of the 468 analyzable participants, 462 had results from both human screeners and the AEYE-DS system and were included in diagnostic accuracy calculations.[37] Gradability for the AEYE-DS system was reported as 99.1% (95% CI, 97.8 to 99.7), with no quantification of how many participants were considered ungradable by the AEYE-DS system (after the original 63 exclusions).[37] All participants in the study had their pupils dilated, and there were no attempts to capture gradable images without dilation.[37]

Number of Participants Identified for Referral

In diagnostic accuracy testing, results of the test being studied are compared to results of a gold standard test that represents the definitive or correct result. In the case of diabetic retinopathy screening, the gold standard is review of images by expert graders (typically board-certified retina specialists at Ophthalmic Reading Centers who remotely analyze and grade fundus photos). Just as AI-enabled diagnostic screening tools consider some images to be ungradable, human graders may also mark images as ungradable and return null results for some patients. Because someone with images judged as ungradable—whether by human screeners or AI—would be considered a referrable case, a true estimate of number of cases that would be referred for further screening should include ungradable cases. Table 8 compares the number of participants identified as referrable for more-than-mild retinopathy using the gold standard method with the number of participants identified as referrable by the AI-enabled diagnostic screening tool. Table 13 is limited to studies that reported on the number of patients with images deemed ungradable by human graders and the number deemed ungradable by AI.

Diagnostic accuracy of AI screening tools show a trend toward high negative predictive value coupled with moderate to low positive predictive value—meaning these autonomous AI-based screening tools are unlikely to miss true cases of diabetic retinopathy but refer a large number of people to further screening who do not have more-than-mild diabetic retinopathy. This tendency toward over-referral should be interpreted in light of the alternative: referral of all individuals meeting diabetic retinopathy screening guidelines to an ophthalmologist for a full dilated eye exam.

Table 8. Participants Identified for Referral (Positive Screening Result or Ungradable)

Author Year No. of Participants Dilation	PPV/NPV	Participants Referred for Further Screening per Gold Standard, n (%)	Participants Referred for Further Screening per AI, n (%)	*P* Value of Between-Group Difference
EyeArt				
Liu 2021 N = 180 No dilation	44.6/100	46 (25.6%)	92 (51.1%)	< .0001
Vought 2023 N = 62 No dilation	72/88	24 (38.7%)	22 (35%)	.6706
Bhaskaranand 2019 N = 101,710 All dilated	72.4/97.6	24,716 (24.3%)	26,110 (25.7%)	< .0001
Heydon 2021 N = 30,405 All dilated	14.0/99.4	2,664 (8.8%)	15,091 (50%)	< .0001
Olvera-Barrios 2021 N = 1,257 All dilated	17.5/99.4	111 (8.8%)	613 (48.8%)	< .0001
Ibáñez-Bruron 2024 N = 366 All dilated	42.4/98.2	63 (17.2%)	79 (21.6%)	.1325
Tufail 2016 N = 20,528 All dilated	19.3/96.2	2,844 (14.0%)	13,918 (68.7%)	< .0001
IDx-DR				
Verbraak 2019 N = 1,616 Reflex dilation	22.5/98.9	429 (26.5%)	538 (33.3%)	< .0001
Dow 2023 N = 80 No dilation	84.0/98.2	22 (27.5%)	25 (31.2%)	.6085

Abbreviations: AI: artificial intelligence; no: number; NPV: negative predictive value; PPV: positive predictive value.

Rates of Follow Up for Patients With AI-Based Diagnostic Screening

Two studies reported on rates of patient follow up with ophthalmology following a finding of referrable diabetic retinopathy in AI-based screening. Liu and colleagues (2021) reported significantly higher rates of follow up for patients with a referrable finding from EyeArt compared to a historical control that received a referral without any screening.[39] Dow and colleagues (2023) reported significantly higher rates of follow up for patients with a referrable finding in IDx-DR screening compared to a historical control group with a referrable finding from human teleophthalmology screeners.[61]

A 2021 publication by Liu and colleagues describes a study that recruited adult patients with type 1 or type 2 diabetes at a hospital-based primary care practice in St. Louis, Missouri who had not attended an ophthalmology appointment within the prior year.[39] Patients were screened

with EyeArt v2.0 and those with more than moderate or ungradable results were referred for follow up.[39] Referrable patients received a phone call within 2 weeks of their EyeArt screening to schedule an appointment at the resident ophthalmology clinic.[39] Rate of adherence to eye screening recommendations was the study's primary outcome.[39] The study used a historical control, comparing follow up for EyeArt screening to the follow-up rate for consecutive adult patients with diabetes seen over a 1-year period at the same primary care clinic.[39] While patients in the historical control were "encouraged to follow up with their previous ophthalmologist" or given a referral to the university eye clinic, there is no indication that they were proactively called to schedule those appointments.[155] Patients were considered "adherent with eye care recommendations" if they attended an eye clinic appointment within 1 year after their reference primary care clinic visit.[39] At 12 months after the index primary care visit, 51 out of 92 patients referred by EyeArt screening (55.4%) had attended an eye care visit. In contrast, only 182 of 974 patients (18.7%) in the historical control had received a general recommendation for follow-up screening ($P < .0001$).[39]

Dow and colleagues (2023)[61] described the implementation of IDx-DR for undilated diabetic retinopathy screening in primary care and endocrinology clinics associated with Stanford Health Care, reporting that the addition of IDx-DR to the workflow increased rate of follow up with an ophthalmologist relative to screening by a human teleophthalmologist (another publication by Dow and colleagues (2023) reports diagnostic accuracy findings and is included in analysis for KQ1[44]). Patients were 18 years or older with type 1 or type 2 diabetes mellitus without a prior diabetic retinopathy diagnosis or a diabetic retinopathy exam in the past 12 months.[61] The primary care physician placed a referral to ophthalmology for all patients with a more-than-mild or ungradable finding.[61] Results for patients with a definitive result from IDx-DR were uploaded to the patient portal within 48 hours.[61] Outcomes for patients who received a more-than-mild or ungradable finding in the AI-enabled workflow were compared to those for patients who had been assessed through a human-based teleophthalmology workflow prior to the implementation of IDx-DR.[61] For all screened patients who received a more-than-mild diabetic retinopathy or ungradable result during the human workflow, AI workflow, or AI-human hybrid workflow periods, researchers searched the electronic medical record at Stanford Health Care for subsequent encounters with an ophthalmologist.[61] Patients reported in a survey whether they received follow up at a site unaffiliated with Stanford.[61] Successful follow up was defined as an in-person encounter with dilated fundus examination within 90 days of the screening encounter.[61] We rated the study by Dow and colleagues as high risk of bias for several methodological issues, including patient self-report of follow up and questions about the large number of patients excluded from analysis.

Analysis included 1,063 patients with a positive (n = 279) or ungradable (n = 784) result from IDx-DR (47% of 2,243 patients screened) and 117 patients with a positive (n = 40) or ungradable (n = 77) result from the historical control of human teleophthalmology screening (15% of 790 patients screened).[61] For patients with a positive result for more-than-mild diabetic retinopathy, 20% of patients with human teleophthalmology screening and 35.5% of those with IDx-DR screening had a follow-up appointment with a Standford-affiliated ophthalmologist within 90 days.[61] An additional 33.7% of patients screened with IDx-DR had a follow-up appointment with a community ophthalmologist within 90 days (not reported for the teleophthalmology workflow), for an overall 69% follow-up rate and a significant improvement ($P < .001$) compared with the

human workflow.[61] For patients who received an ungradable result, 7.8% of patients with human teleophthalmology screening and 13.3% of those with IDx-DR screening had a follow-up appointment with a Standford-affiliated ophthalmologist within 90 days (*P* = .26).[61]

Rates of Follow Up for Patients at Sites Where AI-Based Diagnostic Screening Was Available

In a retrospective cross-sectional study, Huang and colleagues (2024) compared outcomes for all patients with diabetes mellitus who were managed at primary care sites of Johns Hopkins Medicine in the calendar years 2019 (pre-deployment of IDx-DR) and 2021 (post-AI deployment).[62] The version of IDx-DR used was not reported, but no dilation protocol was used.[62] Patients assessed at primary case sites where IDx-DR had been deployed (AI-switched sites) were compared to patients assessed at primary care sites without deployment of IDx-DR (non-AI-switched sites).[62] Analysis included 5,580 patients at sites that implemented IDx-DR and 29,684 patients at sites that did not implement IDx-DR.[62] We could not determine from the information provided in the publication whether pediatric patients were included or excluded and there was no clear exclusion of patients who already had a diabetic retinopathy diagnosis.[62] We also could not determine the number of unique patients included or if there was any overlap of patients from different sites and time periods.[62] The primary outcome measure was adherence to annual diabetic retinopathy testing in a given calendar year.[62] Adherence was defined as either receiving an autonomous AI exam (patients had the option to accept or decline screening with IDx-DR) or a dilated eye exam with an ophthalmologist.[62] The study did not directly measure whether patients were more likely to be screened when screening was immediately available through the AI tool versus being referred to an ophthalmologist for a comprehensive dilated eye exam with an ophthalmologist.[62] Because results were reported at the site level, rather than the patient level, we could not determine if patients who were screened from sites where AI screening was available actually had screening with IDx-DR or whether they accepted a referral to an ophthalmologist for screening.[62] The authors reported a change in adherence to screening recommendations from 2019 to 2021 (Table 9).[62] Patients at sites where IDx-DR was available were more likely to adhere to screening recommendations, although whether they used IDx-DR or traditional ophthalmologist screening is unknown.[62] There were no differences by sex or age group.[62] Patients enrolled in Medicare, Medicare Advantage, or Medicaid were all more likely to adhere to screening recommendations when they were treated at a site where IDx-DR was available.[62] We rated the study by Huang and colleagues as high risk of bias due to lack of clarity on inclusion and exclusion criteria and methods, as well as potential bias related to the authors' affiliation with IDx-DR.

Table 9. Adherence to Screening Recommendations in Study by Huang et al. (2024)[62]

Population	Percent Change in Adherence at AI-Switched Sites (95% CI)	Percent Change in Adherence at Non-AI-Switched Sites (95% CI)	Difference Between Sites
All patients	+8.8 (95 CI, 7.1 to 10.5)	+0.3 (−0.8 to 1.4)	*P* < .001
Male patients	+10.5 (+7.9 to +13.1)	+0.3 (−1.3% to +1.8%)	*P* < .001
Female patients	+7.4 (+5.1 to +9.7)	+0.5 (−1.1% to +2.0%)	*P* < .001
Patients aged ≥ 65 years	+7.8 (+4.7 to +10.8)	−2.1 (−4.2% to +0.0%)	*P* < .001
Patients < 65 years of age	+9.8 (+7.8 to +11.9)	+1.6 (+0.3% to +2.9%)	*P* < .001
White patients	+5.8 (+3.2 to +8.3)	+0.3 (−1.3% to +1.8%)	*P* < .001

Population	Percent Change in Adherence at AI-Switched Sites (95% CI)	Percent Change in Adherence at Non-AI-Switched Sites (95% CI)	Difference Between Sites
Black patients	+12.2 (+9.7 to +14.7)	−0.6 (−2.5% to +1.3%)	*P* < .001
Asian patients	+0.4 (−8.7 to +9.5)	-1.1 (−5.3% to +3.2%)	*P* = .772
Hispanic or Latino patients	+2.7 (−7.2 to +12.7)	+3.8 (−1.2% to +8.7%)	*P* = .858
Medicare patients	+8.5 (+5.5 to +11.6)	−0.8 (−2.9% to +1.3%)	*P* < .001
Medicare Advantage patients	+9.8 (+1.7 to +17.9)	−7.2 (−15.4% to +0.9%)	*P* = .004
Medicaid patients	+13.7 (+6.7 to +20.7)	−4.9 (−10.7% to +1.0%)	*P* < .001

Abbreviations. AI: artificial intelligence; CI: confidence interval.

Modeling of Potential Impact of AI Screening on Vision Loss

Finally, Channa and colleagues and members of the IDx-DR research team (2023) report results of a study that used a Markov model to determine the differential impact on vision loss of autonomous AI-based diabetic retinal exams versus screening performed in the clinic by an eye care provider.[63] Although vision loss is the ultimate outcome of diabetic retinopathy, it could take years to develop and is not measured in diagnostic accuracy studies.[63] To address this issue, the study modeled screening strategies and the downstream care process to estimate the impact on vision loss at 5 years.[63] IDx-DR was compared to referral by a primary care provider to an ophthalmologist or optometrist for dilated diabetic eye exams in the clinic and to a no-screening strategy.[63] The population for the model was adults with diabetes (type 1 or 2) presenting to primary care or another provider managing their diabetes with no known vision loss and no diabetic retinal disease.[63] We rated the study by Channa and colleagues as moderate risk of bias due to concerns about assumptions informing the model and the potential for author conflicts of interest.

The model assumed that while patients may have had some vision loss, they were either unaware of it or did not express it to their primary care provider.[63] This modeling study used data from a publication by Abramoff and colleagues (2018), which is included in the evidence review for KQ1, where reflex dilation was used.[18,63] The primary outcome was the proportion of adults with diabetes who were estimated to develop any vision loss at 5 years (or probability of severe vision loss by 5 years).[63] Patients were assumed to progress by steps: starting with no diabetic retinopathy and progressing to diabetic retinopathy requiring metabolic control, diabetic retinopathy requiring metabolic and ophthalmic control, diabetic retinopathy with vision loss, and finally to diabetic retinopathy with irreversible vision loss.[63] The model assumed that patients who progressed to any diabetic retinopathy would not re-enter the screening pathway, and otherwise would be re-screened annually.[63] Any benefit of ophthalmic encounters with an eye care provider as opposed to AI in detecting diseases other than diabetic retinopathy (i.e., glaucoma, age-related macular degeneration, or cataracts) was not modeled.[63]

For the base case, in the no-screening strategy the proportion of adults with diabetes who were estimated to develop any vision loss at 5 years was 1637/100,000; it was 1625/100,000 for the eye care provider screening strategy, and 1535/100,000 for the AI screening strategy.[63] Thus, the proportion of participants with diabetes who developed vision loss in the model with AI-based screening (1535/100,000) was estimated to be 102/100,000 lower compared with no-

screening (1535/100,000) and 90/100,000 lower compared with eye care provider-based screening (1625/100,000).[63] The difference between no-screening and eye care provider screening was 12/100,000.[63] The authors concluded that the model's results suggest that an AI-based screening strategy is 8.6 times more effective at preventing vision loss than an eye care provider screening strategy, under base-case assumptions.[63]

Usability of the AI-Enabled Diagnostic Screening Systems in Primary Care

Of the 8 prospective diagnostic accuracy studies that took place in primary care settings or diabetes care clinics,[18,20,21,39,40,44,47,49] only 2 provided any details on the practicality of using these autonomous AI-enabled diagnostic screening tools in clinical practice.[20,21] In the study by Wintergerst and colleagues (2022), trained medical assistants in primary care practices in Germany acquired patient images that were graded by EyeArt.[21] The authors reported that image acquisition took an average of 7.5 minutes (range 3–16 minutes) for both eyes.[21] The majority of imaging sessions were completed in less than 10 minutes (64 sessions; 85.3%).[21] The number of attempts to obtain images varied from 1 to 5, with 81.3% of patients successfully completing imaging in 3 or fewer attempts.[21] All of the 14 medical assistants who completed a post-study survey reported that the fundus camera used in the study was easy to use, and just over half (8 medical assistants; 57%) reported that diabetic retinopathy screening could be integrated into their practice's workflow.[21] While most respondents who did not think AI screening would be practical in their clinics did not provide a reason, 4 respondents reported that integrating the screening was too much work or too time-consuming.[21] van der Heijden and colleagues (2018) described their results screening with IDx-DR in a diabetes care center in the Netherlands, noting that staff operating the fundus cameras were prompted by the software to take a new photograph if image quality was low, but "the scheduled time per patient most often did not allow this."[20(p64)] The authors did not quantify "most often" and did not provide any additional information on mean image acquisition time or mean number of imaging attempts per patient.[20]

Gradability in AI-Enabled Systems

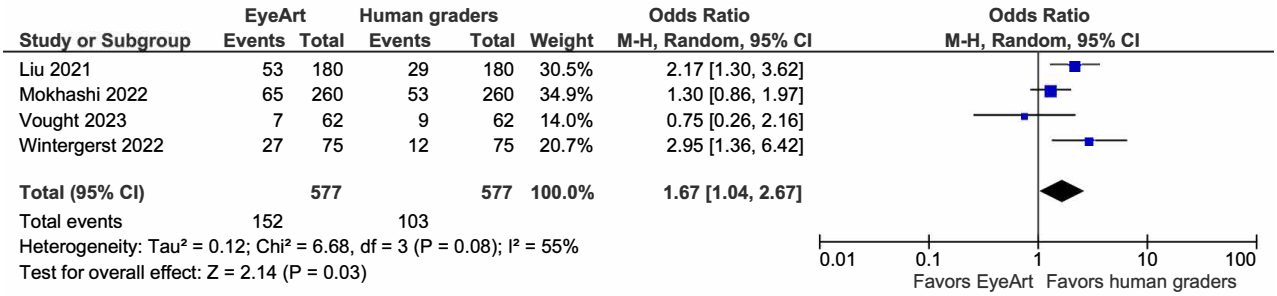
Although diagnostic accuracy studies are not concerned with clinical utility, some studies provide information on usability of the AI-enabled diabetic retinopathy screening systems that provide some information to inform clinical decision making. AI-enabled diabetic retinopathy screening tools are promoted as a practical means of screening without dilation, which would increase clinical utility for primary care practices and endocrinology practices in which dilation of patient pupils is not practical or within the scope of practice. Table 10 summarizes the dilation and gradability results from diagnostic accuracy studies.

Of 15 EyeArt studies, 8 were limited to undilated eyes,[16,21,38-43] 5 used dilation for all participants,[15,19,53,54] 1 used images from a retrospective database that included a mix of dilation protocols,[52] and 1 used a reflex dilation protocol in which patient eyes were dilated after an unspecified number of attempts to capture readable images with undilated eyes.[49] The study by Musetti and colleagues (2025) that used reflex dilation included both EyeArt and IDx-DR and did not report the number of patients that required dilation to obtain gradable images.[49]

Among the 8 EyeArt studies that did not use dilation, the proportion of patients that EyeArt flagged as ungradable ranged from < 1% to 36%. In the 4 studies that also reported ungradable rates for human readers, the proportion of cases considered ungradable was significantly higher for EyeArt (Figure 12):

- Guedes and colleagues (2025) reported that only 1 of 499 patients (0.2%) was excluded due to poor image quality.[43]
- Karabeg and colleagues (2025) reported that 7 of 128 patients (5%) were excluded due to ungradable images.[16]
- Liu and colleagues (2021) reported that 53 of 180 patients (29.4%) were excluded due to ungradable images, compared with 29 (16.1%) for the human graders.[39]
- Mokhashi and colleagues (2022) reported that 38 of 260 patients (14.6%) had images from 1 or both eyes that were ungradable by both EyeArt and the optometrist, while an additional 27 patients (10.4%) were deemed ungradable by EyeArt but gradable by an optometrist.[40]
- Vought and colleagues (2023) reported that 7 of 62 patients (11%) had at least 1 image that was ungradable by EyeArt; in contrast, an onsite human grader considered only 1 patient (2%) ungradable and offsite retina specialists considered 9 patients (15%) ungradable.[41]
- Wintergerst and colleagues (2022) reported that 27 of 75 patients (36%) were determined ungradable by EyeArt, while 12 patients (16%) were classified as ungradable by the ophthalmologist.[21]
- Publications by Ipp and colleagues (2021)[38] and Van and colleagues (2024)[42] did not report on the number of patients that EyeArt found ungradable.

Figure 12. Ungradable Rate for EyeArt vs. Human Graders for Studies in Non-Dilated Eyes



Of 11 IDx-DR studies, 6 analyzed patients without any dilation,[20,44-48] 3 used reflex dilation,[18,50,51] 1 included dilation for all patients,[55] and 1 did not reference dilation.[17] Among the 3 studies using reflex dilation, 2 provided information on the number of patients who required dilation to capture gradable images.[18,50] Abramoff and colleagues (2018) report that 23.6% of 852 patients required dilation in order to obtain gradable images,[18] while a study by Mehra and colleagues (2022) reports that 385 of 965 gradable patients (39.3%) required reflex dilation.[50]

Among the 6 IDx-DR studies that did not use dilation, 3 did not report on gradability. Of the remaining 3 studies, the proportion of patients that IDx-DR considered ungradable ranged from 7% to 34%. In the 2 studies that also reported ungradable rates for human readers, the

proportion of cases considered ungradable was significantly higher for IDx-DR (Figure 13), although heterogeneity was unacceptably high (99%):

- Dow and colleagues (2023) reported that 446 (36.5%) of 1,222 patient encounters were ungradable; in contrast, human graders considered only 6.9% of patients ungradable.[44]
- Poschkamp and colleagues (2025) reported that IDx-DR found 438 of 1716 patients (25.5%) ungradable.[47]
- van der Heijden and colleagues (2018) reported that 477 of 1,415 patients (33.7%) were considered ungradable by IDx-DR, compared with 19.6% of patients considered ungradable by human experts.[20]
- Studies described by Grzybowski and colleagues (2023),[46] Grzybowski and colleagues (2025),[45] and Sedova and colleagues (2022)[48] only included patients that IDx-DR considered gradable and did not report the number of excluded patients.

Figure 13. Ungradable Rate for IDx-DR vs. Human Graders for Studies in Non-Dilated Eyes

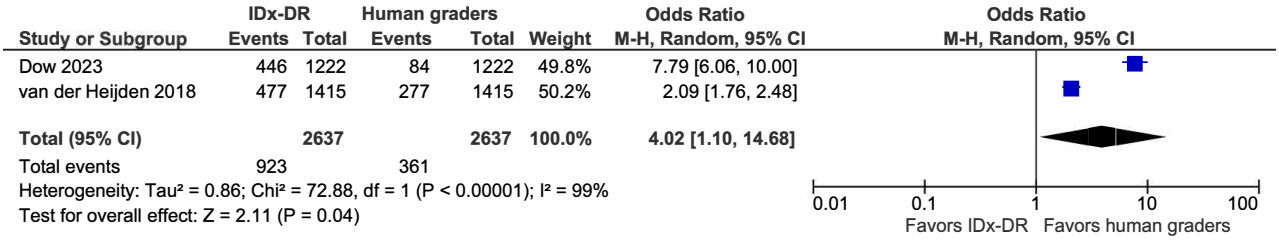


Table 10. Dilation and Gradability in Diagnostic Accuracy Studies

Author Year	Patients Needing Dilation	Patients with Ungradable Images per AI Tool
AEYE-DS		
NCT04612868	NR	11.9% (63 of 531)
Guedes 2025[43]	NA	1 of 499 patients (0.2%)
Ipp 2021[38]	NA	Not reported
Karabeg 2025[16]	NA	7 of 128 patients (5%)
Liu 2021[39]	NA	53 of 180 patients (29.4%), compared to 29 (16.1%) unreadable from human graders
Mokhashi 2022[40]	NA	65 of 260 patients (25%) 38 patients had images from one or both eyes that were ungradable by both the software and optometrist 15 patients were ungradable only by the human 27 patients were ungradable only by the software
Van 2024[42]	NA	Not reported
Vought 2023[41]	NA	7 of 62 patients (11%) had at least 1 image that was ungradable by EyeArt, compared with only 1 (2%) by the onsite grader and 9 (15%) by the retina specialist
Wintergerst 2022[21]	NA	27 of 75 patients (36%) were determined ungradable by EyeArt, while 12 patients (16%) were classified ungradable by the ophthalmologist. *P* = .005

Author Year	Patients Needing Dilation	Patients with Ungradable Images per AI Tool
EyeArt, reflex dilation		
Musetti 2025[49]	Not reported	IDx-DR: 16 of 201 (8.0%) EyeArt 13 of 201 (6.5%) *P* = .56
EyeArt, all patients' eyes dilated		
Heydon 2021[19]	NA	Not reported Human graders categorized 739 of 30,405 patients as ungradable (2.4%) and these were included in analysis (and marked as ungradable) EyeArt cases considered ungradable were considered a positive test and there is no quantification of the number of patients that EyeArt considered ungradable
Ibáñez-Bruron 2024[53]	NA	31 of 366 patients (8.5%)
Olvera-Barrios 2021[54]	NA	Not reported
Sarao 2020[15]	NA	EyeArt judged 4 of 322 eyes (1.2%) as ungradable, but only provided data on a per-eye basis; we do not know how many patients were considered ungradable
Tufail 2016[10]	NA	Not reported
EyeArt, mixed dilation		
Bhaskaranand 2019[52]	NA (not a prospective study)	910 of 101,710 total patient encounters were judged ungradable by EyeArt (0.9%) For 54,481 nonmydriatic encounters: 629 encounters (1.2%) were ungradable For 46,580 mydriatic encounters: 278 (0.6%) were judged ungradable MD 0.6% (95% CI, 0.48 to 0.72); *P* < .0001.
IDx-DR, no eyes dilated		
Dow 2023[44]	NA	36.5% of 1,222 encounters
Grzybowski 2023[46]	NA	Only included 811 patients deemed gradable in the IDx-DR quality check; did not report how many patients were excluded
Grzybowski 2025[45]	NA	Only included 779 patients deemed gradable in the IDx-DR quality check; did not report how many patients were excluded
Poschkamp 2025[47]	NA	438 of 1716 patients (25.5%)
Sedova 2022[48]	NA	Not reported
van der Heijden 2018[20]	NA	477 of 1415 patients (33.7%) Experts rated 277 patients (19.6%) as insufficient quality *P* < .0001

Author Year	Patients Needing Dilation	Patients with Ungradable Images per AI Tool
IDx-DR, reflex dilation		
Abramoff 2018[18]	23.6% of 852 patients	Unclear. First omits 40 studies considered ungradable by the human graders (4.5% of 892). 33 of the 852 remaining (3.9%) had 1 or more images of insufficient quality per IDx-DR
Mehra 2022[50]	For subsample of 965 gradable patients, 39.3% (385) required reflex dilation.	87 of 1052 patients (8.3%) had ungradable images, even after dilation. Gradability decreased as age increased: 18 to 40 years (n = 81): 82.7% 41 to 50 years (n = 114): 71.9% 51 to 60 years (n = 246): 68.3% 61 to 70 years (n = 379): 50.4% 71 to 80 years (n = 196): 33.2% 81 to 90 years (n = 36): 19.4%
Musetti 2025[49]	Not reported	IDx-DR: 16 of 201 (8.0%) EyeArt: 13 of 201 (6.5%) *P* = .56
Verbraak 2019[51]	Not reported	In 191 of 1,616 participants (11.7%), images were graded as insufficient quality by the reference standard The IDx-DR device gave an output of insufficient quality for 280 of 1,616 participants (17.3%). *P* < .0001
IDx-DR, all patient eyes dilated		
Shah 2021[55]	NA	195 of 3281 patients were judged ungradable by the human graders 404 were judged ungradable by IDx-DR 2 were judged ungradable by both human and IDx
EyeArt, unknown dilation		
Riotto 2024[17]	NA	209 of 1350 patients (15.5%)

Abbreviations. AI: artificial intelligence; CI: confidence interval; MD: mean difference; NA: not applicable.

GRADE Summary of Diagnostic Accuracy and Clinical Utility of Autonomous AI-Enabled Diabetic Retinopathy Screeners

Table 11 presents a summary of diagnostic accuracy measures (sensitivity, specificity, and positive and negative predictive values) and percent of images that were considered ungradable by the AI system as a measure of clinical utility for detection of more-than-mild (referable) diabetic retinopathy. Inclusion in the GRADE table was limited to studies with confusion matrices, which were necessary for calculation of pooled estimates. AEYE-DS is not included in the GRADE table, due to the absence of evidence from published, peer-reviewed studies.

When results from all studies with sufficient data were pooled, regardless of dilation protocol or handling of patients with ungradable images (Table 11), sensitivity and specificity were 95% and 71% for EyeArt and 87% and 78% for IDx-DR. Certainty of evidence was low to very low across all diagnostic accuracy measures for both EyeArt and IDx-DR. The mean number of patients who

were deemed ungradable due to one or more unreadable images was 12% for EyeArt and 21% for IDx-DR in the pooled sample. Certainty of evidence for incidence of ungradable results was rated as very low for both EyeArt and IDx-DR.

To be of greatest use as a tool in primary care practices or endocrinology practices, autonomous AI-enabled diabetic retinopathy diagnostic screening tools would be able to reliably capture gradable images without the need for pupil dilation and would provide diagnostic accuracy information based on the assumption that patients who do not receive a definitive result from the system would require referral to an ophthalmologist or retinal specialist for a dilated eye exam.[64] The majority of studies included in this evidence review, however, included dilation for all patients,[10,19,52-55] or called for dilation when attempts to capture gradable images from undilated eyes were unsuccessful.[18,38,49-51] The majority of diagnostic accuracy calculations omitted ungradable images and did not include enough information for us to independently calculate diagnostic accuracy with ungradable images included as referrals.[16,18,20,21,38,40,45-51,55]

Table 12 presents GRADE results for the subset of studies that captured images without dilation and considered ungradable results as referrable cases. Out of 15 EyeArt studies, 6 (40%) captured images without dilation.[16,21,38-41] Only 2 of those (13% of EyeArt studies) treated ungradable cases as referrable.[39,41] Out of 11 IDx-DR studies, 6 (54.5%) captured images without dilation.[20,44-48] Only 1 of those (9% of IDx-DR studies) treated ungradable images as referrals.[44]

Evidence from 2 EyeArt studies provided mixed evidence related to the autonomous AI screener's ability to identify more-than-mild diabetic retinopathy in undilated eyes, with low certainty of evidence across all outcomes.[39,41] Sensitivity was higher and specificity lower in the study by Liu and colleagues (2021) compared with the study by Vought and colleagues.[39,41] High sensitivity in the Liu study (100%) came at the expense of a larger number of false positives (specificity = 65.7%).[39] Differences between the 2 studies may reflect differences in populations.[39,41] Liu and colleagues described a prospective study with 185 patients who were recruited from primary care practices for low-income patients in St. Louis, Missouri.[39] The mean age was 57.4 years and 54% of participants were female.[39] The majority of the sample (78.3%) were African American.[39] Vought and colleagues described a prospective study with 62 participants.[41] Images were captured in an endocrinology clinic and a community screening event in Newark, New Jersey.[41] The mean age was 64 years and 56% of participants were female.[41] The sample was primarily Caucasian (69%), with 21% Hispanic, and 10% African American.[41]

Dow and colleagues described a prospective cohort study that incorporated screening with IDx-DR into primary care practices associated with Stanford University.[44] A total of 1,222 patient encounters were reported during the 18-month study period, with IDx-DR producing gradable results for 776 patients (63.5%).[44] However, only a subset of encounters was simultaneously graded by a human reader and diagnostic accuracy results are based on only 80 patients.[44] Sensitivity (95%) and specificity (93%) were relatively balanced, although high risk of bias and imprecision related to a single study with a small sample size led to very low certainty of evidence across all outcomes.[44] The authors acknowledged differences in their diagnostic accuracy findings compared with the IDx-DR pivotal trial,[18] in which all participants' eyes were dilated, but noted the need for screening tools that are effective in capturing gradable images from undilated eyes for use in primary care settings.[44]

Table 11. Summary of Findings (GRADE)[a] for Detection of More-Than-Mild Diabetic Retinopathy

Metric	Number of Participants (Studies)	Pooled Estimate (95% CI), Range	CoE	Rationale for CoE Rating
EyeArt				
Sensitivity	156,883 (10)	94.97% (92.42 to 97.52)	●●○○ Low	Downgraded 1 level for moderate risk of bias across majority of studies and 1 level for consistency due to variation in outcomes across studies, even when approach to study design and analysis were similar (i.e., all eyes dilated and ungradable tests omitted)
Specificity		71.03% (57.83 to 84.23)	●●○○ Low	
PPV		39.90 (23.70 to 56.09)	●●○○ Low	
NPV		98.70% (97.87 to 99.53)	●●●○ Moderate	Downgraded 1 level for moderate risk of bias across majority of studies
Ungradable rate	102,907 (7)	Mean 12.34% (12.28 to 12.41) Range 1% to 29.4%	●○○○ Very low	Downgraded 1 level for moderate risk of bias in the majority of studies, 1 level for consistency due to wide variation in reported results, and 1 level for imprecision due to the small number of studies reporting this outcome and subsequent lack of clarity on how close this figure is to the true rate
IDx-DR				
Sensitivity	8,857 (9)	88.63 (75.13 to 100)	●○○○ Very low	Downgraded 2 levels for high risk of bias across majority of studies and 1 level for consistency due to variation in outcomes across studies, even when approach to study design and analysis were similar (i.e., all eyes dilated and ungradable tests omitted)
Specificity		78.05 (66.98 to 89.12)	●○○○ Very low	
PPV		41.95 (26.42 to 57.48)	●○○○ Very low	
NPV		97.90 (96.17 to 99.63)	●●○○ Low	Downgraded 2 levels for high risk of bias across majority of studies
Ungradable rate	10,302 (6)	Mean 21.35% (21.12 to 21.58) Range 8.3 to 36.5	●○○○ Very low	Downgraded 2 levels for high risk of bias in the majority of studies and 1 level for imprecision due to the small number of studies reporting this outcome and subsequent lack of clarity on how close this figure is to the true rate

Note. [a] For methods and interpretation of GRADE ratings, see Appendix C.
Abbreviations. CI: confidence interval; CoE: certainty of evidence; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; NPV: negative predictive value; PPV: positive predictive value; RoB: risk of bias.

Table 12. Summary of Findings (GRADE)[a] for Detection of More-Than-Mild Diabetic Retinopathy Without Pupillary Dilation and Counting Ungradable Images as Referrals

Outcome	Study	Results, % (95% CI)	CoE	Rationale for CoE Rating
EyeArt				
Sensitivity	Liu 2021 Vought 2023	100% (90.51 to 100) 74% (no CI)	●●○○ Low	The larger study had moderate RoB (the other was high). Degree of consistency is unknown because 1 study lacked confidence intervals. No downgrade for precision because that issue is already addressed in consistency.
Specificity	Liu 2021 Vought 2023	65.67% (56.98 to 73.65) 87% (no CI)		
PPV	Liu 2021 Vought 2023	44.58% (38.89 to 50.41) 72% (no CI)		
NPV	Liu 2021 Vought 2023	100% (95.89 to 100) 88% (no CI)		
Ungradable rate	Liu 2021 Vought 2023	29.4% EyeArt 16.1% human in Liu 11% EyeArt 2% single grader 15% retina specialist in Vought	●●○○ Low	The larger study had moderate RoB (the other was high). Downgraded 1 level for consistency for large outcome differences between studies.
IDx-DR				
Sensitivity	Dow 2023	95.45% (77.16 to 99.88)	●○○○ Very low	In each case, downgraded 2 levels for high RoB and 1 level for imprecision related to a single study with small sample size.
Specificity	Dow 2023	93.10% (83.27 to 98.09)		
PPV	Dow 2023	84% (67 to 93.14)		
NPV	Dow 2023	98.18% (88.82 to 99.73)		
Ungradable rate	Dow 2023	36.5% IDx-DR, 6.9% human	●○○○ Very low	

Note. [a] For methods and interpretation of GRADE ratings, see Appendix C.
Abbreviations. CI: confidence interval; CoE: certainty of evidence; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; NPV: negative predictive value; PPV: positive predictive value; RoB: risk of bias.

KQ3. Harms

Among the 3 cohort studies that explored the clinical utility of AI-enabled devices for diabetic retinopathy screening, none reported on adverse events or addressed the possibility of harms.[61-63] Diagnostic accuracy studies of AI-enabled diabetic retinopathy screening tools did not reference or report on adverse events. The clinical trial record for AEYE-DS rationalized that, "[s]ince this study was non-interventional with regards to the AEYE-DS device (i.e., it did not come in contact with the study participants) and all interventions were conventional screening exams with FDA-cleared devices used to obtain all of the ophthalmic examinations, information about adverse events was not collected. No safety assessments were necessary."[37]

While a high rate of false-positive results could be considered a harm in some contexts, the founders of IDx-DR addressed the issue of over-identification in a publication by Abramoff and colleagues (2018) noting, "[s]pecificity is also an important consideration, because it affects the number of people with diabetes who receive a referral but do not need one because they have only no or mild DR. Because all referrals will be evaluated by an eye care provider however, this will not increase the risk of that person receiving unnecessary treatment."[18(p39)]

KQ4. Cost and Cost-Effectiveness

Two economic evaluations were identified that met inclusion criteria: published within the past 5 years and utilizing data from the US health care system.[65,66] Both studies modeled use of autonomous AI-enabled diagnostic screening using data from EyeArt studies of undilated screening in primary care practice and found that AI-enabled diabetic retinopathy screening was cost-effective compared with the standard method of referring all patients with diabetes to an ophthalmologist or retinal specialist for a dilated screening exam.[65,66] We rated both cost-effectiveness studies as low risk of bias.[65,66]

Chawla and colleagues (2023) described an economic modeling study designed to compare the cost-effectiveness of fully automated retinal image screening with the current practice of universal ophthalmologist referral for diabetic retinopathy in the US health care system.[65] The authors constructed a Markov transition-state model using a base-case age of 45 years to represent the mean age of onset for type 2 diabetes in the US.[65] Simulated patients were assigned an initial diabetic retinopathy severity state, as well as probabilities of death, progression to a more severe diabetic retinopathy state, and development of diabetic macular edema, based on claims data and large-scale longitudinal studies.[65] The mode used a 1-year cycle length over a 5-year horizon, with supplementary analyses performed at 10 and 20 years.[65] While the study addressed fully automated retinal image screening generally, diagnostic accuracy estimations were based on data from EyeArt reported in the study by Bhaskaranand and colleagues (2019), which is included in the evidence review for KQs 1 and 2.[52,65] Sensitivity and specificity values for both EyeArt screening and manual screening by retinal specialists were converted to true positive versus false-negative rates (for referable cases) and true negative versus false-positive rates (for non-referable cases).[65] Notably, the study by Bhaskaranand used images from a large database that included fundus images that were captured with dilation, without dilation, and dilation unknown.[52] The sensitivity and specificity reported by Bhaskaranand (91.3% and 91.1%, respectively) were derived while treating ungradable cases are referrable.[52] The economic model assumed screening based on undilated fundus images and did not factor in reflex dilation protocols specified in FDA-approval documents.[65] In the model, patients who received a referrable result from the AI-enabled screener were referred for an in-person dilated fundus examination.[65] Ungradable findings were considered to be referrable.[65] Those who did not receive a referrable result were returned to the annual screening pool.[65] Simulated patients with false-negative results were assumed to continue to undergo annual screening, with an annual risk of diabetic retinopathy progression, until they were identified in screening.[65]

All costs were adjusted to 2021 US dollars using the Consumer Price Index.[65] The cost of AI-enabled autonomous diabetic retinopathy screening was set at $48.15 based on information published by CMS in November 2021.[65] Because the study was conducted from a health care payer perspective, the authors did not incorporate provider-oriented costs, such as cameras and software licensing, into the model.[65] Costs were discounted by 3.0% annually.[65] Each health state (no diabetic retinopathy, nonproliferative or proliferative diabetic retinopathy) was assigned a quality-adjusted life years (QALY) value ranging from 0.0 (death) to 1.0 (1 year of perfect health) based on EuroQol 5D scores from a cohort of 2,074 US diabetic patients.[65] Stratification of the QALY scores yielded a mean disutility of 2.1% for patients with diabetic macular edema at each

severity level in the model.[65] Patients with severe vision loss were assigned a utility of 0.640.[65] Deterministic sensitivity analysis was performed to test model stability and identify thresholds at which the cost-effective screening strategy changed, using a willingness-to-pay threshold of $50,000/QALY.[65]

In the final model, AI-enabled diabetic retinopathy screeners demonstrated a cost savings of 18.8%, with net QALY gains identical to those of manual screening, making AI-enabled screening the preferred strategy in the 5-year analysis.[65] AI-enabled diagnostic screening remained less expensive at the extended 10- and 20-year time points, with a net utility gain of 0.001 QALY at 20 years.[65] Multivariate probabilistic sensitivity analysis at 5 years demonstrated that AI-enabled diagnostic screening tools were cost-effective from a health care payer perspective in 99.7% of simulations.[65] The authors also found that cost-effectiveness in the model was highly dependent on specificity, illustrating how excessive false positives could neutralize cost savings through unnecessary referrals and diagnostics.[65] Further, though the authors based their model on a presumption of annual screening for all patients without a diagnosis of diabetic retinopathy, they noted that extending screening intervals for individuals who have a negative reading in screening would reduce baseline costs for both the automated and manual pathways.[65]

Fuller and colleagues (2022) performed a cost-effectiveness analysis of autonomous AI-enabled diabetic retinopathy screening in a primary care medicine clinic that served a low-income patient population.[66] The authors constructed a decision tree to inform a Markov model comparing AI-based screening in primary care to the usual practice of referring all patients with diabetes to an ophthalmologist for a dilated diabetic retinopathy screening exam.[66] The model incorporated data from the study by Liu and colleagues (2020), which used EyeArt in a primary care practice and is included in the evidence review for KQs 1 and 2.[39,66] The Liu study involved screening without dilation and considered all ungradable cases as referrable.[39] The economic modeling study used the study by Liu and colleagues to derive baseline demographic data, referral rates, adherence rates, and diabetic severity distributions for modeling.[66] The authors defined vision-threatening diabetic retinopathy as the presence of any central diabetic macular edema or presence of proliferative or severe nonproliferative diabetic retinopathy.[66] The authors used published epidemiologic data to reflect the racial and ethnic demographics of patients served by their institution in St. Louis, Missouri for use in the economic model.[66] They used data from the Diabetic Retinopathy Clinical Research Network to define treatment and complication rates, as well as rates of progression to severe vision loss.[66] All simulated patients were modeled with good initial visual acuity of 20/30 or better in the better-seeing eye.[66]

Costs were drawn from Medicare 2019 allowable charges using CPT codes and other cost estimates in the published literature and adjusted to reflect 2019 dollars.[66] Using a payor's perspective, annual per-patient treatment and complication costs for years 2 to 5 were modeled as the average for all treatments and complications reported between years 2 to 5 in the respective protocols for the patient's corresponding retinopathy.[66] The primary outcome measure was the incremental cost-utility ratio of current screening practice compared with AI-enabled diagnostic screening, which was used to quantify the incremental cost associated with a 1-unit increase in utility of one health intervention compared to another.[66] The authors provided Markov modeling with microsimulation over a 5-year period.[66] The authors used health utility values associated with vision loss from published sources to calculate QALYs.[66] The willingness-

to-pay, or the dollar amount that health care decision-makers would be willing to pay for a 1-unit increase in effectiveness, was set at $100,000.[66]

At 5 years, the model showed that AI-enabled diagnostic screening had utility comparable to current practice at lower cost.[66] The authors calculated a 23.3% reduction in cost in the AI-enabled diagnostic screening group compared with standard practice ($P < .001$).[66] Comparing current practice to AI-enabled diagnostic screening, the authors computed an incremental cost-utility ratio of $258,721.81. AI-enabled diagnostic screening was cost-effective up to a combined cost of AI-enabled diagnostic screening of $161.14 per screening and up to the standard of care eye examination adherence rate of 71.5%.[66] At a willingness to pay of $50,000, the model favored AI-enabled diagnostic screening in 66% of samples.[66] At a willingness to pay of $100,000, the model favored AI-enabled diagnostic screening in 59% of instances.[66]

KQ5. Clinical Practice Guideline Recommendations

Our searches identified 4 clinical practice guidelines that addressed the use of AI-enabled tools for routine screening for diabetic retinopathy in adult patients with diabetes; all 4 were published, revised, or reaffirmed within the past 5 years (Table 13).[64,67-69] All 4 guidelines described the use of AI-enabled diagnostic screening tools as a promising approach to increase access to routine diabetic retinopathy screening, but only 2 provided official recommendations.[64,67-69] The American Diabetes Association's 2026 Preferred Practice Pattern identifies FDA-cleared AI-enabled diagnostic screening tools as appropriate strategies for screening, as long as there is a pathway for timely referral to an ophthalmologist or retinal specialist.[64] A joint publication from the Asia-Pacific Vitreo-retina Society, the Academy of Asia-Pacific Professors of Ophthalmology, and the Academia Retina Internationalis (2025) includes a consensus statement that notes the potential of AI-enabled diabetic retinopathy screening tools, but advises that more evidence is needed before a full recommendation is issued.[68]

The American Academy of Ophthalmology issued an single-page information statement in June 2020 on use of AI in the diagnosis of diabetic retinopathy.[70] While this is not an official guideline supported by a systematic review and falls outside of our 5-year inclusion window (and is thus not included in Table 13), it does directly address the use of AI-enabled diabetic retinopathy screening tools.[70] The statement notes the recent FDA approval of IDx-DR at the time of publication in 2020.[70] While the organization does not recommend for or against use of AI-enabled diagnostic screening tools, they do recommend that ophthalmologists and policy makers evaluate these technologies as they would any other diagnostic tests, ensuring they are validated, have appropriate regulatory approval before deployment, and are updated as needed.[70] They also note that use of the devices carry some risk of medicolegal liability of harm to the patient, for a missed diagnosis, or a breach of protected health information, although the authors do not expand on potential harms or provide any advice on mitigation strategies.[70]

Table 13. Clinical Practice Guidelines

Organization Title Methodological Quality Assessment	Recommendations Related to Use of AI-Enabled Devices for Diabetic Retinopathy Screening	Discussion of AI-Enabled Devices for Diabetic Retinopathy Screening
American Academy of Ophthalmology (2024)[67] Diabetic Retinopathy Practice Patterns Fair	None	• Notes that new technologies such as telemedicine and autonomous screening systems, are essential to identify, monitor, and guide the treatment of disease. • Provides a brief description of the 3 autonomous systems FDA-cleared for screening to detect referable DR. • Notes that these systems can be deployed in primary care settings to help screen for DR in patients with diabetes. • Advises that the impact of these systems on visual outcomes remains to be seen, but these systems could potentially help improve the DR screening burden. • Cites evidence on cost-effectiveness of AI-enabled diagnostic screening from a single study on a pediatric population.
American Diabetes Association (2026)[64] Standard of Care in Diabetes Good	12.6 Programs that use retinal photography with remote reading or the use of US Food and Drug Administration-cleared AI algorithms to improve access to DR screening are appropriate screening strategies for diabetic retinopathy. Such programs need to provide pathways for timely referral for a comprehensive eye examination when indicated. Grade of Evidence: B	• Notes that retinal photography with remote reading by experts has great potential to provide screening services in areas where qualified eye care professionals are not readily available. • Notes that interpretation of the images should be performed by a trained eye care professional or reading center technician or by FDA-cleared AI-enabled programs.
Asia-Pacific Vitreo-retina Society (APVRS), the Academy of Asia-Pacific Professors of Ophthalmology (AAPPO) and the Academia Retina Internationalis (ARI) (2025)[68] International Consensus and Guidelines on Management of Proliferative Diabetic Retinopathy Fair	Consensus Statement 1.4: Advancements in imaging technologies (e.g., OCT, ultrawide-field imaging) and AI-based tools have the potential to revolutionize DR classification by combining objectivity with comprehensive disease assessment, but further research is needed to validate their integration with existing classification systems. (Consensus score: 100.0 %)	• Notes that AI and machine learning are beginning to play a role in DR classification. • Emphasizes the potential for automation to enhance early detection and management of DR with new technologies.

Organization Title Methodological Quality Assessment	Recommendations Related to Use of AI-Enabled Devices for Diabetic Retinopathy Screening	Discussion of AI-Enabled Devices for Diabetic Retinopathy Screening
Retina Specialists Working Group (2024)[69] Diabetic Disease of the Eye in Canada Poor	None	• Notes that machine-based analysis of retinal photographs for DR detection is a promising technique that could increase the efficiency and reproducibility of screening while alleviating the labor-intensive barrier on providers.

Abbreviations. AI: artificial intelligence; DR: diabetic retinopathy; FDA: US Food and Drug Administration; OCT: optical coherence tomography; RoB: risk of bias.

KQ6. Coverage Policies

Our review focused on the coverage and reimbursement of Category 1 CPT code 92229, which became effective in January 2021 and is defined as: "imaging of retina for detection or monitoring of disease; point-of-care autonomous analysis and report, unilateral or bilateral." [27-30,119,120] This code could apply to all FDA-approved devices for AI-enabled diabetic retinopathy analysis. Prior to 2021, this service did not have its own CPT code.[27-30,119,120]

Providers offering the service typically bill insurers using the CPT code while providing payment to the company for use of their AI-enabled diagnostic screening product.[125] The provider payment to the company is generally structured as: a) a "click fee model" with a fixed payment for each image interpretation; or b) a subscription model with a fee paid (e.g., monthly) to the company for all image interpretations (any quantity).[119,130,131] Providers may also pay the company for leasing the camera equipment.[119]

Medicare

AI-enabled diabetic retinopathy analysis is currently covered by the Medicare program under Category 1 CPT code 92229.[34,71]

The AI-enabled diabetic retinopathy analysis service has been covered under the Medicare Outpatient Prospective Payment (OPPS) system since 2018.[29] It was originally included under a "bridge payment" with a "Q1" status indicator, meaning it was packaged into payment with separately payable services billed during the same visit (through temporary bridge coding with 92250-TC, the technical component of the CPT code for fundus photography).[29,133-135] After receiving a Category 1 CPT code in 2021 (92229), the service was paid separately under the OPPS.[29]

In 2026, CPT code 92229 had an OPPS price of $60.27 and was part of Ambulatory Payment Classification group 5733.[71]

Code 92229 is also covered under the Medicare Physician Fee Schedule.[34] It was initially carrier-priced by individual Medicare Administrative Contractors, and in 2022 it received a national payment rate on the physician fee schedule.[29,34] In 2026, CPT code 92229 was listed on the physician fee schedule with a national reimbursement rate of $46.76.[34]

CMS has not issued a national coverage determination for autonomous screening for diabetic retinopathy, and there are also no local coverage determinations from Medicare Administrative Contractors.[72]

One MAC, Noridian, previously issued a billing and coding article in 2021 titled *Remote Imaging of the Retina to Screen for Retinal Diseases*.[73,74,156] In the article, Noridian specified its coverage for CPT codes 92227, 92228, and 92229 around both the detection and monitoring of diabetic retinopathy.[73,156] The article included specification that 92229 should not be billed if a patient has an in-person ocular examination by an ophthalmologist.[73,156] It also allowed 92229 to be billed for point-of-care follow-up images for patients with established diabetic retinopathy during the rare circumstance when an ophthalmologist is not available.[73,156] The billing article also provided a list of ICD-10 codes that support medical necessity (all for patients with diabetes and/or diabetic retinopathy).[73,156] When Alabama Medicaid activated coverage of CPT code 92229 in 2023, its policy guidance referred to the Noridian billing article for ICD-10 diagnosis codes supporting medical necessity.[157] However, Noridian retired the billing and coding article in November 2023 and it is no longer active.[73,74]

Private Health Plans

Only 2 of the 8 reviewed commercial health plans included specific coverage policy information for AI-enabled diabetic retinopathy analysis (Aetna, Anthem BlueCross BlueShield), and both insurers cover CPT code 92229 for screening of diabetic retinopathy. We did not identify specific coverage policies for any other insurer.

See Table 14 for a summary table of findings, and Appendix I for full detailed policy information.

Table 14. Private Health Plan Coverage

State	Coverage Status (92229)	Policy Criteria and Notes
Aetna[75]	Covered via specific policy	Covered for diabetic retinopathy screening but not for following progression of diabetic retinopathy or screening/evaluating other retinal conditions
Anthem BlueCross BlueShield[76,77,158,159]	Covered via specific policy	Covered for diabetic retinopathy screening but not for following progression of diabetic retinopathy or screening/evaluating other retinal conditions; Medicaid MCO plan in New York could also be providing coverage
Cigna[160,161]	No policy identified	NA
Fidelis Care[78,162-165]	No policy identified	Medicaid MCO plan in New York could also be providing coverage
Healthfirst[166-168]	No policy identified	NA
MetroPlus[169-171]	No policy identified	NA
Molina Healthcare[121,172-175]	No policy identified	No commercial plans in New York; no policy information found for other state commercial plans
UnitedHealthcare[32,176-178]	No policy identified	NA

Source. Health plan policy documentation from Aetna, Anthem BlueCross BlueShield, Cigna, Fidelis Care, Healthfirst, MetroPlusHealth, Molina Healthcare, United Healthcare.
Abbreviations. MCO: managed care organization; NA: not applicable.

Aetna

Covered under specific clinical policy for diabetic retinopathy screening

Aetna maintains a specific policy for retinopathy telescreening systems and considers them medically necessary for screening diabetic retinopathy and retinopathy of prematurity as an alternative to screening by an ophthalmologist or optometrist.[75] The policy includes 92229 as a covered CPT code.[75]

The policy considers retinopathy telescreening systems to be experimental for following the progression of diagnosed diabetic retinopathy, and for screening and evaluating other retinal conditions (e.g., macular degeneration/edema).[75]

Anthem BlueCross BlueShield

Covered under specific clinical policy for diabetic retinopathy screening

Anthem BlueCross BlueShield maintains a specific clinical utilization management policy for retinopathy telescreening systems and considers them medically necessary in the outpatient setting for annual diabetic retinopathy screening as an alternative to screening by an ophthalmologist or optometrist if the patient has not previously been diagnosed and the technique is conducted with an FDA-approved device.[76] The policy includes 92229 as a covered CPT code.[76]

The policy specifies that retinal telescreening systems are not medically necessary for following the progression of disease in patients already diagnosed with diabetic retinopathy, or for screening or evaluating other retinal conditions (e.g., macular degeneration).[76]

Cigna

No specific coverage policy identified

We did not identify any reference to AI-enabled diabetic retinopathy screening or CPT code 92229 within Cigna clinical policies or other plan documentation.[160] The code does appear in Cigna materials about the HEDIS quality metric for diabetic eye exams.[161]

Fidelis Care

No specific coverage policy identified

We did not identify any reference to AI-enabled diabetic retinopathy screening or CPT code 92229 within Fidelis Care clinical policies or other plan documentation.[164] The code does appear in Fidelis materials about the HEDIS quality metric for diabetic eye exams.[165]

Healthfirst

No specific coverage policy identified

We did not identify any reference to AI-enabled diabetic retinopathy screening or CPT code 92229 within Healthfirst clinical policies or other plan documentation.[168]

MetroPlusHealth

No specific coverage policy identified

We did not identify any reference to AI-enabled diabetic retinopathy screening or CPT code 92229 within MetroPlus clinical policies or other plan documentation.[171]

Molina Healthcare

No specific coverage policy identified

Molina Healthcare does not currently offer commercial plans within New York State. We did not identify any reference to AI-enabled diabetic retinopathy screening or CPT code 92229 within Molina clinical policies for commercial plans in other states,[175] The only references identified were associated with the HEDIS quality metric for diabetic eye exams.[121,172]

UnitedHealthcare

No specific coverage policy identified

We did not identify any reference to AI-enabled diabetic retinopathy screening or CPT code 92229 within United clinical policies or other plan documentation.[179] The code does appear in United materials about the HEDIS quality metric for diabetic eye exams.[32]

New York Medicaid MCO Plans

Six of the reviewed private insurers also offer New York Medicaid MCO plans (Anthem,[77,158,159] Fidelis Care,[78,162,163] Healthfirst,[166,167] MetroPlus,[169,170] Molina,[173,174] UnitedHeathcare[176-178]). Although the AI-enabled diabetic retinopathy screening CPT code (92229) is not currently covered by New York's fee-for-service program, some MCOs may offer it on their own:

- Anthem BlueCross BlueShield appears to possibly provide Medicaid MCO coverage, based on the inclusion of 92229 as a service code that does *not* require precertification within the plan's prior authorization look-up tool for its Medicaid line of business,[77] with a reference to the Anthem policy for retinal telescreening systems.[76]
- Fidelis Care also possibly provides Medicaid MCO coverage. Within the Fidelis prior authorization look-up tool for its Medicaid MCO line of business, code 92229 is listed as *not* requiring prior authorization.[78]

We did not identify any information about possible coverage of AI-enabled diabetic retinopathy screening services for the other 4 reviewed insurers offering New York Medicaid MCO plans (Healthfirst, MetroPlus, Molina, United).

Peer Medicaid Agencies

Of the 9 comparator Medicaid agencies, 7 appear to cover AI-enabled diabetic retinopathy analysis, based on their coverage of CPT code 92229. See Table 15 for a summary table of findings, and Appendix I for full detailed policy information.

Table 15. Medicaid Agency Coverage of CPT Code 92229

State	Coverage Status (92229)	Reimbursement Rate, Policy Details, Other Notes
California[79-81]	Covered	No clinical criteria found; no reimbursement price listed
Florida[82,83]	Covered	$35–$36; no clinical criteria found
Massachusetts[84,85]	Covered	$36; no clinical criteria found
New Jersey[86]	Covered	$19–$23; no clinical criteria found

State	Coverage Status (92229)	Reimbursement Rate, Policy Details, Other Notes
New York[33]	No evidence of coverage	NA
North Carolina[87]	Covered	$24; no clinical criteria found
Oregon[91,93,94]	Not covered	HTA body (HERC) put on excluded services list in 2020
Pennsylvania[88,180,181]	Covered	$38; no clinical criteria found
Texas[90,182]	Covered	$36–$38; no clinical criteria found
Washington[92,183,184]	No evidence of coverage	NA

Source. Medicaid fee schedules and documentation from California, Florida, Massachusetts, New Jersey, New York, North Carolina, Oregon, Pennsylvania, Texas, and Washington.
Abbreviations. CPT: current procedural terminology; HERC: Oregon Health Evidence Review Commission. HTA: health technology assessment; NA: not applicable.

California

Covered under fee schedule

California Medicaid lists 92229 as a reimbursable CPT code within both its ophthalmology and professional services policy manuals.[80,81] The agency does not list a price for the service under its fee schedule, implying that it may be priced by-report or invoice-driven.[79] The agency's ophthalmology policy specifies certain codes that may not be billed alongside 92229 on the same date of service, but it does not provide any additional clinical criteria.[80]

Florida

Covered under fee schedule

Florida Medicaid lists CPT code 92229 on both its practitioner and visual services fee schedules.[82,83] The code is reimbursed at $36.37 for the practitioner fee schedule and $34.97 on the visual services fee schedule.[82,83] No clinical criteria or policy was identified.

Massachusetts

Covered under fee schedule

Massachusetts Medicaid lists CPT code 92229 as covered and payable on its vision services policy manual, and the code is reimbursed at $36.09 on the state fee schedule.[84,85] No clinical criteria or policy was identified.

New Jersey

Covered under fee schedule

New Jersey Medicaid lists CPT code 92229 on its fee schedule, and the code is reimbursed at $22.94 for specialists and $19.49 for non-specialists.[86] No clinical criteria or policy was identified.

New York

No evidence of coverage

New York Medicaid does not list CPT code 92229 on any available fee schedules, and the code or a reference to the service does not appear in other agency materials.[33]

North Carolina

Covered under fee schedule

North Carolina Medicaid lists CPT code 92229 on its fee schedule, and the code is reimbursed at $24.11.[87] No clinical criteria or policy was identified.

Oregon

Not covered

Oregon Medicaid does not list CPT code 92229 on any available fee schedules.[91] On the Oregon Health Authority's Prioritized List of Services maintained by the Oregon Health Evidence Review Commission (HERC), the code is included within a list of excluded services that are "unproven, have no clinically important benefit or have harms that outweigh benefits and should be excluded from coverage."[94] The rationale listed is: "[i]nsufficient evidence of effectiveness."[94]

The code was reviewed by HERC in October 2020 just prior to becoming an active CPT Category 1 code.[93] The review specifically looked at the IDx-DR system, several publications, and a private payer policy that considered the product to be investigational at that time (in 2020).[93] The HERC staff summary considered the technology intriguing as a way to increase diabetic retinopathy screening, but found the evidence to date (in 2020) to be insufficient and recommended that it be designated as an excluded service code.[93] The code does not appear to have been re-reviewed in detail since 2020.[94]

Pennsylvania

Covered under fee schedule

Pennsylvania Medicaid lists CPT code 92229 on its fee schedule under a number of provider types and care settings (inpatient, clinic, optometrist, physician), and the code is reimbursed at $37.95.[88] No clinical criteria or policy was identified. In 2022, the agency's managed care operations Technology Assessment Group issued a notice to managed care plans to cover the code (explicitly naming the IDx-DR system), specifying that it would be added to the state Medicaid fee schedule based on well-established medical evidence.[180,181]

Texas

Covered under fee schedule

Texas Medicaid lists CPT code 92229 on its fee schedule and specifies that it is a reimbursable code within its provider manual under the visual and hearing services section.[90,182] The code is reimbursed on the fee schedule at $38.17 for children and $36.35 for adults.[89]

The Medicaid provider manual gives billing guidelines for code 92229, specifying a limitation of 1 service per day and 2 services per calendar year.[90] The Medicaid program also released a bulletin update in 2021 when it activated the CPT code that defined reimbursement-eligible providers as physician assistants, nurse practitioners, clinical nurse specialists, physicians, and optometrist providers in the office, inpatient hospital, and outpatient hospital settings; but that update and the provider manual do not provide additional clinical criteria.[90,182]

Washington

No evidence of coverage

Washington State Medicaid does not list CPT code 92229 on any available fee schedules, and neither the code nor a reference to the service appears in other agency materials.[92,184] The service has not previously been reviewed under the state's Health Technology Assessment program.[183]

Discussion

Our searches identified 26 diagnostic accuracy studies reported in 28 publications (14 studies related to EyeArt, 11 related to IDx-DR, and 1 related to both), 3 cohort studies, 2 cost-effectiveness studies, 4 clinical practice guidelines, and 1 informational statement from the American Academy of Ophthalmology on the use of AI for diabetic retinopathy screening. Diagnostic accuracy studies had wide variability in study designs, including use of prospective or retrospective data, incorporation of pupil dilation into study protocols, and handling of cases the autonomous AI-enabled diagnostic screening tool marked as ungradable due to insufficient image quality. There were wide variations in reported diagnostic accuracy, likely reflecting differences in study protocols and populations.

Autonomous AI-enabled systems have the potential to increase access to diabetic retinopathy screening and improve early detection of diabetic retinopathy.[18] One of the major advantages of AI-based diabetic retinopathy screening is the ability to implement point-of-care testing in primary and community health care settings without the need for specialized equipment or training in ophthalmology.[43] In this context, the performance of the AI-enabled diagnostic screening tools in patients without any dilation is the most important measure of diagnostic accuracy and clinical utility. Studies that estimate diagnostic accuracy based on exclusion of patients with any images the AI tools considered to be of insufficient quality risk inflating estimates of device accuracy.[43,107] In real-world situations, patients with ungradable images would need to be referred to an ophthalmologist or retinal specialist for further review—rather than simply ceasing to exist, as they do in the calculations of diagnostic accuracy studies that omit patients with ungradable results.[17]

Only 1 study related to IDx-DR for detection of more-than-mild diabetic retinopathy included patients who were assessed without dilation and considered ungradable cases as referrals; this study reported a sensitivity of 95% and specificity of 93%.[44] Only 2 diagnostic accuracy studies of EyeArt for detection of more-than-mild diabetic retinopathy met these criteria, reporting a sensitivity of 74% to 100% and specificity of 66% to 87%.[39,41] Variations in outcomes for the 2 EyeArt studies may have been due to differences in the study populations, with one study taking place in a primary care practice with a predominantly African American population[39] and the other and incorporating data from both a primary care practice and a community screening event (where image quality might be expected to be lower than images captured in an office setting) with a primarily Caucasian and Hispanic population.[41]

The balance of sensitivity and specificity across diagnostic accuracy studies, regardless of the use of dilation or the handling of AI-ungradable cases, suggests that the software is unlikely to miss cases of referable diabetic retinopathy, but may refer patients unnecessarily.[40] Autonomous AI-

enabled diagnostic screening systems have several advantages. They may reduce reliance on a scarce pool of human diabetic retinopathy screeners who manually assess digital fundus photographs, and they may increase access to point-of-care testing in primary care, particularly for people residing in areas with a shortage of ophthalmologists and retinal specialists. In theory, AI-based diagnostic screening would limit referrals to those who are most likely to need it. The AI-enabled diagnostic screening systems do not require pupil dilation for all patients, and all 3 systems provide instant feedback to camera operators on image quality, prompting them to retake photos when necessary. The systems provide immediate results, eliminating the need to wait for human screeners to review images and provide results.

The systems also have some disadvantages that may limit their widespread deployment in primary care practices or diabetes care clinics. They require an initial investment in equipment and staff training, as well as ongoing licensing through per-scan costs or monthly fees. The ultimate purpose of the AI-enabled diagnostic screening systems is to limit referrals to human experts to those individuals who most need them; however, high false-positive rates mean that many patients who do not have more-than-mild retinopathy will still be referred for further evaluation. It may also be resource-intensive for practices and frustrating for patients for staff to retake several sets of images during a primary care visit, and the relatively large number of nondiagnostic images may leave staff and patients feeling that time was wasted.[106] Additionally, while the autonomous AI-enabled diagnostic screening tools examined in this report focused solely on identifying referable diabetic retinopathy, a comprehensive dilated exam from an ophthalmologist or retinal specialist would also assess for signs of other eye diseases, including glaucoma, age-related macular degeneration, and cataracts.[63]

The 2 economic evaluations we identified, both of which used data from EyeArt studies and considered ungradable cases to be referrable, concluded that AI-enabled diabetic retinopathy was cost effective compared with usual practice, without any difference in QALYs[65,66] All 4 clinical practice guidelines recognized the potential of FDA-cleared autonomous AI-enabled diabetic retinopathy screening tools to increase access to routine diabetic retinopathy screening,[64,67-69] but only a guideline from the American Academy of Ophthalmology (2024) specifically recommended FDA-cleared AI-enabled diagnostic screening tools as appropriate strategies for screening.[67]

Medicare has provided some level of coverage for AI-enabled diabetic retinopathy screening since 2018 and standalone payment after the service CPT code became active in 2021,[29] with utilization increasing quickly since that time.[35,36] While Medicare provides separate payment exclusively for the autonomous analysis, reimbursement is notably lower than certain other AI-enabled technologies that provide SaaS (e.g., noninvasive cardiac fractional flow reserve measurement).[29,34] The service's CPT code 92229 appears to be covered widely among comparator state Medicaid agencies and by the 2 reviewed health plans that maintain specific policies.

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Appendix A. Search Methods

Clinical Evidence Sources and Search Strategies

We searched selected bibliographic databases and grey literature sources using key words such as *diabetic retinopathy*, *artificial intelligence*, *automated screening*, *machine learning* and device names (e.g., AEye, EyeArt, LumineticsCore) to identify studies evaluating test accuracy, cohort studies, cost-effectiveness studies, as well as clinical practice guidelines. Search results were limited to publications available in the English language. An information specialist constructed and executed all searches. A second information specialist peer reviewed the Ovid MEDLINE search strategy. Searches were conducted January 9, 2026, through January 14, 2026, and April 8, 2026 (clinical trial registries).

Bibliographic Database Sources

- Cochrane Central Register of Controlled Trials (CENTRAL)
- Cochrane Database of Systematic Reviews (CDSR)
- Ovid MEDLINE
- Scopus

Evidence Synthesis Sources

- Agency for Healthcare Research and Quality (AHRQ)
- Canada's Drug Agency
- Epistemonikos
- Health Quality Ontario
- Institute for Clinical and Economic Review (ICER)
- Institute for Health Quality and Efficiency in Health Care
- International Health Technology Assessment (HTA) Database
- National Institute for Health and Care Excellence (NICE)
- Oregon Health Evidence Review Commission (HERC)
- Veterans Administration Evidence Synthesis Program (ESP)
- Washington Health Technology Assessment

Clinical Practice Guideline Sources

- American Academy of Ophthalmology (AAO)
- American Association of Clinical Endocrinology
- American Medical Association (AMA)
- American Society of Retina Specialists
- Association of British Clinical Diabetologists
- Endocrine Society
- Guidelines International Network (GIN) International Guidelines Library
  - National Institute for Health and Care Excellence (NICE)
- Scottish Intercollegiate Guidelines Network (SIGN)
- US Preventive Services Task Force (USPSTF)
- Veterans Administration/Department of Defense Clinical Practice Guidelines

Clinical Trial Sources

- ClinicalTrials.gov
- International Clinical Trials Registry Platform (ICTRP)

MEDLINE Search Strategy

Platform: Ovid
1946 to January 13, 2026
Dates searched (number of results): January 14, 2026 (1,924)

1	diabetic retinopathy/
2	((diabet* or proliferat* or nonproliferat*) adj3 retin*).ti,kf.
3	(diabet* adj3 (eye? or eyesight or macular degenerat* or macular ?edema or sight* or vision or visual*)).ti,kf.
4	or/1-3
5	exp artificial intelligence/
6	artificial intelligen*.ti,kf.
7	(ai adj4 (algorithm* or classif* or detect* or diabet* eye? or diabet* macular or diabet* retinopath* or diagnos* or learn* or predict* or screen* or technolog*)).ti,kf.
8	((automat* or autonomous*) adj4 (classif* or detect* or diagnos* or predict* or screen* or technolog*)).ti,kf.
9	(intelligent adj (classif* or detect* or diagnos* or predict* or screen* or technolog*)).ti,kf.
10	((deep or machine) adj2 learn*).ti,kf.
11	deeplearn*.ti,kf.
12	machinelearn*.ti,kf.
13	large language model*.ti,kf.
14	neural network*.ti,kf.
15	or/5-14
16	aeye.ti,ab,kf,gi,ia,in.
17	(eyeart or eye art or eyenuk or eye nuk).ti,ab,kf,gi,ia,in.
18	(lumineticscore or luminetics core or idxdr or idx-dr).ti,ab,kf.
19	digital diagnostics.gi,ia,in.
20	or/16-19
21	consensus/
22	exp consensus development conferences as topic/
23	exp guidelines as topic/
24	consensus development conference.pt.
25	consensus development conference, NIH.pt.
26	guideline.pt.
27	practice guideline.pt.
28	guideline?.ti,kf.
29	((committee or executive) adj2 (recommendation* or statement* or summar*)).ti,kf.
30	(consensus adj2 (document* or paper* or recommendation* or report* or statement*)).ti,kf.
31	(joint adj2 (document* or recommendation* or statement*)).ti,kf.

32	((policy or position) adj2 (paper* or statement*)).ti,kf.
33	((clinical or critical or practice) adj2 (path? or recommendation? or standard?)).ti,kf.
34	or/22-33
35	and/4,15
36	and/4,34
37	limit 36 to yr="2021 -Current"
38	or/20,35,37
39	(baboon? or bovine? or canine? or cat? or chimpanzee? or chinchilla? or cow? or dog? or feline? or ferret? or goat? or hens or macque? or mice or monkey? or (mouse adj2 model?) or murine? or ovine or pig? or porcine or (non-human adj2 primate?) or (nonhuman adj2 primate?) or sheep or rabbit? or rat or rats or rattus or rhesus or rodent? or swine or zebrafish).ti.
40	38 not 39
41	limit 40 to english language

Cochrane Database of Systematic Reviews (CDSR) and Cochrane Central Register of Controlled Trials (CENTRAL) Search Strategy

Platform: Cochrane Library (Wiley)
CDSR: Issue 1 of 12, January 2026
CENTRAL: Issue 12 of 12, December 2025
Date searched (number of results): January 14, 2026 (CDSR, 0; CENTRAL, 76 uploaded to Distiller)

#1	[mh ^"diabetic retinopathy"]
#2	((diabet* OR proliferat* OR nonproliferat*) NEAR/3 retin*):ti,ab,kw
#3	(diabet* NEAR/3 (eye? OR eyesight OR (macular NEXT degenerat*) OR (macular NEXT ?edema) OR sight* OR vision OR visual*)):ti,ab,kw
#4	#1 OR #2 OR #3
#5	[mh "artificial intelligence"]
#6	(artificial NEXT intelligen*):ti,ab,kw
#7	(ai NEAR/4 (algorithm* OR classif* OR detect* OR (diabet* NEXT eye?) OR (diabet* NEXT macular) OR (diabet* NEXT retinopath*) OR diagnos* OR learn* OR predict* OR screen* OR technolog*)):ti,ab,kw
#8	((automat* OR autonomous*) NEAR/4 (classif* OR detect* OR diagnos* OR predict* OR screen* OR technolog*)):ti,ab,kw
#9	(intelligent NEXT (classif* OR detect* OR diagnos* OR predict* OR screen* OR technolog*)):ti,ab,kw
#10	((deep OR machine) NEAR/2 learn*):ti,ab,kw
#11	deeplearn*:ti,ab,kw
#12	machinelearn*:ti,ab,kw
#13	("large language" NEXT model*):ti,ab,kw
#14	(neural NEXT network*):ti,ab,kw
#15	#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14
#16	(aeye):ti,ab,kw
#17	(eyeart OR "eye art" OR eyenuk OR "eye nuk"):ti,ab,kw
#18	(lumineticscore OR "luminetics core" OR idxdr OR "idx dr"):ti,ab,kw

#19	#16 OR #17 OR #18
#20	#4 AND #15
#21	#19 OR #20

Scopus Search Strategy

Platform: Elsevier
Date searched (number of results): January 14, 2026 (118)

1	TITLE-ABS-KEY (aeye) OR MANUFACTURER (aeye) OR TRADENAME (aeye)
2	TITLE-ABS-KEY (eyeart OR "eye art") OR AFFIL (eyenuk OR "eye nuk") OR MANUFACTURER (eyenuk OR "eye nuk") OR TRADENAME (eyeart OR "eye art")
3	TITLE-ABS-KEY (lumineticscore OR "luminetics core" OR idxdr OR "idx dr") OR AFFIL ("digital diagnostics" OR "idx llc") OR MANUFACTURER ("digital diagnostics" OR "idx llc") OR TRADENAME (lumineticscore OR "luminetics core" OR idxdr OR "idx dr")
4	(TITLE-ABS-KEY (aeye) OR AFFIL (aeye) OR MANUFACTURER (aeye) OR TRADENAME (aeye)) OR (TITLE-ABS-KEY (eyeart OR "eye art") OR AFFIL (eyenuk OR "eye nuk") OR MANUFACTURER (eyenuk OR "eye nuk") OR TRADENAME (eyeart OR "eye art")) OR (TITLE-ABS-KEY (lumineticscore OR "luminetics core" OR idxdr OR "idx dr") OR AFFIL ("digital diagnostics" OR "idx llc") OR MANUFACTURER ("digital diagnostics" OR "idx llc") OR TRADENAME (lumineticscore OR "luminetics core" OR idxdr OR "idx dr"))
5	(TITLE-ABS-KEY (aeye) OR MANUFACTURER (aeye) OR TRADENAME (aeye)) OR (TITLE-ABS-KEY (eyeart OR "eye art") OR AFFIL (eyenuk OR "eye nuk") OR MANUFACTURER (eyenuk OR "eye nuk") OR TRADENAME (eyeart OR "eye art")) OR (TITLE-ABS-KEY (lumineticscore OR "luminetics core" OR idxdr OR "idx dr") OR AFFIL ("digital diagnostics" OR "idx llc") OR MANUFACTURER ("digital diagnostics" OR "idx llc") OR TRADENAME (lumineticscore OR "luminetics core" OR idxdr OR "idx dr")) AND (EXCLUDE (DOCTYPE,"re") OR EXCLUDE (DOCTYPE,"le") OR EXCLUDE (DOCTYPE,"cp") OR EXCLUDE (DOCTYPE,"ch") OR EXCLUDE (DOCTYPE,"ed") OR EXCLUDE (DOCTYPE,"cr"))

Policy Sources and Search Terms

We searched the CMS website and Medicare Coverage Database for local and national coverage determinations and broader coverage policy documentation of autonomous AI-enabled diagnostic screening tools for identification of diabetic retinopathy. We also searched the Medicaid State Waivers List for states with approved, pending, or rejected section 1115a waivers that included coverage of the service. In addition, we searched the websites of the state Medicaid programs and health plans listed below using terms such as *diabetic retinopathy*, *artificial intelligence*, *autonomous*, *diabetes*, *retina*, and CPT code *92229*. Searches were conducted March 6, 2026, through March 13, 2026, and updated June 10, 2026.

State Medicaid Programs

- California Medicaid
- Florida Medicaid
- Massachusetts Medicaid
- New Jersey Medicaid
- New York Medicaid
- North Carolina Medicaid
- Oregon Medicaid and the HERC coverage guidance (including topics under consideration)
- Pennsylvania Medicaid
- Texas Medicaid
- Washington Medicaid and the Washington Health Technology Assessment Program coverage determinations (including topics under consideration)

Health Plans

- Aetna
- Anthem Blue Cross and Blue Shield
- Cigna
- Fidelis Care
- Healthfirst
- MetroPlusHealth
- Molina Healthcare
- UnitedHealthcare

Appendix B. Detailed Inclusion and Exclusion Criteria

Table B1. Detailed Inclusion and Exclusion Criteria

Study Component	Inclusion	Exclusion
Populations	• Adults who meet American Diabetes Association criteria for diabetic retinopathy screening: • Diagnosis of Type 1 diabetes for ≥ 5 years or diagnosis of Type 2 diabetes	• Pediatric patients • Adults without a diagnosis of type 1 or type 2 diabetes • Adults with a previous diagnosis of diabetic retinopathy • Individuals with a diagnosis of eye disease, including macular edema, severe non-proliferative retinopathy, proliferative retinopathy, radiation retinopathy, or retinal vein occlusion
Intervention	• AI-enabled devices FDA-cleared on or before January 1, 2026, for autonomous screening for diabetic retinopathy, including: ○ AEYE-DS (AEYE Health) ○ EyeArt (Eyenuk) ○ LumineticsCore, formerly IDX-DR (Digital Diagnostics)	• Devices without current FDA-clearance
Comparator	• Usual care (retinal screening by an optometrist or ophthalmologist) • Clinical reference standard grading of fundus photographs based on ICDR or ETDRS classification criteria • Another FDA-cleared device for screening for diabetic retinopathy	• No intervention • Comparison with a non-FDA cleared device
Outcomes	Critical (will be presented in GRADE tables) • Measures of diagnostic accuracy (i.e., sensitivity, specificity, positive predictive value, negative predictive value, area under the curve, positive likelihood ration, negative likelihood ratio) • Diagnosis and classification of diabetic retinopathy (i.e., proportion of patients with a finding of any diagnostic retinopathy, more-than-mild diabetic retinopathy, vision-threating diabetic retinopathy, or proliferative diabetic retinopathy) • Adverse events Important (will not be presented in GRADE tables) • Proportion of ungradable results (non-readable images and inconclusive results) • Specialist referral rate compared to reference standard of human grading	• None of the listed outcomes

Study Component	Inclusion	Exclusion
Timing and follow up	• No minimum follow up (KQ1-2) • Cost-effectiveness analyses published within 5 years (KQ3) • Guidelines published, reviewed and reaffirmed, or updated within 5 years (KQ4)	• No restrictions for KQs 2 to 4 • Cost-effectiveness studies or guidelines published more than 5 years prior to the search dates
Setting	• Studies conducted in countries categorized as *very high* on the Human Development Index (KQ2) • Studies conducted in US, or using US-based health systems data (KQ3) • Guidelines developed by organizations in countries categorized as *very high* on the Human Development Index (KQ4)	• Studies conducted in countries not categorized as *very high* on the Human Development Index (KQ2) • Studies not conducted in US, or did not use US-based health systems data (KQ3)
Study design	KQ1 (clinical effectiveness) • Randomized controlled trials • Controlled prospective observational studies • Diagnostic accuracy studies Q2 (clinical utility) • Randomized controlled trials • Controlled prospective observational studies Q3 (harms) • Randomized controlled trials • Observational studies (prospective or retrospective) Q3 (cost-effectiveness) • Comparative studies and economic evaluations • Cost-effectiveness analyses • Economic modeling studies KQ4 (clinical guidelines) • Evidence-based clinical practice guidelines that provide specific diagnostic recommendations	• Studies without extractable data • Studies without a valid comparison group • Uncontrolled studies • Proof-of-principle studies (e.g., program or algorithm development)
Sample size	• Minimum of 20 participants per study arm	• Fewer than 20 participants per study arm randomized • Fewer than 20 participants per study arm included in analysis
Publication type	• Peer-reviewed publication of primary study results • Published in the English language • Ancillary publications with additional comparative follow up	• Abstracts, conference proceedings, posters, editorials, and letters • Studies that have not been formally peer reviewed (i.e., preprint publications) • Studies published in languages other than English • Studies that cannot be found • Duplicate publications of the same study that do not report different outcomes or follow-up times, or single-site reports from published multicenter studies

Abbreviations. ETDRS: Early Treatment Diabetic Retinopathy Study; FDA: US Food and Drug Administration; ICDR: International Clinical Diabetic Retinopathy; GRADE: Grading of Recommendations Assessment, Development, and Evaluation; KQ: key question; US: United States.

Appendix C. Additional Methods

Participant Characteristics and Association with Outcomes

When discussing risk and protective factors or variables in statistical models in Center research products, in almost all cases, we are referring to associations of participant characteristics with outcomes, and not causation of outcomes. This is important because participant characteristics, such as race and ethnicity, serve as proxy or surrogate measures for underlying etiological factors not measured or evaluated in analyses. Etiological factors that might cause differences in outcomes for subgroups of participants could include systemic racism or other forms of systemic discrimination, stress, poverty, housing instability, or epigenetics. For example, by describing any differences in outcomes by race and ethnic groups, we are noting observed associations; these associations are not caused by biological determinants of being Black, White, or Hispanic.

Risk of Bias

Table C1. Risk of Bias Assessment: Nonrandomized Studies

Domain	Domain Elements[a]
Participant selection	For cohort studies: • The 2 groups being studied are selected from source populations comparable in all respects other than factor under investigation, or statistical adjustment is used appropriately to achieve this • The study indicates how many of people asked to take part did so in each of the groups being studied • The likelihood some eligible participants might have outcome at time of enrollment is assessed and considered in analysis • Fewer than 20% of individuals or clusters in each arm of study dropped out before study was completed For case-control studies: • Cases and controls are clearly specified and defined, with inclusion and exclusion criteria applied appropriately • Cases may be selected by meeting inclusion criteria, controls may be selected by meeting inclusion criteria and then being matched to cases • Sampling selection (ratio of cases to control) is justified • Cases and controls selected from same population and same timeframe; when not all cases and controls are selected from same population, these are randomly selected • Among cases, investigators confirm that exposure occurred before development of disease being studied and/or likelihood that some eligible participants might have outcome at time of enrollment is assessed and considered in analysis
Intervention	• The assessment of exposure to intervention is reliable • Exposure level or prognostic factors are assessed at multiple times across length of study, if appropriate • For case-control studies, assessors of (intervention) exposure status are unaware (masked or blinded) to case or control status of participants, and there is a method to limit effects of recall bias on assessment of exposure to intervention
Control	• Control condition represents an appropriate comparator

Domain	Domain Elements[a]
Outcome	• There is a precise definition of outcomes used • Outcomes are measured using valid and reliable measures, evidence from other sources is used to demonstrate method of outcome assessment is valid and reliable • Investigators use single outcome measures and do not rely on composite outcomes, or outcome of interest can be calculated from composite outcome • The study has an appropriate length of follow up for outcome reported and groups are assessed at same time points • Outcome reporting of entire group or subgroups is not selective • When patient-reported outcomes are used, there is a method for validating measure
Masked outcome assessment	• The assessment of outcome(s) is made blind to exposure status. Where outcome assessment blinding was not possible, there is recognition that knowledge of exposure status could have influenced assessment of outcome. • For case-control study: assessors of exposure status are unaware (masked or blinded) of case or control status of participant
Confounding	• The main potential confounders are identified and considered in design and analysis of study
Statistical analysis	• Comparison is made between full participants and those who dropped out or were lost to follow up, by exposure status • If groups were not followed for an equal length of time, analysis was adjusted for differences in length of follow up • All major confounders are adjusted for using multiple variable logistic regression or other appropriate statistical methods • Confidence intervals (or information used to calculate them) are provided • For case-control studies that use matching, conditional analysis is conducted or matching factors are adjusted for in analysis
Other biases (as appropriate)	• List others in table footnote and describe • Sample size adequacy
Interest disclosure	• Disclosures of interest are provided for authors/funders/commissioners of study • Interests are unlikely to significantly affect study validity
Funding source	• There is a description of source(s) of funding • Funding source is unlikely to have a significant impact on study validity

Note. [a] *The elements included in each domain are assessed and rated as yes, no, unclear, or not applicable based on performance and documentation of individual elements in each domain. The overall risk of bias for a study is assessed as high, moderate, or low based on assessment of how well overall study methods and processes were performed to limit bias and ensure validity.*

Table C2. Risk of Bias Assessment: Economic Modeling Studies

Domain	Domain Elements[a]
Target population	• Target population and care setting described • Describe and justify basis for any target population stratification, identify any previously identifiable subgroups • If no subgroup analyses were performed, justify why these were not required
Perspective	• State and justify analytic perspective (e.g., societal, payer, etc.)
Time horizon	• Describe and justify time horizon(s) used in analysis

Domain	Domain Elements[a]
Discount rate	• State and justify discount rate used for costs and outcomes
Comparators	• Describe and justify selected comparators • Competing alternatives appropriate and clearly described
Modelling	• Model structure (e.g., scope, assumptions made) is described and justified • Model diagram provided, if appropriate • Model validation is described (may involve validation of different aspects such as structure, data, assumptions, and coding and different validation models such as comparison with other models) • Data sources listed and assumptions for use justified • Statistical analyses are described
Effectiveness	• Estimates of efficacy/effectiveness of interventions are described and justified • The factors likely to have an impact on effectiveness (e.g., adherence, diagnostic accuracy, values, and preferences) are described and an explanation of how these were factored into analysis is included • The quality of evidence for relationship between intervention and outcomes, and any necessary links, is described
Outcomes	• All relevant outcomes are identified, measured, and valued appropriately (including harms/adverse events) for each intervention, and justification for information/assumptions is given • Any quality-of-life measures used in modelling are described and use justified • Any other outcomes that were considered but rejected are described with rationale for rejection • Ethical and equity-related outcomes are considered and included when appropriate
Resource use/costs	• All resources used are identified, valued appropriately, and included in analyses • Methods for costing are reporting (e.g., patient level) • Resource quantities and unit costs are both reported • Methods for costing time (e.g., lost time, productivity losses) are appropriate and a justification is provided if time costs are not considered
Uncertainty	• Sources of uncertainty in analyses are identified and justification for probability distributions used in probabilistic analyses are given • For scenario analyses, values and assumptions tested are provided and justified
Results	• All results are presented in a disaggregated fashion, by component, in addition to an aggregated manner • All results are presented with undiscounted totals before discounting and aggregation • Natural units are presented along with alternative units (e.g., QALYs) • The components of incremental cost-effectiveness ratio (ICER) are shown (e.g., mean costs of each intervention in numerator and mean outcomes of each intervention in denominator) • Results of scenario analyses, including variability in factors such as practice patterns and costs, are reported and described in relation to reference (base) case
Interest disclosure	• Disclosures of interest are provided for authors/funders/commissioners of study • Interests are unlikely to significantly affect study validity
Funding source	• There is a description of source(s) of funding • Funding source is unlikely to have a significant impact on study validity

Note. [a] The elements included in each domain are assessed and rated as yes, no, unclear, or not applicable based on performance and documentation of individual elements in each domain. The overall risk of bias for a study is assessed as high, moderate, or low based on assessment of how well overall study methods and processes were performed to limit bias and ensure validity.
Abbreviation. ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year.

Table C3. Methodological Quality Assessment: Clinical Practice Guidelines

Domain	Domain Elements[a]
Rigor of development: evidence	• Systematic literature search meets quality standards for a systematic review (i.e., comprehensive search strategy with, at a minimum, 2 or more electronic databases) • The criteria used to select evidence for inclusion is clear and appropriate • The strengths and limitations of individual evidence sources is assessed and overall quality of body of evidence assessed
Rigor of development: recommendations	• Methods for developing recommendations clearly described and appropriate • There is an explicit link between recommendations and supporting evidence • The balance of benefits and harms is considered in formulating recommendations • The guideline has been reviewed by external expert peer reviewers • The updating procedure for guideline is specified in guideline or related materials (e.g., specialty society website)
Editorial independence	• There is a description of source(s) of funding and views of funder(s) are unlikely to have influenced content or validity of guideline • Disclosures of interests for guideline panel members are provided and are unlikely to have a significant impact on overall validity of guideline (e.g., a process for members to recuse themselves from participating on recommendations for which a significant conflict is provided)
Scope and purpose	• Objectives specifically described • Health question(s) specifically described • Target population(s) for guideline recommendations is specified (e.g., patients in primary care) and target users for guideline (e.g., primary care clinicians)
Stakeholder involvement	• Relevant professional groups represented • Views and preferences of target population(s) sought (e.g., clinicians and patients)
Clarity and presentation	• Recommendations are specific and unambiguous • Different management options are clearly presented • Key recommendations are easily identifiable
Applicability	• Provides advice and/or tools on how recommendation(s) can be put into practice • Description of facilitators and barriers to its application • Potential resource implications considered • Criteria for implementation monitoring, audit, and/or performance measures based on guideline are presented

Note. a The elements included in each domain are assessed and rated as yes, no, unclear, or not applicable based on performance and documentation of individual elements in each domain. The overall risk of bias for a study is assessed as high, moderate, or low based on assessment of how well overall study methods and processes were performed to limit bias and ensure validity.

GRADE (Grading of Recommendations Assessment, Development and Evaluation)

Table C4. GRADE System for Rating the Certainty of Evidence for Outcomes

GRADE Rating	Plain Language Description	Detailed Category Description
High	New research is very unlikely to change our understanding of the relationship between this outcome and the health technology.	Center researchers are very confident that the estimate of the effect of the intervention on the outcome lies close to the true effect. Typical sets of studies are RCTs with few or no limitations, and the estimate of effect is likely stable.
Moderate	New research may change our understanding of the relationship between this outcome and the health technology.	Center researchers are moderately confident in the estimate of the effect of the intervention on the outcome. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is different. Typical sets of studies are RCTs with some limitations or well-performed nonrandomized studies with additional strengths that guard against potential bias and have large estimates of effects.
Low	New research is likely to change our understanding of the relationship between this outcome and the health technology.	Center researchers have little confidence in the estimate of the effect of the intervention on the outcome. The true effect may be substantially different from the estimate of the effect. Typical sets of studies are RCTs with serious limitations or nonrandomized studies without special strengths.
Very low	New research is very likely to change our understanding of the relationship between this outcome and the health technology.	Center researchers have no confidence in the estimate of the effect of the intervention on the outcome. The true effect is likely to be substantially different from the estimate of effect. Typical sets of studies are nonrandomized studies with serious limitations or inconsistent results across studies.
Not applicable	There is no research to report.	Center researchers did not identify any eligible articles.

Source. Adapted from 2 publications on GRADE.[185,186]
Abbreviations. GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; RCT: randomized controlled trial.

Appendix D. Included Studies

Table D1. Included Studies by Key Question

Diagnostic Test Accuracy (KQ1)
Abramoff MD, Lavin PT, Birch M, et al. Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices. 2018;1:39.
Bhaskaranand M, Ramachandra C, Bhat S, et al. The value of automated diabetic retinopathy screening with the EyeArt System: a study of more than 100,000 consecutive encounters from people with diabetes. 2019;21(11):635-643.
Dow ER, Khan NC, Chen KM, et al. AI-human hybrid workflow enhances teleophthalmology for the detection of diabetic retinopathy. 2023;3(4):100330.
Grzybowski A, Brona P, Krzywicki T, et al. Diagnostic accuracy of automated diabetic retinopathy image assessment software: IDx-DR and RetCAD. 2025;14(1):73-84.
Grzybowski A, Rao DP, Brona P, et al. diagnostic accuracy of automated diabetic retinopathy image assessment softwares: IDx-DR and Medios Artificial Intelligence. 2023;66(1):1286-1292.
Guedes IIG, Saavedra Santana P, Lopez FC, et al. Evaluation of the degree of agreement in the diagnosis of diabetic retinopathy between ophthalmologists and EyeArt((R)). 2025;11(1):125.
Heydon P, Egan C, Bolter L, et al. Prospective evaluation of an artificial intelligence-enabled algorithm for automated diabetic retinopathy screening of 30 000 patients. 2021;105(5):723-728.
Ibáñez-Bruron MC, Cruzat A, Ordenes-Caviere G, et al. Use of artificial intelligence in diabetic retinopathy screening: experience in a health service in Santiago, Chile. 2024;152(11):1148-1153.
Ipp E, Liljenquist D, Bode B, et al. Pivotal evaluation of an artificial intelligence system for autonomous detection of referrable and vision-threatening diabetic retinopathy. 2021;4(11):e2134254. Ancillary: Lim JI, Regillo CD, Sadda SR, et al. Artificial intelligence detection of diabetic retinopathy: subgroup comparison of the EyeArt System with ophthalmologists' dilated examinations. 2023;3(1):100228.
Karabeg M, Petrovski G, Holen K, et al. Comparison of validity and reliability of manual consensus grading vs. automated AI grading for diabetic retinopathy screening in Oslo, Norway: a cross-sectional pilot study. 2025;14(13):4810.
Liu J, Gibson E, Ramchal S, et al. Diabetic retinopathy screening with automated retinal image analysis in a primary care setting improves adherence to ophthalmic care. 2021;5(1):71-77.
Mehra AA, Softing A, Guner MK, et al. Diabetic retinopathy telemedicine outcomes with artificial intelligence-based image analysis, reflex dilation, and image overread. 2022;244:125-132.
Mokhashi N, Grachevskaya J, Cheng L, et al. A comparison of artificial intelligence and human diabetic retinal image interpretation in an urban health system. 2022;16(4):1003-1007.
Musetti D, Cutolo CA, Bonetto M, et al. Autonomous artificial intelligence versus teleophthalmology for diabetic retinopathy. 2025;35(1):232-238.
Olvera-Barrios A, Heeren TF, Balaskas K, et al. Diagnostic accuracy of diabetic retinopathy grading by an artificial intelligence-enabled algorithm compared with a human standard for wide-field true-colour confocal scanning and standard digital retinal images. 2021;105(2):265-270.
Poschkamp B, Kantz L, Augstein P, et al. Customizing AI-based screening with real-world data: Practical insights from diabetic retinopathy. 2025;11:1-10.
Riotto E, Gasser S, Potic J, et al. Accuracy of autonomous artificial intelligence-based diabetic retinopathy screening in real-life clinical practice. 2024;13(16):14.
Sarao V, Veritti D, Lanzetta P. Automated diabetic retinopathy detection with two different retinal imaging devices using artificial intelligence: a comparison study. 2020;258(12):2647-2654.

Sedova A, Hajdu D, Datlinger F, et al. Comparison of early diabetic retinopathy staging in asymptomatic patients between autonomous AI-based screening and human-graded ultra-widefield colour fundus images. 2022;36(3):510-516.
Shah A, Clarida W, Amelon R, et al. Validation of Automated Screening for Referable Diabetic Retinopathy With an Autonomous Diagnostic Artificial Intelligence System in a Spanish Population. 2021;15(3):655-663.
Tufail A, Kapetanakis VV, Salas-Vega S, et al. An observational study to assess if automated diabetic retinopathy image assessment software can replace one or more steps of manual imaging grading and to determine their cost-effectiveness. 2016;20(92):1-72. Ancillary: Tufail A, Rudisill C, Egan C, et al. Automated diabetic retinopathy image assessment software: diagnostic accuracy and cost-effectiveness compared with human graders. 2017;124(3):343-351.
van der Heijden AA, Abramoff MD, Verbraak F, et al. Validation of automated screening for referable diabetic retinopathy with the IDx-DR device in the Hoorn Diabetes Care System. 2018;96(1):63-68.
Van TN, Thi HLV. Effectiveness of artificial intelligence for diabetic retinopathy screening in community in Binh Dinh Province, Vietnam. 2024;14(3):394-402.
Verbraak FD, Abramoff MD, Bausch GCF, et al. Diagnostic accuracy of a device for the automated detection of diabetic retinopathy in a primary care setting. 2019;42(4):651-656.
Vought R, Vought V, Shah M, et al. EyeArt artificial intelligence analysis of diabetic retinopathy in retinal screening events. 2023;43(12):4851-4859.
Wintergerst MWM, Bejan V, Hartmann V, et al. Telemedical diabetic retinopathy screening in a primary care setting: quality of retinal photographs and accuracy of automated image analysis. 2022;29(3):286-295.
Cohort Studies (KQ2)
Channa R, Wolf RM, Abramoff MD, et al. Effectiveness of artificial intelligence screening in preventing vision loss from diabetes: a policy model. 2023;6(1):53.
Dow ER, Chen KM, Zhao CS, et al. Artificial intelligence improves patient follow up in a diabetic retinopathy screening program. 2023;17:3323-3330.
Huang JJ, Channa R, Wolf RM, et al. Autonomous artificial intelligence for diabetic eye disease increases access and health equity in underserved populations. 2024;7(1):196.
Economic Studies (KQ4)
Chawla H, Uhr JH, Williams JS, et al. Economic evaluation of artificial intelligence systems versus manual screening for diabetic retinopathy in the United States. 2023;54(5):272-280.
Fuller SD, Hu J, Liu JC, et al. Five-Year Cost-Effectiveness modeling of primary care-based, nonmydriatic automated retinal image analysis screening among low-income patients with diabetes. 2022;16(2):415-427.
Clinical Practice Guidelines (KQ5)
American Academy of Ophthalmology. Diabetic retinopathy. Preferred practice pattern. 2024.
American Academy of Ophthalmology. Use of artificial intelligence in the diagnosis of diabetic retinopathy and other conditions. June 2020.
American Diabetes Association Professional Practice Committee. Standards of care in diabetes-2026. 2026(Supplement 1);49:S6-S12.
Lam RF, Radke NV, Bandello FM, et al. International consensuses and guidelines on management of proliferative diabetic retinopathy (PDR) by the Asia-Pacific Vitreo-retina Society (APVRS), the Academy of Asia-Pacific Professors of Ophthalmology (AAPPO) and the Academia Retina Internationalis (ARI). 2025;14(6):100262.
Omar A, Williams RG, Whelan J, et al. Diabetic disease of the eye in Canada: consensus statements from a retina specialist working group. 2024;13(5):1071-1102.

Appendix E. Risk of Bias Assessment

Table E1. Risk of Bias in Diagnostic Accuracy Studies, Part 1

Lead Study Author, Year	Consecutive or Random Sample	Participants Representative of Real-World Population	Clear Inclusion/ Exclusion Criteria	Appropriate Reference Standard	Reference Standard Graders Blinded to Index Test	All Participants Received Reference Standard	Index Test Interpreted Without Knowledge of Reference Standard	Thresholds and Cutoffs Determined a Priori	Uninterpretable Results Reported
Abramoff 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Bhaskaranand 2019	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Dow 2023	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Grzybowski 2025	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Grzybowski 2023	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	No
Guedes 2025	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Heydon 2021	Yes	Unclear	No	Yes	Unclear	Yes	Yes	Yes	No
Ibanez-Bruron 2024	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Ipp 2021	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Karabeg 2025	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Liu 2021	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Mehra 2022	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Mokhashi 2022	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes
Musetti 2025	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	No
Olvera-Barrios 2021	Unclear	Yes	No	Yes	Yes	Yes	Yes	Yes	No
Poschkamp 2025	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Riotto 2024	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sarao 2020	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes

Lead Study Author, Year	Consecutive or Random Sample	Participants Representative of Real-World Population	Clear Inclusion/ Exclusion Criteria	Appropriate Reference Standard	Reference Standard Graders Blinded to Index Test	All Participants Received Reference Standard	Index Test Interpreted Without Knowledge of Reference Standard	Thresholds and Cutoffs Determined a Priori	Uninterpretable Results Reported
Sedova 2022	Unclear	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	No
Shah 2021	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tufail 2016	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear
van der Heijden 2018	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Van 2024	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Verbraak 2019	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Vought 2023	Unclear	Unclear	No	Yes	Yes	Yes	Yes	Yes	Yes
Wintergerst 2022	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table E1. Risk of Bias in Diagnostic Accuracy Studies, Part 2

Lead Study Author, Year	All Participants Included in Analysis	Conflicts of Interest	Sources of Funding	Generalizability	Overall Risk of Bias
Abramoff 2018	No	Yes	Yes	Yes	Moderate. Well done and thoroughly described study. Bias arises from lack of detail on outcomes (no confusion matrix) and limited diagnostic accuracy information (only sensitivity and specificity provided).
Bhaskaranand 2019	Yes	Yes	Yes	Yes	Moderate. Clear methods. Includes all patients (classifying ungradable as referrable), so it's less likely to be overestimating diagnostic accuracy. Most authors are associated with Eyenuk but there's no reason to think it increased RoB. The largest issue here is that we don't know anything about the demographics of these patients. We can't even confirm that they're all adults. We don't know the male:female mix, the proportion with T1D vs T2D, or the average age.

Lead Study Author, Year	All Participants Included in Analysis	Conflicts of Interest	Sources of Funding	Generalizability	Overall Risk of Bias
Dow 2023	No	Yes	Yes	Unclear	High. Too many unanswered questions about the amount of missing data and why numbers are not reported for the full 199 patients with IDx-defined gradable images who were screened by human graders or the 223 people with IDx-defined ungradable images who were screened by human graders.
Grzybowski 2025	No	Yes	Yes	Yes	Moderate. Limited to patients who passed the IDx quality check and we don't have numbers for how many patients were excluded / how many images were deemed to be of insufficient quality.
Grzybowski 2023	No	Yes	Yes	Unclear	High. Lack of detail on the study population limits our ability to gauge how representative these patients were of the general population of people eligible for screening. We also don't know if children were included (IDx is not FDA-cleared for use in children). Omitting any patients who had images deemed ungradable by IDx raises risk that performance of the software will be overstated.
Guedes 2025	No	Yes	Yes	Yes	Moderate. Lacks some detail and limits the primary analysis to any DR vs no DR, but provides a good example of use of EyeArt in a real-world screening context.
Heydon 2021	Yes	Yes	Yes	Yes	Moderate. We don't know if any patients were excluded for any reason, or if there were genuinely 30,000+ consecutive patients. While it's good that patients EyeArt marked as ungradable are included in analysis, we do not have any details on how many patients that was. There's not enough information about the people included in screening (such as the breakdown of T1D and T2D) to know how representative the group was. Given that it was a national screening effort, we can infer it was representative of the British screenable population but can't definitively confirm.
Ibanez-Bruron 2024	Yes	Yes	Unclear	Unclear	High. Very limited detail. Patients all had their eyes dilated, which is not the usual protocol for EyeArt (and the ability to screen without dilation is a selling point for AI screeners). We do not know much about the sample apart from knowing they had diabetes. Can piece together what they did from the numbers they provide, but it is not well described (even after reviewing the second document they refer to for methods).

Lead Study Author, Year	All Participants Included in Analysis	Conflicts of Interest	Sources of Funding	Generalizability	Overall Risk of Bias
Ipp 2021	No	Unclear	Yes	Yes	High. Lacking some detail (for example, could not construct confusion matrices to verify their findings and we don't know how many people required dilation for Eyenuk reading), but the FDA-specified subanalysis was on the whole well done. Risk of bias because the Eyenuk team designed the study, controlled the data, and carried out all analysis. We did not extract data from the main publication, which reported outcomes by eye, rather than by patient, and combined patients who were sequentially enrolled and those who were oversampled for greater likelihood of eye disease.
Karabeg 2025	No	Yes	Yes	Unclear	Moderate. Unknown if this was a consecutive sample of referrals. The double counting of 7 eyes (out of 254 eyes) wouldn't be that much of a concern if results were translated to patients, but all results are provided per eye. Even though it's only 3% of eyes, it raises some concerns.
Liu 2021	Yes	Unclear	Unclear	Yes	Moderate. The use of the historical control isn't too helpful in the absence of other information. What screening, if any, were they getting? Are the 974 included in the historical control 'with recommended visit' just people that the PCP told to go get screened because that's the guideline, or were they getting any other service? As a diagnostic accuracy study, it's fine. The biggest issue is dividing the data into referrable or vision-threatening (vs non-referrable). People who get the vision-threatening flag are still referred. Removing them from the bucket of referrable will have an effect on accuracy numbers.
Mehra 2022	No	Yes	Yes	Yes	Moderate. Likelihood that diagnostic accuracy is over-reported because of omission of ungradable images (which would have been considered referrable and would still have been part of the workflow). Graders would have been aware of which patients were graded not more-than-mild (they were reviewed in batches monthly) and which were graded more-than-mild or ungradable (they were asked to review within 2 to 3 days).

Lead Study Author, Year	All Participants Included in Analysis	Conflicts of Interest	Sources of Funding	Generalizability	Overall Risk of Bias
Mokhashi 2022	No	Yes	Yes	Yes	Moderate. Does not report whether human graders were blinded to the EyeArt findings. Excludes 31% (80 of 260) of patients with ungradable findings, which likely inflates the diagnostic accuracy statistics.
Musetti 2025	Yes	Yes	Yes	Yes	High. Minimal information provided by authors on study design and inclusion/exclusion. Does not provide detailed information on diagnoses—only sensitivity and specificity. Unclear what the sensitivity and specificity calculations relate to. I.e., any diagnosis of DR? More-than-mild diagnosis?
Olvera-Barrios 2021	Unclear	Yes	Yes	Unclear	High. This is the right general population (people 18 and up attending an annual diabetic eye screening program), but there are too many unknowns here. Were all patients who were screened by EyeArt included in analysis? Or were only those who had images judged acceptable by the EyeArt software moved forward (to imaging with the second camera type)? There is no information provided on EyeArt ungradable images and no demographic information. We can assume all of these people had diabetes, since they were in a diabetes screening program, but it is not definitely reported and there's no breakdown by T1D and T2D and no reporting of ages.
Poschkamp 2025	No	Yes	Yes	Yes	Moderate. Excluding uninterpretable results risks overestimating performance. Otherwise, a very well done and clearly explained study.
Riotto 2024	No	Yes	Yes	Yes	High. Lacks important outcome detail. No information to construct a confusion matrix or calculate diagnostic accuracy for the more-than-mild DR group (referable patients). Does not include measures of variability (confidence intervals). Omits 15.5% of patients due to insufficient image quality, which risks creating inflated measured of diagnostic accuracy.

Lead Study Author, Year	All Participants Included in Analysis	Conflicts of Interest	Sources of Funding	Generalizability	Overall Risk of Bias
Sarao 2020	No	Yes	No	Unclear	High. Presented at the per eye level, rather than the per patient level. Patients are referred based on their worst eye, so it is not clear how this would translate to number of patients referred. There are no exclusion criteria so we don't know if people with a prior eye disease diagnosis or history of laser surgery were included or excluded. We can make some general guesses, but we don't really know how many people were excluded from the study. We don't know how many people would be referred for further evaluation based on number of eyes alone. Images marked as ungradable by EyeArt were omitted from diagnostic accuracy calculations, although in practice they would be considered as referrable. There is a lack of information to construct a confusion matrix and the authors reported only sensitivity, specificity, and AUC.
Sedova 2022	Unclear	Yes	No	Unclear	High. Doesn't address the issue of ungradable images, and we don't know if images deemed ungradable by IDx were excluded, or whether there weren't any ungradable images (which would be surprising, even in this small sample). We don't know when this took place and we don't know if human graders were aware of the IDx results. Presence or absence of funding isn't directly reported.
Shah 2021	No	Unclear	Unclear	Unclear	High. Study is sponsored by IDx and most authors are affiliated with IDx. Does not report ages included in the study, so we don't know if pediatric patients were included. Omits patients with ungradable results, which has the potential to inflate diagnostic accuracy outcomes (even though ungradable patients would be considered referrable and would still be part of the clinic workflow).
Tufail 2016	Unclear	Yes	Yes	Yes	Moderate. NHS counts ungradable images as referrable. No indication that EyeArt found any images ungradable, which would be a surprise. The study was well done and the downgrade is solely for questions about ungradable images in the EyeArt system.

Lead Study Author, Year	All Participants Included in Analysis	Conflicts of Interest	Sources of Funding	Generalizability	Overall Risk of Bias
van der Heijden 2018	No	Unclear	Unclear	Yes	High. Does not report age ranges and pediatric patients aren't excluded, so we don't know if children were included in the study (and if so, how many). Omits patients who had ungradable images per IDx, so likely overestimates diagnostic accuracy. If you consider ungradable images as referrable (which they generally are in practice), they would still be included in comparison with human grader results. Study is funded by IDx and authors included IDx's founder, but unclear if that introduced any bias.
Van 2024	Yes	Yes	Yes	Yes	Moderate. Gives insight into use of EyeArt in a real-world context in a resource-limited setting, and performance of the system with non-Caucasian eyes. Unclear whether the cases used represent a random sample or all patients screened during this time period who met inclusion/exclusion criteria. Does not provide information on number of unreadable images or how many patients were excluded because they had unreadable images. Reports that there were no differences by age or sex, but only provides p values (no detailed data)
Verbraak 2019	No	Unclear	Yes	Yes	Moderate. The authors report results for the subset of data that IDx was able to grade, which could overestimate diagnostic accuracy, but give us enough information to run comparative numbers if ungradable cases were considered referable. The biggest issue here is that we don't know if this sample included children (IDx is not FDA-cleared for pediatric use).
Vought 2023	Yes	Yes	Yes	Unclear	High. Really light on details. Not enough information to construct a confusion matrix and what information they do give does not have measures of dispersal (i.e., confidence intervals). Includes but is not limited to the population of interest.
Wintergerst 2022	No	Yes	Yes	Yes	High. Not a consecutive or random sample. Omission of ungradable images likely inflated diagnostic accuracy figures. Does not provide data sufficient to create confusion matrix.

Table E2. Risk of Bias in 3 Observational Studies, Part 1

Lead Study Author, Year	Comparable Groups	Reliable and Consistent Exposure Assessment	Reliable and Consistent Outcome Measure	Blinding of Study Analysts	Appropriate Length of Follow Up	Groups Followed for Equal Time	Comparison by Exposure Status	Adjustment for Confounders	Appropriate Effect Size Used
Channa 2023	Yes	Yes	Yes	NA	Unclear	Yes	Yes	Unclear	Yes
Dow 2023	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes
Huang 2024	Yes	Yes	Yes	NA	NA	NA	Yes	Yes	Yes

Table E2. Risk of Bias in 3 Observational Studies, Part 2

Lead Study Author, Year	Loss to Follow Up Unlikely to Bias Results	Disclosures of Interest for Authors	Description of Funding Source	Results Applicable to Purpose of Report	Overall Risk of Bias
Channa 2023	Yes	Unclear	Yes	Unclear	Moderate. Some concerns related to the role of IDx's founder and some of the assumptions that inform the model, but it is well described and transparent. Unclear how applicable this is to the intended purpose of the report and the use of IDx in practice.
Dow 2023	No	Unclear	Yes	Yes	High. Within the constraints of the study design, provides valuable and relevant information. Results represent the workflow in this particular system, where results flagged as ungradable were reviewed by human graders. In that context, the omission of ungradable patients from IDx analysis makes sense, but in systems where ungradable results are considered referrals (and aren't reviewed by a human), the high percent follow up reported here would likely be lower. The biggest question here is what happened to the 120 patients with ungradable results in IDx who disappear from analysis. Additionally, the only group who had both human and AI grading were those who had ungradable results returned by IDx. Human graders would have been aware of that (so not blinded to outcomes).

Lead Study Author, Year	Loss to Follow Up Unlikely to Bias Results	Disclosures of Interest for Authors	Description of Funding Source	Results Applicable to Purpose of Report	Overall Risk of Bias
Huang 2024	NA	Unclear	Yes	Unclear	Moderate. Reportedly includes all adult patients with diabetes managed within Johns Hopkins Medicine's primary care sites. Does not describe if any patients were excluded (i.e., those who were not candidates for IDx, those who had a DR diagnosis, etc.) or if those criteria were factored into their calculations of 'adherence'. Methods section lacks detail and does not provide enough information for another researcher to replicate their data gathering steps or analysis methods. Numbers do not represent unique patients. Patients could be seen more than once in a given clinic in a given year and there's only a general reference to controlling for such occurrences. Does not provide detail on how IDx was rolled out in the clinics where it was used and what protocols were in place (were all patients screened with IDx? Only those who met certain requirements, etc.). Tracks the proportion of patients in any given year who received recommended screening, but makes some leaps about what that says about access and health equity.

Table E3. Risk of Bias in Cost-Effectiveness Studies, Part 1

Lead Study Author, Year	Target Population Described and Justified	Analytic Perspective Defined	Time Horizon Described and Justified	Discount Rate Used for Costs and Outcomes Defined	Appropriate Comparators and Competing Alternatives	Analytic Model Well Defined and Justified	Estimates of Effectiveness of Interventions Described	Relevant Outcomes Identified, Measured, and Valued Appropriately	Resources Used in Evaluation Identified and Valued Appropriately
Chawla 2023	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Fuller 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table E3. Risk of Bias in Cost-Effectiveness Studies, Part 2

Lead Study Author, Year	Sources of Uncertainty Identified and Addressed	Disaggregated Results Presented	Disclosures of Interest	Disclosures of Funding Source	Generalizability	Overall Risk ff Bias
Chawla 2023	Yes	Yes	Yes	Yes	Yes	Low. Well described. Sources and assumptions defined and justified. Sensitivity analysis included. Results of costs modeled across various scenarios provided. Directly relevant.
Fuller 2022	Yes	Yes	Yes	Yes	Yes	Low. Very well described. Thoroughly catalogs and justifies sources and assumptions. Detailed model with visuals. Well-defined inputs. Discussion of limitations.

Table E4. Risk of Bias in Clinical Practice Guidelines, Part A

Organization Lead Author, Year	Comprehensive Systematic Review	Clear and Appropriate Inclusion Criteria	Assessed Strengths and Limitations of Evidence	Clear Methods for Recommendation Development	Explicit Link Between Recommendations and Evidence	Balanced of Benefits and Harms
American Academy of Ophthalmology 2024	Yes	NR	Yes	Somewhat	Yes	Yes
American Diabetes Association 2026	Yes	Yes	Yes	Yes	Yes	Yes

Organization Lead Author, Year	Comprehensive Systematic Review	Clear and Appropriate Inclusion Criteria	Assessed Strengths and Limitations of Evidence	Clear Methods for Recommendation Development	Explicit Link Between Recommendations and Evidence	Balanced of Benefits and Harms
Lam 2025	Unclear	Unclear	Yes	Somewhat	Yes	Yes
Omar 2024	Unclear	Unclear	Unclear	Somewhat	Yes	Yes

Table E4. Methodological Quality of Clinical Practice Guidelines, Part B

Organization Lead Author, Year	External Peer Review	Process for Guideline Updates	Editorial Independence	Panel Member Disclosures	Overall Methodological Quality Assessment
American Academy of Ophthalmology 2024	Not reported	Yes	Yes	Yes	Fair. Limited information on search strategies and inclusion and exclusion criteria. No information on screening strategies. General references to methods development but no apparent external peer review.
American Diabetes Association 2026	Yes	Yes	Yes	Yes	Good. Very thorough methods and well-defined processes for searching for and grading evidence, developing recommendations, and soliciting external peer review.
Lam 2025	Not reported	Not reported	Yes	Yes	Fair. No information on literature search, no methods section for evidence review, and no link to another document that might provide more information. Limited information on guideline development process and no reference to peer review or processes for updates.
Omar 2024	Not reported	Not reported	Yes	Yes	Poor. Only basic information on literature search and no detail in main document or supplemental file. Only details on recommendation development involve a single workshop and surveys completed by work group members. No details on processes for recommendation development or grading strength of evidence. No references to guideline update process.

Appendix F. GRADE Assessment

Table F1. GRADE Summary for Studies of AI-Enabled Tools for Detection of More-Than-Mild Diabetic Retinopathy

Outcome	Study	Overall RoB	Consistency (Degree of Similarity in Effect Sizes)	Directness (Relevance to Population of Interest)	Precision (Degree of Certainty	GRADE	Justification
AEYE, reflex dilation with ungradable omitted							
Sensitivity Specificity PPV NPV Ungradable rate	NCT04612868	Cannot evaluate certainty of evidence. No published peer-reviewed studies.					
EyeArt							
Sensitivity Specificity PPV NPV	Bhaskaranand 2019 Heydon 2021 Olvera-Barrios 2021 Ibáñez-Bruron 2024 Tufail 2016	Moderate (-1)	Some concerns (-1) Differences across studies in design and approach, but even in studies that shared similar approaches (i.e., undilated eyes and ungradable considered referrable) there is wide variation in accuracy metrics	No concerns	No concerns	Low	Downgraded 1 level for moderate risk of bias across majority of studies and 1 level for consistency due to variation in outcomes across studies, even when approach to study design and analysis were similar (i.e., all eyes dilated and ungradable tests omitted)
Ungradable rate	Liu 2021 Vought 2023 Karabeg 2025 Mokhashi 2022 Musetti 2025	Moderate (-1)	Some concerns (-1)	No concerns	Some concerns (-1) Reported in only a small subset of	Very Low	Downgraded 1 level for moderate risk of bias in the majority of studies, 1 level for consistency due to wide variation in reported results, and 1 level for imprecision due to the small number of studies reporting this outcome and

Outcome	Study	Overall RoB	Consistency (Degree of Similarity in Effect Sizes)	Directness (Relevance to Population of Interest)	Precision (Degree of Certainty	GRADE	Justification
	Bhaskaranand 2019 Ibanez-Bruron 2024				studies, so unclear how close this is to the true rate		subsequent lack of clarity on how close this figure is to the true rate.
IDxDR							
Sensitivity Specificity PPV NPV	Dow 2023 Grzybowski 2023 Grzybowski 2025 Mehra 2022 Poschkamp 2025 Shah 2021 Sedova 2022 van der Heijden 2018 Shah 2021 Verbraak 2019	High	Some concerns (-1) Differences across studies in design and approach, but even in studies that shared similar approaches (i.e., undilated eyes and ungradable considered referrable) there is wide variation in accuracy metrics	No concerns	No concerns	Very Low	Downgraded 2 levels for risk of bias across majority of studies and 1 level for consistency due to variation in outcomes across studies, even when approach to study design and analysis were similar (i.e., all eyes dilated and ungradable tests omitted)
Ungradable rate	Dow 2023 Poschkamp 2025 van der Heijden 2018 Merha 2022 Verbraak 2019 Shah 2021	High (-2)	No concerns Differences likely reflect use of dilation or reflex dilations vs no dilation	No concerns	Some concerns (-1) Reported in only a small subset of studies, so unclear how close this is to the true rate	Very Low	Downgraded 2 levels for high risk of bias in the majority of studies and 1 level for imprecision due to the small number of studies reporting this outcome and subsequent lack of clarity on how close this figure is to the true rate.

Abbreviations. RoB: risk of bias; NPV: negative predictive value; PPV: positive predictive value.

Appendix G. Excluded Studies With Primary Reason for Exclusion

Table G1 lists the publications that were excluded during full text review and the primary reason for exclusion. There may be multiple reasons for exclusion for any given publication, and the table lists only the most influential reason for exclusion.

Table G1. Excluded Studies With Primary Reason for Exclusion

Citation	Reason for Exclusion
Abramoff M, Staal J, Suttorp M, Polak B, Viergever M. Low level screening of exudates and hemorrhages in background diabetic retinopathy. Comp Assi Fun Image Anal. 2000;15.	Intervention. This predates IDx-DR and does not relate to the FDA-cleared autonomous system.
Abràmoff MD, Folk JC, Han DP, et al. Automated analysis of retinal images for detection of referable diabetic retinopathy. JAMA Ophthalmol. 2013;131(3):351-357. doi: 10.1001/jamaophthalmol.2013.1743	Intervention. Iowa Detection Program is a precursor of IDx, but it is not IDx. It is not an autonomous system.
Abramoff MD, Lavin PT, Jakubowski JR, et al. Mitigation of AI adoption bias through an improved autonomous AI system for diabetic retinal disease. NPJ Digit Med. 2024;7(1):369. doi: 10.1038/s41746-024-01389-x	Intervention. Not FDA cleared for use with a handheld camera, but provides information for background and discussion sections.
Abramoff MD, Leng T, Ting DSW, et al. Automated and Computer-Assisted Detection, Classification, and Diagnosis of Diabetic Retinopathy. Telemed J E Health. 2020;26(4):544-550. doi: 10.1089/tmj.2020.0008	Publication Type. General overview.
Abramoff MD, Lou Y, Erginay A, et al. Improved Automated Detection of Diabetic Retinopathy on a Publicly Available Dataset Through Integration of Deep Learning. Invest Ophthalmol Vis Sci. 2016;57(13):5200-5206. doi: 10.1167/iovs.16-19964	Intervention. Compares performance of 2 different versions of the IDx device.
Abramoff MD, Niemeijer M, Russell SR. Automated detection of diabetic retinopathy: barriers to translation into clinical practice. Expert Rev Med Devices. 2010;7(2):287-296. doi: 10.1586/erd.09.76	Publication Type. Commentary.
Abramoff MD, Niemeijer M, Suttorp-Schulten MS, Viergever MA, Russell SR, van Ginneken B. Evaluation of a system for automatic detection of diabetic retinopathy from color fundus photographs in a large population of patients with diabetes. Diabetes Care. 2008;31(2):193-198. doi: 10.2337/dc07-1312	Intervention. Developer of IDx, but these early versions are testing individual algorithms, not the autonomous screening system they eventually develop.
Abramoff MD, Reinhardt JM, Russell SR, et al. Automated early detection of diabetic retinopathy. Ophthalmology. 2010;117(6):1147-1154. doi: 10.1016/j.ophtha.2010.03.046	Intervention. Not an FDA-cleared AI device.
Abramoff MD, Whitestone N, Patnaik JL, et al. Autonomous artificial intelligence increases real-world specialist clinic productivity in a cluster-randomized trial. NPJ Digit Med. 2023;6(1):184. doi: 10.1038/s41746-023-00931-7	Outcomes. Sole outcomes are productivity and number of encounters. Not relevant to the clinical utility KQ, reference for clinical utility because of Bangledeshi setting (not high HDI).

Citation	Reason for Exclusion
Agurto C, Barriga ES, Murray V, et al. Automatic detection of diabetic retinopathy and age-related macular degeneration in digital fundus images. Invest Ophthalmol Vis Sci. 2011;52(8):5862-5871. doi: 10.1167/iovs.10-7075	Intervention. Not an FDA-cleared AI device.
Ahmed M, Dai T, Channa R, Abramoff MD, Lehmann HP, Wolf RM. Cost-effectiveness of AI for pediatric diabetic eye exams from a health system perspective. NPJ Digit Med. 2025;8(1):3. doi: 10.1038/s41746-024-01382-4	Population. Pediatric population.
AlQahtani AS, Hazzazi MA, Waheeb SA, et al. Saudi Arabia Guidelines for diabetic macular edema: A consensus of the Saudi Retina Group. Saudi Med J. 2021;42(2):131-145. doi: 10.15537/smj.2021.2.25623	Intervention. No reference to AI, machine learning, or autonomous screening systems.
Arenas-Cavalli JT, Abarca I, Rojas-Contreras M, Bernuy F, Donoso R. Correction: Clinical validation of an artificial intelligence-based diabetic retinopathy screening tool for a national health system. Eye (Lond). 2021;35(10):2910. doi: 10.1038/s41433-021-01690-z	Publication Type. Original article has been corrected.
Attiku Y, Nittala MG, Velaga SB, et al. Comparison of diabetic retinopathy severity grading on ETDRS 7-field versus ultrawide-field assessment. Eye (Lond). 2023;37(14):2946-2949. doi: 10.1038/s41433-023-02445-8	Aim. Compares 2 camera types.
Bhambhwani V, Whitestone N, Patnaik JL, Ojeda A, Scali J, Cherwek DH. Feasibility and Patient Experience of a Pilot Artificial Intelligence-Based Diabetic Retinopathy Screening Program in Northern Ontario. Ophthalmic Epidemiol. 2025;32(5):518-524. doi: 10.1080/09286586.2024.2434738	Comparator. Jenny was right that there's no comparator. Provides some useful background information though.
Bhaskaranand M, Ramachandra C, Bhat S, et al. Automated Diabetic Retinopathy Screening and Monitoring Using Retinal Fundus Image Analysis. J Diabetes Sci Technol. 2016;10(2):254-261. doi: 10.1177/1932296816628546	Intervention. This is actually the right intervention, but a later publication by Bhaskaranand (2019) uses the same database (EyePACS data) and has double the sample size, so we'll use that one.
Bhuiyan A, Govindaiah A, Alauddin S, Otero-Marquez O, Smith RT. Combined automated screening for age-related macular degeneration and diabetic retinopathy in primary care settings. Ann Eye Sci. 2021;6. doi: 10.21037/aes-20-114	Intervention. Not an FDA-cleared AI device.
Bhuiyan A, Govindaiah A, Deobhakta A, et al. Development and Validation of an Automated Diabetic Retinopathy Screening Tool for Primary Care Setting. Diabetes Care. 2020;43(10):e147-e148. doi: 10.2337/dc19-2133	Intervention. Not an FDA-cleared AI device.

Citation	Reason for Exclusion
Boucher MC, Qian J, Brent MH, et al. Evidence-based Canadian guidelines for tele-retina screening for diabetic retinopathy: recommendations from the Canadian Retina Research Network (CR2N) Tele-Retina Steering Committee. Can J Ophthalmol. 2020;55(1 Suppl 1):14-24. doi: 10.1016/j.jcjo.2020.01.001	Publication Date. If you decide to go with 2021 to 2026 for guidelines, then exclude.
Bressler I, Aviv R, Margalit D, et al. Autonomous Screening for Diabetic Macular Edema Using Deep Learning Processing of Retinal Images. Ophthalmol Sci. 2025;5(4):100722. doi: 10.1016/j.xops.2025.100722	Outcomes. AEYE is FDA cleared for detection of more-than-mild diabetic retinopathy in adults with diabetes. This is an exploratory study about detection of diabetic macular edema (not a cleared indication).
Bressler I, Aviv R, Margalit D, Rom Y, Ianchulev T, Dvey-Aharon Z. Autonomous screening for laser photocoagulation in fundus images using deep learning. Br J Ophthalmol. 2024;108(5):742-746. doi: 10.1136/bjo-2023-323376	Population. Training AEYE to discern laser patterns in patients who have received laser photocoagulation, for the purpose of potentially using AEYE for disease management and follow up (i.e., different indication than what it is currently cleared for).
Bressler I, Dollberg D, Aviv R, et al. Non-Contact Optical Blood Pressure Biometry Using AI-Based Analysis of Non-Mydriatic Fundus Imaging. medRxiv. 2025;07:07. doi: 10.1101/2025.01.06.25320084	Intervention. AEYE research group, but not diagnostic retinopathy (identification of hypertension).
Bryan JM, Bryar PJ, Mirza RG. Convolutional Neural Networks Accurately Identify Ungradable Images in a Diabetic Retinopathy Telemedicine Screening Program. Telemed J E Health. 2023;29(9):1349-1355. doi: 10.1089/tmj.2022.0357	Intervention. Not an FDA-cleared AI device.
Channa R, Wolf R, Abramoff MD. Autonomous Artificial Intelligence in Diabetic Retinopathy: From Algorithm to Clinical Application. J Diabetes Sci Technol. 2021;15(3):695-698. doi: 10.1177/1932296820909900	Publication Type. Commentary.
Chen EM, Chen D, Chilakamarri P, Lopez R, Parikh R. Economic Challenges of Artificial Intelligence Adoption for Diabetic Retinopathy. Ophthalmology. 2021;128(3):475-477. doi: 10.1016/j.ophtha.2020.07.043	Publication Type. Research letter, not a published study.
Chen KM, Zhao CS, Knapp A, et al. Targeted Interventions Lead to Quality Improvement in Year 2 of an Artificial Intelligence-Based Diabetic Retinopathy Detection Program in Northern California. Retina. 2025;30:30. doi: 10.1097/IAE.0000000000004499	Comparator. The study describes the implementation of IDx-DR into workflow in the Stanford Teleophthalmology Automated Testing and Universal Screening (STATUS) program, but does not include any comparator. Human graders were only involved if IDx-DR produced an ungradable result. Keep for background.

Citation	Reason for Exclusion
Chen Y, Song F, Zhao Z, et al. Acceptability, applicability, and cost-utility of artificial-intelligence-powered low-cost portable fundus camera for diabetic retinopathy screening in primary health care settings. Diabetes Res Clin Pract. 2025;223:112161. doi: 10.1016/j.diabres.2025.112161	Intervention. Does not include any of the 3 FDA-cleared screening systems.
Chudzik P, Majumdar S, Caliva F, Al-Diri B, Hunter A. Microaneurysm detection using fully convolutional neural networks. Comput Methods Programs Biomed. 2018;158:185-192. doi: 10.1016/j.cmpb.2018.02.016	Intervention. Not an FDA-cleared device and aim is to detect microaneurysm.
Cicinelli MV, Gravina S, Rutigliani C, et al. Assessing Diabetic Retinopathy Staging With AI: A Comparative Analysis Between Pseudocolor and LED Imaging. Transl Vis Sci Technol. 2024;13(3):11. doi: 10.1167/tvst.13.3.11	Comparator. Compares performance with 2 different cameras, rather than comparing performance with a human grader.
Crane AB, Choudhry HS, Dastjerdi MH. Effect of simulated cataract on the accuracy of artificial intelligence in detecting diabetic retinopathy in color fundus photos. Indian J Ophthalmol. 2024;72(Suppl 1):S42-S45. doi: 10.4103/IJO.IJO_1163_23	Intervention. Does not include any of the 3 FDA-cleared screening systems.
Cuadros J. The Real-World Impact of Artificial Intelligence on Diabetic Retinopathy Screening in Primary Care. J Diabetes Sci Technol. 2021;15(3):664-665. doi: 10.1177/1932296820914287	Publication Type. Commentary.
Das T, Takkar B, Sivaprasad S, et al. Recently updated global diabetic retinopathy screening guidelines: commonalities, differences, and future possibilities. Eye (Lond). 2021;35(10):2685-2698. doi: 10.1038/s41433-021-01572-4	Intervention. Not an FDA-cleared AI device.
Delavari P, Ozturan G, Navajas EV, Yilmaz O, Oruc I. AI-Assisted identification of sex-specific patterns in diabetic retinopathy using retinal fundus images. PLoS One. 2025;20(8):e0327305. doi: 10.1371/journal.pone.0327305	Intervention. Not one of the 3 FDA-cleared screening tools.
Diaz EA, Seifert ML, Gruning V, et al. Diabetic Retinopathy Screening Among Federally Qualified Health Center Patients Using Point-of-Care AI: DRES-POCAI: A Trial Protocol. JAMA Netw Open. 2025;8(10):e2538114. doi: 10.1001/jamanetworkopen.2025.38114	Publication Type. Protocol. Will attach to any publication of results (but likely haven't published yet).
Dismuke C. Progress in examining cost-effectiveness of AI in diabetic retinopathy screening. Lancet Digit Health. 2020;2(5):e212-e213. doi: 10.1016/S2589-7500(20)30077-7	Publication Type. Commentary.

Citation	Reason for Exclusion
Duggal M, Chauhan A, Gupta V, et al. Real-World Evaluation of AI-Driven Diabetic Retinopathy Screening in Public Health Settings: Validation and Implementation Study. JMIR Med Inform. 2025;13:e67529. doi: 10.2196/67529	Intervention. Not one of the 3 FDA-cleared screening tools.
Eszes DJ, Szabo DJ, Russell G, et al. Diabetic Retinopathy Screening in Patients with Diabetes Using a Handheld Fundus Camera: The Experience from the South-Eastern Region in Hungary. J Diabetes Res. 2021;2021:6646645. doi: 10.1155/2021/6646645	Intervention. Although one of the authors is associated with Eyenuk, they were testing a different AI program.
Font O, Torrents-Barrena J, Royo D, et al. Validation of an autonomous artificial intelligence-based diagnostic system for holistic maculopathy screening in a routine occupational health checkup context. Graefes Arch Clin Exp Ophthalmol. 2022;260(10):3255-3265. doi: 10.1007/s00417-022-05653-2	Intervention. Not an FDA-cleared AI device.
Gandor M, Palka F, Ksiazek W, et al. Diagnostics of diabetic retinopathy based on fundus photos using machine learning methods with advanced feature engineering algorithms. Sci Rep. 2025;15(1):34486. doi: 10.1038/s41598-025-06973-z	Intervention. Not one of the 3 FDA-cleared screening tools.
Gargeya R, Leng T. Automated Identification of Diabetic Retinopathy Using Deep Learning. Ophthalmology. 2017;124(7):962-969. doi: 10.1016/j.ophtha.2017.02.008	Intervention. Not an FDA-cleared AI device.
Goldstein J, Weitzman D, Lemerond M, Jones A. Determinants for scalable adoption of autonomous AI in the detection of diabetic eye disease in diverse practice types: key best practices learned through collection of real-world data. Front Digit Health. 2023;5:1004130. doi: 10.3389/fdgth.2023.1004130	Publication Type. Feasibility/implementation study, but does not report patient-specific outcomes that might be related to clinical utility.
Gomez Rossi J, Rojas-Perilla N, Krois J, Schwendicke F. Cost-effectiveness of Artificial Intelligence as a Decision-Support System Applied to the Detection and Grading of Melanoma, Dental Caries, and Diabetic Retinopathy. JAMA Netw Open. 2022;5(3):e220269. doi: 10.1001/jamanetworkopen.2022.0269	Setting. Economic data is modeled from Brazilian patient data set.
Grzybowski A, Brona P, Krzywicki T, Gaca-Wysocka M, Berlinska A, Swiech A. Variability of Grading DR Screening Images among Non-Trained Retina Specialists. J Clin Med. 2022;11(11):31. doi: 10.3390/jcm11113125	Intervention. Not an FDA-cleared AI device.
Grzybowski A, Brona P. A pilot study of autonomous artificial intelligence-based diabetic retinopathy screening in Poland. Acta Ophthalmol. 2019;97(8):e1149-e1150. doi: 10.1111/aos.14132	Publication Type. Research letter.

Citation	Reason for Exclusion
Grzybowski A, Brona P. Analysis and Comparison of Two Artificial Intelligence Diabetic Retinopathy Screening Algorithms in a Pilot Study: IDx-DR and Retinalyze. J Clin Med. 2021;10(11):27. doi: 10.3390/jcm10112352	Population. All three Grzybowski studies use the same dataset (each one compares IDx to another AI screener). Using the study with the largest sample size (Grzybowski 2023).
Grzybowski A, Peeters F, Barao RC, et al. Evaluating the efficacy of AI systems in diabetic retinopathy detection: A comparative analysis of Mona DR and IDx-DR. Acta Ophthalmol. 2025;103(4):388-395. doi: 10.1111/aos.17428	Population. All three Grzybowski studies use the same dataset (each one compares IDx to another AI screener). Using the study with the largest sample size (Grzybowski 2023).
Gul MF, Polat O, Bakir H. TL-GWO: Fine-tuned transfer learning with grey wolf optimizer for accurate fundus image-based eye disease classification. Exp Eye Res. 2025;260:110598. doi: 10.1016/j.exer.2025.110598	Intervention. Not one of the 3 FDA-cleared screening tools.
Hajabdollahi M, Esfandiarpoor R, Najarian K, Karimi N, Samavi S, Reza Soroushmehr SM. Hierarchical Pruning for Simplification of Convolutional Neural Networks in Diabetic Retinopathy Classification. Annu Int Conf IEEE Eng Med Biol Soc. 2019;2019:970-973. doi: 10.1109/EMBC.2019.8857769	Publication Type. Conference abstract.
Hamati J, Prashanthi S, Narayanan R, et al. Prevalence of age-related macular degeneration and associated factors in Indian cohort in a tertiary care setting. Indian J Ophthalmol. 2023;71(10):3361-3366. doi: 10.4103/IJO.IJO_199_23	Intervention. Not an FDA-cleared AI device.
Hammes HP, Lemmen KD, Bertram B. Diabetic Retinopathy and Maculopathy. Exp Clin Endocrinol Diabetes. 2021;129(S 01):S64-S69. doi: 10.1055/a-1284-6223	Publication Type. Overview of DR, for German practitioners.
Hansen MB, Abràmoff MD, Folk JC, Mathenge W, Bastawrous A, Peto T. Results of Automated Retinal Image Analysis for Detection of Diabetic Retinopathy from the Nakuru Study, Kenya. PLoS One. 2015;10(10):e0139148. doi: 10.1371/journal.pone.0139148	Intervention. Iowa Detection Program is a precursor to IDX, but it is not the same as IDX. It was not an autonomous system.
Helmchen LA, Lehmann HP, Abramoff MD. Automated detection of retinal disease. Am J Manag Care. 2014;20(11 Spec No. 17):eSP48-52.	Publication Type. Commentary.
Horton MB, Brady CJ, Cavallerano J, et al. Practice Guidelines for Ocular Telehealth-Diabetic Retinopathy, Third Edition. Telemed J E Health. 2020;26(4):495-543. doi: 10.1089/tmj.2020.0006	Publication Date. Practice guidelines are more than 5 years old.
Huang JJ, Channa R, Wolf RM, et al. Author Correction: Autonomous artificial intelligence for diabetic eye disease increases access and health equity in underserved populations. NPJ Digit Med. 2024;7(1):220. doi: 10.1038/s41746-024-01229-y	Publication Type. Correction to funding statement, but it does not add anything of substance to change our analysis or risk of bias assessment. I have appended to refid 701 (the main article).

Citation	Reason for Exclusion
Huber SL, Parzer V, Ludvik B, Pollreisz A, Mahnert N, Brix JM. Evaluation of IDx-DR software for diabetic retinopathy screening in outpatient clinics: Efficacy, safety, and feasibility in a real-world setting. J Diabetes Complications. 2025;39(10):109120. doi: 10.1016/j.jdiacomp.2025.109120	Comparator. Description of the integration of IDx-DR into the workflow at the Austrian center. No comparison to manual grading or tests of diagnostic accuracy.
Jamison C, Cushley L, Curran K, Peto T. Grading images for diabetic retinopathy: tips and guidelines. Community eye health. 2023;36(119):11-13.	Publication Type. General overview.
Jin L, Behabadi BF, Jadi MP, Ramachandra CA, Mel BW. Classical-Contextual Interactions in V1 May Rely on Dendritic Computations. Neuroscience. 2022;489:234-250. doi: 10.1016/j.neuroscience.2022.02.033	Intervention. Not an FDA-cleared AI device.
Joseph S, Wang Y, Drinkwater JJ, et al. Effectiveness of artificial intelligence-based diabetic retinopathy screening in primary care and endocrinology settings in Australia: a pragmatic trial. Br J Ophthalmol. 2025;110(1):76-82. doi: 10.1136/bjo-2025-327447	Intervention. None of the 3 FDA-cleared systems.
Kanagasingam Y, Xiao D, Vignarajan J, Preetham A, Tay-Kearney ML, Mehrotra A. Evaluation of Artificial Intelligence-Based Grading of Diabetic Retinopathy in Primary Care. JAMA Netw Open. 2018;1(5):e182665. doi: 10.1001/jamanetworkopen.2018.2665	Intervention. Not an FDA-cleared AI device.
Kapetanakis VV, Rudnicka AR, Liew G, et al. A study of whether automated Diabetic Retinopathy Image Assessment could replace manual grading steps in the English National Screening Programme. J Med Screen. 2015;22(3):112-118. doi: 10.1177/0969141315571953	Publication Type. Protocol
Karabeg M, Petrovski G, Hertzberg SN, et al. A pilot cost-analysis study comparing AI-based EyeArt(R) and ophthalmologist assessment of diabetic retinopathy in minority women in Oslo, Norway. Int J Retina Vitreous. 2024;10(1):40. doi: 10.1186/s40942-024-00547-3	Intervention. The EU doesn't put restrictions on brand of fundus camera, but this uses a confocal scanner rather than a traditional fundus camera.
Keel S, Wu J, Lee PY, Scheetz J, He M. Visualizing Deep Learning Models for the Detection of Referable Diabetic Retinopathy and Glaucoma. JAMA Ophthalmol. 2019;137(3):288-292. doi: 10.1001/jamaophthalmol.2018.6035	Intervention. Not an FDA-cleared AI device.
Khan Z, Gaidhane AM, Singh M, et al. Diagnostic Accuracy of IDX-DR for Detecting Diabetic Retinopathy: A Systematic Review and Meta-Analysis. Am J Ophthalmol. 2025;273:192-204. doi: 10.1016/j.ajo.2025.02.022	Publication Type.

Citation	Reason for Exclusion
Kim TN, Aaberg MT, Li P, et al. Comparison of automated and expert human grading of diabetic retinopathy using smartphone-based retinal photography. Eye (Lond). 2021;35(1):334-342. doi: 10.1038/s41433-020-0849-5	Intervention. EyeArt is not FDA cleared for use with smartphone cameras.
Kubin AM, Huhtinen P, Ohtonen P, Keskitalo A, Wirkkala J, Hautala N. Comparison of 21 artificial intelligence algorithms in automated diabetic retinopathy screening using handheld fundus camera. Ann Med. 2024;56(1):2352018. doi: 10.1080/07853890.2024.2352018	Outcomes. Compared manual grading to assessment of 21 AI-based algorithms. Does not provide outcomes for individual products and no supplemental file with additional detail.
La Franca L, Rutigliani C, Checchin L, Lattanzio R, Bandello F, Cicinelli MV. Rate and Predictors of Misclassification of Active Diabetic Macular Edema as Detected by an Automated Retinal Image Analysis System. Ophthalmol Ther. 2024;13(6):1553-1567. doi: 10.1007/s40123-024-00929-8	Intervention. Focus is on identifification of diabetic macular edema. All patients received pupil dilation and optical coherence tomography. Not being used to identify more-than-mild DR or vision-threatening DR generally in patients with diabetes.
Larsen M, Gondolf T, Godt J, et al. Assessment of automated screening for treatment-requiring diabetic retinopathy. Curr Eye Res. 2007;32(4):331-336. doi: 10.1080/02713680701215587	Intervention. Not an FDA-cleared AI device.
Larsen N, Godt J, Grunkin M, Lund-Andersen H, Larsen M. Automated detection of diabetic retinopathy in a fundus photographic screening population. Invest Ophthalmol Vis Sci. 2003;44(2):767-771. doi: 10.1167/iovs.02-0417	Intervention. Not an FDA-cleared AI device.
Lee AY, Lee CS, Hunt MS, Yanagihara RT, Blazes M, Boyko EJ. Multicenter, Head-to-Head, Real-World Validation Study of Seven Automated Artificial Intelligence Diabetic Retinopathy Screening Systems. Diabetes Care 2021;44:XXXX-XXXX. Diabetes Care. 2021;44(5):e108-e109. doi: 10.2337/dci21-0007	Publication Type. Response to comment.
Lee AY, Yanagihara RT, Lee CS, et al. Multicenter, Head-to-Head, Real-World Validation Study of Seven Automated Artificial Intelligence Diabetic Retinopathy Screening Systems. Diabetes Care. 2021;44(5):1168-1175. doi: 10.2337/dc20-1877	Outcomes. Companies are masked and cannot tell which results relate to our 3 interventions.
Lim WX, Chen Z. Enhancing deep learning pre-trained networks on diabetic retinopathy fundus photographs with SLIC-G. Med Biol Eng Comput. 2024;62(8):2571-2583. doi: 10.1007/s11517-024-03093-0	Intervention. Does not include any of the 3 FDA-cleared screening systems.
Liu TYA, Huang J, Channa R, et al. Autonomous Artificial Intelligence Increases Access and Health Equity in Underserved Populations with Diabetes. Res Sq. 2024;13:13. doi: 10.21203/rs.3.rs-3979992/v1	Publication Type. Preprint. Not peer reviewed. Subsequently published in NPJ Digit Med. 2024 Jul 22;7(1):196.

Citation	Reason for Exclusion
Liu TYA, Wolf RM. Autonomous Artificial Intelligence for Diabetic Eye Disease Testing Improves Access and Equity in the Pediatric and Adult Populations: The Johns Hopkins Medicine Experience. Diabetes Spectr. 2025;38(1):19-22. doi: 10.2337/dsi24-0016	Study Design. Descriptive. Keep for background or discussion.
Luong A, Cheung J, McMurtry S, et al. Comparison of Machine Learning Models to a Novel Score in the Identification of Patients at Low Risk for Diabetic Retinopathy. Ophthalmol Sci. 2025;5(1):100592. doi: 10.1016/j.xops.2024.100592	Intervention. Does not include any of the 3 FDA-cleared screening systems.
Lupidi M, Danieli L, Fruttini D, et al. Artificial intelligence in diabetic retinopathy screening: clinical assessment using handheld fundus camera in a real-life setting. Acta Diabetol. 2023;60(8):1083-1088. doi: 10.1007/s00592-023-02104-0	Intervention. Not an FDA-cleared AI device.
Malerbi FK, Melo GB. Feasibility of screening for diabetic retinopathy using artificial intelligence, Brazil. Bull World Health Organ. 2022;100(10):643-647. doi: 10.2471/BLT.22.288580	Publication Type. Description of another study focused on a non FDA-cleared detection device.
Management of Type 2 Diabetes Mellitus Work Group. VA/DoD clinical practice guideline for the management of type 2 diabetes mellitus. Department of Veterans Affairs and Department of Defense. 2023. Accessed January 9, 2026. https://www.healthquality.va.gov/HEALTHQUALITY/guidelines/CD/diabetes/VADOD-Diabetes-CPG_Final_508.pdf	Intervention. Does not address diabetic retinopathy screening (only screening for diabetes).
Mathenge W, Whitestone N, Nkurikiye J, et al. Impact of Artificial Intelligence Assessment of Diabetic Retinopathy on Referral Service Uptake in a Low-Resource Setting: The RAIDERS Randomized Trial. Ophthalmol Sci. 2022;2(4):100168. doi: 10.1016/j.xops.2022.100168	Intervention. Not an FDA-cleared AI device.
McAllister M, Ko S, Bawa K, et al. Clinical practice guidelines for the treatment and management of diabetic macular oedema: a systematic review. Eye (Lond). 2025;39(17):3121-3128. doi: 10.1038/s41433-025-04043-2	Study Design.
Mel GC, Ramachandra CA, Mel BW. Object Boundary Detection in Natural Images May Depend on "Incitatory" Cell-Cell Interactions. J Neurosci. 2022;42(48):8960-8979. doi: 10.1523/JNEUROSCI.2581-18.2022	Study Design. Exploration of boundary detection in hypothetical cases.
Men Y, Fhima J, Celi LA, Ribeiro LZ, Nakayama LF, Behar JA. Deep learning generalization for diabetic retinopathy staging from fundus images. Physiol Meas. 2025;13(1):22. doi: 10.1088/1361-6579/ada86a	Intervention. Does not include any of the 3 FDA-cleared screening systems. Does cite several papers by Abramoff, but does not use the IDx-DR/LumineticsCore system.

Citation	Reason for Exclusion
Meredith S, van Grinsven M, Engelberts J, et al. Performance of an artificial intelligence automated system for diabetic eye screening in a large English population. Diabet Med. 2023;40(6):e15055. doi: 10.1111/dme.15055	Intervention. Not an FDA-cleared AI device.
Messica S, Cohen S, Hadad A, et al. Temporal Integrative Machine Learning for Early Detection of Diabetic Retinopathy Using Fundus Imaging and Electronic Health Records. IEEE J Biomed Health Inform. 2025;PP:09. doi: 10.1109/JBHI.2025.3578197	Intervention. Does not involve any of the FDA-cleared screening tools.
Nagasawa T, Tabuchi H, Masumoto H, et al. Accuracy of Diabetic Retinopathy Staging with a Deep Convolutional Neural Network Using Ultra-Wide-Field Fundus Ophthalmoscopy and Optical Coherence Tomography Angiography. J Ophthalmol. 2021;2021:6651175. doi: 10.1155/2021/6651175	Intervention. Not an FDA-cleared AI device.
National Institute for Health and Care Excellence (NICE). AI technologies for detecting diabetic retinopathy. July 6, 2021. Accessed January 9, 2026. https://www.nice.org.uk/advice/mib265	Study Design. General review. Not underpinned by an SR.
National Institute for Health and Care Excellence (NICE). Diabetes (type 1 and type 2) in children and young people: diagnosis and management. August 1, 2015 (last updated May 11, 2023). Accessed January 9, 2026. https://www.nice.org.uk/guidance/ng18	Population. Children and teens.
National Institute for Health and Care Excellence (NICE). Diabetic retinopathy: management and monitoring. August 13, 2024. Accessed January 9, 2026. https://www.nice.org.uk/guidance/ng242	Intervention. Not underpinned by a systematic review. Refers readers to NICE guidelines for diabetic retinopathy screening.
National Institute for Health and Care Excellence (NICE). Type 1 diabetes in adults: diagnosis and management. August 26, 2015 (last updated August 17, 2022). Accessed January 9, 2026. https://www.nice.org.uk/guidance/ng17	Intervention. Refers readers to NICE's guidelines on diabetic retinopathy.
Nderitu P, Nunez do Rio JM, Webster L, et al. Augmenting a prognostic deep learning system for referable diabetic retinopathy and maculopathy with synthetic retinal images. Commun Med (Lond). 2025;20:20. doi: 10.1038/s43856-025-01316-5	Intervention. Test of a conditional cascaded diffusion model to generate synthetic retinal images, not a test of the accuracy of any of our 3 devices. One author included work for EyeArt in their disclosure statement, but this paper is not about the EyeArt product and was not funded by EyeArt.
Niemeijer M, Abramoff MD, van Ginneken B. Fast detection of the optic disc and fovea in color fundus photographs. Med Image Anal. 2009;13(6):859-870. doi: 10.1016/j.media.2009.08.003	Intervention. This work has authors associated with IDx-DR (Iowa Development Program) and is likely a predecessor to this tool, but a tool is not specified.

Citation	Reason for Exclusion
Niemeijer M, Abramoff MD, van Ginneken B. Segmentation of the optic disc, macula and vascular arch in fundus photographs. IEEE Trans Med Imaging. 2007;26(1):116-127. doi: 10.1109/TMI.2006.885336	Intervention. May describe preliminary development of IDx-DR (Neimeijer and Abramoff are authors), but does not mention IDx-DR or Iowa Development Program.
Niemeijer M, van Ginneken B, Russell SR, Suttorp-Schulten MS, Abramoff MD. Automated detection and differentiation of drusen, exudates, and cotton-wool spots in digital color fundus photographs for diabetic retinopathy diagnosis. Invest Ophthalmol Vis Sci. 2007;48(5):2260-2267. doi: 10.1167/iovs.06-0996	Intervention. Does not seem to use one of the tools of interest. Also, looking at ability to detect specific lesions rather than determine DR.
Niemeijer M, van Ginneken B, Staal J, Suttorp-Schulten MS, Abramoff MD. Automatic detection of red lesions in digital color fundus photographs. IEEE Trans Med Imaging. 2005;24(5):584-592. doi: 10.1109/TMI.2005.843738	Intervention. Another paper that may describe preliminary development of IDx-DR (Abramoff and Niemeijer are authors), but neither IDx-DR nor Iowa Development Program are mentioned.
Nolan B, Daybranch ER, Barton K, Korsen N. Patient and Provider Experience with Artificial Intelligence Screening Technology for Diabetic Retinopathy in a Rural Primary Care Setting. J Maine Med Cent. 2023;5(2). doi: 10.46804/2641-2225.1144	Study Design. No comparator group, survey data only.
Ogunyemi OI, Gandhi M, Lee M, et al. Detecting diabetic retinopathy through machine learning on electronic health record data from an urban, safety net healthcare system. JAMIA open. 2021;4(3):ooab066. doi: 10.1093/jamiaopen/ooab066	Intervention. Not an FDA-cleared AI device.
Pandey PU, Ballios BG, Christakis PG, et al. Ensemble of deep convolutional neural networks is more accurate and reliable than board-certified ophthalmologists at detecting multiple diseases in retinal fundus photographs. Br J Ophthalmol. 2024;108(3):417-423. doi: 10.1136/bjo-2022-322183	Intervention. Does not include any of the 3 FDA-cleared screening systems.
Paul S, Tayar A, Morawiec-Kisiel E, et al. Use of artificial intelligence in screening for diabetic retinopathy at a tertiary diabetes center. Ophthalmologie. 2022;119(7):705-713. doi: 10.1007/s00347-021-01556-5	Non-English.
Peris-Martinez C, Shaha A, Clarida W, et al. Use in clinical practice of an automated screening method of diabetic retinopathy that can be derived using a diagnostic artificial intelligence system. Arch Soc Esp Oftalmol (Engl Ed). 2021;96(3):117-126. doi: 10.1016/j.oftal.2020.08.007	Intervention. Not an FDA-cleared AI device.
Pires R, Avila S, Wainer J, Valle E, Abramoff MD, Rocha A. A data-driven approach to referable diabetic retinopathy detection. Artif Intell Med. 2019;96:93-106. doi: 10.1016/j.artmed.2019.03.009	Intervention. Not an FDA-cleared AI device.

Citation	Reason for Exclusion
Quellec G, Lamard M, Abramoff MD, et al. A multiple-instance learning framework for diabetic retinopathy screening. Med Image Anal. 2012;16(6):1228-1240. doi: 10.1016/j.media.2012.06.003	Intervention. Abramoff is one of the authors on this paper, but does not mention IDx-DR.
Rajalakshmi R, Subashini R, Anjana RM, Mohan V. Automated diabetic retinopathy detection in smartphone-based fundus photography using artificial intelligence. Eye (Lond). 2018;32(6):1138-1144. doi: 10.1038/s41433-018-0064-9	Intervention. EyeArt is not FDA-cleared for use with a smartphone camera.
Rajesh AE, Davidson OQ, Lee CS, Lee AY. Artificial Intelligence and Diabetic Retinopathy: AI Framework, Prospective Studies, Head-to-head Validation, and Cost-effectiveness. Diabetes Care. 2023;46(10):1728-1739. doi: 10.2337/dci23-0032	Publication Type. General overview.
Raman R, Ramasamy K, Rajalakshmi R, Sivaprasad S, Natarajan S. Diabetic retinopathy screening guidelines in India: All India Ophthalmological Society diabetic retinopathy task force and Vitreoretinal Society of India Consensus Statement. Indian J Ophthalmol. 2021;69(3):678-688. doi: 10.4103/ijo.IJO_667_20	Setting. India (not very high HDI).
Ran AR, Ding JL, Tang Z, et al. Real-World Prospective Validation and Economic Evaluation of Deep Learning-Based Diabetic Retinopathy Detection From Fundus Photographs: A Systematic Review and Meta-analysis. Diabetes Care. 2025;19:19. doi: 10.2337/dc25-1493	Study Design. Review bibliography
Robin A, Giovingo M. Screening recommendations for diabetics. Dis Mon. 2021;67(5):101116. doi: 10.1016/j.disamonth.2020.101116	Publication Type. Review.
Rodriguez-Miguel A, Arruabarrena C, Allendes G, Olivera M, Zarranz-Ventura J, Teus MA. Hybrid deep learning models for the screening of Diabetic Macular Edema in optical coherence tomography volumes. Sci Rep. 2024;14(1):17633. doi: 10.1038/s41598-024-68489-2	Intervention. Does not include any of the 3 FDA-cleared screening systems. Use of optical coherence tomography, rather than fundus photography.
Rogers WA, Draper H, Carter SM. Evaluation of artificial intelligence clinical applications: Detailed case analyses show value of healthcare ethics approach in identifying patient care issues. Bioethics. 2021;35(7):623-633. doi: 10.1111/bioe.12885	Intervention. Not an FDA-cleared AI device.
Rom Y, Aviv R, Cohen GY, Friedman YE, Ianchulev T, Dvey-Aharon Z. Diabetes detection from non-diabetic retinopathy fundus images using deep learning methodology. Heliyon. 2024;10(16):e36592. doi: 10.1016/j.heliyon.2024.e36592	Intervention. This is the AEYE group, but the goal is diagnosis of diabetes in eyes without any disease.

Citation	Reason for Exclusion
Romero-Oraa R, Herrero-Tudela M, Lopez MI, Hornero R, Garcia M. Attention-based deep learning framework for automatic fundus image processing to aid in diabetic retinopathy grading. Comput Methods Programs Biomed. 2024;249:108160. doi: 10.1016/j.cmpb.2024.108160	Intervention. Does not include any of the 3 FDA-cleared screening systems.
Roser P, Grohmann C, Aberle J, Spitzer MS, Kromer R. Evaluation der Implementierung eines zugelassenen Künstliche-Intelligenz-Systems zur Erkennung der diabetischen Retinopathie. Diabetologie und Stoffwechsel. 2021;16(05):402-408. doi: 10.1055/a-1484-9678	Non-English.
Ruamviboonsuk P, Krause J, Chotcomwongse P, et al. Erratum: Author Correction: Deep learning versus human graders for classifying diabetic retinopathy severity in a nationwide screening program. NPJ Digit Med. 2019;2:68. doi: 10.1038/s41746-019-0146-5	Publication Type. Immaterial if the referenced article is included or excluded, since it has been corrected and does not need to be attached to this correction.
Russell G, Hertzberg SNW, Anisimova N, Gavrilova N, Petrovski BE, Petrovski G. Digital Image Analysis of the Angle and Optic Nerve: A Simple, Fast, and Low-Cost Method for Glaucoma Assessment. J Ophthalmol. 2020;2020:3595610. doi: 10.1155/2020/3595610	Intervention. Glaucoma. Not diabetic retinopathy.
Salongcay RP, Aquino LAC, Alog GP, et al. Accuracy of Integrated Artificial Intelligence Grading Using Handheld Retinal Imaging in a Community Diabetic Eye Screening Program. Ophthalmol Sci. 2024;4(3):100457. doi: 10.1016/j.xops.2023.100457	Intervention. Tested system is not one of the 3 FDA cleared products.
Sanchez CI, Niemeijer M, Abramoff MD, van Ginneken B. Active learning for an efficient training strategy of computer-aided diagnosis systems: application to diabetic retinopathy screening. Med Image Comput Comput Assist Interv. 2010;13(Pt 3):603-610. doi: 10.1007/978-3-642-15711-0_75	Intervention. Not an FDA-cleared AI device.
Seth PK, Senthil S, Das AV, Garudadri C. Prevalence of glaucoma types, clinical profile and disease severity at presentation: Tertiary Institute based cross-sectional study from South India. Indian J Ophthalmol. 2023;71(10):3305-3312. doi: 10.4103/IJO.IJO_3305_22	Intervention. Not an FDA-cleared AI device.
Shi M, Afzal MM, Huang H, et al. Equitable Deep Learning for Diabetic Retinopathy Detection Using Multidimensional Retinal Imaging With Fair Adaptive Scaling. Transl Vis Sci Technol. 2025;14(7):1. doi: 10.1167/tvst.14.7.1	Intervention. Not one of the 3 FDA-cleared screening tools.

Citation	Reason for Exclusion
Shou BL, Venkatesh K, Chen C, et al. Risk Factors for Nondiagnostic Imaging in a Real-World Deployment of Artificial Intelligence Diabetic Retinal Examinations in an Integrated Healthcare System: Maximizing Workflow Efficiency Through Predictive Dilation. J Diabetes Sci Technol. 2024;18(2):302-308. doi: 10.1177/19322968231201654	Comparator. No comparator.
Shuang Y, Di X, Kanagasingam Y. Exudate detection for diabetic retinopathy with convolutional neural networks. Annu Int Conf IEEE Eng Med Biol Soc. 2017;2017:1744-1747. doi: 10.1109/EMBC.2017.8037180	Intervention. Not an FDA-cleared AI device.
Similie DE, Andersen JKH, Dinesen S, Savarimuthu TR, Grauslund J. Grading of diabetic retinopathy using a pre-segmenting deep learning classification model: Validation of an automated algorithm. Acta Ophthalmol. 2025;103(2):215-221. doi: 10.1111/aos.16781	Intervention. References IDX and EyeArt in the background section, but uses a screening system they developed themselves.
Skevas C, de Olaguer NP, Lleo A, et al. Implementing and evaluating a fully functional AI-enabled model for chronic eye disease screening in a real clinical environment. BMC Ophthalmol. 2024;24(1):51. doi: 10.1186/s12886-024-03306-y	Intervention. Does not include any of the 3 FDA-cleared screening systems.
Staal J, Abramoff MD, Niemeijer M, Viergever MA, van Ginneken B. Ridge-based vessel segmentation in color images of the retina. IEEE Trans Med Imaging. 2004;23(4):501-509. doi: 10.1109/TMI.2004.825627	Intervention. Not an FDA-cleared AI device.
Studnicka J, Nemcansky J, Vyslouzilova D, Ernest J, Nemec P. Diabetic Retinopathy - Diagnostics and Treatment Guidelines. Cesk Slov Oftalmol. 2023;79(5):238-247. doi: 10.31348/2023/28	Non-English.
Surya J, Garima, Pandy N, et al. Efficacy of deep learning-based artificial intelligence models in screening and referring patients with diabetic retinopathy and glaucoma. Indian J Ophthalmol. 2023;71(8):3039-3045. doi: 10.4103/IJO.IJO_11_23	Intervention. Not an FDA-cleared AI device.
Takkar B, Das T, Thamarangsi T, et al. Development of Diabetic retinopathy screening guidelines in South-East Asia region using the context, challenges, and future technology. Semin Ophthalmol. 2022;37(1):97-104. doi: 10.1080/08820538.2021.1925308	Publication Type. Guidelines focused on low-resource settings in Southeast Asia. AI screening is mentioned, but no specific recommendations for or against the use of AI devices is provided.
Talcott KE, Baxter SL, Chen DK, et al. American Society of Retina Specialists Artificial Intelligence Task Force Report. J Vitreoretin Dis. 2024;8(4):373-380. doi: 10.1177/24741264241247602	Publication Type. Not a guideline. Useful for background.

Citation	Reason for Exclusion
Talcott KE, Kim JE, Modi Y, Moshfeghi DM, Singh RP. The American Society of Retina Specialists Artificial Intelligence Task Force Report. J Vitreoretin Dis. 2020;4(4):312-319. doi: 10.1177/2474126420914168	Study Design. Updated version is refid 662 (Talcott 2024).
Tan TE, Ng YP, Calhoun C, et al. Detection of Center-Involved Diabetic Macular Edema With Visual Impairment Using Multimodal Artificial Intelligence Algorithms. Ophthalmol Retina. 2025;9(10):955-963. doi: 10.1016/j.oret.2025.04.016	Intervention. Not one of the 3 FDA-cleared screening tools.
Teegavarapu RR, Sanghvi HA, Belani T, Gill GS, Chalam KV, Gupta S. Evaluation of Convolutional Neural Networks (CNNs) in Identifying Retinal Conditions Through Classification of Optical Coherence Tomography (OCT) Images. Cureus. 2025;17(1):e77109. doi: 10.7759/cureus.77109	Intervention. Does not include any of the 3 FDA-cleared screening systems.
Teng CW, Patel SD, Barkmeier AJ, et al. Autonomous Artificial Intelligence in Diabetic Retinopathy Testing-Lessons Learned on Successful Health System Adoption. Ophthalmol Sci. 2026;6(1):100935. doi: 10.1016/j.xops.2025.100935	Study Design. Review included studies
Ting DSW, Carin L, Abramoff MD. Observations and Lessons Learned From the Artificial Intelligence Studies for Diabetic Retinopathy Screening. JAMA Ophthalmol. 2019;137(9):994-995. doi: 10.1001/jamaophthalmol.2019.1997	Publication Type. Review.
Tobin KW, Abramoff MD, Chaum E, et al. Using a patient image archive to diagnose retinopathy. Annu Int Conf IEEE Eng Med Biol Soc. 2008;2008:5441-5444. doi: 10.1109/IEMBS.2008.4650445	Intervention. Abramoff is the developer/founder of IDx, but the algorithms tested here are not the autonomous IDx product.
Varadarajan AV, Bavishi P, Ruamviboonsuk P, et al. Predicting optical coherence tomography-derived diabetic macular edema grades from fundus photographs using deep learning. Nat Commun. 2020;11(1):130. doi: 10.1038/s41467-019-13922-8	Intervention. Not an FDA-cleared AI device.
Venkatesh KP, Brito G. Lessons on regulation and implementation from the first FDA-cleared autonomous AI - Interview with Chairman and Founder of Digital Diagnostics Michael Abramoff. Healthc (Amst). 2023;11(2):100692. doi: 10.1016/j.hjdsi.2023.100692	Publication Type. Lessons learned.
Vought R, Vought V, Szirth B, Khouri AS. Future direction for the deployment of deep learning artificial intelligence: Vision threatening disease detection in underserved communities during COVID-19. Saudi J Ophthalmol. 2023;37(3):193-199. doi: 10.4103/sjopt.sjopt_16_23	Study Design. Overview of system deployment during the COVID-19 pandemic.
Wagle N, Morkos J, Liu J, et al. aEYE: A deep learning system for video nystagmus detection. Front Neurol. 2022;13:963968. doi: 10.3389/fneur.2022.963968	Intervention. Nystagmus, not diabetic retinopathy.

Citation	Reason for Exclusion
Wang K, Jayadev C, Nittala MG, et al. Automated detection of diabetic retinopathy lesions on ultrawidefield pseudocolour images. Acta Ophthalmol. 2018;96(2):e168-e173. doi: 10.1111/aos.13528	Intervention. Uses an experimental camera (ultra-wide field), while EyeArt is FDA cleared for use with a traditional fundus camera.
Wang TW, Luo WT, Tu YK, Chou YB, Wu YT. Diagnostic Accuracy of EyeArt for Fundus-Based Detection of Diabetic Retinopathy: A Systematic Review and Meta-analysis. Am J Ophthalmol. 2026;281:465-479. doi: 10.1016/j.ajo.2025.09.045	Study Design. Pulled full text in order to cross reference included studies with our search results and make sure we didn't miss any studies.
Wang Y, Liu C, Hu W, et al. Economic evaluation for medical artificial intelligence: accuracy vs. cost-effectiveness in a diabetic retinopathy screening case. NPJ Digit Med. 2024;7(1):43. doi: 10.1038/s41746-024-01032-9	Setting. Cost-effectiveness in the Chinese healthcare system.
Wolf RM, Abramoff MD, Channa R, Tava C, Clarida W, Lehmann HP. Potential reduction in healthcare carbon footprint by autonomous artificial intelligence. NPJ Digit Med. 2022;5(1):62. doi: 10.1038/s41746-022-00605-w	Publication Type. Potential reduction in carbon emissions.
Wolf RM, Channa R, Abramoff MD, Lehmann HP. Cost-effectiveness of Autonomous Point-of-Care Diabetic Retinopathy Screening for Pediatric Patients With Diabetes. JAMA Ophthalmol. 2020;138(10):1063-1069. doi: 10.1001/jamaophthalmol.2020.3190	Population. IDx is not FDA cleared for pediatric patients.
Wolf RM, Channa R, Lehmann HP, Abramoff MD, Liu TYA. Clinical Implementation of Autonomous Artificial Intelligence Systems for Diabetic Eye Exams: Considerations for Success. Clin Diabetes. 2024;42(1):142-149. doi: 10.2337/cd23-0019	Publication Type. Opinion piece from the IDx team.
Wolf RM, Channa R, Liu TYA, et al. Autonomous artificial intelligence increases screening and follow-up for diabetic retinopathy in youth: the ACCESS randomized control trial. Nat Commun. 2024;15(1):421. doi: 10.1038/s41467-023-44676-z	Population. Pediatric patients ages 8 to 21 years (mean 15.3 years for AI group and 15.9 years for control group).
Wolf RM, Liu TYA, Thomas C, et al. The SEE Study: Safety, Efficacy, and Equity of Implementing Autonomous Artificial Intelligence for Diagnosing Diabetic Retinopathy in Youth. Diabetes Care. 2021;44(3):781-787. doi: 10.2337/dc20-1671	Population. IDx is not FDA cleared for use in pediatric populations.
Wongchaisuwat N, Wang J, White ES, Hwang TS, Jia Y, Bailey ST. Detection of Macular Neovascularization in Eyes Presenting with Macular Edema using OCT Angiography and a Deep Learning Model. Ophthalmol Retina. 2025;9(4):378-385. doi: 10.1016/j.oret.2024.10.017	Intervention. Does not include any of the 3 FDA-cleared screening systems.

Citation	Reason for Exclusion
Yang WH, Zheng B, Wu MN, et al. An Evaluation System of Fundus Photograph-Based Intelligent Diagnostic Technology for Diabetic Retinopathy and Applicability for Research. Diabetes Ther. 2019;10(5):1811-1822. doi: 10.1007/s13300-019-0652-0	Intervention. Not an FDA-cleared AI device.
Youssef A, Nichol AA, Martinez-Martin N, et al. Ethical Considerations in the Design and Conduct of Clinical Trials of Artificial Intelligence. JAMA Netw Open. 2024;7(9):e2432482. doi: 10.1001/jamanetworkopen.2024.32482	Study Design. Interview-based study to determine the applicability of NIH ethical principles for clinical trials to trials of AI, and unique ethical considerations of AI trials.
Zhang Y, Ma X, Huang K, Li M, Heng PA. Semantic-Oriented Visual Prompt Learning for Diabetic Retinopathy Grading on Fundus Images. IEEE Trans Med Imaging. 2024;43(8):2960-2969. doi: 10.1109/TMI.2024.3383827	Intervention. Does not include any of the 3 FDA-cleared screening systems.
Zhu A, Tailor P, Verma R, et al. Implementation of deep learning artificial intelligence in vision-threatening disease screenings for an underserved community during COVID-19. J Telemed Telecare. 2024;30(10):1590-1597. doi: 10.1177/1357633X231158832	Intervention. Does not include any of the 3 FDA-cleared screening systems. Computer-aided (not autonomous) diagnosis.

Appendix H. Detailed Diagnostic Accuracy Outcomes

Table H1. Diagnostic Accuracy of Autonomous AI for More-Than-Mild (Referable) Diabetic Retinopathy, With Ungradable Cases Omitted[a]

Dilation	Study	Version	Notes	Sensitivity	Specificity	PPV	NPV	LR+	LR-
AEYE-DS									
Reflex dilation	NCT 04612868	NR	2 images (1 per eye)	92.98 (83.3 to 97.24)	91.36 (88.22 to 93.72)	NR	NR	10.76 (CI NR)	0.08 (CI NR)
Reflex dilation	NCT 04612868	NR	4 images (2 per eye)	94.74 (85.63 to 98.19)	88.64 (85.18 to 91.38)	NR	NR	8.34 (CI NR)	0.06 (CI NR)
EyeArt									
No dilation	Van 2024	2.0		96.64% (91.62 to 99.08)	90.09% (87.00 to 92.65)	71.43% (65.47 to 76.72)	99.05% (97.55 to 99.64)	9.75 (7.39 to 12.85)	0.04 (0.01 to 0.10)
	Ipp 2021	2.1.0	Correction for oversampling of high-risk patients	95.5% (92.6 to 97.7)	87.7% (86.0 to 89.5)	62.7% (57.8 to 64.7)	98.9% (98.3 to 99.5)	7.76 (CI NR)	0.05 (CI NR)
	Wintergerst 2022	2.1.0	No confusion matrix	75% (19 to 99)	98% (88 to 100)	NR	NR	37.5 (CI NR)	0.26 (CI NR)
	Karabeg 2025	2.1.0		89.66% (72.65 to 97.81)	83.03% (77.37 to 87.76)	41.27% (33.82 to 49.14)	98.37% (95.38 to 99.44)	5.28 (3.84 to 7.26)	0.12 (0.04 to 0.36)
	Mokhashi 2022	NR		100% (66.37 to 100)	77.78% (70.80 to 83.77)	19.15% (15.18 to 23.87)	100% (97.26 to 100)	4.50 (3.40 to 5.96)	0
Reflex dilation	Ipp 2021	2.1.0	Correction for oversampling of high-risk patients	95.5% (92.9 to 97.7)	87.8% (86.3 to 89.5)	62.8% (58.1 to 64.7)	98.9% (98.4 to 99.5)	7.83 (CI NR)	0.05 (CI NR)
	Musetti 2025	2.0	No confusion matrix	100% (89.94 to 100)	72.9% (65.2 to 97.7)	NR	NR	3.69 (CI NR)	0 (CI NR)
All dilated	Ibáñez-Bruron 2024	NR		92.31% (81.46 to 97.86)	78.80% (73.57 to 83.41)	44.44% (38.67 to 50.37)	98.24 (95.60 to 99.31)	4.35 (3.43 to 5.52)	0.10 (0.04 to 0.25)

Dilation	Study	Version	Notes	Sensitivity	Specificity	PPV	NPV	LR+	LR-
IDx-DR									
No dilation	Dow 2023	NR		95.54% (77.16 to 99.88)	98.18% (90.28 to 99.95)	95.45% (75.03 to 99.32)	98.18% (88.83 to 99.73)	52.50 (7.51 to 366.89)	0.05 (0.01 to 0.31)
	Grzybowski 2023	NR		98.85% (95.51 to 99.86)	68.09 (64.30 to 71.71)	3.10 (2.76 to 3.47)	0.02 (0.0 to 0.07)	3.10 (2.76 to 3.47)	0.02 (0.0 to 0.07)
	Grzybowski 2025	NR		99.30% (96.14 to 99.98)	68.99% (65.18 to 72.63)	42.47% (39.60 to 45.39)	99.77% (98.37 to 99.97)	3.20 (2.84 to 3.61)	0.01 (0.00 to 0.07)
	Poschkamp 2025	NR		90.16% (84.90 to 94.07)	82.95% (80.42 to 85.28)	50.15% (46.47 to 53.83)	97.79 (96.62 to 98.57)	5.29 (4.56 to 6.13)	0.12 (0.08 to 0.18)
	Sedova 2022	2.2	Vs. single manual grader	95.45% (77.16 to 99.88)	46.88% (20.09 to 65.26)	55.26% (46.84 to 63.40)	93.75% (60.09 to 99.06)	1.80 (1.28 to 2.52)	0.10 (0.01 to 0.68)
	Sedova 2022	2.2	Vs. 2 graders with overlay	100% (83.16 to 100)	47.06% (29.78 to 64.87)	52.63% (44.73 to 60.40)	100% (79.41 to 100)	1.89 (1.38 to 2.59)	0
	van der Heijden 2018	2.0		68.49% (56.56 to 78.87)	86.18% (83.64 to 88.46)	30.49% (25.83 to 35.59)	96.87% (95.66 to 97.75)	4.96 (3.94 to 6.24)	0.37 (0.26 to 0.51)
Reflex dilation	Abramoff 2018	NR	No confusion matrix	87.2% (81.8 to 91.2)	90.7% (88.3 to 92.7)	NR	NR	9.38 (CI NR)	0.14 (CI NR)
	Mehra 2022	NR		100% (90.75 to 100)	89.21% (87.04 to 91.14)	27.54% (24.00 to 31.38)	100% (99.55 to 100)	9.27 (7.70 to 11.16)	0
	Musetti 2025	NR	No confusion matrix	94.3% (80.4 to 99.3)	66.0% (57.8 to 73.5)	NR	NR	2.77 (CI NR)	0.09 (CI NR)
	Verbraak 2019	2.1		79.37% (67.30 to 88.53)	93.82% (92.33 to 95.10)	39.68% (33.84 to 44.83)	98.89% (98.20 to 99.31)	12.84 (9.99 to 16.52)	0.22 (0.14 to 0.36)
All dilated	Shah 2021	NR		100% (96.73 to 100)	81.82% (80.27 to 83.30)	19.20% (17.96 to 20.51)	100 (99.82 to 100)	5.50 (5.07 to 5.97)	0

[a] Test values with 95% confidence intervals.

Abbreviations: CI: confidence interval; LR+: positive likelihood ratio; LR-: negative likelihood ratio; NR: not reported. NVP: negative predictive value; PPV: positive predictive value.

Table H2. Diagnostic Accuracy of Autonomous AI for More-Than-Mild (Referable) Diabetic Retinopathy, With Ungradable Cases Considered Referable[a]

Dilation	Author Year	Version	Notes	Sensitivity	Specificity	PPV	NPV	LR+	LR-
EyeArt									
No dilation	Liu 2021	2.0		100% (90.51 to 100)	65.67% (56.98 to 73.65)	44.58% (38.89 to 50.41)	100% (95.89 to 100)	2.91 (2.30 to 3.68)	0
	Vought 2023	NR	No confusion matrix	74% (no CI)	87% (no CI)	72% (no CI)	88% (no CI)	5.69 (CI NR)	0.30 (CI NR)
All dilated	Bhaskaranand 2019	2.0	Mix of all dilated, undilated, unknown	91.30% (90.91 to 91.68)	91.12% (90.92 to 91.31)	72.45% (72.0 to 72.90)	97.62% (97.51 to 97.72)	10.28 (10.05 to 10.51)	0.10 (0.09 to 0.10)
	Heydon 2021	2.1		95.69% (94.75 to 96.50)	53.96% (53.38 to 54.55)	13.96% (13.78 to 14.15)	99.38% (99.25 to 99.49)	2.08 (2.05 to 2.11)	0.08 (0.07 to 0.10)
	Olvera-Barrios 2021	2.1		96.40% (91.03 to 99.01)	55.85% (52.92 to 58.75)	17.46% (16.41 to 18.55)	99.38% (98.39 to 99.76)	2.18 (2.03 to 2.35)	0.06 (0.02 to 0.17)
	Ibáñez-Bruron 2024	NR		93.65% (84.53 to 98.24)	73.60 (68.25 to 78.47)	42.45% (37.68 to 47.36)	98.24% (95.56 to 99.31)	3.55 (2.91 to 4.33)	0.09 (0.03 to 0.22)
	Tufail 2016	NR		91.08% (89.94 to 92.13)	37.30% (36.56 to 38.05)	19.30% (19.04 to 19.56)	96.21% (95.74 to 96.64)	1.45 (1.43 to 1.48)	0.24 (0.21 to 0.27)
IDx									
No dilation	Dow 2023	NR		95.45% (77.16 to 99.88)	93.10% (83.27 to 98.09)	84% (67 to 93.14)	98.18% (88.82 to 99.73)	13.84 (5.35 to 35.79)	0.05 (0.01 to 0.33)
Reflex dilation	Verbraak 2019	2.1		81.69% (70.73 to 89.87)	85.23% (83.23 to 87.08)	22.48% (19.68 to 25.56)	98.89% (98.19 to 99.32)	5.53 (4.67 to 6.55)	0.21 (0.13 to 0.35)

[a] *Test values with 95% confidence intervals.*

Abbreviations: CI: confidence interval; LR+: positive likelihood ratio; LR-: negative likelihood ratio; NR: not reported. NVP: negative predictive value; PPV: positive predictive value.

Table H3. Diagnostic Accuracy of EyeArt for Detection of Vision-Threatening Diabetic Retinopathy[a]

Protocol	Author Year	Version	Definition	Sensitivity	Specificity	PPV	NPV	LR+	LR-
Ungradable = referable, no dilation	Liu 2021	2	Vision-threatening	66.67% (29.93 to 92.51)	89.47% (83.87 to 93.64)	25% (15. 0 to 38.63)	98.08% (95.29 to 99.23)	6.33 (3.35 to 11.96)	0.37 (0.15 to 0.94)
Ungradable = referable, all dilated	Ibáñez-Bruron 2024	NR	Severe DR	100% (89.42 to 100)	84.38% (80.03 to 88.11)	38.82% (33.08 to 44.89)	100 (98.7 to 100)	6.40 (4.99 to 8.22)	0
	Olvera-Barrios 2021	2.1	Vision-threatening	100% (99.53 to 100)	NR	NR	NR	2.21 (2.06 to 2.37)	NR
	Tufail 2016	NR	Vision-threatening	93.81% (92.86 to 94.67)	15.84% (15.30 to 16.39)	15.40% (15.25 to 15.55)	94.00% (93.12 to 94.78)	1.11 (1.10 to 1.13)	0.39 (0.34 to 0.45)
Ungradable omitted, no dilation	Karabeg 2025	2.1.0	Severe	50.00% (1.26 to 98.74)	99.18% (97.08 to 99.90)	33.33% (6.60 to 77.95)	99.59% (98.38 to 99.90)	61.25 (8.66 to 433.10)	0.50 (0.13 to 2.02)
	Van 2024	2	Vision-threatening	100% (93.84 to 100)	92.19% (89.55 to 94.34)	59.59% (51.32 to 65.49)	100% (99.24 to 100)	12.80 (9.54 to 17.18)	0
	Ipp 2021	2.1.0	Vision-threatening, correction for oversampling of high-risk patients	96.9% (91.2 to 100)	90.0% (89.2 to 91.5)	29.6% (24.4 to 29.9)	99.8% (99.6 to 100)	9.69 (CI NR)	0.03 (CI NR)
Ungradable omitted, reflex dilation	Ipp 2021	2.1.0	Vision-threatening, correction for oversampling of high-risk patients	97.0% (91.2 to 100)	90.1% (89.4 to 91.5)	29.9% (24.7 to 30.1)	99.9% (99.6 to 100)	9.80 (CI NR)	0.03 (CI NR)
Ungradable omitted, all dilated	Ibáñez-Bruron 2024	NR	Severe	100% (85.75 to 100)	90.35% (86.52 to 93.40)	44.44% (36.28 to 52.92)	100 (98.70 to 100)	10.37 (7.38 to 14.57)	0

[a] *Test values with 95% confidence intervals.*

Abbreviations: LR+: positive likelihood ratio; LR-: negative likelihood ratio; NR: note reported. NVP: negative predictive value; PPV: positive predictive value.

Table H4. Subgroup Analysis of Diagnostic Accuracy for EyeArt in a Study With National Health Service Data[a10]

Subgroup	Sensitivity	Specificity	PPV	NPV	LR+	LR-
Sex						
Female	92.44% (90.79 to 93.87)	16.47% (15.67 to 17.30)	14.07% (13.84 to 14.30)	93.64% (92.31 to 94.75)	1.11 (1.09 to 1.13)	0.46 (0.37 to 0.56)
Male	94.82% (93.63 to 95.84)	15.27% (14.55 to 16.02)	16.43% (16.23 to 16.62)	94.37% (93.13 to 95.40)	1.12 (1.10 to 1.14)	0.34 (0.27 to 0.42)
Ethnicity						
White	92.32% (90.43 to 93.93)	18.05% (17.18 to 18.94)	12.62% (12.39 to 12.86)	94.82% (93.60 to 95.83)	1.13 (1.10 to 1.15)	0.43 (0.34 to 0.53)
Asian	95.13% (93.66 to 96.34)	12.89% (12.05 to 13.77)	16.39% (16.16 to 16.62)	93.65% (91.82 to 95.09)	1.09 (1.07 to 1.11)	0.38 (0.29 to 0.50)
Black	93.98% (91.90 to 95.67)	15.89 (14.65 to 17.18)	18.41% (18.05 to 18.78)	92.90% (90.55 to 94.69)	1.12 (1.09 to 1.14)	0.38 (0.28 to 0.52)
Age group						
< 50 years	96.19% (94.43 to 97.52)	16.78% (15.66 to 17.94)	15.21% (14.95 to 15.48)	96.60% (95.06 to 97.67)	1.16 (1.13 to 1.18)	0.23 (0.15 to 0.34)
50 to < 65 years	94.34% (92.88 to 95.58)	15.52% (14.66 to 16.42)	16.83% (16.59 to 17.07)	93.81% (92.27 to 95.05)	1.12 (1.10 to 1.14)	0.36 (0.29 to 0.46)
65 to 98 years	91.56% (89.63 to 93.23)	15.52% (14.65 to 16.42)	13.91% (13.65 to 14.17)	92.50% (90.86 to 93.86)	1.08 (1.06 to 1.11)	0.54 (0.44 to 0.67)

Protocol = all patients dilated, patients with ungradable images considered as referrals, EyeArt version not reported. [a] Test values with 95% confidence intervals. Abbreviations: LR+: positive likelihood ratio; LR-: negative likelihood ratio; NR: note reported. NVP: negative predictive value; PPV: positive predictive value.

Table H5. Diagnostic Accuracy of Autonomous AI in Situations Varying From FDA-Indications[a]

Protocol	Author Year	Version	Notes	Sensitivity	Specificity	PPV	NPV	LR+	LR-
EyeArt									
Ungradable omitted, no dilation	Guedes 2025	2.1	Any DR, not more than mild	100% (98.07 to 100)	93.53% (90.18 to 96.00)	90.43% (86.08 to 93.52)	100% (98.73 to 100)	15.45 (10.11 to 23.60)	0
Ungradable omitted, all dilated	Sarao 2020	2.1	Per eye, and no confusion matrix	90.8% (85.0 to 94.9)	75.3% (68.0 to 81.7)	NR	NR	3.68 (CI NR)	0.12 (CI NR)
IDx-DR									
Ungradable omitted, dilation not reported	Riotto 2024	NR	Any DR, no confusion matrix	100% (no CI)	78.4% (no CI)	36.7% (no CI)	100% (no CI)	4.63 (CI NR)	0 (CI NR)

[a] *Test values with 95% confidence intervals.*

Abbreviations: CI: confidence interval; DR: diabetic retinopathy; FDA: US Food and Drug Administration; LR+: positive likelihood ratio; LR-: negative likelihood ratio; NR: note reported. NPV: negative predictive value; PPV: positive predictive value.

Appendix I: Description of Coverage Policies

Health Plan or State	Coverage Status	Relevant Policy Information and Excerpts
Medicare[29,34,71-73,125]		
OPPS payment started 2018 (originally as part of a "bridge payment" package) National payment rate under Medicare Physician Fee Schedule started 2022, after initial carrier pricing No LCDs or NCDs found; prior billing and coding article issued by MAC, but retired 2023	Covered under Outpatient Prospective Payment System (OPPS) and Physician Fee Schedule	OPPS payment began in 2018, originally included under a "bridge payment" with a "Q1" status indicator, meaning it was packaged into payment with separately payable services billed during the same visit; paid separately under OPPS since 2021 • 2026 pricing: $60.27 Paid through Medicare national physician fee schedule • Prior to 2022, service was carrier (MAC) priced; national rate established in 2022 • 2026 pricing: $46.76 There is no current Medicare national coverage determination or local coverage determination from a Medicare Administrative Contractor (MAC). One MAC (Noridian) previously published a billing and coding article in 2021 titled, "Remote Imaging of the Retina to Screen for Retinal Diseases," that provided billing and coding guidance for CPT codes 92227, 92228, and 92229, along with a list of ICD-10 codes that support medical necessity. The billing article stood alone and was not tied to a local coverage determination. Noridian retired this billing and coding article in 2023. Excerpts from archived version of the Noridian billing and coding article (no longer active)[73]: **Article Guidance** *Article Text* Noridian allows coverage for CPT® Code 92227 Imaging of Retina for detection or monitoring of disease; with remote clinical staff review and report, unilateral or bilateral, for the early detection of diabetic retinopathy in patients with Type I diabetes for greater than five years or Type II diabetes at the time of diagnosis on an annual basis until such time as such retinopathy is detected. CPT® 92229 allows coverage for Imaging of retina for detection or monitoring of disease; point-of-care autonomous analysis and report, unilateral or bilateral. Once retinopathy is detected the patient should be under the direct care of an ophthalmologist but on occasion a need may arise where remote acquisition of retinal images is medically necessary. For those times 92228 or 92229 is billed. Please note that the CPT code encompasses either unilateral or bilateral. Noridian will not pay for 92227 more frequently than annually. Medicare benefits covers an eye exam for diabetic retinopathy screening once each year if you have diabetes. 92227 or 92229 should not be billed if the patient has had an in person ocular examination by an ophthalmologist.

Health Plan or State	Coverage Status	Relevant Policy Information and Excerpts
		In a patient with established diabetic retinopathy, a remote image process may be done and the images transmitted to an ophthalmologist for review and guidance. The image review must be done by an ophthalmologist. For imaging of retina for detection or monitoring of disease; with remote physician or other qualified health care professional, interpretation and report, unilateral or bilateral (92228), an ophthalmologist must interpret the image and submit a formal report with any treatment or follow up recommendations. In the rare instance where an ophthalmologist is not available in a patient with established diabetic retinopathy, point of care follow up images may be done using 92229 with automated analysis and report. The imaging device must be FDA approved for the intended use. In addition, transmission of the images and beneficiary information must adhere to applicable HIPAA laws for patient privacy. The originating office must be able to demonstrate that the person acquiring the image(s) has been fully trained in the acquisition of such images for the respective device. In review, once diabetic retinopathy is diagnosed the use of CPT 92227 no longer applies as the care is no longer screening in nature.
Health plans		
Aetna[75] Last reviewed 2025	Covered for diabetic retinopathy screening by specific policy	Policy Excerpts:[75] **Scope of Policy** This Clinical Policy Bulletin addresses retinopathy telescreening systems. **I. Medical Necessity** Aetna considers retinopathy telescreening systems medically necessary for screening diabetic retinopathy and retinopathy of prematurity as an alternative to retinopathy screening by an ophthalmologist or optometrist. **II. Experimental, Investigational, or Unproven** A. Aetna considers artificial intelligence-based systems experimental, investigational, or unproven for screening of retinopathy of prematurity because the effectiveness of this approach has not been established. B. Aetna considers retinopathy telescreening systems experimental, investigational, or unproven for the following because of insufficient evidence of their clinical value for these indications (not an all-inclusive list): • Following the progression of disease in members who are diagnosed with diabetic retinopathy • Screening or evaluating retinal conditions other than diabetic retinopathy or retinopathy of prematurity, including, but not limited to macular degeneration/edema.

Health Plan or State	Coverage Status	Relevant Policy Information and Excerpts
Anthem BlueCross BlueShield[76,77] Last reviewed 2026	Covered for diabetic retinopathy screening by specific policy	Policy Excerpts:[76] **Description** This document addresses retinal telescreening in the outpatient setting, including its use for the detection of diabetic retinopathy. **Medically Necessary:** Retinal telescreening systems in the outpatient setting are considered **medically necessary** for annual diabetic retinopathy screening as an alternative to retinopathy screening by an ophthalmologist or optometrist when **both** of the following criteria are met: • The individual does not have prior known diabetic retinopathy; **and** • The imaging and grading technique is performed with a U.S. Food and Drug Administration (FDA) approved device for retinal telescreening. **Not Medically Necessary:** All other uses of retinal telescreening systems in the outpatient setting are considered **not medically necessary,** including, but not limited to those listed below: • To follow the progression of disease in individuals who have been diagnosed with diabetic retinopathy • To screen or evaluate retinal conditions other than diabetic retinopathy, including, but not limited to macular degeneration. Within prior authorization look-up tool for New York Medicaid MCO line of business, 92229 is listed as *not* requiring prior authorization with reference to Anthem's retinal telescreening policy; implying possible Medicaid MCO coverage in the state
Cigna[160,161]	No specific policy information identified	Only references to diabetic eye exam HEDIS quality metric
Fidelis Care[78,162-165]	No specific policy information identified	Only references to diabetic eye exam HEDIS quality metric Within prior authorization look-up tool for New York Medicaid MCO line of business, 92229 is listed as *not* requiring prior authorization; implying possible Medicaid MCO coverage in the state
Healthfirst[166-168]	No specific policy information identified	No references found in New York Medicaid MCO provider or member materials
MetroPlusHealth[169-171]	No specific policy information identified	No references found in New York Medicaid MCO provider or member materials

Health Plan or State	Coverage Status	Relevant Policy Information and Excerpts
Molina Healthcare[121,172-175]	No specific policy information identified	No commercial plans in New York; no policy information found within commercial plan documentation for other states or New York Medicaid MCO provider or member materials (aside from references to HEDIS quality metric for diabetic eye exams)
UnitedHealthcare[32,176,177,179]	No specific policy information identified	Only references to diabetic eye exam HEDIS quality metric; no references found in New York Medicaid MCO provider or member materials
Medicaid		
California[79-81] *Updated 2026*	Covered on fee schedule	92229 appears on Medi-Cal ophthalmology and professional services policy manuals as a covered CPT code, though no price provided on fee schedule Excerpts from ophthalmology policy[80]: The following CPT 90000 series of codes (*including 92229*) for eye procedures are considered bilateral services. Therefore, a code should be billed only once, regardless of whether the procedure was performed on one or both eyes. However, in the case of eye surgeries, this does not apply, and the appropriate code should be used to specify whether the procedure was unilateral or bilateral. When performed as a bilateral procedure, claims must be billed on a single line using modifier 50 (bilateral procedure) with a quantity of "1", for CPT codes 92132 thru 92134, 92202 and 92227 thru 92229. The allowed service is one per day, whether it is unilateral or bilateral. No documentation is required for CPT codes listed above. CPT codes 92227, 92228, and 92229 are not reimbursable for the same recipient on the same date of service by any provider in conjunction with codes 92002 thru 92014, 92133, 92134, 92227, 92228, 92250 or Evaluation and Management (E&M) codes 99202 thru 99350 and 99417.
Florida[82,83] *Updated 2026*	Covered on fee schedule	92229 appears on practitioner ($36.37) and visual services ($34.97) fee schedules; no other criteria or guidance identified
Massachusetts[84,85] *Updated 2026*	Covered on fee schedule	92229 listed on vision services manual as a covered CPT code, appears on fee schedule with reimbursement price of $36.09; no other criteria or guidance identified
New Jersey[86] *Updated 2026*	Covered on fee schedule	92229 appears on fee schedule with reimbursement price of $22.94 for specialists and $19.49 for non-specialists; no other criteria or guidance identified
New York[33] *Updated 2026*	No evidence of coverage	92229 does not appear on any agency fee schedules or materials

<table>
<tr><th>Health Plan or State</th><th>Coverage Status</th><th>Relevant Policy Information and Excerpts</th></tr>
<tr><td>North Carolina[87]

Updated 2026</td><td>Covered on fee schedule</td><td>92229 appears on fee schedule with reimbursement price of $24.11; no other criteria or guidance identified</td></tr>
<tr><td>Oregon[91,93,94]

Updated 2026</td><td>Not covered</td><td>92229 does not appear on agency fee schedule; Oregon Health Evidence Review Commission (HERC) program includes 92229 on its list of excluded services, based on a review in October 2020 prior to the CPT code becoming active. The 2020 review included a description of the technology, review of 2 publications and a private payer policy (BlueCross BlueShield) that considered the service investigational at the time.

Excerpt from Oregon HERC Prioritized List of Health Services[94]:
EXCLUDED SERVICES GUIDELINE E2, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS
The following Interventions are unproven, have no clinically important benefit or have harms that outweigh benefits and should be excluded from coverage:

<table>
<tr><th>Procedure Code</th><th>Intervention</th><th>Rationale</th><th>Last Review</th></tr>
<tr><td>92229</td><td>Imaging of retina for detection or monitoring of disease; point-of-care automated analysis and report, unilateral or bilateral</td><td>Insufficient evidence of effectiveness</td><td>October, 2020</td></tr>
</table>

Excerpt from HERC October 2020 Meeting Materials[93]:
HERC staff summary
Digital retinal imaging with automated image interpretation is an intriguing technology to increase diabetic retinopathy screening. However, the evidence to date is insufficient to determine the effectiveness of this technology.

HERC staff recommendation:
1) Place 92229 Imaging of retina for detection or monitoring of disease; point-of-care automated analysis and report, unilateral or bilateral on line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS and update the GN173 reference as shown below</td></tr>
</table>

<table>
<tr><th>Health Plan or State</th><th>Coverage Status</th><th>Relevant Policy Information and Excerpts</th></tr>
<tr><td>Pennsylvania[88,180,181]

Updated 2026</td><td>Covered on fee schedule</td><td>92229 appears on fee schedule under a number of provider types and care settings (inpatient, clinic, optometrist, physician) with reimbursement price of $37.95; no other criteria or guidance identified.

In 2022, the agency's managed care operations Technology Assessment Group issued a notice to managed care plans to cover the code.

Excerpt from technology assessment memo[180]:
Purpose
The Office of Medical Assistance Programs (OMAP) is issuing this Operations Memorandum to provide MCOs coverage updates on new technologies as discussed in regular TAG meetings.
Background
The Technology Assessment Group (TAG) workgroup meets quarterly on the first Wednesday of February, May, August, and November to discuss issues and evidence-based research pertaining to evolving new technologies and previously reviewed technologies or services that were determined to be covered only through a program exception request. During the TAG meeting, decisions are made as to whether certain technologies or services will be covered under the Medical Assistance (MA) Program and the option under which it will be covered. TAG's coverage options are as follows:
• Option # 1: Indicates service, device, or procedure will be added to the MA Program Fee Schedule because of well-established medical evidence. MCOs or MA Fee-for-service (FFS) program may require prior authorization.
Discussion
Below is the updated list of codes/descriptions discussed at the August 3, 2022, TAG Meeting and the decision that was made:
<table><tr><th>HCPCS/CPT Code</th><th>Description</th><th>Decision</th></tr><tr><td>CPT 92229</td><td>IDx-DR System:
Imaging of retina for detection or monitoring of disease; point-of care automated analysis and report, unilateral or bilateral</td><td>Option #1</td></tr></table></td></tr>
</table>

Health Plan or State	Coverage Status	Relevant Policy Information and Excerpts
Texas[89,90,182] *Updated 2026*	Covered on fee schedule	92229 listed in provider manual under visual and hearing services section as a covered CPT code, appears on fee schedule with reimbursement price of $38.17 for children and $36.35 for adults; provider guide gives additional billing guidance, but no other clinical criteria Excerpts from provider manual[90]: Procedure codes 92201, 92202, 92227, 92229, 92230, and 92260 are reimbursed for the total component only. Remote retinal imaging (procedure codes 92227, 92228, and 92229) is a benefit of Medicaid when the images are obtained by a provider at one facility, and then transmitted electronically, to be reviewed and interpreted at another site by an ophthalmologist or other qualified health care professional under the direction of a retinal specialist. Procedure codes 92227, 92228, 92229, 92235, 92240, 92242, 92250 and 92260 are limited to one service per day and two services per calendar year by any provider. Procedure code 92230 must be billed with modifier LT or RT to identify the eye on which the service was performed. Procedure codes S0620 and S0621 will be denied if billed on the same date of service as procedure codes 92227, 92228, 92229, 92230, 92235, 92240, 92242, 92250 or 92260. Excerpts from 2021 Medicaid bulletin update activating reimbursement for CPT code 92229[182]: **Limitations for added procedure code** Procedure code 92229 may be reimbursed as follows: • To PA, NP, CNS, physician, and optometrist providers for services rendered in the office, inpatient hospital, and outpatient hospital settings. Procedure code 92229 is limited to one service per day and two services per calendar year by any provider. Refer to: The Texas Medicaid Provider Procedures Manual, Vision and Hearing Services Handbook, subsection 4.3.5.11, “Other Specialized Vision Services” for additional information.
Washington[92,183,184] *Updated 2026*	No evidence of coverage	92229 does not appear on any agency fee schedules or materials; no prior review of technology by state’s Health Technology Assessment (HTA) program.

Source. Medicare coverage database and Centers for Medicare and Medicaid Services coverage policy documentation. Health plan websites for Aetna, Anthem BlueCross BlueShield, Cigna, Fidelis Care, Healthfirst, MetroPlusHealth, Molina Healthcare, UnitedHealthcare. State Medicaid agency websites for California, Florida, Massachusetts, New Jersey, New York, North Carolina, Oregon, Pennsylvania, Texas, Washington.
Abbreviations. MCO: managed care organization.

Appendix J: Relevant Codes

Table J1. Applicable Codes for AI-Enabled Diabetic Retinopathy Analysis

Code	Description
ICD-10-CM codes	
Various E08 codes	Diabetes mellitus due to underlying conditions
Various E09 codes	Drug or chemical induced diabetes mellitus
Various E10 codes	Type 1 diabetes mellitus
Various E11 codes	Type 2 diabetes mellitus
Various E13 codes	Other specified diabetes mellitus
CPT code[27]	
92229	Imaging of retina for detection or monitoring of disease; point-of-care autonomous analysis and report, unilateral or bilateral

Abbreviations. AI: artificial intelligence; CPT: Current Procedural Terminology; HCPCS: Healthcare Common Procedure Coding System; ICD-10-CM: International Classification of Diseases, Tenth Revision, Clinical Modification.

Appendix K: Prevalence of Diabetic Retinopathy in New York Counties

Table K1. Adjusted* Prevalence of Diabetic Retinopathy Among People With Diabetes

County	Adjusted Prevalence	County	Adjusted Prevalence
Albany County	27.01 (22.41 to 32.19)	Niagara County	23.43 (19.43 to 28.17)
Allegany County	18.52 (15.22 to 22.33)	Oneida County	25.95 (21.5 to 31.18)
Bronx County	26.44 (21.94 to 31.67)	Onondaga County	24.89 (20.72 to 29.83)
Broome County	17.56 (14.45 to 21.08)	Ontario County	25.01 (20.84 to 30.37)
Cattaraugus County	19.84 (16.31 to 23.91)	Orange County	27.76 (23.08 to 33.16)
Cayuga County	31.2 (25.89 to 37.31)	Orleans County	22.33 (18.34 to 27.29)
Chautauqua County	28.03 (23.41 to 33.46)	Oswego County	26.78 (22.05 to 32.16)
Chemung County	21.95 (18.12 to 26.38)	Otsego County	26.13 (21.52 to 31.26)
Chenango County	29.59 (24.49 to 35.66)	Putnam County	27.31 (22.62 to 32.68)
Clinton County	20.3 (16.83 to 24.28)	Queens County	26.83 (22.35 to 32.03)
Columbia County	29.19 (24.33 to 34.97)	Rensselaer County	33.41 (27.73 to 40.07)
Cortland County	24.38 (20.25 to 29.28)	Richmond County	26.2 (21.76 to 31.38)
Delaware County	26 (21.4 to 30.98)	Rockland County	30.65 (25.44 to 36.51)
Dutchess County	22.04 (18.32 to 26.34)	Saratoga County	26.58 (21.97 to 31.96)
Erie County	25.16 (20.8 to 30.01)	Schenectady County	24.15 (20.03 to 28.99)
Essex County	24.43 (20.28 to 29.36)	Schoharie County	35.12 (28.94 to 42)
Franklin County	22.72 (18.61 to 27.49)	Schuyler County	19.49 (15.73 to 23.83)
Fulton County	19.78 (16.33 to 24.06)	Seneca County	22.54 (18.49 to 27.49)
Genesee County	25.63 (21.01 to 30.89)	St. Lawrence County	19.88 (16.45 to 23.64)
Greene County	35.53 (29.43 to 42.5)	Steuben County	23.97 (19.81 to 28.65)
Hamilton County	21.33 (16.69 to 26.98)	Suffolk County	24.54 (20.45 to 29.3)
Herkimer County	28.44 (23.35 to 34.3)	Sullivan County	25.38 (21.05 to 30.31)
Jefferson County	34.37 (28.53 to 41.11)	Tioga County	20.7 (17.23 to 24.97)
Kings County	27.73 (23.04 to 33.15)	Tompkins County	34.55 (28.48 to 41.24)
Lewis County	26.39 (21.65 to 31.98)	Ulster County	25.27 (20.91 to 30.34)
Livingston County	22.92 (18.87 to 27.77)	Warren County	28.05 (23.37 to 33.65)
Madison County	26.25 (21.59 to 31.41)	Washington County	28.08 (23.2 to 33.7)
Monroe County	22.55 (18.74 to 26.87)	Wayne County	21.37 (17.53 to 25.61)
Montgomery County	26.08 (21.6 to 31.46)	Westchester County	24.8 (20.61 to 29.57)
Nassau County	23.25 (19.33 to 27.77)	Wyoming County	23.35 (19.18 to 28.38)
New York County	21.02 (17.42 to 25.11)	Yates County	22.24 (17.99 to 26.97)

** Adjusted for age, sex, and race/ethnicity.*

Source: Centers for Disease Control and Prevention Vision & Eye Health Surveillance System.[4]