Objective: To evaluate whether single-field fundus photography can be used as a screening tool to identify diabetic retinopathy for referral for further ophthalmic care.

Methods: A MEDLINE search of the peer-reviewed literature was conducted in June 2001 for the years 1968 to 2001 and updated in September 2003, yielding 145 articles. The search was limited to articles published in English. The Cochrane Library of clinical trials was also investigated. The authors reviewed the abstracts of these articles and selected 63 of possible clinical relevance for review by the panel. Of these 63 articles, the panel selected 32 for the panel methodologist to review and rate according to the strength of evidence.

Results: Three of the 32 articles reviewed were classified as level I evidence, and 4 were classified as level II evidence. Evidence from level I studies demonstrates that as a tool to detect vision-threatening retinopathy, single-field fundus photography interpreted by trained readers has sensitivity ranging from 61% to 90% and specificity ranging from 85% to 97% when compared with the gold standard reference of stereophotographs of 7 standard fields. When compared with dilated ophthalmoscopy by an ophthalmologist, single-field fundus photography has sensitivity ranging from 38% to 100% and specificity ranging from 75% to 100%.

Conclusions: Single-field fundus photography is not a substitute for a comprehensive ophthalmic examination, but there is level I evidence that it can serve as a screening tool for diabetic retinopathy to identify patients with retinopathy for referral for ophthalmic evaluation and management. The advantages of single-field fundus photography interpreted by trained readers are ease of use (only one photograph is required), convenience, and ability to detect retinopathy. Further studies will be required to assess the implementation of single-field photography–based programs to confirm the clinical and cost-effectiveness of these techniques in improving population visual outcomes. Future research also should include establishing standardized protocols and satisfactory performance standards for diabetic retinopathy screening programs. Ophthalmology 2004;111:1055–1062 © 2004 by the American Academy of Ophthalmology.
results in appropriate photocoagulation.\textsuperscript{13–16} In conjunction with other organizations such as the American Diabetes Association, the American Academy of Ophthalmology has established examination guidelines for individuals with diabetes mellitus that take into consideration the type of diabetes, severity of retinopathy, and metabolic status.\textsuperscript{12,17,18} Unfortunately, despite the consensus that examinations for the presence of diabetic retinopathy can reduce the risk of blindness, a large number of individuals with diabetes do not receive such examinations.\textsuperscript{19–23} As a result, diabetic retinopathy remains a leading cause of visual impairment and blindness in the working population.\textsuperscript{24,25}

A variety of techniques can be used to detect and classify diabetic retinopathy, including direct and indirect ophthalmoscopy, stereoscopic color film fundus photography, fluorescein angiography, and mydriatic or nonmydriatic digital color or monochromatic photography. Ophthalmoscopy is the most commonly used technique to screen for diabetic retinopathy. However, undilated ophthalmoscopy, especially that done by nonophthalmologists, has poor sensitivity relative to 7-field stereoscopic color photography.\textsuperscript{26} Under typical clinical conditions, direct ophthalmoscopy done by nonophthalmologists has a sensitivity of approximately 50\% for the detection of proliferative retinopathy.\textsuperscript{27}

The gold standard for the detection and classification of diabetic retinopathy is stereoscopic color fundus photographs in 7 standard fields, as defined by the Early Treatment Diabetic Retinopathy Study (ETDRS) group.\textsuperscript{28} Although this technique is accurate and reproducible, it is labor intensive and requires skilled photographers; skilled photograph readers; and sophisticated photography equipment, film processing, and archiving. The turnaround time from acquisition of the data to interpretation can take weeks in clinical trials. Finally, from the patient’s perspective, it can be time consuming and uncomfortable. In short, 7-field stereoscopic fundus photography is not an ideal screening technique, but it can serve as the standard with which to compare other screening technologies.

Single-field fundus photography interpreted by trained readers is used to detect retinopathy that requires referral to an ophthalmologist; it is not used to comprehensively grade the level of retinopathy in the eye. One advantage of single-field fundus photography is the convenience to patients who do not have vision-threatening retinopathy. It requires less time and less light (only one flash is required), and unlike photography of multiple fields, it may not require mydriasis in the majority of patients. Finally, the use of single-field photography may be a cost-effective way to use ophthalmic services because only patients with vision-threatening retinopathy are referred to an ophthalmologist.

**Description of the Technique**

Single-field fundus photography requires a fundus camera such as the Canon Cr6-45NM (Canon USA, Lake Success, NY) or the Topcon TRC-NW6S (Topcon America Corp., Paramus, NJ). The photography can be performed with and without mydriasis, and can be film based (prints or slides) or digital. The photographs are interpreted by trained readers or forwarded to a reading center for interpretation and grading.

**Resource Requirements**

Photoscreening for diabetic retinopathy requires digital or nondigital fundus photographic systems, which may be mydriatic or nonmydriatic; software for image analysis; photographic personnel trained in fundus photography; and trained fundus photograph readers.

**Question for Assessment**

The focus of this assessment is to address the following question:

- Is single-field fundus photography an effective screening tool for identifying patients with diabetic retinopathy who need to be referred for further ophthalmic care?

**Description of Evidence**

The MEDLINE search of the peer-reviewed literature was conducted in June 2001 for the years 1968 to 2001 and updated in September 2003. The search was limited to articles published in English. The Cochrane Library of clinical trials was also investigated. The search strategy used the MeSH terms *diabetic retinopathy/diagnosis* and the text words *retinal, photography, single, field, and fundus*. The searches yielded 145 articles.

The authors reviewed the abstracts of the 145 articles and selected 63 of possible clinical relevance for review by the panel. The panel selected 32 of these articles of sufficient clinical relevance for review by the panel methodologist. Using a rating scale based on that developed by the British Centre for Evidence-Based Medicine\textsuperscript{29} for reviewing diagnostic studies, the panel methodologist assigned one of the following ratings to each of the selected articles based on her review of the study design, methods, and results.

- A level I rating was assigned to studies reporting an independent, masked comparison of an appropriate spectrum of consecutive patients, all of whom have undergone both the diagnostic test and the reference standard test. An appropriate spectrum implies that the cohort of study patients includes a good mix of mild and severe, treated and untreated disease, plus individuals with different but commonly confused disorders.
- A level II rating was assigned to any independent, masked, or objective comparison, or to a study performed in a set of nonconsecutive patients or confined to a narrow spectrum of study individuals (or both), all of whom have undergone both the diagnostic test and the reference standard test. This rating also applies to an independent, masked comparison of an appropriate spectrum of patients in which the reference standard test was not applied to all patients.
A level III rating was applied to studies in which the reference standard test was unobjective, was applied without masking, or was not conducted independently from the diagnostic test. This rating was also used if positive and negative tests were verified using separate reference standards, or if the study was performed in an inappropriate spectrum of patients (e.g., if patients known to have the target disorder were compared with patients known to have another condition clearly different from the target disorder).

Of the 32 articles reviewed by the methodologist, 14 involved multiple-field rather than single-field fundus photography, and 1 did not evaluate photoscreening. An additional 2 articles did not provide information concerning the number of photographic fields. It is also important to note that ungradable photographs were excluded from analyses in some studies. Eleven studies lacked any reference standard, and an additional 11 studies used a suboptimal reference standard. Because ophthalmoscopy is the most widely performed technique in clinical practice, studies comparing single-field fundus photography with ophthalmoscopy also were included. The level of retinopathy detected that required referral to an ophthalmologist varied in the studies.

Published Results

Using stereoscopic color fundus photographs in 7 standard fields as defined by the ETDRS group as the gold standard for comparison, 3 studies (level I evidence) evaluated the effectiveness of single-field fundus photography as a screening tool for diabetic retinopathy (Table 1).

In the largest of these studies, Pugh et al screened 352 patients using 4 screening methods that were compared with a reference standard of stereoscopic 30° retinal photographs of 7 standard fields read in a standardized fashion by trained readers at the University of Wisconsin Fundus Photographic Reading Center. The 4 screening methods were an examination by an ophthalmologist through dilated pupils using direct and indirect ophthalmoscopy, an examination by a physician's assistant through dilated pupils using direct ophthalmoscopy, a single 45° retinal photograph without pharmacological dilation, and a set of 3 dilated 45° retinal photographs.

In this study, patients received dilated ophthalmoscopy done by an ophthalmologist. They also received a single-field nonmydriatic 45° retinal photograph using color slide film and 7 standard fields as the reference standard. The sensitivity and specificity were, respectively, 33% and 99% for ophthalmoscopy and 61% and 85% for nonmydriatic single-field photographs. Thus, the photographs were demonstrated to be superior to clinical examination (level I evidence). However, 12% of the patients without pharmacologic dilation had ungradable photographs, usually due to cataract. Only 54% of nonmydriatic photographs were graded as good or fair, compared with 65% of mydriatic photographs. The authors concluded that mydriasis was usually necessary in older patients.

In another study, single-field dilated 45° Polaroid (Polaroid Corp., Waltham, MA) fundus photographs and single-field dilated 45° digital images were compared with a reference standard of 7 overlapping stereoscopic 30°-field photographs graded by a central reading center according to the ETDRS scale. An additional image could be obtained from a 20° field once features of concern had been identified. The photographs and digital images demonstrated a sensitivity of 72% and 74%, respectively, for detecting any retinopathy, and a sensitivity of 90% and 85% for detecting sight-threatening retinopathy.

In a third study, dilated ophthalmoscopy by an ophthalmologist and nonstereoscopic 45° single-field nonmydriatic monochromatic digital photography (SNMDP) was compared with 7-standard field photography. Lin et al reported a screening technique utilizing SNMDP with remote interpretation. In a prospective comparative observational case series, 197 patients with type 1 or type 2 diabetes mellitus were sequentially examined by SNMDP, dilated ophthalmoscopy done by an ophthalmologist, and the reference standard, 7-standard field photography. There was excellent agreement (κ = 0.97) between the SNMDP and 7-standard field photographs for the degree of diabetic retinopathy utilizing a referral (ETDRS level ≥ 35) or no referral (ETDRS level = 20) dichotomization (level I evidence). This dichotomization was also used for specificity and sensitivity analysis. The sensitivity of the SNMDP compared with 7-standard field photographs was 78%, and the specificity was 86%. Single-field digital monochromatic nonmydriatic photography was superior to dilated ophthalmoscopy when compared with 7-standard field photographs. It demonstrated 100% sensitivity and 71% specificity when compared with ophthalmoscopy. No patient identified by ophthalmoscopy for referral was missed by the SNMDP. Single-field digital monochromatic nonmydriatic photography demonstrated 25% overcalls (a higher retinopathy level diagnosed by the tested modality than the standard) for referral, compared with ophthalmoscopy. However, when adjudicated against 7-standard field photographs, this difference was due to the reduced sensitivity of ophthalmoscopy. With a sensitivity of 78%, SNMDP did miss some patients who required a referral based on 7-standard field photographs. The lack of stereopsis also diminishes the ability to diagnose clinically significant macular edema in the absence of lipid, hemorrhage, or microaneurysms. This study also utilized a skilled remote reading center. The authors emphasize that SDMNP is superior to dilated ophthalmoscopy.

Four additional studies (level II evidence) evaluated the effectiveness of single-fundus photography using ophthalmologic examination as the reference standard. In the first of these studies, single-field nonmydriatic 45° fundus photographs were found to have sensitivity and specificity of 96% and 98%, respectively, for detecting any diabetic retinopathy; 100% and 96% for detecting diabetic maculopathy; and 82% and 100% for detecting proliferative diabetic retinopathy. However, ungradable photographs were excluded from analysis. Another study using single-field mydriatic 60° retinal photography found sensitivity and specificity of 93% and 89%, respectively, for detecting
<table>
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<tr>
<th>Study</th>
<th>Level of Evidence</th>
<th>N</th>
<th>Reference Standard</th>
<th>Referral Threshold</th>
<th>Results</th>
<th>Comments</th>
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<tr>
<td>Pugh et al (1993)*</td>
<td>I</td>
<td>352</td>
<td>7 standard fields, as per ETDRS</td>
<td>Moderate to severe nonproliferative disease and any proliferative disease</td>
<td>Dilated direct and indirect ophthalmoscopy performed by ophthalmologist: sensitivity, 33% specificity, 99% positive likelihood ratio, 72</td>
<td>42 of 50 ungradable photographs became gradable after dilation.</td>
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<td>Single-field 45° nonmydriatic retinal photograph (color slide film): sensitivity, 61% specificity, 85% positive likelihood ratio, 4.1</td>
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<td>3 dilated 45° retinal photographs (color slide film): sensitivity, 81% specificity, 97% positive likelihood ratio, 24</td>
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<td>42 of 50 ungradable photographs became gradable after dilation.</td>
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<td>Taylor et al (1999)†</td>
<td>I</td>
<td>118</td>
<td>7 standard fields, as per ETDRS</td>
<td>Sight-threatening diabetic retinopathy</td>
<td>Single-field dilated 45° Polaroid fundus photograph: sensitivity, 72% for detecting any retinopathy specificity, 88% for detecting any retinopathy sensitivity, 90% for detecting sight-threatening retinopathy specificity, 97% for detecting sight-threatening retinopathy</td>
<td>For digital images, an additional image could be obtained from a 20° field once features of concern had been identified.</td>
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<td>Single-field dilated 45° digital images: sensitivity, 74% for detecting any retinopathy specificity, 88% for detecting any retinopathy sensitivity, 85% for detecting sight-threatening retinopathy specificity, 97% for detecting sight-threatening retinopathy</td>
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<td>Lin et al (2002)‡</td>
<td>I</td>
<td>197</td>
<td>7 standard fields, as per ETDRS</td>
<td>ETDRS level ≥ 35</td>
<td>Single-field nonmydriatic 45° monochromatic digital images: sensitivity, 78% for detecting retinopathy at ETDRS level ≥ 35 specificity, 86% for detecting retinopathy at ETDRS level ≥ 35</td>
<td></td>
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<td>Williams et al (1986)§</td>
<td>II</td>
<td>62</td>
<td>Ophthalmologist-performed dilated ophthalmoscopy</td>
<td>Not reported</td>
<td>Single-field nonmydriatic 45° fundus photographs (color Polaroid or color slide film): sensitivity, 96% for detecting any retinopathy specificity, 98% for detecting any retinopathy sensitivity, 100% for detecting diabetic maculopathy specificity, 96% for detecting diabetic maculopathy sensitivity, 82% for detecting proliferative diabetic retinopathy specificity, 100% for detecting proliferative diabetic retinopathy</td>
<td>Ungradable photographs were excluded from analysis.</td>
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<td>Joannou et al (1996)†</td>
<td>II</td>
<td>24</td>
<td>Ophthalmologist-performed dilated ophthalmoscopy</td>
<td>Severe background retinopathy, preproliferative and proliferative retinopathy, maculopathy</td>
<td>Single-field mydriatic 60° retinal photography (color slide film): sensitivity, 93% for detecting any retinopathy specificity, 89% for detecting any retinopathy sensitivity, 100% for detecting severe retinopathy specificity, 75% for detecting severe retinopathy</td>
<td>Compared to a 60° field, one 45° field missed 31% of cases of retinopathy and two 45° fields missed 11% of cases of retinopathy. (Continued)</td>
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any retinopathy, and 100% and 75% for detecting severe retinopathy. Compared with a 60° field, one 45° field missed 31% of cases of retinopathy and two 45° fields missed 11% of retinopathy cases. In another study, mydriatic 45° digital fundus photographs were found to have sensitivity, specificity, and a positive predictive value of 84.4%, 79.2%, and 73.0%, respectively, for detecting any retinopathy; 91.2%, 82.2%, and 67.8% for detecting non-proliferative diabetic retinopathy; and 93.3%, 96.8%, and 70.0% for detecting proliferative diabetic retinopathy or clinically significant macular edema. The last study described in Table 1 reported low sensitivity (38%) but acceptable specificity (95%) for detecting any retinopathy. Although most patients can be photographed without mydriasis, lens opacities in older patients can result in photographs that are ungradable. In the studies above, Pugh et al. found that 42 of 50 ungradable photographs became gradable after dilation. Taylor et al. and Joannou et al. evaluated only dilated single-field photography. Based on these studies, eyes with ungradable pictures should have dilation and repeat photography. Eyes with photographs that remain ungradable after dilation would be considered screening positives and require referral for ophthalmic evaluation.

Multiple-field fundus photography systems offer advantages of greater coverage of the fundus and stereoscopy and have reported improved sensitivity compared with single-field fundus photography. Multiple-field systems may be more costly in terms of time taken to obtain and interpret the images and in requiring a skilled ophthalmic photographer.

Conclusions

There is level I evidence that single-field fundus photography with interpretation by trained readers can serve as a screening tool to identify patients with diabetic retinopathy for referral for ophthalmic evaluation and management, but it is not a substitute for a comprehensive ophthalmic exam.

### Table 1. (Continued.)

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<tr>
<th>Study</th>
<th>Level of Evidence</th>
<th>N</th>
<th>Reference Standard</th>
<th>Referral Threshold</th>
<th>Results</th>
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<tr>
<td>Herbert et al (2003)*</td>
<td>II</td>
<td>145</td>
<td>Ophthalmologist-performed dilated ophthalmoscopy</td>
<td>Not reported</td>
<td>Single-field 45° digital retinal photography: sensitivity, 38.2% for detecting any retinopathy; specificity, 95.5% for detecting any retinopathy</td>
<td>If images obtained without mydriasis were deemed inadequate, photography was repeated after mydriasis. Four percent of images were excluded from the study because they were blurred despite mydriasis.</td>
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ETDRS = Early Treatment of Diabetic Retinopathy Study.
The likelihood ratio is the likelihood that a given test result would be expected in a patient with the target disorder versus the likelihood that the same result would be expected in a patient without that disorder.


A comprehensive eye examination is an opportunity to diagnose other treatable eye diseases such as cataract or glaucoma. In addition, ophthalmologists may educate patients about the importance of all aspects of diabetes care, such as blood glucose and blood pressure control. The advantages of single-field fundus photography interpreted by trained readers are ease of use (only one photograph is required), convenience, and ability to detect retinopathy. The disadvantage is that reported sensitivity values are less than ideal when compared with 7–standard field photography. When compared with ophthalmoscopy, however, single-field fundus photography has the potential to improve the quality of the evaluation and the numbers of patients evaluated. The use of nonmydriatic fundus photography systems represents a compromise. Although it is apparent that mydriasis improves image quality and sensitivity, particularly in older patients, it is uncertain whether this is outweighed by the disadvantage of dilation related to patient compliance. In other words, the diminished sensitivity of a nonmydriatic photograph may be acceptable if more patients complete the process.

It is unknown whether or not patients are willing to undergo such evaluation on a yearly basis, as recommended by current guidelines. Whether any of the systems discussed can accommodate the tens of thousands of photographs necessary to appreciably improve detection rates for diabetic retinopathy in the general population is unknown. Caution should be exercised in strictly applying the test characteristics from the reported studies; most tests perform less well in the real world setting. Further studies will be required to assess the implementation of programs that are based on single-field fundus photography in a real clinical setting to confirm the clinical effectiveness and cost-effectiveness of these techniques in improving population visual outcomes. Future research also should include establishing standardized protocols and satisfactory performance standards for diabetic retinopathy screening programs.

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