Retinal telescreening for diabetic retinopathy

Clinical Policy ID: CCP.1230

Recent review date: 5/2021

Next review date: 9/2022

Policy contains: Diabetic retinopathy; retinal telescreening; telemedicine.

Coverage policy

Diabetic retinopathy telescreening is clinically proven and, therefore, medically necessary for detection of diabetic retinopathy, as an alternative to on-site retinopathy screening by an ophthalmologist or optometrist, when all of the following criteria are met (American Academy of Ophthalmology, 2018; Flaxel, 2020; Li, 2011):

- Member is diagnosed with diabetes.
- Member has no prior-known diabetic retinopathy.
- Detection is by fundus photography (standardized Early Treatment Diabetic Retinopathy Study photos using stereoscopic color fundus photographs in seven standard fields or single-field fundus photography), with or without mydriasis.
- Photograph is manually interpreted by an ophthalmologist or optometrist (subject to state licensure requirements).
- Screening intervals are:
    - Members with Type 1 diabetes — annually beginning five years after the onset of diabetes; for diabetes diagnosed before puberty, screening should begin at puberty, unless other considerations would suggest otherwise.
    - Members with Type 2 diabetes — at the time of diabetes diagnosis and at least annually thereafter.
    - Members with either Type 1 or Type 2 diabetes who become pregnant — initial exam soon after conception and early in the first trimester. Additional screening through pregnancy may be indicated on a case-by-case basis.

Limitations

All other indications for telescreening diabetic retinopathy are investigational/not clinically proven and, therefore, not medically necessary, including (Flaxel, 2020; Hooper, 2012):

- Disease surveillance in members with an existing diagnosis of diabetic retinopathy.
- Screening or evaluating retinal conditions other than diabetic retinopathy, including, but not limited to, macular degeneration/edema or retinopathy of prematurity.
- Screening in women with gestational diabetes, as these members are not at risk of developing diabetic retinopathy.

Automated digital image analysis using integrated artificial intelligence-based algorithms is investigational/not clinically proven and, therefore, not medically necessary (Islam, 2020; Wang, 2020).

Alternative covered services

No alternative covered services were identified during the writing of this policy.

Background

Diabetic retinopathy is a leading cause of vision loss in the United States and occurs as a result of long-term pathologic changes of the retinal vasculature (Shukla, 2020). The prevalence and severity of diabetic retinopathy increases with the duration of diabetes; however, it is inversely correlated to glycemic and blood pressure control. Early stage disease (called nonproliferative diabetic retinopathy) may be asymptomatic and only discovered incidentally on fundus examination. Advanced disease (called proliferative diabetic retinopathy) may involve retinal leakage within the macula that progresses to severe vision loss occurring as a result of neovascularization with subsequent hemorrhage or fibrosis; it may or may not be symptomatic. Diabetic retinopathy can worsen during pregnancy due to the physiologic changes of pregnancy itself or changes in overall metabolic control.

Diabetic retinopathy treatment is aimed at reducing the risk of disease onset and limiting disease progression (Shukla, 2020). Early identification and treatment of diabetic retinopathy is important for reducing vision loss, and an important component of disease management involves regular retinal assessments. However, a significant portion of patients with diabetes have never had their eyes examined. They tend to be older, less educated, more recently diagnosed, live in rural areas, and receive health care from a primary care practitioner.

Techniques used to detect and classify diabetic retinopathy include testing for visual acuity and intraocular pressure, slit-lamp examination, gonioscopy, and dilated fundus examination with an indirect ophthalmoscope (Shukla, 2020). The gold standard for the detection and classification of diabetic retinopathy is stereoscopic color fundus photographs in seven standard fields, as defined by the Early Treatment Diabetic Retinopathy Study group (Solomon, 2019). However, it is labor-intensive and requires skilled staff, often in short supply, and sophisticated equipment, making it impractical for widespread use. Fluorescein angiography, optical coherence tomography with or without angiography, and ultrasonography may also be used to confirm a diagnosis.

Across income settings, availability of skilled personnel, training programs, and retinal imaging infrastructure is a major factor affecting access to diabetic retinal screening services (Piyasena, 2019). To improve screening compliance and overcome these limitations, several interventions have been proposed or developed (Kalogeropoulos, 2020; Lawrenson, 2018). In any one region, the screening program that is adopted is likely to be a compromise between patient need and efficacy of the method, the existing infrastructure, and local expertise. Most involve multiple components to affect the behavior of either the provider or the patient, as no single modality satisfies all the requirements for a screening program.

Telescreening

Screening programs can be tailored to different population needs, from basic screening (a program that differentiates those with no or mild disease from those with more significant disease) to evaluative screening (a program that can replace standardized Early Treatment Diabetic Retinopathy Study photos for any clinical or research purpose). A telescreening program that can accurately and reliably perform basic screening may lessen the burden of screening by a traditional dilated fundus exam (Kalogeropoulos, 2020; Lawrenson, 2018).

Diabetic retinopathy telescreening is a digital solution that involves taking digital pictures of the retina of diabetic patients in the primary care physician's office, and electronically transmitting these pictures to a reading center for evaluation for diabetic retinopathy and macular edema by trained non-physician technicians (Kalogeropoulos, 2020; Lawrenson, 2018). Because diabetic retinopathy telescreening can be performed in conjunction with a primary care physician office visit without referral to an ophthalmologist or optometrist, these systems have the potential to improve compliance with retinopathy screening. A telehealth program's goals and desired performance may affect choice of screening protocol and technology. Ultimately, good-quality retinal imaging and accurate diagnosis are essential to minimizing inappropriate referrals.

Nonmydriatic single-field fundus photography has the potential to improve the quality of the evaluation and the number of patients evaluated (Shukla, 2020). Although mydriasis improves image quality and sensitivity, particularly in older patients, it is uncertain whether the disadvantages of dilation outweigh the benefits. In other words, the diminished sensitivity of a nonmydriatic photograph may be acceptable if more patients complete the process.

Other screening options include ultra-wide-field imaging, smartphone-based fundus cameras, and hand-held fundus cameras that allow immediate transmittal to trained ophthalmologists for grading of diabetic retinopathy (Rajalakshmi, 2021). Fundus cameras with integrated artificial intelligence-based algorithms offer automated digital image analysis of fundus images. A positive result is intended to trigger a referral to an ophthalmologist. An example of an automated retinal image analysis device is the IDx-DR (Digital Diagnostics Inc, Coralville, Iowa).

Findings

The American Telemedicine Association (Li, 2011) published recommendations for designing, implementing, and maintaining an ocular telehealth program, including recommendations for evaluating diabetic retinopathy telehealth methods and technologies. Ocular telehealth programs can be an essential component of primary care in that they can integrate diabetes eye care into the patient's overall health care. The goals of an ocular telehealth program in diabetes are to extend access to people with diabetes, regardless of geography or socioeconomic status, the ability to receive an evidence-based retinal evaluation to determine the presence and severity of diabetic retinopathy.

These program recommendations also provide guidance for assessing the clinical value of retinal telescreening for diabetic retinopathy (Li, 2011). Program objectives should address specific patient outcome measures such as reduction in the incidence of vision loss due to diabetic retinopathy. System measures should emphasize improving diagnosis and management of diabetic retinopathy, efficiency, clinical effectiveness, and availability, quality, efficiency, and cost-effectiveness of remote evaluation for diabetic retinopathy.

A validated telescreening program should state the reference standard used for validation and relevant datasets used for comparison. For example, it should demonstrate an ability to compare favorably with Early Treatment Diabetic Retinopathy Study film or digital photography as reflected in kappa values for agreement of diagnosis, false-positive and false-negative readings, and diagnostic operating characteristics (predictive values, sensitivity, and specificity) of diagnosing levels of retinopathy and macular edema. Unobtainable or unreadable images should be considered a positive finding, and patients should be promptly re-imaged or referred for evaluation by an eye care specialist. Regardless of an image's origin, the quality of medical images must meet specified

standards. Quality control should encompass all program components, such as image acquisition, transmission, and reading.

The Canadian Ophthalmological Society (Hooper, 2012) recommended implementing properly designed teleophthalmology programs “to improve access to, and compliance with, monitoring in culturally, economically or geographically isolated populations of individuals with diabetes. They cited strong evidence from eight diagnostic accuracy studies (n = 1,412 total participants) that the sensitivity and specificity exceeded 95% in detection of nonproliferative diabetic retinopathy by various teleophthalmology algorithms. Teleophthalmology systems with this diagnostic performance using mydriatic and nonmydriatic digital cameras would be acceptable for diabetic retinopathy screening to identify patients with diabetic retinopathy who require further evaluation and management.

An American Academy of Ophthalmology Preferred Practice Pattern on Diabetic Retinopathy (2016) states: “Some studies have shown that screening programs using digital images taken with or without dilation may enable early detection of diabetic retinopathy along with an appropriate referral. Digital cameras with stereoscopic capabilities are useful for identifying subtle neovascularization and macular edema. Studies have found a positive association between participating in a photographic screening program and subsequent adherence to receiving recommended comprehensive dilated eye examinations by a clinician. Of course, such screening programs are more relevant when access to ophthalmic care is limited. Screening programs should follow established guidelines. Given the known gap in accessibility of direct ophthalmologic screening, fundus photographic screening programs may help increase the chances that at-risk individuals will be promptly referred for more detailed evaluation and management.”

The choice of screening strategies depends on the rates of appearance and progression of diabetic retinopathy and on risk factors that alter these rates (American Academy of Ophthalmology, 2016; Hooper, 2012). Patients with Type 1 diabetes should have annual screenings for diabetic retinopathy beginning five years after the onset of their disease; for disease diagnosed before puberty, screening should begin at puberty, unless other considerations would suggest otherwise. Patients with Type 2 diabetes should have screening at the time of diagnosis and at least annually thereafter. During pregnancy, the initial exam should occur soon after conception and early in the first trimester. Once nonproliferative diabetes retinopathy is detected, examination should be conducted at least annually for mild disease, or more frequently (at three- to six-month intervals) for pregnant patients or patients with moderate or severe disease based on the severity of diabetic retinopathy. Women who develop gestational diabetes do not require an eye examination during pregnancy and do not appear to be at increased risk for diabetic retinopathy during pregnancy.

Validated telescreening for diabetic retinopathy should be based on fundus photography. The evidence suggests that either conventional 35-mm color photography or digital seven-field imaging systems can meet the relevant quality standards for annual eye examination to detect diabetic retinopathy, with the advantage that image acquisition can be performed in the primary care setting (American Academy of Ophthalmology, 2016; Hooper, 2012). Questions regarding the accuracy of imaging that involves fewer than seven fields or does not involve dilation of the pupil require additional study. An assessment of three high-quality comparative studies found single-field fundus photography was an effective screening tool for identifying patients with diabetic retinopathy who need to be referred for further ophthalmic care (Williams, 2004). Both single-field and nonmydriatic fundus photography have lower sensitivity than seven-standard field photography or ophthalmoscopy, but they represent a compromise for improving patient compliance with screening.

In 2018, we added an evidence-based Danish guideline on screening for diabetic retinopathy (Grauslund, 2018). The recommended screening intervals are consistent with our policy with the additional consideration of how well the underlying diabetes is controlled. In the presence of suboptimal diabetic control, they recommended tailoring screening intervals. The results of the Diabetes Control and Complication Trial (2017) showed a close

correlation between glycemic regulation (mean glycated hemoglobin levels) and the risk of five-year progression from no diabetic retinopathy to proliferative diabetic retinopathy. The risk of progression from no retinopathy to proliferative diabetic retinopathy or clinically significant macular edema was 1.0% over five years among patients with a glycated hemoglobin level of 6%, compared with 4.3% over three years among patients with a glycated hemoglobin level of 10%. Establishing an individualized schedule for retinopathy screening on the basis of the patient's current state of retinopathy and glycated hemoglobin level reduced the frequency of eye examinations by 58% without delaying the diagnosis of clinically significant disease.

In 2019, the policy ID was changed from 14.02.15 to CCP.1369.

In 2020, we added no new relevant literature to the policy.

In 2021, we updated the American Academy of Ophthalmology Preferred Practice Pattern on Diabetic Retinopathy (Flaxel, 2020, update of 2016) and added a systematic review (Avidor, 2020) of seven economic evaluations, which confirm the difficulty in quantifying the cost-effectiveness of retinal telescreening programs due to the lack of data from randomized controlled trials, the high risk of bias in the available data from observational studies, and the inability to generalize results from one screening program to another.

We added two systematic reviews and meta-analyses (Islam, 2020; Wang, 2020) of automated diabetic retinopathy screening systems that apply deep learning-based algorithms (artificial intelligence) to classify diabetic retinopathy. From these two analyses, the pooled sensitivity ranged from 83% to 91.9% and pooled specificity ranged from 91.3% to 92% for detecting referable diabetic retinopathy from retinal fundus photographs. Advantages of implementing automated diabetic retinopathy classification include reduction in staffing, cost of screening, and intra- and inter-grader variability. Limitations include ethical concerns regarding lack of trust in computerized systems compared with human-based readings. At best, the current evidence supports the feasibility of automated telescreening systems, but their routine implementation and impact on patient outcomes require further study.

The purpose of an effective screening program for diabetic retinopathy is to determine who needs to be referred to an ophthalmologist for close follow-up and possible treatment and who may simply be screened annually (Flaxel, 2020). To improve diabetic retinopathy screening compliance, telescreening can be performed as part of a primary care physician office visit. In this setting, a positive result is intended to trigger a referral to an ophthalmologist. We modified the coverage criteria to focus the policy on patients with diabetes and no known diabetic retinopathy as the target telescreening population, in accordance with contemporary guidelines.

References

On February 3, 2021, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "ophthalmology," "diabetic retinopathy," "photography," "telescreening," "teleophthalmology," and "retina." We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

4/2016: initial review date and clinical policy effective date: 7/2016

4/2018: Policy references updated.

4/2019: Policy references updated. The policy ID was changed.

3/2020: Policy references updated.

5/2021: Policy references updated. Coverage modified.