MEDICAL POLICY	Eye: Retinopathy Telescreening (All Lines of Business Except Medicare)
Effective Date: 6/1/2022  6/1/2022 Medical Officer Date	Medical Policy Number: 185 Technology Assessment Committee Approved Date: 10/09 Medical Policy Committee Approved Date: 8/11; 5/13; 6/14; 9/15; 5/16; 7/17; 9/17; 12/18; 2/19; 3/2020; 5/2020; 12/2020; 07/2021; 4/2022

See Policy CPT CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:

All lines of business except Medicare

BENEFIT APPLICATION

Medicaid Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

POLICY CRITERIA

I. Retinal photography may be considered **medically necessary and is covered** to screen for diabetic retinopathy in patients with diabetes mellitus when all of the following criteria (A.-C.) are met:

   A. The individual does not have prior diagnosis of diabetic retinopathy; **and**
   B. The imaging technique is performed with a U.S. Food and Drug Administration (FDA) approved device; **and**
   C. The final images are graded for diabetic retinopathy using a manual process.

II. Retinal photography is considered **not medically necessary and is not covered** in patients with diabetes mellitus who currently have a diagnosis of diabetic retinopathy when the above criteria are not met, including but not limited to:

A. Monitoring potential progression of a disease process; **or**
B. Guidance in evaluating the need for or response to a specific treatment or intervention.

III. Retinal photography is considered **investigational and is not covered** for any other situation, including, but not limited to:

A. When criterion I. above is not met; **or**
B. For screening of a condition other than diabetes mellitus, including, but not limited to:
    1. Suspected diabetes, pre-diabetes, or gestational diabetes; **or**
    2. Macular degeneration; **or**
    3. Retinopathy of prematurity; **or**
C. When the final retinal images are graded using an automatic process only (e.g., Intelligent Retinal Imaging System [IRIS], IDx-DR).

Link to Policy Summary

BILLING GUIDELINES

Code 92227 for diabetic retinopathy screening may only be covered when medical necessity criteria above are met and code 92227 is billed with any of the following ICD-10 codes below:

E08.0 – E08.29
E08.36 – E08.9
E09.0 – E09.29
E09.36 – E09.9
E10.0 – E10.29
E10.36 – E10.9
E11.0 – E11.29
E11.36 – E11.9
E12.0 – E10.29
E12.36 – E12.9
E13.0 – E13.29
E13.36 – E13.9
O24.0 – O24.33
O24.8 – O24.93

CPT CODES

All Lines of Business Except Medicare	
No Prior Authorization Required	
92227	Remote imaging for detection of retinal disease (eg, retinopathy in a patient with diabetes) with analysis and report under physician supervision, unilateral or bilateral
Not Covered	
92228	Remote imaging for monitoring and management of active retinal disease (eg, diabetic retinopathy) with physician review, interpretation and report, unilateral or bilateral
92229	Imaging of retina for detection or monitoring of disease; point-of-care automated analysis and report, unilateral or bilateral

DESCRIPTION

Diabetic retinopathy is a microvascular complication of diabetes mellitus that is the most common ophthalmologic complication of diabetes and the leading cause of new blindness in the United States. The risk of developing retinopathy increases with duration of disease. After 20 years of diabetes, nearly all patients with type 1 diabetes and over 60% of patients with type 2 diabetes have some degree of retinopathy, which can lead to retinal detachments, retinal tears, and macular edema, with subsequent partial or total loss of vision.[1]

The standard of care for prevention of vision loss due to diabetic retinopathy includes a comprehensive annual eye examination, including measurement of visual acuity, intraocular pressure, and an examination of the retina performed with the pupils pharmacologically dilated. This is generally performed by an ophthalmologist or retinal specialist. If diagnosed in an early stage, laser photocoagulation can be effective in preventing or reducing vision loss in patients with proliferative retinopathy or macular edema if lesions.[1]

Access to the expertise of a specialist and equipment may not always be available and retinal telescreening systems have emerged as a way to increase screening for diabetic retinopathy. Photographic methods have been developed to allow images of the retina to be documented and examined by expert readers who are not located conveniently to the patient. The gold standard for screening is currently the seven-field stereoscopic color fundus photography. Recently, digital fundus photography, which may or may not involve dilation of the pupils, has become popular. Digital imaging has the advantage of allowing for evaluation by trained examiners at distant locations thereby enhancing patient access to retinal specialists.

More recently, nonmydriatic digital retinal imaging allows remote interpretation by an ophthalmologist, which may improve retinopathy screening in areas with a shortage of eye care specialists, and is reported to have good sensitivity and specificity for detecting diabetic retinopathy.

Retinopathy telescreening is also currently being investigated for detection of other conditions including macular degeneration and retinopathy of prematurity (ROP). Currently, the use of telescreening for ROP evaluations consists of fundus images acquired with a digital, fiber optic, wide-angle, color fundus camera. Images are taken in the NICU and then transmitted to a remote location for interpretation.[2]

REVIEW OF EVIDENCE

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of various forms of retinal imaging as a screen for diabetic retinopathy. Below is a summary of the available evidence identified through June 2021.

Diabetic Retinopathy

Mydriatic versus Nonmydriatic Status

Systematic Reviews

In 2011, Bragge et al. reported a meta-analysis, which examined how pupil dilation affected the accuracy of screening for diabetic retinopathy, including 20 studies that measured the sensitivity and specificity of imaging tests used for screening for diabetic retinopathy.[3] Studies measured sensitivity and specificity for the detection of diabetic retinopathy, using either digital photography; film photography; direct examination; Polaroid photography; various combinations of camera types or camera plus examination and scanning laser ophthalmoscope. All included studies used either seven-field mydriatic photography or dilated fundus examination (by an ophthalmologist or equivalent specialist) as the reference standard. Compared to a reference standard for imaging, the overall estimate of sensitivity was 82.5% (95% CI, 75.6% to 87.9%) and specificity was 88.4% (95% CI, 84.5% to 91.4%) for alternative imaging methods. The reviewers reported that mydriatic status did not significantly influence sensitivity (odds ratio [OR], 0.89; 95% CI, 0.56-1.41; p = 0.61) or specificity (OR, 0.94; 95% CI, 0.57-1.54; p = 0.80). The authors concluded that outreach screening was an effective alternative to on-site specialist examination, regardless of imaging technique used or mydriatic status.

In 2019, Piyasena et al. conducted a meta-analysis comparing the diagnostic accuracy of mydriatic versus non-mydriatic strategies for digital retinal imaging using one or more fields of view for the detection of any level of diabetic retinopathy.[4] The analysis reviewed 21 cross-sectional studies with acceptable levels of bias and heterogeneity evaluating the accuracy of diabetes retinopathy screening. Sensitivity was shown to be highest when mydriatic strategies were used with greater than two fields (92%, 95% CI: 90-94%). After excluding ungradable images from the dataset, pooled sensitivity was shown to be the same in non-mydriatic and mydriatic strategies at 86% (95% CI: 85-87%).Specificity was not effected by choice of non-mydriatic and mydriatic strategy, and was observed to be highest when using greater than two field methods (94%, 95% CI: 93-96%). The authors concluded that non-mydriatic two-field strategy is a practical approach for creating diabetes retinopathy screening programs in low-income settings.

Randomized Controlled Trials (RCTs)

In 2015, Mansberger et al. published the results of a study that randomized 567 participants to either receive telemedicine with a nonmydriatic camera in a primary care clinic (n=296) or traditional surveillance with an eye care professional (n=271).[5] Patients were followed for 5 years. After 2 years, telemedicine was offered to all participants. During the 6-month or less time period, the telemedicine group participants were more likely to receive a diabetic retinopathy screening examination when compared with the traditional surveillance group (94.6% versus 43.9%; 95%; confidence interval [CI], 46.6%-54.8%; p<0.001). In addition, in the 6-18 month timeframe, the telemedicine group was also more likely to receive diabetic retinopathy screening exams (53.0% versus 33.2%; 95% CI, 16.5%-23.1%; p<0.001). After 2 years when telemedicine was offered to both groups, there was no difference between the groups in the percentage of diabetic retinopathy screening examinations.

Nonrandomized Studies

In 2004, Murgatroyd reported on the effect of pupillary dilation on screening for diabetic retinopathy, including 398 individuals (794 eyes). Slit lamp examination findings were compared to non-mydriatic fundus images. Three photographic strategies were used: undilated single field, dilated single field, and dilated multiple fields. The photographs were presented randomly to retinal screeners and the screeners were masked to the use of mydriatics. Although mydriasis significantly reduced the proportion of ungradable photographs from 26% to 5% (p<0.001), the sensitivity and specificity were no different for dilated versus undilated pupils. The sensitivity and specificity for detecting retinopathy using undilated single field photography was 77% (95% CI: 71 to 84) and 95 % (95% CI: 93 to 97), respectively. Using dilated single field photography the figures were 81% (95% CI: 76 to 87) and 92% (95% CI: 90 to 94), respectively. Using dilated three field photography the figures were 83% (95% CI 78 to 88) and 93% (95% CI: 91 to 96), respectively.

<u>Digital Imaging Screening Methods</u>

The validity of digital image acquisition and the reliability of digital image evaluation have been established to be acceptable for diagnostic purposes. Key studies comparing the accuracy of high-resolution digital stereoscopic fundus photographs to plain film stereoscopic fundus photographs (the gold standard), are described below.

Nonrandomized Studies

In 2002, Fransen et al. published the results of a case series including 290 diabetic participants. All pts had seven standard field color stereo photos taken on film and captured digitally.[6] Photos and digital images were each graded in a blinded fashion by trained graders. Concordance was 80.1%. The sensitivity of digital photography in detecting threshold events was 98.2% and the specificity was 89.7%. The positive predictive value was 69.5% and the negative predictive value was 99.5% for this sample. The authors concluded that evaluation of film and digital images provided substantially equivalent results.

In 2005, Schiffman et al. published the results from a masked prospective image validation study, including 111 patients with diabetes (222 eyes) who were imaged with both the DigiScope and with seven-field stereo color fundus photography.[7] The authors reported that there was high correlation between the DigiScope and seven-field stereo color fundus photography between "no diabetic retinopathy" and "any diabetic retinopathy" (Kappa statistic 0.97 for the right eye [OD] and 0.94 for the left eye [OS]). This was reflected in the sensitivities (0.99 OD, 1.00 OS) and specificities (1.00 OD, 0.92 OS) of the DigiScope test. The investigators concluded that the DigiScope has excellent agreement, sensitivity, and specificity compared with the "gold-standard" seven-field color stereo photography for identifying patients with any or low levels of diabetic retinopathy that should be referred to ophthalmologist. The authors noted, however, that the DigiScope is not designed as a diabetic retinopathy disease management tool or to replace a comprehensive eye examination.

In 2006, Zimmer-Galler published a case series that included 2,771 individuals with diabetes who had not undergone an eye examination in the past year who were imaged with the DigiScope (EyeTel Imaging, Inc.) in the primary care physician's office.[8] A total of 9% of those screened were referred for a conventional comprehensive ophthalmological examination based on DigiScope findings, while 11% were referred due to unreadable images. The authors concluded that implementation of the DigiScope in the primary care setting was practical as it allowed screening of patients with diabetes who were otherwise not receiving recommended comprehensive eye examinations.

In 2010, Wilson et al. published the results of a large study that evaluated the sensitivity and specificity of wide-field scanning laser ophthalmoscopy (WSLO) for screening of diabetic retinopathy, comparing its performance with digital retinal photography.[9] A total of 380 patients (759 eyes) underwent non-mydriatic WSLO imaging, single- and dual-field mydriatic digital retinal photography, and examination with slit lamp biomicroscopy, the reference standard. Grading of retinopathy was performed in a masked fashion. Screening sensitivities for dilated single-field retinal photography, dual-field retinal photography and WSLO were not significantly different (82.9, 82.9 and 83.6%; $p > 0.2$). Specificities for the three types of imaging were also similar (92.1, 91.1 and 89.5%, respectively; $p > 0.2$). However, the technical failure rate (number of ungradable images) with undilated WSLO was greater than that obtained with dilated 2-field retinal photography (10.8 vs. 5.8%, $p = 0.005$) and with dilated 1-field retinal photography (10.8 vs. 6.3%, $p = 0.02$). Additional limitations of implementing WSLO into telecreening includes lack of studies performed in a mobile setting, low resolution to detect small lesions, and significantly more time spent on image analysis.

In 2013, Ku et al. published a study that assessed the accuracy of grading diabetic retinopathy using a single-field digital fundus photograph compared to clinical grading from a dilated slit-lamp fundus exam, including 360 participants (706 eyes) from remote communities in central Australia.[10] On clinical grading, 163 eyes had diabetic retinopathy, 51 eyes were vision-threatening. The sensitivity and specificity for detecting diabetic retinopathy were 74% (95% CI, 67%-80%) and 92% (95% CI, 90%-94%), respectively. The sensitivity and specificity for detecting vision-threatening diabetic retinopathy were 86% (95% CI, 77%-96%) and 95% (95% CI, 93%-97%), respectively. The authors concluded that even single-field digital fundus photography is a valid screening tool for DR in remote communities and may be used to provide eye care services with acceptable accuracy.

Telemedicine

Since there is sufficient evidence of the relative equivalence of digital imaging to plain film photography, retinal telescreening systems can be a valid alternative to conventional exams by an eye specialist. Recent studies reporting on the validity of telescreening are described below.

Systematic Review

In 2015, Shi et al. conducted a systematic review assessing the diagnostic accuracy of telemedicine in various clinical levels of diabetic retinopathy (DR), including 20 studies (N= 1960 participants).[11] Pooled sensitivity and specificity of telemedicine in detecting the absence of DR were 86% and 95%, respectively. For non-proliferative diabetic retinopathy (NPDR) sensitivities (53-76%) and specificities (89-99%) varied by severity (low-, medium, and high). For proliferative diabetic retinopathy (PDR), sensitivities (75-76%) and specificities (95-97%) varied by risk (low versus high). In addition, subgroup analysis of non-mydriasis versus mydriasis in telemedicine detection of absence of DR indicated that non-mydriasis-based methods were less sensitive than mydriasis (sensitivity of 80% versus 91%, respectively). Limitations of this review included heterogeneity between included studies and three included studies had missing data for several outcomes.

Nonrandomized Studies

In 2014, Raman et al. published the results of a randomized study that compared the diagnostic accuracy of telescreening (using single-field 45-degree fundus photography) to that of traditional ophthalmologist-based diabetic retinopathy screening in rural India.[12] Overall 3522 people with diabetes mellitus underwent ophthalmologist-based screening and 4456 people with diabetes underwent ophthalmologist-led telescreening. A total of 519 people (14.7%) were diagnosed to have diabetic retinopathy in the ophthalmologist-based model, and 853 people (19.1%) in the ophthalmologist-led model $p < 0.0001$). More sight-threatening retinopathies were found in the ophthalmologist-led model than in the ophthalmologist-based model (6.3% vs. 5%). Thus the investigators concluded that telescreening did not underestimate the prevalence of diabetic retinopathy.

Automated Processing of Images

Technology Assessment

In 2016, Tufail et al. published a technology assessment of automated diabetic retinopathy image assessment software on behalf of the U.K.-based National Institute for Health Research (NHS) Diabetic Eye Screening Programme (DESP).[13] The assessment compared three automated retinal image analysis systems (ARIASs); iGradingM, Retmarker and EyeArt; to determine their screening performance, compared to each other and manual grading of images. Currently, only EyeArt is available in the United States. This was an observational retrospective measurement comparison study that evaluated 102,856 images from consecutive diabetic patients who attended a routine annual NHS DESP visit. The sensitivity estimates of the ARIASs were as follows: EyeArt 94.7% (95% CI 94.2% to 95.2%) for any retinopathy, 93.8% (95% CI 92.9% to 94.6%) for referable retinopathy and 99.6% (95% CI 97.0% to 99.9%) for

proliferative retinopathy; and Retmarker 73.0% (95% CI 72.0% to 74.0%) for any retinopathy, 85.0% (95% CI 83.6% to 86.2%) for referable retinopathy and 97.9% (95% CI 94.9 to 99.1%) for proliferative retinopathy. iGradingM classified all images as either 'disease' or 'ungradable', which limited iGradingM analysis. The sensitivity and false-positive rates for EyeArt were not affected by ethnicity, sex or camera type but sensitivity declined with increasing patient age. The screening performance of Retmarker varied with patient's age, ethnicity and camera type.

The assessment reported a number of limitations of some of these ARIASs, including scaling and infrastructure issues due to uploading and processing a large number of images, lacking of blinding of certain manual graders to previous manual grades and automated grading classification, and not assessing referral or rescreening as an outcome. Observational trials evaluating ARIAS effectiveness by way of correct patient referral or rescreen rates are needed to validate this hypothesis. The assessment concluded that Retmarker and EyeArt achieved acceptable sensitivity for referable retinopathy and false-positive rates (compared with human graders as reference standard), but observational trials evaluating ARIAS effectiveness by way of correct patient referral or rescreen rates are needed.

Nonrandomized Studies

In 2013, Abramoff et al. evaluated the Iowa Detection Program (IDP) automated screening system, analyzing digital color photographs from 1748 eyes (874 patients with diabetes) who were at risk for diabetic retinopathy.[14] The IDP sensitivity was 96.8% (95% CI, 94.4%-99.3%) and specificity was 59.4% (95% CI, 55.7%-63.0%). In addition, the PPV was 39.8% (95% CI, 35.2%-44.3%) and the NPV was 98.5% (95% CI, 97.4%-99.7%). In 2016, authors reported on a deep learning algorithm add-on to the IDP algorithm, using the same dataset as in their 2013 study.[15] The authors reported that the sensitivity and the NPV were not statistically different from their earlier published IDP sensitivity, but specificity (59.4% to 87.0%) and PPV (39.8% to 67.4%) had significantly improved. The authors stated that prospective studies were needed in order to determine "real world" performance of the device.
In 2016, Walton et al. conducted a retrospective cohort study designed to determine the efficacy of an automated algorithm in interpreting screening ophthalmoscopic photographs from patients with diabetes compared with a reading center interpretation, including 15 015 patients with type 1 or 2 diabetes.[16] Patients who had undergone a retinal screening examination and nonmydriatic fundus photography via the Intelligent Retinal Imaging System (IRIS) from June 2013 to April 2014 were included. The sensitivity of the IRIS algorithm in detecting sight-threatening diabetic eye disease compared with the reading center interpretation was 66.4% (95% CI, 62.8%-69.9%) with a false-negative rate of 2%. The specificity was 72.8% (95% CI, 72.0%-73.5%). The IRIS algorithm had a positive predictive value of 10.8% (95% CI, 9.6%-11.9%) and a negative predictive value of 97.8% (95% CI, 96.8%-98.6%). The authors noted that although the algorithm shows promise as a screening program, algorithm refinement is needed to achieve better performance and that further studies are needed to assess test performance and patient safety.

In 2018 van der Heijden et al., evaluated the performance of the IDx-DR automated device compared to retinal specialists for the detection of referable diabetic retinopathy (RDR), including analyzable images from 898 participants.[17] In this study, three retinal specialists manually graded the images using the International Clinical Diabetic Retinopathy Severity Scale (ICDR) classification score and the EURODIAB

classification systems. When compared to manual grading using EURODIAB, the IDx-DR device showed a sensitivity for RDR of 91% (95% CI: 0.69–0.98), specificity of 84% (95% CI: 0.81–0.86), positive predictive value of 12% (95% CI: 0.08–0.18) and negative predictive value of 100% (95% CI: 0.99–1.00). When compared to human grading using the ICDR classification, the IDx-DR system showed a sensitivity of 68% (95% CI: 0.56–0.79), specificity of 86% (95% CI: 0.84–0.88), positive predictive value of 30% (95% CI: 0.24–0.38), and negative predictive value of 97% (95% CI: 0.95–0.98). The small number of participants deemed to have RDR and the high number of retinal images that were considered of insufficient quality (approximately 35%) limited this study.

Retinopathy of Prematurity (ROP)

In 2015, Fierson et al. conducted a systematic review evaluating the use of telemedicine for the evaluation of retinopathy of prematurity (ROP), including 11 observational studies.[2] The review stated that the included studies were heterogeneous in design, including differences in:

1. the number of photographs taken (range:1 to 15 per examination)
2. the background of personnel taking photographs (ophthalmologists, ophthalmic photographers, and/or NICU nurses)
3. the image readers (retinal specialists, pediatric ophthalmologists, and/or general ophthalmologists)
4. the diagnostic outcome measures (detection of moderate ROP, detection of severe ROP). Studies reporting of detection of any ROP were excluded from the review.
5. the metrics of accuracy that were reported

Of the eight included studies deemed of good quality, only one study included greater than 108 patients. Quinn et al. evaluated 1257 infants and reported a telemedicine sensitivity of 90.0%, a specificity of 87.0%, a negative predictive value of 97.3%, and a positive predictive value of 62.5%.[18] This study was limited by a high degree of variability in grading results among ophthalmologist examiners, resulting in false positive and false negative cases. In addition, this study was limited to infants at high risk of ROP, and may not be generalizable to all infants eligible for ROP examinations.

Three included studies reported sensitivity below 80% and five studies reported positive predictive values below 70%. The reviewers conceded that differences in methods do not permit direct comparison between studies with respect to sensitivity and specificity.

The review cited a number of limitations of telemedicine for ROP in general, including “difficulty in imaging the retinal periphery, limited image quality in certain circumstances (eyes with poor dilation, media haze, or dark fundus pigmentation), variability in image interpretation even among experienced clinicians, and high implementation cost (hardware, software, and nonphysician personnel)”.

An additional 2015 systematic review by Athikarisamy et al., including three prospective (N=120 individuals) and three retrospective (N=579) studies, cited overall limitations to the body of evidence for telescreening for ROP similar to those listed above, including some studies reporting less than desirable sensitivities, specificities, PPVs and/or NPVs.[19] The reviewers concluded that diagnostic accuracy of telemedicine imaging with digital retinal photography (DRP) must be established in prospective studies

with adequate sample size where DRP is compared against the simultaneously performed gold standard, the binocular indirect ophthalmoscope (BIO) examination.

Two recent large observational studies (n = 100 and 281 infants) were identified after the publication of the systematic reviews above.[20,21] The sole U.S.-based study (Biten et al.), reported that among the 281 infants evaluated, ophthalmoscopy and telemedicine each had similar sensitivity for zone I disease (n=165) (78% [95% CI, 71%-84%] vs 78% [95% CI, 73%-83%]), plus disease (n=50) (74% [95% CI, 61%-87%] vs 79% [95% CI, 72%-86%]), and type 2 ROP (stage 3, zone I, or plus disease; n=251) (86% [95% CI, 80%-92%] vs 79% [95% CI, 75%-83%]). However, ophthalmoscopy was significantly more sensitive in identifying stage 3 disease (n=136)(85% [95% CI, 79%-91%] vs 73% [95% CI, 67%-78%]; p = 0.004). Of note, the 1553 examinations used in the analyses included serial assessments of the same infant and the two eyes of each infant were regarded as separate study participants making these observations not truly independent of each other. However, no statistical adjustment was used to account for this.

Macular Degeneration

In 2018, Kawaguchi et al. conducted a systematic review of the use of tele-ophthalmology compared to in-person care for age-related macular degeneration (AMD), including only two RCTs which examined choroidal neovascularization (CNV) in AMD.[22-24] The included RCTs evaluated tele-ophthalmology in two different patient populations: AMD patients progressing to neovascularization[24] and patients being monitored for AMD recurrence[23]. In addition, one RCT used a self-administered home monitoring device whose data was transmitted to clinical staff via mobile phone, while the other RCT utilized a stand-alone teleophthalmologic site, where imaging studies were acquired and electronically sent over to tertiary hospital-based retina specialists. The reviewers also noted that the duration of exposure and follow-up for outcome measures were significantly different in each study.

A small number of nonrandomized studies were identified that evaluated the use of telescreening for AMD.[25-27] However, these studies assessed images from heterogeneous patient populations in an effort to diagnose and/or classify and/or manage patients with AMD.

CLINICAL PRACTICE GUIDELINES

Diabetic Retinopathy

American Diabetes Association (ADA)

The 2020 ADA Standards of Medical Care in Diabetes recommended the following for screening for diabetic retinopathy:[28]

- "Adults with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 5 years after the onset of diabetes. (Evidence grade: B = well-conducted cohort, case-control, registry studies)

- Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist at the time of the diabetes diagnosis. (Evidence grade: B = well-conducted cohort, case-control, registry studies)
- If there is no evidence of retinopathy for one or more annual eye exams and glycemia is well controlled, then screening every 1–2 years may be considered. If any level of diabetic retinopathy is present, subsequent dilated retinal examinations should be repeated at least annually by an ophthalmologist or optometrist. If retinopathy is progressing or sight-threatening, then examinations will be required more frequently. (Evidence grade: B = well-conducted cohort, case-control, registry studies)
- Women with preexisting type 1 or type 2 diabetes who are planning pregnancy or who are pregnant should be counseled on the risk of development and/or progression of diabetic retinopathy. (Evidence grade: B = well-conducted cohort, case-control, registry studies)
- Eye examinations should occur before pregnancy or in the first trimester in patients with preexisting type 1 or type 2 diabetes, and then patients should be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy. (Evidence grade: B = well-conducted cohort, case-control, registry studies)"

Regarding pregnant women, the ADA states:

- "Women with preexisting type 1 or type 2 diabetes who are planning pregnancy or who have become pregnant should be counseled on the risk of development and/or progression of diabetic retinopathy. Dilated eye examinations should occur ideally before pregnancy or in the first trimester, and then patients should be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy and as recommended by the eye care provider. (Evidence grade: B = well-conducted cohort, case-control, registry studies)
- Eye examinations should occur before pregnancy or in the first trimester in patients with preexisting type 1 or type 2 diabetes, and then patients should be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy. (Evidence grade: B = well-conducted cohort, case-control, registry studies)"

Regarding telescreening, the ADA states:

"Programs that use retinal photography (with remote reading or use of a validated assessment tool) to improve access to diabetic retinopathy screening can be appropriate screening strategies for diabetic retinopathy. Such programs need to provide pathways for timely referral for a comprehensive eye examination when indicated. (Evidence grade: B = well-conducted cohort, case-control, registry studies)"

American Academy of Ophthalmology (AAO)

The 2019 updated Preferred Practice Pattern on Diabetic Retinopathy published the following strong recommendations, based on good quality evidence (high-quality systematic reviews of case-control or cohort studies):[29]

"People with type 1 diabetes should have annual screenings for diabetic retinopathy beginning 5 years after the onset of their disease, whereas those with type 2 diabetes should have a prompt screening at the time of diagnosis and at least yearly screenings thereafter. Women with diabetes who become pregnant should be examined early and closely in the course of the pregnancy because the disease can progress rapidly. However, an eye examination is not required when gestational diabetes occurs during pregnancy. Patients with diabetes have an accelerated rate of diabetic retinopathy progression during puberty and should be followed more closely."

Regarding telescreening, the AAO states:

> "Diabetic retinopathy may be asymptomatic for years, even at an advanced stage, so screening, using new technologies such as telemedicine, is essential to identify, monitor, and guide the treatment of disease.
> 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, retinal imagining screening programs may help increase the chances that at-risk individuals will be promptly referred for more detailed evaluation and management."

Retinopathy of Prematurity

American Academy of Pediatrics (AAP) / American Academy of Ophthalmology (AAO) / American Association for Pediatric Ophthalmology and Strabismus (AAPOS) / American Association of Certified Orthoptists (AACO)

In 2018, the AAP updated their clinical practice guidelines on the screening of premature infants for retinopathy of prematurity (ROP),[30] recommending the following:

> "Retinal screening examinations should be performed after pupillary dilation by using binocular indirect ophthalmoscopy with a lid speculum and scleral depression (as needed) to detect ROP. In recent literature, authors suggest that a carefully organized program of remotely interpreted wide-angle fundus camera ROP screening may initially be used in place of binocular indirect ophthalmoscope examinations up to the point at which treatment of ROP is believed to be indicated; at this point, indirect ophthalmoscopy is required."

However, the guideline states that "the use of digital photographic retinal images that are captured and sent for remote interpretation is a developing alternative approach to ophthalmoscopic ROP screening; however, few outcome comparisons between large-scale operational digital-imaging systems with remote interpretation versus binocular indirect ophthalmoscopy have been published."

POLICY SUMMARY

Diabetic Retinopathy

There is enough research to show that overall health outcomes may be comparable between retinal photography with manual image interpretation by an ophthalmologist or retinal specialist (telescreening) and in-person retinal examinations for or individuals who have diabetes mellitus without a diagnosis of diabetic retinopathy. Clinical practice guidelines based on research recommend retinal photography (with remote reading or use of a validated assessment tool) to help screening strategies for diabetic retinopathy. Therefore, retinal photography with manual image interpretation by an ophthalmologist or retinal specialist may be considered medically necessary and covered when policy criteria are met.

For those who have a diagnosis of diabetic retinopathy, there is enough research to show that overall health outcomes are not improved with the use of retinal photography for any reason, including but not limited to monitoring and treatment selection. Therefore, retinal photography with manual image interpretation by an ophthalmologist or retinal specialist (telescreening) is considered not medically necessary and not covered for those who already have a diagnosis of diabetic retinopathy.

Other Conditions

There is not enough research to know if retinal photography with manual image interpretation by an ophthalmologist or retinal specialist (telescreening) leads to improved overall health outcomes in other conditions of the eye including retinopathy of prematurity and age-related macular degeneration, or in those who are not currently diagnosed with diabetes mellitus. That does not mean it doesn't work. More research is needed to know for sure. No clinical practice guidelines based on research have been identified that recommend the use of telescreening other patient populations other than in those with diabetes mellitus as described in the section above. Therefore, retinal photography with manual image interpretation by an ophthalmologist or retinal specialist (telescreening) is considered investigational and not covered for other conditions of the eye.

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

U.S. Food & Drug Administration (FDA)

In April of 2018, the FDA approved the use of the IDx-DR as a retinal diagnostic software device under the De Novo premarket review pathway, with the following indications for use:[31]

> "for use by health care providers to automatically detect more than mild diabetic retinopathy (mtmDR) in adults diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy. IDx-DR is indicated for use with the Topcon NW400."

According to the FDA, "IDx-DR was granted Breakthrough Device designation, meaning the FDA provided intensive interaction and guidance to the company on efficient device development, to expedite evidence generation and the agency's review of the device."

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

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