PREFERRED PRACTICE PATTERN®

Primary Open-Angle Glaucoma Suspect

AMERICAN ACADEMY® OF OPHTHALMOLOGY
The Eye M.D. Association

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GLAUCOMA PREFERRED PRACTICE PATTERN® DEVELOPMENT PROCESS AND PARTICIPANTS

The **Glaucoma Preferred Practice Pattern® Panel** members wrote the Primary Open-Angle Glaucoma Suspect Preferred Practice Pattern® guidelines ("PPP"). The PPP Panel members discussed and reviewed successive drafts of the document, meeting in person twice and conducting other review by e-mail discussion, to develop a consensus over the final version of the document.

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The **Preferred Practice Patterns Committee** members reviewed and discussed the document during a meeting in April 2015. The document was edited in response to the discussion and comments.

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The Primary Open-Angle Glaucoma Suspect PPP was then sent for review to additional internal and external groups and individuals in July 2015. 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 PPP Panel reviewed and discussed these comments and determined revisions to the document.

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FINANCIAL DISCLOSURES

In compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies (available at www.cmss.org/codeforinteractions.aspx), 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 (56%) of the members of the Glaucoma Preferred Practice Pattern Panel 2014–2015 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 August 2015 are available online at www.aao.org/ppp.

TABLE OF CONTENTS

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 Relationship with Industry Procedures (available at www.aao.org/about-preferred-practice-patterns) to comply with the Code.

Appendix 2 contains the International Statistical Classification of Diseases and Related Health Problems (ICD) codes for the disease entities that this PPP covers. Appendix 3 has an algorithm for the management of primary open-angle glaucoma (POAG) suspect. The intended users of the Primary Open-Angle Glaucoma Suspect 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:

I++	High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias
I+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
I-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
II++	High-quality systematic reviews of case-control or cohort studies 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
II+	Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
II-	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
III	Nonanalytic studies (e.g., case reports, case series)

- 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:

Good quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Insufficient quality	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 Any estimate of effect is very uncertain

- Key recommendations for care are defined by GRADE[2] as follows:

Strong recommendation	Used when the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not
Discretionary recommendation	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

- The Highlighted Findings and Recommendations for Care section lists points determined by the PPP Panel 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 June 2014 in the PubMed and Cochrane databases. Complete details of the literature search are available in Appendix 4.

HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

A diagnosis for primary open-angle glaucoma (POAG) suspect is established by the presence of one of the following conditions: a consistently elevated intraocular pressure (IOP), a suspicious-appearing optic nerve, or abnormal visual field.

Highlights of established risk factors for a POAG suspect diagnosis include an elevated IOP, family history of glaucoma or glaucoma suspect, thin central cornea, race, older age, myopia, and type 2 diabetes.

The decision to treat a POAG suspect patient may depend on evidence of optic nerve changes, any visual field defect, level of IOP, and other associated risk factors.

In the Ocular Hypertension Treatment Study (OHTS) overall, 90% to 95% of patients with ocular hypertension did not go on to develop glaucoma over 5 years, but treatment to reduce IOP also reduced the risk of developing POAG from 9.5% to 4.5%.[4]

A reasonable target for IOP reduction in a POAG suspect patient is 20%, based on the OHTS.

Appropriate testing to evaluate and monitor patients with OAG includes gonioscopy, pachymetry, tonometry, perimetry, careful observation of the optic nerve, and ocular imaging.

If a decision is made to treat IOP, options include medical eye drops or laser trabeculoplasty.

INTRODUCTION

DISEASE DEFINITION

A glaucoma suspect is an individual with clinical findings and/or a constellation of risk factors that indicate an increased likelihood of developing primary open-angle glaucoma (POAG).

CLINICAL FINDINGS CHARACTERISTIC OF PRIMARY OPEN-ANGLE GLAUCOMA SUSPECT

The clinical findings in one or both eyes of an individual with an open anterior chamber angle that define a glaucoma suspect patient are any of the following: 1) an appearance of the optic disc or retinal nerve fiber layer (RNFL) that is suspicious for glaucomatous damage; 2) a visual field suspicious for glaucomatous damage in the absence of clinical signs of other optic neuropathies; or 3) consistently elevated intraocular pressure (IOP) associated with normal appearance of the optic disc, RNFL, and visual field.

This definition excludes the angle-closure glaucomas and known secondary causes for open-angle glaucoma, such as pseudoexfoliation (exfoliation syndrome), pigment dispersion, and traumatic angle recession.

PATIENT POPULATION

The patient population includes adults with open anterior chamber angles with one of the clinical findings or risk factors listed in the Clinical Findings Characteristic of Primary Open-Angle Glaucoma Suspect section.

CLINICAL OBJECTIVES

- Identify patients at high risk of developing POAG
- Document the status of the optic nerve structure at presentation by clinical evaluation and imaging, and document visual function by visual field testing
- Consider treatment of high-risk individuals to prevent or delay the development of POAG
- Minimize the side effects of treatment and the impact of treatment on the patient's vision, general health, and quality of life
- Educate and involve the patient and appropriate family members/caregivers in the management of the patient's condition

BACKGROUND

PREVALENCE

Studies have not documented the cumulative prevalence of glaucoma suspect because there are multiple definitions for abnormal visual fields, IOP, optic disc damage, and retinal nerve fiber abnormalities. Furthermore, several studies suggest that features of the eye such as cup-to-disc ratio and IOP may be associated with myopia,[5] ethnoracial groups,[6-8] and family history.[9]

However, studies have documented the prevalence of ocular hypertension in the United States. Ocular hypertension may be defined as IOP in the highest 97.5% percentile for the population that does not have optic disc or visual field damage.[6]

In the United States, this definition usually includes an IOP greater than 21 mmHg. Using this definition, the prevalence of ocular hypertension in non-Hispanic whites who are age 40 years and older and live in the United States is 4.5% (ranging from 2.7% in persons 43 to 49 years old to 7.7% in those 75 to 79 years old).[10] In Latinos age 40 years and older, the overall prevalence is 3.5% (ranging from 1.7% in persons 40 to 49 years old to 7.4% in those 80 and older).[11] There are no published population-based estimates for the prevalence of ocular hypertension in African Americans and Asian Americans. Overall, 3 to 6 million persons in the United States have ocular hypertension.[12]

The prevalence of ocular hypertension may be even higher because the majority of people with ocular hypertension may be undiagnosed. For example, the Los Angeles Latino Eye Study (LALES) showed that 75% of Latinos with IOP greater than 21 mmHg were previously undiagnosed.[11] Because ocular hypertension is a major risk factor for development of glaucoma, eye care providers should measure IOP in all of their patients over 40. However, the overall likelihood of *developing* glaucomatous optic neuropathy increases with the number and relative strength of risk factors.

RISK FACTORS

The findings of epidemiological investigations and clinical trials provide a framework for assessing the risk factors associated with POAG. Numerous studies have identified risk factors associated with POAG:

- Higher IOP[4,13-23]
- Older age[4,13,16,17,24-26]
- Family history of glaucoma[17,27]
- African race or Latino/Hispanic ethnicity
- Thinner central cornea[4,13,28]
- Lower ocular perfusion pressure[27,29,30]
- Type 2 diabetes mellitus[31-34]
- Myopia[29,35-37]
- Lower systolic and diastolic blood pressure[27]
- Disc hemorrhage[38-42]
- Larger cup-to-disc ratio[4,13]
- Higher pattern standard deviation on threshold visual field testing[23,43]

Although disc hemorrhage, increased cup-disc ratio, and higher pattern standard deviation are considered to be risk factors for the development of POAG, it can also be argued that these signs represent early optic nerve damage and visual field damage from glaucoma.

Even though there are some conflicting data on the association between type 2 diabetes mellitus and POAG,[17,31-33,44-49] there is increasing evidence from population-based studies suggesting that type 2 diabetes mellitus is an important risk factor for POAG.[31-33,45,47] Population-based assessments of Hispanics (in Los Angeles, California),[32] non-Hispanic whites (in Beaver Dam, Wisconsin, and Blue Mountains, Australia),[31,47] and a large cohort enrolled in the Nurses' Health Study[45] have shown that persons with type 2 diabetes mellitus are more likely (40% higher odds in Hispanics, twofold higher odds in non-Hispanic whites) to have POAG. Further, in the LALES,[32] longer duration of type 2 diabetes mellitus was associated with a higher risk of having POAG. One explanation for this observation is that microvascular changes in the optic nerve may contribute to the greater susceptibility of optic nerve damage in persons with type 2 diabetes mellitus.[46] A recent meta-analysis of 47 studies concluded that diabetes mellitus is associated with increased risk of glaucoma and may be associated with elevated IOP.[34]

Other risk factors that have been associated with open-angle glaucoma include migraine headache, peripheral vasospasm, concurrent cardiovascular disease, systemic hypertension, and myopia.[13,50-54] However, the association between these risk factors and the development of glaucomatous optic nerve damage has not been demonstrated consistently.[13,25,29,35,55-59]

DETECTION

Patients suspected of having POAG can be identified during a comprehensive adult medical eye evaluation.[60] Although an assessment of IOP can identify individuals who are ocular hypertensive, an assessment of the optic nerve and the visual field is required to identify patients who have glaucoma without ocular hypertension.

In 2000, Medicare began providing a benefit for a glaucoma screening for patients with the following risk factors:

- Family history of glaucoma
- History of diabetes
- African American and age 50 or older
- Hispanic and age 65 or older (risk factor added in 2006)

CARE PROCESS

PATIENT OUTCOME CRITERIA

- Preservation of visual function
- Maintenance of quality of life
- Detection of progression to POAG at the earliest possible stage

DIAGNOSIS

The comprehensive initial glaucoma suspect evaluation (history and physical examination) includes all components of the comprehensive adult medical eye evaluation[60] in addition to and with special attention to those factors that specifically bear upon the diagnosis, course, and treatment of POAG. The evaluation may require more than one visit. For instance, an individual might be suspected of having POAG on one visit but may return for further evaluation to confirm the diagnosis, including additional IOP measurements, gonioscopy, central corneal thickness (CCT) determination, visual field assessment, and optic nerve head (ONH) and RNFL evaluation and documentation.

History

- Ocular history (e.g., refractive error, trauma requiring surgery)
- Family history.[18,61,62] The severity and outcome of glaucoma in family members, including a history of visual loss from glaucoma, should be obtained during initial evaluation.[61,62]
- Systemic history (e.g., asthma, migraine headache, vasospasm, cardiovascular disease)
- Review of pertinent records, with particular reference to the IOP and the status of the optic nerve and visual field
- Ocular and nonocular medications (e.g., corticosteroids) and known local or systemic intolerance to ocular or nonocular medications
- Ocular surgery

It is important to note that a history of LASIK or photorefractive keratectomy has been associated with a falsely low IOP measurement due to thinning of the cornea.[63-65] In addition, cataract surgery may lower the IOP when compared with the presurgical baseline.[66,67]

Evaluation of Visual Function

Self-reported functional status or difficulty with vision can be assessed either through patient complaints or by using specific questionnaires, including the National Eye Institute - Visual Function Questionnaire-25 and Glau-QOL.[68-76] Patients who are glaucoma suspects are likely to be asymptomatic, but patients who have progressed to definite glaucoma may have sufficient visual field loss to impair night driving, near vision, reading speed, and outdoor mobility.[77-84]

Physical Examination

The ophthalmic evaluation focuses specifically on the following elements in the comprehensive adult medical eye evaluation:[60]

- Visual acuity measurement
- Pupil examination
- Anterior segment examination
- IOP measurement
- Gonioscopy
- ONH and RNFL examination
- Fundus examination

Visual acuity measurement

The best-corrected visual acuity, at distance and at near, should be determined.

Pupil examination

The pupils are examined for reactivity and for a relative afferent pupillary defect.[85-87]

Anterior segment examination

Slit-lamp biomicroscopic examination of the anterior segment can provide evidence of physical findings associated with narrow angles, such as shallow peripheral anterior chamber depth and crowded anterior chamber angle anatomy,[88,89] corneal pathology, or a secondary mechanism for elevated IOP. Secondary mechanisms for elevated IOP can include pseudoexfoliation material on the pupil margin; anterior lens capsule or corneal endothelium (exfoliation syndrome); pigment dispersion with spoke-like; mid-peripheral radial iris transillumination defects; iris and angle neovascularization; or inflammation.

Intraocular pressure measurement

Results from the OHTS demonstrate that lowering an elevated IOP reduces the risk of progression of glaucomatous visual field and optic nerve damage.[4] It is important to determine the full extent of IOP fluctuation over time to determine who is most at risk of developing glaucoma and, therefore, whom to treat to prevent future glaucoma. Intraocular pressure is measured in each eye, preferably by Goldmann applanation tonometry, before gonioscopy or dilation of the pupil.[90] Recording time of day of IOP measurements may be helpful to assess diurnal variation. Unrecognized IOP fluctuations may be associated with an increased risk of developing glaucomatous damage.[91-100] Therefore, additional IOP measurements may be indicated, either at different hours of the day on the same day or on different days.

Gonioscopy

The diagnosis of POAG requires careful evaluation of the anterior chamber angle to exclude angle closure or secondary causes of IOP elevation, such as angle recession, pigment dispersion, peripheral anterior synechiae, angle neovascularization, and inflammatory precipitates.[101] A useful technique for examining the angle in an eye with a narrow anterior chamber is to have the patient look towards the mirror of the gonioprism into which the examiner is looking.

(See www.gonioscopy.org and Selected Reference Texts section for discussion of the techniques of gonioscopy.)

Optic nerve head and retinal nerve fiber layer examination

There is evidence that glaucomatous changes detected by optic disc and RNFL examination may precede defects detected by standard automated perimetry.[102-108] In OHTS, optic nerve damage alone without visual field loss occurred in 69 eyes and accounted for 55% of the study endpoints reached.[4]

Examination of the ONH and RNFL provides valuable structural information about glaucomatous optic nerve damage.[104,106,109-111] Physical features that may indicate glaucomatous optic neuropathy include the following:

- Vertical elongation of the optic cup, with associated decrease in neuroretinal rim width
- Excavation of the cup
- Thinning of the RNFL
- Notching of the neuroretinal rim
- Thinning of the inferior and/or superior neuroretinal rim
- Disc hemorrhage
- Parapapillary atrophy
- Nasalization of central ONH vessels
- Baring of the circumlinear vessel
- Absence of neuroretinal rim pallor

Normally, the neuroretinal rim of the optic nerve is widest inferiorly and narrowest temporally. The abbreviated corollary for this anatomic feature is called the ISNT rule: it is widest at the inferior rim, followed by the superior rim, followed by the nasal rim, and lastly by the temporal rim. In approximately 80% of patients with glaucomatous cupping, the nerve contour does not follow this rule, and both the inferior and superior rims are thinned.[112,113]

Visible structural alterations of the ONH or RNFL and development of parapapillary choroidal atrophy in early glaucoma may precede the onset of visual field defects.[104,114-116] Other investigations have reported functional deficits occurring in advance of structural change.[117,118] Careful study of the optic disc neural rim for small hemorrhages is important because these hemorrhages sometimes herald focal disc damage and visual field loss, and they may signify ongoing optic nerve damage in patients with glaucoma.[119-132] In the OHTS, the incidence of POAG in eyes with disc hemorrhage was 13.6% compared with 5.2% in eyes without disc hemorrhage over 8 years.[127] In the Early Manifest Glaucoma Trial, 13% of patients had disc hemorrhages at baseline examination, and hemorrhages were associated with progression.[120]

The appearance of the optic nerve should be documented.[106,110,133] The preferred technique for ONH evaluation involves magnified stereoscopic visualization (as with the slit-lamp biomicroscope), preferably through a dilated pupil. In some cases, direct ophthalmoscopy complements magnified stereoscopic visualization, providing additional information of optic nerve detail as a result of the greater magnification of the direct ophthalmoscope. Red-free illumination of the posterior pole may aid in evaluating the RNFL.[134] Color stereophotography is an accepted method for documenting qualitative ONH appearance. Computer-based imaging analysis of the ONH and RNFL is a complementary method for documenting of the optic nerve and is discussed in the Diagnostic Ophthalmic Testing section below. Computer-based imaging and stereoscopic photography of the optic nerve provide different information about optic nerve status, and both are useful adjuncts to a good clinical examination.

Fundus examination

Examination of the fundus through a dilated pupil whenever feasible includes a search for other abnormalities that may account for optic nerve changes and/or visual field defects (e.g., optic nerve pallor, disc drusen, optic nerve pits, disc edema from central nervous system disease, macular degeneration, retinovascular occlusion, or other retinal disease).

Diagnostic Testing

Important ophthalmic testing includes the following components:

- Central corneal thickness measurement
- Visual field evaluation
- ONH and RNFL imaging

Central corneal thickness measurement

Measurement of CCT aids the interpretation of IOP readings and helps to stratify patient risk for ocular damage.[13,135-137] In the OHTS and European Glaucoma Prevention Study (EGPS) trials, the average CCT in the ocular hypertension group was 570 μm, and the risk of developing POAG was greater in eyes with corneal thickness less than 555 μm compared with eyes with corneal thickness 588 μm or greater. An overestimation of the real IOP as measured by Goldmann applanation tonometry may occur in eyes with corneas that are thicker than average, whereas an underestimation of the real IOP tends to occur in eyes with corneas that are thinner than average. An exception to this is that the measurement of IOP is underestimated in eyes with large amounts of corneal edema.[138] Several studies have sought to quantify the relationship between measured IOP level and CCT, but there is no generally accepted correction formula. The World Glaucoma Association Consensus on IOP suggests that a correction factor should not be used to adjust values measured in individual patients.[138] There is a controversy over whether CCT represents a risk factor for glaucoma because of its effect on IOP measurement or whether CCT is a risk factor itself, unrelated to IOP.[139-144] Although it is clear that thinner CCT is a risk factor for the development of POAG,[13] studies of progression have had variable findings. Some (but not all) studies found an association with thin CCT (see Table 1).[132]

TABLE 1 SUMMARY OF RESULTS FOR CENTRAL CORNEAL THICKNESS AS A RISK FACTOR FOR PROGRESSION OF GLAUCOMA

Study	No. of Patients	Level of Evidence	Risk	Comments
Early Manifest Glaucoma Trial[122]	255	I	+	Thin CCT is a risk factor for progression of glaucoma (in patients with baseline IOP ≥21 mmHg)
Kim and Chen[145]	88	II	+	Thin CCT is associated with visual field progression in glaucoma
Chauhan, et al[146]	54	II	-	CCT did not predict visual field or optic disc progression
Jonas, et al[147]	454	II	-	CCT is not associated with progression of visual field damage
Jonas, et al[148]	390	II	-	CCT is not associated with optic disc hemorrhages
Congdon, et al[149]	230	II	-	CCT is not associated with glaucoma progression (although low corneal hysteresis is associated with glaucoma progression)
Stewart, et al[150]	310	III	+/-	CCT is associated with progression on univariate analysis but is not associated on multivariate analysis

CCT = central corneal thickness

Adapted with permission from Dueker D, Singh K, Lin SC, et al. Corneal thickness measurement in the management of primary open-angle glaucoma: a report by the American Academy of Ophthalmology. Ophthalmology 2007;114:1784.

Visual field evaluation

Eye care providers evaluate the visual field using automated static threshold perimetry (SAP) with white-on-white stimuli. It is the gold standard test for comparing other types of visual field testing.[151] Careful manual combined kinetic and static threshold testing (e.g., Goldmann visual fields) is an acceptable alternative when patients cannot perform automated perimetry reliably or if it is not available. If visual field glaucomatous damage is newly detected in a glaucoma suspect patient, it is best to repeat the testing to confirm the changes.[152] *(II++, good quality, strong recommendation)*

Frequency doubling technology and short-wavelength automated perimetry (SWAP) are two of several alternative testing methods shown to be helpful in screening for early visual field damage especially when SAP is normal.[151,153,154] The frequency doubling technology measures contrast sensitivity for a frequency doubling stimulus and has been shown to demonstrate high sensitivity and specificity to detect glaucomatous defects that have later been predictive of functional loss measured by SAP in glaucoma suspect patients.[155-159] Visual field testing based on SWAP[160] isolates short-wavelength sensitive cells using a narrow band of blue-light stimulus on a yellow background-illuminated perimeter bowl. Clinicians may use these selective functional tests to diagnose early visual loss in glaucoma suspects, but studies have not demonstrated clear advantages over standard automated achromatic visual field testing (e.g., SAP).[161-163]

Optic nerve head and retinal nerve fiber layer imaging

The appearance of the optic nerve and, if possible, the RNFL, should be documented for the glaucoma suspect patient.[106,133] *(II++, good quality, strong recommendation)* Although they are distinctly different methodologies, stereoscopic disc photographs and computerized images of the nerve are complementary with regard to the information they provide the clinician who must manage the patient.[164] In the absence of these methodologies, a nonstereoscopic photograph or a drawing of the ONH should be recorded, but this is a less desirable alternative to stereophotography or computer-based imaging.[165-168] *(III, insufficient evidence, strong recommendation)* In some cases, the topography of the disc is difficult to appreciate on stereo photographs. When the optic disc is saucerized with a paucity of vessels, the topography is often not easily seen on photographs, and a disc drawing obtained by using a narrow slit beam of light moving across the disc may be needed for additional documentation of this anatomic variation. There is limited benefit of using stereophotography or digital imaging to identify progressive optic nerve change in patients with advanced glaucomatous optic neuropathy because there is little if any nerve tissue to evaluate or measure.[169,170]

Computer-based digital imaging of the ONH and RNFL is routinely used to provide quantitative information to supplement the clinical examination of the optic nerve. A substantial number of patients demonstrate structural alterations in the ONH, parapapillary RNFL, and macular areas of the RNFL before functional change occurs. One rationale for using computerized imaging is to distinguish glaucomatous damage from eyes without glaucoma when thinning of the RNFL is measured, thereby facilitating earlier diagnosis and detection of optic nerve damage.[107,108,171] There are three types of computer-based optic nerve imaging devices available for glaucoma: confocal scanning laser ophthalmoscopy (CSLO), optical coherence tomography (OCT), and scanning laser polarimetry. The versions of these devices that were studied in a systematic review were similar in their ability to distinguish glaucoma from controls.[106,172,173] It is important to remember that reported results from these devices do not always represent disease.[174] Criteria used to establish normative databases vary between different imaging devices. Some individual disc findings will not fall into the normative database that is used to establish abnormality, and results should be interpreted cautiously. Therefore, results from these tests must be interpreted in the context of the clinical examination and other supplementary tests in order to avoid falsely concluding that a statistically abnormal result on imaging represents true abnormality. As in these instruments continue to improve, they may become more reliable in helping the clinician diagnose glaucoma and to identify progressive nerve

damage.[107,108,171] Furthermore, progression analysis programs for computer-based imaging devices are evolving to better detect optic nerve and RNFL changes that may be secondary to glaucoma,[175,176] though these programs are still limited by a lack of longitudinal information on whether these structural changes eventually lead to visual field loss.[176]

Because some patients show visual field loss without corresponding optic nerve progression,[4,102,175-178] both structural and functional assessments remain integral to patient care. Even though digital imaging technology is approved as an adjunct to aid in glaucoma diagnosis, the clinician should include all perimetric and other structural information when formulating patient management decisions.[164] (*III, insufficient quality, strong recommendation)* As device technology evolves (e.g., specific reference databases, higher resolution spectral domain OCT), the performance of diagnostic imaging devices is expected to improve accordingly.

Differential Diagnosis

Glaucoma is a chronic, progressive optic neuropathy associated with several risk factors, including IOP, that contribute to damage. A characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons result in progressive visual field loss. Other entities associated with optic disc damage or abnormalities of the visual field should be considered prior to accepting the diagnosis of glaucoma. These nonglaucomatous diseases (and examples) are categorized as follows:

- Optic disc abnormalities
  - Anterior ischemic optic neuropathies
  - Optic nerve drusen
  - Myopic tilted optic nerves
  - Toxic optic neuropathies
  - Congenital pit
  - Congenital disc anomalies (e.g., coloboma, periventricular leukomalacia, Morning Glory syndrome)
  - Leber hereditary optic neuropathy and dominant optic atrophy
  - Optic neuritis
- Retinal abnormalities
  - Age-related macular degeneration
  - Panretinal photocoagulation
  - Retinitis pigmentosa
  - Retinal arterial and venous occlusions
- Central nervous system abnormalities
  - Compressive optic neuropathy
  - Demyelination from multiple sclerosis
  - Nutritional optic neuropathy
  - Dominant optic atrophy

MANAGEMENT

Goals

The goals of managing patients with POAG suspect are as follows:

- Monitor or lower IOP through treatment if an eye is likely to progress to POAG or to develop progressive optic disc, RNFL, or visual damage
- Monitor for changes in the optic disc and RNFL
- Monitor for changes in the visual field

Intraocular pressure is the only modifiable parameter in glaucoma and glaucoma suspect patients. The decision to begin treatment to lower IOP in the glaucoma suspect patient is complex and based on the ophthalmologist's analysis of the examination results, risk assessment, and evaluation of the patient and the patient's preferences. The number and severity of risk factors present, the prognosis, management plan, and likelihood that therapy, once started, can be long term, should be discussed with the patient and, when feasible, with the patient's family. *(good quality, strong recommendations)* Risk assessment based on OHTS and EGPS may be helpful in managing the patient with glaucoma suspect.[43]

In the OHTS overall, 90% to 95% of patients with ocular hypertension did not go on to develop glaucoma over 5 years, but treatment to reduce IOP also reduced the risk of developing POAG from 9.5% to 4.5%.[4] And, since therapy exposes patients to the risks, side effects, and expense of long-term treatment, the decision to begin treatment for a glaucoma suspect patient is particularly important. For some patients, the risk of developing POAG is sufficiently high to justify starting treatment.[4,13,179] For example, in the OHTS, untreated patients with a baseline IOP of 26 mmHg or above and a CCT of 555 µm or below had a 36% chance of developing optic nerve damage during long-term follow-up compared with a 2% risk for patients with a baseline IOP of less than 24 mmHg and a CCT greater than 588 µm.[13] Whether or not a patient is treated, long-term monitoring for the development of glaucoma is essential.

When treatment is appropriate, an effective medication regimen requires attention to its effect on IOP, side effects, and to the possibility of nonadherence to therapy. Laser trabeculoplasty should be considered when nonadherence, cost, convenience, side effects, or risks of medication are factors. *(good quality, strong recommendation)* The ophthalmologist should consider these issues in choosing a regimen that works well to lower IOP with the least possible side effects. *(good quality, strong recommendation)* The diagnosis, number and severity of risk factors, prognosis and management plan, and likelihood of long-term therapy should be discussed with the patient. *(good quality, strong recommendation)*

Deciding When to Treat a Glaucoma Suspect Patient

The decision to treat a glaucoma suspect patient may arise in various settings.

- Any patient who shows evidence of optic nerve deterioration based on ONH appearance, RNFL loss, or visual field changes consistent with glaucomatous damage has developed POAG and should be treated as described in the Primary Open-Angle Glaucoma PPP.[180] Clinicians can recognize subtle abnormalities in the optic disc and RNFL using periodic fundus imaging with disc and RNFL photography and computerized imaging of the optic nerve and nerve fiber layer.[104,181]
- A new visual field defect that is consistent with a pattern of glaucomatous visual field defect, confirmed on retesting of visual fields, may indicate that the patient has developed POAG.[152,182]
- A patient who demonstrates very high IOP in which optic nerve damage is likely to occur may require treatment.
- In some cases, initiating treatment to lower the risk of glaucomatous damage may be appropriate if the patient has risk factors for glaucoma. Established risk factors for a patient who goes from a diagnosis of "POAG suspect" to "developing POAG" include a higher IOP, older age, family history of glaucoma, African ancestry or Latino/Hispanic ethnicity, type 2 diabetes mellitus, myopia, lower ocular perfusion pressure, lower systolic and diastolic blood pressure, thinner central cornea, disc hemorrhage, larger cup-to-disc ratio, and higher pattern standard deviation on threshold visual field testing.
- Clinicians may consider using a risk calculator for determining the risk of glaucoma from ocular hypertension.[43,183-185] These calculators determine the overall risk of developing glaucoma in 5 years using the risk factors of age, vertical cup-to-disc ratio, pattern standard deviation (from standard automated achromatic visual field testing), CCT, and IOP. Risk calculators are available for free from http://ohts.wustl.edu/risk/calculator.html. They are also available as applications for smartphones.

Whatever the scenario, a discussion must occur between the physician and patient to outline the risks and benefits of treatment versus observation.

Target Intraocular Pressure

When deciding to treat a glaucoma suspect patient, it is important to remember that the goal of treatment is to maintain the IOP in a range at which visual field loss is unlikely to significantly affect a patient's health-related quality of life over his or her lifetime.[186] *(II+, moderate quality, discretionary recommendation)* The estimated upper limit of this range is considered the "target pressure." Target pressure can vary among these patients, and in the same patient it may need adjustment during the clinical course. In any patient, target pressure is an estimate and a means toward the ultimate goal of protecting the patient's vision. It is reasonable to begin by choosing a target pressure of 20% lower than the mean of several baseline IOP measurements based on criteria from OHTS.[4] *(I+, moderate quality, discretionary recommendation)* Current IOP and its relationship to target IOP should be evaluated at each visit and individualized for each patient.

A definite deterioration in optic nerve structure or visual field (i.e., conversion to glaucoma patient) in a patient who is a glaucoma suspect suggests that the target pressure should be lower,[120,187] and the patient should be managed as described in the Primary Open-Angle Glaucoma PPP.[180]

Choice of Therapy

Clinicians have many suitable medications for lowering IOP in glaucoma suspects. Their choice of medication may be influenced by costs, side effects, and dosing schedules. (See Table 2 for an overview of options available.) Patients adhere to therapy best when they are using the fewest number of eye drops with the least side effects to achieve the target IOP. If target IOP is not achieved by one medication, then additional separate medications, combination therapies, switching treatments, or laser trabeculoplasty may be considered.

TABLE 2 GLAUCOMA MEDICATIONS

Drug Classification	Methods of Action	IOP Reduction*	Potential Side Effects	Potential Contraindications	FDA Pregnancy Safety Category†
Prostaglandin analogs	Increase uveoscleral and/or trabecular outflow	25%–33%	• Increased and misdirected eyelash growth • Periocular hyperpigmentation • Conjunctival injection • Allergic conjunctivitis/contact dermatitis • Keratitis • Possible herpes virus activation • Increased iris pigmentation • Uveitis • Cystoid macular edema • Periorbitopathy • Migraine-like headache • Flu-like symptoms	• Macular edema • History of herpetic keratitis • Active uveitis	C
Beta-adrenergic antagonists (beta-blockers)	Decrease aqueous production	20%–25%	• Allergic conjunctivitis/contact dermatitis • Keratitis • Bronchospasm (seen with nonselective) • Bradycardia • Hypotension • CHF (classic teaching, although cardiologists use beta-blockers as first line treatment in CHF) • Reduced exercise tolerance • Depression • Impotence	• Chronic obstructive pulmonary disease (nonselective) • Asthma (nonselective) • CHF • Bradycardia • Hypotension • Greater than first-degree heart block	C

TABLE 2 GLAUCOMA MEDICATIONS (CONTINUED)

Drug Classification	Methods of Action	IOP Reduction*	Potential Side Effects	Potential Contraindications	FDA Pregnancy Safety Category†
Alpha-adrenergic agonists	Nonselective: improve aqueous outflow Selective: decrease aqueous production; decrease episcleral venous pressure or increase uveoscleral outflow	20%–25%	• Allergic conjunctivitis/contact dermatitis • Follicular conjunctivitis • Dry mouth and nose • Hypotension • Headache • Fatigue • Somnolence	• Monoamine oxidase inhibitor therapy • Infants and children younger than 2 years	B
Parasympathomimetic agents	Increase trabecular outflow	20%–25%	• Increased myopia • Decreased vision • Cataract • Periocular contact dermatitis • Allergic conjunctivitis/contact dermatitis • Conjunctival scarring • Conjunctival shrinkage • Keratitis • Paradoxical angle closure • Retinal tears/detachment • Eye or brow ache/pain • Increased salivation • Abdominal cramps	• The need to regularly assess the fundus • Neovascular, uveitic, or malignant glaucoma	C
Topical carbonic anhydrase inhibitors (mainly with systemic use)	Decrease aqueous production	15%–20%	• Allergic dermatitis/conjunctivitis • Corneal edema • Keratitis • Metallic taste	• Sulfonamide allergy • Kidney stones • Aplastic anemia • Thrombocytopenia • Sickle cell disease	C
Oral carbonic anhydrase inhibitors	Decrease aqueous production	20%–30%	• Stevens-Johnson syndrome • Malaise, anorexia, depression • Serum electrolyte imbalance • Renal calculi • Blood dyscrasias (aplastic anemia, thrombocytopenia) • Metallic taste • Enuresis • Parasthesia • Diarrhea • Abdominal cramps	• Sulfonamide allergy • Kidney stones • Aplastic anemia • Thrombocytopenia • Sickle cell disease	C
Hyperosmotic agents	Dehydration of vitreous	No data	• Headache • CHF • Nausea, vomiting • Diarrhea • Renal failure • Diabetic complications • Mental confusion	• Renal failure • CHF	C

CHF = congestive heart failure; IOP = intraocular pressure

* Data from the Heijl A, Traverso CE, eds. Terminology and Guidelines for Glaucoma. European Glaucoma Society. 4th ed. Savona, Italy: PubliComm; 2014:146-51. Available at: www.eugs.org/eng/EGS_guidelines4.asp. Accessed May 29, 2015.

† FDA Pregnancy Category B = Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies on pregnant women. FDA Pregnancy Category C = Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Adapted with permission from the American Academy of Ophthalmology Practicing Ophthalmologists Curriculum (POC) Panel Chairs and Vice Chairs. Practicing Ophthalmologists Curriculum 2014–2016. Glaucoma. Available at: http://one.aao.org/POCTopics. Accessed May 29, 2015.

Prostaglandin analogs are the most frequently used initial eye drops for lowering IOP.[188,189] They are the most effective drugs at lowering IOP, and they are relatively safe. They are, therefore, often considered as initial medical therapy unless other considerations such as contraindications, cost, side effects, intolerance, or patient refusal preclude this.[190,191] Other agents include beta-adrenergic antagonists, alpha$_2$ adrenergic agonists, topical and oral carbonic anhydrase inhibitors, and parasympathomimetics.[192,193]

To determine the effectiveness of topical therapy, it is necessary to distinguish between the therapeutic impact of an agent on IOP and ordinary background spontaneous fluctuations of IOP. Though the monocular trial has been recommended in the past to determine whether a glaucoma medication is effective, recent studies have shown that it is not a good predictor of long-term efficacy.[194,195] A monocular trial is defined as the initiation of treatment in only one eye, followed by a comparison of the relative change of the IOP in both eyes at follow-up visits to account for spontaneous fluctuations in IOP. However, the trial may not work because the two eyes of an individual may respond differently to the same medication, asymmetric spontaneous fluctuations in IOP may occur, and monocular topical medications may have a contralateral effect.[196] A better way to assess IOP-lowering response is to compare the effect in one eye with multiple baseline measurements in the same eye, but the number of necessary baseline measurements will vary among patients.[197] *(II+, moderate quality, discretionary recommendation)*

If a drug fails to reduce IOP sufficiently, then either switching to an alternative medication as monotherapy or adding additional medication is appropriate until the desired IOP level is attained.[133] *(III, good quality, strong recommendation)* Since some studies have shown that adding a second medication decreased adherence to glaucoma treatment,[198,199] fixed combination therapy may improve patient adherence even though it is not recommended for initial treatment.

The patient and the ophthalmologist together decide on a practical and feasible regimen to follow in terms of dosing, cost, and adherence in the context of the patient's age and preferences.[133] The ophthalmologist should assess the patient for local ocular and systemic side effects and toxicity, including interactions with other medications and potential life-threatening adverse reactions. *(good quality, strong recommendation)* Patients can be educated about eyelid closure or nasolacrimal occlusion to reduce systemic absorption after medication instillation (see Related Academy Materials section for patient education brochures).[200]

Adequate treatment to lower IOP requires a high level of adherence to therapy, but this is frequently not achieved. Several studies indicate relatively poor adherence to therapy.[201-204] Even with instruction, free medication, once-daily administration, use of a dosing aid, and electronic monitoring of adherence, nearly 45% of patients with glaucoma in one study took fewer than 75% of their prescribed doses.[204] Fixed combinations of two medications may improve patient adherence by reducing the number of drops required for therapy. Instilling eye drops correctly is difficult for many patients, and their ability to do so may worsen with aging, comorbidities, and as glaucoma progresses.[205,206] Repeated instruction and counseling about proper techniques for using medication as well as a clearly written medication regimen and follow-up telephone calls may improve adherence to therapy.[204,207,208] At each examination, medication dosage and frequency of use should be recorded. *(good quality, strong recommendation)* Reviewing the time of day when medication was taken may be useful to help patients link eye-drop administration to activities of daily living and to be sure patients are actually using their eye drops. Adherence to the therapeutic regimen and recommendations for therapeutic alternatives, such as laser trabeculoplasty, or diagnostic procedures should be discussed. *(good quality, strong recommendation)* Cost may be a factor in adherence, especially when multiple medications are used.[208,209] Patient education and informed participation in treatment decisions may improve adherence[208] and overall effectiveness of management. Adherence is also handicapped when patients run out of medication before they are permitted to refill their prescription. However, patients with Medicare insurance may now refill their medication after they have completed at least 70% of the month, or approximately 21 days of therapy.[210]

Laser trabeculoplasty may also benefit high-risk glaucoma suspect patients. For example, in patients who are at risk of not receiving continuous follow-up care or in patients who have very high IOP who prefer laser over medical therapy. If incisional surgery is to be considered, the patient can be managed as described in the Primary Open-Angle Glaucoma PPP.[180]

Special circumstances in pregnancy and during breast feeding

Pregnancy

Glaucoma medical management of the pregnant or nursing patient presents challenges with respect to balancing glaucoma progression[211] against concerns for the safety of the fetus or the infant.[212-214] Data on the risks of topical ocular hypotensive agents during pregnancy are limited. The FDA has established drug pregnancy categories of A, B, C, D, and X.[215] Pregnancy Category A indicates evidence from studies in pregnant women that the drug failed to show fetal risk, in any trimester. Category B indicates animal reproductive studies failed to show fetal risk, and that there are no well-controlled studies in pregnant women. Category C indicates that animal reproductive studies showed adverse effects on the fetus and that there are no well-controlled studies on pregnant women. Category D indicates evidence of human fetal risk. Category X indicates that animal and human studies showed fetal abnormalities. Brimonidine has a Pregnancy Category B rating. All other topical ocular hypotensive agents have a Pregnancy Category C rating. The beta-blockers tend to be used during pregnancy because there is long-term experience with this drug class. Very few data exist on the risk of taking latanoprost in pregnancy, although a small case series of 11 subjects who took it while pregnant revealed no adverse effects on pregnancy and no birth defects.[216] In general, most ophthalmologists avoid the use of prostaglandins during pregnancy because of the theoretical risk of premature labor, but these medications may be considered for use in the breast-feeding mother.[214]

Breast-feeding

Some topical glaucoma medications have been detected in breast milk, such as timolol and carbonic anhydrase inhibitors. The data are controversial as to whether timolol poses a threat to the breast-feeding infant. The American Academy of Pediatrics has approved the use of both oral and topical forms of carbonic anhydrase inhibitors during lactation, although the infant should be carefully monitored when the former are used.[214,217] Brimonidine is known to cross the blood-brain barrier and can cause apnea in infants. For this reason, it is usually recommended that the medication not be used in mothers who are breast-feeding.[213] *(III, good quality, strong recommendation)* In summary, managing glaucoma in the pregnant or lactating patient involves an interdisciplinary approach to balance disease progression in the mother while minimizing risks to the fetus and nursing infant.

Follow-up Evaluation

The purpose of follow-up examination is to evaluate IOP level, visual field status, optic disc appearance, and RNFL status to determine if damage has occurred. The interaction between patient and disease is unique for every patient, and management for each patient must always be individualized. Primary open-angle glaucoma suspect patients who are being observed should be seen at least every 12 to 24 months, depending on individual risk factors. *(good quality, strong recommendation)* However, if a patient has high risk factors for progression, then more-frequent reassessment is justified. Primary open-angle glaucoma suspect patients who are being treated may need to be seen more often until they are stable, and then they may be followed annually. These guidelines represent the consensus of an expert panel in the absence of conclusive scientific evidence in the literature.

History

The following interval history should be elicited during all follow-up visits for POAG suspect patients:

- Interval ocular history
- Interval systemic medical and medication history
- Side effects of ocular medications if the patient is being treated
- Frequency and time of last IOP-lowering medications and review of medication use if the patient is being treated

Ophthalmic examination

The following components of the ophthalmic examination should be performed during all follow-up visits for POAG suspect patients:

- Visual acuity measurement
- Slit-lamp biomicroscopy
- IOP measurement

The frequency of periodic ONH evaluation and documentation[165,218-220] and visual field evaluation[221-223] is based on an assessment of each patient's individual risk. A comprehensive adult medical eye evaluation and additional eye assessments can be performed on follow-up examination,[60] with more frequent follow-up if the patient is at higher risk for developing glaucoma. Patients with a thinner cornea,[4,13] higher IOP,[4,13-23] disc hemorrhage,[38-42,224] larger cup-to-disc, larger mean pattern standard deviation, evidence of pseudoexfoliation or pigment dispersion, or family history of glaucoma may warrant closer follow-up than patients with lower IOP, normal corneal thickness, and no disc hemorrhage. Gonioscopy is indicated when there is a suspicion of an angle-closure component, anterior chamber shallowing, anterior chamber angle abnormalities, or if there is an unexplained change in IOP. Gonioscopy should be performed periodically.

Adjustment of therapy

In glaucoma suspect patients, decisions for therapeutic intervention should aim to minimize risks from treatment, whereas in POAG, the decision to treat aims to minimize the risks of glaucoma disease progression. *(good quality, strong recommendation)* The indications for adjusting therapy in glaucoma suspect patients are as follows:

- Target IOP is not achieved and the benefits of a change in therapy outweigh the risks for the patient
- The patient is intolerant of the prescribed medical regimen
- The patient does not adhere to the prescribed medical regimen
- Contraindications to individual medicines develop
- The patient under treatment has been stable for a prolonged period without progression to POAG; in this case, cautious withdrawal of therapy may be considered

PROVIDER AND SETTING

The performance of certain diagnostic procedures (e.g., tonometry, pachymetry, perimetry, fundus imaging, and photography) may be delegated to appropriately trained and supervised personnel. However, the interpretations of results and the medical and surgical management of disease require the medical training, clinical judgment, and the experience of an ophthalmologist.

COUNSELING AND REFERRAL

It is important to educate and engage patients in the management of their condition by providing oral and written take-home and online information. This may be especially true for patients who are primary open-angle glaucoma suspects, since some authors have shown that follow-up is poor in patients with this diagnosis.[225,226] One reason for this was patients' perception that their disease was "not serious enough."[225] Patients should be educated about their condition and its potential to lead to the blinding disease glaucoma, the rationale and goals of intervention, the status of their condition, and the relative benefits and risks of alternative interventions so that they can participate meaningfully in developing an appropriate plan of action. *(good quality, strong recommendation)* Patients should be encouraged to alert their ophthalmologist to physical or emotional changes that occur when taking glaucoma medications, if prescribed. *(good quality, strong recommendation)* The ophthalmologist should be sensitive to these problems and provide support and encouragement.

Patients considering keratorefractive surgery should be informed about the possible impact laser vision correction has on reducing contrast sensitivity and decreasing the accuracy of IOP measurements.[65] *(good quality, strong recommendation)*

SOCIOECONOMIC CONSIDERATIONS

Although there is strong evidence that treatment of patients with bona fide open-angle glaucoma is cost-effective, it is less clear whether it is cost-effective to treat glaucoma suspects or patients with ocular hypertension. Results from the landmark OHTS clearly demonstrate that lowering IOP reduces the risk of progressing to glaucoma, yet the majority of patients in both the treated and untreated study arms never went on to develop glaucoma. Therefore, the additional costs of treating all of these patients need to be carefully considered relative to the benefits conferred by delaying or preventing glaucoma for a small subset of patients. Based on findings from OHTS, researchers studied the incremental cost-effectiveness of treating patients with ocular hypertension and determined that it was not considered cost-effective to treat all patients with this condition. However, they determined that treatment of patients with ocular hypertension who have an IOP of 24 mmHg or higher and a 2% or higher annual risk of developing glaucoma was indeed cost-effective.[209] These researchers also showed that patient life expectancy is an important consideration. For example, a 45-year old with ocular hypertension and a 2% or higher annual risk of glaucoma would require a life expectancy of at least 18 years for treatment to be considered cost-effective. Patients who are older at the time of first diagnosis of ocular hypertension would have to live even longer for treatment to be considered cost-effective.[227] Other authors performed a similar set of analyses and also concluded that treatment of all patients with ocular hypertension did not confer high value. However, treatment of persons with ocular hypertension who had risk factors for progressing to glaucoma (e.g., higher levels of IOP, thinner corneas, and greater cup-to-disc ratios) was indeed cost-effective.[228]

Another important question is whether it is cost-effective to screen patients for glaucoma. A systematic review of the literature on this topic concluded that screening an entire population for glaucoma is not cost-effective, but targeted screening of high-risk groups may be.[229] Since 2000, Medicare has continued to provide benefits for screening high-risk groups such as African Americans, Latinos, persons with a family history of glaucoma, and those with diabetes.[230] As the sensitivity, specificity, efficiency, and safety of equipment used to properly diagnose patients with glaucoma continue to improve, it is hoped that there will soon be ways to perform screenings of large numbers of patients for glaucoma in a manner that is cost-effective.

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. 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. INTERNATIONAL STATISTICAL CLASSIFICATION OF DISEASES AND RELATED HEALTH PROBLEMS (ICD) CODES

Primary open-angle glaucoma suspect includes the entity of primary open-angle suspect or borderline glaucoma and related entities with the following ICD-9 and ICD-10 classifications:

	ICD-9 CM	ICD-10 CM
Primary open-angle glaucoma suspect	365.00	H40.001
		H40.002
		H40.003
Preglaucoma, unspecified	365.00	H40.001
		H40.002
		H40.003
Open angle with borderline findings, low risk (e.g., borderline IOP or optic disc appearance suspicious of glaucoma)	365.01	H40.011
		H40.012
		H40.013
1–2 risk factors*		
Steroid responders	365.03	H40.041
		H40.042
		H40.043
Ocular hypertension	365.04	H40.051
		H40.052
		H40.053
Open angle with borderline findings, high risk	365.05	H40.021
3 or more risk factors*		H40.022
		H40.023

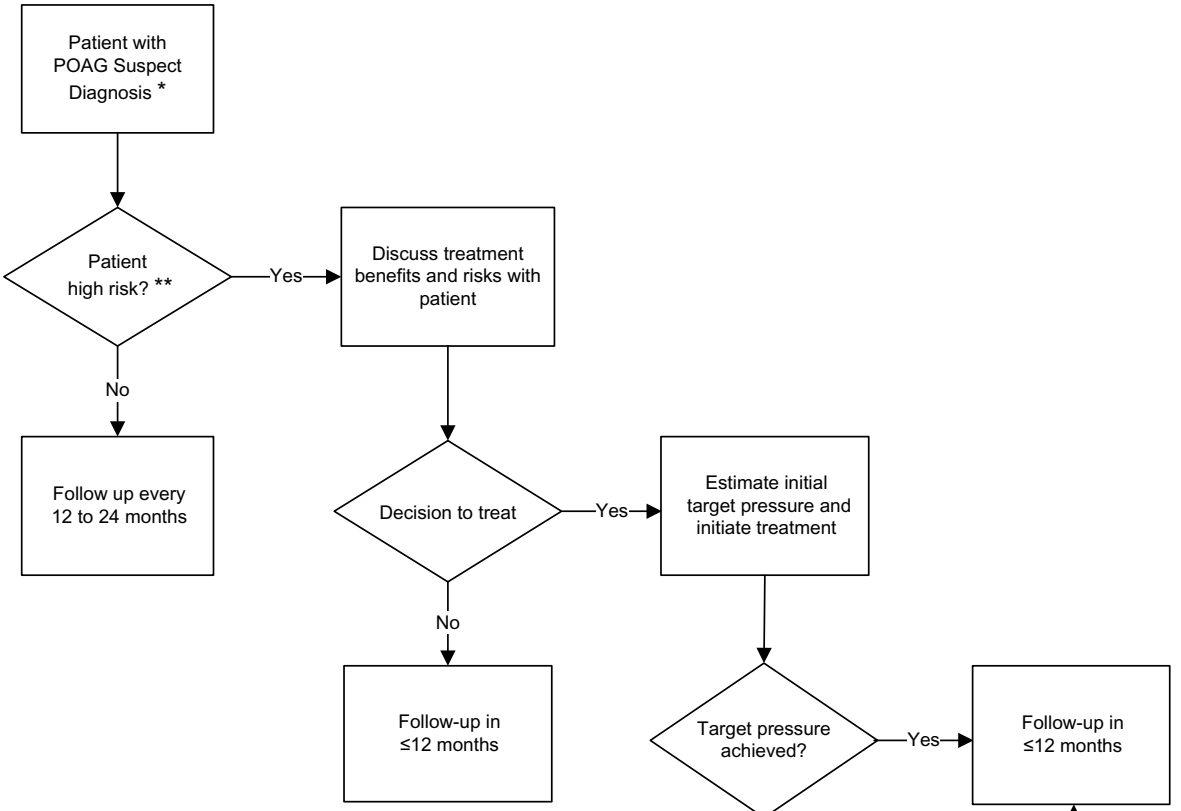
CM = Clinical Modification used in the United States; IOP = intraocular pressure

* Risk factors include family history of glaucoma, higher IOP, thinner central cornea, disc hemorrhage, larger cup-to-disc ratio, pigment dispersion syndrome, and pseudoexfoliation.

Additional information for ICD-10 codes:

- Certain ICD-10 CM categories have applicable 7th characters. The applicable 7th character is required for all codes within the category, or as the notes in the Tabular List instruct. The 7th character must always be the 7th character in the data field. If a code that requires a 7th character is not 6 characters, a placeholder X must be used to fill in the empty characters.
- For bilateral sites, the final character of the codes in the ICD-10 CM indicates laterality. If no bilateral code is provided and the condition is bilateral, separate codes for both the left and right side should be assigned. Unspecified codes should be used only when there is no other code option available.
- When the diagnosis code specifies laterality, regardless of which digit it is found in (i.e., 4th digit, 5th digit, or 6th digit):
  - Right is always 1
  - Left is always 2
  - Bilateral is always 3

APPENDIX 3. MANAGEMENT ALGORITHM FOR PATIENTS WITH PRIMARY OPEN-ANGLE GLAUCOMA SUSPECT



* The clinical findings that define a glaucoma suspect are characterized by one of the following in at least one eye in an individual with open anterior-chamber angles by gonioscopy.

- Appearance of the optic disc or retinal nerve fiber layer that is suspicious for glaucomatous damage.
- A visual field suspicious for glaucomatous damage.
- Consistently elevated IOP associated with appearance of the optic disc and retinal nerve fiber layer and with normal visual field test results.

** The overall likelihood of developing glaucomatous optic neuropathy increases with the number and relative strength of risk factors, which include the following:

- Elevated IOP
- Older age
- Family history of glaucoma
- Increased cup-to-disc ratio
- Thinner central corneal thickness
- Disc hemorrhage
- Larger mean pattern standard deviation on threshold visual field testing
- Lower ocular perfusion pressure
- Lower systolic and diastolic blood pressure
- Pigment dispersion syndrome
- Pseudoexfoliation

APPENDIX 4. LITERATURE SEARCHES FOR THIS PPP

Literature searches of the PubMed and Cochrane databases were conducted in June 2014; the search strategies were as follows. Specific limited update searches were conducted after June 2014.

PubMed Searches

Optic nerve imaging (4/29/09 – 6/10/14)

("Glaucoma"[Mesh] OR "Ocular Hypertension"[Mesh]) AND ("Optic Atrophy"[Mesh] OR "Optic Nerve"[Mesh] OR "Optic Nerve Diseases"[Mesh] OR "Optic Disk"[Mesh] OR "Nerve Fibers"[Mesh] OR "retinal nerve fiber layer") AND ((2009/04/29[edat]:3000[edat]) AND (Humans[Mesh]) AND (English[lang])): 1187 references as of 6/10/14; 1185 imported; 2 duplicates.

Central corneal thickness (4/29/09 – 6/10/14)

("Glaucoma"[Mesh] OR glaucoma OR "Ocular Hypertension"[Mesh] OR "Intraocular Pressure"[Mesh]) AND ("corneal thickness" OR CCT OR "Cornea/pathology"[Mesh]) AND ((2009/04/29[EDat]:3000[EDat]) AND (English[lang])): 829 references as of 6/10/14.

("Glaucoma"[Mesh] OR glaucoma OR "Ocular Hypertension"[Mesh] OR "Intraocular Pressure"[Mesh]) AND pachymetry AND ((2009/04/29[EDat]:3000[EDat]) AND (English[lang])): 198 references as of 6/10/14.

Diurnal/nocturnal variation in IOP (4/29/09 – 6/10/14)

("Circadian Rhythm"[Mesh] OR "circadian rhythm" OR diurnal OR nocturnal) AND ("Intraocular Pressure"[Mesh] OR "intraocular pressure" OR IOP) AND ((2009/04/29[EDat]:3000[EDat]) AND (English[lang])): 208 references as of 6/10/14; 207 imported; 1 duplicate.

Primary open-angle suspect update (4/29/09 – 6/10/14)

(("Glaucoma, Open-Angle"[Mesh] AND suspect*) OR (POAG AND Suspect*) OR (glaucoma AND suspect*)) AND (randomized controlled trial [PT] OR controlled clinical trial [PT] OR randomized [TIAB] OR placebo [TIAB] OR drug therapy [SH] OR randomly [TIAB] OR trial [TIAB] OR groups [TIAB]) NOT (animals[MH] NOT (humans [MH] AND animals[MH])) AND (("2008/08/01"[PDat]:"2009"[PDat])): 149 references as of 6/10/14; 148 imported; 1 duplicate.

(("Glaucoma, Open-Angle"[Mesh] AND suspect*) OR (POAG AND Suspect*) OR (glaucoma AND suspect*)) AND ((2009/04/29[PDat]:3000[PDat]) AND (Clinical Trial[ptyp])): 37 references as of 6/10/14.

Cochrane searches

Optic nerve imaging (4/2009 – 6/2014)

("Glaucoma"[Mesh] OR glaucoma OR "Ocular Hypertension"[Mesh]) AND ("Optic Atrophy"[Mesh] OR "Optic Nerve"[Mesh] OR "optic nerve" OR "Optic Nerve Diseases"[Mesh] OR "Optic Disk"[Mesh] OR "optic disk" OR "Nerve Fibers"[Mesh] OR "nerve fibers" OR "retinal nerve fiber layer"): 5 results in Cochrane Database of Systematic Reviews as of 6/23/14.

Central corneal thickness (4/2009 – 6/2014)

Hypertension"[Mesh] OR "Intraocular Pressure"[Mesh] OR IOP OR "intraocular pressure") AND (("corneal thickness") OR (CCT AND corneal*) OR "Cornea/pathology"[Mesh])): 105 results in Cochrane Central Register of Controlled Trials as of 6/17/14.

("Glaucoma"[Mesh] OR glaucoma OR "Ocular Hypertension"[Mesh] OR "Intraocular Pressure"[Mesh]) AND pachymetry: 28 results in Cochrane Central Register of Controlled Trials as of 6/17/14.

Diurnal/nocturnal variation in IOP (4/2009 - 6/2014)

(Circadian Rhythm[Mesh] OR “circadian rhythm” OR diurnal OR nocturnal) AND (Intraocular Pressure[Mesh] OR “intraocular pressure” OR IOP): 12 results in Database of Abstracts of Reviews of Effects as of 6/13/14.

POAG suspect update (4/24/09 – 6/23/14)

("Glaucoma, Open-Angle"[Mesh] AND suspect) OR (POAG AND Suspect) OR (glaucoma AND suspect): 2 results in Cochrane Database of Systematic Reviews as of 6/23/14.

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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.

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