Comprehensive Adult Medical Eye Evaluation Preferred Practice Pattern®
COMPREHENSIVE ADULT MEDICAL EYE EVALUATION PREFERRED PRACTICE PATTERN® DEVELOPMENT PROCESS AND PARTICIPANTS

The Preferred Practice Patterns Committee members wrote the Comprehensive Adult Medical Eye Evaluation Preferred Practice Pattern® guidelines (PPP). The committee members discussed and reviewed successive drafts of the document, meeting in person once and conducting other review by e-mail discussion, to develop a consensus over the final version of the document.

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The Comprehensive Adult Medical Eye Evaluation PPP was then sent for review to additional internal and external groups and individuals in June 2020. All those who returned comments were required to provide disclosure of relevant relationships with industry to have their comments considered (indicated with an asterisk below). Members of the Preferred Practice Patterns Committee reviewed and discussed these comments and determined revisions to the document.

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In compliance with the Council of Medical Specialty Societies’ Code for Interactions with Companies (available at https://cmss.org/code-signers-pdf), relevant relationships with industry are listed. The Academy has Relationship with Industry Procedures to comply with the Code (available at www.aao.org/about-preferred-practice-patterns). A majority (75%) of the members of the Preferred Practice Patterns Committee 2020 had no related financial relationship to disclose.

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The disclosures of relevant relationships to industry of other reviewers of the document from January to October 2020 are available online at www.aao.org/ppp.
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Comprehensive Adult Medical Eye Evaluation Preferred Practice Pattern®

**Background:**
Patients may seek to undergo a comprehensive adult medical eye evaluation for a variety of reasons. An evaluation is typically recommended for patients who have not been seen by an ophthalmologist for an extended period of time or for those who have never been examined. Recommended intervals between comprehensive examinations vary with age and risk factors. A thorough ophthalmic evaluation can detect common abnormalities of the visual system and its related structures as well as less common yet extremely serious issues. Such evaluations can also uncover evidence of systemic disease through its associated ophthalmic manifestations. With appropriate and timely intervention, visually impairing conditions such as cataract, and potentially blinding diseases such as glaucoma, age-related macular degeneration, and diabetic retinopathy often have favorable outcomes.

**Rationale for Treatment:**
The rationale for performing periodic comprehensive medical eye examinations in adults without known ocular conditions or risk factors is to detect ocular diseases, visual dysfunction, or ophthalmic signs of systemic disease. Early recognition, counseling, and treatment may preserve visual function or, in the case of systemic disease, prevent serious illness or even premature death from occurring. Irreversible vision loss has been associated with adverse effects on quality of life and mental health, and self-reported visual loss has been found to be associated with depression. Comprehensive medical eye evaluations are also performed to evaluate new symptoms and to monitor patients with previously identified eye conditions or risk factors. The public health impact of eye disease is substantial.

**Care Process:**
The components of a comprehensive medical eye evaluation include a history, medical eye examination and any needed laboratory tests, diagnosis, and initiation of management. The examination includes a careful evaluation for ophthalmic disorders; the treatment plan addresses refractive errors and ocular disease; and referrals are initiated when systemic disease is detected.
OBJECTIVES OF PREFERRED PRACTICE PATTERN® GUIDELINES

As a service to its members and the public, the American Academy of Ophthalmology has developed a series of Preferred Practice Pattern® guidelines that identify characteristics and components of quality eye care. Appendix 1 describes the core criteria of quality eye care.

The Preferred Practice Pattern® guidelines are based on the best available scientific data as interpreted by panels of knowledgeable health professionals. In some instances, such as when results of carefully conducted clinical trials are available, the data are particularly persuasive and provide clear guidance. In other instances, the panels have to rely on their collective judgment and evaluation of available evidence.

These documents provide guidance for the pattern of practice, not for the care of a particular individual. While they should generally meet the needs of most patients, they cannot possibly best meet the needs of all patients. Adherence to these PPPs will not ensure a successful outcome in every situation. These practice patterns should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the best results. It may be necessary to approach different patients’ needs in different ways. The physician must make the ultimate judgment about the propriety of the care of a particular patient in light of all of the circumstances presented by that patient. The American Academy of Ophthalmology is available to assist members in resolving ethical dilemmas that arise in the course of ophthalmic practice.

Preferred Practice Pattern® guidelines are not medical standards to be adhered to in all individual situations. The Academy specifically disclaims any and all liability for injury or other damages of any kind, from negligence or otherwise, for any and all claims that may arise out of the use of any recommendations or other information contained herein.

References to certain drugs, instruments, and other products are made for illustrative purposes only and are not intended to constitute an endorsement of such. Such material may include information on applications that are not considered community standard, that reflect indications not included in approved U.S. Food and Drug Administration (FDA) labeling, or that are approved for use only in restricted research settings. The FDA has stated that it is the responsibility of the physician to determine the FDA status of each drug or device he or she wishes to use, and to use them with appropriate patient consent in compliance with applicable law.

Innovation in medicine is essential to ensure the future health of the American public, and the Academy encourages the development of new diagnostic and therapeutic methods that will improve eye care. It is essential to recognize that true medical excellence is achieved only when the patients’ needs are the foremost consideration.

All Preferred Practice Pattern® guidelines are reviewed by their parent panel annually or earlier if developments warrant and updated accordingly. To ensure that all PPPs are current, each is valid for 5 years from the “approved by” date unless superseded by a revision. Preferred Practice Pattern guidelines are funded by the Academy without commercial support. Authors and reviewers of PPPs are volunteers and do not receive any financial compensation for their contributions to the documents. The PPPs are externally reviewed by experts and stakeholders, including consumer representatives, before publication. The PPPs are developed in compliance with the Council of Medical Specialty Societies’ Code for Interactions with Companies. The Academy has Relationships with Industry Procedures (available at www.aao.org/about-preferred-practice-patterns) to comply with the Code.

The intended users of the Comprehensive Medical Adult Eye Evaluation PPP are ophthalmologists.
METHODS AND KEY TO RATINGS

Preferred Practice Pattern guidelines should be clinically relevant and specific enough to provide useful information to practitioners. Where evidence exists to support a recommendation for care, the recommendation should be given an explicit rating that shows the strength of evidence. To accomplish these aims, methods from the Scottish Intercollegiate Guideline Network\(^1\) (SIGN) and the Grading of Recommendations Assessment, Development and Evaluation\(^2\) (GRADE) group are used. GRADE is a systematic approach to grading the strength of the total body of evidence that is available to support recommendations on a specific clinical management issue. Organizations that have adopted GRADE include SIGN, the World Health Organization, the Agency for Healthcare Research and Policy, and the American College of Physicians.\(^3\)

- All studies used to form a recommendation for care are graded for strength of evidence individually, and that grade is listed with the study citation.
- To rate individual studies, a scale based on SIGN\(^1\) is used. The definitions and levels of evidence to rate individual studies are as follows:

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I++</td>
<td>High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias</td>
</tr>
<tr>
<td>I+</td>
<td>Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias</td>
</tr>
<tr>
<td>I-</td>
<td>Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias</td>
</tr>
<tr>
<td>II++</td>
<td>High-quality systematic reviews of case control or cohort studies</td>
</tr>
<tr>
<td></td>
<td>High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal</td>
</tr>
<tr>
<td>II+</td>
<td>Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal</td>
</tr>
<tr>
<td>II-</td>
<td>Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal</td>
</tr>
<tr>
<td>III</td>
<td>Non-analytic studies (e.g., case reports, case series)</td>
</tr>
</tbody>
</table>

- Recommendations for care are formed based on the body of the evidence. The body of evidence quality ratings are defined by GRADE\(^2\) as follows:

<table>
<thead>
<tr>
<th>Quality</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good quality</td>
<td>Further research is very unlikely to change our confidence in the estimate of effect</td>
</tr>
<tr>
<td>Moderate quality</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate</td>
</tr>
<tr>
<td>Insufficient quality</td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate</td>
</tr>
<tr>
<td></td>
<td>Any estimate of effect is very uncertain</td>
</tr>
</tbody>
</table>

- Key recommendations for care are defined by GRADE\(^2\) as follows:

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong recommendation</td>
<td>Used when the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not</td>
</tr>
<tr>
<td>Discretionary</td>
<td>Used when the trade-offs are less certain—either because of low quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced</td>
</tr>
</tbody>
</table>

- The Highlighted Recommendations for Care section lists points determined by the PPP Committee to be of particular importance to vision and quality of life outcomes.
- All recommendations for care in this PPP were rated using the system described above. Ratings are embedded throughout the PPP main text in italics.
- Literature searches to update the PPP were undertaken in February 2020 and June 2020 in the PubMed database. Complete details of the literature searches are available in Appendix 2.
HIGHLIGHTED RECOMMENDATIONS FOR CARE

The recommended frequency for adult comprehensive medical eye examinations for asymptomatic patients, and for patients who do not have risk factors for eye disease, is as follows: under 40 years—every 5 to 10 years; 40 to 54 years—every 2 to 4 years; 55 to 64 years—every 1 to 3 years; and 65 years or older—every 1 to 2 years.

An increased frequency of comprehensive medical eye examinations is recommended for adults who have risk factors for glaucoma, such as African Americans and Hispanics.

The first recommended adult comprehensive medical eye examination, and subsequent frequency of examination for patients who have diabetes mellitus, depends on the type of diabetes and pregnancy status. The recommendations are as follows: (1) type 1 diabetes mellitus—first examination 5 years after onset and yearly thereafter; (2) type 2 diabetes mellitus—first examination at the time of diagnosis and yearly thereafter; and (3) for women with type 1 or type 2 diabetes—first examination prior to conception and then early in the first trimester of pregnancy. Interval recommendations thereafter will be based on findings at first examination. (Note: Women who develop gestational diabetes do not require an eye examination during pregnancy, and they do not appear to be at increased risk for developing diabetic retinopathy during pregnancy.)

Smoking is a risk factor for many ocular diseases.
INTRODUCTION

PATIENT POPULATION
Adults with no known ocular conditions or risk factors, adults with previously identified conditions or risk factors, or adults with recurrent or new symptoms.

CLINICAL OBJECTIVES
- Detect and diagnose ocular abnormalities and diseases
- Identify risk factors for ocular disease
- Identify risk factors for systemic disease based on ocular findings
- Establish the presence or absence of ocular signs or symptoms of systemic disease
- Determine the refractive state and health status of the eye, visual system, and related structures
- Discuss the results and implications of the examination with the patient
- Initiate an appropriate management plan, including determination of the frequency of future visits, further diagnostic tests, referral, or treatment

BACKGROUND

Patients may seek a comprehensive adult medical eye evaluation for a variety of reasons. It is recommended for patients who have not been examined for an extended period of time by an ophthalmologist or those who are being seen for the first time. Recommended intervals between comprehensive examinations vary with age and risk factors. A thorough ophthalmic evaluation can detect common abnormalities of the visual system and related structures as well as less common yet extremely serious ones, such as ocular tumors. Such an evaluation can also uncover evidence of systemic disease that has associated ophthalmic manifestations. All patients, particularly those with risk factors for ocular disease, should be re-examined periodically to prevent or minimize vision loss by detecting and treating the disease at an early stage. Patients in whom ophthalmic disease(s) is identified require periodic comprehensive examinations for optimal monitoring and treatment of the condition(s). With appropriate and timely intervention, potentially blinding diseases such as glaucoma, cataract, age-related macular degeneration (AMD) and diabetic retinopathy often have a more favorable outcome. Studies have indicated that up to 40% of legal blindness found among nursing home residents, as well as in both urban and rural communities, could have been prevented or ameliorated if those individuals had received timely ophthalmic screening and care. In a population-based study, 63% of the participants who had eye disease were not aware of it.

RATIONALE FOR COMPREHENSIVE MEDICAL EYE EVALUATIONS
The rationale for performing periodic comprehensive medical eye examinations in adults without known ocular conditions or risk factors is to detect ocular diseases, visual dysfunction, or ophthalmic signs of systemic disease in the adult population. Early recognition, counseling, or treatment may preserve visual function or, in the case of systemic diseases, could prevent serious illness or even premature death. Irreversible vision loss has been associated with adverse effects on quality of life and mental health, and self-reported visual loss has been found to be significantly associated with depression. Comprehensive medical eye evaluations are also performed periodically to evaluate new symptoms and monitor patients with previously identified eye conditions or risk factors.

The public health impact of eye disease is substantial, because vision affects daily functioning. Improvement in visual function that occurs as a result of treatment of ocular disorders is accompanied by improvement in life satisfaction and mental health and by participation in home and community activities. Vision plays a critical role in mobility and in fall prevention. Untreated visual impairment has been associated with cognitive decline and Alzheimer's disease. A higher risk of motor vehicle collisions was found among drivers with glaucoma who had severe visual field defects. Cataract surgery in older drivers has been shown to reduce the subsequent motor vehicle
collision rate. Visual impairment, AMD, and cataract have been associated with an increased risk of mortality. In women 65 and older, poorer visual acuity and reduced contrast sensitivity have been associated with a higher risk of mortality.

**OCULAR DISEASES**

In 2015, about 1.02 million adults 40 and older in the United States were legally blind (distance corrected visual acuity of ≤20/200, or a visual field of ≤20 degrees in the better seeing eye), and an additional 3.22 million were visually impaired (distance corrected visual acuity of <20/40 in the better-seeing eye). The highest frequencies of visual impairment and legal blindness were found in individuals 80 years and older and generally correlated with age. Rates of visual impairment and legal blindness were disproportionately higher among individuals of African descent compared with individuals of European descent. Rates of visual impairment were higher among individuals of Hispanic/Latino descent compared with individuals of European or African descent.

Many patients will be unaware that they have a vision-threatening ocular condition because of the lack of early symptoms (see Table 1). These conditions include common and often treatable diseases such as glaucoma, diabetic retinopathy, and some forms of macular degeneration.

**Open-Angle Glaucoma**

Primary open-angle glaucoma (POAG) is a significant public health problem. It is estimated that 76 million people in the world have glaucoma in the year 2020. Glaucoma (both open-angle and angle-closure) is the second leading cause of blindness worldwide. Overall, the prevalence of POAG for adults aged 40 and older in the United States was estimated to be about 3.05% in 2013. Prevalence studies suggest that POAG will increase by 50% worldwide from 52.7 million in 2020 to 79.8 million in 2040 as the population ages.

Large differences exist in the prevalence of glaucoma among different ethnорacial groups. Overall, there appears to be a threefold higher prevalence of open-angle glaucoma (OAG) in African Americans relative to non-Hispanic whites in the United States. It is also the leading cause of blindness in African Americans. Further, the prevalence of OAG is even higher in Afro-Caribbeans relative to African Americans. Recent evidence on Hispanics/Latinos suggests that they have high prevalence rates of OAG that are comparable to the prevalence rates for African Americans. An analysis of claims data from a large U.S.-based managed care plan suggests that the prevalence of OAG among Asian Americans is comparable to the prevalence among Latinos and is higher than that of non-Hispanic white Americans.

**Primary Angle Closure Glaucoma**

Considerable differences exist in the prevalence of angle closure among ethnорacial groups, with highest rates in Inuit, Chinese, and other Asian populations; lower rates are reported in populations of African and African-derived origin and European and European-derived origin. In some Asian populations, primary angle-closure glaucoma (PACG) is reported to account for nearly as many cases of glaucoma as OAG. Worldwide, 0.7% of people over 40 years of age are estimated to have angle-closure glaucoma; in 2013, this represented 20.2 million people, with most (15.5 million) in Asia. In China, PACG is estimated to cause unilateral blindness (visual acuity <20/200 or visual field ≤10°) in 1.5 million individuals and bilateral blindness in another 1.5 million.

**Diabetes-Related Ocular Disease**

An estimated 100 million Americans aged 18 years and older have either been diagnosed with diabetes or are prediabetic, according to a 2015 report by the Centers for Disease Control and Prevention (CDC). As reported by the CDC, 30.3 million Americans 18 or older have diabetes (9.4% of people in this age group), and about one-quarter are not aware that they have the disease. An additional 79 million persons have impaired fasting blood glucose levels (based on both fasting blood glucose levels and HbA1c levels). In 2015, an estimated 1.5 million new cases of diabetes were diagnosed among people aged 18 and older.

Rates of diagnosed diabetes increased with age: 4% of individuals 18 to 44 years old had diabetes, as did 17% of those 45 to 64 years old and 25% of those 65 and older. Rates of diagnosed diabetes were higher among Native Americans and Alaskan Natives (15.1%), non-
Hispanic blacks (12.7%), and Hispanics (12.1%) compared with Asians (8.0%) and non-Hispanic whites (7.4%).

Rates of prediabetes (HbA1c levels between 5.7% and 6.4%) are also increasing. It is estimated that 33.9% of U.S. adults 18 or older (84.1 million people) have prediabetes based on their fasting glucose or HbA1c level. Nearly half (48.3%) of adults 65 or older had prediabetes. The age-adjusted incidence of diabetes was two times higher for people with less than a high school education (10.4/1000 persons) compared with those with more than a high school education (5.3/1000 persons) from 2013 to 2015. Rates of diabetes and prediabetes are similarly high among children and adolescents (younger than 20). Compared with members of other U.S. racial and ethnic groups, non-Hispanic whites had the highest rate of new cases of type 1 diabetes. Among children and adolescents aged 10 to 19, U.S. minority populations had higher rates of new cases of type 2 diabetes compared with non-Hispanic whites.

The 2015 CDC report notes a higher prevalence of diabetes among American Indians/Alaska Natives (15.1%), non-Hispanic blacks (12.7%), and people of Hispanic ethnicity (12.1%) than among non-Hispanic whites (7.4%) and Asians (8.0%) among adults aged 18 years or older. Americans of African descent or Hispanic ethnicity have a disproportionately high prevalence of diabetes compared with Americans of European descent (12.6%, 11.8%, 7.0%, respectively), whereas Asian Americans have only a slightly higher prevalence (8.4%). American Indians and Alaska Natives had an approximate diabetes prevalence of 6.4 per 1000 in 1990, which increased to 9.3 per 1000 in 1998 (approximately 45% increase) in children and young adults under the age of 35 years. Other research suggests a high prevalence of diabetes in Asia.

According to a recently published study in the Lancet estimating the lifetime risk and years of life lost due to diabetes in the United States from 1985–2011, approximately 40% of Americans over the age of 20 years are at risk for developing diabetes during their lifetime. With increasing industrialization and globalization, there is a concomitant increasing prevalence of diabetes that is leading to a worldwide epidemic. An alarming increase in the frequency of type 2 diabetes in the pediatric age group has been noted in several countries, including in the United States, and has been associated with the increased frequency of childhood obesity. Diabetes is one of the most common diseases in school-aged children. Clearly, these trends predict an increase in the number of individuals with diabetes as well as the associated increased costs for health care and the burdens of disability associated with diabetes and its complications. In addition, there is evidence suggesting that diabetes develops at earlier ages and carries a higher incidence of complications among ethnic minorities.

**TABLE 1 PREVALENCE OF MAJOR OCULAR DISEASES AND CONDITIONS THAT MAY BE ASYMPTOMATIC**

<table>
<thead>
<tr>
<th>Disease or Condition</th>
<th>Prevalence</th>
<th>Risk Factors for Disease or Disease Progression</th>
<th>Potentially Positive Findings on Examinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choroidal nevi</td>
<td>5%–8%, increases with age, and more common in white Americans. (Note: Findings are based on 45° fundus images centered on the fovea and optic nerve.)</td>
<td>White American populations and increasing age</td>
<td>Clearly defined margins, often flat or slightly elevated; typically stable in size. Over time, choroidal nevi may display overlying drusen, retinal pigment epithelial atrophy, hyperplasia, or fibrous metaplasia.</td>
</tr>
<tr>
<td>Open-angle glaucoma</td>
<td>African Americans ≥40: 3.4%, White Americans ≥40: 1.7%</td>
<td>African, Hispanic, or Latino descent, increased age, 66, 69, 74 family history of glaucoma, 65, 66 elevated IOP, 67, 68 thin central cornea, 67, 68</td>
<td>Abnormal optic disc and nerve fiber layer defect, characteristic visual field defect, elevated IOP, decreased vision (late stages), exfoliation material on the lens capsule, signs of pigment dispersion syndrome (including Krukenberg spindle)</td>
</tr>
<tr>
<td>Primary angle-closure glaucoma</td>
<td>0.009%/65–2.6%/6 (highest rates in Inuit and Asian populations)</td>
<td>Hyperopia, family history of angle closure, increasing age, 64 female gender, 66, 67 Inuit or Asian descent</td>
<td>Narrow angles, elevated IOP, peripheral anterior synechiae</td>
</tr>
</tbody>
</table>
### Diabetic Retinopathy

<table>
<thead>
<tr>
<th>General population age ≥ 40:</th>
<th>Increasing duration of diabetes, high levels of glycated hemoglobin, high systolic blood pressure, elevated serum lipid levels.</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.4%(^{103})</td>
<td>Retinal microaneurysms, hemorhages, lipid exudates, intraretinal microvascular anomalies, macular edema, retinal or anterior segment neovascularization, preretinal or vitreous hemorrhage, tractional retinal detachment</td>
</tr>
<tr>
<td>Individuals age ≥ 40 with type 1 or type 2 diabetes: 28.5%(^{104}-40.3%(^{103})</td>
<td></td>
</tr>
<tr>
<td>Individuals of Hispanic descent with type 1 or type 2 diabetes age ≥ 40: 46.9%(^{105})</td>
<td></td>
</tr>
</tbody>
</table>

### Early AMD

<table>
<thead>
<tr>
<th>White Americans age ≥ 45: 4.8%(^{119})</th>
<th>Increasing age, bilateral soft drusen, large drusen, confluent drusen, clumping or atrophy of retinal pigment epithelium, family history, genetic polymorphisms, smoking, poor diet/nutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals of African descent age ≥ 45: 2.1%(^{119})</td>
<td>Retinal pigment epithelial disturbances/atrophy, intermediate or large drusen, geographic atrophy, or retinal pigmented epithelial detachments</td>
</tr>
<tr>
<td>Individuals of Hispanic descent age ≥ 45: 4.0%(^{119})</td>
<td></td>
</tr>
<tr>
<td>Individuals of Hispanic descent age ≥ 40: 7.5%(^{120})</td>
<td></td>
</tr>
<tr>
<td>Individuals of Asian descent age 40–79: 6.8%(^{121})</td>
<td></td>
</tr>
</tbody>
</table>

### Late AMD

<table>
<thead>
<tr>
<th>White Americans age ≥ 45: 0.6%(^{119})</th>
<th>Increasing age, family history, smoking, bilateral soft drusen, large drusen, confluent drusen, clumping or atrophy of retinal pigment epithelium, body mass index and genetic factors.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals of African descent age ≥ 45: 0.3%(^{119})</td>
<td>Drusen and associated retinal pigment epithelial changes, geographic atrophy, evidence of choroidal neovascularization (intra- or subretinal hemorrhage, lipid, intra- or subretinal fluid)</td>
</tr>
<tr>
<td>Individuals of Hispanic descent age ≥ 45: 0.2%(^{120})</td>
<td></td>
</tr>
<tr>
<td>Individuals of Hispanic descent age ≥ 40: 0.2%(^{120})</td>
<td></td>
</tr>
<tr>
<td>Individuals of Asian descent age 40–79: 0.56%(^{121})</td>
<td></td>
</tr>
</tbody>
</table>

AMD = age-related macular degeneration; IOP = intraocular pressure.

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P13
Age-Related Macular Degeneration

Age-related macular degeneration (AMD) is a leading cause of severe vision impairment among white Americans. In 2004, it was estimated that approximately 1.75 million people aged 40 years or older in the United States have either neovascular AMD or geographic atrophy in at least one eye and that 7.3 million have high-risk features, such as large drusen (≥125 µm), in one or both eyes. A report published in JAMA Ophthalmology in 2011 notes that the prevalence of any AMD in the 2005–2008 National Health and Nutrition Examination Survey was 6.5%, which is lower than the 9.4% prevalence reported in the 1988–1994 Third National Health and Nutrition Examination Survey. Overall, these estimates show a decreasing incidence of AMD. The prevalence, incidence, and progression of AMD and most associated features (e.g., large drusen) increase significantly with age. For example, the prevalence of AMD in white females 60 to 64 is 0.3%, increasing to 16.4% in those 80 and older. Age-related macular degeneration is usually asymptomatic in its early stages, although a fundus examination is helpful in identifying patients with an increased risk of developing choroidal neovascularization or advanced AMD. The Age Related Eye Disease Study (AREDS) defined a role for nutritional supplements for slowing the progression of AMD. It is important to identify those patients at higher risk because the AREDS2 supplement formulation (i.e., vitamin C, vitamin E, zinc, copper, lutein, zeaxanthin) has been shown to have preventive efficacy in this higher-risk group. An estimated 8 million persons at least 55 years old in the United States have monocular or binocular intermediate AMD or monocular advanced AMD. They should be considered to be at high risk for progression of advanced AMD and are the population for whom the AREDS2 formulation should be considered. If all the patients at risk were given supplements, then more than 300,000 could delay disease progression and associated vision loss.

Cigarette smoking has been consistently identified in numerous studies as a risk factor for progression of AMD, and the risk increases relative to the number of pack-years smoked. Smoking-cessation counseling may influence patients to stop smoking, reducing the risk of AMD progression. Patients with neovascular AMD report a substantial decline in their quality of life and have an increased need for assistance with activities of daily living that progresses as visual acuity worsens. Early treatment of AMD is associated with a more favorable prognosis. Anti-vascular endothelial growth factor (VEGF) treatment given within 2 years after diagnosis of neovascular AMD in non-Hispanic white patients has been shown to reduce legal blindness and visual impairment. It is important to note that since the registration trials for the currently approved anti-VEGF medications, the standard of care is to treat neovascular AMD as soon as diagnosis has been made. Because early symptoms may be subtle, a comprehensive eye examination may represent a patient’s best opportunity to be diagnosed and treated at an earlier and potentially more favorable stage.

Cataract

Cataract remains a significant cause of visual disability in the United States, accounting for approximately 50% of low-vision cases in adults over 40. Cataract is the leading cause of treatable blindness among Americans of African descent who are 40 years of age and older, and it is the leading cause of low vision among individuals of African, Hispanic/Latino, and European descent. Because smoking increases the risk of cataract progression, informing smokers about this and other associated ocular and systemic diseases may influence them to stop smoking.

Other Ocular Disorders

Other examples of high-risk conditions or diseases that necessitate a medical eye examination include a history of ocular trauma or the presence of abnormalities of the anterior segment, such as corneal ectasia, corneal dystrophies, or peripheral anterior synechiae. Conditions that increase the risk of OAG (e.g., exfoliation syndrome and pigment dispersion syndrome) and angle-closure glaucoma (narrow anterior chamber angle) should also be evaluated. High myopia and abnormalities of the posterior segment, such as retinal tears or retinal degenerations

P14
SYSTEMIC DISEASES AND CONDITIONS

Important ophthalmic manifestations associated with systemic infectious, neoplastic, autoimmune, vascular, and nutrition-related diseases may be discovered during the ocular comprehensive ophthalmic evaluation.

The following components of the comprehensive examination may identify signs of systemic diseases or other serious medical conditions:

- External examination: orbital tumor, Graves’ disease, metabolic storage diseases
- Pupillary function: Horner’s syndrome, pharmacologic toxicity, midbrain tumor, aneurysm
- Ocular alignment and motility: neurological disorders (e.g., myasthenia gravis, central nervous system defects or aneurysm, multiple sclerosis), Graves’ disease
- Visual fields by confrontation: cerebrovascular accidents, chiasmal tumors
- Anterior segment: drug or heavy-metal toxicity; immune-mediated diseases (e.g., rheumatoid arthritis); infectious diseases; vitamin A deficiency; metabolic, endocrine, or storage diseases
- Posterior segment: systemic hypertension, diabetes mellitus, infectious diseases (e.g., acquired immunodeficiency syndrome, tuberculosis, syphilis, histoplasmosis, toxoplasmosis), immune-mediated diseases, vasculitis, primary or metastatic tumors, metabolic storage diseases, phakomatoses, hematologic diseases, cerebrovascular disease, increased intracranial pressure, toxicity from hydroxychloroquine, tamoxifen, or phenothiazines

SOCIOECONOMIC CONSIDERATIONS

In 2006, the societal cost of major visual disorders (AMD, cataract, diabetic retinopathy, POAG, refractive errors) among U.S. residents 40 and older was estimated to be $35.4 billion. This total comprised $16.2 billion in direct medical costs, $11.1 billion in other direct costs, and $8 billion in productivity losses. Not included in this total are costs associated with comorbid conditions, such as depression or injury.

In another study, U.S. residents 40 and older with blindness or visual impairment had estimated excess medical expenditures of $5.1 billion annually. This estimate includes the cost of home care and informal care for blind and visually impaired adults. The study also estimated that the total number of quality-adjusted life years (QALY) lost for individuals with blindness or visual impairment was 209,000. Valuing each QALY lost at $50,000 would add $10.4 billion to the estimate of the annual economic impact of visual impairment and blindness.

In 2012, the costs of vision loss and eye disorders among the population younger than 40 years were estimated at $27.5 billion (95% confidence interval, $21.5–$37.2 billion), including $5.9 billion for children and $21.6 billion for adults 18 to 39 years of age in the United States. This total included $14.5 billion in direct costs: $7.3 billion for diagnosed eye disorders, $4.9 billion in refraction correction, and $0.5 billion for undiagnosed vision loss. The indirect costs were $13 billion, due mainly to productivity losses. In addition, this cumulative vision loss cost society 215,000 QALYs. There were significant differences in the use of eye care services by adults with eye diseases in the United States with respect to socioeconomic position, as measured by poverty-income ratio and educational attainment.

In Australia, researchers estimated that the economic impact and cost in 2004 was A$9.85 billion (≈ US$9.5 billion), with vision disorders ranking seventh in the direct health care costs of various health conditions. Vision loss was also the seventh leading cause of disability in Australia, with the years of life lost to disability valued at A$4.8 billion (≈ US$4.64 billion) annually.

In 2006, the annual nonmedical costs related to visual impairment in France, Germany, Italy, and the United Kingdom were estimated at €10,749 million (≈ US$17,439 million) in France, €9,214 million (≈ US$14,948 million) in Germany, €12,069 million (≈ US$19,580 million) in Italy, and €15,180 million (≈ US$24,627 million) in the United Kingdom.
CARE PROCESS

A comprehensive medical eye evaluation includes a history, examination, diagnosis, and initiation of management. The examination includes a careful and thorough detection and diagnosis of ophthalmic disorders, develops a treatment plan for addressing refractive error and ocular disease, and refers detected systemic disease to the appropriate medical care provider. The items listed are basic areas of evaluation or investigation and are not meant to exclude additional elements when appropriate. For example, because history taking is an interactive process, the patient's responses may guide the clinician to pursue additional questions and evaluation.

HISTORY

In general, a thorough history may include the following items:
- Demographic data (e.g., name, date of birth, gender, and ethnicity or race)
- Patient’s other pertinent health care providers
- Chief complaint and history of present illness
- Present status of visual function (e.g., patient’s self-assessment of visual status, visual needs, any recent or current visual symptoms, and use of eyeglasses or contact lenses)
- Ocular symptoms (e.g., eyelid swelling, diplopia, redness, photophobia)
- Ocular history (e.g., prior eye diseases, injuries, surgery, including cosmetic eyelid and refractive surgery, or other treatments and medications)
- Systemic history: medical conditions and previous surgery
- Medications: ophthalmic and systemic medications currently used, including nutritional supplements and other over-the-counter products
- Allergies or adverse reactions to medications
- Family history: pertinent familial ocular (e.g., glaucoma, AMD) and systemic disease
- Social history (e.g., occupation; tobacco, alcohol, illicit drug use; family and living situation, as appropriate)
- Sexual history
- Directed review of systems

OCULAR EXAMINATION

The comprehensive eye examination consists of an evaluation of the physiological function and the anatomical status of the eye, visual system, and its related structures. This usually includes the following elements:
- Visual acuity with current correction (the power of the present correction recorded) at distance and, when appropriate, at near
- Refraction when indicated
- Visual fields by confrontation
- External examination (e.g., eyelid position and character, lashes, lacrimal apparatus and tear function; globe position; and pertinent skin and facial features)
- Pupillary function (e.g., size and response to light, relative afferent pupillary defect)
- Ocular alignment and motility (e.g., cover/uncover test, alternate cover test, ductions and versions)
- Slit-lamp biomicroscopic examination: eyelid margins and lashes; tear film; conjunctiva; sclera; cornea; anterior chamber; and assessment of central and peripheral anterior chamber depth, iris, lens, and anterior vitreous
- Intraocular pressure measurement, preferably using a contact applanation method (typically a Goldmann tonometer). Contact tonometry may be deferred in the setting of suspected ocular infection or corneal trauma.
- Fundus examination: mid and posterior vitreous, retina (including posterior pole and periphery), vasculature, and optic nerve
- Assessment of relevant aspects of patient’s mental and physical status

Examination of anterior segment structures routinely involves gross and biomicroscopic evaluation before and after dilation. Evaluation of structures situated posterior to the iris is best performed.
through a dilated pupil. Optimal examination of the optic nerve, macula, and peripheral retina requires the use of an indirect ophthalmoscope or slit-lamp fundus biomicroscopy with appropriate accessory diagnostic lenses.

Based on the patient's history and findings, additional tests or evaluations might be indicated to evaluate further a particular structure or function. These are not routinely part of the comprehensive medical eye clinical evaluation. Specialized clinical evaluation may include the following:

- Monocular near-vision testing
- Potential acuity testing
- Glare testing
- Contrast sensitivity testing
- Color-vision testing
- Testing of stereoscopy and fusion
- Testing of accommodation and convergence
- Central visual field testing (Amsler grid)
- Expanded evaluation of ocular motility and alignment in multiple fields of gaze at distance and near
- Exophthalmometry (e.g., Hertel)
- Tear breakup time
- Ocular surface vital dye staining
- Corneal sensation
- Gonioscopy
- Functional evaluation of the nasolacrimal system
- Indirect ophthalmoscopy with scleral indentation
- Contact lens stereoscopic biomicroscopy (e.g., Goldmann three-mirror lens)

Additional diagnostic testing may include the following:

- Keratometry (e.g., to assess surface quality and power)
- Corneal topography/tomography, including analysis
- Measurement of corneal thickness (optical and ultrasonic pachymetry)
- Corneal endothelial cell analysis
- Meibomography
- Tear osmolarity
- External, slit-lamp, or fundus photography
- Anterior and posterior segment optical coherence tomography
- Confocal microscopy
- Wavefront analysis
- Visual fields by automated and/or manual perimetry
- Biometry
- Stereophotography or computer-based image analysis of the optic disc and retinal nerve fiber layer or macula
- Ophthalmic ultrasonography (A-scan, B-scan, ultrasound biomicroscopy)
- Fluorescein, indocyanine green, and optical coherence tomography angiography
- Electrophysiological testing
- Microbiology and cytology of ocular or periorcular specimens
- In-office point-of-care testing (e.g., immunochromatography)
- Radiologic imaging
- Laboratory tests for systemic disease

**DIAGNOSIS AND MANAGEMENT**

The ophthalmologist evaluates and integrates the findings of the comprehensive ophthalmic examination with all aspects of the patient's health status and social situation in determining an appropriate course of action. Patients are considered in one of three general categories based on the results of the evaluation: patients with no risk factors, patients with risk factors, and patients with conditions that require intervention.
Category I: Patients With No Risk Factors

When the initial comprehensive evaluation is normal or involves only refractive errors that require corrective lenses, the ophthalmologist reviews the findings with the patient and renders advice regarding an appropriate interval for re-examination. Although this is considered a low-risk category, periodic re-examination is indicated to detect new, potentially asymptomatic, or unrecognized ocular disease, such as glaucoma, diabetic retinopathy, and AMD, the incidence of which increases with age.

A 5-year observational study of a nationally representative cohort of Medicare beneficiaries showed that patients 65 and older who had more regular eye examinations experienced less decline in vision and functional status than those who had less frequent examinations.\(^{154}\) For each additional year in which a patient received an eye examination, there was an increased likelihood of continuing to read newspapers and maintaining activities of daily living. There was also a decreased risk of developing new limitations in activities of daily living and instrumental activities of daily living. Instrumental activities of daily living are activities related to independent living and include preparing meals, managing money, shopping for groceries or personal items, performing light or heavy housework, and using a telephone.

There is little evidence in the literature to define the optimal frequency of eye examinations of patients under 65 with no eye symptoms or signs. There is some evidence that clinically significant fundus abnormalities in asymptomatic patients increase with age.\(^{155}\) But other evidence suggests that the diagnostic yield of dilated fundus examination in asymptomatic patients is low, particularly in younger age groups.\(^{156}\) In the absence of symptoms or other indications following the initial comprehensive medical eye evaluation, periodic evaluations are recommended at the frequency indicated in Table 2, which takes into account the relationship between increasing age and the risk of asymptomatic or undiagnosed disease. At the time of each comprehensive medical eye evaluation, the ophthalmologist will reassess the patient to determine the appropriate follow-up interval. Adults with no signs or risk factors for eye disease should have a comprehensive medical eye evaluation at age 40 if they have not previously received one.\(^{157}\)

Interim evaluations, such as screenings, refractions, or less extensive evaluations, are indicated to address episodic minor problems and complaints, or for patient reassurance. Other situations may warrant a comprehensive medical eye evaluation. The extent of the interim evaluation to be performed is determined by the patient's condition, symptoms, and the ophthalmologist's medical judgment.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Frequency of Evaluation*</th>
</tr>
</thead>
<tbody>
<tr>
<td>65 or older(^{154})</td>
<td>Every 1–2 years</td>
</tr>
<tr>
<td>55–64</td>
<td>Every 1–3 years</td>
</tr>
<tr>
<td>40–54</td>
<td>Every 2–4 years</td>
</tr>
<tr>
<td>Under 40</td>
<td>Every 5–10 years</td>
</tr>
</tbody>
</table>

* Interim eye evaluations, consisting of vision examinations (e.g., refractions, eyeglasses, contact lens evaluations), may be performed during these periods as well.

Category II: Patients With Risk Factors

A patient is considered to be at increased risk when the evaluation reveals signs that are suggestive of a potentially abnormal condition or when risk factors for developing ocular disease are identified but the patient does not yet require intervention. These situations may merit closer follow-up to monitor the patient's ocular health and to detect early signs of disease with additional testing.

The ophthalmologist determines an appropriate follow-up interval for each patient based on the presence of early symptoms and signs, risk factors, the onset of ocular disease, and the potential rate of progression of a given disease. For example, individuals of African descent might
require more frequent examinations because they are at higher risk for an earlier onset and more rapid progression of glaucoma. It is recommended that patients with the conditions and risk factors noted in Table 3 undergo a comprehensive medical eye evaluation at the listed intervals.

### TABLE 3  COMPREHENSIVE MEDICAL EYE EVALUATION FOR PATIENTS WITH DIABETES MELLITUS OR RISK FACTORS FOR GLAUCOMA

<table>
<thead>
<tr>
<th>Condition/Risk Factor*</th>
<th>Frequency of Evaluation†</th>
</tr>
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<tbody>
<tr>
<td><strong>Diabetes Mellitus</strong></td>
<td></td>
</tr>
<tr>
<td>Type 1158</td>
<td>5 years after onset†</td>
</tr>
<tr>
<td>Type 2159</td>
<td>At time of diagnosis</td>
</tr>
<tr>
<td>Prior to pregnancy160–162 (Type 1 or 2)</td>
<td>Prior to conception and early in the first trimester</td>
</tr>
<tr>
<td></td>
<td>See Diabetic Retinopathy PPP163 for interval recommendations based on findings at first examination</td>
</tr>
<tr>
<td><strong>Risk Factors for Glaucoma164</strong></td>
<td></td>
</tr>
<tr>
<td>Age 65 years or older</td>
<td>Every 1–2 years*</td>
</tr>
<tr>
<td>Age 55–64 years</td>
<td>Every 1–2 years</td>
</tr>
<tr>
<td>Age 40–54 years</td>
<td>Every 1–3 years</td>
</tr>
<tr>
<td>Under 40 years</td>
<td>Every 2–5 years</td>
</tr>
</tbody>
</table>

* The Center for Medicare and Medicaid Services covers glaucoma examinations by eye care professionals in the office for beneficiaries who have diabetes mellitus, those with a family history of glaucoma, African Americans 50 years or older, and Hispanics 65 years or older.

† The ophthalmologist’s assessment of degree of risk, abnormal findings, or potential loss of visual function may dictate more frequent follow-up examinations than listed in this table. If the patient has additional glaucoma risk factors, the Primary Open-Angle Glaucoma Suspect PPP should be consulted.165

‡ Some patients may require refractive management during this period.

### Category III: Conditions That Require Intervention

For a patient with ophthalmic or refractive abnormalities, the ophthalmologist prescribes glasses, contact lenses, or other optical devices; treats with medications; arranges for additional evaluation, testing, and follow-up as appropriate; and performs nonsurgical or surgical procedures, including laser surgery when indicated.

The ophthalmologist should ensure that the patient is informed of relevant examination findings and any need for further evaluation, testing, treatment, or follow-up. Also, relevant ophthalmic findings should be shared with the patient's primary care physician or other specialists, as appropriate. For a patient with systemic abnormalities, the ophthalmologist may advise further evaluation or referral, as appropriate.

Vision rehabilitation attempts to restore as much functional ability as possible,166 and patients with reduced visual function may be referred for vision rehabilitation and social services (see Vision Rehabilitation PPP).167, 168 More information on vision rehabilitation, including materials for patients, is available at [www.ao.org/smart-sight-low-vision](http://www.ao.org/smart-sight-low-vision).

### PROVIDER AND SETTING

Of all health care providers, the ophthalmologist, as a physician with full medical training, best combines a thorough understanding of ocular pathology and disease processes; familiarity with systemic disorders that have ocular manifestations; and clinical skills and experience in ocular diagnosis, treatment, and medical decision making. This makes the ophthalmologist the most qualified professional to perform, oversee, and interpret the results of a comprehensive medical eye evaluation. Frequently, and appropriately, specific testing and data collection are conducted by trained personnel working under the ophthalmologist’s supervision.
APPENDIX 1. QUALITY OF OPHTHALMIC CARE CORE CRITERIA

Providing quality care is the physician's foremost ethical obligation, and is the basis of public trust in physicians.
AMA Board of Trustees, 1986

Quality ophthalmic care is provided in a manner and with the skill that is consistent with the best interests of the patient. The discussion that follows characterizes the core elements of such care.

The ophthalmologist is first and foremost a physician. As such, the ophthalmologist demonstrates compassion and concern for the individual, and utilizes the science and art of medicine to help alleviate patient fear and suffering. The ophthalmologist strives to develop and maintain clinical skills at the highest feasible level, consistent with the needs of patients, through training and continuing education. The ophthalmologist evaluates those skills and medical knowledge in relation to the needs of the patient and responds accordingly. The ophthalmologist also ensures that needy patients receive necessary care directly or through referral to appropriate persons and facilities that will provide such care, and he or she supports activities that promote health and prevent disease and disability.

The ophthalmologist recognizes that disease places patients in a disadvantaged, dependent state. The ophthalmologist respects the dignity and integrity of his or her patients and does not exploit their vulnerability.

Quality ophthalmic care has the following optimal attributes, among others.

- The essence of quality care is a meaningful partnership relationship between patient and physician. The ophthalmologist strives to communicate effectively with his or her patients, listening carefully to their needs and concerns. In turn, the ophthalmologist educates his or her patients about the nature and prognosis of their condition and about proper and appropriate therapeutic modalities. This is to ensure their meaningful participation (appropriate to their unique physical, intellectual, and emotional state) in decisions affecting their management and care, to improve their motivation and compliance with the agreed plan of treatment, and to help alleviate their fears and concerns.

- The ophthalmologist uses his or her best judgment in choosing and timing appropriate diagnostic and therapeutic modalities as well as the frequency of evaluation and follow-up, with due regard to the urgency and nature of the patient's condition and unique needs and desires.

- The ophthalmologist carries out only those procedures for which he or she is adequately trained, experienced, and competent, or, when necessary, is assisted by someone who is, depending on the urgency of the problem and availability and accessibility of alternative providers.

- Patients are assured access to, and continuity of, needed and appropriate ophthalmic care, which can be described as follows.
  - The ophthalmologist treats patients with due regard to timeliness, appropriateness, and his or her own ability to provide such care.
  - The operating ophthalmologist makes adequate provision for appropriate pre- and postoperative patient care.
  - When the ophthalmologist is unavailable for his or her patient, he or she provides appropriate alternate ophthalmic care, with adequate mechanisms for informing patients of the existence of such care and procedures for obtaining it.
  - The ophthalmologist refers patients to other ophthalmologists and eye care providers based on the timeliness and appropriateness of such referral, the patient's needs, the competence and qualifications of the person to whom the referral is made, and access and availability.

- The ophthalmologist seeks appropriate consultation with due regard to the nature of the ocular or other medical or surgical problem. Consultants are suggested for their skill, competence, and accessibility.

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They receive as complete and accurate an accounting of the problem as necessary to provide efficient and effective advice or intervention, and in turn they respond in an adequate and timely manner. The ophthalmologist maintains complete and accurate medical records.

- On appropriate request, the ophthalmologist provides a full and accurate rendering of the patient's records in his or her possession.
- The ophthalmologist reviews the results of consultations and laboratory tests in a timely and effective manner and takes appropriate actions.
- The ophthalmologist and those who assist in providing care identify themselves and their profession.
- For patients whose conditions fail to respond to treatment and for whom further treatment is unavailable, the ophthalmologist provides proper professional support, counseling, rehabilitative and social services, and referral as appropriate and accessible.
- Prior to therapeutic or invasive diagnostic procedures, the ophthalmologist becomes appropriately conversant with the patient's condition by collecting pertinent historical information and performing relevant preoperative examinations. Additionally, he or she enables the patient to reach a fully informed decision by providing an accurate and truthful explanation of the diagnosis; the nature, purpose, risks, benefits, and probability of success of the proposed treatment and of alternative treatment; and the risks and benefits of no treatment.
- The ophthalmologist adopts new technology (e.g., drugs, devices, surgical techniques) in judicious fashion, appropriate to the cost and potential benefit relative to existing alternatives and to its demonstrated safety and efficacy.
- The ophthalmologist enhances the quality of care he or she provides by periodically reviewing and assessing his or her personal performance in relation to established standards, and by revising or altering his or her practices and techniques appropriately.
- The ophthalmologist improves ophthalmic care by communicating to colleagues, through appropriate professional channels, knowledge gained through clinical research and practice. This includes alerting colleagues of instances of unusual or unexpected rates of complications and problems related to new drugs, devices, or procedures.
- The ophthalmologist provides care in suitably staffed and equipped facilities adequate to deal with potential ocular and systemic complications requiring immediate attention.
- The ophthalmologist also provides ophthalmic care in a manner that is cost effective without unacceptably compromising accepted standards of quality.

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APPENDIX 2. LITERATURE SEARCHES FOR THIS PPP

Literature searches of the PubMed and Cochrane databases were conducted in March 2020; the search strategies were as follows. Specific limited update searches were conducted after June 2020.

"activities of daily living"[mh] AND ("vision disorders"[mh] OR "visual acuity"[mh] OR "visual fields"[mh] OR "visually impaired persons"[mh])

"quality of life"[mh] AND ("vision disorders"[mh] OR "visual acuity"[mh] OR "visual fields"[mh] OR "visually impaired persons"[mh])

"diagnosis"[mh] AND "vision disorders"[mh]

RELATED ACADEMY MATERIALS

Basic and Clinical Science Course
Fundamentals and Principles of Ophthalmology (Section 2, 2019–2020)

Clinical Education

To order any of these products, except for the free materials, please contact the Academy’s Customer Service at 866.561.8558 (U.S. only) or 415.561.8540 or www.aao.org/store.
REFERENCES

3. GRADE working group. Organizations that have endorsed or that are using GRADE. Available at www.gradeworkinggroup.org/. Accessed November 2020.


