



Complete Summary

GUIDELINE TITLE

Retinopathy in diabetes.

BIBLIOGRAPHIC SOURCE(S)

Fong DS, Aiello L, Gardner TW, King GL, Blankenship G, Cavallerano JD, Ferris FL 3rd, Klein R. Retinopathy in diabetes. Diabetes Care 2004 Jan; 27(Suppl 1):S84-7. [10 references] [PubMed](#)

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SCOPE

DISEASE/CONDITION(S)

- Diabetes mellitus, type 1
- Diabetes mellitus, type 2
- Diabetic retinopathy (i.e., nonproliferative diabetic retinopathy; proliferative diabetic retinopathy)

GUIDELINE CATEGORY

Management
Prevention
Screening
Treatment

CLINICAL SPECIALTY

Endocrinology
Family Practice
Internal Medicine

Ophthalmology
Optometry
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Optometrists
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To prevent, reverse, or delay the visual loss associated with the disease process of diabetic retinopathy

TARGET POPULATION

- Individuals 10 years of age or older with type 1 diabetes
- Individuals with type 2 diabetes
- Pregnant women with pre-existing diabetes

INTERVENTIONS AND PRACTICES CONSIDERED

1. Screening for diabetic retinopathy, including dilated and comprehensive eye examinations
2. Intensive diabetes management (i.e., glycemic and blood pressure control)
3. Aspirin treatment (considered but not recommended)
4. Laser photocoagulation therapy: scatter (panretinal) laser photocoagulation surgery and focal laser photocoagulation surgery
5. Vitrectomy
6. Fluorescein angiography
7. Dilated indirect ophthalmoscopy coupled with biomicroscopy and seven-standard field stereoscopic 30 degree fundus photography
8. Film and digital nonmydriatic images (considered but not recommended)
9. Visual rehabilitation

MAJOR OUTCOMES CONSIDERED

- Incidence of nonproliferative diabetic retinopathy and proliferative diabetic retinopathy
- Visual loss associated with diabetes
- Morbidity associated with diabetic retinopathy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendations have been assigned ratings of A, B, or C, depending on the quality of evidence (see table below). Expert opinion (E) is a separate category for recommendations in which there is as yet no evidence from clinical trials, in which clinical trials may be impractical, or in which there is conflicting evidence. Recommendations with an "A" rating are based on large, well-designed clinical trials or well done meta-analyses. Generally, these recommendations have the best chance of improving outcomes when applied to the population to which they are appropriate. Recommendations with lower levels of evidence may be equally important but are not as well supported.

American Diabetes Association's evidence grading system for clinical practice recommendations:

A

Clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered, including:

- Evidence from a well-conducted multicenter trial
- Evidence from a meta-analysis that incorporated quality ratings in the analysis
- Compelling non-experimental evidence, i.e., "all or none" rule developed by the Center for Evidence Based Medicine at Oxford*

Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including:

- Evidence from a well-conducted trial at one or more institutions
- Evidence from a meta-analysis that incorporated quality ratings in the analysis

*Either all patients died before therapy and at least some survived with therapy, or some patients died without therapy and none died with therapy. Example: use of insulin in the treatment of diabetic ketoacidosis.

B

Supportive evidence from well-conducted cohort studies, including:

- Evidence from a well-conducted prospective cohort study or registry
- Evidence from a well-conducted meta-analysis of cohort studies

Supportive evidence from a well-conducted case-control study

C

Supportive evidence from poorly controlled or uncontrolled studies:

- Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results
- Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls)
- Evidence from case series or case reports

Conflicting evidence with the weight of evidence supporting the recommendation

E

Expert consensus or clinical experience

COST ANALYSIS

Cost analyses have suggested that annual examination for some patients with type 2 diabetes may not be cost-effective and that consideration should be given

to increasing the screening interval. However, these analyses may not have completely considered all the factors:

1. The analyses assumed that legal blindness was the only level of visual loss with economic consequences, but other visual function outcomes, such as visual acuity worse than 20/40, are clinically important, occur much more frequently, and have economic consequences.
2. The analyses used nonproliferative diabetic retinopathy progression figures from newly diagnosed patients with diabetes. Although rates of progression are stratified by glycosylated hemoglobin (HbA1c) levels, newly diagnosed patients are different from those with the same level of retinopathy and have a longer diabetes duration. While rates of progression correlate with HbA1c levels, newly diagnosed patients with the same level of retinopathy progress differently than those with longer duration of disease. A person with a longer duration of diabetes is more likely to progress during the next year of observation.
3. The rates of progression were derived from diabetic individuals of northern European extraction and are not applicable to other ethnic and racial groups who have higher rates of retinopathy progression, such as African- and Hispanic-Americans.

In determining the examination interval for an individual patient, the eye care provider should also consider the implications of less frequent eye examinations. Older people are at higher risk for cataract, glaucoma, age-related macular degeneration, and other potentially blinding disorders. Detection of these problems adds value to the examination but is rarely considered in analyses of screening interval. Patient education also occurs during examinations. Patients know the importance of controlling their blood glucose, blood pressure, and serum lipids, and this importance can be reinforced at a time when patients are particularly aware of the implications of vision loss. In addition, long intervals between follow-up visits may lead to difficulties in maintaining contact with patients. Patients may be unlikely to remember that they need an eye examination after several years have passed.

After considering these issues, and in the absence of empirical data showing otherwise, persons with diabetes should have an annual eye examination.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The paper was reviewed and approved by the American Diabetes Association's Professional Practice Committee and Executive Committee of the Board of Directors.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Treatment modalities exist that can prevent or delay the onset of diabetic retinopathy, as well as prevent loss of vision, in a large proportion of patients with diabetes. The Diabetes Control and Complications Trial and the United Kingdom Prospective Diabetes Study established that glycemic and blood pressure control can prevent and delay the progression of diabetic retinopathy in patients with diabetes. Timely laser photocoagulation therapy can also prevent loss of vision in a large proportion of patients with severe nonproliferative diabetic retinopathy and proliferative diabetic retinopathy and/or macular edema. Because a significant number of patients with vision-threatening disease may not have symptoms, ongoing evaluation for retinopathy is a valuable and required strategy.

The recommendations for initial and subsequent ophthalmologic evaluation of patients with diabetes are stated below. The evidence grading system (A through C, E) is defined at the end of the "Major Recommendations" field.

- Patients with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 3 to 5 years after the onset of diabetes. In general, evaluation for diabetic eye disease is not necessary before 10 years of age. However, some evidence suggests that the prepubertal duration of diabetes may be important in the development of microvascular complications; therefore, clinical judgment should be used when applying these recommendations to individual patients. (B)
- Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist shortly after diabetes diagnosis. (B)
- Subsequent examinations for both type 1 and type 2 diabetic patients should be repeated annually by an ophthalmologist or optometrist who is knowledgeable and experienced in diagnosing the presence of diabetic retinopathy and is aware of its management. Examinations will be required more frequently if retinopathy is progressing. This follow-up interval is recommended recognizing that there are limited data addressing this issue. (B)
- When planning pregnancy, women with preexisting diabetes should have a comprehensive eye examination and should be counseled on the risk of development and/or progression of diabetic retinopathy. Women with diabetes who become pregnant should have a comprehensive eye examination in the 1st trimester and close follow-up throughout pregnancy. This guideline does not apply to women who develop gestational diabetes because such individuals are not at increased risk for diabetic retinopathy. (B)
- Patients with any level of macular edema, severe nonproliferative diabetic retinopathy, or any proliferative diabetic retinopathy require the prompt care of an ophthalmologist who is knowledgeable and experienced in the management and treatment of diabetic retinopathy. Referral to an ophthalmologist should not be delayed until proliferative diabetic retinopathy has developed in patients who are known to have severe nonproliferative or more advanced retinopathy. Early referral to an ophthalmologist is particularly important for patients with type 2 diabetes and severe nonproliferative diabetic retinopathy, since laser treatment at this stage is associated with a 50% reduction in the risk of severe visual loss and vitrectomy. (E)

- Patients who experience vision loss from diabetes should be encouraged to pursue visual rehabilitation with an ophthalmologist or optometrist who is trained or experienced in low-vision care. (E)

Definitions

American Diabetes Association's evidence grading system for clinical practice recommendations:

A

Clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered, including:

- Evidence from a well-conducted multicenter trial
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- Compelling non-experimental evidence, i.e., "all or none" rule developed by the Center for Evidence Based Medicine at Oxford*

Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including:

- Evidence from a well-conducted trial at one or more institutions
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- Evidence from case series or case reports

Conflicting evidence with the weight of evidence supporting the recommendation

E

Expert consensus or clinical experience

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field). The recommendations were based on the evidence reviewed in the companion document "Diabetic retinopathy" (Technical Review). In that publication, the efficacy of various treatments was primarily defined by four national multicenter randomized clinical trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Glycemic Control

- The Diabetes Control and Complications Trial (DCCT) demonstrated that intensive therapy reduced the mean risk of retinopathy by 76% (95% confidence interval [CI] 62-85). In the secondary intervention cohort, the intensive group had a higher cumulative incidence of sustained progression during the first year. However, by 36 months, the intensive group had lower risks of progression. Intensive therapy reduced the risk of progression by 54% (95% CI 39-66).
- The protective effect of glycemic control has also been confirmed for patients with type 2 diabetes. The U.K. Prospective Diabetes Study (UKPDS) demonstrated that improved blood glucose control reduced the risk of developing retinopathy and nephropathy and possibly reduces neuropathy. The overall rate of microvascular complications was decreased by 25% in patients receiving intensive therapy versus conventional therapy.

Blood Pressure Control

The UKPDS also investigated the influence of tight blood pressure control. With a median follow-up of 8.4 years, patients assigned to tight control had a 34% reduction in progression of retinopathy and a 47% reduced risk of deterioration in visual acuity of three lines in association with a 10/5 mmHg reduction in blood pressure. In addition, there were reductions in deaths related to diabetes and strokes.

Laser Photocoagulation

- The Diabetic Retinopathy Study (DRS) investigated whether scatter (panretinal) photocoagulation, compared with indefinite deferral, could reduce the risk of vision loss from proliferative diabetic retinopathy (PDR). After only 2 years, photocoagulation was shown to significantly reduce severe visual loss (i.e., best acuity of 5/200 or worse). The benefit persisted through the entire duration of follow-up and was greatest among patients whose eyes had high-risk characteristics (HRCs) (i.e., disc neovascularization or vitreous hemorrhage with any retinal neovascularization). The treatment effect was much smaller for eyes that did not have HRCs.
- To determine the timing of photocoagulation, the Early Treatment Diabetic Retinopathy Study (ETDRS) examined the effect of treating eyes with mild nonproliferative diabetic retinopathy (NPDR) to early PDR. The rates of visual loss were low with either treatment applied early or delayed until development of HRCs. Because of this low rate and the risk of complications, the report suggested that scatter photocoagulation be deferred in eyes with mild-to-moderate NPDR. The ETDRS also demonstrated the effectiveness of focal photocoagulation in eyes with macular edema. In patients with clinically significant macular edema, 24% of untreated eyes, compared with 12% of treated eyes, developed doubling of the visual angle.

POTENTIAL HARMS

- Visual and functional side effects of therapy provided to individuals at risk of visual loss
- Scatter photocoagulation can exacerbate macular edema
- Vitreous surgery has the potential for serious complications, including profound visual loss and permanent pain and blindness
- Risks associated with fluorescein angiography include death and severe medical sequelae

Subgroups Most Likely to Experience These Harms

- Although detrimental effects of fluorescein dye on the fetus have not been documented, fluorescein does cross the placenta into the fetal circulation. Fluorescein angiography during pregnancy is therefore generally not indicated.
- Patients with high-risk proliferative diabetic retinopathy where clinically significant macular edema is also present

CONTRAINDICATIONS

CONTRAINDICATIONS

Fluorescein angiography is usually contraindicated in patients with known allergy to fluorescein dye.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline does not apply to women who develop gestational diabetes because such individuals are not at increased risk for diabetic retinopathy.
- Some evidence suggests that prepubertal duration of diabetes may be important in the development of microvascular complications; therefore, clinical judgment should be used when applying these recommendations to individual patients.
- Evidence is only one component of decision-making. Clinicians care for patients, not populations; guidelines must always be interpreted with the needs of the individual patient in mind. Individual circumstances such as comorbid and coexisting diseases, age, education, disability, and above all, patient's values and preferences must also be considered and may lead to different treatment targets and strategies. Also, conventional evidence hierarchies such as the one adapted by the American Diabetes Association may miss some nuances that are important in diabetes care.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Fong DS, Aiello L, Gardner TW, King GL, Blankenship G, Cavallerano JD, Ferris FL 3rd, Klein R. Retinopathy in diabetes. Diabetes Care 2004 Jan;27(Suppl 1):S84-7. [10 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1997 Nov (revised 1998; republished 2004 Jan)

GUIDELINE DEVELOPER(S)

American Diabetes Association - Professional Association

SOURCE(S) OF FUNDING

The American Diabetes Association (ADA) received an unrestricted educational grant from LifeScan, Inc., a Johnson and Johnson Company, to support publication of the 2004 Diabetes Care Supplement.

GUIDELINE COMMITTEE

Professional Practice Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors of Position Statement, Initial Draft: Donald S. Fong, MD, MPH; Lloyd Aiello, MD, PhD; Thomas W. Gardner, MD; George L. King, MD; George Blankenship, MD; Jerry D. Cavallerano, OD, PhD; Frederick L. Ferris, III, MD; Ronald Klein, MD, MPH

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

The guideline was originally approved in November 1997; the most recent review/revision was completed in 1998.

American Diabetes Association (ADA) position statements are reissued annually.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [American Diabetes Association \(ADA\) Web site](#).

Print copies: Available from American Diabetes Association, 1701 North Beauregard Street, Alexandria, VA 22311.

AVAILABILITY OF COMPANION DOCUMENTS

The recommendations in this paper are based on the evidence reviewed in the following publication:

- Aiello LP, Gardner TW, King GL, Blankenship G, Cavallerano JD, Ferris FL, Klein R: Diabetic retinopathy (Technical Review). Diabetes Care 1998;21:143-56.

Print copies: Available from American Diabetes Association (ADA), 1701 North Beauregard Street, Alexandria, VA 22311.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on November 1, 1998. The information was verified by the guideline developer on December 15, 1998. The summary was updated by ECRI on April 1, 2001, January 29, 2002, July 29, 2003, and March 24, 2004.

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