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Primary Open-Angle Glaucoma Preferred Practice Pattern®

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Preferred Practice Pattern® guidelines are developed by the Academy's H. Dunbar Hoskins Jr., MD Center for Quality Eye Care without any external financial support. Authors and reviewers of the guidelines are volunteers and do not receive any financial compensation for their contributions to the documents. The guidelines are externally reviewed by experts and stakeholders before publication.

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GLAUCOMA PREFERRED PRACTICE PATTERN® DEVELOPMENT PROCESS AND PARTICIPANTS

The **Glaucoma Preferred Practice Pattern Committee** members wrote the Primary Open-Angle Glaucoma Preferred Practice Pattern guidelines (PPP). The PPP Committee 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.

Glaucoma Preferred Practice Pattern Committee 2024-2025

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We thank our partners, the Cochrane Eyes and Vision US Satellite (CEV@US), for identifying reliable systematic reviews that we cite and discuss in support of the PPP recommendations.

The Preferred Practice Patterns Committee members reviewed and discussed the document during a meeting in June 2025. The document was edited in response to the discussion and comments.

Preferred Practice Patterns Committee 2025

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The Primary Open-Angle Glaucoma PPP was sent for review in July 2025 to improve the quality of the guideline, to gather feedback on the draft recommendations and to assess feasibility for and applicability to the target audience, including assessing the facilitators and barriers to implementing recommendations (e.g., U.S. ophthalmologists and other important groups, including patients, other physicians, international ophthalmologists, research organizations, ophthalmological organizations, and experts in the field). The PPP was sent for review to the following patient organizations to solicit the views and preferences of patients and the public: Consumers United for Evidence-Based Healthcare, American Foundation for the Blind, Foundation Fighting Blindness, Lighthouse Guild, National Federation of the Blind, and Prevent Blindness. All those who were returning comments were required to provide disclosure of relevant relationships with industry to have their comments considered (indicated with an asterisk below). Members of the Glaucoma Preferred Practice Pattern Committee reviewed these comments and determined revisions to the document.

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This guideline will be formally re-evaluated and updated on a 5-year cycle in 2030. A Summary Benchmark is a resource to facilitate application of the guideline and to provide criteria that could be used to measure the application of recommendations, which will be available to all at www.ao.org/ppp.

FINANCIAL DISCLOSURES

There is no external funding, including industry/commercial support, for the development of this PPP or for the distribution of the guidelines. The Academy has fully funded the development of this PPP, and the views or interests of the Academy have not influenced the final recommendations, which are based on evidence from systematic reviews. All those individuals significantly involved in the guideline development process, including guideline committee members, PPP Committee members, Secretary for Quality of Care, and Academy staff, have declared competing/financial interests through a financial interest disclosure process as well as an assessment of the Open Payments website (available at <https://openpaymentsdata.cms.gov/>). The interests of the guideline committee members are provided at the beginning of each meeting and those with competing interests in a guideline topic do not participate in voting on areas of disagreement. In compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies (available at <https://cmss.org/code-for-interactions-with-companies/>), relevant relationships with industry are listed. As per CMSS code, direct financial relationships with companies do not include food and beverage, research funds paid to the institution and relationships outside of the topic of the PPP. The Academy has Relationship with Industry Procedures to comply with the Code (available at www.aao.org/about-preferred-practice-patterns). A majority (57%) of the members of the Glaucoma Preferred Practice Pattern Committee 2024–2025 had no direct financial relationships to disclose.

Glaucoma Preferred Practice Pattern Committee 2024-2025

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The disclosures of relevant relationships to industry of other reviewers of the document from January to October 2025 are available online at www.aao.org/ppp.

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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 committees 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 committees 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 committee 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. The intended users of the Primary Open-Angle Glaucoma 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 Network¹ (SIGN) and the Grading of Recommendations Assessment, Development and Evaluation² (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.²

- ◆ 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 SIGN¹ 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 GRADE³ 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 GRADE³ 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 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 on March 1, 2024 and July 31, 2025 in the PubMed database. Complete details of the literature searches are available in Appendix 3.
- ◆ Recommendations are based on systematic reviews, as per the Institute of Medicine (Clinical Practice Guidelines We Can Trust, 2011). In formulating the recommendations, the health benefits, side

effects/harms/risks, and the balance of benefits and risks are reviewed and considered. Final decisions are arrived at through informal consensus techniques. If there are areas of disagreement, a vote will be conducted among the members of the guideline committee. If there are individuals with direct financial relationships in the area of disagreement, these individuals will refrain from the vote.

HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

Established risk factors for the development of primary open-angle glaucoma (POAG) include elevated intraocular pressure (IOP), older age, family history of glaucoma, Black race or Latino/Hispanic ethnicity, diabetes mellitus, lower systolic and diastolic blood pressure, lower ocular perfusion pressure, myopia, thinner central cornea, lower corneal hysteresis, disc hemorrhage, larger cup-to-disc ratio, and higher pattern standard deviation on threshold visual field testing.

Many patients with POAG have untreated IOP consistently within the normal range (i.e., normal-tension glaucoma). Lowering IOP in these patients is beneficial.

Characteristic clinical features of POAG include an open angle on gonioscopy, glaucomatous optic nerve cupping, thinning of the circumpapillary retinal nerve fiber layer (RNFL)/macular ganglion cell layer on imaging, and typical glaucomatous visual field defects in the absence of any secondary causes of IOP elevation.

Adjusting automated visual field programs (30 degrees, 24 degrees, 10 degrees) and stimulus size (III, V) can aid in detecting and monitoring for progressive visual field loss.

Clinical trials have shown that lowering IOP reduces the risk of developing POAG and slows the progression of POAG. Effective laser surgical, medical, and incisional surgical approaches exist for lowering IOP.

Individuals differ in the susceptibility of their optic nerves to IOP-related damage. A reasonable initial treatment goal in a patient with POAG is to reduce IOP 20% to 30% below baseline and to adjust up or down as indicated by disease course and severity.

Functional testing with visual fields and structural testing with optical coherence tomography (OCT) provide complementary information used to monitor for glaucomatous progression.

INTRODUCTION

DISEASE DEFINITION

Primary open-angle glaucoma (POAG) in adults is a chronic, progressive optic neuropathy in which there is a characteristic acquired atrophy of the optic nerve and irreversible loss of retinal ganglion cells and their axons. In POAG, the anterior chamber is open by gonioscopy and secondary causes of IOP elevation are absent. Primary open-angle glaucoma is a potentially blinding eye disease, but early diagnosis and treatment can generally prevent visual disability.

CLINICAL FINDINGS CHARACTERISTIC OF PRIMARY OPEN-ANGLE GLAUCOMA

Primary open-angle glaucoma is a chronic ocular disease process that is progressive, generally bilateral, but often asymmetric.⁴ It is associated with the following characteristics:

- ◆ Evidence of optic nerve damage based on either, or both, of the following:
 - ◆ Optic disc retinal nerve fiber layer (RNFL) structural abnormalities
 - Diffuse or focal narrowing, or notching, of the optic disc rim, especially at the inferior or superior poles, which forms the basis for the ISNT rule⁵ (see Optic Nerve Head and Retinal Nerve Fiber Layer Clinical Examination subsection in the Physical Examination section)
 - Progressive narrowing of the neuroretinal rim with an associated increase in cupping of the optic disc
 - Diffuse or localized thinning of the parapapillary RNFL, especially at the inferior or superior poles. Highly myopic individuals without glaucoma may have a diffusely thin parapapillary RNFL.
 - Optic disc hemorrhages involving the disc rim, parapapillary RNFL, or lamina cribrosa
 - Optic disc neural rim asymmetry of the two eyes consistent with loss of neural tissue
 - Beta-zone parapapillary atrophy
 - Thinning of the circumpapillary RNFL and/or macular ganglion cell layer on imaging
 - ◆ Corresponding reliable and reproducible visual field defects
 - Characteristic visual field defects consistent with structural damage (e.g., nasal step, arcuate field defect, or paracentral depression in clusters of test sites)⁶
 - Visual field loss respecting the horizontal midline in one hemifield that exceeds loss in the opposite hemifield (in early/moderate cases)
 - Absence of other known explanations (e.g., optic disc drusen, optic nerve pit, retinal or neurological pathology)
- ◆ Adult onset
- ◆ Open anterior chamber angles on gonioscopy
- ◆ Absence of other known explanations (i.e., secondary glaucoma) for glaucomatous optic nerve change (e.g., pigment dispersion syndrome, pseudoexfoliation syndrome, uveitis, trauma, and corticosteroid use)

Primary open-angle glaucoma represents a spectrum of disease in adults in which the susceptibility of the optic nerve to damage varies among patients. Although many patients with POAG present with elevated intraocular pressure (IOP), 30% to 92% of those with characteristic findings of POAG have normal IOP measurements depending upon the population.⁷⁻¹⁸ The vast majority of patients with POAG have disc changes or disc and visual field changes,¹⁹ but there are cases where early visual field changes may develop before there are detectable changes to the optic nerve.

The severity of glaucoma damage can be estimated according to the following categories:

- ◆ Mild: Definite optic disc, circumpapillary RNFL, or macular ganglion cell layer imaging abnormalities consistent with glaucoma as detailed above, and a normal visual field as tested with standard automated perimetry (SAP)
- ◆ Moderate: Definite optic disc, circumpapillary RNFL, or macular ganglion cell layer imaging abnormalities consistent with glaucoma as detailed above, and visual field abnormalities in one hemifield that are not within 5 degrees of fixation as tested with SAP

- ◆ **Severe:** Definite optic disc, circumpapillary RNFL, or macular ganglion cell layer imaging abnormalities consistent with glaucoma as detailed above, and visual field abnormalities in both hemifields and/or loss within 5 degrees of fixation in at least one hemifield as tested with SAP
- ◆ **Indeterminate:** Definite optic disc, circumpapillary RNFL, or macular ganglion cell layer imaging abnormalities consistent with glaucoma as detailed above, inability of patient to perform visual field testing, unreliable/uninterpretable visual field test results, or visual fields not yet performed

PATIENT POPULATION

The patient population consists of adults with open anterior chamber angles and demonstrated optic nerve or circumpapillary RNFL damage, and/or visual field loss.

CLINICAL OBJECTIVES

- ◆ Document the status of the optic nerve structure at baseline by clinical evaluation and imaging, and document visual function by visual field testing
- ◆ Estimate an IOP below which further optic nerve damage is unlikely to occur (see Target Intraocular Pressure subsection in the Care Process section)
- ◆ Perform and document gonioscopy
- ◆ Attempt to maintain IOP at or below an individualized target level by initiating appropriate medical and/or surgical intervention(s) after discussing the options with the patient
- ◆ Monitor the structure and function of the optic nerve for further damage and adjust the target IOP to a lower level if deterioration occurs
- ◆ Minimize the side effects of treatment and their impact 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 disease
- ◆ Maintain quality of vision and preserve quality of life

BACKGROUND

PREVALENCE

Primary open-angle glaucoma is a significant public health problem.²⁰⁻²⁸ It was estimated that 52.68 million people in the world had POAG in the year 2020.²¹ Glaucoma (both open-angle and angle-closure) is the leading cause of irreversible blindness worldwide.²⁹ Glaucoma is estimated to be responsible for between 11% and 14% of all cases of blindness globally, and 26% of those who are blind are in high income countries.^{29, 30} The global prevalence of POAG among adults aged 40 to 80 years was estimated to be about 3.05% in 2013.²¹ 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,²¹ and that it will disproportionately affect African and Asian countries.^{20, 21, 23, 24}

Large differences exist in the prevalence of glaucoma among different ethnic and racial groups (see Table 1 and Figure 1). Overall, there appears to be a threefold higher prevalence of open-angle glaucoma (OAG) in Black individuals relative to non-Hispanic White individuals in the United States.^{25, 26} It is also the leading cause of blindness in Black individuals.²⁶ Furthermore, the prevalence of OAG is even higher in West African and Afro-Caribbean individuals relative to African American individuals.^{31, 32} Recent evidence suggests that Latino individuals have high prevalence rates of OAG that are comparable to those of Black individuals.²⁷ An analysis of claims data from a large U.S.-based managed care plan and another analysis in the Medicare population suggests that the prevalence of OAG among Asian American individuals is comparable to the prevalence among Latino individuals and is higher than that of non-Hispanic White American individuals.^{28, 33}

There is a growing recognition that racial and ethnic categories are socially constructed and not biologically coherent, and concerns about the use of these terms in medical research have been increasingly acknowledged.^{34, 35} Many studies have reported associations between race or ethnicity and health outcomes, but outcomes may also be related to ancestry and heritage, as well as socioeconomic, structural, institutional, cultural, demographic, and other factors.³⁶⁻³⁸ Identifying the

race and ethnicity of study participants may provide information about the generalizability of results. However, many individuals identify with more than one race and ethnicity, and categories should not be viewed as absolute. Whenever possible, rather than solely relying on self-identified race and ethnicity, researchers should identify which other factors (e.g., economic, environmental, social) might be conflated with race and ethnicity and incorporate multiple types of measures into the study design. Race and ethnicity categories should be clearly and specifically defined, including how the data were collected. The use of nonspecific categories such as “Other” or “non-White” should be avoided, and participants should be able to select more than one category to account for multiracial and multiethnic individuals.³⁵

TABLE 1 PREVALENCE (%) OF DEFINITE OPEN-ANGLE GLAUCOMA

Study, Year	Ethnic and Racial Group	Age-Specific Prevalence					
		Age Groups (years)					Total
		40–49	50–59	60–69	70–79	80+	
Baltimore Eye Study, 1991 ³⁹	Black	1.3	4.2	6.2	8.9	12.9	5.0
Barbados Eye Study, 1994 ⁴⁰	Black+	1.4	4.1	6.7	14.8	23.2	6.8
Los Angeles Latino Eye Study, 2004 ²⁷	Latino	1.3	2.9	7.4	14.7	21.8	4.7
Proyecto Vision Evaluation Research, 2001 ⁴¹	Hispanic	0.5	0.6	1.7	5.7	12.6	2.0
Baltimore Eye Study, 1991 ³⁹	NHW	0.2	0.3	1.5	3.3	1.94	1.4
Blue Mountains Eye Study, 1996 ⁴²	NHW		0.4*	1.3	4.7	11.4	3.0
Visual Impairment Project, 1998 ⁴³	NHW	0.5	1.5	4.5	8.6	9.9	3.4
Beaver Dam Eye Study, 1992 ¹²	NHW						2.1
Roscommon, 1993 ⁴⁴	NHW		0.7	1.8	3.2	3.1	1.9

NHW = non-Hispanic White.

NOTE: The studies reporting prevalence used different definitions of disease; therefore, caution should be exercised when comparing these studies.

* The study combined ages 40–59 into one group.

Adapted with permission from Varma R, Ying-Lai M, Francis B, et al. Los Angeles Latino Eye Study Group. Prevalence of open-angle glaucoma and ocular hypertension in Latinos: the Los Angeles Latino Eye Study. *Ophthalmology*. 2004;111:1445.

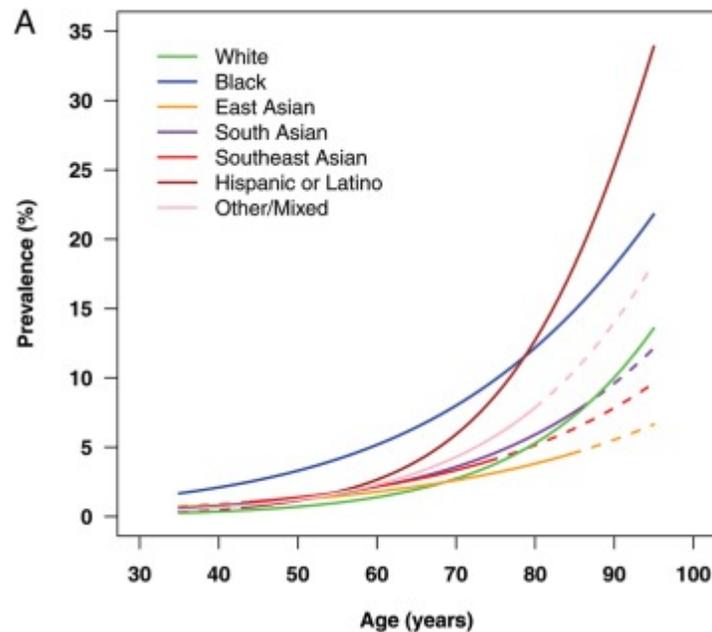


FIGURE 1. Estimated prevalence (%) of primary open-angle glaucoma with age for men and women combined by race and ethnicity. Colored lines come from regression models adjusting for age, fitted separately for different races and ethnicities. Solid lines are given across the age range of available data for each group.

Adapted from Kapetanakis V, Chan M, Foster P, et al. Global variations and time trends in the prevalence of primary open angle glaucoma (POAG): a systematic review and meta analysis. *Br J Ophthalmol.* 2016 Jan;100(1):86-93.

RISK FACTORS

Numerous prospective and retrospective studies have identified risk factors associated with the development of POAG with varying levels of evidence:

- ◆ Elevated IOP^{12, 15, 19, 40-42, 45-52}
- ◆ Older age^{19, 39, 45, 47, 48, 51-54}
- ◆ Family history of glaucoma^{48, 55-57}
- ◆ Black race or Latino/Hispanic ethnicity^{20, 21}
- ◆ Diabetes mellitus⁵⁸⁻⁶¹
- ◆ Lower systolic and diastolic blood pressure^{55, 62}
- ◆ Lower ocular perfusion pressure^{55, 62-64}
- ◆ Myopia^{52, 64-68}
- ◆ Thinner central cornea^{19, 45, 56, 69}
- ◆ Lower corneal hysteresis⁷⁰⁻⁷²
- ◆ Disc hemorrhage⁷³⁻⁷⁷
- ◆ Larger cup-to-disc ratio^{19, 45}
- ◆ Higher pattern standard deviation on threshold visual field testing^{45, 50, 78}

Other factors that have been associated with OAG include migraine headache, sleep apnea, peripheral vasospasm (Raynaud's syndrome), low intracranial pressure, cardiovascular disease, systemic hypertension, hypothyroidism, and male sex.^{45, 70, 79-83} However, the association between these risk factors and the development of glaucomatous optic nerve damage has not been demonstrated consistently.^{45, 53, 64, 65, 84-89}

Intraocular Pressure

A number of population-based studies have demonstrated that the prevalence of POAG^{12, 15, 40-42, 46, 49, 52, 90} increases as the level of IOP increases (see Figure 2). In the Baltimore Eye Survey, nearly 7% of White individuals and 25% of Black individuals had POAG at an IOP of 30 mmHg or greater.⁴⁶ These studies provide strong evidence that IOP plays a prominent role in the optic neuropathy of

POAG. Furthermore, studies have demonstrated that reducing IOP decreases the risk of visual field progression in OAG (see Table 2).^{45, 91-96}

In spite of the relationship between the level of IOP and POAG, there is great inter-individual variation in the susceptibility of the optic nerve to IOP-related damage. Population-based studies indicate that a variable proportion of patients with IOP greater than 21 mmHg (Northern Italy [13%],¹⁷ Los Angeles [18%],²⁷ Arizona [20%],⁴¹ Blue Mountains [25%],⁴² Melbourne [39%],⁴³ Baltimore [45%],³⁹ Rotterdam [61%],¹⁵ Barbados [71%]⁶⁴) have glaucomatous optic nerve damage.⁴⁶ This suggests that an IOP level of greater than 21 mmHg is arbitrary and highlights the poor predictive value of utilizing a specific IOP cutoff as a measure for screening or diagnosing POAG.

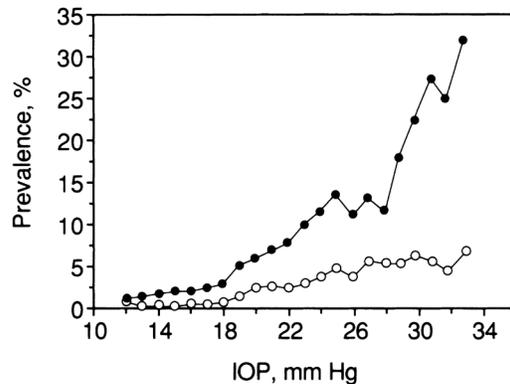


Figure 2: Prevalence of primary open-angle glaucoma in relation to screening intraocular pressure. Black subjects, n = 4,674 eyes (closed circles); White subjects, n = 5,700 eyes (open circles).

IOP = intraocular pressure.

Reprinted with permission from the American Medical Association. Sommer AE, Tielsch JM, Katz J, et al. Relationship between intraocular pressure and primary open angle glaucoma among White and /Black Americans. The Baltimore Eye Survey. *Arch Ophthalmol.* 1991;109(8):1090-5. Copyright 1991. All rights reserved.

TABLE 2 RELATIONSHIP BETWEEN IOP REDUCTION AND GLAUCOMA PROGRESSION IN MAJOR CLINICAL TRIALS

Study, Year	Study Design	No. of Patients	Follow-up Duration (years)	Finding
Scottish Glaucoma Trial, 1988–1989 ^{97, 98}	Newly diagnosed POAG: medical therapy vs. trabeculectomy	116	4.6 (mean)	Trabeculectomy lowered IOP (58% reduction) more than medicine (42% IOP reduction). Medical therapy group had more deterioration in visual fields than trabeculectomy group.
Moorfields Primary Treatment Trial, 1994 ⁹⁹	Newly diagnosed POAG: medical therapy vs. laser trabeculoplasty surgery vs. trabeculectomy	168	5+	Trabeculectomy lowered IOP the most (60% IOP reduction). Laser trabeculoplasty surgery (38% IOP reduction) and medical therapy groups (49% IOP reduction) had more deterioration in visual fields than trabeculectomy group.
Collaborative Normal-Tension Glaucoma Study, 1998 ⁹¹	POAG in eyes with normal IOP: rate of progression, effect of IOP reduction on progression rate	230	5+	Lowering IOP (37% IOP reduction) slowed the rate of visual field loss compared with untreated eyes (1% IOP reduction).

Primary Open-Angle Glaucoma PPP

Early Manifest Glaucoma Trial, 2002–2007 ^{93, 94, 100}	Newly diagnosed POAG: medical therapy and laser trabeculectomy vs. no treatment	255	8 (median)	Lowering IOP with medical therapy and laser trabeculectomy surgery (25% IOP reduction) slowed progression of optic disc and visual field damage.
Collaborative Initial Glaucoma Treatment Study, 2001 ¹⁰¹	Newly diagnosed POAG: medicine vs. trabeculectomy	607	5+	Lowering IOP with initial filtering surgery (46% IOP reduction) was as effective as medical therapy (38% IOP reduction) to slow the progression of visual field damage.
Advanced Glaucoma Intervention Study, 2000, 2004 ^{95, 102}	POAG after medical therapy failure with no previous surgery: laser trabeculectomy first vs. trabeculectomy first	591	10–13	Surgical outcome varied by race. Black patients did better with laser trabeculectomy first (30% IOP reduction), whereas White patients did better with trabeculectomy first (48% IOP reduction). No further visual field deterioration was seen on average in patients who maintained IOP <18 mmHg at all study visits (mean IOP = 12.3 mmHg).
United Kingdom Glaucoma Treatment Study, 2014 ⁹⁶	Newly diagnosed OAG: latanoprost 0.005% vs. placebo	516	2	Latanoprost lowered IOP (3.8 mmHg) more than placebo (0.9 mmHg). Latanoprost group had a reduced risk of visual field deterioration than placebo group.

HR = hazard ratio; IOP = intraocular pressure; POAG = primary open-angle glaucoma.

Age

Older age is an important risk factor for the presence and progression of POAG.^{39-43, 100, 103-106} A number of epidemiological studies demonstrate that the prevalence of glaucoma increases dramatically with age, particularly among Latino, Hispanic, and Black individuals (see Table 1 and Figure 1).

Family History

Family history is a risk factor for glaucoma. In the Rotterdam Eye Study, in which all siblings of glaucoma cases and controls were examined, the odds of having POAG were 9.2-fold higher for individuals who have a first-degree relative (sibling or parent) with confirmed POAG.¹⁰⁷ Other studies in which family members were not examined depended on patient reports of the status of family members, and these are known to be subject to several biases. Nonetheless, they support the concept that first-degree relatives of those with OAG are at greater risk. For example, in the Baltimore Eye Survey and the Los Angeles Latino Eye Study (LALES), the odds were twice as high for individuals with POAG (1.92 and 2.85, respectively) of reporting a first-degree relative (parent, child, or sibling) with glaucoma compared with individuals who did not have glaucoma. However, the odds increased to over three times as high if they reported that they had a sibling with glaucoma (LALES, 3.5¹⁰⁸; Baltimore, 3.7¹⁰⁹). Interestingly, the odds rose to fivefold higher if there were two or more siblings who were reported to have a history of glaucoma.

Race, Ethnicity, and Social Determinants of Health

Despite a growing recognition that racial and ethnic categories are socially constructed, these characteristics remain an important risk factor for POAG (see Figure 1).^{34, 35} However, it is important to acknowledge that self-identified race and ethnicity categories used in research studies are inherently limited and intertwined with other aspects of health, such as socioeconomic, structural, institutional, cultural, demographic factors.³⁵ Nonetheless, the prevalence of POAG is higher in individuals of West African, Afro-Caribbean, or Latino/Hispanic origin than in other groups.^{13, 27, 39-41, 110} The prevalence is three times higher in Black and Hispanic individuals of Mexican ancestry compared with non-Hispanic White

individuals.^{27, 39} Blindness from glaucoma is at least six times more prevalent in Black individuals than in White individuals.²⁶ Systematic reviews and meta-analysis studies suggest that POAG disproportionately affects African and Asian countries.^{20, 21}

Various studies have also noted differences in outcomes tied to social or economic conditions (disparities), including race and ethnicity, in utilization of eye care services. Studies have demonstrated that Black individuals are less likely to undergo examinations for glaucoma compared with White individuals,^{111, 112} have lower rates of undergoing visual field testing in the year before glaucoma surgery,¹¹³ and have lower rates of using medical and surgical interventions for glaucoma.¹¹⁴ A study found that despite possessing health insurance, Latino individuals were significantly less likely to undergo monitoring for glaucoma compared with White individuals.¹¹⁵ In response to this information, in 2000 Medicare began providing a benefit for glaucoma screening in individuals with the following risk factors: a family history of glaucoma, a history of diabetes, African American descent and age 50 or older, or Latino ethnicity and age 65 or older.¹¹⁶

In the ever-evolving health care environment, it will be important to incorporate interventions that address not just racial and ethnic disparities but also disparities in glaucoma diagnosis and management associated with life conditions like income, housing, and education that affect health (social determinants of health).¹¹⁷⁻¹¹⁹ Glaucoma diagnosis is associated with higher area deprivation indices and lower income levels, including potential underdiagnosis of individuals in areas with high social vulnerability.¹²⁰⁻¹²² Residing in areas with a higher social vulnerability index and area deprivation index is associated with delayed glaucoma surgery and higher incidence of surgery when controlling for other demographic and ocular parameters.^{122, 123} A higher social vulnerability index may also be associated with glaucoma-related severe visual impairment.¹²⁴ Further research will clarify health care disparities and also interventions that can improve glaucoma diagnosis and management.

Genetic Factors

Our understanding of the complex genetic architecture of OAG and how it relates to an increased risk of developing glaucomatous optic neuropathy is rapidly growing. Traditional linkage methods have identified various genes for some of the heritable forms of glaucoma.¹²⁵⁻¹²⁷ Population-based studies have expanded from national collaborations to international consortia to determine the complex genetic architecture of OAG¹²⁸ and the OAG endophenotypes of IOP,¹²⁹⁻¹³¹ central corneal thickness (CCT),¹³²⁻¹³⁴ and optic disc parameters.^{135, 136} With advances in sequencing technology and reduced costs, studies have utilized large-scale genome-level interrogation that has led to the identification of the common genetic variants associated with OAG and/or IOP elevation.^{130, 136-138} Newer genetic sequencing platforms and larger sample sizes of glaucoma cases and controls have resulted in the identification of rare genetic variants associated with OAG. Population-based studies suggest that multiple genetic polymorphisms, post-translational, and environmental interactions are associated with the phenotype of POAG.¹³⁹⁻¹⁴¹ These genetic variants, or risk alleles, or gene-environmental interactions will require further investigation to determine if these factors are protective, are associated with disease progression, or represent potential new therapeutic targets. At this time, genetic tests are available for select inherited eye diseases.¹⁴² With the exception of genetic testing for children of patients with juvenile open-angle glaucoma,¹⁴³ routine genetic testing for glaucoma risk alleles is not recommended for patients with POAG.¹⁴⁴

Genetics may play a key role in the risk of developing glaucoma. Recent genome-wide association studies in patients of African ancestry have identified multiple unique loci associated with POAG.^{145, 146} Studies of mitochondrial DNA have recently identified three haplotypes as risk factors for POAG, which have been found in approximately 25% of patients who self-identified as African American.¹⁴⁷ Polygenic risk scores estimate the combined effect of many genetic variants on an individual's relative risk of disease, and they have been used in glaucoma to predict progression and response to treatment. Although this approach may hold promise for the future, no polygenic risk scores are currently validated for clinical use.

Diabetes Mellitus

Even though conflicting data exist on the association between diabetes mellitus and POAG,^{48, 58-60, 148-153} there is increasing evidence from population-based studies suggesting that diabetes

mellitus is an important risk factor for POAG.^{58-60, 149, 151} Population-based assessments of Hispanic individuals (in Los Angeles, California);⁵⁹ non-Hispanic White individuals (in Beaver Dam, Wisconsin; and Blue Mountains, Australia),^{58, 151} and a large cohort enrolled in the Nurses' Health Study¹⁴⁹ have shown that persons with diabetes mellitus are more likely (40% higher odds in Hispanic individuals, twofold higher odds in non-Hispanic White individuals) to have POAG. Furthermore, in the LALES,⁵⁹ longer duration of 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 greater susceptibility to glaucomatous optic nerve damage in persons with diabetes mellitus.¹⁵⁰ Interestingly, authors have suggested that diabetes may be directly associated with a higher IOP reading, likely related to a change in corneal biomechanics.¹⁵⁴ Although this may act as a confounder, a meta-analysis of 47 studies concluded that diabetes mellitus is associated with increased risk of glaucoma and may be associated with elevated IOP.⁶¹

Ocular Perfusion Pressure

Ocular perfusion pressure is the difference between blood pressure (at systole or diastole) and IOP. Low ocular perfusion pressure may lead to alterations in blood flow and contribute to progressive glaucomatous optic nerve damage. Population-based studies have provided evidence that low diastolic perfusion pressure (<50 mmHg) is associated with a higher prevalence of POAG.^{41, 55, 63, 84, 155} In addition, in the Early Manifest Glaucoma Trial (EGMT), systolic perfusion pressure of 125 mmHg or below was associated with a higher risk of glaucoma progression (relative risk of 1.42) over an 8-year period.¹⁰⁰ Other data suggest that a nocturnal mean arterial pressure 10 mmHg lower than daytime mean arterial pressure may predict progression of normal-tension glaucoma and increased risk of visual field loss.¹⁵⁶ Recent evidence suggests that low diastolic perfusion pressure is associated with increased risk for glaucoma only in patients receiving treatment for systemic hypertension.¹⁵⁷ However, statistical analysis was unable to determine whether perfusion pressure is associated with glaucoma because of its individual components (systolic blood pressure, diastolic blood pressure, or IOP), a combination of these components, or an interaction between these components.¹⁵⁸

Myopia

Large cross-sectional epidemiologic studies in Afro-Caribbean, Hispanic, non-Hispanic White, Chinese, Asian Indian, and Japanese individuals suggest that persons with myopia have a higher prevalence of OAG than those without myopia.^{64-67, 159-162} More recently, data from the LALES have provided evidence of an independent relationship between longer axial length (axial myopia) and a higher prevalence of OAG.⁸² The underlying hypothesis is that individuals with axial myopia have weaker scleral support at the optic nerve, and this contributes to a greater susceptibility of the optic nerve to glaucomatous damage.

Central Corneal Thickness

Because applanation tonometry measurements are derived from resistance to corneal indentation and corneal stiffness, differences in CCT may introduce artifacts in IOP measurement.^{45, 69, 163-169} The mean CCT in healthy human eyes varies with ethnic and racial characteristics. The average CCT measured ultrasonically in White American individuals is 556 μm ,¹⁷⁰ in Latino individuals it is 546 μm ,¹⁷¹ in Asian individuals it is 552 μm ,¹⁷² in American Indian/Alaska Native individuals it is 555 μm ,¹⁷³ and in Black individuals it is 534 μm .¹⁶⁸ If IOP is underestimated in eyes with thinner CCT, the relationship between IOP level and OAG damage may be underestimated, since the IOP is actually higher than measured. Conversely, if IOP is overestimated in eyes with a non-edematous, thicker CCT, the relationship between IOP level and OAG damage may be overestimated, since the IOP is actually lower than measured. Although several tables and figures have been published, no standard nomogram that corrects applanation IOP measurements for CCT has yet been validated,^{163, 167, 174-176} and applying a specific correction should be avoided. In all these studies, eyes with forme-fruste keratoconus, Fuchs endotheliopathy, or postkeratorefractive surgery were not considered. Therefore, clinicians diagnose glaucoma using the clinical examination of the optic nerve head (ONH);

imaging of the ONH, circumpapillary RNFL, and macular ganglion cell layer; and assessment of the visual field.

A thinner central cornea has been reported as a risk factor for POAG (see Figure 3).¹⁷⁷⁻¹⁷⁹ Central corneal thickness may be a biomarker for structural or physical factors involved in the pathogenesis of POAG.¹⁷⁷ Corneal biomechanical properties such as hysteresis may also have an impact on IOP measurement, glaucoma risk, and risk of glaucoma progression.¹⁸⁰⁻¹⁸⁵ In particular, in eyes with a thinner CCT following keratorefractive surgery IOP may be significantly underestimated by Goldmann applanation tonometry. A tonometer device that aims to correct for dynamic corneal properties may be optimal, and careful monitoring of visual fields and optical coherence tomography (OCT) in glaucoma patients is required even in those with apparently low IOP.^{176, 186-189} Although controversy exists about CCT as a risk factor because CCT alters the measurement of IOP and hysteresis, clinicians should measure CCT when evaluating patients with POAG.

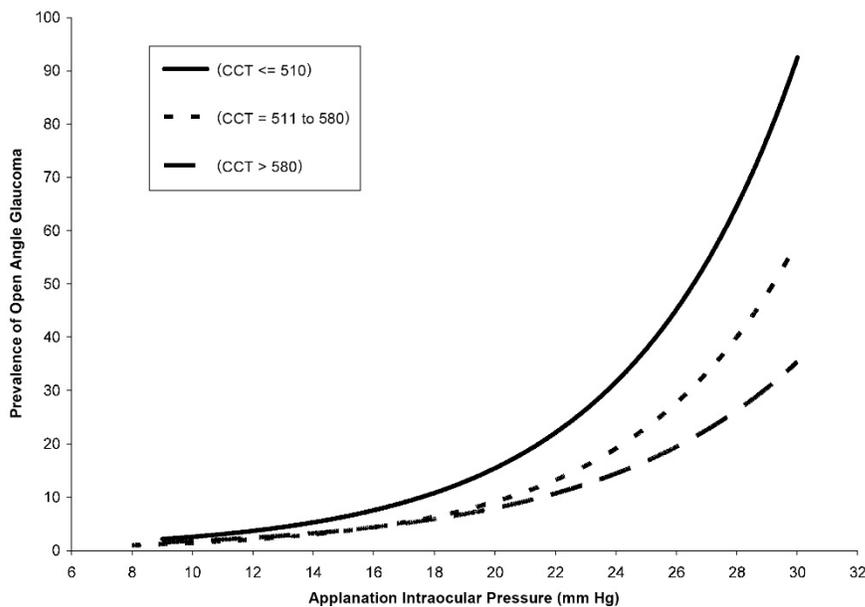


FIGURE 3. Trendlines showing the relationship between the prevalence of open-angle glaucoma and applanation intraocular pressure stratified by central corneal thickness in micrometers in the Latino individuals (n = 5970) in the Los Angeles Latino Eye Study.

Adapted with permission from Francis B, Varma R, Chopra V, et al, Los Angeles Latino Eye Study Group. Intraocular pressure, central corneal thickness, and prevalence of open-angle glaucoma: the Los Angeles Latino Eye Study. *Am J Ophthalmol.* 2008;146:743.

Other Factors

Migraine headache and peripheral vasospasm (Raynaud's syndrome) have been identified as risk factors for glaucomatous optic nerve damage, particularly in normal-tension glaucoma.^{79, 80, 83, 91, 190-192} These conditions may decrease autoregulation of optic disc blood flow when compared with patients without this history.¹⁹³ Although migraine headaches alone may actually decrease visual field sensitivity during the attack,¹⁹⁴ overall, clinicians should consider migraine and peripheral vasospasm as risk factors for progressive glaucoma.

A number of large population-based studies have noted an association between systemic arterial hypertension and OAG,^{63, 84, 85, 195-197} though there are also multiple studies reporting no association between these conditions.^{41, 64, 198-200} A possible explanation for the conflicting findings among these studies may be related to the extent to which the studies adjusted for potential confounding factors. After adjustment for diabetes and hyperlipidemia, one study found that patients with systemic arterial hypertension (and no diabetes or hyperlipidemia) had a 17% increased risk of developing OAG ($P < 0.001$). Those with concomitant systemic arterial hypertension and diabetes had a 48% increased risk of glaucoma ($P < 0.001$).¹⁹⁶ The reasons for why systemic arterial hypertension may influence risk of glaucoma are poorly understood and

could be related to increased perfusion of the ciliary body, resulting in greater aqueous production and higher IOP, a known risk factor for glaucoma.^{195, 201} Decreased perfusion to the optic disc from sclerotic arterioles may also be involved.²⁰² Finally, treatment of systemic arterial hypertension with antihypertensives may cause systemic hypotension and a reduction in perfusion of the optic nerve.²⁰³ Interestingly, low diastolic perfusion pressure was found to be associated with increased risk for glaucoma only in patients receiving treatment for systemic hypertension.^{105, 157, 204} Overall, the association of systemic arterial hypertension with glaucoma is controversial.^{195, 201}

Another interesting association may occur between the translaminar pressure gradient (pressure difference between IOP and intracranial pressure) and glaucoma.²⁰⁵⁻²⁰⁹ A retrospective study in 30,000 patients who underwent diagnostic lumbar puncture showed lower intracranial pressure in patients with glaucoma compared with age-matched controls.²⁰⁶ Another prospective study demonstrated that patients with POAG had lower intracranial pressure compared with controls.²⁰⁸ Follow-up studies from both groups demonstrated that patients with normal-tension glaucoma had even lower intracranial pressure, whereas patients with ocular hypertension had higher levels of intracranial pressure.^{207, 209} Overall, additional research is needed to determine whether intracranial pressure is a risk factor for glaucoma.^{210, 211}

Reports suggest that hypothyroidism may be associated with glaucoma. The biologic explanation may include decreased cellular metabolism with increased susceptibility to ganglion cell loss and/or alterations in mucopolysaccharides in the trabecular meshwork that increase IOP.²¹²⁻²¹⁴ Also, male sex may be associated with a higher risk of glaucoma, which may be due to a protective effect of female hormones on ganglion cell loss. However, women have a larger population burden of glaucoma due to longer survival.^{20, 51}

POPULATION SCREENING FOR GLAUCOMA

Primary open-angle glaucoma may be an ideal disease to detect by targeted screening because it is often asymptomatic until later stages of the disease, it creates significant morbidity, and treatment slows or prevents the progression of visual field loss.²¹⁵ Visual field loss in glaucoma decreases health-related quality of life.^{216, 217} However, screening for glaucoma in the general population is not cost-effective.^{218, 219} Screening is more useful and cost-effective when it is targeted at populations at high risk for glaucoma, such as older adults,²⁵ those with a first-degree relative with glaucoma,^{107, 109, 220-222} Black or Hispanic individuals, or those with social and economic factors affecting access to care and health outcomes.²⁵ Although screening in the general population for glaucoma alone is not cost-effective, screening programs may be more efficacious when they include screening for other major causes of blindness, such as age-related macular degeneration and diabetic retinopathy. Targeted community-based glaucoma screenings in populations with high levels of poverty and high proportions of people who identify as African American or Hispanic/Latino found a 27% rate of glaucoma and suspected glaucoma, which was 3 times the national average.^{223, 224} Continuing to improve community-based screening strategies as well as the validity and efficiency of portable diagnostic technology may facilitate cost-effective glaucoma screening and reduction in the incidence of glaucoma in high-risk populations in the future.

There are 3 main approaches to screening patients for POAG: measuring the IOP, assessing the ONH and circumpapillary RNFL, and evaluating the visual field, either alone or in combination.

Measuring IOP is not an effective method for screening populations for glaucoma. Using an IOP above 21 mmHg, the sensitivity for the diagnosis of POAG by tonometry was 47.1% and the specificity was 92.4% in one population survey.²²⁵ Population-based studies suggest that half of all individuals with POAG have IOP levels below 22 mmHg, the usual screening cutoff.^{15, 42, 46} Additionally, most individuals with elevated pressures at a screening measurement do not have, and may never develop, optic nerve damage, although risk increases with higher IOP.^{42, 46} Studies show that approximately 1 of every 10 to 15 individuals with elevated IOP at screening has demonstrable optic nerve damage, and half of these (1 in 20 to 30 individuals) may not have been previously diagnosed with glaucoma.^{42, 44, 46, 226}

A second method of screening for glaucoma is to assess the ONH and circumpapillary RNFL. Clinicians have used several techniques to examine the ONH and circumpapillary RNFL. Some techniques, such as ophthalmoscopy and optic disc photography, may require minimal technology but are highly subjective and

have poor agreement and high interobserver variation.²²⁷⁻²²⁹ Optical coherence tomography can be used to examine the ONH, circumpapillary RNFL, and macular ganglion cell layer. Studies suggest that these have poor to moderate diagnostic precision for glaucoma when used in isolation for population-based screening.²³⁰⁻²³² Additional processing of OCT measurements may increase their predictive value for screening.^{233, 234} Optical coherence tomography can also provide further diagnostic value for screening for other diseases such as age-related macular degeneration and diabetic retinopathy; however, barriers to implementing OCT include its expense and lack of portability.²³⁰⁻²³²

A third method of screening for glaucoma is to evaluate the visual field. Visual field testing has been used in mass screening but may be nonspecific for glaucoma. It may show abnormalities in normal eyes because of inexperience with visual field testing, small pupils, inaccuracies due to uncorrected refractive error, and ocular media abnormalities.²³⁵ Frequency doubling technology perimetry does not require correction of moderate refractive error and is useful as a screening tool to detect moderate to severe glaucomatous damage due to portability and speed of the test.^{236, 237} However, combining structural assessments of the ONH or circumpapillary RNFL with perimetry likely produces better diagnostic sensitivity and specificity.²³⁸

Clinicians and researchers have evaluated telemedicine to screen for glaucoma. Telemedicine uses telecommunication equipment to remotely diagnose and recommend treatment. The same considerations for screening discussed above apply to telemedicine, but one of the advantages of this approach is increased access to screening outside of the ophthalmologist's office and the rapid transfer of information.²³⁹⁻²⁴¹ Another potential tool for population-based screening is artificial intelligence.²⁴²⁻²⁴⁴ Artificial intelligence is used for multiple purposes, including natural language processing, transportation navigation, and image processing. Artificial intelligence based on deep learning has been applied to fundus photographs, OCT images, and visual fields. It provides discrimination of diseased eyes from normal eyes without the restrictions of human graders and conventional statistical techniques, and it has a higher diagnostic performance compared with these methods.²⁴¹⁻²⁴⁴ Limitations of artificial intelligence include difficulty understanding discriminatory factors and generalizability to different patient groups.

The Medicare glaucoma screening benefit covers glaucoma evaluations in the office for beneficiaries who have diabetes mellitus, those with a family history of glaucoma, African American individuals who are aged 50 or older, and Hispanic individuals who are aged 65 years or older.¹¹⁶

CARE PROCESS

PATIENT OUTCOME CRITERIA

- ◆ Preservation of visual function
- ◆ Maintenance of quality of life

DIAGNOSIS

The comprehensive initial glaucoma evaluation (history and physical examination) includes all components of the comprehensive adult medical eye evaluation²⁴⁵ and focuses attention on those features that specifically pertain to the diagnosis, course, and treatment of POAG. The evaluation may require more than one visit. For instance, an individual might be suspected of having glaucoma on one visit but may return for further evaluation to confirm the diagnosis, including additional IOP measurements; gonioscopy; CCT determination; visual field assessment; and ONH, circumpapillary RNFL, and macular ganglion cell layer imaging.

History

- ◆ Ocular history (e.g., refractive error, trauma, prior ocular surgery)
- ◆ Race, ethnicity, and socioeconomic factors
- ◆ Family history.^{15, 107, 109} The severity and outcome of glaucoma in family members, including a history of visual loss from glaucoma, should be obtained during the initial evaluation.^{107, 109}
- ◆ Systemic history (e.g., asthma/chronic obstructive pulmonary disease, migraine headache, Raynaud's syndrome, diabetes mellitus, cardiovascular disease, blood pressure abnormalities, sleep apnea, hypothyroidism)

- ◆ Review of pertinent records, with particular attention to IOP levels, status of the optic nerve, and visual field testing
- ◆ Current and prior ocular and nonocular medications (e.g., corticosteroids, anti-hypertensives) and known local or systemic intolerance to ocular or nonocular medications

Cataract surgery may also lower the IOP compared with the presurgical baseline.^{246, 247} A history of laser-assisted in situ keratomileusis (LASIK), small-incision lenticule extraction (SMILE), or photorefractive keratectomy can be associated with a falsely low IOP measurement due to thinning of the cornea.^{186, 188, 248-251} A history of prior glaucoma laser surgery or incisional ocular surgical procedures should also be elicited.

Evaluation of Visual Function

Self-reported functional status or difficulty with vision can be assessed either through the patient's description or by using specific questionnaires, such as the National Eye Institute - Visual Function Questionnaire-25, Glaucoma Quality of Life-15, and Glau-QOL.^{216, 252-259} Patients who have glaucoma may have sufficient visual field loss to impair driving (especially at night), near vision, reading speed, and outdoor mobility.^{217, 260-266}

Physical Examination

The ophthalmic evaluation focuses specifically on the following elements in the comprehensive adult medical eye evaluation:²⁴⁵

- ◆ Visual acuity measurement
- ◆ Pupil examination
- ◆ Confrontational visual fields
- ◆ Slit-lamp biomicroscopy
- ◆ IOP measurement
- ◆ Gonioscopy
- ◆ ONH and circumpapillary 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 a relative afferent pupillary defect.²⁶⁷⁻²⁷⁰

Confrontation visual field

Confrontation visual fields may be evaluated as an adjunct to automated visual field testing.

Slit-lamp biomicroscopy

Slit-lamp biomicroscopic examination of the anterior segment can reveal evidence of physical findings associated with narrow angles, such as shallow peripheral anterior chamber depth and crowded anterior chamber angle anatomy.^{271, 272} Secondary mechanisms for elevated IOP can be detected on anterior segment examination and can include pseudoexfoliation material on the pupil margin, anterior lens capsule or corneal endothelium (pseudoexfoliation syndrome); pigment dispersion syndrome with spoke-like, mid-peripheral radial iris transillumination defects, Krukenberg spindle, and/or Scheie stripe; iris and angle neovascularization; or inflammation.

Intraocular pressure measurement

Intraocular pressure is measured in each eye, preferably by Goldmann applanation tonometry, and before gonioscopy or dilation of the pupil. Recording the time of day of IOP measurements may be helpful to assess diurnal variation and its relation to the timing of topical ocular hypotensive agents. The significance of diurnal IOP fluctuation and

progression of visual field loss has yet to be fully established in the literature.^{100, 106, 273-280} Similarly, since IOP may vary within individuals even at the same time of the day, ophthalmologists should consider making therapeutic decisions based on several IOP measurements rather than on a single measurement.²⁸¹ Patients may benefit from IOP measurement at different times of the day.²⁸²

Gonioscopy

The diagnosis of POAG requires careful evaluation of the anterior chamber angle to exclude angle-closure glaucoma or secondary causes for IOP elevation, such as angle recession, pigment dispersion, pseudoexfoliation syndrome, peripheral anterior synechiae, angle neovascularization, and inflammatory precipitates.²⁸³ A useful technique to examine a narrow anterior chamber angle, especially in the setting of a high lens vault or steep iris insertion, is to tilt the gonioprism slightly toward the quadrant of interest or have the patient look slightly towards the mirror of the gonioprism into which the examiner is looking. A description of angle structures observed during gonioscopy should be documented (i.e., Schwalbe's line, anterior/nonpigmented trabecular meshwork, posterior/pigmented trabecular meshwork, scleral spur, ciliary body band), or a standard grading system may be used. The Spaeth gonioscopy grading system describes the anterior chamber angle anatomy in detail with a high correlation to ultrasound biomicroscopy.²⁸⁴

(See www.gonioscopy.org for discussion and videos describing techniques of gonioscopy.)

Optic nerve head and retinal nerve fiber layer clinical examination

Examination of the ONH and circumpapillary RNFL provides valuable structural information about glaucomatous optic nerve damage.^{4, 285-288} Ocular features that may indicate glaucomatous optic neuropathy include the following:

- ◆ Vertical elongation of the optic nerve cup with an associated decrease in neuroretinal rim width
- ◆ Large optic nerve cup size
- ◆ Asymmetric optic nerve cupping
- ◆ Diffuse or focal narrowing of the neuroretinal rim, especially superior and/or inferior
- ◆ Optic disc hemorrhages involving the disc rim, parapapillary RNFL, or lamina cribrosa
- ◆ Nasalization of central ONH vessels
- ◆ Baring of the circumlinear vessel
- ◆ Diffuse or focal thinning of the circumpapillary RNFL
- ◆ Beta-zone parapapillary atrophy
- ◆ Optic disc hemorrhages

The size of the physiologic cup is related to the size of the optic disc. Larger overall disc area is associated with a larger optic nerve cup. Commonly, the neuroretinal rim of the optic nerve is widest inferiorly and narrowest temporally. This anatomic feature is referred to as the ISNT rule: the neuroretinal rim is widest at the inferior rim, followed by the superior rim, followed by the nasal rim, and lastly by the temporal rim.²⁸⁹⁻²⁹¹ In approximately 80% of patients with glaucoma, cupping does not follow this rule because both the inferior and superior rims show thinning.^{289, 290} However, a study has demonstrated that normal eyes follow the ISNT rule less than 45% of the time.²⁹¹

Visible structural alterations of the ONH or circumpapillary RNFL and development of parapapillary choroidal atrophy in early glaucoma may precede the onset of visual field defects.^{286, 292-294} Other investigations have reported functional deficits occurring in advance of structural change.^{295, 296} Careful examination 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.^{77, 91-93, 100, 104, 191, 297-303} In the Ocular Hypertension Treatment Study, the incidence of POAG in eyes with disc hemorrhage was 13.6% compared with 5.2% in eyes without disc hemorrhage over 8 years.⁷⁷ In the EGM, 13% of patients had disc hemorrhages at baseline examination, and hemorrhages were associated with progression.⁹³

The optic nerve should be carefully examined for the above signs of glaucomatous damage, and its appearance should be documented.^{4, 287, 304} The preferred technique for ONH evaluation involves magnified stereoscopic visualization (as obtained with the slit-lamp biomicroscope), preferably through a dilated pupil. In some cases, direct ophthalmoscopy complements magnified stereoscopic visualization, providing additional information about 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 circumpapillary RNFL.³⁰⁵ Color stereophotography is an accepted method for documenting qualitative ONH appearance. Computer-based image analysis of the ONH and circumpapillary RNFL/macular ganglion cell layer is a complementary method for documenting the optic nerve and is discussed in the Diagnostic 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 comprehensive 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, macular degeneration, retinovascular occlusion, or other retinal disease).

Diagnostic Testing

Diagnostic tests that are used to further evaluate patients with POAG include the following:

- ◆ CCT measurement
- ◆ Corneal hysteresis measurement
- ◆ Visual field evaluation
- ◆ ONH, circumpapillary RNFL, and macular ganglion cell layer imaging

Central corneal thickness measurement

Measurement of CCT aids the interpretation of IOP readings and helps to stratify patient risk for ocular damage.^{45, 69, 169, 178, 306} In the Ocular Hypertension Treatment Study and European Glaucoma Prevention Study trials, the average CCT in the ocular hypertension group was 570 μm , and the risk of developing POAG was greater in eyes with a corneal thickness less than 555 μm compared with eyes with a corneal thickness 588 μm or greater.^{45, 307} (Additional information is available in the Central Corneal Thickness subsection under Risk Factors.) Applanation tonometry may overestimate the true IOP in eyes with corneas that are thicker than average, whereas an underestimation of the true IOP tends to occur in eyes with corneas that are thinner than average. An exception to this is that measurement of IOP may be underestimated in eyes with corneal edema.¹⁷⁸ Several studies have sought to quantify the relationship between measured IOP level and CCT, but there is no generally accepted correction formula.^{163, 167, 174-176} The World Glaucoma Association Consensus on IOP suggests that a correction factor should not be used to adjust values measured in individual patients.³⁰⁸ Although it is clear that thinner CCT is a risk factor for the development of POAG,⁴⁵ studies of progression have had variable findings. Some (but not all) studies found an association between glaucoma progression and thinner CCT.^{100, 182, 309-313}

Corneal hysteresis measurement

Hysteresis is a measure of the cornea's response to an applied pressure. Corneal hysteresis appears to provide additional, independent information associated with the risk of POAG development. In retrospective and prospective studies, lower hysteresis values have been reported to be associated with both a higher risk of POAG development and visual field progression in patients with glaucoma.^{70-72, 183, 314-316} Each 1 mmHg lower hysteresis value correlated with a 0.2% per year rate of visual field index decline, and the highest rates of progression occurred in eyes with lower hysteresis and higher IOP values. This has been described as a measure of elasticity or viscoelastic dampening. Therefore, a lower hysteresis value may indicate that the lamina cribosa and peripapillary sclera have less

ability to absorb applied energy and potentially subject optic nerve axons to greater mechanical stress.³¹⁷ Although corneal hysteresis is not routinely used in clinical practice, it complements current structural and functional assessments in guiding disease risk.¹⁸⁰

Visual field evaluation

Eye care clinicians evaluate the visual field using SAP with white-on-white stimuli.³¹⁸ Testing strategies can be tailored to the patient and degree of visual field loss by using specific programs that evaluate the central threshold sensitivity at 30 degrees, 24 degrees, and 10 degrees, and by varying stimulus size. 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. In patients with visual field damage that encroaches on or involves fixation, use of central 10-degree programs facilitates measurement of this area by sampling more points near fixation than do either the 24- and 30-degree testing strategies. Testing with a 10-2 program may also be useful to detect early visual field damage in the central 10 degrees before such abnormalities are obvious in a 24- or 30-degree testing strategy.³¹⁹ When a visual field defect is present on initial testing, repeat testing should be performed to establish a good baseline for future comparisons. Repeat visual field examination using the same testing strategy is recommended to confirm test results that show a new or progressive glaucomatous defect.^{91, 320-322} Poorly reliable tests or those with presumed artifacts (e.g., lens rim or ptosis) should be repeated after addressing the underlying cause.

Frequency doubling technology and short-wavelength automated perimetry (SWAP) are two alternative testing methods to detect visual field damage.³²³⁻³²⁶ Frequency doubling technology measures contrast sensitivity for a frequency doubling stimulus.³²⁷⁻³³¹ Visual field testing using SWAP isolates short-wavelength sensitive cells using a narrow band of blue-light stimulus on a yellow background-illuminated perimeter bowl.³³² Although SWAP and frequency doubling technology were developed to identify glaucomatous field loss earlier than SAP, they are not recommended for routine glaucoma management. See Tables 8 and 9 in the Follow-up Evaluation section below for recommended guidelines for follow-up timing and frequency for visual field evaluation.³¹⁸

Virtual reality visual field testing may offer a more accessible and patient-friendly alternative to traditional methods for detecting glaucomatous visual field loss.³³³ Multiple studies have demonstrated good agreement between virtual reality visual field testing and SAP in identifying glaucomatous visual field defects.³³⁴⁻³⁴¹ Virtual reality allows for portable and home-based testing, potentially enhancing patient monitoring and early detection of glaucomatous progression. Technical limitations, such as restricted luminance range and lack of advanced eye-tracking, may impact the precision of visual field assessments.³³³ Additionally, current studies have been conducted primarily in controlled settings with selective populations. Further research is needed to determine the capacity of virtual reality visual field testing to detect glaucoma and monitor disease progression in real-world conditions.

Optic nerve head, circumpapillary retinal nerve fiber layer, and macular ganglion cell layer imaging

The appearance of the optic nerve and circumpapillary RNFL should be documented for the patient with POAG, if possible.^{287, 304} The disc damage likelihood scale may be used and takes into account the optic disc size and the thickness of the neuroretinal rim.³⁴² Stereoscopic disc photographs and computerized images of the nerve are complementary with regard to the information they provide to the clinician.³⁴³ In the absence of these methodologies, a nonstereoscopic photograph or a drawing of the optic nerve should be recorded, but this is a less desirable alternative to stereophotography or computer-based imaging.³⁴⁴⁻³⁴⁷ 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 in 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 in using stereophotography to identify

progressive optic nerve change in patients with advanced glaucomatous cupping because there is little, if any, nerve tissue to evaluate or measure.^{348, 349}

Computer-based digital imaging of the ONH, circumpapillary RNFL, and macular ganglion cell layer is routinely used to provide quantitative information to supplement the clinical examination of the optic nerve. Some patients demonstrate structural alterations in the ONH and parapapillary RNFL before functional change occurs. In many, but not all, cases, computerized imaging can be useful to distinguish between glaucomatous and nonglaucomatous RNFL thinning, based on the presence or absence of progression, respectively.³⁵⁰⁻³⁵² There are 3 types of computer-based optic nerve imaging devices that have been used to evaluate glaucoma: confocal scanning laser ophthalmoscopy, OCT, and scanning laser polarimetry. The versions of these devices that were studied in a systematic review were similar in their ability to distinguish glaucomatous eyes from control eyes.^{287, 353-355}

Results outside of the normative range (i.e., red disease) from these devices do not always represent disease.³⁵⁶ Criteria used to establish normative databases vary between different imaging devices, and ONH or circumpapillary RNFL/macular ganglion cell layer measurements may fall outside normative ranges for reasons other than glaucoma. Their interpretation should include an evaluation of all components of the report and not just their summary statistics, after an adequate assessment of scan quality is performed. 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 any quantitative imaging study represents true disease.³⁵⁷ As these instruments continue to improve, they may become more reliable in helping the clinician diagnose glaucoma and identify progressive nerve damage.³⁵⁰⁻³⁵² Furthermore, progression analysis programs for computer-based imaging devices are evolving to better detect optic nerve, circumpapillary RNFL, and macular ganglion cell layer imaging changes that may be secondary to glaucoma.^{358, 359}

Because some patients show visual field loss without corresponding optic nerve progression,^{19, 358-362} both structural and functional assessments remain integral to patient care. Even though quantitative 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.³⁴³ 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 pathogenic factors, including IOP, that contribute to damage. The characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons can result in progressive visual field loss. Other entities associated with optic disc damage or abnormalities of the visual field should be considered prior to confirming the diagnosis of glaucoma. Optic nerve pallor in excess of cupping and visual field defects aligning with the vertical meridian suggest nonglaucomatous disorders.³⁶³ Nonglaucomatous diseases associated with optic nerve and visual abnormalities include the following:

- ◆ Optic disc abnormalities
 - ◆ Anterior ischemic optic neuropathies
 - ◆ Optic nerve drusen
 - ◆ Myopic tilted optic nerves
 - ◆ Toxic optic neuropathies
 - ◆ Congenital disc anomalies (e.g., congenital pit, coloboma, periventricular leukomalacia in prematurity, morning glory syndrome, optic disc hypoplasia)
 - ◆ Hereditary optic neuropathies (e.g., Leber hereditary optic neuropathy, dominant optic atrophy)

- ◆ Optic neuritis
- ◆ Nutritional optic neuropathy
- ◆ Compressive optic neuropathy
- ◆ Traumatic optic neuropathy
- ◆ Retinal abnormalities
 - ◆ Age-related macular degeneration
 - ◆ Choriorretinal scars (e.g., from panretinal photocoagulation)
 - ◆ Retinitis pigmentosa
 - ◆ Retinal arterial and venous occlusions
 - ◆ Myelinated nerve fibers
 - ◆ Retinal colobomas
 - ◆ Neuroretinitis
 - ◆ Retinal detachment
 - ◆ Prior retinal procedures (e.g., vitrectomy with membrane peeling)

MANAGEMENT

Goals

The goals of managing patients with POAG are as follows:

- ◆ Control of IOP in the target range
- ◆ Stable optic nerve/circumpapillary RNFL status
- ◆ Stable visual fields

Ophthalmologists can lower IOP using laser surgery, medications, or incisional surgery. Results from randomized controlled trials (summarized in Table 2) and other studies provide evidence that these treatments reduce IOP and decrease the incidence and rate of progressive POAG.^{19, 45, 91-96, 99, 100, 102, 364-377}

Glaucoma medications have historically been used as the initial treatment for glaucoma. However, several multicenter, randomized clinical trials have challenged the traditional paradigm for glaucoma management. The Glaucoma Laser Trial (GLT) and Laser in Glaucoma and Ocular Hypertension Trial (LiGHT) compared eye drops and laser trabeculoplasty surgery as first-line treatments for open-angle glaucoma.^{378, 379} The Collaborative Initial Glaucoma Treatment Study (CIGTS) and Treatment of Advanced Glaucoma Study (TAGS) assessed whether patients with newly diagnosed OAG are better managed with initial medication or surgery.^{380, 381} The Moorfields Primary Therapy Trial evaluated the relative efficacy of medical therapy, laser trabeculoplasty surgery, and trabeculectomy as primary therapy in open-angle glaucoma.⁹⁹

Target Intraocular Pressure

When deciding to treat a patient with glaucoma, it is important to remember that the goal of treatment is to maintain the IOP within a range at which visual field loss is unlikely to substantially reduce a patient's health-related quality of life over his or her lifetime.³⁸² The estimated upper limit of this range is considered the "target pressure." The initial target pressure is an estimate and a means toward the ultimate goal of protecting the patient's vision. The target pressure should be individualized and may need adjustment further down or even up during the course of the disease.³⁸³

When initiating therapy, the ophthalmologist assumes that the measured pretreatment pressure range contributed to optic nerve damage and is likely to cause additional damage in the future. Factors to consider when choosing a target pressure include the stage of overall glaucomatous damage as determined by the degree of structural optic nerve injury and/or functional visual field loss, baseline IOP at which damage occurred, age of patient, and additional considerations (e.g., CCT, life expectancy, prior rate of progression). Lowering the pretreatment IOP by 25% or more has been shown to slow the progression of POAG.^{91, 93-95, 101, 102} Choosing a lower target

IOP can be justified if there is more severe optic nerve damage, if the damage is progressing rapidly, or if other risk factors such as family history, age, or disc hemorrhages are present (see Risk Factors for Progression section below). Choosing a less aggressive target IOP may be reasonable if the risks of treatment outweigh the benefits (e.g., if a patient does not tolerate medical treatment, laser or incisional surgical intervention would be difficult, or if the patient's anticipated life expectancy is limited). It should be noted, however, that high-quality prospective data comparing different target IOP levels are not currently available; as such, the trade-off between risks and benefits associated with different thresholds is unclear.³⁸⁴

The adequacy and validity of the target pressure should periodically be reassessed by comparing optic nerve status (by optic disc appearance and quantitative assessments of the ONH, circumpapillary RNFL, and macular ganglion cell layer) and visual field tests with results from previous examinations. Target IOP may change depending on the results of long-term monitoring. Target pressure is an estimate, and all treatment decisions must be individualized according to the needs of the patient. Although algorithms are useful in clinical practice, no validated algorithm for determining whether to lower or raise any given target IOP currently exists.³⁰⁸

Choice of Therapy

The IOP can be lowered by laser surgery, medical treatment, or incisional surgery (alone or in combination). Thorough discussion about the relative risks and benefits of a given treatment should be conducted with the patient prior to its initiation. The patient and 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, preferences, and degree of optic nerve damage.³⁰⁴ Systemic comorbidities that deserve consideration when choosing medical therapy for glaucoma include asthma/chronic obstructive pulmonary disease, cardiac arrhythmia, and depression. Patients who are pregnant or nursing also deserve special consideration.

Laser trabeculoplasty surgery

Laser trabeculoplasty surgery may be used as initial or adjunctive therapy in patients with POAG.^{366, 385-388} Laser trabeculoplasty surgery lowers IOP by improving aqueous outflow and can be performed using argon or solid-state lasers.^{389, 390} Laser trabeculoplasty surgery may be performed to 180 degrees or to 360 degrees of the angle. Several randomized clinical trials have evaluated the safety and efficacy of laser trabeculoplasty surgery (see Table 3).

Argon and diode laser trabeculoplasty surgery

The GLT, as well as other studies using continuous-wave argon laser with a wavelength spectrum that peaks at 488 nm (argon laser trabeculoplasty surgery [ALT]), found that treatment provides a clinically significant reduction of IOP in more than 75% of initial treatments on previously unoperated eyes.^{102, 391} More compact solid-state diode lasers have mostly replaced the original argon laser used in these initial studies with equal IOP-lowering efficacy and safety.^{392, 393}

For patients initially treated with ALT, the amount of medical treatment required for glaucoma control is often reduced.^{366, 394} Results from long-term studies of patients receiving maximum medical therapy who subsequently had laser surgery and incisional surgery indicate that 30% to more than 50% of eyes require additional surgical treatment within 5 years after ALT.^{102, 395-398} For eyes that have failed to maintain a previously adequate response, repeat ALT has a low long-term rate of success, with failure occurring in nearly 90% of these eyes by 2 years.³⁹⁹⁻⁴⁰³ Repeat ALT confers an increased risk of complications such as IOP spikes compared with initial ALT.^{399, 400, 403, 404}

Selective laser trabeculoplasty surgery

The introduction of selective laser trabeculoplasty surgery (SLT) is most likely responsible for the increase in use of laser trabeculoplasty surgery beginning in 2001 after a previous decline.⁴⁰⁵⁻⁴⁰⁷ Recent data further support its use as an initial therapy.⁴⁰⁸ Selective laser trabeculoplasty surgery uses a 532-nm, Q-switched, frequency-doubled Nd:YAG laser that

delivers less energy and is selectively absorbed by pigmented cells in the trabecular meshwork,⁴⁰⁹ producing less thermal damage than ALT.⁴¹⁰ However, several prospective and retrospective studies indicate that SLT appears to have a similar IOP-lowering effect to ALT.⁴¹¹⁻⁴¹⁹ Selective laser trabeculoplasty surgery also appears to be comparable in efficacy to medical therapy with prostaglandin analogs,^{385, 388, 420, 421} although in one prospective study, IOP lowering was only similar between treatments when 360 degrees (but not 90 or 180 degrees) of the trabecular meshwork was treated with SLT.⁴²⁰ A small, multicenter, randomized clinical trial comparing SLT and medical therapy (i.e., prostaglandin analog) as initial treatment for OAG found similar IOP reduction between groups after 1 year of follow-up.³⁸⁶ The LiGHT Trial was a larger multicenter, randomized trial comparing initial treatment with 360-degree SLT and medications in patients with OAG and ocular hypertension.³⁸⁷ Selective laser trabeculoplasty surgery was associated with better cost-effectiveness than medical therapy over 3 years, and it resulted in similar IOP lowering and quality-of-life scores. Rapid visual field progression occurred in more eyes in the medication-treated group than in the SLT-treated group.⁴²² Extension of the LiGHT Trial to 6 years of follow-up showed a significantly lower rate of disease progression and reduced need for glaucoma and cataract surgery for eyes initially treated with SLT compared with those initially treated with IOP-lowering drops.⁴⁰⁸ The West Indies Glaucoma Laser Study (WIGLS) demonstrated safe and effective IOP lowering 1 year after monotherapy with 360-degree SLT in Black patients in St. Lucia and Dominica.⁴²³

Several studies have demonstrated that repeat SLT is both safe and effective and that it achieves a similar reduction in IOP and duration of response as the initial treatment.^{390, 424-433} The choice of initial laser surgery treatment – selective or argon – does not appear to influence the effectiveness of repeat SLT.^{433, 434} In contrast, repeat ALT is less effective and carries risks such as post-procedure IOP elevation.^{399-402, 404, 435, 436}

The safety profile of SLT appears to be good, with only mild anterior chamber inflammation after treatment and less ocular discomfort compared with ALT.⁴¹⁵ Intraocular pressure spikes have been noted after SLT in 4.5% to 27% of eyes in various studies,^{408, 412, 416, 420, 433} which are similar to rates observed with ALT.^{412, 416} Clinical experience suggests that eyes with more heavily pigmented trabecular meshwork are more prone to IOP spikes.⁴³⁷

A 2022 Cochrane Systematic Review found that laser trabeculoplasty surgery may be more effective than topical drops in slowing the progression of visual field loss in OAG and may be similar to topical drops in controlling IOP at a lower cost.⁴³⁸ (*I-, Moderate Quality, Discretionary Recommendation*)

Although conventional SLT is performed with gonioscopic visualization of the trabecular meshwork during the procedure, a novel device has been developed to perform noncontact translimbal direct SLT (DSLTL). The automated Voyager™ DSLTL device (Alcon, Fort Worth, TX) uses a Q-switched, frequency-doubled Nd:YAG laser with a wavelength of 532 nm to direct laser energy to the limbus region without requiring contact with the patient's eye. A predefined number of laser pulses are applied 360 degrees around the limbus, passing directly to the trabecular meshwork.⁴³⁹ The GLAUrious Study is a multicenter, randomized clinical trial that compared DSLTL with conventional SLT.⁴⁴⁰ Direct selective laser trabeculoplasty surgery did not achieve statistical noninferiority compared with conventional SLT after 6 months of follow-up.⁴⁴¹

TABLE 3 RANDOMIZED CLINICAL TRIALS OF LASER TRABECULOPLASTY SURGERY

Study, Year	Study Design	No. of Patients	Follow-up Duration (years)	Finding
Glaucoma Laser Trial (GLT), 1990–1995 ^{391, 442}	Newly diagnosed POAG: medical therapy vs. ALT	271	2.5–5.5	Initial ALT lowered IOP more (9 mmHg) than initial treatment with topical timolol maleate (7 mmHg) over 2 years. Initial ALT was at least as effective in preserving visual field and optic disc status over 5.5 years.

TABLE 3 RANDOMIZED CLINICAL TRIALS OF LASER TRABECULOPLASTY SURGERY

Study, Year	Study Design	No. of Patients	Follow-up Duration (years)	Finding
Glaucoma Laser Trial Follow-up Study, 1995 ³⁹¹	Participants in the GLT	203	6–9	Longer follow-up reinforced the earlier findings that initial ALT lowered IOP more (1.2 mmHg greater IOP reduction) than initial treatment with topical timolol maleate and was at least as effective in preserving visual field and optic disc status.
Moorfields Primary Therapy Trial, 1994 ⁹⁹	Newly diagnosed POAG: medical therapy vs. ALT vs. trabeculectomy	168	5+	Trabeculectomy lowered IOP the most (60% IOP reduction). The ALT group (38% IOP reduction) and medical therapy group (49% IOP reduction) had more deterioration in visual fields than the trabeculectomy group.
Early Manifest Glaucoma Trial (EMGT), 2002–2007 ^{93, 94, 100}	Newly diagnosed POAG: medical therapy and ALT vs. no treatment	255	4–10	Lowering IOP with medical therapy and ALT (25% IOP reduction) slowed progression of optic disc and visual field damage.
Advanced Glaucoma Intervention Study (AGIS), 2000–2004 ^{95, 102}	POAG after medical-therapy failure with no previous surgery: ALT vs. trabeculectomy	591	10–13	Surgical outcome varied by race. Black patients did better with ALT first (30% IOP reduction), whereas White patients did better with trabeculectomy first (48% IOP reduction). No further visual field deterioration was seen on average in patients who maintained IOP <18 mmHg at all study visits (mean IOP = 12.3 mmHg).
Selective Laser Trabeculoplasty vs. Medical Therapy as Initial Treatment for Glaucoma, 2012 ³⁸⁶	POAG and OHTN: initial medical therapy vs. SLT	69	1	Medical therapy with prostaglandin analogs and 360-degree SLT showed similar IOP lowering at 1 year.
West Indies Glaucoma Laser Study (WIGLS), 2017 ⁴²³	POAG: immediate medication washout and SLT vs. 3-month delay then washout and SLT vs. 6-month delay then washout and SLT	72	1	360-degree SLT monotherapy reduced IOP by 20% in 78% of patients of Afro-Caribbean descent through 1 year.
Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial, 2019 ³⁸⁷	POAG and OHTN; initial medical therapy vs. SLT	718	3	Medical therapy resulted in similar IOP lowering and quality-of-life scores compared with 360-degree SLT at 3 years. SLT was more cost-effective than medication.
LiGHT Extension, 2023 ⁴⁰⁸	Participants in the LiGHT Trial	524	6	SLT provided better long-term disease control than initial medical therapy with reduced need for incisional glaucoma and cataract surgery.

ALT = argon laser trabeculoplasty surgery; IOP = intraocular pressure; OHTN = ocular hypertension; POAG = primary open-angle glaucoma; SLT = selective laser trabeculoplasty surgery.

Perioperative care for laser trabeculoplasty surgery

The ophthalmologist who performs the laser surgery has the following responsibilities.^{443, 444}

- ◆ To obtain informed consent from the patient or the patient's surrogate decision maker after discussing the risks, benefits, and expected outcomes of surgery

- ◆ To ensure that the preoperative evaluation confirms that surgery is indicated
- ◆ To perform at least one IOP check immediately prior to surgery and within 30 minutes to 2 hours after surgery⁴⁴⁵
- ◆ To perform a follow-up examination within 6 weeks of surgery or sooner if there is concern about IOP-related damage to the optic nerve during this time^{395, 446-448}

Randomized clinical trials have compared different short-term anti-inflammatory regimens after SLT and provide mixed results regarding their influence on IOP outcomes. While some studies have demonstrated no effect of anti-inflammatory eye drops on postoperative IOP,⁴⁴⁹⁻⁴⁵¹ others have shown improved IOP reduction with the use of prednisolone acetate 1%^{452, 453} or ketorolac 0.5%.⁴⁵²

Medications that are not being used chronically may be used perioperatively to avert temporary IOP elevations, particularly in those patients with severe disease.^{445, 454, 455} A 2017 Cochrane Systematic Review found that perioperative medications are superior to no medication to prevent the occurrence of spikes in IOP.⁴⁵⁶ Therefore, in consultation with the individual patient, treating ophthalmologists should use perioperative medications if temporary IOP elevations are a concern. (*I+*, *Moderate Quality*, *Strong Recommendation*) Brimonidine has been shown to be as effective as apraclonidine in preventing immediate IOP elevation after laser trabeculoplasty surgery.^{457, 458} Treating 180 degrees reduces the incidence and magnitude of postoperative IOP elevation compared with 360-degree treatment.⁴⁵⁹⁻⁴⁶¹

Medical treatment

Topical medical therapy is currently the most common initial intervention to lower IOP (see Table 4 for an overview of options available). Prostaglandin analogs are the most frequently prescribed eye drops for lowering IOP in patients with glaucoma because they are most efficacious and well tolerated, and they need to be instilled only once daily.^{96, 462-464} Therefore, prostaglandin analogs are often selected as initial medical therapy unless other considerations, such as contraindications, cost, side effects, intolerance, or patient refusal preclude this.⁴⁶⁵⁻⁴⁶⁷

Topical beta adrenergic antagonists are commonly prescribed to treat glaucoma and have demonstrated good efficacy and tolerability.⁴⁶⁴ Nonselective beta adrenergic antagonists (e.g., timolol) block both beta-1 (primarily cardiac) and beta-2 (primarily pulmonary) receptors. Cardioselective beta-blockers (e.g., betaxolol) target beta-1 receptors and minimize, but do not completely eliminate, the risk of pulmonary adverse effects in patients with obstructive airway disease.⁴⁶⁸ Topical beta-blockers may be dosed once or twice daily. However, nighttime dosing of beta-blockers is associated with limited efficacy⁴⁶⁹ and may contribute to visual field progression via nocturnal reduction of systemic blood pressure.⁴⁷⁰ Other glaucoma medications used to provide long-term IOP reduction include alpha₂ adrenergic agonists, parasympathomimetics, rho-kinase inhibitors, and topical and oral carbonic anhydrase inhibitors.⁴⁷¹⁻⁴⁷³

TABLE 4 GLAUCOMA MEDICATIONS

Drug Classification	Agents	Mechanism of Action	IOP Reduction*	Potential Side Effects	Potential Contraindications	FDA Pregnancy Safety Category†
Prostaglandin analogs	Bimatoprost Latanoprost Latanoprostene bunod ^{†§} Omidenedapag [§] Tafluprost Travoprost	Increase uveoscleral outflow	25%–33%	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • Macular edema • History of herpetic keratitis • Active uveitis 	C
Beta-adrenergic antagonists (beta-blockers)	<u>Nonselective</u> Carteolol Levobunolol Timolol <u>Selective</u> Betaxolol	Decrease aqueous production	20%–25%	<ul style="list-style-type: none"> • Allergic conjunctivitis/contact dermatitis • Keratitis • Bronchospasm • Bradycardia • Hypotension • CHF • Reduced exercise tolerance • Depression • Impotence 	<ul style="list-style-type: none"> • Chronic obstructive pulmonary disease • Asthma • CHF • Bradycardia • Hypotension • Greater than first-degree heart block 	C
Alpha-2-adrenergic agonists	Apraclonidine Brimonidine	Decrease aqueous production; decrease episcleral venous pressure or increase uveoscleral outflow	20%–25%	<ul style="list-style-type: none"> • Allergic/follicular conjunctivitis/contact dermatitis • Dry mouth and nose • Hypotension • Headache • Fatigue • Somnolence • Respiratory depression (in infants and children) 	<ul style="list-style-type: none"> • Monoamine oxidase inhibitor therapy • Infants and children 	B

TABLE 4 GLAUCOMA MEDICATIONS

Drug Classification	Agents	Mechanism of Action	IOP Reduction*	Potential Side Effects	Potential Contraindications	FDA Pregnancy Safety Category†
Parasympathomimetic agents	<u>Cholinergic agonist</u> Pilocarpine <u>Anticholinesterase agent</u> Echothiophate	Increase trabecular outflow	20%–25%	<ul style="list-style-type: none"> • Increased myopia • Decreased vision • Cataract • Allergic conjunctivitis/contact dermatitis • Conjunctival scarring • Keratitis • Paradoxical angle closure • Retinal tears/detachment • Eye or brow ache/pain • Increased salivation • Abdominal cramps 	<ul style="list-style-type: none"> • Areas of peripheral retina that predispose to breaks • The need to regularly assess the fundus • Neovascular, uveitic, or malignant glaucoma 	C
Rho kinase inhibitors	Netarsudil [§]	Increase trabecular outflow. Decrease episcleral venous pressure. Decrease aqueous production.	10%–20%	<ul style="list-style-type: none"> • Conjunctival hyperemia • Corneal verticillate • Instillation site pain • Conjunctival hemorrhage • Keratitis • Allergic conjunctivitis/contact dermatitis 	<ul style="list-style-type: none"> • None 	--- [§]
Topical carbonic anhydrase inhibitors	Brinzolamide Dorzolamide	Decrease aqueous production	15%–20%	<ul style="list-style-type: none"> • Allergic conjunctivitis/contact dermatitis • Corneal edema • Keratitis • Metallic taste 	<ul style="list-style-type: none"> • Sulfonamide allergy • Sickle cell disease with hyphema 	C
Oral carbonic anhydrase inhibitors	Acetazolamide Methazolamide	Decrease aqueous production	20%–30%	<ul style="list-style-type: none"> • Stevens-Johnson syndrome • Malaise, anorexia, depression • Serum electrolyte imbalance • Renal calculi • Blood dyscrasias (aplastic anemia, thrombocytopenia) • Metallic taste • Enuresis • Parasthesia • Diarrhea • Abdominal cramps 	<ul style="list-style-type: none"> • Sulfonamide allergy • Kidney stones • Aplastic anemia • Thrombocytopenia • Sickle cell disease 	C
Hyperosmotic agents	Glycerol Mannitol	Dehydration of vitreous	No data	<ul style="list-style-type: none"> • Headache • CHF • Nausea, vomiting • Diarrhea • Renal failure • Diabetic complications • Mental confusion 	<ul style="list-style-type: none"> • Renal failure • CHF • Potential CNS pathology 	C

CHF = congestive heart failure; CNS = central nervous system; FDA = Food and Drug Administration; 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: http://www.icoph.org/dynamic/attachments/resources/egs_guidelines_4_english.pdf Accessed October 16, 2020.
- † 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.
- ‡ Latanoprostene bunod is rapidly metabolized to latanoprost (a prostaglandin analog) and butanediol mononitrate (a nitric oxide-donating moiety). It enhances aqueous humor outflow through both the uveoscleral and trabecular meshwork pathways.⁴⁷⁴⁻⁴⁷⁷
- § The FDA replaced the ABCDX drug pregnancy categories with descriptive information on medication risks to the developing fetus, breastfed infant, and individual of reproductive potential under the Pregnancy and Lactation Labeling Rule in 2015. Therefore, this drug is not assigned a pregnancy category. No data exist in pregnant women.

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 monocular trials have been recommended in the past to determine whether a topical ocular hypotensive agent is effective, studies have shown that such trials are not good predictors of long-term efficacy.^{478, 479} A monocular trial is defined as the initiation of treatment in only one eye, followed by a comparison of the relative change in 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 agents may have a contralateral effect.⁴⁸⁰ 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.⁴⁸¹

If a drug fails to reduce IOP sufficiently, then either switching to an alternative medication as monotherapy or adding medication is appropriate until the desired IOP level is attained.³⁰⁴ Because some studies have shown that adding a second medication decreased adherence to glaucoma treatment,^{482, 483} fixed combination therapy may improve patient adherence and reduce exposure to preservatives, although it is not recommended for initial treatment in most circumstances. However, when the necessary reduction of IOP exceeds the expected efficacy of a single drug, combination therapy may be prescribed in selected patients. Addition of a second, third, or fourth glaucoma medication has been shown to result in an incremental reduction in IOP, but the effect is usually smaller than for the first medication.^{484, 485} A study evaluating the IOP following a pre-randomization glaucoma medication washout in the HORIZON and COMPASS Trials noted a 24% reduction in IOP with the first medication, whereas each additional drop conferred only about 4% further reduction.⁴⁸⁴ Retrospective studies have reported additional IOP lowering of 3 to 4 mmHg or approximately 15% to 25% by adding a third or fourth agent to an existing regimen.⁴⁸⁶⁻⁴⁸⁹

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.³⁰⁴ 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. Patients should be educated about eyelid closure or nasolacrimal occlusion to reduce systemic absorption after eye drop instillation (see Related Academy Materials section for patient education brochures).⁴⁹⁰

Adequate treatment of glaucoma requires a high level of adherence to therapy. Frequently this is not achieved, and studies indicate relatively poor adherence to therapy.⁴⁹¹⁻⁴⁹⁴ Multiple dosing requirements or side effects (such as depression, exercise intolerance, and impotence that might occur with topical beta-blockers) may impact adherence to therapy.^{483, 495} Cost may be a factor in adherence, especially when multiple medications are used.⁴⁹⁶ Even with instruction, free medication, once-daily administration, use of a dosing aid, and electronic monitoring of adherence, nearly 45% of patients in one study took fewer than 75% of their prescribed doses.⁴⁹⁴ Instilling eye drops correctly is difficult for many patients, and their ability to instill them may worsen with aging and comorbidities and as glaucoma progresses.^{496, 497} Repeated instruction and counseling about proper techniques

for using medication, including waiting at least 5 minutes between multiple drop regimens, as well as a clearly written medication regimen and follow-up telephone calls or smartphone reminders, may improve adherence to therapy.^{494, 498, 499} (*I-, Insufficient Quality, Strong Recommendation*) One randomized controlled trial studied a multifaceted intervention involving comprehensive and personalized patient and companion education and the use of a reminder aid on glaucoma medications. In this study, the average proportion of glaucoma medication taken on time over a 6-month period was significantly better for patients receiving the intervention compared with patients in the control arm.⁵⁰⁰ A 2022 Cochrane Systematic Review further indicated that interventions involving face-to-face assessments and the creation of personalized, tailored care plans improved ocular hypotensive therapy adherence. Moreover, multifaceted interventions were superior to single interventions in increasing adherence. However, the review did not determine which intervention strategy produced better clinical outcomes for patients.⁵⁰¹ Thus, adherence interventions are left to the judgment of the treating ophthalmologist. (*I-, Moderate Quality, Discretionary Recommendation*) At each examination, medication dosage and frequency of use should be reviewed and recorded. Reviewing the time medication was taken may help patients link eye-drop administration to common activities of daily living and help to ensure patients are actually using their eye drops. Adherence to the therapeutic regimen and recommendations for therapeutic alternatives should be discussed.

Adherence to medical therapy may be reduced when patients run out of medication, due to inadvertent drop wastage or inability to properly instill eye drops, before they are permitted to refill their prescription. One study found this was more likely for patients who self-administered eye drop medications when visual acuity was worse than 20/70 in either eye.⁵⁰² However, patients who have Medicare prescription drug coverage may now refill their medication after they have completed at least 70% of the month, or approximately 21 days of therapy.⁵⁰³ Some states have enacted legislation that allows access to early refills for all beneficiaries. Multiple drug delivery systems have been developed to address the problems of patient adherence and side effects associated with glaucoma medical therapy. Enhanced drug delivery targets include punctal plugs,⁵⁰⁴ rings placed in the fornix,⁵⁰⁵ contact lenses,⁵⁰⁶ subconjunctival injections⁵⁰⁷/devices,⁵⁰⁸ intracameral delivery systems,⁵⁰⁹ and drug-eluting intraocular devices.⁵¹⁰

In 2020, a bimatoprost intracameral implant (Durysta, Allergan, an Abbvie company, North Chicago, IL) received U.S. Food and Drug Administration (FDA) approval for use in patients with ocular hypertension and POAG. This biodegradable implant, which is injected with a 28-gauge delivery system, demonstrated noninferiority to twice-daily timolol in phase 3 clinical trials.⁵¹¹ In phase 1 and 2 studies, a single bimatoprost sustained-release implant showed similar efficacy to topical bimatoprost 0.03% through 4 months of follow-up, and 68% of patients had a persistent effect at 6 months.⁵⁰⁹ This implant is currently FDA approved only for a single administration because repeat intracameral implants were associated with a higher degree of corneal endothelial cell loss. Several studies are underway to investigate the mechanisms of sustained action and to better understand safe and effective dosing.

In 2023, a travoprost-eluting implant (iDose TR, Glaukos, Aliso Viejo, CA) was FDA approved to be surgically implanted into the trabecular meshwork based on two prospective, randomized, multicenter, double-masked phase 3 trials that showed noninferiority to topical timolol.⁵⁰⁹ At 3 years, a greater percentage of patients receiving the implant (versus patients receiving timolol) were well controlled on the same or fewer topical IOP-lowering medications.²⁶⁹

Special circumstances in pregnancy and during breastfeeding

Managing glaucoma in the pregnant or lactating patient involves an interdisciplinary approach to prevent disease progression in the mother while minimizing risks to the fetus and nursing infant. Punctal occlusion should be emphasized when caring for patients who are pregnant or nursing and using glaucoma drop therapy. Laser trabeculoplasty surgery may be considered as an alternative or adjunct to medical therapy in select patients during pregnancy and breastfeeding. Detailed practical recommendations on IOP lowering in these

patients are available in a guide by the American Glaucoma Society and Canadian Glaucoma Society.⁵¹²

Pregnancy

Glaucoma medical management of the pregnant patient presents challenges with respect to balancing the risk of glaucoma progression⁵¹³ against concerns for the safety of the fetus.⁵¹⁴⁻⁵¹⁶ Given the high risk of teratogenicity in the first trimester, a treatment strategy before and during pregnancy should be discussed with women with glaucoma who are of childbearing age and interested in conceiving. Because IOP levels may decrease during pregnancy, temporarily discontinuing treatment may be considered in select patients under strict follow-up. Data on the risks of topical ocular hypotensive agents during pregnancy are limited. The FDA established drug pregnancy categories of A, B, C, D, and X in 1979.⁵¹⁷ Pregnancy Category A indicates evidence from studies in pregnant women that the drug failed to show fetal risk in any trimester. Category B indicates that 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. Beta-blockers, prostaglandin analogs, topical carbonic anhydrase inhibitors, parasympathomimetics, and hyperosmotics have a Pregnancy Category C rating. Beta-blockers tend to be used during pregnancy because there is long-term experience with this drug class. A paucity of data exists 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.⁵¹⁸ 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 breastfeeding mother.⁵¹⁶ Oral carbonic anhydrase inhibitors have been shown to cause teratogenicity when delivered in high doses to animals.⁵¹⁹

The FDA replaced the ABCDX drug pregnancy categories with descriptive information on medication risks to the developing fetus, breastfed infant, and individual of reproductive potential under the Pregnancy and Lactation Labeling Rule in 2015. Therefore, rho kinase inhibitors and other medications approved after 2015 are not assigned a pregnancy category. No data exist on the use of netarsudil in pregnant women. Animal studies did not demonstrate adverse effects on the developing fetus with clinically relevant intravenous exposures.⁵²⁰

Breastfeeding

Some topical glaucoma medications have been detected in breast milk, such as timolol, carbonic anhydrase inhibitors, and brimonidine. The data are inconsistent as to whether timolol poses a threat to the breastfeeding 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.^{516, 521} Brimonidine is known to cross the blood-brain barrier and can cause apnea in infants, toddlers, and children. Therefore, brimonidine should be avoided in mothers who are breastfeeding.⁵¹⁵

Incisional glaucoma surgery

Glaucoma surgery lowers IOP by enhancing aqueous outflow. Minimally invasive (or micro-invasive) glaucoma surgery (MIGS) is a newer group of non bleb-forming procedures that augment aqueous drainage through the physiologic outflow pathway. Trabeculectomy and aqueous shunts are commonly referred to as traditional glaucoma surgery, and these procedures create a bleb by diverting aqueous into the subconjunctival space. Traditional glaucoma surgery generally produces greater IOP reduction than MIGS but also has a higher risk of complications. The continued expansion of surgical options for managing glaucoma has allowed surgeons to tailor the selection of a procedure to the

individual patient.⁵²² Multicenter, randomized clinical trials have provided valuable information to guide the surgical care of patients with glaucoma.

Minimally invasive glaucoma surgery

The term MIGS refers to a group of surgical procedures that are performed using an ab interno approach and involve minimal trauma to ocular tissues.^{523, 524} The number of MIGS procedures continues to grow, and their use has become widespread among glaucoma and cataract specialists. Modest IOP reduction has been reported following MIGS, and postoperative pressures are typically in the mid to upper teens.⁵²⁵ Although less effective in lowering IOP than trabeculectomy and aqueous shunt surgery, MIGS has a more favorable safety profile. Currently available FDA-approved MIGS includes procedures targeting the trabecular meshwork/Schlemm's canal. They are commonly combined with phacoemulsification; some are FDA approved only to be performed concurrently with phacoemulsification. Large, prospective trials have evaluated the efficacy of MIGS procedures (see Table 5). These trials generally enrolled patients with mild to moderate OAG with elevated IOP.

Trabecular meshwork/Schlemm's canal-based MIGS

Trabecular MIGS includes the cutting or removal, dilation, or stenting of varying extents of the trabecular meshwork and inner wall of Schlemm's canal under gonioscopic guidance. These procedures enhance aqueous access to collector channels and increase outflow.⁵²⁶ The IOP-lowering effect of trabecular MIGS is limited by resistance in distal outflow pathways and the episcleral venous pressure.

Tissue cutting/removing procedures

Trabectome: Trabectome (MicroSurgical Technology, Redmond, WA) uses high-frequency electrocautery to remove up to 180 degrees of trabecular meshwork through a single corneal incision.⁵²⁷⁻⁵³³ In a meta-analysis of 5091 patients, the rate of surgical success was 46% for stand-alone Trabectome and 85% for cataract extraction and Trabectome at 2 years.⁵²⁸ Prior laser trabeculoplasty does not appear to significantly affect the results of Trabectome.^{534, 535} A failed Trabectome did not affect the success rate of subsequent trabeculectomy in one cohort study.⁵³⁶ The most common complications include hyphema (up to 100%), peripheral anterior synechiae (14%), and IOP spikes (6%).⁵²⁸ Spontaneous, delayed hyphema has been reported up to 31 months after uncomplicated Trabectome.⁵³⁷

Kahook Dual Blade (KDB): The KDB (New World Medical, Rancho Cucamonga, CA) is a single-use instrument with two parallel blades on a footplate/ramp that allows excision of a strip of trabecular meshwork of Schlemm's canal with minimal collateral damage to adjacent structures. The single-use goniotomy blade may be used with cataract surgery or as a stand-alone procedure. Retrospective studies with short-term follow-up demonstrate modest IOP-lowering when KDB goniotomy is performed with or without phacoemulsification, with minimal associated complications.⁵³⁸⁻⁵⁴⁰ A single-center, randomized, controlled trial found that KDB combined with cataract surgery did not offer significant additional IOP and glaucoma medication reduction compared with phacoemulsification alone after 1 year of follow-up.⁵⁴¹ Another randomized, controlled clinical trial demonstrated that combined phacoemulsification and KDB goniotomy had a higher rate of surgical success at 1 year compared with combined phacoemulsification and iStent microbypass (Glaukos Corporation, Aliso Viejo, CA) implantation.⁵⁴² Transient hyphema (up to 17%) and IOP spikes (up to 17%) were the most common early postoperative complications.⁵⁴³ Infrequent complications included injury to Descemet's membrane (3.8%) and creation of a cyclodialysis cleft (up to 1.2%).

Tanito Microhook (TMH): The TMH (Imami & Co., Ltd, Tokyo, Japan) is a reusable instrument with a sharpened, bent tip that cleaves the trabecular meshwork and Schlemm's canal. The TMH is available straight, right-angled, and left-angled. A randomized, single-center trial reported greater IOP reduction and surgical success with TMH combined with phacoemulsification than phacoemulsification alone after 1 year of follow-up.⁵⁴⁴ The most frequent complication of TMH was hyphema (7%).

SION Surgical Instrument: The SION Surgical Instrument (Sight Sciences, Menlo Park, CA) is a single-use device used to excise trabecular meshwork. A rounded toe punctures the trabecular meshwork, a lower foot guides the instrument along Schlemm's canal, and an upper foot directs excised trabecular meshwork into the trap and tissue collection window.

iAccess Precision Blade: The iAccess Precision Blade (Glaukos Corporation, Aliso Viejo, CA) is a single-use, circular blade with a 300-micron deep backstop that is used to create multiple incisions and excisions of 220-micron segments of trabecular meshwork and the inner wall of Schlemm's canal or a continuous incision over at least 90 degrees.

Gonioscopy-assisted transluminal trabeculotomy (GATT): In GATT, circumferential cannulation and subsequent cleaving of Schlemm's canal is performed with the iTrack illuminated microcatheter (Nova Eye Medical, Fremont, CA) or suture. A meta-analysis of 537 eyes showed that GATT produced a 9.81-mmHg reduction in IOP, and a decrease in the number of glaucoma medications by 1.67.⁵⁴⁵ The most frequent complications were hyphema (12.5%–80.6%), IOP spikes (1.9%–32.3%), and transient hypotony (4.5%–6.5%). Descemet's detachment (0.5%), iridodialysis (0.5%), and vitreous hemorrhage (2.9%) occurred less commonly. Ciliochoroidal detachment has been detected using anterior segment OCT in 47.7% of patients undergoing GATT, although they are typically asymptomatic and self-limited.⁵⁴⁶

OMNI Surgical System: The OMNI Surgical System (Sight Sciences, Menlo Park, CA) is an alternative means of performing viscodilation of Schlemm's canal and collector channels and a trabeculotomy over 180- to 360-degrees (previously TRAB360) using a retractable microcatheter. In a prospective, multicenter study, viscodilation and trabeculotomy using the OMNI Surgical System combined with cataract surgery resulted in a 35% reduction in mean IOP and an 80% decrease in the number of glaucoma medications at 1 year.⁵⁴⁷ Hyphema (6%) and IOP spikes (2%) were the most common complications.

Dilation procedures

Ab interno canaloplasty (ABiC): In ABiC, the iTrack illuminated microcatheter is used to circumferentially dilate Schlemm's canal with cohesive viscoelastic. Unlike ab externo canaloplasty, ABiC does not involve incision of the conjunctiva or placement of a tension suture. Small retrospective studies have demonstrated IOP lowering to the midteens 1 year after ABiC, with or without concomitant cataract surgery. The success of ABiC in reducing postoperative glaucoma medication burden is less clear.^{548, 549} Efficacy of ABiC appears to be comparable to that of ab externo canaloplasty.⁵⁵⁰ A randomized controlled trial comparing GATT with ABiC in patients with OAG demonstrated lower mean IOP after GATT, but similar success rates were seen with both procedures at 1 year.⁵⁵¹ Hyphema (47%), IOP spikes (42%), and supraciliary effusion (71%) were common complications after ABiC.

OMNI Surgical System: The OMNI Surgical System utilizes a flexible microcatheter to perform viscodilation of Schlemm's canal and collector channels (previously VISCO360). No prospective studies evaluating only viscodilation are currently available.

Streamline Surgical System: The Streamline Surgical System (New World Medical, Inc., Rancho Cucamonga, CA) involves cannulation and viscodilation of Schlemm's canal and collector channels. A multicenter, randomized clinical trial found similar reduction of IOP and medical therapy when phacoemulsification was combined with viscodilation using the Streamline Surgical System or iStent implantation after 6 months of follow-up.⁵⁵²

Stenting procedures

iStent/iStent inject: The first-generation trabecular microbypass stent, or iStent (Glaukos Corporation, Aliso Viejo, CA), is a single snorkel-shaped device manufactured from heparin-coated titanium that is implanted into Schlemm's canal using a preloaded inserter. The iStent is FDA approved for implantation in combination with cataract surgery in patients with mild to moderate OAG. A multicenter, randomized clinical trial showed that the proportion of patients with an unmedicated IOP of 21 mmHg or lower

was higher in patients who received cataract surgery combined with an iStent compared with cataract surgery alone at 2 years.⁵⁵³ Studies suggest that implantation of multiple stents may provide better IOP lowering than a single stent; however, placement of more than one first-generation iStent is considered off-label use in the United States.⁵⁵⁴⁻⁵⁵⁷

The second-generation iStent inject (Glaukos Corporation, Aliso Viejo, CA) includes two conical implantable stents in a preloaded injector and has the same indications as its predecessor. A randomized trial comparing implantation of two iStent inject devices with fixed-combination latanoprost/timolol found comparable efficacy between the two groups.⁵⁵⁸ Another multicenter, randomized clinical trial found that patients randomized to cataract extraction with iStent inject were more likely to achieve an IOP reduction of 20% or more from baseline after washout compared with those undergoing cataract extraction alone.⁵⁵⁹ A 2019 Cochrane Systematic Review found very low-quality evidence that iStent/iStent inject achieves better IOP control or reduction in medications and that future research should include more quality-of-life outcomes. Thus, the selection of iStent or medications should be left to the discretion of the treating ophthalmologist, in consultation with the individual patient.⁵⁶⁰ (*I-, Insufficient Quality, Strong Recommendation*)

In 2022, the FDA approved the iStent infinite system (Glaukos Corporation, Aliso Viejo, CA) to be used as a stand-alone procedure without concomitant cataract surgery. The iStent infinite includes three heparin-coated implantable stents in a preloaded auto-injector. In a multicenter pivotal trial, implantation of iStent infinite was performed in eyes with OAG uncontrolled by prior incisional or cilioablativ surgery or on maximum tolerated medical therapy. The stand-alone procedure achieved clinically significant IOP reduction with a favorable safety profile at 1 year.⁵⁶¹

Similar surgical complications occur with the iStent and iStent inject. Adverse events reported in randomized clinical trials included hyphema (1.2%–1.9%), IOP spikes (1%–33%), corneal injury (3.1%), peripheral anterior synechiae formation (1.8%), and cyclodialysis cleft (1.2%).⁵⁴³ Stent-related complications included obstruction (1%–13.2%) and malposition (3%–18%).

Hydrus Microstent: The intracanalicular scaffold, or Hydrus Microstent (Alcon, Fort Worth, TX), is an 8-mm nitinol implant that is inserted into Schlemm’s canal via an ab interno approach using a preloaded injector. Like the iStent, the Hydrus Microstent is approved for use in patients with mild to moderate POAG who are undergoing concurrent phacoemulsification. Studies have demonstrated IOP reductions to the midteens, with a decreased need for glaucoma medications after Hydrus Microstent implantation combined with cataract surgery compared with cataract surgery alone.^{562,}

⁵⁶³ At 1 year, stand-alone Hydrus Microstent implantation resulted in higher success rates and use of fewer glaucoma medications compared with placement of two iStents in a randomized clinical trial.⁵⁶⁴ A 2020 Cochrane Systematic Review found moderate evidence that the Hydrus Microstent in the short term is more effective when compared with iStent for lowering IOP of patients with OAG.⁵⁶⁵ (*I, Moderate Quality, Strong Recommendation*) Most complications of the Hydrus Microstent were self-limited, included hyphema (0.5%–36%), IOP spikes (0.5%–20%), and corneal edema (1.4%–28.0%).⁵⁴³ Adverse events relating to the microstent itself include focal peripheral anterior synechiae (8.7%–20.0%), device obstruction (1.1%–12.2%), and device malposition (1.1%).

Suprachoroidal MIGS

CyPass Micro-Stent: The CyPass Micro-Stent (Alcon Laboratories, Fort Worth, TX) is an ab interno suprachoroidal shunt that was FDA approved for implantation at the time of cataract surgery in patients with mild to moderate POAG.⁵⁶⁶ A 2021 Cochrane Systematic Review reported data from a single randomized, controlled trial that showed superiority of combined CyPass and cataract surgery compared with cataract surgery alone in achieving medication-free control of POAG.⁵⁶⁷ (*I-, Moderate Quality, Discretionary Recommendation*) However, the CyPass underwent market withdrawal and an FDA Class I recall in 2018 after a post-approval study demonstrated significantly greater endothelial cell loss at 5 years in patients who received combined CyPass and

TABLE 5 LARGE, PROSPECTIVE CLINICAL TRIALS ON EFFICACY OF MINIMALLY INVASIVE GLAUCOMA SURGERY (MIGS)*

Study, Year	Treatment Groups (n)	Follow-up	Efficacy Outcome Measures	Results	P-value
			Glaucoma medications	Mean glaucoma medications CE-IOL/KDB: 0.27 (-79.1%) CE-IOL/iStent: 0.41 (-70.5%)	<i>P</i> = 0.17
			IOP ≤18 mmHg	IOP ≤18 mmHg CE-IOL/KDB: 72.2% CE-IOL/iStent: 67.9%	<i>P</i> = 0.19
Tanito Microhook					
Maheshwari et al, 2023 ⁵⁴⁴	CE-IOL/TMH (57) CE-IOL (57)	1 year	IOP	Mean IOP CE-IOL/TMH: 12.5 ± 3.6 mmHg (-51.5%) CE-IOL: 20.0 ± 2.7 mmHg (-20.1%)	<i>P</i> < 0.001
			Glaucoma medications	Mean glaucoma medications CE-IOL/TMH: 0.2 ± 0.5 CE-IOL: 1.1 ± 0.9	<i>P</i> < 0.001
			Success criteria Criterion 1: IOP 6–18 mmHg or ≥20% reduction from baseline Criterion 2: IOP 6–15 mmHg or ≥25% reduction from baseline	Complete success criterion 1 CE-IOL/TMH: 90.3% CE-IOL: 0%	<i>P</i> < 0.001
			Success/failure definitions Complete success: Success without use of glaucoma medications	Complete success criterion 2 CE-IOL/TMH: 86.9% CE-IOL: 0%	<i>P</i> < 0.001
			Qualified success: Success with use of same or fewer glaucoma medications	Qualified success criterion 1 CE-IOL/TMH: 90.9% CE-IOL: 49.1%	<i>P</i> < 0.001
			Failure: Inability to meet success criteria or requiring glaucoma surgery	Qualified success criterion 2 CE-IOL/TMH: 87.4% CE-IOL: 31.6%	<i>P</i> < 0.001
Omni Surgical System					
GEMINI Study, 2022 ⁵⁴⁷	CE-IOL/360° canaloplasty and 180° trabeculotomy with OMNI (149)	1 year	Unmedicated diurnal IOP	Mean unmedicated diurnal IOP:† 15.6 ± 4.0 mmHg (-35%)	–
			Glaucoma medications	Mean glaucoma medications: 0.4 ± 0.9 (-80%)	
			Unmedicated diurnal IOP reduced ≥20% from baseline	Unmedicated diurnal IOP reduced ≥20% from baseline:† 84.2%	
			Unmedicated diurnal IOP 6–18 mmHg	Unmedicated diurnal IOP 6–18 mmHg:† 76%	
iStent					
US iStent Study, 2012 ⁵⁵³	CE-IOL/iStent (117) CE-IOL (123)	2 years	Unmedicated IOP ≤21 mmHg (primary)	Unmedicated IOP ≤21 mmHg CE-IOL/iStent: 61% CE-IOL: 50%	<i>P</i> = 0.036

TABLE 5 LARGE, PROSPECTIVE CLINICAL TRIALS ON EFFICACY OF MINIMALLY INVASIVE GLAUCOMA SURGERY (MIGS)*

Study, Year	Treatment Groups (n)	Follow-up	Efficacy Outcome Measures	Results	P-value
			Unmedicated IOP reduced $\geq 20\%$ from baseline (secondary)	Unmedicated IOP reduced $\geq 20\%$ from baseline CE-IOL/iStent: 53% CE-IOL: 544%	$P = 0.090$
			Glaucoma medications	Mean glaucoma medications CE-IOL/iStent: CE-IOL/iStent: $0.3 \pm 0.6 (-1.3)$ CE-IOL: CE-IOL: $0.5 \pm 0.7 (-0.9)$	NR
Katz et al, 2018 ⁵⁷³	1 iStent (38) 2 iStents (41) 3 iStents (40)	42 months	Unmedicated IOP reduced $\geq 20\%$ from baseline†	Unmedicated IOP reduced $\geq 20\%$ from baseline 1 iStent: 61% 2 iStents: 91% 3 iStents: 91%	NR
			IOP	Mean IOP 1 iStent: 15.0 ± 2.8 mmHg 2 iStents: 15.7 ± 1.0 mmHg 3 iStents: 14.8 ± 1.3 mmHg	NR
Fechtner et al, 2019 ⁵⁷⁴	2 iStents (54) Travoprost (47)	5 years	Success (IOP 6–18 mmHg without additional glaucoma surgery or medications)	Success 2 iStents: 77% Travoprost: 53%	$P = 0.04$
			Diurnal IOP	Mean diurnal IOP 2 iStents: 16.5 ± 1.2 mmHg (-35.3%) Travoprost: 16.3 ± 1.9 mmHg (-35.1%)	NR
iStent inject					
Second Line Study, 2014 ⁵⁵⁸	iStent Inject (94) Latanoprost/timolol (98)	1 year	Diurnal IOP reduction $\geq 20\%$ from baseline	Diurnal IOP reduction $\geq 20\%$ from baseline iStent Inject: 94.7% Latanoprost/timolol: 91.8%	NR
			Diurnal IOP ≤ 18 mmHg	Diurnal IOP ≤ 18 mmHg iStent Inject: 92.6% Latanoprost/timolol: 89.8%	NR
			Diurnal IOP	Mean diurnal IOP iStent Inject: 13.0 ± 2.3 mmHg (-8.1 mmHg) Latanoprost/timolol: 13.2 ± 2.0 mmHg (-7.3 mmHg)	NR
iStent Inject Study, 2019 ⁵⁵⁹	CE-IOL/iStent Inject (387) CE-IOL (118)	2 years	Unmedicated diurnal IOP reduced $\geq 20\%$ from baseline (primary)	Unmedicated diurnal IOP reduced $\geq 20\%$ from baseline† CE-IOL/iStent Inject: 75.8% CE-IOL: 61.9%	$P = 0.005$
			Unmedicated reduction in diurnal IOP from baseline (secondary)	Mean unmedicated reduction in diurnal IOP from baseline† CE-IOL/iStent inject: -7.0 ± 4.0 mmHg (31.1%) CE-IOL: -5.4 ± 3.7 mmHg (27.3%)	$P < 0.001$
			Glaucoma medications	Mean glaucoma medications CE-IOL/iStent Inject: $0.4 \pm 0.8 (-1.2)$ CE-IOL: $0.8 \pm 1.0 (-0.8)$	NR
Hydrus Microstent					

TABLE 5 LARGE, PROSPECTIVE CLINICAL TRIALS ON EFFICACY OF MINIMALLY INVASIVE GLAUCOMA SURGERY (MIGS)*

Study, Year	Treatment Groups (n)	Follow-up	Efficacy Outcome Measures	Results	P-value
Hydrus II Study, 2015 ⁵⁶²	CE-IOL/Hydrus (50) CE-IOL (50)	2 years	Unmedicated diurnal IOP reduced $\geq 20\%$ from baseline (primary)	Unmedicated diurnal IOP reduced $\geq 20\%$ from baseline† CE-IOL/Hydrus: 80% CE-IOL: 46%	$P = 0.0008$
			Diurnal IOP	Unmedicated diurnal IOP† CE-IOL/Hydrus: 16.9 ± 3.3 mmHg CE-IOL: 19.2 ± 4.7 mmHg	$P = 0.0093$
			Glaucoma medications	Mean glaucoma medications CE-IOL/Hydrus: 0.5 ± 1.0 CE-IOL: 1.0 ± 1.0	$P = 0.0189$
			Freedom from medications	Freedom from medications CE-IOL/Hydrus: 72.9% CE-IOL: 37.8%	$P = 0.0008$
HORIZON Study, 2022 ⁵⁷⁵	CE-IOL/Hydrus (369) CE-IOL (187)	5 years	Unmedicated diurnal IOP ≤ 18 mmHg	Unmedicated diurnal IOP ≤ 18 mmHg CE-IOL/Hydrus: 49.5% CE-IOL: 33.8%	$P = 0.003$
			Diurnal IOP	Mean diurnal IOP: CE-IOL/Hydrus: 16.8 ± 3.1 mmHg CE-IOL: 17.2 ± 3.2 mmHg	$P = 0.24$
			Glaucoma medications	Mean glaucoma medications: CE-IOL/Hydrus: 0.5 ± 0.9 CE-IOL: 0.9 ± 0.9	$P < 0.001$
			Freedom from medications	Freedom from medications: CE-IOL/Hydrus: 66% CE-IOL: 46%	$P < 0.001$
			Repeat glaucoma surgery	Cumulative probability of incisional glaucoma surgery CE-IOL/Hydrus: 2.4% CE-IOL: 6.2%	$P = 0.027$
COMPARE Study, 2020 ⁵⁶⁴	Hydrus (74) 2 iStents (76)	1 year	Success (IOP ≤ 18 mmHg, no glaucoma medications, no glaucoma surgery)	Cumulative probability of success Hydrus: 35.6% 2 iStents: 10.5%	$P = 0.001$
			Unmedicated diurnal IOP ≤ 18 mmHg	Unmedicated diurnal IOP ≤ 18 mmHg Hydrus: 30.1% 2 iStents: 9.3%	$P = 0.002$
			Change in diurnal IOP	Mean change in diurnal IOP Hydrus: -1.7 ± 4.0 mmHg 2 iStents: -1.0 ± 4.0 mmHg	$P = 0.3$
			Change in glaucoma medications	Mean change in glaucoma glaucoma medications Hydrus: -1.6 ± 1.2 2 iStents: -1.0 ± 1.2	$P = 0.004$
			Freedom from medications	Freedom from medications Hydrus: 46.6% 2 iStents: 24.0%	$P = 0.0057$

CyPass Micro-Stent

TABLE 5 LARGE, PROSPECTIVE CLINICAL TRIALS ON EFFICACY OF MINIMALLY INVASIVE GLAUCOMA SURGERY (MIGS)*

Study, Year	Treatment Groups (n)	Follow-up	Efficacy Outcome Measures	Results	P-value
COMPASS Trial, 2016 ⁵⁶⁶	CE-IOL/CyPass (374)	2 years	Unmedicated diurnal IOP reduced $\geq 20\%$ from baseline (primary)	Unmedicated diurnal IOP reduced $\geq 20\%$ from baseline† CE-IOL/CyPass: 77% CE-IOL: 60%	P = 0.001
	CE-IOL (131)		Unmedicated reduction in diurnal IOP from baseline	Unmedicated reduction in diurnal IOP from baseline† CE-IOL/CyPass: -7.4 mmHg (30%) CE-IOL: -5.4 mmHg (21%)	P < 0.001
			Unmedicated IOP 6–18 mmHg	Unmedicated IOP 6–18 mmHg† CE-IOL/CyPass: 65% CE-IOL: 44%	P < 0.001
COMPASS-XT Trial, 2019 ⁵⁶⁸	CE-IOL/CyPass (215)	5 years	Same	Unmedicated IOP reduced $\geq 20\%$ from baseline CE-IOL/CyPass: 46.0% CE-IOL: 32.1%	NR
	CE-IOL (67)			Mean reduction in IOP CE-IOL/CyPass: -8.4 mmHg CE-IOL: -8.0 mmHg	NR
				Unmedicated IOP 6–18 mmHg CE-IOL/CyPass: 44.0% CE-IOL: 28.3%	NR

CE-IOL = cataract extraction with intraocular lens implantation; IOP = intraocular pressure; KDB = Kahook Dual Blade; NR = not reported; POAG = primary open-angle glaucoma; PXG = pseudoexfoliation glaucoma; TMH = Tanito Microhook.

* Studies that enrolled at least 100 patients are included in the table.

† Medication washout.

Bleb-forming surgery

Minimally invasive bleb surgery (MIBS), trabeculectomy, and aqueous shunts drain aqueous humor into the subconjunctival space, which results in the formation of a bleb. These techniques have the potential for greater IOP reduction, and they are generally used in cases of moderate to advanced glaucoma. Several large, prospective clinical trials have evaluated the efficacy of traditional glaucoma surgery (see Table 6).

Minimally invasive bleb surgery

Minimally invasive bleb surgery should be considered separately from MIGS because it is bleb forming, commonly involves implantation of a device from an ab externo approach, and has different safety and efficacy profiles.⁵²³

XEN Gel Stent

The XEN Gel Stent (AbbVie, North Chicago, IL) is a 6-mm gelatinous tube that is designed for placement into the subconjunctival space via an ab interno approach using a preloaded 27-gauge needle inserter. Some surgeons prefer to insert the device via an ab externo approach, either through the intact conjunctiva or following a limited peritomy. Although several models have been studied, only the 45-micron lumen stent is FDA approved for use in refractory glaucoma. As in trabeculectomy, the use of intraoperative antifibrotic agents enhances surgical success.⁵⁷⁶ A pivotal single-arm prospective trial demonstrated IOP in the midteens 1 year after XEN Gel Stent implantation with mitomycin C (MMC). Transient postoperative hypotony was common, as was the frequency of needling.⁵⁷⁶ An interim analysis of a multicenter,

randomized clinical trial found that implantation of the XEN gel stent with opening of the conjunctiva resulted in lower IOP with greater success and a lower needling rate compared with eyes surgically treated using a closed conjunctiva technique.⁵⁷⁷ A 2022 systematic review and meta-analysis showed that XEN Gel Stent implantation demonstrated similar postoperative IOP compared with trabeculectomy but with a higher bleb needling rate.⁵⁷⁸ (*II++*, *Moderate Quality*, *Discretionary Recommendation*) A multicenter, randomized clinical trial comparing the XEN Gel Stent with MMC and trabeculectomy with MMC found lower mean IOP following trabeculectomy, but both procedures had similar rates of surgical success at 1 year.⁵⁷⁹

Trabeculectomy

Trabeculectomy remains the most effective surgical procedure to lower IOP; it is generally indicated when medications and appropriate laser surgery are insufficient to control disease and can be considered in selected cases as initial therapy.^{278, 580} In the CIGTS, initial trabeculectomy was more effective than initial medical therapy in reducing IOP, and it was more effective at slowing visual field progression among patients who presented with more advanced visual field loss.²⁷⁸ Patients who underwent primary trabeculectomy in the Moorfields Primary Therapy Trial showed no visual field deterioration over 5 years, in contrast to those treated with medications. Early surgery also resulted in lower IOP than medical therapy and laser surgery over the same time period.^{99, 581} Patients with advanced OAG underwent primary trabeculectomy in the TAGS, a multicenter, randomized, unblinded controlled trial conducted in the UK. At 5 years of follow-up, primary trabeculectomy was more effective in lowering IOP and preventing disease progression than primary medical treatment in patients with advanced glaucoma, and both randomized treatments had a similar safety profile.⁵⁸²

Trabeculectomy provides an alternative path for the escape of aqueous humor into the subconjunctival space, and it often reduces IOP and the need for medical treatment. Estimates of success rates over time range from 31% to 88% in different populations and with varying definitions of success and failure.⁵⁸³⁻⁵⁸⁶ The failure rate of trabeculectomy, without the use of adjunctive antifibrotic medications alone or combined with medical therapy, in a previously unoperated eye in the Advanced Glaucoma Intervention Study¹⁰² reached approximately 30% in Black patients and 20% in White patients over a 10-year period.¹⁰² Preoperative medical treatment with benzalkonium chloride-preserved drugs may be a risk factor for surgical failure.^{587, 588} Even though long-term control is often achieved, many patients require further therapy or additional ocular surgery, with a higher associated long-term failure rate.^{102, 589-592} Furthermore, filtering surgery increases the likelihood that phakic eyes will develop a visually significant cataract.^{101, 593, 594} A history of glaucoma surgery also increases the risk of corneal graft failure after penetrating keratoplasty.⁵⁹⁵

In eyes that have undergone previous cataract surgery involving a conjunctival incision, the success rate of initial glaucoma filtering surgery has been reported to be reduced.^{367, 590, 596-598} However, a retrospective case comparison study observed a similar success rate of initial trabeculectomy with MMC in phakic eyes and in eyes after clear-corneal phacoemulsification.⁵⁹⁹

A 2005 Cochrane Systematic Review concluded that antifibrotic agents may be used intraoperatively and postoperatively to reduce the subconjunctival scarring after trabeculectomy that can result in failure of the operation, and therefore intraoperative MMC should be used.⁶⁰⁰ (*I+*, *Moderate Quality*, *Strong Recommendation*) More recent studies confirm this outcome in eyes at high risk of surgical failure⁶⁰¹ and eyes that have not undergone previous surgery.⁶⁰²⁻⁶⁰⁴ A 2015 Cochrane Systematic Review concluded that there is low-quality evidence that MMC may be more effective than intraoperative 5-fluorouracil (5-FU) in achieving long-term lower IOP. A 2014 Cochrane Systematic Review reported evidence that intraoperative 5-FU may improve the success rate of lowering IOP compared with no antifibrotic agents, but multiple subconjunctival injections are usually required postoperatively. Additionally, subconjunctival 5-FU injections may be used in an attempt to abort impending bleb failure. Intraoperative 5-FU and MMC were found to be equally safe and effective adjuncts to primary

trabeculectomy in a multicenter, randomized clinical trial.⁶⁰⁵ Therefore, the selection of intraoperative MMC or 5-FU should be left to the discretion of the treating ophthalmologist, in consultation with the individual patient.^{606, 607} (*I++*, *Moderate Quality*, *Strong Recommendation*)

The use of postoperative injections of 5-FU also reduces the likelihood of surgical failure in both high-risk eyes^{367, 608, 609} and eyes that have not undergone previous surgery.^{607, 610, 611} A 2014 Cochrane Systematic Review reported that postoperative injections of 5-FU were rarely utilized in postoperative regimens, perhaps because of patient preference and an increased risk of complications. Use of 5-FU should generally be avoided in patients with corneal epithelial disease. Thus, the routine administration of postoperative 5-FU is not recommended but should be based on individualized considerations for the patient.⁶⁰⁷ (*I++*, *Moderate Quality*, *Strong Recommendation*) Aqueous outflow may be enhanced in the early postoperative period with laser suture lysis or removal of releasable sutures.^{612, 613} Transconjunctival needling with 5-FU or MMC has been shown to be effective in reviving failing filtering blebs.⁶¹⁴⁻⁶²⁶ Open trabeculectomy revision with MMC has also demonstrated success in reestablishing aqueous outflow.^{627, 628}

The use of an antifibrotic agent carries with it an increased risk of complications such as hypotony,⁶²⁹⁻⁶³¹ hypotony maculopathy,⁶²⁹ late-onset bleb leak,^{607, 632} and late-onset infection⁶³³⁻⁶³⁵ that must be weighed against the benefits when deciding whether to use these agents. These complications may be even more common in primary filtering surgery of phakic patients.⁶³⁶⁻⁶³⁸ A trend toward a lower concentration and shorter exposure time of MMC has been observed over time,⁶³⁹ and use of a fornix-based conjunctival flap with broad application of MMC has been advocated to avoid bleb-related complications.^{640, 641} Cochrane systematic reviews have reported similar IOP control and complications with fornix-based and limbus-based conjunctival flaps.^{642, 643} (*I+*, *Moderate Quality*, *Discretionary Recommendation*)

The Ex-PRESS Glaucoma Filtration Device (Alcon Laboratories, Fort Worth, TX) is a nonvalved, stainless steel implant originally designed for subconjunctival insertion at the limbus. A high rate of hypotony and device extrusion⁶⁴⁴⁻⁶⁴⁶ prompted a modification in surgical technique, which involved placing the device under a partial-thickness scleral flap.⁶⁴⁷ The procedure is similar to trabeculectomy, but sclerectomy and iridectomy are not performed. Retrospective studies⁶⁴⁷⁻⁶⁵² and randomized clinical trials⁶⁵³⁻⁶⁵⁵ have reported similar IOP reduction and surgical success rates with standard trabeculectomy and trabeculectomy with the Ex-PRESS Glaucoma Filtration Device. A 2023 Cochrane Systematic Review reported low-certainty evidence that the use of an Ex-PRESS Glaucoma Filtration Device plus trabeculectomy may produce greater IOP reduction at 1-year follow-up compared with standard trabeculectomy.⁶⁵⁶ (*I+*, *Moderate Quality*, *Discretionary Recommendation*) Several studies comparing trabeculectomy plus the Ex-PRESS Glaucoma Filtration Device with standard trabeculectomy found no significant differences in the rates of intraoperative and postoperative complications,^{649, 650, 652-655} but others have reported a higher incidence of early hypotony and cataract progression following standard trabeculectomy.^{648, 651, 657} Notably, use of the Ex-PRESS Glaucoma Filtration Device was shown to result in greater endothelial cell loss than standard trabeculectomy in one randomized clinical trial.⁶⁵⁷ Use of the Ex-PRESS Glaucoma Filtration Device is associated with greater surgical cost relative to standard trabeculectomy due to the additional expense of the implant itself.⁶⁵⁸

Aqueous shunts

Aqueous shunts (also known as tube shunts, glaucoma drainage devices, and setons) consist of a tube that diverts aqueous humor to an end plate located within the subconjunctival space in the equatorial region of the eye. The primary resistance to flow through these devices occurs across the fibrous capsule that develops around the end plate. Aqueous shunts differ in their design with respect to the size, shape, and material composition of the end plate. They may be further subdivided into valved and nonvalved implants, depending on whether a valve mechanism is present to limit flow through the shunt if the IOP becomes too low. Examples of nonvalved implants are the

Baerveldt glaucoma implant (Abbott Medical Optics, Santa Ana, CA), ClearPath (New World Medical, Inc., Rancho Cucamonga, CA), and the Molteno implant (Molteno Ophthalmic Ltd., Dunedin, New Zealand). An example of a valved implant is the Ahmed glaucoma valve (New World Medical, Inc., Rancho Cucamonga, CA).

Aqueous shunts have traditionally been used to manage medically uncontrolled glaucoma when trabeculectomy has failed to control IOP or is deemed unlikely to succeed. This includes eyes with neovascular glaucoma, uveitic glaucoma, conjunctival scarring from previous ocular surgery or cicatrizing diseases of the conjunctiva, congenital glaucoma in which angle surgery has failed, or other secondary glaucomas (e.g., post pars plana vitrectomy, iridocorneal endothelial syndrome). However, the indications for using aqueous shunts have been broadening, and these devices are being increasingly used in the surgical management of glaucoma. Medicare data show a steady rise in the annual number of shunts placed from 1994 to 2016, and there has been a concurrent decline in the number of trabeculectomies performed each year.^{522, 659}

Several randomized clinical trials have investigated the efficacy of aqueous shunts, and studies have compared aqueous shunts with trabeculectomy. A 2017 Cochrane Systematic Review found that there was insufficient information to conclude whether aqueous shunts or trabeculectomy yielded superior results, with heterogeneous methodology and data quality across studies. Therefore, the selection of aqueous shunts or trabeculectomy should be left to the discretion of the treating ophthalmologist, in consultation with the individual patient.⁶⁶⁰ (*I-, Insufficient Quality, Strong Recommendation*) A retrospective study evaluating surgical results in matched patient groups reported similar IOP reduction with the single-plate Molteno implant and trabeculectomy with 5-FU.⁶⁶¹ However, another retrospective case-controlled study observed a higher 5-year success rate after trabeculectomy with MMC than with Ahmed glaucoma valve implantation.⁶⁶² A randomized clinical trial in Sri Lanka comparing the Ahmed implant and trabeculectomy in patients with POAG and angle-closure glaucoma found comparable IOP reduction and success rates, with a mean follow-up of 31 months.⁶⁶³ The Tube Versus Trabeculectomy (TVT) Study was a multicenter, randomized clinical trial that compared the safety and efficacy of tube-shunt surgery using the 350-mm² Baerveldt glaucoma implant and trabeculectomy with MMC in patients with previous cataract extraction and/or failed trabeculectomy. Tube-shunt surgery had a higher success rate than trabeculectomy during 5 years of follow-up, but both surgical procedures were associated with similar IOP reduction, use of supplemental medical therapy, serious complications, reoperation for glaucoma, vision loss, quality of life, and visual field progression at 5 years.⁶⁶⁴⁻⁶⁶⁸ The Primary Tube Versus Trabeculectomy (PTVT) Study was a multicenter, randomized clinical trial comparing 350-mm² Baerveldt glaucoma implant surgery versus trabeculectomy with MMC in eyes without previous incisional surgery. Trabeculectomy with MMC and tube shunt surgery produced similar IOPs at 5 years of follow-up, but fewer glaucoma medications were required after trabeculectomy with MMC.⁶⁶⁹ There was no significant difference in the rate of surgical failure, serious complications, reoperation for glaucoma, vision loss, and visual field progression between the two procedures.⁶⁶⁹⁻⁶⁷²

Numerous studies have compared aqueous shunts that differ in size and design.^{667, 671, 673-682} Shunts with larger surface area end plates have been associated with lower levels of IOP⁶⁷³⁻⁶⁷⁵ and use of fewer topical ocular hypotensive agents^{674, 676, 677} in several retrospective case series. A randomized clinical trial evaluating the single-plate (135 mm²) and double-plate (270 mm²) Molteno implants observed a higher success rate with the double-plate implant at 2 years.⁶⁷⁸ However, a prospective study of the 350-mm² and 500-mm² Baerveldt implants found a higher success rate with the 350-mm² implant at 5 years.⁶⁷⁹ A prospective randomized trial comparing the Ahmed glaucoma valve (184 mm²) and single-plate Molteno implant noted similar success with both implants at 2 years.⁶⁸⁰ The Ahmed Baerveldt Comparison (ABC) Study and Ahmed Versus Baerveldt (AVB) Study are both multicenter, randomized clinical trials designed to compare the safety and efficacy of the Ahmed glaucoma valve (model FP7) and 350-mm² Baerveldt implant. Greater reductions in IOP and use of glaucoma medical therapy were seen following Baerveldt implantation at 3 months and thereafter, and these differences were

statistically significant at multiple time points during 5 years of follow-up in both studies.⁶⁸¹⁻⁶⁸³ Serious complications in the ABC Study and hypotony-related vision-threatening complications in the AVB Study occurred less frequently with the Ahmed implant. In a pooled analysis of the ABC Study, the AVB Study, and the TVT Study, the cumulative probability of failure 5 years after the tube shunt surgery was 38.3%. Predictors of tube shunt failure were lower preoperative IOP, neovascular glaucoma, Ahmed implantation, and younger age.⁶⁸⁴

Aqueous shunts are associated with intraoperative and postoperative complications that are similar to those occurring with trabeculectomy. In addition, they have unique complications related to implantation of a foreign body. Erosion of the tube may occur through the conjunctiva (5% in TVT Study,⁶⁶⁵ 1% in PTVT Study,⁶⁷⁰ 1%–2.9% in ABC Study,⁶⁸² 2%–4% in AVB Study⁶⁸¹), and this typically develops a few millimeters behind the limbus following anterior chamber insertion. Patch allografts of sclera, cornea, or pericardium are commonly used to prevent tube erosion, and a long scleral tunnel may also mitigate this risk.^{685, 686} Diplopia and motility disorders may result from extraocular muscle fibrosis or a mass effect of the bleb overlying the end plate (6% in TVT Study,⁶⁶⁵ 4% in PTVT Study,⁶⁷⁰ 11.8%–12.7% in ABC Study,⁶⁸² 2%–5% in AVB Study⁶⁸¹). Progressive endothelial cell loss can produce persistent corneal edema (16% in TVT Study,⁶⁶⁵ 0% in PTVT Study,⁶⁷⁰ 11.7%–11.9% in ABC Study,⁶⁸² 11%–12% in AVB Study⁶⁸¹). Potential causes of corneal decompensation include mechanical tube-cornea touch, foreign body reaction to the tube, disruption of the blood-aqueous barrier, and changes in aqueous composition with increased inflammatory mediators.⁶⁸⁷ Iris, vitreous, blood, or fibrin may obstruct the tube.

TABLE 6 LARGE, PROSPECTIVE CLINICAL TRIALS OF TRABECULECTOMY AND AQUEOUS SHUNTS SURGERY

Study, Year	Treatment Groups (n)	Follow-up	Efficacy Outcome Measures	Results	P-value
Trabeculectomy					
Moorfields Primary Treatment Trial, 1994 ⁹⁹	Medical treatment (56) Laser trabeculoplasty surgery (55) Trabeculectomy (57)	5 years	Failure (IOP >22 mmHg on 2 visits)	Cumulative probability of failure Meds: 17% Laser: 32% Trab: 2%	P = 0.0001
			IOP	Mean IOP Meds: 18.5 mmHg Laser: 18.5 mmHg Trab: 14.1 mmHg	P < 0.0001*
FFSS Study, 1996 ⁶⁸⁸	Trabeculectomy with 5-FU (105) Trabeculectomy without 5-FU (108)	5 years	Failure (IOP >21 mmHg, reoperation for glaucoma)	Cumulative probability of failure Trab with 5-FU: 52% Trab without 5-FU: 79%	P < 0.001
AGIS, 2004 ^{95, 102}	ATT TAT	10 years	Sustained decrease of visual field (increase in visual field defect score ≥4)	Cumulative probability of sustained decrease in visual field Black patients ATT: 37.6% TAT: 34.7%	P = 0.99
				White patients ATT: 39.9% TAT: 29.2%	P = 0.012

TABLE 6 LARGE, PROSPECTIVE CLINICAL TRIALS OF TRABECULECTOMY AND AQUEOUS SHUNTS SURGERY

Study, Year	Treatment Groups (n)	Follow-up	Efficacy Outcome Measures	Results	P-value
			Sustained visual field impairment (visual field defect score ≤ 18)	Cumulative probability of sustained visual field impairment Black patients ATT: 11.9% TAT: 18.5%	$P = 0.25$
				White patients ATT: 9.9% TAT: 7.3%	$P = 0.15$
			Sustained decrease of visual acuity (loss ≥ 3 Snellen lines)	Cumulative probability of sustained decrease of visual acuity Black patients ATT: 35.6% TAT: 43.6%	$P = 0.012$
				White patients ATT: 26.8% TAT: 35.9%	$P = 0.25$
			Sustained visual acuity impairment (Snellen visual acuity $< 20/100$)	Cumulative probability of sustained visual acuity impairment Black patients ATT: 10.8% TAT: 15.3%	$P = 0.79$
				White patients ATT: 11.6% TAT: 12.5%	$P = 0.91$
CIGTS, 2011 ⁶⁸⁹	Trabeculectomy with or without 5-FU (300)	3–9 years	IOP	Mean IOP Trab: 13.8 ± 3.8 mmHg Meds: 17.1 ± 2.4 mmHg	
	Medical treatment (307)		Visual fields	Visual field MD Trab: -7.9 ± 6.2 dB Meds: -6.2 ± 6.0 dB	
TAGS, 2024 ⁵⁸²	Trabeculectomy with MMC (227)	5 years	IOP	Mean IOP Trab: 12.07 ± 5.18 mmHg Meds: 14.76 ± 4.14 mmHg	$P < 0.001$
	Medical treatment (226)		Visual fields	Visual field MD Trab: -14.30 ± 7.14 dB Meds: -16.74 ± 6.78 dB	$P < 0.001$

Trabeculectomy and Aqueous Shunts

TABLE 6 LARGE, PROSPECTIVE CLINICAL TRIALS OF TRABECULECTOMY AND AQUEOUS SHUNTS SURGERY

Study, Year	Treatment Groups (n)	Follow-up	Efficacy Outcome Measures	Results	P-value
Wilson et al, 2003 ⁶⁶³	Ahmed implant (59)	41–52 months	Failure (IOP \geq 21 mmHg or $<$ 15% reduction from baseline, IOP \leq 5 mmHg, reoperation for glaucoma, loss of LP vision)	Cumulative probability of failure	$P = 0.86$
	Trabeculectomy with or without MMC (64)			Ahmed: 30.2% Trab: 31.9%	
				IOP	
		Number of glaucoma meds	Mean glaucoma meds Ahmed: 1.13 \pm 0.14 Trab: 0.93 \pm 0.11	$P = 0.34$	
TVT Study, 2012 ⁶⁶⁴	Baerveldt implant (107)	5 years	Failure (IOP $>$ 21 mmHg or $<$ 20% reduction from baseline, IOP \leq 5 mmHg, reoperation for glaucoma, loss of LP vision)	Cumulative probability of failure	$P = 0.002$
	Trabeculectomy with MMC (105)			Tube: 29.8% Trab: 46.9%	
				IOP	
		Number of glaucoma meds	Mean glaucoma meds Tube: 1.4 \pm 1.3 Trab: 1.2 \pm 1.5	$P = 0.23$	
Islamaj et al, 2020 ⁶⁹⁰	Baerveldt implant (59)	5 years	Failure (IOP $>$ 21 mmHg or $<$ 20% reduction from baseline, IOP \leq 5 mmHg, reoperation for glaucoma)	Failure	$P = 0.72$
	Trabeculectomy with MMC (60)			Baerveldt: 37% Trab: 40%	
				IOP	
		Number of glaucoma meds	Mean glaucoma meds Baerveldt: 1.9 \pm 1.2 Trab: 0.5 \pm 0.9	NR	
PTVT Study, 2022 ⁶⁶⁹	Baerveldt implant (125)	5 years	Failure (IOP $>$ 21 mmHg or $<$ 20% reduction from baseline, IOP \leq 5 mmHg, reoperation for glaucoma, loss of LP vision)	Cumulative probability of failure	$P = 0.21$
	Trabeculectomy with MMC (117)			Tube: 42% Trab: 35%	
		IOP	Mean IOP Tube: 13.4 \pm 3.5 mmHg Trab: 13.0 \pm 5.2 mmHg	$P = 0.52$	

TABLE 6 LARGE, PROSPECTIVE CLINICAL TRIALS OF TRABECULECTOMY AND AQUEOUS SHUNTS SURGERY

Study, Year	Treatment Groups (n)	Follow-up	Efficacy Outcome Measures	Results	P-value
			Number of glaucoma meds	Mean glaucoma meds Tube: 2.2 ± 1.3 Trab: 1.3 ± 1.4	P < 0.001
Aqueous Shunts					
Heuer et al, 1992 ⁶⁷⁸	SP Molteno implant (50)	2 years	Failure (IOP >21 mmHg, IOP <6 mmHg, reoperation for glaucoma, devastating complication)	Cumulative probability of failure SP Molteno: 54%	P = 0.0035
	DP Molteno implant (51)			DP Molteno: 29%	
Britt et al, 1999 ⁶⁷⁹	350-mm ² Baerveldt implant (53)	5 years	Failure (IOP >21 mmHg, IOP <6 mmHg, reoperation for glaucoma, loss of LP vision)	Cumulative probability of failure 350-mm ² Baerveldt: 21%	P = 0.05
	500-mm ² Baerveldt implant (50)			500-mm ² Baerveldt: 34%	
				IOP	
			Number of glaucoma meds	Mean glaucoma meds 350-mm ² Baerveldt: 1 500-mm ² Baerveldt: 1.6	P = 0.63
ABC Study, 2015 ⁶⁸²	Ahmed implant (143)	5 years	Failure (IOP >21 mmHg or <20% reduction from baseline, IOP ≤5 mmHg, reoperation for glaucoma or removal of implant, loss of LP vision)	Cumulative probability of failure Ahmed: 44.7%	P = 0.65
	Baerveldt implant (133)			Baerveldt: 39.4%	
				IOP	
			Number of glaucoma meds	Mean glaucoma meds Ahmed: 2.2 ± 1.4 Baerveldt: 1.8 ± 1.5	P = 0.28
AVB Study, 2016 ⁶⁸¹	Ahmed implant (124)	5 years	Failure (IOP >18 mmHg or <20% reduction from baseline, IOP <5 mmHg, vision-threatening complication, additional glaucoma procedure, loss of LP vision)	Cumulative probability of failure Ahmed: 53%	P = 0.04
	Baerveldt implant (114)			Baerveldt: 40%	

TABLE 6 LARGE, PROSPECTIVE CLINICAL TRIALS OF TRABECULECTOMY AND AQUEOUS SHUNTS SURGERY

Study, Year	Treatment Groups (n)	Follow-up	Efficacy Outcome Measures	Results	P-value
			IOP	Mean IOP Ahmed: 16.6 ± 5.9 mmHg Baerveldt: 13.6 ± 5.0 mmHg	P = 0.001
			Number of glaucoma meds	Mean glaucoma meds Ahmed: 1.8 ± 1.5 Baerveldt: 1.2 ± 1.3	P = 0.03
Yazdani et al, 2017 ⁶⁹¹	Ahmed implant with TA (52)	1 year	Failure (IOP >21 mmHg, IOP <6 mmHg, > glaucoma meds)	Cumulative probability of failure Ahmed with TA: 33.5%	P = 0.24
	Ahmed implant without TA (52)			Ahmed without TA: 44.9%	
			IOP	Mean IOP Ahmed with TA: 14.2 ± 3.6 mmHg Ahmed without TA: 14.9 ± 5.4 mmHg	P = 0.57
			Number of glaucoma meds	Mean glaucoma meds Ahmed with TA: 2.0 ± 1.5 Ahmed without TA: 2.1 ± 0.9	NR

ABC = Ahmed Baerveldt Comparison; AGIS = Advanced Glaucoma Intervention Study; ATT = argon laser trabeculoplasty-trabeculectomy-trabeculectomy; AVB = Ahmed Versus Baerveldt; CIGTS = Collaborative Initial Glaucoma Treatment Study; DP = doubleplate; FFSS = Fluorouracil Filtering Surgery Study; 5-FU = 5 fluorouracil; IOP = intraocular pressure; NR = not reported; Laser = Laser Trabeculoplasty Surgery; LP = light perception; Meds = medications; MD = mean deviation; MMC = mitomycin C; PTVT = Primary Tube Versus Trabeculectomy; SP = single-plate; TA = triamcinolone acetonide; TAGS = Treatment of Advance Glaucoma Study; TAT = trabeculectomy-argon laser trabeculoplasty-trabeculectomy; Trab = Trabeculectomy; TVT = Tube Versus Trabeculectomy.

*Comparison between surgery and the other two treatment groups throughout the 5-year follow-up period.

Nonpenetrating glaucoma surgery

Nonpenetrating glaucoma surgery avoids creating a continuous passageway from the anterior chamber to the subconjunctival space and thereby helps to reduce the risk of bleb-related complications and hypotony. There is generally a longer learning curve associated with nonpenetrating glaucoma surgery than with trabeculectomy.

Deep sclerectomy

Deep sclerectomy involves excision of sclerocorneal tissue under a partial thickness scleral flap, leaving a thin window of trabecular meshwork and Descemet membrane to provide some resistance to aqueous outflow. Antifibrotic agents are frequently used as adjuncts to deep sclerectomy, and it has been suggested that placement of collagen drainage devices under the scleral flap can improve aqueous humor filtration.⁶⁹²⁻⁶⁹⁴ One randomized clinical trial found that trabeculectomy was more effective than deep sclerectomy at lowering IOP,⁶⁹⁵ but several other trials found that the two surgeries were equally effective.^{692-694, 696-699}

Viscocanalostomy

Viscocanalostomy includes deep sclerectomy along with expansion of Schlemm's canal using an ophthalmic viscoelastic device. The procedure is intended to allow passage of aqueous humor through the trabeculodescemetic membrane window and into the physiologic outflow pathway through Schlemm's canal. Randomized clinical trials comparing viscocanalostomy with trabeculectomy suggest greater IOP reduction with trabeculectomy but fewer complications with viscocanalostomy.^{613, 700-707} A 2014 Cochrane Systematic Review found limited evidence that control of IOP was better with trabeculectomy than with viscocanaloplasty, but conclusions could not be drawn for deep sclerectomy, and quality-of-life outcomes may be needed to differentiate among procedures. Thus, the selection of viscocanalostomy and deep sclerectomy over trabeculectomy should be left to the discretion of the treating ophthalmologist, in consultation with the individual patient.⁷⁰⁸ (*I-, Insufficient Quality, Strong Recommendation*)

Canaloplasty

In canaloplasty, circumferential viscodilation of Schlemm's canal using a flexible microcatheter is performed in combination with deep sclerectomy. Dilating the entire canal aims to provide aqueous humor access to a greater number of collector channels. A 10-0 polypropylene (Prolene) suture is placed with appropriate tension within Schlemm's canal when possible to apply inward directed tension on the trabecular meshwork. The safety and efficacy of canaloplasty alone and combined with phacoemulsification was described in a nonrandomized, multicenter clinical trial through 3 years of follow-up.⁷⁰⁹ A retrospective case series found lower postoperative IOP with trabeculectomy compared with canaloplasty.⁷¹⁰ In a randomized clinical trial comparing trabeculectomy and canaloplasty, patients in the trabeculectomy group achieved higher success rates and required fewer medications than those in the canaloplasty group, but they also experienced a higher rate of late hypotony.⁷¹¹

Cycloablation surgery

Currently performed cycloablation surgeries reduce ciliary body function and the rate of aqueous production by delivering laser energy to the ciliary processes. Cycloablation procedures have evolved from initial techniques such as cyclodiathermy⁷¹² and cyclocryotherapy to cyclophotocoagulation, which can be performed using a transscleral or endoscopic approach. Cycloablation procedures had traditionally been used for refractory glaucomas, eyes with limited visual potential, or poor candidates for incisional glaucoma surgery due to their unpredictable results and unsatisfactory safety profile. However, advances in laser surgery technique have broadened their use, and they are more commonly being offered to patients earlier in the disease course.⁷¹³⁻⁷²¹ Complications that may occur with cycloablative procedures include persistent inflammation, cystoid macular edema, hyphema, corneal decompensation, hypotony, and phthisis bulbi.

Transscleral diode cyclophotocoagulation

Transscleral diode cyclophotocoagulation (TS-CPC) surgery is commonly performed with a probe that applies 810-nm diode laser energy to the sclera. The laser is transmitted to the ciliary epithelium and stroma, where it has a coagulative effect. Analysis of Medicare claims data shows that the number of TS-CPC procedures performed on Medicare enrollees increased 113.7% from 2008 to 2016.⁵²²

Continuous wave cyclophotocoagulation

The original form of TS-CPC delivers continuous high-intensity laser energy to the ciliary body while the laser is being applied and has been termed continuous-wave transscleral cyclophotocoagulation surgery (CW-TSCP).⁷²² A common conventional technique recommends starting with a laser energy power of 1750–2000 milliwatts for 2 seconds and incrementally increasing the laser energy until an audible “pop” sound is heard. In an alternative technique, termed the slow-coagulation technique, the laser energy power is set to 1250 milliwatts and applied for a 4.0-second duration.⁷²³ Retrospective studies of

CW-TSCP have demonstrated efficacy in lowering IOP in patients with glaucoma, including refractory cases, with a reasonable safety profile.^{722, 724-728}

Micropulse cyclophotocoagulation

Micropulse transscleral cyclophotocoagulation surgery (MP-CPC) is an alternative approach to traditional diode laser cyclophotocoagulation that delivers repetitive short bursts of diode laser energy with intervening rest periods.⁷²⁹ A 2019 review of MP-CPC literature suggests that this technique provides similar efficacy to CW-TSCP with less risk of severe complications, such as hypotony and phthisis bulbi.⁷³⁰ A 2023 meta-analysis further describes MP-CPC as an efficacious procedure for IOP lowering in various stages of glaucoma, with a favorable safety profile when compared with conventional CW-TSCP.⁷³¹

Endoscopic cyclophotocoagulation

Analysis of Medicare claims data shows that the overall number of endocyclophotocoagulation surgeries performed on Medicare enrollees increased 28.5% from 2008 to 2016.⁵²² Endoscopic cyclophotocoagulation (ECP) uses a solid-state 810-nm laser, a video camera, aiming beam, and xenon light source housed together, and the laser energy is delivered through a fiberoptic cable⁷¹⁴ that can be introduced inside the eye for direct visualization and treatment of the ciliary processes. This allows better titration of laser treatment.^{732, 733} The IOP reduction reported with ECP has ranged from 34% to 57%.⁷³⁴⁻⁷³⁶ Most studies treat 270 to 360 degrees of the ciliary body.^{734, 736} Fibrin exudates, hyphema, cystoid macular edema, vision loss, hypotony, choroidal detachment,⁷³⁴ and phthisis⁷³⁷ have been noted after ECP in eyes with advanced glaucoma, but more recent studies involving eyes with less advanced glaucomatous damage report fewer of these complications.⁷³⁵

Endoscopic cyclophotocoagulation surgery^{734, 735, 738} may be combined with cataract surgery. One randomized trial comparing cataract surgery combined with either ECP or trabeculectomy suggested that IOP-lowering efficacy is similar for both.⁷³⁹ Another study comparing ECP with the Ahmed drainage implant also showed comparable efficacy in lowering IOP, although the rate of complications with the latter surgery was higher.⁷⁴⁰ A 2019 Cochrane Systematic Review found inconclusive evidence whether cycloablation procedures for refractory glaucoma result in better outcomes and fewer complications than other glaucoma treatments, or whether one cycloablation surgery is better than another.⁷⁴¹ Another 2019 Cochrane Systematic Review identified no studies on the effects of endocyclophotocoagulation surgery for OAG.⁷⁴² Additional randomized clinical trials are needed to further elucidate the merits of each type of cyclophotocoagulation relative to one another as well as to other types of glaucoma surgery.^{741, 742} Therefore, the selection of cyclophotocoagulation over other procedures should be left to the discretion of the treating ophthalmologist, in consultation with the individual patient. (*I-, Insufficient Quality, Discretionary Recommendation*)

Combined glaucoma and cataract surgery

Patients with POAG who have visually significant cataracts have a range of options available. If IOP control is at target on one or two medications, cataract surgery alone may be adequate, with the additional benefit that it may lower IOP slightly. If IOP is poorly controlled on several medications or there is evidence of glaucomatous progression in a patient with a moderate cataract, glaucoma surgery may be indicated initially, with the plan to perform cataract surgery once IOP is adequately controlled. Between these two extremes, the decision of which procedure(s) to perform first or whether to combine cataract and glaucoma surgery is determined by the ophthalmologist and patient after discussion of the risks and benefits of each course of action.

Cataract surgery alone consistently produces modest reductions in IOP and glaucoma medical therapy in patients with POAG.^{247, 743} Patients with higher preoperative IOP generally experience greater IOP reduction with cataract extraction. Although cataract surgery frequently results in lowering of IOP, patients with glaucoma are at higher risk of IOP spikes in the early postoperative period that can be deleterious to the optic nerve. Generally, combined cataract and trabeculectomy is not as effective as trabeculectomy

alone in lowering IOP,^{247, 744} so patients who require filtration surgery who also have mild cataract may be better served by filtration surgery alone and cataract surgery later. An evidence-based review of combined cataract surgery and trabeculectomy concluded that the use of MMC, but not 5-FU, results in lower IOP in combined procedures.⁷⁴⁴ A 2005 Cochrane Systematic Review concluded that MMC may be used intraoperatively to reduce the subconjunctival scarring after trabeculectomy that can result in failure of the operation, but there was no evidence with combined cataract surgery and trabeculectomy.⁶⁰⁰ A review published in 2002 found moderate-quality evidence that separating the cataract and trabeculectomy incisions results in lower IOP than a one-site combined procedure, but the differences in outcomes were small.⁷⁴⁴ Subsequent publications have found no difference between the two approaches.⁷⁴⁴⁻⁷⁴⁷

Potential benefits of a combined procedure (cataract extraction with IOL implantation and trabeculectomy) are protection against the IOP rise that may complicate cataract surgery alone, the possibility of achieving long-term glaucoma control with a single operation, and elimination of the risk of bleb failure with subsequent cataract surgery when glaucoma surgery is performed first.⁷⁴⁸⁻⁷⁵⁰ A 2015 Cochrane Systematic Review identified low-quality evidence for better IOP control with combined surgery over glaucoma surgery alone. More high-quality studies are required with outcomes that are relevant to patients. Therefore, the selection of a combined surgery or cataract surgery alone can be left to the discretion of the treating ophthalmologist, in consultation with the individual patient.⁷⁵¹ (*I-, Insufficient Quality, Strong Recommendation*)

Intraocular lens selection merits special consideration in cases where trabeculectomy is performed first and cataract surgery is deferred until IOP is optimized. Myopic surprises have been described following phacoemulsification in patients with prior filtering surgery and lower preoperative IOP,⁷⁵²⁻⁷⁵⁴ even when using fourth-generation formulas and noncontact (laser) interferometry.⁷⁵³ Multifocal intraocular lenses may have adverse effects on contrast sensitivity⁷⁵⁵ and visual field performance⁷⁵⁶ in patients with glaucoma. Intraocular lens choices and refractive goals should be individualized for each patient based on history of filtering surgery, IOP level, and severity of glaucomatous damage.

Other types of glaucoma surgery can also be combined with cataract surgery, such as implantation of aqueous shunts, nonpenetrating glaucoma surgery, MIGS, and ECP.

Perioperative care in glaucoma surgery

The ophthalmologist who performs glaucoma surgery and cycloablation has the following responsibilities:^{443, 444}

- ◆ Perform gonioscopy preoperatively, especially when considering trabecular meshwork/Schlemm's canal-based MIGS
- ◆ Obtain informed consent from the patient or the patient's surrogate decision maker after discussing the risks, benefits, alternatives, and expected outcomes of surgery⁷⁵⁷
- ◆ Ensure that the preoperative evaluation accurately documents the findings and indications for surgery
- ◆ Prescribe topical corticosteroids in the postoperative period^{758, 759}
- ◆ Perform follow-up evaluations as indicated based on the procedure and specific clinical scenario to evaluate visual acuity, IOP, the status of the anterior segment and posterior segments,⁷⁶⁰⁻⁷⁶⁵ and the need for and timing of medication adjustments
- ◆ Schedule more frequent follow-up visits, as necessary, for patients with postoperative complications such as a flat or shallow anterior chamber or evidence of early bleb failure, increased inflammation, or Tenon's cyst (encapsulated bleb)⁷⁶⁰⁻⁷⁶⁵
- ◆ Undertake additional treatments as necessary to improve aqueous flow into the bleb and lower IOP if evidence of bleb failure develops, including injection of antifibrotic agents, bleb massage, suture adjustment, release or lysis, or bleb needling^{615, 617, 766}
- ◆ Manage postoperative complications as they develop, such as repair of bleb leak or reformation of a flat anterior chamber

- ◆ Explain that filtration surgery places the eye at risk for endophthalmitis for the duration of the patient's life, and that if the patient has symptoms of pain and decreased vision and the signs of redness and discharge he or she should notify the ophthalmologist immediately⁷⁶⁷

Other therapies

There is a growing interest in complementary approaches to the treatment of glaucoma. The FYSX ocular pressure adjusting pump (Balance Ophthalmics, Sioux Falls, South Dakota) is a novel device consisting of a pair of goggles connected to a pressure-modulating pump that creates a localized decrease in atmospheric pressure on the eye. In a multicenter, randomized clinical trial enrolling patients with normal-tension glaucoma, the device produced a mean reduction of IOP of 39.1% during negative-pressure application. The most common device-related adverse event was periorbital edema (13%).⁷⁶⁸

There is a lack of conclusive scientific evidence that herbal medicines or nutritional supplements are beneficial in treating glaucoma.⁷⁶⁹⁻⁷⁷² Although marijuana can lower IOP, its side effects and short duration of action prompted the American Glaucoma Society to not support its use in the treatment of glaucoma.⁷⁷³ Results of a study of UK Biobank data suggest that habitual caffeine consumption is weakly associated with lower IOP. However, in participants with a genetic predisposition for elevated IOP, greater caffeine consumption is associated with higher IOP and higher glaucoma prevalence.⁷⁷⁴ Results from the National Health and Nutrition Examination Survey suggest that higher intensity exercise may reduce the risk of developing glaucoma.⁷⁷⁵ A 2024 Cochrane systematic review demonstrated a correlation between mindfulness-based relaxation practices and IOP reduction.⁷⁷⁶ (*I-, Moderate Quality, Discretionary Recommendation*) There has been interest in the neuroprotective role of nicotinamide in glaucoma. One randomized clinical trial demonstrated that oral nicotinamide and pyruvate may result in short-term improvement in visual function in patients with glaucoma.⁷⁷⁷ Drug-induced liver injury has been reported with nicotinamide use.^{778, 779} Longer-term studies of these agents are needed to establish their role in managing glaucoma.⁷⁷⁸

Follow-up Evaluation

Guidelines for follow-up glaucoma care of patients with POAG are summarized in Table 7. These recommendations apply to ongoing glaucoma management and not to visits for other purposes. The purpose of follow-up examination is to evaluate IOP level, visual field status, and optic disc appearance as well as ONH, circumpapillary RNFL, and macular ganglion cell layer imaging to determine if progressive damage has occurred. Guidelines for the frequency of visual field and optic nerve evaluation of patients with POAG are provided in Table 8.

TABLE 7 CONSENSUS-BASED GUIDELINES FOR FOLLOW-UP OF PRIMARY OPEN-ANGLE GLAUCOMA

Target IOP Achieved	Progression of Damage	Duration of Control (months)	Approximate Follow-up Interval (months)*	
			Mild-Moderate	Severe
Yes	No	≤6	3–6	3–4
Yes	No	>6	6–12	3–6
Yes	Yes	NA	1–3	1–2
No	Yes	NA	1–2	1–2
No	No	NA	1–6	1–3

IOP = intraocular pressure; NA = not applicable.

*Consider more frequent follow-up intervals following adjustments to therapy and for monocular patients.

TABLE 8 CONSENSUS-BASED GUIDELINES FOR VISUAL FIELD AND OPTIC NERVE EVALUATION FOR PRIMARY OPEN-ANGLE GLAUCOMA

Target IOP Achieved	Progression of Damage	Duration of Control (months)	Approximate Follow-up Interval (months)*			
			Visual Field Evaluation [†]		Optic Nerve Evaluation [‡]	
			Mild-Moderate	Severe	Mild-Moderate	Severe
Yes	No	≤6	6–12	6–9	6–12	6–9
Yes	No	>6	6–18	6–12	6–18	6–12
Yes	Yes	NA	1–6	1–4	6–12	6–9
No	Yes	NA	1–6	1–4	6–12	6–9
No	No	NA	1–6	1–6	6–12	6–9

IOP = intraocular pressure; NA = not applicable.

*Consider more frequent testing intervals for monocular patients.

[†]Clustering visual field tests shortly after diagnosis and at follow-up may assist in detecting fast progressors.

[‡]Optic nerve evaluation may involve optical coherence tomography or disc photos.

History

The following interval history can be elicited at POAG follow-up visits:

- ◆ Interval ocular history
- ◆ Interval systemic medical history
- ◆ Side effects of ocular medications
- ◆ Review of pertinent medication use, including time of last administration

Ophthalmic examination

The following components of the ophthalmic examination should be performed at POAG follow-up visits:

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

Based on the understanding of the effect of CCT on IOP measurements,^{19, 45, 780} measurement of CCT should be repeated after any event (e.g., refractive surgery⁷⁸¹) that may alter CCT.

Home tonometry is a promising development to aid in glaucoma management. In a prospective study of the iCare Home device (iCare Finland Oy, Vantaa, Finland), the agreement between iCare Home readings and Goldmann applanation tonometry was good, with 91% of readings within 5 mmHg. However, 1 in 6 participants was unable to use the device appropriately, indicating the importance of patient selection and education.⁷⁸² A contact lens sensor is commercially available (Triggerfish CLS, Sensimed AG, Lausanne, Switzerland) to measure 24-hour IOP-related patterns in an ambulatory setting.⁷⁸³⁻⁷⁸⁵ This technology is based on the assumption that variation in IOP leads to changes in ocular volume and dimension, which the device captures through embedded strain gauges.⁷⁸³⁻⁷⁸⁶

Gonioscopy

Repeat gonioscopy is indicated when there is a suspicion of an angle-closure component, anterior chamber shallowing or anterior chamber angle abnormalities, or if there is an unexplained change in IOP.

Optic nerve head, circumpapillary retinal nerve fiber layer, macular ganglion cell layer, and visual field evaluation

Optic nerve head evaluation should be performed regularly. Documentation by imaging, photography, or drawing,^{344, 787-789} OCT,⁷⁹⁰⁻⁷⁹⁴ and visual field evaluation⁷⁹⁵⁻⁷⁹⁸ should be performed at initial visits to establish a baseline and then repeated at least yearly. Periodic photography may also reveal disc hemorrhages not seen on examination⁷⁷ and, in view of the quickly advancing imaging field, may provide a more stable baseline for comparison than a new imaging baseline every few years.

A study of participants in the multicenter African Descent and Glaucoma Evaluation Study demonstrated that more frequent testing with circumpapillary OCT resulted in earlier detection of progression.⁷⁹⁹ A 6-month interval of testing was suggested to balance between statistical power to detect progression and the burden for the patient and healthcare system. Patients at high risk for progression may benefit from shorter intervals of OCT testing, such as 4 months.

Measurements of the inner retinal thickness of the central macula may aid in detecting glaucoma, including pre-perimetric glaucoma. Rates of change of inner retinal thickness measurements have also been shown to be helpful in monitoring glaucoma progression.⁸⁰⁰

Studies have shown that more frequent visual field testing improves the ability to detect glaucoma progression, especially in patients with rapid disease progression or those with high variability in visual field measurements.^{382, 801-806} A study using patient data, computer simulation, and statistical analysis showed that performing 1 visual field per year led to failure to detect significant visual field loss.³⁸² The authors recommended that 6 visual fields be performed in the first 2 years in order to detect clinically meaningful change. The Fast-PACE prospective, observational cohort study determined that rapid visual field progression may be detected with 2 clusters of 5 visits scheduled 6 months apart.⁸⁰² In the study, each cluster consisted of 5 visits scheduled at weekly intervals during which patients underwent IOP measurement, 24-2 and 10-2 SAP testing, and spectral-domain OCT testing. While the approach used in this study may not be practical for routine clinical practice, it may be a useful guide in monitoring patients who are newly diagnosed or at high risk of progression.

Factors that influence the frequency of evaluations include the severity of damage (mild, moderate, severe, with more frequent evaluations for more severe disease), the rate of progression,³⁸² the extent to which the IOP exceeds the target pressure, and the number and significance of other risk factors for damage to the optic nerve. In certain cases, follow-up visual field testing and imaging may be required more frequently (e.g., a second test to establish a baseline for future comparisons, to clarify a suspicious test result or apparent testing artifact, or to include an alternate visual field testing strategy).

Risk Factors for Progression

Risk factors for progression of glaucoma include the following:

- ◆ IOP: Several multicenter, randomized clinical trials have investigated the relationship between IOP and risk of glaucomatous progression (see Table 2). Higher baseline IOP,⁹³ higher mean IOP during follow-up,^{95, 807} higher peak IOP during follow-up^{104, 808, 809} and higher yearly average IOP⁸¹⁰ were associated with greater progression of glaucoma as measured by visual field or optic nerve changes. Greater diurnal IOP fluctuation has inconsistently been shown to be related to visual field progression and requires further study.^{100, 106, 273-280}
- ◆ Older age^{93, 100, 278, 807, 811, 812}
- ◆ Disc hemorrhage: The presence of a disc hemorrhage^{77, 811, 813-819} and the percentage of visits with disc hemorrhage^{93, 100} have been associated with progression of visual field defect or optic nerve damage. The association has been reported in both normal-tension and in high-pressure glaucoma.
- ◆ Large cup-to-disc ratio or small optic nerve rim area^{820, 821}
- ◆ Beta-zone parapapillary atrophy: The baseline presence^{813, 820} and the size^{811, 822} of parapapillary atrophy adjacent to the optic nerve (beta zone) has been related to visual field or optic nerve progression in several large prospective and retrospective studies.

- ◆ Thinner CCT: Strong evidence exists for thinner central cornea as a risk factor for progression from ocular hypertension to POAG, but evidence is mixed for thinner central cornea as a risk factor for progression in glaucoma (see Table 9).^{100, 169, 178, 182, 309, 313, 780, 823, 824}
- ◆ Lower corneal hysteresis: Corneal hysteresis is a measure of the viscoelastic dampening of the cornea and has been shown to be associated with the risk of glaucoma progression.¹⁸¹⁻¹⁸⁴
- ◆ Lower ocular perfusion pressure^{100, 156}
- ◆ Poor adherence with medications⁸²⁵⁻⁸²⁸
- ◆ Progression in fellow eye: Glaucomatous progression in one eye is associated with an increased risk of progression in the fellow eye, and unilateral disease commonly becomes bilateral.^{100, 829-832}

TABLE 9 SUMMARY OF RESULTS FOR CENTRAL CORNEAL THICKNESS AS A RISK FACTOR FOR PROGRESSION OF GLAUCOMA

Study, Year	No. of Patients	Level of Evidence	Risk	Comments
Early Manifest Glaucoma Trial, 2007 ¹⁰⁰	255	I	+	Thinner CCT is a risk factor for progression of glaucoma (in those patients with baseline IOP \geq 21 mmHg)
Kim and Chen, 2004 ³⁰⁹	88	II	+	Thinner CCT is associated with visual field progression in glaucoma
Chauhan et al, 2005 ³¹⁰	54	II	-	CCT did not predict visual field or optic disc progression
Jonas et al, 2005 ⁸³³	454	II	-	CCT is not associated with progression of visual field damage
Jonas et al, 2005 ³¹¹	390	II	-	CCT is not associated with optic disc hemorrhages
Congdon et al, 2006 ¹⁸²	230	II	-	CCT is not associated with glaucoma progression (although low corneal hysteresis is associated with glaucoma progression)
Stewart et al, 2006 ³¹³	310	III	+/-	CCT is associated with progression on univariate analysis but is not associated on multivariate analysis

CCT = central corneal thickness; IOP = intraocular pressure.

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.

Adjustment of Therapy

The indications for adjusting therapy are as follows:

- ◆ Target IOP is not achieved and the benefits of a change in therapy outweigh the risks for the patient
- ◆ A patient has progressive optic nerve damage despite achieving the target IOP
- ◆ The patient does not tolerate the prescribed medical regimen
- ◆ The patient is unable to adhere to the prescribed medical regimen
- ◆ Contraindications to individual medicines develop
- ◆ Stable optic nerve status and lower IOP occur for a prolonged period in a patient taking topical ocular hypotensive agents. Under these circumstances, a carefully monitored attempt to reduce the medical regimen may be appropriate.

Downward adjustment of target pressure should be made in the face of progressive optic disc, imaging, or visual field change.^{826, 834-837}

Upward adjustment of target pressure can be considered if the patient has been stable and if the patient either requires (because of side effects) or desires less medication. A follow-up visit in 2

to 8 weeks, depending on disease severity, may help to assess the response and side effects from washout of the old medication or onset of maximum effect of the new medication.

CLINICIAN AND SETTING

The performance of certain diagnostic procedures (e.g., tonometry, pachymetry, perimetry, ONH imaging, circumpapillary RNFL, and macular ganglion cell layer imaging) may be delegated to appropriately trained and supervised personnel. However, the interpretation of results and medical and surgical management of the disease require the medical training, clinical judgment, and experience of the ophthalmologist. Most diagnostic and therapeutic procedures can be safely undertaken on an outpatient basis. In some instances, however, hospitalization may be required. This includes, for example, patients who have special medical or social needs.

COUNSELING AND REFERRAL

It is important to educate and engage with patients in the management of their condition. Patients should be educated through in-person, written, and online information about the disease process, 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. Patients using medical therapy should be encouraged to alert their ophthalmologist to side effects of glaucoma medications and barriers to adherence. They should also be reminded to inform their primary care physician and other clinicians about their use of these medications. Ophthalmologists should remain mindful that the diagnosis of glaucoma can itself lead to negative psychological effects and to fear of blindness.⁸³⁸⁻⁸⁴²

Ophthalmologists should strive to provide education that is clear, relevant, and accessible to the patient and their caregiver(s). Patients with poor health literacy skills may be especially vulnerable to worse visual outcomes.⁸⁴³ Limiting dense text and using “teach-back” techniques such as asking patients to explain what they understand about glaucoma may be helpful for patients with limited literacy skills. Patients with higher levels of literacy may ask questions that lead to a more complex discussion, but patients who do not understand the information provided to them initially may miss the opportunity to engage in their disease management.

Even patients with experience using glaucoma drops may struggle to administer drops successfully.⁴⁹⁶ Many patients depend on companions to assist with their drops.⁸⁴⁴ Ophthalmologists or trained staff should consider providing instructions to patients, and companions if applicable, on drop administration techniques and having patients demonstrate their preferred technique in the office. Drop administration may be exceedingly difficult for some patients, and laser trabeculoplasty surgery, sustained medication delivery methods, or other surgery may be better options for these patients. Adherence to medical therapy should be assessed and addressed at each visit (see Medical Management section for more details). A majority of states have legislation that permits early drop refills; although the exact technicalities are variable, it is important to empower patients with this knowledge.⁸⁴⁵

Glaucoma affects the patient’s vision and health-related quality of life in many ways,^{217, 846} including employment issues (e.g., fear of loss of job and insurance from diminished ability to read and drive), social issues (e.g., isolation, fear of negative impact on relationships and sexuality), and loss of independence and activities that require good visual acuity (e.g., sports and other hobbies). The ophthalmologist should be sensitive to these problems and provide support and encouragement. Some patients may find peer-support groups or counseling helpful.

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.^{186, 847} During LASIK, SMILE, and femtosecond laser-assisted cataract surgery, IOP briefly increases upon application of the suction ring and vacuum. This may cause additional damage in patients whose optic nerves already have advanced damage.⁸⁴⁸ Therefore, these procedures may be relatively contraindicated in such individuals, but photorefractive keratectomy may be possible.⁸⁴⁸ In addition, postoperative fluid may develop in the stromal interface and lead to temporary underestimation of the applanation IOP in patients treated aggressively with topical corticosteroids to resolve diffuse lamellar keratitis. These patients may have an undetected corticosteroid-induced elevation of IOP.⁸⁴⁹ Conversely, elevated IOP may be associated with stromal keratitis, a condition known as pressure-induced intralamellar stromal keratitis.⁸⁴⁹ This can be caused by corticosteroid-

induced IOP elevation, which may be associated with interface fluid accumulation and lead to IOP underestimation.^{850, 851} Inflammation subsides as the IOP is reduced using glaucoma medications. Patients with glaucomatous optic neuropathy considering implantation of a multifocal intraocular lens should be informed of the risk of reduced contrast sensitivity.⁷⁵⁵ Limited data exist, and therefore intraocular lens selection should be guided by patients' expectations, glaucoma type and severity, number of glaucoma medications, ocular surface disease, and intraocular lens specifications.⁸⁵² It is important to establish preoperative and baseline documentation of ONH status and visual field to facilitate subsequent glaucoma management.⁷⁵⁵

If the diagnosis or management of POAG is in question, or if the condition is refractory to treatment, consultation with or referral to an ophthalmologist with special training or experience in managing glaucoma should be considered. Patients with glaucoma can be referred for and encouraged to use appropriate vision rehabilitation, social services, and counseling.⁸⁵³ Empathetic communication and questioning by the physician is helpful to elicit patients' or family members' concerns. Fall prevention measures, such as improved lighting and home modification, and additional training, should be considered in high-risk patients as well.^{854, 855} Consider referrals for peer support groups for patients with depression, anxiety, and loss of independence or employment.⁸⁵⁶ More information on vision rehabilitation, including materials for patients, is available at <https://www.aao.org/education/low-vision-and-vision-rehab>.

SOCIOECONOMIC CONSIDERATIONS

The number of adults 40 to 80 years old worldwide with glaucoma was estimated to be more than 76 million in 2020. As the prevalence of glaucoma increases with age, this number is projected to increase to more than 111 million in 2040.²¹ Thus, the burden of disease, both to the individual patient and the economic burden to society, is substantial.⁸⁵⁷

Patients with glaucoma may struggle with daily activities such as reading, walking, and driving.⁸⁵⁸ Performance on these activities deteriorates with worsening of glaucoma severity or when both eyes are affected.⁸⁵⁸ Patients with glaucoma are more likely to experience falls and more likely to be involved in motor vehicle collisions compared with people without glaucoma.⁸⁵⁹ Quality of life is affected for patients with all stages of glaucoma, even those with early disease.⁸⁶⁰

The costs of managing a chronic disease like glaucoma can be broken down into direct medical costs, direct nonmedical costs, and indirect costs. Direct costs include costs of visits to eye care clinicians, ancillary testing, and medical and surgical interventions. One study from 2005 estimated that nearly \$3 billion per year was spent in the United States on direct medical costs from glaucoma.⁸⁶¹ Direct nonmedical costs (e.g., costs for transportation to appointments and nursing home care) and indirect costs (e.g., loss of productivity of the patient or caregivers) can be more difficult to quantify but are substantial. Using Medicare claims data and Markov modeling, one study from 2010 estimated that the average direct and indirect medical costs for patients with POAG are \$1688 higher over a lifetime than other patients without this condition.⁸⁶²

Costs of glaucoma are greater in more severe disease.^{863, 864} One study from 2006 determined that the average annual direct medical costs for patients with early glaucoma, advanced glaucoma, and end-stage glaucoma were \$623, \$1915, and \$2511, respectively.⁸⁶⁴ Among patients with early glaucoma, most of the costs of care are for medications.⁸⁶⁵ For those with advanced disease, indirect costs such as costs for home health care and rehabilitation predominate.^{866, 867} Secondary forms of glaucoma may confer an even greater economic burden. In particular, the cost of care for patients with pseudoexfoliation glaucoma is significantly more than the cost of care for patients with POAG due to the increased number of office visits, surgeries, and medications.⁸⁶⁸

Using computer modeling, researchers found that the treatment of patients with glaucoma was highly cost-effective when making optimistic assumptions about therapy effectiveness and still reasonably cost-effective when making more conservative estimates of therapy effectiveness.⁸⁶⁹ Other studies have compared the cost-effectiveness of using different treatment modalities. One study found use of generic prostaglandin analogues and laser trabeculoplasty to both be cost-effective treatment strategies for patients with early glaucoma.⁸⁷⁰ The use of generic prostaglandin analogues was found to be the more cost-effective treatment option compared with laser trabeculoplasty when assuming optimal medication adherence. However, when assuming more realistic estimates of medication adherence, laser trabeculoplasty surgery was found to confer greater value compared with prostaglandin analogues. The results of the LiGHT Study support this finding.³⁸⁷ Indeed, poor

medication adherence has been identified as contributing to the high cost of glaucoma care across multiple studies and in different health care systems.⁸⁷¹ Interventions that improve medication adherence can be cost-effective, based on several models.⁸⁷²⁻⁸⁷⁴

The TAGS comparing primary trabeculectomy versus primary glaucoma eye drops for newly diagnosed advanced glaucoma reported medications as more cost-effective in the first 2 years; however, trabeculectomy had greater IOP reduction and was hypothesized to be more cost-effective over time.⁸⁷⁵ Markov modeling based on estimates from the TVT Study suggested that both trabeculectomy and tube shunt surgery were cost-effective over a 5-year period compared with medical management, with trabeculectomy incurring a lower cost per quality-adjusted life year.⁸⁷⁶ A separate study comparing standard trabeculectomy versus trabeculectomy with the ExPress Glaucoma Filtration Device found that ExPress Glaucoma Filtration Device surgery incurred significantly greater cost than standard trabeculectomy.⁶⁵⁸ Even though glaucoma surgeries have varying safety profiles, indications, and efficacy, conventional surgeries and SLT were found to be more cost-effective per mmHg of IOP lowering compared with MIGS procedures in one analysis.⁸⁷⁷ Ongoing studies are exploring the cost-effectiveness of MIGS procedures.⁸⁷⁸ Analyses across various models and systems suggest a reasonable likelihood that combination cataract extraction and trabecular meshwork bypass devices are cost-effective compared with cataract extraction alone.⁸⁷⁹⁻⁸⁸² Notably, several studies had commercial relationships with the device manufacturer, so bias cannot be excluded. However, one paper without notable bias reported that the combination of cataract extraction and iStent inject or Hydrus microstent were cost-effective at a conservative quality-adjusted life year threshold within 5 years.⁸⁸³

Finally, when considering the economic burden of glaucoma, it is important to appreciate that glaucoma has a greater negative effect on certain groups, including communities facing systemic challenges such as a higher social vulnerability index or those in racial and ethnic minorities (see Race, Ethnicity, and Social Determinants of Health section).

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 includes the entity of open-angle glaucoma and related entities with the following ICD-10 classifications:

	ICD-10 CM
Unspecified open-angle glaucoma	H40.10X-
Primary open-angle glaucoma	H40.111- H40.112- H40.113-
Low-tension glaucoma	H40.121- H40.122- H40.123-
Residual stage of open-angle glaucoma	H40.151 H40.152 H40.153
Glaucomatous atrophy of the optic disc	H47.231 H47.232 H47.233

CM = Clinical Modification used in the United States; (-) = requires 7th digit for staging 0, stage unspecified; 1, mild stage; 2, moderate stage; 3, severe stage; 4, indeterminate stage

ICD-10 stages of glaucoma:

- Unspecified, 0: Stage is not documented in medical record
- Mild, 1: No visual field defects
- Moderate, 2: Visual field defect in one hemifield and not within 5 degrees of fixation
- Severe, 3: Visual fields in both hemifields and/or within 5 degrees of fixation
- Indeterminate, 4: Visual field testing is unreliable/uninterpretable, not yet performed, or cannot be performed

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. LITERATURE SEARCHES FOR THIS PPP

Literature searches of the PubMed database were conducted on March 1, 2024; the search strategies are listed below. Specific limited update searches were conducted on July 31, 2025. The searches had added filters for human, English-language randomized controlled trials and systematic reviews and date limiters to capture literature published since June 15, 2020. The committee analyzed 3,349 studies, of which 178 were included in the PPP. The literature searches with the disease condition and the search term, patient values, and patient preferences yielded 135 results, all of which were provided to the committee, 4 of which merited inclusion in the PPP. The literature searches for economic evaluation and treatment cost yielded 53 studies, all of which were provided to the committee, 8 of which merited inclusion in the PPP.

Anterior Segment Imaging: ("Tomography, Optical Coherence"[mh] OR (ultrasound AND biomicroscopy) OR ("anterior segment" AND imaging) OR ("anterior segment" AND image*)) AND ("Glaucoma"[mh] OR glaucoma OR "Glaucoma, Open-Angle"[mh] OR poag)

Diagnosis: (Glaucoma/diagnosis[MeSH] OR "Glaucoma, Open Angle/diagnosis"[MeSH]) OR ((glaucoma[tiab] OR poag[tiab]) AND diagnosis[tiab])

Diode Cyclophotocoagulation: ("Glaucoma"[mh] OR "Glaucoma, Open-Angle"[mh] OR glaucoma) AND ((diode[tiab] AND cyclophotocoagulation[tiab]) OR "diode photocoagulation"[tiab])

Cost Benefit: ("Glaucoma/economics"[MeSH] OR "Glaucoma, Open Angle/economics"[MeSH]) OR ((Glaucoma[MeSH] OR "Glaucoma, Open Angle"[Mesh] OR glaucoma[tiab]) AND "Cost-Benefit Analysis"[MeSH]) NOT "Cost of Illness"[MeSH]

Cost of Illness: (Glaucoma[MeSH] OR "Glaucoma, Open Angle"[MeSH] OR glaucoma[tiab]) AND "Cost of Illness"[MeSH]

Endoscopic Cyclophotocoagulation: ("Glaucoma"[mh] OR "Glaucoma, Open-Angle"[mh] OR glaucoma) AND (("endoscopic photocoagulation") OR (endoscopic AND cyclophotocoagulation))

IOP Fluctuation and Risk of Progression: ("Glaucoma"[mh] OR "Glaucoma, Open-Angle"[mh] OR glaucoma) AND ("Intraocular Pressure"[mh] OR "intraocular pressure" OR IOP) AND (fluctuation OR fluctuating OR fluctuates OR fluctu* OR variation* OR varying OR varie* OR variabl*)

Natural History: (Glaucoma[MeSH] OR "Glaucoma, Open Angle"[MeSH] OR glaucoma[tiab] OR poag[tiab]) AND ("natural history"[tiab])

Nutrition and POAG: ("Nutrition Therapy"[mh] OR "Nutritional Status"[mh] OR nutrition* OR nutrient* OR "Diet"[mh] OR "Diet Therapy"[mh] OR diet OR "Dietary Supplements"[mh] OR "Vitamins"[mh] OR vitamin* OR "Antioxidants"[mh] OR antioxidant*) AND ("Glaucoma"[mh] OR "Glaucoma, Open-Angle"[mh] OR glaucoma OR poag)

Patient Values and Preferences: (Glaucoma[MeSH] OR "Glaucoma, Open Angle"[MeSH] OR glaucoma[tiab]) AND (("patient values"[tiab] OR "patient preferences"[tiab]) OR (patient[tiab] AND (values[tiab] OR preferences[tiab])))

POAG Update: ("Glaucoma, Open-Angle"[mh] OR poag)

Prevalence: (Glaucoma/epidemiology[MeSH] OR "Glaucoma, Open Angle/epidemiology"[MeSH]) OR (glaucoma[tiab] AND (prevalence[tiab] OR epidemiology[tiab]))

Progression: ("Intraocular Pressure"[mh] OR IOP) AND ("Glaucoma"[mh] OR glaucoma) AND "optic nerve damage" AND ("disease progression"[mh] OR past OR future OR predict* OR progressive)

Psychological Effects: ("Glaucoma"[mh] OR glaucoma OR "Glaucoma, Open-Angle"[mh]) AND ("Psychology"[mh] OR psychology OR psychological OR "Quality of Life"[mh] OR "quality of life" OR "Personality"[mh]) OR "Glaucoma/psychology"[mh]

Quality of Life: ("Quality of Life"[mh] OR "quality of life" OR qol OR hrqol OR "Sickness Impact Profile"[mh] OR "sickness impact" OR "Activities of Daily Living"[mh] OR "daily activities" OR "daily activity" OR "Karnofsky Performance Status"[mh] OR "Illness Behavior"[mh] OR "illness impact") AND ("Glaucoma, Open-Angle"[mh] OR "Glaucoma"[mh] OR glaucoma OR POAG)

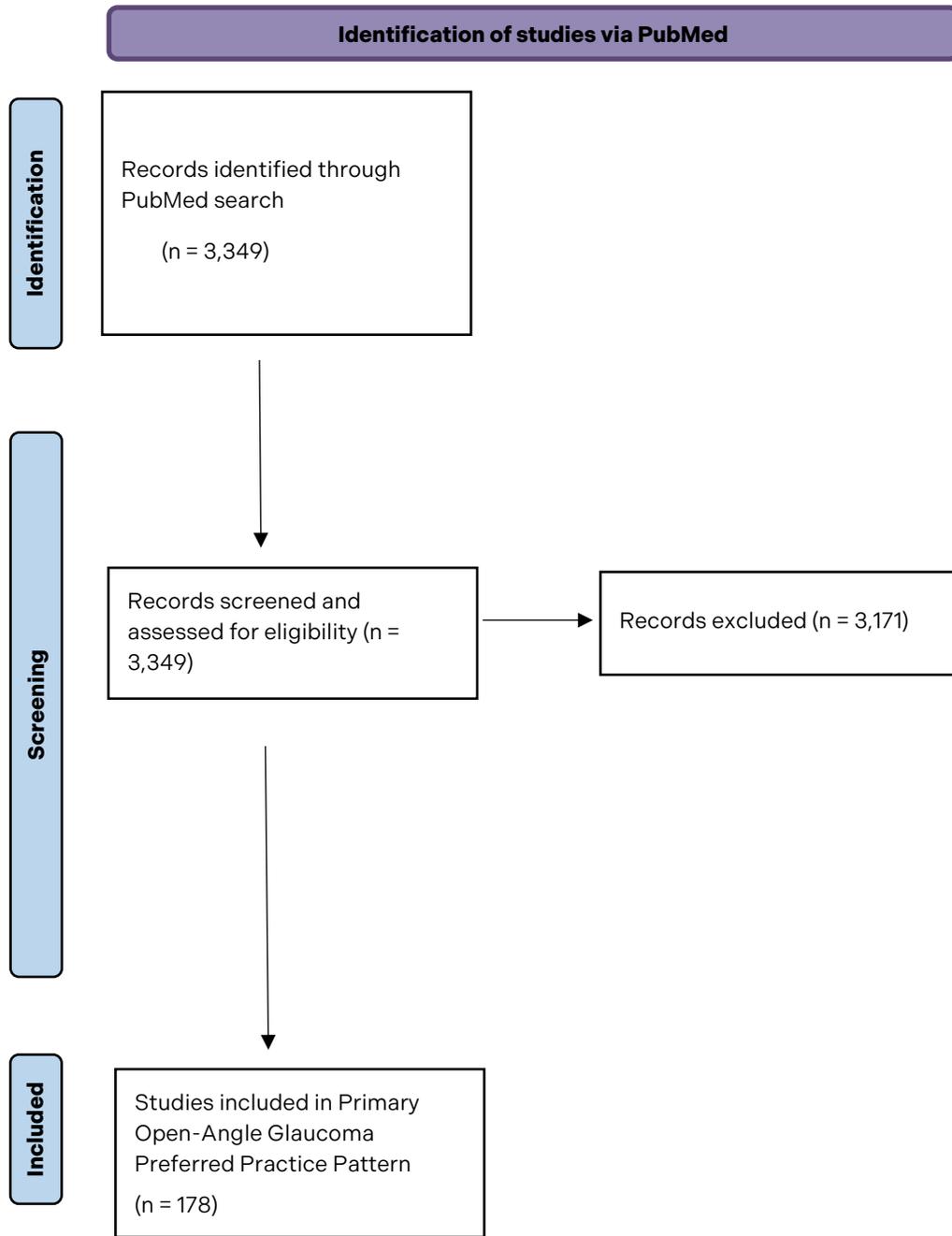
Refractive Surgery in Patients with POAG or Glaucoma Suspect: ("Refractive Surgical Procedures"[mh] OR "refractive surgery") AND ("Glaucoma"[mh] OR "Glaucoma, Open-Angle"[mh] OR glaucoma OR poag)

Risk Factors: (Glaucoma[MeSH] OR "Glaucoma, Open Angle"[MeSH] OR glaucoma[tiab] OR poag[tiab]) AND (Risk Factors[MeSH] OR ("risk"[tiab] AND "factors"[tiab]))

Selective Laser Trabeculoplasty: "selective laser trabeculoplasty"[tiab]

Sleep Disturbances and POAG: ("Sleep"[mh] OR "Sleep Apnea, Central"[mh] OR "Sleep Disorders, Circadian Rhythm"[mh] OR "Sleep Apnea Syndromes"[mh] OR "Sleep Apnea, Obstructive"[mh] OR "Sleep Disorders"[tiab] OR "Sleep Disorders, Intrinsic"[mh] OR "Dyssomnias"[mh] OR "Sleep Deprivation"[mh] OR "Sleep Initiation and Maintenance Disorders"[mh] OR "sleep disturbance" OR "sleep disturbances" OR "sleep apnea") AND ("Glaucoma"[mh] OR "Glaucoma, Open-Angle"[mh] OR glaucoma OR poag)

Stereographic Photography of the Optic Nerve Head: (("Photography"[mh] AND stereophotography) OR "stereographic photography")) AND ("Optic Nerve"[mh] OR "Optic Disk"[mh] OR "optic nerve") AND ("Glaucoma"[mh] OR "Glaucoma, Open-Angle"[mh] OR glaucoma OR poag)



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

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Trabecular Procedures Combined with Cataract Surgery for Open-Angle Glaucoma OTA (2023)

Selective Laser Trabeculoplasty for the Treatment of Glaucoma OTA (2023)

Corneal Hysteresis for the Diagnosis of Glaucoma and Assessment of Progression Risk OTA (2023)

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The Effect of Phacoemulsification on Intraocular Pressure in Glaucoma Patients OTA (2015)

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REFERENCES

1. Scottish Intercollegiate Guidelines Network. Annex B: Key to evidence statements and grades of recommendations. In: SIGN 50: A guideline developer's handbook. 2008 edition, revised 2011. Edinburgh, Scotland: Scottish Intercollegiate Guidelines Network. Available at: <https://www.sign.ac.uk/>. Accessed September 6, 2025.
2. GRADE Working Group. Organizations that have endorsed or that are using GRADE. Available at: <https://www.gradeworkinggroup.org/>. Accessed September 6, 2025.
3. Guyatt GH, Oxman AD, Vist GE, et al. Grade: An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924-6.
4. Jonas JB, Budde WM, Panda-Jonas S. Ophthalmoscopic evaluation of the optic nerve head. *Surv Ophthalmol* 1999;43:293-320.
5. Morgan JE, Bourtsoukli I, Rajkumar KN, et al. The accuracy of the inferior>superior>nasal>temporal neuroretinal rim area rule for diagnosing glaucomatous optic disc damage. *Ophthalmology* 2012;119:723-30.
6. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. *Br J Ophthalmol* 2002;86:238-42.
7. Liang YB, Friedman DS, Zhou Q, et al. Prevalence of primary open angle glaucoma in a rural adult Chinese population: The Handan Eye Study. *Invest Ophthalmol Vis Sci* 2011;52:8250-7.
8. Vijaya L, George R, Baskaran M, et al. Prevalence of primary open-angle glaucoma in an urban South Indian population and comparison with a rural population. The Chennai Glaucoma Study. *Ophthalmology* 2008;115:648-54 e1.
9. Leung DY, Tham CC. Normal-tension glaucoma: Current concepts and approaches-a review. *Clin Exp Ophthalmol* 2022;50:247-59.
10. Shen SY, Wong TY, Foster PJ, et al. The prevalence and types of glaucoma in Malay people: The Singapore Malay Eye Study. *Invest Ophthalmol Vis Sci* 2008;49:3846-51.
11. Wang D, Huang W, Li Y, et al. Intraocular pressure, central corneal thickness, and glaucoma in Chinese adults: The Liwan Eye Study. *Am J Ophthalmol* 2011;152:454-62 e1.
12. Klein BE, Klein R, Sponsel WE, et al. Prevalence of glaucoma: The Beaver Dam Eye Study. *Ophthalmology* 1992;99:1499-504.
13. Rotchford AP, Johnson GJ. Glaucoma in Zululand: A population-based cross-sectional survey in a rural district in South Africa. *Arch Ophthalmol* 2002;120:471-8.
14. Pakravan M, Yazdani S, Javadi MA, et al. A population-based survey of the prevalence and types of glaucoma in central Iran: The Yazd Eye Study. *Ophthalmology* 2013;120:1977-84.
15. Dielemans I, Vingerling JR, Wolfs RC, et al. The prevalence of primary open-angle glaucoma in a population-based study in the Netherlands: The Rotterdam Study. *Ophthalmology* 1994;101:1851-5.
16. Jonasson F, Damji KF, Arnarsson A, et al. Prevalence of open-angle glaucoma in Iceland: Reykjavik Eye Study. *Eye* 2003;17:747-53.
17. Bonomi L, Marchini G, Marraffa M, et al. Prevalence of glaucoma and intraocular pressure distribution in a defined population: The Egna-Neumarkt Study. *Ophthalmology* 1998;105:209-15.
18. Varma R, Ying-Lai M, Francis BA, et al. Prevalence of open-angle glaucoma and ocular hypertension in Latinos: The Los Angeles Latino Eye Study. *Ophthalmology* 2004;111:1439-48.
19. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: A randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002;120:701-13; discussion 829-30.
20. Kapetanakis VV, Chan MP, Foster PJ, et al. Global variations and time trends in the prevalence of primary open angle glaucoma (POAG): A systematic review and meta-analysis. *Br J Ophthalmol* 2016;100:86-93.
21. Tham YC, Li X, Wong TY, et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040: A systematic review and meta-analysis. *Ophthalmology* 2014;121:2081-90.
22. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol* 2006;90:262-7.
23. Klein BE, Klein R. Projected prevalences of age-related eye diseases. *Invest Ophthalmol Vis Sci* 2013;54:ORSF14-7.
24. Vajaranant TS, Wu S, Torres M, Varma R. The changing face of primary open-angle glaucoma in the United States: Demographic and geographic changes from 2011 to 2050. *Am J Ophthalmol* 2012;154:303-14.
25. Friedman DS, Wolfs RC, O'Colmain BJ, et al. Eye diseases prevalence research group. Prevalence of open-angle glaucoma among adults in the United States. *Arch Ophthalmol* 2004;122:532-8.

26. Sommer A, Tielsch JM, Katz J, et al. Racial differences in the cause-specific prevalence of blindness in east Baltimore. *N Engl J Med* 1991;325:1412-7.
27. Varma R, Ying-Lai M, Francis BA, et al. Los Angeles Latino Eye Study group. Prevalence of open-angle glaucoma and ocular hypertension in Latinos: The Los Angeles Latino Eye Study. *Ophthalmology* 2004;111:1439-48.
28. Stein JD, Kim DS, Niziol LM, et al. Differences in rates of glaucoma among Asian Americans and other racial groups, and among various Asian ethnic groups. *Ophthalmology* 2011;118:1031-7.
29. GBD 2019 Blindness and Vision Impairment Collaborators, Vision Loss Expert Group of the Global Burden of Disease Study. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to vision 2020: The right to sight: An analysis for the global burden of disease study. *Lancet Glob Health* 2021;9:e144-e60.
30. Vision Loss Expert Group of the Global Burden of Disease Study, GBD Blindness and Vision Impairment Collaborators. Global estimates on the number of people blind or visually impaired by glaucoma: A meta-analysis from 2000 to 2020. *Eye (Lond)* 2024;38:2036-46.
31. Kyari F, Entekume G, Rabi M, et al. A population-based survey of the prevalence and types of glaucoma in Nigeria: Results from the Nigeria National Blindness and Visual Impairment Survey. *BMC Ophthalmol* 2015;15:176.
32. Budenz DL, Barton K, Whiteside-de Vos J, et al. Prevalence of glaucoma in an urban West African population: The Tema Eye Survey. *JAMA Ophthalmol* 2013;131:651-8.
33. Tseng VL, Kitayama K, Yu F, Coleman AL. Prevalence and severity of glaucoma in the California Medicare population. *Am J Ophthalmol* 2024;259:25-34.
34. Flanagin A, Frey T, Christiansen SL, AMA Manual of Style Committee. Updated guidance on the reporting of race and ethnicity in medical and science journals. *JAMA* 2021;326:621-7.
35. National Academies of Sciences, Engineering, and Medicine. Rethinking race and ethnicity in biomedical research. Washington, DC: *The National Academies Press*, 2025; 270.
36. Borrell LN, Elhawary JR, Fuentes-Afflick E, et al. Race and genetic ancestry in medicine - a time for reckoning with racism. *N Engl J Med* 2021;384:474-80.
37. Ioannidis JPA, Powe NR, Yancy C. Recalibrating the use of race in medical research. *JAMA* 2021;325:623-4.
38. Bauchner H. Race, poverty, and medicine in the United States. *JAMA* 2015;313:1423.
39. Tielsch JM, Sommer A, Katz J, et al. Racial variations in the prevalence of primary open-angle glaucoma: The Baltimore Eye Survey. *JAMA* 1991;266:369-74.
40. Leske MC, Connell AM, Schachat AP, Hyman L. The Barbados Eye Study: Prevalence of open angle glaucoma. *Arch Ophthalmol* 1994;112:821-9.
41. Quigley HA, West SK, Rodriguez J, et al. The prevalence of glaucoma in a population-based study of Hispanic subjects: Proyecto VER. *Arch Ophthalmol* 2001;119:1819-26.
42. Mitchell P, Smith W, Attebo K, Healey PR. Prevalence of open-angle glaucoma in Australia: The Blue Mountains Eye Study. *Ophthalmology* 1996;103:1661-9.
43. Wensor MD, McCarty CA, Stanislavsky YL, et al. The prevalence of glaucoma in the Melbourne Visual Impairment Project. *Ophthalmology* 1998;105:733-9.
44. Coffey M, Reidy A, Wormald R, et al. Prevalence of glaucoma in the west of Ireland. *Br J Ophthalmol* 1993;77:17-21.
45. Gordon MO, Beiser JA, Brandt JD, et al. The Ocular Hypertension Treatment Study: Baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002;120:714-20; discussion 829-30.
46. Sommer A, Tielsch JM, Katz J, et al. Relationship between intraocular pressure and primary open angle glaucoma among White and Black Americans: The Baltimore Eye Survey. *Arch Ophthalmol* 1991;109:1090-5.
47. Leske MC, Connell AM, Wu SY, et al. Barbados Eye Studies group. Incidence of open-angle glaucoma: The Barbados Eye Studies. *Arch Ophthalmol* 2001;119:89-95.
48. Le A, Mukesh BN, McCarty CA, Taylor HR. Risk factors associated with the incidence of open-angle glaucoma: The Visual Impairment Project. *Invest Ophthalmol Vis Sci* 2003;44:3783-9.
49. Leibowitz HM, Krueger DE, Maunder LR, et al. The Framingham Eye Study monograph: An ophthalmological and epidemiological study of cataract, glaucoma, diabetic retinopathy, macular degeneration, and visual acuity in a general population of 2631 adults, 1973-1975. *Surv Ophthalmol* 1980;24:335-610.
50. Miglior S, Pfeiffer N, Torri V, et al. European Glaucoma Prevention Study (EGPS) Group. Predictive factors for open-angle glaucoma among patients with ocular hypertension in the European Glaucoma Prevention Study. *Ophthalmology* 2007;114:3-9.
51. Kim KE, Kim MJ, Park KH, et al. Prevalence, awareness, and risk factors of primary open-angle glaucoma: Korea National Health and Nutrition Examination Survey 2008-2011. *Ophthalmology* 2016;123:532-41.

52. Pan CW, Yang WY, Hu DN, et al. Longitudinal cohort study on the incidence of primary open-angle glaucoma in Bai Chinese. *Am J Ophthalmol* 2017;176:127-33.
53. Armaly MF, Krueger DE, Maunder L, et al. Biostatistical analysis of the collaborative glaucoma study: I. Summary report of the risk factors for glaucomatous visual-field defects. *Arch Ophthalmol* 1980;98:2163-71.
54. Mason RP, Kosoko O, Wilson MR, et al. National survey of the prevalence and risk factors of glaucoma in St. Lucia, West Indies. Part I. Prevalence findings. *Ophthalmology* 1989;96:1363-8.
55. Leske MC, Wu SY, Hennis A, et al. BESs study group. Risk factors for incident open-angle glaucoma: The Barbados Eye Studies. *Ophthalmology* 2008;115:85-93.
56. Chiam N, Baskaran M, Li Z, et al. Social, health and ocular factors associated with primary open-angle glaucoma amongst Chinese Singaporeans. *Clin Exp Ophthalmol* 2018;46:25-34.
57. Karti O, Yuksel B, Uzunel UD, et al. The assessment of optical coherence tomographic parameters in subjects with a positive family history of glaucoma. *Clin Exp Optom* 2017;100:663-7.
58. Mitchell P, Smith W, Chey T, Healey PR. Open-angle glaucoma and diabetes: The Blue Mountains Eye Study, Australia. *Ophthalmology* 1997;104:712-8.
59. Chopra V, Varma R, Francis BA, et al. Los Angeles Latino Eye Study group. Type 2 diabetes mellitus and the risk of open-angle glaucoma: The Los Angeles Latino Eye Study. *Ophthalmology* 2008;115:227-32.
60. Bonovas S, Peponis V, Filioussi K. Diabetes mellitus as a risk factor for primary open-angle glaucoma: A meta-analysis. *Diabet Med* 2004;21:609-14.
61. Zhao D, Cho J, Kim MH, et al. Diabetes, fasting glucose, and the risk of glaucoma: A meta-analysis. *Ophthalmology* 2015;122:72-8.
62. Tham YC, Lim SH, Gupta P, et al. Inter-relationship between ocular perfusion pressure, blood pressure, intraocular pressure profiles and primary open-angle glaucoma: The Singapore Epidemiology of Eye Diseases Study. *Br J Ophthalmol* 2018;102:1402-6.
63. Tielsch JM, Katz J, Sommer A, et al. Hypertension, perfusion pressure, and primary open-angle glaucoma. A population-based assessment. *Arch Ophthalmol* 1995;113:216-21.
64. Leske MC, Connell AM, Wu SY, et al. Risk factors for open-angle glaucoma. The Barbados Eye Study. *Arch Ophthalmol* 1995;113:918-24.
65. Mitchell P, Hourihan F, Sandbach J, Wang JJ. The relationship between glaucoma and myopia: The Blue Mountains Eye Study. *Ophthalmology* 1999;106:2010-5.
66. Grodum K, Heijl A, Bengtsson B. Refractive error and glaucoma. *Acta Ophthalmol Scand* 2001;79:560-6.
67. Xu L, Wang Y, Wang S, Jonas JB. High myopia and glaucoma susceptibility the Beijing Eye Study. *Ophthalmology* 2007;114:216-20.
68. Shen L, Melles RB, Metlapally R, et al. The association of refractive error with glaucoma in a multiethnic population. *Ophthalmology* 2016;123:92-101.
69. Brandt JD, Beiser JA, Kass MA, Gordon MO. Central corneal thickness in the ocular hypertension treatment study (OHTS). *Ophthalmology* 2001;108:1779-88.
70. Susanna CN, Diniz-Filho A, Daga FB, et al. A prospective longitudinal study to investigate corneal hysteresis as a risk factor for predicting development of glaucoma. *Am J Ophthalmol* 2018;187:148-52.
71. Zhang B, Shweikh Y, Khawaja AP, et al. Associations with corneal hysteresis in a population cohort: Results from 96 010 UK Biobank participants. *Ophthalmology* 2019;126:1500-10.
72. Wurster P, Harris A, Gonzalez AC, et al. Risk factors for open-angle glaucoma in persons of Latin American descent. *J Glaucoma* 2020;29:217-25.
73. Drance SM, Fairclough M, Butler DM, Kottler MS. The importance of disc hemorrhage in the prognosis of chronic open angle glaucoma. *Arch Ophthalmol* 1977;95:226-8.
74. Diehl DL, Quigley HA, Miller NR, et al. Prevalence and significance of optic disc hemorrhage in a longitudinal study of glaucoma. *Arch Ophthalmol* 1990;108:545-50.
75. Airaksinen PJ, Mustonen E, Alanko HI. Optic disc haemorrhages precede retinal nerve fibre layer defects in ocular hypertension. *Acta Ophthalmol (Copenh)* 1981;59:627-41.
76. Siegner SW, Netland PA. Optic disc hemorrhages and progression of glaucoma. *Ophthalmology* 1996;103:1014-24.
77. Budenz DL, Anderson DR, Feuer WJ, et al. Ocular Hypertension Treatment Study Group. Detection and prognostic significance of optic disc hemorrhages during the Ocular Hypertension Treatment Study. *Ophthalmology* 2006;113:2137-43.
78. Gordon MO, Torri V, Miglior S, et al. Ocular Hypertension Treatment Study Group, European Glaucoma Prevention Study Group. Validated prediction model for the development of primary open-angle glaucoma in individuals with ocular hypertension. *Ophthalmology* 2007;114:10-9.
79. Broadway DC, Drance SM. Glaucoma and vasospasm. *Br J Ophthalmol* 1998;82:862-70.

80. Cursiefen C, Wisse M, Cursiefen S, et al. Migraine and tension headache in high-pressure and normal-pressure glaucoma. *Am J Ophthalmol* 2000;129:102-4.
81. Fan YY, Su WW, Liu CH, et al. Correlation between structural progression in glaucoma and obstructive sleep apnea. *Eye (Lond)* 2019;33:1459-65.
82. Kuzin AA, Varma R, Reddy HS, et al. Ocular biometry and open-angle glaucoma: The Los Angeles Latino Eye Study. *Ophthalmology* 2010;117:1713-9.
83. Wang J, Mitchell P, Smith W. Is there an association between migraine headache and open-angle glaucoma?: Findings from the Blue Mountains Eye Study. *Ophthalmology* 1997;104:1714-19.
84. Bonomi L, Marchini G, Marraffa M, et al. Vascular risk factors for primary open angle glaucoma: The Egna-Neumarkt Study. *Ophthalmology* 2000;107:1287-93.
85. Dielemans I, Vingerling JR, Algra D, et al. Primary open-angle glaucoma, intraocular pressure, and systemic blood pressure in the general elderly population: The Rotterdam Study. *Ophthalmology* 1995;102:54-60.
86. Jonas JB, Martus P, Budde WM. Anisometropia and degree of optic nerve damage in chronic open-angle glaucoma. *Am J Ophthalmol* 2002;134:547-51.
87. Leske MC, Wu SY, Nemesure B, Hennis A. Incident open-angle glaucoma and blood pressure. *Arch Ophthalmol* 2002;120:954-9.
88. Mitchell P, Lee AJ, Rochtchina E, Wang JJ. Open-angle glaucoma and systemic hypertension: The Blue Mountains Eye Study. *J Glaucoma* 2004;13:319-26.
89. Swaminathan SS, Bhakta AS, Shi W, et al. Is obstructive sleep apnea associated with progressive glaucomatous optic neuropathy? *J Glaucoma* 2018;27:1-6.
90. Weih LM, Nanjan M, McCarty CA, Taylor HR. Prevalence and predictors of open-angle glaucoma: Results from the Visual Impairment Project. *Ophthalmology* 2001;108:1966-72.
91. Collaborative Normal-Tension Glaucoma Study Group. Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. *Am J Ophthalmol* 1998;126:487-97.
92. Collaborative Normal-Tension Glaucoma Study Group. The effectiveness of intraocular pressure reduction in the treatment of normal-tension glaucoma. *Am J Ophthalmol* 1998;126:498-505.
93. Leske MC, Heijl A, Hussein M, et al. Early Manifest Glaucoma Trial Group. Factors for glaucoma progression and the effect of treatment: The Early Manifest Glaucoma Trial. *Arch Ophthalmol* 2003;121:48-56.
94. Heijl A, Leske MC, Bengtsson B, et al. Early Manifest Glaucoma Trial Group. Reduction of intraocular pressure and glaucoma progression: Results from the Early Manifest Glaucoma Trial. *Arch Ophthalmol* 2002;120:1268-79.
95. AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. *Am J Ophthalmol* 2000;130:429-40.
96. Garway-Heath DF, Crabb DP, Bunce C, et al. Latanoprost for open-angle glaucoma (UKGTS): A randomised, multicentre, placebo-controlled trial. *Lancet* 2015;385:1295-304.
97. Jay JL, Murray SB. Early trabeculectomy versus conventional management in primary open angle glaucoma. *Br J Ophthalmol* 1988;72:881-9.
98. Jay JL, Allan D. The benefit of early trabeculectomy versus conventional management in primary open angle glaucoma relative to severity of disease. *Eye* 1989;3 (Pt 5):528-35.
99. Migdal C, Gregory W, Hitchings R. Long-term functional outcome after early surgery compared with laser and medicine in open-angle glaucoma. *Ophthalmology* 1994;101:1651-6; discussion 7.
100. Leske MC, Heijl A, Hyman L, et al. Early Manifest Glaucoma Trial Group. Predictors of long-term progression in the Early Manifest Glaucoma Trial. *Ophthalmology* 2007;114:1965-72.
101. Lichter PR, Musch DC, Gillespie BW, et al. CIGTS study group. Interim clinical outcomes in the Collaborative Initial Glaucoma Treatment Study comparing initial treatment randomized to medications or surgery. *Ophthalmology* 2001;108:1943-53.
102. AGIS investigators. The Advanced Glaucoma Intervention Study (AGIS): 13. Comparison of treatment outcomes within race: 10-year results. *Ophthalmology* 2004;111:651-64.
103. Friedman DS, Jampel HD, Munoz B, West SK. The prevalence of open-angle glaucoma among Blacks and Whites 73 years and older: The Salisbury Eye Evaluation Glaucoma Study. *Arch Ophthalmol* 2006;124:1625-30.
104. De Moraes CG, Juthani VJ, Liebmann JM, et al. Risk factors for visual field progression in treated glaucoma. *Arch Ophthalmol* 2011;129:562-8.
105. De Moraes CG, Liebmann JM, Greenfield DS, et al. Low-pressure glaucoma treatment study group. Risk factors for visual field progression in the low-pressure glaucoma treatment study. *Am J Ophthalmol* 2012;154:702-11.
106. Caprioli J, Coleman AL. Intraocular pressure fluctuation a risk factor for visual field progression at low intraocular pressures in the Advanced Glaucoma Intervention Study. *Ophthalmology* 2008;115:1123-9.

107. Wolfs RC, Klaver CC, Ramrattan RS, et al. Genetic risk of primary open-angle glaucoma. Population-based familial aggregation study. *Arch Ophthalmol* 1998;116:1640-5.
108. Doshi V, Ying-Lai M, Azen SP, Varma R. Los Angeles Latino Eye Study Group. Sociodemographic, family history, and lifestyle risk factors for open-angle glaucoma and ocular hypertension. The Los Angeles Latino Eye Study. *Ophthalmology* 2008;115:639-47.
109. Tielsch JM, Katz J, Sommer A, et al. Family history and risk of primary open angle glaucoma. The Baltimore Eye Survey. *Arch Ophthalmol* 1994;112:69-73.
110. Rotchford AP, Kirwan JF, Muller MA, et al. Temba Glaucoma Study: A population-based cross-sectional survey in urban South Africa. *Ophthalmology* 2003;110:376-82.
111. Sloan FA, Brown DS, Carlisle ES, et al. Monitoring visual status: Why patients do or do not comply with practice guidelines. *Health Serv Res* 2004;39:1429-48.
112. Wang F, Javitt JC, Tielsch JM. Racial variations in treatment for glaucoma and cataract among Medicare recipients. *Ophthalmic Epidemiol* 1997;4:89-100.
113. Coleman AL, Yu F, Rowe S. Visual field testing in glaucoma medicare beneficiaries before surgery. *Ophthalmology* 2005;112:401-6.
114. Devgan U, Yu F, Kim E, Coleman AL. Surgical undertreatment of glaucoma in Black beneficiaries of medicare. *Arch Ophthalmol* 2000;118:253-6.
115. Stein JD, Talwar N, Laverne AM, et al. Racial disparities in the use of ancillary testing to evaluate individuals with open-angle glaucoma. *Arch Ophthalmol* 2012;130:1579-88.
116. Centers for Medicare and Medicaid Services. Your medicare coverage: Glaucoma tests. <https://www.Medicare.Gov/coverage/glaucoma-screenings>. Accessed September 6, 2025.
117. Acuff K, Wu JH, Varkhedi V, Baxter SL. Social determinants of health and health disparities in glaucoma: A review. *Clin Exp Ophthalmol* 2024;52:276-93.
118. Davuluru SS, Jess AT, Kim JSB, et al. Identifying, understanding, and addressing disparities in glaucoma care in the United States. *Transl Vis Sci Technol* 2023;12:18.
119. Kitayama K, Tsugawa Y, Nishi A, Coleman AL. Socioeconomic status mediates and modifies racial and ethnic disparities in incisional glaucoma surgical outcomes. *Am J Ophthalmol* 2025.
120. Newman-Casey PA, Aliancy J, Lu MC, et al. Social deprivation and the risk of screening positive for glaucoma in the mi-SIGHT telemedicine-based glaucoma detection program. *Ophthalmology* 2023;130:1053-65.
121. Shweikh Y, Ko F, Chan MP, et al. Measures of socioeconomic status and self-reported glaucoma in the U.K. Biobank cohort. *Eye (Lond)* 2015;29:1360-7.
122. Tseng VL, Kitayama K, Yu F, et al. Social vulnerability, prevalence of glaucoma, and incidence of glaucoma surgery in the California Medicare population. *Ophthalmol Glaucoma* 2023;6:616-25.
123. Shaheen A, Medeiros FA, Swaminathan SS. Association between greater social vulnerability and delayed glaucoma surgery. *Am J Ophthalmol* 2024;268:123-35.
124. Swaminathan SS, Medeiros FA, Gedde SJ. Impact of social vulnerability index on the development of severe visual impairment or blindness from glaucoma. *Am J Ophthalmol* 2024;267:172-81.
125. Stone EM, Fingert JH, Alward WL, et al. Identification of a gene that causes primary open angle glaucoma. *Science* 1997;275:668-70.
126. Rezaie T, Child A, Hitchings R, et al. Adult-onset primary open-angle glaucoma caused by mutations in optineurin. *Science* 2002;295:1077-9.
127. Pasutto F, Keller KE, Weisschuh N, et al. Variants in ASB10 are associated with open-angle glaucoma. *Hum Mol Genet* 2012;21:1336-49.
128. Burdon KP, Macgregor S, Hewitt AW, et al. Genome-wide association study identifies susceptibility loci for open angle glaucoma at TMC01 and CDKN2B-AS1. *Nat Genet* 2011;43:574-8.
129. Hysi PG, Cheng CY, Springelkamp H, et al. Genome-wide analysis of multi-ancestry cohorts identifies new loci influencing intraocular pressure and susceptibility to glaucoma. *Nat Genet* 2014;46:1126-30.
130. Ozel AB, Moroi SE, Reed DM, et al. Genome-wide association study and meta-analysis of intraocular pressure. *Hum Genet* 2014;133:41-57.
131. van Koolwijk LM, Ramdas WD, Ikram MK, et al. Common genetic determinants of intraocular pressure and primary open-angle glaucoma. *PLoS Genet* 2012;8:e1002611.
132. Gao X, Gauderman WJ, Liu Y, et al. A genome-wide association study of central corneal thickness in Latinos. *Invest Ophthalmol Vis Sci* 2013;54:2435-43.
133. Lu Y, Vitart V, Burdon KP, et al. Genome-wide association analyses identify multiple loci associated with central corneal thickness and keratoconus. *Nat Genet* 2013;45:155-63.
134. Ulmer M, Li J, Yaspan BL, et al. Genome-wide analysis of central corneal thickness in primary open-angle glaucoma cases in the NEIGHBOR and GLAUGEN consortia. *Invest Ophthalmol Vis Sci* 2012;53:4468-74.

135. Springelkamp H, Hohn R, Mishra A, et al. Meta-analysis of genome-wide association studies identifies novel loci that influence cupping and the glaucomatous process. *Nat Commun* 2014;5:4883.
136. Wiggs JL, Yaspan BL, Hauser MA, et al. Common variants at 9p21 and 8q22 are associated with increased susceptibility to optic nerve degeneration in glaucoma. *PLoS Genet* 2012;8:e1002654.
137. Carnes MU, Liu YP, Allingham RR, et al. Discovery and functional annotation of six6 variants in primary open-angle glaucoma. *PLoS Genet* 2014;10:e1004372.
138. Loomis SJ, Kang JH, Weinreb RN, et al. Association of CAV1/CAV2 genomic variants with primary open-angle glaucoma overall and by gender and pattern of visual field loss. *Ophthalmology* 2014;121:508-16.
139. Chen M, Yu X, Xu J, et al. Association of gene polymorphisms with primary open angle glaucoma: A systematic review and meta-analysis. *Invest Ophthalmol Vis Sci* 2019;60:1105-21.
140. Wiggs JL, Pasquale LR. Genetics of glaucoma. *Hum Mol Genet* 2017;26:R21-R7.
141. Stamenkovic M, Lukic V, Suvakov S, et al. GSTM1-null and GSTT1-active genotypes as risk determinants of primary open angle glaucoma among smokers. *Int J Ophthalmol* 2018;11:1514-20.
142. Consugar MB, Navarro-Gomez D, Place EM, et al. Panel-based genetic diagnostic testing for inherited eye diseases is highly accurate and reproducible, and more sensitive for variant detection, than exome sequencing. *Genet Med* 2015;17:253-61.
143. Ciociola EC, Klifto MR. Juvenile open angle glaucoma: Current diagnosis and management. *Curr Opin Ophthalmol* 2022;33:97-102.
144. American Academy of Ophthalmology. Policy statement. Recommendations for genetic testing of inherited eye diseases. San Francisco, CA: American Academy of Ophthalmology; 2014. Available at: <https://www.aaopt.org/education/clinical-statement/recommendations-genetic-testing-of-inherited-eye-d>. Accessed September 6, 2025.
145. Genetics of Glaucoma in People of African Descent Consortium, Hauser MA, Allingham RR, et al. Association of genetic variants with primary open-angle glaucoma among individuals with African ancestry. *JAMA* 2019;322:1682-91.
146. Verma SS, Gudiseva HV, Chavali VRM, et al. A multi-cohort genome-wide association study in African ancestry individuals reveals risk loci for primary open-angle glaucoma. *Cell* 2024;187:464-80 e10.
147. Collins DW, Gudiseva HV, Trachtman B, et al. Association of primary open-angle glaucoma with mitochondrial variants and haplogroups common in African Americans. *Mol Vis* 2016;22:454-71.
148. Dielemans I, de Jong PT, Stolk R, et al. Primary open-angle glaucoma, intraocular pressure, and diabetes mellitus in the general elderly population. The Rotterdam Study. *Ophthalmology* 1996;103:1271-5.
149. Pasquale LR, Kang JH, Manson JE, et al. Prospective study of type 2 diabetes mellitus and risk of primary open-angle glaucoma in women. *Ophthalmology* 2006;113:1081-6.
150. de Voogd S, Ikram MK, Wolfs RC, et al. Is diabetes mellitus a risk factor for open-angle glaucoma?: The Rotterdam Study. *Ophthalmology* 2006;113:1827-31.
151. Klein BE, Klein R, Jensen SC. Open-angle glaucoma and older-onset diabetes: The Beaver Dam Eye Study. *Ophthalmology* 1994;101:1173-7.
152. Nakamura M, Kanamori A, Negi A. Diabetes mellitus as a risk factor for glaucomatous optic neuropathy. *Ophthalmologica* 2005;219:1-10.
153. Vijaya L, George R, Paul PG, et al. Prevalence of open-angle glaucoma in a rural South Indian population. *Invest Ophthalmol Vis Sci* 2005;46:4461-7.
154. Luo XY, Tan NYQ, Chee ML, et al. Direct and indirect associations between diabetes and intraocular pressure: The Singapore Epidemiology of Eye Diseases Study. *Invest Ophthalmol Vis Sci* 2018;59:2205-11.
155. Memarzadeh F, Ying-Lai M, Chung J, et al. Los Angeles Latino Eye Study Group. Blood pressure, perfusion pressure, and open-angle glaucoma: The Los Angeles Latino Eye Study. *Invest Ophthalmol Vis Sci* 2010;51:2872-7.
156. Charlson ME, de Moraes CG, Link A, et al. Nocturnal systemic hypotension increases the risk of glaucoma progression. *Ophthalmology* 2014;121:2004-12.
157. Topouzis F, Wilson MR, Harris A, et al. Association of open-angle glaucoma with perfusion pressure status in the Thessaloniki Eye Study. *Am J Ophthalmol* 2013;155:843-51.
158. Khawaja AP, Crabb DP, Jansonius NM. The role of ocular perfusion pressure in glaucoma cannot be studied with multivariable regression analysis applied to surrogates. *Invest Ophthalmol Vis Sci* 2013;54:4619-20.
159. Wong TY, Klein BE, Klein R, et al. Refractive errors, intraocular pressure, and glaucoma in a white population. *Ophthalmology* 2003;110:211-7.
160. Ramakrishnan R, Nirmalan PK, Krishnadas R, et al. Glaucoma in a rural population of southern India: The Aravind Comprehensive Eye Survey. *Ophthalmology* 2003;110:1484-90.
161. Suzuki Y, Iwase A, Araie M, et al. Risk factors for open-angle glaucoma in a Japanese population: The Tajimi Study. *Ophthalmology* 2006;113:1613-7.

162. Wu SY, Nemesure B, Leske MC. Glaucoma and myopia. *Ophthalmology* 2000;107:1026-7.
163. Shah S, Chatterjee A, Mathai M, et al. Relationship between corneal thickness and measured intraocular pressure in a general ophthalmology clinic. *Ophthalmology* 1999;106:2154-60.
164. Whitacre MM, Stein RA, Hassanein K. The effect of corneal thickness on applanation tonometry. *Am J Ophthalmol* 1993;115:592-6.
165. Goldmann H, Schmidt T. Applanation tonometry [in German]. *Ophthalmologica* 1957;134:221-42.
166. Ehlers N, Bramsen T, Sperling S. Applanation tonometry and central corneal thickness. *Acta Ophthalmol (Copenh)* 1975;53:34-43.
167. Stodtmeister R. Applanation tonometry and correction according to corneal thickness. *Acta Ophthalmol Scand* 1998;76:319-24.
168. Doughty MJ, Zaman ML. Human corneal thickness and its impact on intraocular pressure measures: A review and meta-analysis approach. *Surv Ophthalmol* 2000;44:367-408.
169. Medeiros FA, Sample PA, Zangwill LM, et al. Corneal thickness as a risk factor for visual field loss in patients with preperimetric glaucomatous optic neuropathy. *Am J Ophthalmol* 2003;136:805-13.
170. Aghaian E, Choe JE, Lin S, Stamper RL. Central corneal thickness of Caucasians, Chinese, Hispanics, Filipinos, African Americans, and Japanese in a glaucoma clinic. *Ophthalmology* 2004;111:2211-9.
171. Hahn S, Azen S, Ying-Lai M, Varma R. Los Angeles Latino Eye Study Group. Central corneal thickness in Latinos. *Invest Ophthalmol Vis Sci* 2003;44:1508-12.
172. Chua J, Tham YC, Liao J, et al. Ethnic differences of intraocular pressure and central corneal thickness: The Singapore Epidemiology of Eye Diseases Study. *Ophthalmology* 2014;121:2013-22.
173. Torres RJ, Jones E, Edmunds B, et al. Central corneal thickness in northwestern American Indians/Alaskan natives and comparison with white and African-American persons. *Am J Ophthalmol* 2008;146:747-51.
174. Shimmyo M, Ross AJ, Moy A, Mostafavi R. Intraocular pressure, Goldmann applanation tension, corneal thickness, and corneal curvature in Caucasians, Asians, Hispanics, and African Americans. *Am J Ophthalmol* 2003;136:603-13.
175. Orsengo GJ, Pye DC. Determination of the true intraocular pressure and modulus of elasticity of the human cornea in vivo. *Bull Math Biol* 1999;61:551-72.
176. Weinreb RN, Brandt JD, Garway-Heath D, Medeiros FA, eds. Intraocular pressure: Reports and consensus statements of the 4th global AIGS consensus meeting on intraocular pressure. The Netherlands: *Kugler Publications*, 2007.
177. Brandt JD, Gordon MO, Gao F, et al. Adjusting intraocular pressure for central corneal thickness does not improve prediction models for primary open-angle glaucoma. *Ophthalmology* 2012;119:437-42.
178. Dueker DK, 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;114:1779-87.
179. Francis BA, Varma R, Chopra V, et al. Intraocular pressure, central corneal thickness, and prevalence of open-angle glaucoma: The Los Angeles Latino Eye Study. *Am J Ophthalmol* 2008;146:741-6.
180. Sit AJ, Chen TC, Takusagawa HL, et al. Corneal hysteresis for the diagnosis of glaucoma and assessment of progression risk: A report by the American Academy of Ophthalmology. *Ophthalmology* 2023;130:433-42.
181. Liu J, Roberts CJ. Influence of corneal biomechanical properties on intraocular pressure measurement: Quantitative analysis. *J Cataract Refract Surg* 2005;31:146-55.
182. Congdon NG, Broman AT, Bandeen-Roche K, et al. Central corneal thickness and corneal hysteresis associated with glaucoma damage. *Am J Ophthalmol* 2006;141:868-75.
183. Medeiros FA, Meira-Freitas D, Lisboa R, et al. Corneal hysteresis as a risk factor for glaucoma progression: A prospective longitudinal study. *Ophthalmology* 2013;120:1533-40.
184. De Moraes CV, Hill V, Tello C, et al. Lower corneal hysteresis is associated with more rapid glaucomatous visual field progression. *J Glaucoma* 2012;21:209-13.
185. Jammal AA, Medeiros FA. Corneal hysteresis: Ready for prime time? *Curr Opin Ophthalmol* 2022;33:243-9.
186. Shin J, Kim TW, Park SJ, et al. Changes in biomechanical properties of the cornea and intraocular pressure after myopic laser in situ keratomileusis using a femtosecond laser for flap creation determined using ocular response analyzer and Goldmann applanation tonometry. *J Glaucoma* 2015;24:195-201.
187. Pepose JS, Feigenbaum SK, Qazi MA, et al. Changes in corneal biomechanics and intraocular pressure following LASIK using static, dynamic, and noncontact tonometry. *Am J Ophthalmol* 2007;143:39-47.
188. Kirwan C, O'Keefe M. Measurement of intraocular pressure in LASIK and LASEK patients using the Reichert ocular response analyzer and Goldmann applanation tonometry. *J Refract Surg* 2008;24:366-70.
189. Qazi MA, Sanderson JP, Mahmoud AM, et al. Postoperative changes in intraocular pressure and corneal biomechanical metrics laser in situ keratomileusis versus laser-assisted subepithelial keratectomy. *J Cataract Refract Surg* 2009;35:1774-88.

190. Krupin T, Liebmann JM, Greenfield DS, et al. Low-Pressure Glaucoma Study Group. The low-pressure glaucoma treatment study (LOGTS) study design and baseline characteristics of enrolled patients. *Ophthalmology* 2005;112:376-85.
191. Drance S, Anderson DR, Schulzer M. Risk factors for progression of visual field abnormalities in normal-tension glaucoma. *Am J Ophthalmol* 2001;131:699-708.
192. Huang JY, Su CC, Wang TH, Tsai IJ. Migraine and increased risk of developing open angle glaucoma: A population-based cohort study. *BMC Ophthalmol* 2019;19:50.
193. Park HY, Park SH, Park CK. Central visual field progression in normal-tension glaucoma patients with autonomic dysfunction. *Invest Ophthalmol Vis Sci* 2014;55:2557-63.
194. Nguyen BN, Vingrys AJ, McKendrick AM. The effect of duration post-migraine on visual electrophysiology and visual field performance in people with migraine. *Cephalalgia* 2014;34:42-57.
195. Bulpitt CJ, Hodes C, Everitt MG. Intraocular pressure and systemic blood pressure in the elderly. *Br J Ophthalmol* 1975;59:717-20.
196. Newman-Casey PA, Talwar N, Nan B, et al. The relationship between components of metabolic syndrome and open-angle glaucoma. *Ophthalmology* 2011;118:1318-26.
197. Wilson MR, Hertzmark E, Walker AM, et al. A case-control study of risk factors in open angle glaucoma. *Arch Ophthalmol* 1987;105:1066-71.
198. Tan GS, Wong TY, Fong CW, Aung T. Diabetes, metabolic abnormalities, and glaucoma. *Arch Ophthalmol* 2009;127:1354-61.
199. Wormald RP, Basauri E, Wright LA, Evans JR. The African Caribbean Eye Survey: Risk factors for glaucoma in a sample of African Caribbean people living in London. *Eye (Lond)* 1994;8 (Pt 3):315-20.
200. Kaimbo Wa Kaimbo D, Missotten L. Risk factors for open-angle glaucoma in 260 Black subjects in Congo. *Bull Soc Belge Ophthalmol* 1997;267:29-34.
201. Shiose Y, Kawase Y. A new approach to stratified normal intraocular pressure in a general population. *Am J Ophthalmol* 1986;101:714-21.
202. Wolf S, Arend O, Sponsel WE, et al. Retinal hemodynamics using scanning laser ophthalmoscopy and hemorrheology in chronic open-angle glaucoma. *Ophthalmology* 1993;100:1561-6.
203. Graham SL, Drance SM. Nocturnal hypotension: Role in glaucoma progression. *Surv Ophthalmol* 1999;43 (suppl):S10-6.
204. Müskens RP, de Voogd S, Wolfs RC, et al. Systemic antihypertensive medication and incident open-angle glaucoma. *Ophthalmology* 2007;114:2221-6.
205. Fleischman D, Allingham RR. The role of cerebrospinal fluid pressure in glaucoma and other ophthalmic diseases: A review. *Saudi J Ophthalmol* 2013;27:97-106.
206. Berdahl JP, Allingham RR, Johnson DH. Cerebrospinal fluid pressure is decreased in primary open-angle glaucoma. *Ophthalmology* 2008;115:763-8.
207. Berdahl JP, Fautsch MP, Stinnett SS, Allingham RR. Intracranial pressure in primary open angle glaucoma, normal tension glaucoma, and ocular hypertension: A case-control study. *Invest Ophthalmol Vis Sci* 2008;49:5412-8.
208. Ren R, Jonas JB, Tian G, et al. Cerebrospinal fluid pressure in glaucoma: A prospective study. *Ophthalmology* 2010;117:259-66.
209. Ren R, Zhang X, Wang N, et al. Cerebrospinal fluid pressure in ocular hypertension. *Acta Ophthalmol* 2011;89:e142-8.
210. Abegão Pinto L, Vandewalle E, Pronk A, Stalmans I. Intraocular pressure correlates with optic nerve sheath diameter in patients with normal tension glaucoma. *Graefes Arch Clin Exp Ophthalmol* 2012;250:1075-80.
211. Ford RL, Frankfort BJ, Fleischman D. Cerebrospinal fluid and ophthalmic disease. *Curr Opin Ophthalmol* 2022;33:73-9.
212. Wang S, Liu Y, Zheng G. Hypothyroidism as a risk factor for open angle glaucoma: A systematic review and meta-analysis. *PLoS One* 2017;12:e0186634.
213. Lin HC, Kang JH, Jiang YD, Ho JD. Hypothyroidism and the risk of developing open-angle glaucoma: A five-year population-based follow-up study. *Ophthalmology* 2010;117:1960-6.
214. Thvilum M, Brandt F, Brix TH, Hegedus L. The interrelation between hypothyroidism and glaucoma: A critical review and meta-analyses. *Acta Ophthalmol* 2017;95:759-67.
215. Coleman AL, Mansberger SL, Wilson MR. Epidemiology of primary open-angle glaucoma. In: Albert DM, Miller JW, Azar DT, Blodi BA, eds. *Albert & Jakobiec's principles & practice of ophthalmology*, 3rd ed. Philadelphia, PA: *Saunders/Elsevier*, 2008;Chapter 36.
216. Freeman EE, Munoz B, West SK, et al. Glaucoma and quality of life: The Salisbury Eye Evaluation. *Ophthalmology* 2008;115:233-8.

217. McKean-Cowdin R, Wang Y, Wu J, et al. Los Angeles Latino Eye Study Group. Impact of visual field loss on health-related quality of life in glaucoma: The Los Angeles Latino Eye Study. *Ophthalmology* 2008;115:941-8.
218. Burr JM, Mowatt G, Hernandez R, et al. The clinical effectiveness and cost-effectiveness of screening for open angle glaucoma: A systematic review and economic evaluation. *Health Technol Assess* 2007;11:III-IV, IX-X, 1-190.
219. Hernandez RA, Burr JM, Vale LD. Economic evaluation of screening for open-angle glaucoma. *Int J Technol Assess Health Care* 2008;24:203-11.
220. Klein BE, Klein R, Lee KE. Heritability of risk factors for primary open-angle glaucoma: The Beaver Dam Eye Study. *Invest Ophthalmol Vis Sci* 2004;45:59-62.
221. Duggal P, Klein AP, Lee KE, et al. A genetic contribution to intraocular pressure: The Beaver Dam Eye Study. *Invest Ophthalmol Vis Sci* 2005;46:555-60.
222. Mitchell P, Rochtchina E, Lee AJ, Wang JJ. Bias in self-reported family history and relationship to glaucoma: The Blue Mountains Eye Study. *Ophthalmic Epidemiol* 2002;9:333-45.
223. Newman-Casey PA, Hark LA, Lu MC, et al. Social determinants of health and glaucoma screening and detection in the SIGHT studies. *J Glaucoma* 2024;33:S60-S5.
224. Kolomeyer NN, Katz LJ, Hark LA, et al. Lessons learned from 2 large community-based glaucoma screening studies. *J Glaucoma* 2021;30:875-7.
225. Tielsch JM, Katz J, Singh K, et al. A population-based evaluation of glaucoma screening: The Baltimore Eye Survey. *Am J Epidemiol* 1991;134:1102-10.
226. Hollows FC, Graham P. Intraocular pressure, glaucoma and glaucoma suspects in a defined population. *Br J Ophthalmol* 1966;50:570-86.
227. Sommer A. Disabling visual disorders. Public health and preventive medicine 12th ed. Norwalk: *Appleton-Century-Crofts*, 1986.
228. Lichter PR. Variability of expert observers in evaluating the optic disc. *Trans Am Ophthalmol Soc* 1976;74:532-72.
229. Kahn HA, Leibowitz HM, Ganley JP. Standardizing diagnostic procedures. *Am J Ophthalmol* 1975;79:768-75.
230. Springelkamp H, Lee K, Wolfs RC, et al. Population-based evaluation of retinal nerve fiber layer, retinal ganglion cell layer, and inner plexiform layer as a diagnostic tool for glaucoma. *Invest Ophthalmol Vis Sci* 2014;55:8428-38.
231. Francis BA, Varma R, Vigen C, et al. Population and high-risk group screening for glaucoma: The Los Angeles Latino Eye Study. *Invest Ophthalmol Vis Sci* 2011;52:6257-64.
232. Li G, Fansi AK, Harasymowycz P. Screening for glaucoma using GDx-VCC in a population with ≥ 1 risk factors. *Can J Ophthalmol* 2013;48:279-85.
233. Fukai K, Terauchi R, Noro T, et al. Real-time risk score for glaucoma mass screening by spectral domain optical coherence tomography: Development and validation. *Transl Vis Sci Technol* 2022;11:8.
234. Hood DC, La Bruna S, Tsamis E, et al. Detecting glaucoma with only OCT: Implications for the clinic, research, screening, and ai development. *Prog Retin Eye Res* 2022;90:101052.
235. Anderson DR, Patella VM. Automated static perimetry, 2nd ed. St. Louis, MO: *Mosby*, 1999:10-31, 121-188, 281-282, 317-320.
236. Quigley HA. Identification of glaucoma-related visual field abnormality with the screening protocol of frequency doubling technology. *Am J Ophthalmol* 1998;125:819-29.
237. Tatemichi M, Nakano T, Tanaka K, et al. Glaucoma Screening Project (GSP) Study Group. Performance of glaucoma mass screening with only a visual field test using frequency-doubling technology perimetry. *Am J Ophthalmol* 2002;134:529-37.
238. Mwanza JC, Warren JL, Hochberg JT, et al. Combining frequency doubling technology perimetry and scanning laser polarimetry for glaucoma detection. *J Glaucoma* 2015;24:561-7.
239. Hark LA, Adegate J, Katz LJ, et al. Philadelphia telemedicine glaucoma detection and follow-up study: Cataract classifications following eye screening. *Telemed J E Health* 2019.
240. Maa AY, Medert CM, Lu X, et al. Diagnostic accuracy of technology-based eye care services: The technology-based eye care services compare trial part I. *Ophthalmology* 2020;127:38-44.
241. Jo JJ, Pasquale LR. Recent developments of telemedicine in glaucoma. *Curr Opin Ophthalmol* 2024;35:116-23.
242. Ting DSW, Pasquale LR, Peng L, et al. Artificial intelligence and deep learning in ophthalmology. *Br J Ophthalmol* 2019;103:167-75.
243. Liu S, Graham SL, Schulz A, et al. A deep learning-based algorithm identifies glaucomatous discs using monoscopic fundus photographs. *Ophthalmology Glaucoma* 2018;1:15-22.
244. Shigueoka LS, Vasconcellos JPC, Schimitti RB, et al. Automated algorithms combining structure and function outperform general ophthalmologists in diagnosing glaucoma. *PLoS One* 2018;13:e0207784.

245. American Academy of Ophthalmology Preferred Practice Patterns Committee. Preferred Practice Pattern[®] guidelines. Comprehensive adult medical eye evaluation. San Francisco, CA: American Academy of Ophthalmology; 2025.
246. Mansberger SL, Gordon MO, Jampel H, et al. Reduction in intraocular pressure after cataract extraction: The Ocular Hypertension Treatment Study. *Ophthalmology* 2012;119:1826-31.
247. Friedman DS, Jampel HD, Lubomski LH, et al. Surgical strategies for coexisting glaucoma and cataract: An evidence-based update. *Ophthalmology* 2002;109:1902-13.
248. Svedberg H, Chen E, Hamberg-Nystrom H. Changes in corneal thickness and curvature after different excimer laser photorefractive procedures and their impact on intraocular pressure measurements. *Graefes Arch Clin Exp Ophthalmol* 2005;243:1218-20.
249. Montes-Mico R, Charman WN. Intraocular pressure after excimer laser myopic refractive surgery. *Ophthalmic Physiol Opt* 2001;21:228-35.
250. Rashad KM, Bahnassy AA. Changes in intraocular pressure after laser in situ keratomileusis. *J Refract Surg* 2001;17:420-7.
251. Hosny M, Aboalazayem F, El Shiwiy H, Salem M. Comparison of different intraocular pressure measurement techniques in normal eyes and post small incision lenticule extraction. *Clin Ophthalmol* 2017;11:1309-14.
252. Gutierrez P, Wilson MR, Johnson C, et al. Influence of glaucomatous visual field loss on health-related quality of life. *Arch Ophthalmol* 1997;115:777-84.
253. Lee BL, Gutierrez P, Gordon M, et al. The glaucoma symptom scale: A brief index of glaucoma-specific symptoms. *Arch Ophthalmol* 1998;116:861-6.
254. Parrish RK, 2nd, Gedde SJ, Scott IU, et al. Visual function and quality of life among patients with glaucoma. *Arch Ophthalmol* 1997;115:1447-55.
255. Wilson MR, Coleman AL, Yu F, et al. Functional status and well-being in patients with glaucoma as measured by the medical outcomes study short form-36 questionnaire. *Ophthalmology* 1998;105:2112-6.
256. Aspinall PA, Johnson ZK, Azuara-Blanco A, et al. Evaluation of quality of life and priorities of patients with glaucoma. *Invest Ophthalmol Vis Sci* 2008;49:1907-15.
257. Goldberg I, Clement CI, Chiang TH, et al. Assessing quality of life in patients with glaucoma using the glaucoma quality of life-15 (GQL-15) questionnaire. *J Glaucoma* 2009;18:6-12.
258. Spaeth G, Walt J, Keener J. Evaluation of quality of life for patients with glaucoma. *Am J Ophthalmol* 2006;141:S3-14.
259. Bechettille A, Arnould B, Bron A, et al. Measurement of health-related quality of life with glaucoma: Validation of the Glau-QoL 36-item questionnaire. *Acta Ophthalmol* 2008;86:71-80.
260. McKean-Cowdin R, Varma R, Wu J, et al. Los Angeles Latino Eye Study Group. Severity of visual field loss and health-related quality of life. *Am J Ophthalmol* 2007;143:1013-23.
261. Ringsdorf L, McGwin G, Jr., Owsley C. Visual field defects and vision-specific health-related quality of life in African Americans and whites with glaucoma. *J Glaucoma* 2006;15:414-8.
262. Varma R, Wu J, Chong K, et al. Los Angeles Latino Eye Study Group. Impact of severity and bilaterality of visual impairment on health-related quality of life. *Ophthalmology* 2006;113:1846-53.
263. Lisboa R, Chun YS, Zangwill LM, et al. Association between rates of binocular visual field loss and vision-related quality of life in patients with glaucoma. *JAMA Ophthalmol* 2013;131:486-94.
264. Crabb DP, Smith ND, Glen FC, et al. How does glaucoma look?: Patient perception of visual field loss. *Ophthalmology* 2013;120:1120-6.
265. Ramulu PY, West SK, Munoz B, et al. Glaucoma and reading speed: The Salisbury Eye Evaluation project. *Arch Ophthalmol* 2009;127:82-7.
266. Gracitelli CP, Abe RY, Tatham AJ, et al. Association between progressive retinal nerve fiber layer loss and longitudinal change in quality of life in glaucoma. *JAMA Ophthalmol* 2015;133:384-90.
267. Kohn AN, Moss AP, Podos SM. Relative afferent pupillary defects in glaucoma without characteristic field loss. *Arch Ophthalmol* 1979;97:294-6.
268. Brown RH, Zilis JD, Lynch MG, Sanborn GE. The afferent pupillary defect in asymmetric glaucoma. *Arch Ophthalmol* 1987;105:1540-3.
269. Kerrison JB, Buchanan K, Rosenberg ML, et al. Quantification of optic nerve axon loss associated with a relative afferent pupillary defect in the monkey. *Arch Ophthalmol* 2001;119:1333-41.
270. Chang DS, Xu L, Boland MV, Friedman DS. Accuracy of pupil assessment for the detection of glaucoma: A systematic review and meta-analysis. *Ophthalmology* 2013;120:2217-25.
271. Foster PJ, Devereux JG, Alsbirk PH, et al. Detection of gonioscopically occludable angles and primary angle closure glaucoma by estimation of limbal chamber depth in Asians: Modified grading scheme. *Br J Ophthalmol* 2000;84:186-92.

272. Van Herick W, Shaffer RN, Schwartz A. Estimation of width of angle of anterior chamber. Incidence and significance of the narrow angle. *Am J Ophthalmol* 1969;68:626-9.
273. Barkana Y, Anis S, Liebmann J, et al. Clinical utility of intraocular pressure monitoring outside of normal office hours in patients with glaucoma. *Arch Ophthalmol* 2006;124:793-7.
274. Hasegawa K, Ishida K, Sawada A, et al. Diurnal variation of intraocular pressure in suspected normal-tension glaucoma. *Jpn J Ophthalmol* 2006;50:449-54.
275. Dinn RB, Zimmerman MB, Shuba LM, et al. Concordance of diurnal intraocular pressure between fellow eyes in primary open-angle glaucoma. *Ophthalmology* 2007;114:915-20.
276. Bagga H, Liu JH, Weinreb RN. Intraocular pressure measurements throughout the 24 h. *Curr Opin Ophthalmol* 2009;20:79-83.
277. Nouri-Mahdavi K, Hoffman D, Coleman AL, et al. Predictive factors for glaucomatous visual field progression in the Advanced Glaucoma Intervention Study. *Ophthalmology* 2004;111:1627-35.
278. Musch DC, Gillespie BW, Lichter PR, et al. CIGTS Study Investigators. Visual field progression in the Collaborative Initial Glaucoma Treatment Study the impact of treatment and other baseline factors. *Ophthalmology* 2009;116:200-7.
279. Nouri-Mahdavi K, Medeiros FA, Weinreb RN. Fluctuation of intraocular pressure as a predictor of visual field progression. *Arch Ophthalmol* 2008;126:1168-9; author reply 9-70.
280. Asrani S, Zeimer R, Wilensky J, et al. Large diurnal fluctuations in intraocular pressure are an independent risk factor in patients with glaucoma. *J Glaucoma* 2000;9:134-42.
281. Zhang ML, Chon BH, Wang J, et al. Single vs multiple intraocular pressure measurements in glaucoma surgical trials. *JAMA Ophthalmol* 2014;132:956-62.
282. Konstas AG, Kahook MY, Araie M, et al. Diurnal and 24-h intraocular pressures in glaucoma: Monitoring strategies and impact on prognosis and treatment. *Adv Ther* 2018;35:1775-804.
283. Tasman W, Jaeger EA, eds. Duane's ophthalmology, 15th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2009.
284. Spaeth GL, Aruajo S, Azuara A. Comparison of the configuration of the human anterior chamber angle, as determined by the Spaeth gonioscopic grading system and ultrasound biomicroscopy. *Trans Am Ophthalmol Soc* 1995;93:337-47; discussion 47-51.
285. Quigley HA, Enger C, Katz J, et al. Risk factors for the development of glaucomatous visual field loss in ocular hypertension. *Arch Ophthalmol* 1994;112:644-9.
286. Sommer A, Katz J, Quigley HA, et al. Clinically detectable nerve fiber atrophy precedes the onset of glaucomatous field loss. *Arch Ophthalmol* 1991;109:77-83.
287. Lin SC, Singh K, Jampel HD, et al. Optic nerve head and retinal nerve fiber layer analysis: A report by the American Academy of Ophthalmology. *Ophthalmology* 2007;114:1937-49.
288. Lloyd MJ, Mansberger SL, Fortune BA, et al. Features of optic disc progression in patients with ocular hypertension and early glaucoma. *J Glaucoma* 2013;22:343-8.
289. Harizman N, Oliveira C, Chiang A, et al. The ISNT rule and differentiation of normal from glaucomatous eyes. *Arch Ophthalmol* 2006;124:1579-83.
290. Hwang YH, Kim YY. Application of the ISNT rule to neuroretinal rim thickness determined using Cirrus HD optical coherence tomography. *J Glaucoma* 2015;24:503-7.
291. Poon LY, Sola-Del Valle D, Turalba AV, et al. The ISNT rule: How often does it apply to disc photographs and retinal nerve fiber layer measurements in the normal population? *Am J Ophthalmol* 2017;184:19-27.
292. Johnson CA, Cioffi GA, Liebmann JR, et al. The relationship between structural and functional alterations in glaucoma: A review. *Semin Ophthalmol* 2000;15:221-33.
293. Medeiros FA, Alencar LM, Zangwill LM, et al. Prediction of functional loss in glaucoma from progressive optic disc damage. *Arch Ophthalmol* 2009;127:1250-6.
294. Teng CC, De Moraes CG, Prata TS, et al. The region of largest beta-zone parapapillary atrophy area predicts the location of most rapid visual field progression. *Ophthalmology* 2011;118:2409-13.
295. Harwerth RS, Vilupuru AS, Rangaswamy NV, Smith EL, III. The relationship between nerve fiber layer and perimetry measurements. *Invest Ophthalmol Vis Sci* 2007;48:763-73.
296. Hood DC, Kardon RH. A framework for comparing structural and functional measures of glaucomatous damage. *Prog Retin Eye Res* 2007;26:688-710.
297. Miglior S, Torri V, Zeyen T, et al. Intercurrent factors associated with the development of open-angle glaucoma in the European Glaucoma Prevention Study. *Am J Ophthalmol* 2007;144:266-75.
298. De Moraes CG, Prata TS, Liebmann CA, et al. Spatially consistent, localized visual field loss before and after disc hemorrhage. *Invest Ophthalmol Vis Sci* 2009;50:4727-33.

299. Jeoung JW, Park KH, Kim JM, et al. Optic disc hemorrhage may be associated with retinal nerve fiber loss in otherwise normal eyes. *Ophthalmology* 2008;115:2132-40.
300. Hwang YH, Kim YY, Kim HK, Sohn YH. Changes in retinal nerve fiber layer thickness after optic disc hemorrhage in glaucomatous eyes. *J Glaucoma* In press.
301. Bengtsson B, Leske MC, Yang Z, Heijl A. Early Manifest Glaucoma Trial Group. Disc hemorrhages and treatment in the Early Manifest Glaucoma Trial. *Ophthalmology* 2008;115:2044-8.
302. de Beaufort HC, De Moraes CG, Teng CC, et al. Recurrent disc hemorrhage does not increase the rate of visual field progression. *Graefes Arch Clin Exp Ophthalmol* 2010;248:839-44.
303. Laemmer R, Nguyen TK, Horn FK, Mardin CY. Morphologic and functional glaucomatous change after occurrence of single or recurrent optic disc hemorrhages. *Graefes Arch Clin Exp Ophthalmol* 2010;248:1683-4; author reply 5.
304. Singh K, Lee BL, Wilson MR. Glaucoma Modified Rand-Like Methodology Group. A panel assessment of glaucoma management: Modification of existing rand-like methodology for consensus in ophthalmology. Part II: Results and interpretation. *Am J Ophthalmol* 2008;145:575-81.
305. Quigley HA, Sommer A. How to use nerve fiber layer examination in the management of glaucoma. *Trans Am Ophthalmol Soc* 1987;85:254-72.
306. Agudelo LM, Molina CA, Alvarez DL. Changes in intraocular pressure after laser in situ keratomileusis for myopia, hyperopia, and astigmatism. *J Refract Surg* 2002;18:472-4.
307. Miglior S, Pfeiffer N, Torri V, et al. Predictive factors for open-angle glaucoma among patients with ocular hypertension in the European Glaucoma Prevention Study. *Ophthalmology* 2007;114:3-9.
308. Weinreb RN, Brandt JD, Garway-Heath D, Medeiros FA, eds. Intraocular pressure. World Glaucoma Association consensus series - 4. The Netherlands: *Kugler Publications*, 2007.
309. Kim JW, Chen PP. Central corneal pachymetry and visual field progression in patients with open-angle glaucoma. *Ophthalmology* 2004;111:2126-32.
310. Chauhan BC, Hutchison DM, LeBlanc RP, et al. Central corneal thickness and progression of the visual field and optic disc in glaucoma. *Br J Ophthalmol* 2005;89:1008-12.
311. Jonas JB, Stroux A, Oberacher-Velten IM, et al. Central corneal thickness and development of glaucomatous optic disk hemorrhages. *Am J Ophthalmol* 2005;140:1139-41.
312. Jonas JB, Holbach L. Central corneal thickness and thickness of the lamina cribrosa in human eyes. *Invest Ophthalmol Vis Sci* 2005;46:1275-9.
313. Stewart WC, Day DG, Jenkins JN, et al. Mean intraocular pressure and progression based on corneal thickness in primary open-angle glaucoma. *J Ocul Pharmacol Ther* 2006;22:26-33.
314. Susanna BN, Ogata NG, Jammal AA, et al. Corneal biomechanics and visual field progression in eyes with seemingly well-controlled intraocular pressure. *Ophthalmology* 2019;126:1640-6.
315. Jimenez-Santos MA, Saenz-Frances F, Sanchez-Jean R, et al. Synergic effect of corneal hysteresis and central corneal thickness in the risk of early-stage primary open-angle glaucoma progression. *Graefes Arch Clin Exp Ophthalmol* 2021;259:2743-51.
316. Estrela T, Jammal AA, Mariottoni EB, et al. The relationship between asymmetries of corneal properties and rates of visual field progression in glaucoma patients. *J Glaucoma* 2020;29:872-7.
317. Pan M, Kwok S, Pan X, Liu J. Biomechanical correlations between the cornea and the optic nerve head. *Invest Ophthalmol Vis Sci* 2024;65:34.
318. Jampel HD, Singh K, Lin SC, et al. Assessment of visual function in glaucoma: A report by the American Academy of Ophthalmology. *Ophthalmology* 2011;118:986-1002.
319. De Moraes CG, Hood DC, Thenappan A, et al. 24-2 visual fields miss central defects shown on 10-2 tests in glaucoma suspects, ocular hypertensives, and early glaucoma. *Ophthalmology* 2017;124:1449-56.
320. Gordon MO, Kass MA. The Ocular Hypertension Treatment Study: Design and baseline description of the participants. *Arch Ophthalmol* 1999;117:573-83.
321. Keltner JL, Johnson CA, Quigg JM, et al. Ocular Hypertension Treatment Study Group. Confirmation of visual field abnormalities in the Ocular Hypertension Treatment Study. *Arch Ophthalmol* 2000;118:1187-94.
322. Keltner JL, Johnson CA, Levine RA, et al. Normal visual field test results following glaucomatous visual field end points in the Ocular Hypertension Treatment Study. *Arch Ophthalmol* 2005;123:1201-6.
323. Delgado MF, Nguyen NT, Cox TA, et al. Automated perimetry: A report by the American Academy of Ophthalmology. *Ophthalmology* 2002;109:2362-74.
324. Liu S, Lam S, Weinreb RN, et al. Comparison of standard automated perimetry, frequency-doubling technology perimetry, and short-wavelength automated perimetry for detection of glaucoma. *Invest Ophthalmol Vis Sci* 2011;52:7325-31.

325. Tafreshi A, Sample PA, Liebmann JM, et al. Visual function-specific perimetry to identify glaucomatous visual loss using three different definitions of visual field abnormality. *Invest Ophthalmol Vis Sci* 2009;50:1234-40.
326. van der Schoot J, Reus NJ, Colen TP, Lemij HG. The ability of short-wavelength automated perimetry to predict conversion to glaucoma. *Ophthalmology* 2010;117:30-4.
327. Johnson CA, Samuels SJ. Screening for glaucomatous visual field loss with frequency-doubling perimetry. *Invest Ophthalmol Vis Sci* 1997;38:413-25.
328. Cello KE, Nelson-Quigg JM, Johnson CA. Frequency doubling technology perimetry for detection of glaucomatous visual field loss. *Am J Ophthalmol* 2000;129:314-22.
329. Medeiros FA, Sample PA, Weinreb RN. Frequency doubling technology perimetry abnormalities as predictors of glaucomatous visual field loss. *Am J Ophthalmol* 2004;137:863-71.
330. Meira-Freitas D, Tatham AJ, Lisboa R, et al. Predicting progression of glaucoma from rates of frequency doubling technology perimetry change. *Ophthalmology* 2014;121:498-507.
331. Landers JA, Goldberg I, Graham SL. Detection of early visual field loss in glaucoma using frequency-doubling perimetry and short-wavelength automated perimetry. *Arch Ophthalmol* 2003;121:1705-10.
332. Demirel S, Johnson CA. Incidence and prevalence of short wavelength automated perimetry deficits in ocular hypertensive patients. *Am J Ophthalmol* 2001;131:709-15.
333. Babel AT, Soumakieh MM, Chen AY, et al. Virtual reality visual field testing in glaucoma: Benefits and drawbacks. *Clin Ophthalmol* 2025;19:933-7.
334. Chia ZK, Kong AW, Turner ML, et al. Assessment of remote training, at-home testing, and test-retest variability of a novel test for clustered virtual reality perimetry. *Ophthalmol Glaucoma* 2024;7:139-47.
335. Heinzman Z, Linton E, Marin-Franch I, et al. Validation of the Iowa head-mounted open-source perimeter. *Transl Vis Sci Technol* 2023;12:19.
336. McLaughlin DE, Savatovsky EJ, O'Brien RC, et al. Reliability of visual field testing in a telehealth setting using a head-mounted device: A pilot study. *J Glaucoma* 2024;33:15-23.
337. Montelongo M, Gonzalez A, Morgenstern F, et al. A virtual reality-based automated perimeter, device, and pilot study. *Transl Vis Sci Technol* 2021;10:20.
338. Narang P, Agarwal A, Srinivasan M, Agarwal A. Advanced vision analyzer-virtual reality perimeter: Device validation, functional correlation and comparison with Humphrey field analyzer. *Ophthalmol Sci* 2021;1:100035.
339. Sayed AM, Kashem R, Abdel-Mottaleb M, et al. Toward improving the mobility of patients with peripheral visual field defects with novel digital spectacles. *Am J Ophthalmol* 2020;210:136-45.
340. Stapelfeldt J, Kucur SS, Huber N, et al. Virtual reality-based and conventional visual field examination comparison in healthy and glaucoma patients. *Transl Vis Sci Technol* 2021;10:10.
341. Tsapakis S, Papaconstantinou D, Diagourtas A, et al. Visual field examination method using virtual reality glasses compared with the Humphrey perimeter. *Clin Ophthalmol* 2017;11:1431-43.
342. Spaeth GL, Lopes JF, Junk AK, et al. Systems for staging the amount of optic nerve damage in glaucoma: A critical review and new material. *Surv Ophthalmol* 2006;51:293-315.
343. Chong GT, Lee RK. Glaucoma versus red disease: Imaging and glaucoma diagnosis. *Curr Opin Ophthalmol* 2012;23:79-88.
344. Shaffer RN, Ridgway WL, Brown R, Kramer SG. The use of diagrams to record changes in glaucomatous disks. *Am J Ophthalmol* 1975;80:460-4.
345. Coleman AL, Sommer A, Enger C, et al. Interobserver and intraobserver variability in the detection of glaucomatous progression of the optic disc. *J Glaucoma* 1996;5:384-9.
346. Iester M, De Ferrari R, Zanini M. Topographic analysis to discriminate glaucomatous from normal optic nerve heads with a confocal scanning laser: New optic disk analysis without any observer input. *Surv Ophthalmol* 1999;44 Suppl 1:S33-40.
347. Watkins RJ, Broadway DC. Intraobserver and interobserver reliability indices for drawing scanning laser ophthalmoscope optic disc contour lines with and without the aid of optic disc photographs. *J Glaucoma* 2005;14:351-7.
348. Jampel HD, Friedman D, Quigley H, et al. Agreement among glaucoma specialists in assessing progressive disc changes from photographs in open-angle glaucoma patients. *Am J Ophthalmol* 2009;147:39-44.
349. Gaasterland DE, Blackwell B, Dally LG, et al. Advanced Glaucoma Intervention Study Investigators. The Advanced Glaucoma Intervention Study (AGIS): 10. Variability among academic glaucoma subspecialists in assessing optic disc notching. *Trans Am Ophthalmol Soc* 2001;99:177-84; discussion 84-5.
350. Alencar LM, Bowd C, Weinreb RN, et al. Comparison of HRT-3 glaucoma probability score and subjective stereophotograph assessment for prediction of progression in glaucoma. *Invest Ophthalmol Vis Sci* 2008;49:1898-906.

351. Baraibar B, Sanchez-Cano A, Pablo LE, Honrubia FM. Preperimetric glaucoma assessment with scanning laser polarimetry (GDx VCC): Analysis of retinal nerve fiber layer by sectors. *J Glaucoma* 2007;16:659-64.
352. Lalezary M, Medeiros FA, Weinreb RN, et al. Baseline optical coherence tomography predicts the development of glaucomatous change in glaucoma suspects. *Am J Ophthalmol* 2006;142:576-82.
353. Medeiros FA, Zangwill LM, Bowd C, Weinreb RN. Comparison of the GDx VCC scanning laser polarimeter, HRT II confocal scanning laser ophthalmoscope, and Stratus OCT optical coherence tomograph for the detection of glaucoma. *Arch Ophthalmol* 2004;122:827-37.
354. Weinreb RN, Zangwill LM, Jain S, et al. OHTS CSLO Ancillary Study Group. Predicting the onset of glaucoma: The confocal scanning laser ophthalmoscopy ancillary study to the Ocular Hypertension Treatment Study. *Ophthalmology* 2010;117:1674-83.
355. Chen TC, Hogue A, Junk AK, et al. Spectral-domain OCT: Helping the clinician diagnose glaucoma: A report by the American Academy of Ophthalmology. *Ophthalmology* 2018;125:1817-27.
356. Mansberger SL, Menda SA, Fortune BA, et al. Automated segmentation errors when using optical coherence tomography to measure retinal nerve fiber layer thickness in glaucoma. *Am J Ophthalmol* 2017;174:1-8.
357. Meier KL, Greenfield DS, Hilmantel G, et al. Special commentary: Food and Drug Administration and American Glaucoma Society co-sponsored workshop: The validity, reliability, and usability of glaucoma imaging devices. *Ophthalmology* 2014;121:2116-23.
358. Leung CK. Diagnosing glaucoma progression with optical coherence tomography. *Curr Opin Ophthalmol* 2014;25:104-11.
359. Kotowski J, Wollstein G, Ishikawa H, Schuman JS. Imaging of the optic nerve and retinal nerve fiber layer: An essential part of glaucoma diagnosis and monitoring. *Surv Ophthalmol* 2014;59:458-67.
360. Miglior S, Zeyen T, Pfeiffer N, et al. European Glaucoma Prevention Study (EGPS) Group. Results of the European Glaucoma Prevention Study. *Ophthalmology* 2005;112:366-75.
361. Chauhan BC, McCormick TA, Nicoletta MT, LeBlanc RP. Optic disc and visual field changes in a prospective longitudinal study of patients with glaucoma: Comparison of scanning laser tomography with conventional perimetry and optic disc photography. *Arch Ophthalmol* 2001;119:1492-9.
362. Wollstein G, Schuman JS, Price LL, et al. Optical coherence tomography longitudinal evaluation of retinal nerve fiber layer thickness in glaucoma. *Arch Ophthalmol* 2005;123:464-70.
363. Greenfield DS, Siatkowski RM, Glaser JS, et al. The cupped disc. Who needs neuroimaging? *Ophthalmology* 1998;105:1866-74.
364. Higginbotham EJ, Gordon MO, Beiser JA, et al. Ocular Hypertension Treatment Study Group. The Ocular Hypertension Treatment Study: Topical medication delays or prevents primary open-angle glaucoma in African American individuals. *Arch Ophthalmol* 2004;122:813-20.
365. Jay JL, Allan D. The benefit of early trabeculectomy versus conventional management in primary open angle glaucoma relative to severity of disease. *Eye (Lond)* 1989;3 (Pt 5):528-35.
366. Glaucoma laser trial research group. The Glaucoma Laser Trial (GLT) and Glaucoma Laser Trial follow-up study: 7. Results. *Am J Ophthalmol* 1995;120:718-31.
367. Fluorouracil Filtering Surgery Study Group. Five-year follow-up of the Fluorouracil Filtering Surgery Study. *Am J Ophthalmol* 1996;121:349-66.
368. Odberg T. Visual field prognosis in advanced glaucoma. *Acta Ophthalmol* 1987;65 (suppl):27-9.
369. Mao LK, Stewart WC, Shields MB. Correlation between intraocular pressure control and progressive glaucomatous damage in primary open-angle glaucoma. *Am J Ophthalmol* 1991;111:51-5.
370. Kolker AE. Visual prognosis in advanced glaucoma: A comparison of medical and surgical therapy for retention of vision in 101 eyes with advanced glaucoma. *Trans Am Ophthalmol Soc* 1977;75:539-55.
371. Quigley HA, Maumenee AE. Long-term follow-up of treated open-angle glaucoma. *Am J Ophthalmol* 1979;87:519-25.
372. Greve EL, Dake CL, Klaver J, Mutsaerts E. Ten year prospective follow-up of a glaucoma operation. The double flap Scheie in primary open angle glaucoma. In: Greve EL, Leydhecker W, Raitta C, eds. Second European Glaucoma Symposium, Helsinki 1984. Dordrecht, Netherlands: *Dr. W Junk*, 1985.
373. Werner EB, Drance SM, Schulzer M. Trabeculectomy and the progression of glaucomatous visual field loss. *Arch Ophthalmol* 1977;95:1374-7.
374. Kidd MN, O'Connor M. Progression of field loss after trabeculectomy: A five-year follow-up. *Br J Ophthalmol* 1985;69:827-31.
375. Rollins D, Drance S. Five-year follow-up of trabeculectomy in the management of chronic open-angle glaucoma. New Orleans Acad Ophthalmol, Symposium on Glaucoma 1981.
376. Chandler PA. Long-term results in glaucoma therapy. *Am J Ophthalmol* 1960;49:221-46.

377. Abedin S, Simmons RJ, Grant WM. Progressive low-tension glaucoma: Treatment to stop glaucomatous cupping and field loss when these progress despite normal intraocular pressure. *Ophthalmology* 1982;89:1-6.
378. Glaucoma Laser Trial Research Group. The Glaucoma Laser Trial (GLT): 3. Design and methods. *Control Clin Trials* 1991;12:504-24.
379. Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. Laser in Glaucoma and ocular Hypertension (LiGHT) Trial. A multicentre, randomised controlled trial: Design and methodology. *Br J Ophthalmol* 2018;102:593-8.
380. Musch DC, Lichter PR, Guire KE, Standardi CL. The Collaborative Initial Glaucoma Treatment Study: Study design, methods, and baseline characteristics of enrolled patients. *Ophthalmology* 1999;106:653-62.
381. King AJ, Fernie G, Azuara-Blanco A, et al. Treatment of Advanced Glaucoma Study: A multicentre randomised controlled trial comparing primary medical treatment with primary trabeculectomy for people with newly diagnosed advanced glaucoma-study protocol. *Br J Ophthalmol* 2018;102:922-8.
382. Chauhan BC, Garway-Heath DF, Goni FJ, et al. Practical recommendations for measuring rates of visual field change in glaucoma. *Br J Ophthalmol* 2008;92:569-73.
383. Jampel HD. Target pressure in glaucoma therapy. *J Glaucoma* 1997;6:133-8.
384. Clement CI, Bhartiya S, Shaarawy T. New perspectives on target intraocular pressure. *Surv Ophthalmol* 2014;59:615-26.
385. McIlraith I, Strasfeld M, Colev G, Hutnik CM. Selective laser trabeculoplasty as initial and adjunctive treatment for open-angle glaucoma. *J Glaucoma* 2006;15:124-30.
386. Katz LJ, Steinmann WC, Kabir A, et al. Selective laser trabeculoplasty versus medical therapy as initial treatment of glaucoma: A prospective, randomized trial. *J Glaucoma* 2012;21:460-8.
387. Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): A multicentre randomised controlled trial. *Lancet* 2019;393:1505-16.
388. Wong MO, Lee JW, Choy BN, et al. Systematic review and meta-analysis on the efficacy of selective laser trabeculoplasty in open-angle glaucoma. *Surv Ophthalmol* 2015;60:36-50.
389. American Academy of Ophthalmology Basic and Clinical Science Course Subcommittee. Basic and clinical science course. Section 10: Glaucoma, 2025-2026. San Francisco, CA: American Academy of Ophthalmology; 2025.
390. Takusagawa HL, Hoguet A, Sit AJ, et al. Selective laser trabeculoplasty for the treatment of glaucoma: A report by the American Academy of Ophthalmology. *Ophthalmology* 2024;131:37-47.
391. Glaucoma laser trial research group. The Glaucoma Laser Trial (GLT) and glaucoma laser trial follow-up study: 7. Results. *Am J Ophthalmol* 1995;120:718-31.
392. Brancato R, Carassa R, Trabucchi G. Diode laser compared with argon laser for trabeculoplasty. *Am J Ophthalmol* 1991;112:50-5.
393. Chung PY, Schuman JS, Netland PA, et al. Five-year results of a randomized, prospective, clinical trial of diode vs argon laser trabeculoplasty for open-angle glaucoma. *Am J Ophthalmol* 1998;126:185-90.
394. Glaucoma laser trial research group. The Glaucoma Laser Trial (GLT). 2. Results of argon laser trabeculoplasty versus topical medicines. *Ophthalmology* 1990;97:1403-13.
395. Spaeth GL, Baez KA. Argon laser trabeculoplasty controls one third of cases of progressive, uncontrolled, open angle glaucoma for 5 years. *Arch Ophthalmol* 1992;110:491-4.
396. Schwartz AL, Love DC, Schwartz MA. Long-term follow-up of argon laser trabeculoplasty for uncontrolled open-angle glaucoma. *Arch Ophthalmol* 1985;103:1482-4.
397. Krupin T, Patkin R, Kurata FK, et al. Argon laser trabeculoplasty in Black and White patients with primary open-angle glaucoma. *Ophthalmology* 1986;93:811-6.
398. Shingleton BJ, Richter CU, Dharma SK, et al. Long-term efficacy of argon laser trabeculoplasty. A 10-year follow-up study. *Ophthalmology* 1993;100:1324-9.
399. Starita RJ, Fellman RL, Spaeth GL, Poryzees E. The effect of repeating full-circumference argon laser trabeculoplasty. *Ophthalmic Surg* 1984;15:41-3.
400. Brown SV, Thomas JV, Simmons RJ. Laser trabeculoplasty re-treatment. *Am J Ophthalmol* 1985;99:8-10.
401. Richter CU, Shingleton BJ, Bellows AR, et al. Retreatment with argon laser trabeculoplasty. *Ophthalmology* 1987;94:1085-9.
402. Weber PA, Burton GD, Epitropoulos AT. Laser trabeculoplasty retreatment. *Ophthalmic Surg* 1989;20:702-6.
403. Feldman RM, Katz LJ, Spaeth GL, et al. Long-term efficacy of repeat argon laser trabeculoplasty. *Ophthalmology* 1991;98:1061-5.
404. Jorizzo PA, Samples JR, Van Buskirk EM. The effect of repeat argon laser trabeculoplasty. *Am J Ophthalmol* 1988;106:682-5.

405. Reynolds AC, Skuta GL. Current trends and challenges in glaucoma care. Focal points: Clinical modules for ophthalmologists. Module 6. San Francisco, CA: American Academy of Ophthalmology; 2008:2.
406. Ramulu PY, Corcoran KJ, Corcoran SL, Robin AL. Utilization of various glaucoma surgeries and procedures in medicare beneficiaries from 1995 to 2004. *Ophthalmology* 2007;114:2265-70.
407. Rachmiel R, Trope GE, Chipman ML, et al. Laser trabeculoplasty trends with the introduction of new medical treatments and selective laser trabeculoplasty. *J Glaucoma* 2006;15:306-9.
408. Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. Laser in Glaucoma and ocular Hypertension (LiGHT) Trial: Six-year results of primary selective laser trabeculoplasty versus eye drops for the treatment of glaucoma and ocular hypertension. *Ophthalmology* 2023;130:139-51.
409. Latina MA, Park C. Selective targeting of trabecular meshwork cells: In vitro studies of pulsed and CW laser interactions. *Exp Eye Res* 1995;60:359-71.
410. Kramer TR, Noecker RJ. Comparison of the morphologic changes after selective laser trabeculoplasty and argon laser trabeculoplasty in human eye bank eyes. *Ophthalmology* 2001;108:773-9.
411. McAlinden C. Selective laser trabeculoplasty (SLT) vs other treatment modalities for glaucoma: Systematic review. *Eye (Lond)* 2014;28:249-58.
412. Russo V, Barone A, Cosma A, et al. Selective laser trabeculoplasty versus argon laser trabeculoplasty in patients with uncontrolled open-angle glaucoma. *Eur J Ophthalmol* 2009;19:429-34.
413. Damji KF, Shah KC, Rock WJ, et al. Selective laser trabeculoplasty v argon laser trabeculoplasty: A prospective randomised clinical trial. *Br J Ophthalmol* 1999;83:718-22.
414. Popiela G, Muzyka M, Szelepin L, et al. Use of YAG-selecta laser and argon laser in the treatment of open angle glaucoma [in Polish]. *Klin Oczna* 2000;102:129-33.
415. Martinez-de-la-Casa JM, Garcia-Feijoo J, Castillo A, et al. Selective vs argon laser trabeculoplasty: Hypotensive efficacy, anterior chamber inflammation, and postoperative pain. *Eye (Lond)* 2004;18:498-502.
416. Damji KF, Bovell AM, Hodge WG, et al. Selective laser trabeculoplasty versus argon laser trabeculoplasty: Results from a 1-year randomised clinical trial. *Br J Ophthalmol* 2006;90:1490-4.
417. Best UP, Domack H, Schmidt V. Pressure reduction after selective laser trabeculoplasty with two different laser systems and after argon laser trabeculoplasty--a controlled prospective clinical trial on 284 eyes [in German]. *Klin Monatsbl Augenheilkd* 2007;224:173-9.
418. Juzych MS, Chopra V, Banitt MR, et al. Comparison of long-term outcomes of selective laser trabeculoplasty versus argon laser trabeculoplasty in open-angle glaucoma. *Ophthalmology* 2004;111:1853-9.
419. Van de Veire S, Zeyen T, Stalmans I. Argon versus selective laser trabeculoplasty. *Bull Soc Belge Ophthalmol* 2006;299:5-10.
420. Nagar M, Ogunyomade A, O'Brart DP, et al. A randomised, prospective study comparing selective laser trabeculoplasty with latanoprost for the control of intraocular pressure in ocular hypertension and open angle glaucoma. *Br J Ophthalmol* 2005;89:1413-7.
421. Li X, Wang W, Zhang X. Meta-analysis of selective laser trabeculoplasty versus topical medication in the treatment of open-angle glaucoma. *BMC Ophthalmol* 2015;15:107.
422. Wright DM, Konstantakopoulou E, Montesano G, et al. Visual field outcomes from the multicenter, randomized controlled Laser in Glaucoma and ocular Hypertension Trial. *Ophthalmology* 2020.
423. Realini T, Shillingford-Ricketts H, Burt D, Balasubramani GK. West Indies glaucoma laser study (WIGLS): 1. 12-month efficacy of selective laser trabeculoplasty in Afro-Caribbeans with glaucoma. *Am J Ophthalmol* 2017;184:28-33.
424. Polat J, Grantham L, Mitchell K, Realini T. Repeatability of selective laser trabeculoplasty. *Br J Ophthalmol* 2016;100:1437-41.
425. Hong BK, Winer JC, Martone JF, et al. Repeat selective laser trabeculoplasty. *J Glaucoma* 2009;18:180-3.
426. Francis BA, Loewen N, Hong B, et al. Repeatability of selective laser trabeculoplasty for open-angle glaucoma. *BMC Ophthalmol* 2016;16:128.
427. Copparam S, Kuley B, Zheng CX, et al. Outcomes of repeat selective laser trabeculoplasty for open-angle glaucoma. *Investigative Ophthalmology & Visual Science* 2019;60:689-.
428. Avery N, Ang GS, Nicholas S, Wells A. Repeatability of primary selective laser trabeculoplasty in patients with primary open-angle glaucoma. *Int Ophthalmol* 2013;33:501-6.
429. Jang HJ, Yu B, Hodge W, Malvankar-Mehta MS. Repeat selective laser trabeculoplasty for glaucoma patients: A systematic review and meta-analysis. *J Curr Glaucoma Pract* 2021;15:117-24.
430. Garg A, Vickerstaff V, Nathwani N, et al. Efficacy of repeat selective laser trabeculoplasty in medication-naive open-angle glaucoma and ocular hypertension during the LiGHT trial. *Ophthalmology* 2020;127:467-76.
431. Durr GM, Harasymowycz P. The effect of repeat 360-degree selective laser trabeculoplasty on intraocular pressure control in open-angle glaucoma. *J Fr Ophthalmol* 2016;39:261-4.

432. Khouri AS, Lari HB, Berezina TL, et al. Long term efficacy of repeat selective laser trabeculoplasty. *J Ophthalmic Vis Res* 2014;9:444-8.
433. Latina MA, Sibayan SA, Shin DH, et al. Q-switched 532-nm nd:YAG laser trabeculoplasty (selective laser trabeculoplasty): A multicenter, pilot, clinical study. *Ophthalmology* 1998;105:2082-8; discussion 9-90.
434. Birt CM. Selective laser trabeculoplasty retreatment after prior argon laser trabeculoplasty: 1-year results. *Can J Ophthalmol* 2007;42:715-9.
435. Messner D, Siegel LI, Kass MA, et al. Repeat argon laser trabeculoplasty. *Am J Ophthalmol* 1987;103:113-5.
436. Hutnik C, Crichton A, Ford B, et al. Selective laser trabeculoplasty versus argon laser trabeculoplasty in glaucoma patients treated previously with 360 degrees selective laser trabeculoplasty: A randomized, single-blind, equivalence clinical trial. *Ophthalmology* 2019;126:223-32.
437. Harasymowycz PJ, Papamatheakis DG, Latina M, et al. Selective laser trabeculoplasty (SLT) complicated by intraocular pressure elevation in eyes with heavily pigmented trabecular meshworks. *Am J Ophthalmol* 2005;139:1110-3.
438. Rolim-de-Moura CR, Paranhos A, Jr., Loutfi M, et al. Laser trabeculoplasty for open-angle glaucoma and ocular hypertension. *Cochrane Database Syst Rev* 2022;8:CD003919.
439. Goldenfeld M, Belkin M, Dobkin-Bekman M, et al. Automated direct selective laser trabeculoplasty: First prospective clinical trial. *Transl Vis Sci Technol* 2021;10:5.
440. Congdon N, Azuara-Blanco A, Solberg Y, et al. Direct selective laser trabeculoplasty in open angle glaucoma study design: A multicentre, randomised, controlled, investigator-masked trial (glaurious). *Br J Ophthalmol* 2023;107:62-5.
441. Gazzard G, Congdon N, Azuara-Blanco A, et al. Randomized noninferiority trial of direct selective laser trabeculoplasty in open-angle glaucoma and ocular hypertension: GLAUrious study. *Ophthalmology* 2025.
442. Glaucoma Laser Trial Research Group. The Glaucoma Laser Trial (GLT): 2. Results of argon laser trabeculoplasty versus topical medicines. *Ophthalmology* 1990;97:1403-13.
443. American Academy of Ophthalmology. Policy statement. An ophthalmologist's duties concerning postoperative care. San Francisco, CA: American Academy of Ophthalmology; 2012. .
444. American Academy of Ophthalmology. Policy statement. Preoperative assessment: Responsibilities of the ophthalmologist. San Francisco, CA: American Academy of Ophthalmology; 2012. .
445. Robin AL. Argon laser trabeculoplasty medical therapy to prevent the intraocular pressure rise associated with argon laser trabeculoplasty. *Ophthalmic Surg* 1991;22:31-7.
446. Wickham MG, Worthen DM. Argon laser trabeculotomy: Long-term follow-up. *Ophthalmology* 1979;86:495-503.
447. Wise JB, Witter SL. Argon laser therapy for open-angle glaucoma. A pilot study. *Arch Ophthalmol* 1979;97:319-22.
448. Schwartz AL, Whitten ME, Bleiman B, Martin D. Argon laser trabecular surgery in uncontrolled phakic open angle glaucoma. *Ophthalmology* 1981;88:203-12.
449. Realini T, Charlton J, Hettlinger M. The impact of anti-inflammatory therapy on intraocular pressure reduction following selective laser trabeculoplasty. *Ophthalmic Surg Lasers Imaging* 2010;41:100-3.
450. Champagne S, Anctil JL, Goyette A, et al. Influence on intraocular pressure of anti-inflammatory treatments after selective laser trabeculoplasty. *J Fr Ophthalmol* 2015;38:588-94.
451. De Keyser M, De Belder M, De Groot V. Randomized prospective study of the use of anti-inflammatory drops after selective laser trabeculoplasty. *J Glaucoma* 2017;26:e22-e9.
452. Groth SL, Albeiruti E, Nunez M, et al. SALT Trial: Steroids after laser trabeculoplasty: Impact of short-term anti-inflammatory treatment on selective laser trabeculoplasty efficacy. *Ophthalmology* 2019;126:1511-6.
453. Miranda JF, Maestrini HA, Barbosa CCP, et al. Effect of anti-inflammatory regimen on selective laser trabeculoplasty outcomes: A randomized controlled trial. *J Glaucoma* 2025;34:421-7.
454. Holmwood PC, Chase RD, Krupin T, et al. Apraclonidine and argon laser trabeculoplasty. *Am J Ophthalmol* 1992;114:19-22.
455. Robin A, Pollack I, House B, Enger C. Effects of ALO 2145 on intraocular pressure following argon laser trabeculotomy. *Arch Ophthalmol* 1987;105:646-50.
456. Zhang L, Weizer JS, Musch DC. Perioperative medications for preventing temporarily increased intraocular pressure after laser trabeculoplasty. *Cochrane Database Syst Rev* 2017;2:CD010746.
457. Barnes SD, Campagna JA, Dirks MS, Doe EA. Control of intraocular pressure elevations after argon laser trabeculoplasty: Comparison of brimonidine 0.2% to apraclonidine 1.0%. *Ophthalmology* 1999;106:2033-7.
458. Chen TC. Brimonidine 0.15% versus apraclonidine 0.5% for prevention of intraocular pressure elevation after anterior segment laser surgery. *J Cataract Refract Surg* 2005;31:1707-12.

459. Weinreb RN, Ruderman J, Juster R, Zweig K. Immediate intraocular pressure response to argon laser trabeculoplasty. *Am J Ophthalmol* 1983;95:279-86.
460. Hoskins HD, Jr., Hetherington J, Jr., Minckler DS, et al. Complications of laser trabeculoplasty. *Ophthalmology* 1983;90:796-9.
461. Alif BE, Shields MB. Early intraocular pressure response to laser trabeculoplasty 180 degrees without apraclonidine versus 360 degrees with apraclonidine. *Ophthalmic Surg* 1991;22:539-42.
462. Whitson JT. Glaucoma: A review of adjunctive therapy and new management strategies. *Expert Opin Pharmacother* 2007;8:3237-49.
463. McKinnon SJ, Goldberg LD, Peeples P, et al. Current management of glaucoma and the need for complete therapy. *Am J Manag Care* 2008;14:S20-7.
464. Li T, Lindsley K, Rouse B, et al. Comparative effectiveness of first-line medications for primary open-angle glaucoma: A systematic review and network meta-analysis. *Ophthalmology* 2016;123:129-40.
465. Stewart WC, Konstas AG, Nelson LA, Krufft B. Meta-analysis of 24-hour intraocular pressure studies evaluating the efficacy of glaucoma medicines. *Ophthalmology* 2008;115:1117-22.
466. Bhosle MJ, Reardon G, Camacho FT, et al. Medication adherence and health care costs with the introduction of latanoprost therapy for glaucoma in a medicare managed care population. *Am J Geriatr Pharmacother* 2007;5:100-11.
467. Boland MV, Ervin AM, Friedman DS, et al. Comparative effectiveness of treatments for open-angle glaucoma: A systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2013;158:271-9.
468. Weinreb RN, van Buskirk EM, Cherniack R, Drake MM. Long-term betaxolol therapy in glaucoma patients with pulmonary disease. *Am J Ophthalmol* 1988;106:162-7.
469. Gulati V, Fan S, Zhao M, et al. Diurnal and nocturnal variations in aqueous humor dynamics of patients with ocular hypertension undergoing medical therapy. *Arch Ophthalmol* 2012;130:677-84.
470. Hayreh SS, Podhajsky P, Zimmerman MB. Beta-blocker eyedrops and nocturnal arterial hypotension. *Am J Ophthalmol* 1999;128:301-9.
471. van der Valk R, Webers CA, Schouten JS, et al. Intraocular pressure-lowering effects of all commonly used glaucoma drugs: A meta-analysis of randomized clinical trials. *Ophthalmology* 2005;112:1177-85.
472. Cheng JW, Cai JP, Wei RL. Meta-analysis of medical intervention for normal tension glaucoma. *Ophthalmology* 2009;116:1243-9.
473. Serle JB, Katz LJ, McLaurin E, et al. Two phase 3 clinical trials comparing the safety and efficacy of Netarsudil to timolol in patients with elevated intraocular pressure: Rho kinase elevated IOP treatment trial 1 and 2 (ROCKET-1 and ROCKET-2). *Am J Ophthalmol* 2018;186:116-27.
474. Weinreb RN, Ong T, Scassellati Sforzolini B, et al. A randomised, controlled comparison of latanoprostene bunod and latanoprost 0.005% in the treatment of ocular hypertension and open angle glaucoma: The VOYAGER study. *Br J Ophthalmol* 2015;99:738-45.
475. Weinreb RN, Scassellati Sforzolini B, Vittitow J, Liebmann J. Latanoprostene bunod 0.024% versus timolol maleate 0.5% in subjects with open-angle glaucoma or ocular hypertension: The APOLLO study. *Ophthalmology* 2016;123:965-73.
476. Medeiros FA, Martin KR, Peace J, et al. Comparison of latanoprostene bunod 0.024% and timolol maleate 0.5% in open-angle glaucoma or ocular hypertension: The LUNAR study. *Am J Ophthalmol* 2016;168:250-9.
477. Liu JHK, Slight JR, Vittitow JL, et al. Efficacy of latanoprostene bunod 0.024% compared with timolol 0.5% in lowering intraocular pressure over 24 hours. *Am J Ophthalmol* 2016;169:249-57.
478. Bhorade AM, Wilson BS, Gordon MO, et al. The utility of the monocular trial: Data from the Ocular Hypertension Treatment Study. *Ophthalmology* 2010;117:2047-54.
479. Realini TD. A prospective, randomized, investigator-masked evaluation of the monocular trial in ocular hypertension or open-angle glaucoma. *Ophthalmology* 2009;116:1237-42.
480. Piltz J, Gross R, Shin DH, et al. Contralateral effect of topical beta-adrenergic antagonists in initial one-eyed trials in the Ocular Hypertension Treatment Study. *Am J Ophthalmol* 2000;130:441-53.
481. Realini T, Fechtner RD, Atreides SP, Gollance S. The unocular drug trial and second-eye response to glaucoma medications. *Ophthalmology* 2004;111:421-6.
482. Robin AL, Covert D. Does adjunctive glaucoma therapy affect adherence to the initial primary therapy? *Ophthalmology* 2005;112:863-8.
483. Robin AL, Novack GD, Covert DW, et al. Adherence in glaucoma: Objective measurements of once-daily and adjunctive medication use. *Am J Ophthalmol* 2007;144:533-40.
484. Johnson TV, Jampel HD. Intraocular pressure following prandomization glaucoma medication washout in the HORIZON and COMPASS trials. *Am J Ophthalmol* 2020;216:110-20.

485. Jampel HD, Chon BH, Stamper R, et al. Effectiveness of intraocular pressure-lowering medication determined by washout. *JAMA Ophthalmol* 2014;132:390-5.
486. Bro T, Linden C. The more, the better? The usefulness of brimonidine as the fourth antiglaucoma eye drop. *J Glaucoma* 2018;27:643-6.
487. Lee DA, Gornbein JA. Effectiveness and safety of brimonidine as adjunctive therapy for patients with elevated intraocular pressure in a large, open-label community trial. *J Glaucoma* 2001;10:220-6.
488. Neelakantan A, Vaishnav HD, Iyer SA, Sherwood MB. Is addition of a third or fourth antiglaucoma medication effective? *J Glaucoma* 2004;13:130-6.
489. thoe Schwartzenberg GW, Buys YM. Efficacy of brimonidine 0.2% as adjunctive therapy for patients with glaucoma inadequately controlled with otherwise maximal medical therapy. *Ophthalmology* 1999;106:1616-20.
490. Zimmerman TJ, Kooner KS, Kandarakis AS, Ziegler LP. Improving the therapeutic index of topically applied ocular drugs. *Arch Ophthalmol* 1984;102:551-3.
491. Nordstrom BL, Friedman DS, Mozaffari E, et al. Persistence and adherence with topical glaucoma therapy. *Am J Ophthalmol* 2005;140:598-606.
492. Friedman DS, Quigley HA, Gelb L, et al. Using pharmacy claims data to study adherence to glaucoma medications: Methodology and findings of the Glaucoma Adherence and Persistency Study (GAPS). *Invest Ophthalmol Vis Sci* 2007;48:5052-7.
493. Schwartz GF, Reardon G, Mozaffari E. Persistency with latanoprost or timolol in primary open-angle glaucoma suspects. *Am J Ophthalmol* 2004;137:S13-6.
494. Okeke CO, Quigley HA, Jampel HD, et al. Adherence with topical glaucoma medication monitored electronically the travatan dosing aid study. *Ophthalmology* 2009;116:191-9.
495. Tsai JC. A comprehensive perspective on patient adherence to topical glaucoma therapy. *Ophthalmology* 2009;116:S30-6.
496. Stone JL, Robin AL, Novack GD, et al. An objective evaluation of eyedrop instillation in patients with glaucoma. *Arch Ophthalmol* 2009;127:732-6.
497. Aptel F, Masset H, Burillon C, et al. The influence of disease severity on quality of eye-drop administration in patients with glaucoma or ocular hypertension [letter]. *Br J Ophthalmol* 2009;93:700-1.
498. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med* 2005;353:487-97.
499. Waterman H, Evans JR, Gray TA, et al. Interventions for improving adherence to ocular hypotensive therapy. *Cochrane Database Syst Rev* 2013:CD006132.
500. Muir KW, Rosdahl JA, Hein AM, et al. Improved glaucoma medication adherence in a randomized controlled trial. *Ophthalmol Glaucoma* 2022;5:40-6.
501. Ha A. JM, Shim R. S., Kim C. Y., Chang I. B., Kim Y. K. Interventions for glaucoma medication adherence improvement: A network meta-analysis of randomized controlled trials. *Ophthalmology* 2022;129:1294-304.
502. Moore DB, Walton C, Moeller KL, et al. Prevalence of self-reported early glaucoma eye drop bottle exhaustion and associated risk factors: A patient survey. *BMC Ophthalmol* 2014;14:79.
503. Department of Health & Human Services Centers for Medicare & Medicaid Services. Early refill edits on topical ophthalmic products [memorandum]. June 2, 2010. .
504. Perera SA, Ting DS, Nongpiur ME, et al. Feasibility study of sustained-release travoprost punctum plug for intraocular pressure reduction in an Asian population. *Clin Ophthalmol* 2016;10:757-64.
505. Brandt JD, DuBiner HB, Benza R, et al. Long-term safety and efficacy of a sustained-release Bimatoprost ocular ring. *Ophthalmology* 2017;124:1565-6.
506. Gote V, Sikder S, Sicotte J, Pal D. Ocular drug delivery: Present innovations and future challenges. *J Pharmacol Exp Ther* 2019;370:602-24.
507. Wong TT, Novack GD, Natarajan JV, et al. Nanomedicine for glaucoma: Sustained release latanoprost offers a new therapeutic option with substantial benefits over eyedrops. *Drug Deliv Transl Res* 2014;4:303-9.
508. Gutierrez-Hernandez JC, Caffey S, Abdallah W, et al. One-year feasibility study of replenish micropump for intravitreal drug delivery: A pilot study. *Transl Vis Sci Technol* 2014;3:8.
509. Craven ER, Walters T, Christie WC, et al. 24-month phase I/II clinical trial of Bimatoprost sustained-release implant (Bimatoprost SR) in glaucoma patients. *Drugs* 2020;80:167-79.
510. Dick HB, Schultz T, Gerste RD. Miniaturization in glaucoma monitoring and treatment: A review of new technologies that require a minimal surgical approach. *Ophthalmol Ther* 2019;8:19-30.
511. Allergan, inc. Durysta (bimatoprost implant) [drug approval] U.S. Food and Drug Administration website. Revised March 2020.
512. Belkin A, Chen T, DeOliveria AR, et al. A practical guide to the pregnant and breastfeeding patient with glaucoma. *Ophthalmol Glaucoma* 2020;3:79-89.

513. Brauner SC, Chen TC, Hutchinson BT, et al. The course of glaucoma during pregnancy: A retrospective case series. *Arch Ophthalmol* 2006;124:1089-94.
514. Johnson SM, Martinez M, Freedman S. Management of glaucoma in pregnancy and lactation. *Surv Ophthalmol* 2001;45:449-54.
515. Razeghinejad MR, Tania Tai TY, Fudenberg SJ, Katz LJ. Pregnancy and glaucoma. *Surv Ophthalmol* 2011;56:324-35.
516. Salim S. Glaucoma in pregnancy. *Curr Opin Ophthalmol* 2014;25:93-7.
517. U.S. Food and Drug Administration Center for Drug Evaluation and Research. FDA background package for meeting of drug safety and risk management advisory committee (DSARM): Management of drug related teratogenic risk - day one. December 12, 2012:11-13. Available at: <https://web.archive.org/web/20150926060200/http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm307385.htm>. Accessed September 6, 2025.
518. De Santis M, Lucchese A, Carducci B, et al. Latanoprost exposure in pregnancy. *Am J Ophthalmol* 2004;138:305-6.
519. Holmes LB, Kawanishi H, Munoz A. Acetazolamide: Maternal toxicity, pattern of malformations, and litter effect. *Teratology* 1988;37:335-42.
520. Aerie Pharmaceuticals Inc. Rhopressa (netarsudil ophthalmic solution) [package insert]. U.S. Food and Drug Administration website. Revised December 2017.
521. Sachs HC. The transfer of drugs and therapeutics into human breast milk: An update on selected topics. *Pediatrics* 2013;132:e796-809.
522. Rathi S, Andrews CA, Greenfield DS, Stein JD. Trends in glaucoma surgeries performed by glaucoma subspecialists versus nonspecialists on medicare beneficiaries from 2008 through 2016. *Ophthalmology* 2021;128:30-8.
523. Gedde SJ, Vinod K, Bowden EC, et al. Special commentary: Reporting clinical endpoints in studies of minimally invasive glaucoma surgery. *Ophthalmology* 2025;132:141-53.
524. Saheb H, Ahmed II. Micro-invasive glaucoma surgery: Current perspectives and future directions. *Curr Opin Ophthalmol* 2012;23:96-104.
525. Richter GM, Takusagawa HL, Sit AJ, et al. Trabecular procedures combined with cataract surgery for open-angle glaucoma: A report by the American Academy of Ophthalmology. *Ophthalmology* 2024;131:370-82.
526. Fellman RL, Mattox C, Singh K, et al. American Glaucoma Society position paper: Microinvasive glaucoma surgery. *Ophthalmology Glaucoma* 2020;3:1-6.
527. Chow JTY, Hutnik CML, Solo K, Malvankar-Mehta MS. When is evidence enough evidence? A systematic review and meta-analysis of the trabectome as a solo procedure in patients with primary open-angle glaucoma. *J Ophthalmol* 2017;2017:2965725.
528. Kaplowitz K, Bussell II, Honkanen R, et al. Review and meta-analysis of ab-interno trabeculectomy outcomes. *Br J Ophthalmol* 2016;100:594-600.
529. Minckler D, Baerveldt G, Ramirez MA, et al. Clinical results with the trabectome, a novel surgical device for treatment of open-angle glaucoma. *Trans Am Ophthalmol Soc* 2006;104:40-50.
530. Mosaed S, Rhee DJ, Filippopoulos T, et al. Trabectome outcomes in adult open-angle glaucoma patients: One-year follow-up. *Clin Surg Ophthalmol* 2010;28:182-6.
531. Maeda M, Watanabe M, Ichikawa K. Evaluation of trabectome in open-angle glaucoma. *J Glaucoma* 2013;22:205-8.
532. Jordan JF, Wecker T, van Oterendorp C, et al. Trabectome surgery for primary and secondary open angle glaucomas. *Graefes Arch Clin Exp Ophthalmol* 2013;251:2753-60.
533. Ahuja Y, Ma Khin Pyi S, Malihi M, et al. Clinical results of ab interno trabeculectomy using the trabectome for open-angle glaucoma: The Mayo Clinic series in Rochester, Minnesota. *Am J Ophthalmol* 2013;156:927-35.
534. Vold SD, Dustin L. Trabectome study group. Impact of laser trabeculoplasty on trabectome® outcomes. *Ophthalmic Surg Lasers Imaging* 2010;41:443-51.
535. Klamann MK, Gonnermann J, Maier AK, et al. Influence of selective laser trabeculoplasty (SLT) on combined clear cornea phacoemulsification and trabectome outcomes. *Graefes Arch Clin Exp Ophthalmol* 2014;252:627-31.
536. Jea SY, Mosaed S, Vold SD, Rhee DJ. Effect of a failed trabectome on subsequent trabeculectomy. *J Glaucoma* 2012;21:71-5.
537. Ahuja Y, Malihi M, Sit AJ. Delayed-onset symptomatic hyphema after ab interno trabeculectomy surgery. *Am J Ophthalmol* 2012;154:476-80 e2.
538. Berdahl JP, Gallardo MJ, ElMallah MK, et al. Six-month outcomes of goniotomy performed with the Kahook dual blade as a stand-alone glaucoma procedure. *Adv Ther* 2018;35:2093-102.

539. Dorairaj SK, Kahook MY, Williamson BK, et al. A multicenter retrospective comparison of goniotomy versus trabecular bypass device implantation in glaucoma patients undergoing cataract extraction. *Clin Ophthalmol* 2018;12:791-7.
540. Le C, Kazaryan S, Hubbell M, et al. Surgical outcomes of phacoemulsification followed by iStent implantation versus goniotomy with the Kahook dual blade in patients with mild primary open-angle glaucoma with a minimum of 12-month follow-up. *J Glaucoma* 2019;28:411-4.
541. Ventura-Abreu N, Garcia-Feijoo J, Pazos M, et al. Twelve-month results of ab interno trabeculectomy with Kahook dual blade: An interventional, randomized, controlled clinical study. *Graefes Arch Clin Exp Ophthalmol* 2021;259:2771-81.
542. Falkenberry S, Singh IP, Crane CJ, et al. Excisional goniotomy vs trabecular microbypass stent implantation: A prospective randomized clinical trial in eyes with mild to moderate open-angle glaucoma. *J Cataract Refract Surg* 2020;46:1165-71.
543. Vinod K, Gedde SJ. Safety profile of minimally invasive glaucoma surgery. *Curr Opin Ophthalmol* 2021;32:160-8.
544. Maheshwari D, Grover DS, Ramakrishnan R, et al. Early outcomes of combined phacoemulsification and ab interno Tanito microhook trabeculotomy in open-angle glaucoma. *Ophthalmol Glaucoma* 2024;7:123-30.
545. Guo CY, Qi XH, Qi JM. Systematic review and meta-analysis of treating open angle glaucoma with gonioscopy-assisted transluminal trabeculotomy. *Int J Ophthalmol* 2020;13:317-24.
546. Sato T, Kawaji T, Hirata A. Transient ciliochoroidal detachment after 360-degree suture trabeculotomy ab interno for open-angle glaucoma: 12-month follow-up. *Eye (Lond)* 2019;33:1081-9.
547. Gallardo MJ, Pyfer MF, Vold SD, et al. Canaloplasty and trabeculotomy combined with phacoemulsification for glaucoma: 12-month results of the gemini study. *Clin Ophthalmol* 2022;16:1225-34.
548. Gallardo MJ, Supnet RA, Ahmed IIK. Viscodilation of Schlemm's canal for the reduction of IOP via an ab-interno approach. *Clin Ophthalmol* 2018;12:2149-55.
549. Davids AM, Pahlitzsch M, Boeker A, et al. Ab interno canaloplasty (ABIC)-12-month results of a new minimally invasive glaucoma surgery (MIGS). *Graefes Arch Clin Exp Ophthalmol* 2019;257:1947-53.
550. Gallardo MJ, Supnet RA, Ahmed IIK. Circumferential viscodilation of Schlemm's canal for open-angle glaucoma: Ab-interno vs ab-externo canaloplasty with tensioning suture. *Clin Ophthalmol* 2018;12:2493-8.
551. Yin P, Li J, Shi Y, et al. Ab interno canaloplasty versus gonioscopy-assisted transluminal trabeculotomy in open-angle glaucoma: A randomised controlled trial. *Br J Ophthalmol* 2024;108:687-94.
552. Goldberg DF, Orlich C, Flowers BE, et al. A randomized controlled trial comparing streamline canaloplasty to trabecular micro-bypass stent implantation in primary open-angle glaucoma. *Clin Ophthalmol* 2024;18:2917-28.
553. Craven ER, Katz LJ, Wells JM, Giamporcaro JE. Cataract surgery with trabecular micro-bypass stent implantation in patients with mild-to-moderate open-angle glaucoma and cataract: Two-year follow-up. *J Cataract Refract Surg* 2012;38:1339-45.
554. Fernandez-Barrientos Y, Garcia-Feijoo J, Martinez-de-la-Casa JM, et al. Fluorophotometric study of the effect of the glaukos trabecular microbypass stent on aqueous humor dynamics. *Invest Ophthalmol Vis Sci* 2010;51:3327-32.
555. Belovay GW, Naqi A, Chan BJ, et al. Using multiple trabecular micro-bypass stents in cataract patients to treat open-angle glaucoma. *J Cataract Refract Surg* 2012;38:1911-7.
556. Katz LJ, Erb C, Carceller GA, et al. Prospective, randomized study of one, two, or three trabecular bypass stents in open-angle glaucoma subjects on topical hypotensive medication. *Clin Ophthalmol* 2015;9:2313-20.
557. Popovic M, Campos-Moller X, Saheb H, Ahmed IIK. Efficacy and adverse event profile of the iStent and iStent inject trabecular micro-bypass for open-angle glaucoma: A meta-analysis. *J Curr Glaucoma Pract* 2018;12:67-84.
558. Fea AM, Belda JI, Rekas M, et al. Prospective unmasked randomized evaluation of the iStent inject® versus two ocular hypotensive agents in patients with primary open-angle glaucoma. *Clin Ophthalmol* 2014;8:875-82.
559. Samuelson TW, Sarkisian SR, Jr., Lubeck DM, et al. Prospective, randomized, controlled pivotal trial of an ab interno implanted trabecular micro-bypass in primary open-angle glaucoma and cataract: Two-year results. *Ophthalmology* 2019;126:811-21.
560. Le JT, Bicket AK, Wang L, Li T. Ab interno trabecular bypass surgery with iStent for open-angle glaucoma. *Cochrane Database Syst Rev* 2019;3:CD012743.
561. Sarkisian SR, Jr., Grover DS, Gallardo MJ, et al. Effectiveness and safety of iStent infinite trabecular micro-bypass for uncontrolled glaucoma. *J Glaucoma* 2023;32:9-18.
562. Pfeiffer N, Garcia-Feijoo J, Martinez-de-la-Casa JM, et al. A randomized trial of a schlemm's canal microstent with phacoemulsification for reducing intraocular pressure in open-angle glaucoma. *Ophthalmology* 2015;122:1283-93.

563. Samuelson TW, Chang DF, Marquis R, et al. A Schlemm canal microstent for intraocular pressure reduction in primary open-angle glaucoma and cataract: The HORIZON study. *Ophthalmology* 2019;126:29-37.
564. Ahmed IIK, Fea A, Au L, et al. A prospective randomized trial comparing Hydrus and iStent microinvasive glaucoma surgery implants for stand-alone treatment of open-angle glaucoma: The COMPARE study. *Ophthalmology* 2020;127:52-61.
565. Otarola F, Virgili G, Shah A, et al. Ab interno trabecular bypass surgery with Schlemm's canal microstent (Hydrus) for open angle glaucoma. *Cochrane Database Syst Rev* 2020;3:CD012740.
566. Vold S, Ahmed, II, Craven ER, et al. Two-year compass trial results: Supraciliary microstenting with phacoemulsification in patients with open-angle glaucoma and cataracts. *Ophthalmology* 2016;123:2103-12.
567. Sandhu A, Jayaram H, Hu K, et al. Ab interno supraciliary microstent surgery for open-angle glaucoma. *Cochrane Database Syst Rev* 2021;5:CD012802.
568. Reiss G, Clifford B, Vold S, et al. Safety and effectiveness of cypass supraciliary micro-stent in primary open-angle glaucoma: 5-year results from the COMPASS XT study. *Am J Ophthalmol* 2019;208:219-25.
569. Rhee D, Radcliffe N, Mah F, et al. ASCRS Cypass Withdrawal Task Force. Preliminary ASCRS Cypass withdrawal consensus statement. 2018.
570. Alcon Laboratories. Cypass microstent [instructions for use]. U.S. Food and Drug Administration website.
571. Francis BA, Minckler D, Dustin L, et al. Combined cataract extraction and trabeculotomy by the internal approach for coexisting cataract and open-angle glaucoma: Initial results. *J Cataract Refract Surg* 2008;34:1096-103.
572. Ting JL, Damji KF, Stiles MC, Trabectome Study G. Ab interno trabeculectomy: Outcomes in exfoliation versus primary open-angle glaucoma. *J Cataract Refract Surg* 2012;38:315-23.
573. Katz LJ, Erb C, Carceller Guillamet A, et al. Long-term titrated IOP control with one, two, or three trabecular micro-bypass stents in open-angle glaucoma subjects on topical hypotensive medication: 42-month outcomes. *Clin Ophthalmol* 2018;12:255-62.
574. Fechtner RD, Voskanyan L, Vold SD, et al. Five-year, prospective, randomized, multi-surgeon trial of two trabecular bypass stents versus prostaglandin for newly diagnosed open-angle glaucoma. *Ophthalmol Glaucoma* 2019;2:156-66.
575. Ahmed IIK, De Francesco T, Rhee D, et al. Long-term outcomes from the horizon randomized trial for a Schlemm's canal microstent in combination cataract and glaucoma surgery. *Ophthalmology* 2022;129:742-51.
576. Grover DS, Flynn WJ, Bashford KP, et al. Performance and safety of a new ab interno gelatin stent in refractory glaucoma at 12 months. *Am J Ophthalmol* 2017;183:25-36.
577. McGlumphy EJ, Do A, Du A, et al. Interim analysis of clinical outcomes with open versus closed conjunctival implantation of the Xen45 gel stent. *Ophthalmol Glaucoma* 2024;7:116-22.
578. Yang X, Zhao Y, Zhong Y, Duan X. The efficacy of Xen gel stent implantation in glaucoma: A systematic review and meta-analysis. *BMC Ophthalmol* 2022;22:305.
579. Sheybani A, Vera V, Grover DS, et al. Gel stent versus trabeculectomy: The randomized, multicenter, gold-standard pathway study (GPS) of effectiveness and safety at 12 months. *Am J Ophthalmol* 2023;252:306-25.
580. Parrish RK, 2nd, Feuer WJ, Schiffman JC, et al. Five-year follow-up optic disc findings of the Collaborative Initial Glaucoma Treatment Study. *Am J Ophthalmol* 2009;147:717-24.
581. King AJ, Hudson J, Fernie G, et al. Primary Trabeculectomy for Advanced Glaucoma: Pragmatic multicentre randomised controlled trial (TAGS). *BMJ* 2021;373:n1014.
582. King AJ, Hudson J, Azuara-Blanco A, et al. Evaluating primary treatment for people with advanced glaucoma: Five-year results of the treatment of Advanced Glaucoma Study. *Ophthalmology* 2024;131:759-70.
583. Law SK, Modjtahedi SP, Mansury A, Caprioli J. Intermediate-term comparison of trabeculectomy with intraoperative mitomycin-C between Asian American and Caucasian glaucoma patients: A case-controlled comparison. *Eye (Lond)* 2007;21:71-8.
584. Kim HY, Egbert PR, Singh K. Long-term comparison of primary trabeculectomy with 5-fluorouracil versus mitomycin C in West Africa. *J Glaucoma* 2008;17:578-83.
585. Wong MH, Husain R, Ang BC, et al. The Singapore 5-fluorouracil trial: Intraocular pressure outcomes at 8 years. *Ophthalmology* 2013;120:1127-34.
586. Kirwan JF, Lockwood AJ, Shah P, et al. Trabeculectomy outcomes group audit study group. Trabeculectomy in the 21st century: A multicenter analysis. *Ophthalmology* 2013;120:2532-9.
587. Boimer C, Birt CM. Preservative exposure and surgical outcomes in glaucoma patients: The PESO study. *J Glaucoma* 2013;22:730-5.
588. Broadway DC, Grierson I, O'Brien C, Hitchings RA. Adverse effects of topical antiglaucoma medication. II. The outcome of filtration surgery. *Arch Ophthalmol* 1994;112:1446-54.

589. Heuer DK, Gressel MG, Parrish RK, 2nd, et al. Trabeculectomy in aphakic eyes. *Ophthalmology* 1984;91:1045-51.
590. Gross RL, Feldman RM, Spaeth GL, et al. Surgical therapy of chronic glaucoma in aphakia and pseudophakia. *Ophthalmology* 1988;95:1195-201.
591. Shirato S, Kitazawa Y, Mishima S. A critical analysis of the trabeculectomy results by a prospective follow-up design. *Jpn J Ophthalmol* 1982;26:468-80.
592. Law SK, Shih K, Tran DH, et al. Long-term outcomes of repeat vs initial trabeculectomy in open-angle glaucoma. *Am J Ophthalmol* 2009;148:685-95.
593. AGIS investigators. The Advanced Glaucoma Intervention Study: 8. Risk of cataract formation after trabeculectomy. *Arch Ophthalmol* 2001;119:1771-9.
594. Hylton C, Congdon N, Friedman D, et al. Cataract after glaucoma filtration surgery. *Am J Ophthalmol* 2003;135:231-2.
595. Writing Committee for the Cornea Donor Study Research Group; Sugar A, Gal RL, Kollman C, et al. Factors associated with corneal graft survival in the cornea donor study. *JAMA Ophthalmol* 2015;133:246-54.
596. Lee LC, Pasquale LR. Surgical management of glaucoma in pseudophakic patients. *Semin Ophthalmol* 2002;17:131-7.
597. Fontana H, Nouri-Mahdavi K, Caprioli J. Trabeculectomy with mitomycin C in pseudophakic patients with open-angle glaucoma: Outcomes and risk factors for failure. *Am J Ophthalmol* 2006;141:652-9.
598. Takihara Y, Inatani M, Seto T, et al. Trabeculectomy with mitomycin for open-angle glaucoma in phakic vs pseudophakic eyes after phacoemulsification. *Arch Ophthalmol* 2011;129:152-7.
599. Supawavej C, Nouri-Mahdavi K, Law SK, Caprioli J. Comparison of results of initial trabeculectomy with mitomycin C after prior clear-corneal phacoemulsification to outcomes in phakic eyes. *J Glaucoma* 2013;22:52-9.
600. Wilkins M, Indar A, Wormald R. Intra-operative mitomycin C for glaucoma surgery. *Cochrane Database Syst Rev* 2005:CD002897.
601. Andreanos D, Georgopoulos GT, Vergados J, et al. Clinical evaluation of the effect of mitomycin-C in re-operation for primary open angle glaucoma. *Eur J Ophthalmol* 1997;7:49-54.
602. Robin AL, Ramakrishnan R, Krishnadas R, et al. A long-term dose-response study of mitomycin in glaucoma filtration surgery. *Arch Ophthalmol* 1997;115:969-74.
603. Costa VP, Comegno PE, Vasconcelos JP, et al. Low-dose mitomycin C trabeculectomy in patients with advanced glaucoma. *J Glaucoma* 1996;5:193-9.
604. Martini E, Laffi GL, Sprovieri C, Scorolli L. Low-dosage mitomycin C as an adjunct to trabeculectomy. A prospective controlled study. *Eur J Ophthalmol* 1997;7:40-8.
605. Singh K, Mehta K, Shaikh N. Trabeculectomy with intraoperative mitomycin C versus 5-fluorouracil. Prospective randomized clinical trial. *Ophthalmology* 2000;107:2305-9.
606. Cabourne E, Clarke JC, Schlottmann PG, Evans JR. Mitomycin C versus 5-fluorouracil for wound healing in glaucoma surgery. *Cochrane Database Syst Rev* 2015:CD006259.
607. Green E, Wilkins M, Bunce C, Wormald R. 5-fluorouracil for glaucoma surgery. *Cochrane Database Syst Rev* 2014:CD001132.
608. Ruderman JM, Welch DB, Smith MF, Shoch DE. A randomized study of 5-fluorouracil and filtration surgery. *Am J Ophthalmol* 1987;104:218-24.
609. Fluorouracil Filtering Surgery Study Group. Fluorouracil filtering surgery study one-year follow-up. *Am J Ophthalmol* 1989;108:625-35.
610. Goldenfeld M, Krupin T, Ruderman JM, et al. 5-fluorouracil in initial trabeculectomy. A prospective, randomized, multicenter study. *Ophthalmology* 1994;101:1024-9.
611. Ophir A, Ticho U. A randomized study of trabeculectomy and subconjunctival administration of fluorouracil in primary glaucomas. *Arch Ophthalmol* 1992;110:1072-5.
612. Ralli M, Nouri-Mahdavi K, Caprioli J. Outcomes of laser suture lysis after initial trabeculectomy with adjunctive mitomycin C. *J Glaucoma* 2006;15:60-7.
613. Kobayashi H, Kobayashi K, Okinami S. A comparison of the intraocular pressure-lowering effect and safety of viscocanalostomy and trabeculectomy with mitomycin C in bilateral open-angle glaucoma. *Graefes Arch Clin Exp Ophthalmol* 2003;241:359-66.
614. Rotchford AP, King AJ. Needling revision of trabeculectomies bleb morphology and long-term survival. *Ophthalmology* 2008;115:1148-53.
615. Kapasi MS, Birt CM. The efficacy of 5-fluorouracil bleb needling performed 1 year or more posttrabeculectomy: A retrospective study. *J Glaucoma* 2009;18:144-8.
616. Amini H, Esmaili A, Zarei R, et al. Office-based slit-lamp needle revision with adjunctive mitomycin-C for late failed or encapsulated filtering blebs. *Middle East Afr J Ophthalmol* 2012;19:216-21.

617. Anand N, Khan A. Long-term outcomes of needle revision of trabeculectomy blebs with mitomycin C and 5-fluorouracil: A comparative safety and efficacy report. *J Glaucoma* 2009;18:513-20.
618. Del Noce C, Vagge A, Traverso CE. Bleb needling with mitomycin C as adjunctive therapy in failing blebs: A retrospective study. *Ophthalmic Res* 2019;62:55-60.
619. Lin S, Byles D, Smith M. Long-term outcome of mitomycin C-augmented needle revision of trabeculectomy blebs for late trabeculectomy failure. *Eye (Lond)* 2018;32:1893-9.
620. Liu W, Wang J, Zhang M, et al. Comparison of subconjunctival mitomycin C and 5-fluorouracil injection for needle revision of early failed trabeculectomy blebs. *J Ophthalmol* 2016;2016:3762674.
621. Maestrini HA, Cronemberger S, Matoso HD, et al. Late needling of flat filtering blebs with adjunctive mitomycin C: Efficacy and safety for the corneal endothelium. *Ophthalmology* 2011;118:755-62.
622. Mardelli PG, Lederer CM, Jr., Murray PL, et al. Slit-lamp needle revision of failed filtering blebs using mitomycin C. *Ophthalmology* 1996;103:1946-55.
623. Panarelli JF, Vinod K, Huang G, Sidoti PA. Transconjunctival revision with mitomycin-C following failed trabeculectomy. *J Glaucoma* 2016;25:618-22.
624. Pathak-Ray V, Choudhari N. Rescue of failing or failed trabeculectomy blebs with slit-lamp needling and adjunctive mitomycin C in Indian eyes. *Indian J Ophthalmol* 2018;66:71-6.
625. Shetty RK, Wartluft L, Moster MR. Slit-lamp needle revision of failed filtering blebs using high-dose mitomycin C. *J Glaucoma* 2005;14:52-6.
626. Tulidowicz-Bielak M, Kosior-Jarecka E, Zarnowski T. Revision of trabeculectomy filtering blebs with mitomycin C: Long term results. *Indian J Ophthalmol* 2016;64:822-8.
627. Anand N, Arora S. Surgical revision of failed filtration surgery with mitomycin C augmentation. *J Glaucoma* 2007;16:456-61.
628. Chen PP, Moeller KL. Smaller-incision revision of trabeculectomy with mitomycin: Long-term outcomes and complications. *J Glaucoma* 2019;28:27-31.
629. Costa VP, Wilson RP, Moster MR, et al. Hypotony maculopathy following the use of topical mitomycin C in glaucoma filtration surgery. *Ophthalmic Surg* 1993;24:389-94.
630. Zacharia PT, Deppermann SR, Schuman JS. Ocular hypotony after trabeculectomy with mitomycin C. *Am J Ophthalmol* 1993;116:314-26.
631. Kupin TH, Juzych MS, Shin DH, et al. Adjunctive mitomycin C in primary trabeculectomy in phakic eyes. *Am J Ophthalmol* 1995;119:30-9.
632. Greenfield DS, Liebmann JM, Jee J, Ritch R. Late-onset bleb leaks after glaucoma filtering surgery. *Arch Ophthalmol* 1998;116:443-7.
633. Soltau JB, Rothman RF, Budenz DL, et al. Risk factors for glaucoma filtering bleb infections. *Arch Ophthalmol* 2000;118:338-42.
634. Jampel HD, Quigley HA, Kerrigan-Baumrind LA, et al. Risk factors for late-onset infection following glaucoma filtration surgery. *Arch Ophthalmol* 2001;119:1001-8.
635. Kim EA, Law SK, Coleman AL, et al. Long-term bleb-related infections after trabeculectomy: Incidence, risk factors and influence of bleb revision. *Am J Ophthalmol* In press.
636. Whiteside-Michel J, Liebmann JM, Ritch R. Initial 5-fluorouracil trabeculectomy in young patients. *Ophthalmology* 1992;99:7-13.
637. Suner IJ, Greenfield DS, Miller MP, et al. Hypotony maculopathy after filtering surgery with mitomycin C. Incidence and treatment. *Ophthalmology* 1997;104:207-14; discussion 14-5.
638. Scott DR, Quigley HA. Medical management of a high bleb phase after trabeculectomies. *Ophthalmology* 1988;95:1169-73.
639. Desai MA, Gedde SJ, Feuer WJ, et al. Practice preferences for glaucoma surgery: A survey of the American Glaucoma Society in 2008. *Ophthalmic Surg Lasers Imaging* 2011;42:202-8.
640. Jones E, Clarke J, Khaw PT. Recent advances in trabeculectomy technique. *Curr Opin Ophthalmol* 2005;16:107-13.
641. Wells AP, Cordeiro MF, Bunce C, Khaw PT. Cystic bleb formation and related complications in limbus- versus fornix-based conjunctival flaps in pediatric and young adult trabeculectomy with mitomycin C. *Ophthalmology* 2003;110:2192-7.
642. Theventhiran AB, Kim G, Yao W. Fornix-based versus limbal-based conjunctival trabeculectomy flaps for glaucoma. *Cochrane Database Syst Rev* 2021;8:CD009380.
643. Al-Haddad C, Abdulaal M, Al-Moujahed A, Ervin AM. Fornix-based versus limbal-based conjunctival trabeculectomy flaps for glaucoma. *Cochrane Database Syst Rev* 2015;11:CD009380.
644. Rivier D, Roy S, Mermoud A. Ex-PRESS R-50 miniature glaucoma implant insertion under the conjunctiva combined with cataract extraction. *J Cataract Refract Surg* 2007;33:1946-52.

645. Stewart RM, Diamond JG, Ashmore ED, Ayyala RS. Complications following Ex-PRESS glaucoma shunt implantation. *Am J Ophthalmol* 2005;140:340-1.
646. Wamsley S, Moster MR, Rai S, et al. Results of the use of the Ex-PRESS miniature glaucoma implant in technically challenging, advanced glaucoma cases: A clinical pilot study. *Am J Ophthalmol* 2004;138:1049-51.
647. Dahan E, Carmichael TR. Implantation of a miniature glaucoma device under a scleral flap. *J Glaucoma* 2005;14:98-102.
648. Maris PJ, Jr., Ishida K, Netland PA. Comparison of trabeculectomy with Ex-PRESS miniature glaucoma device implanted under scleral flap. *J Glaucoma* 2007;16:14-9.
649. Good TJ, Kahook MY. Assessment of bleb morphologic features and postoperative outcomes after Ex-PRESS drainage device implantation versus trabeculectomy. *Am J Ophthalmol* 2011;151:507-13.
650. Sugiyama T, Shibata M, Kojima S, et al. The first report on intermediate-term outcome of Ex-PRESS glaucoma filtration device implanted under scleral flap in Japanese patients. *Clin Ophthalmol* 2011;5:1063-6.
651. Marzette L, Herndon LW. A comparison of the Ex-PRESS mini glaucoma shunt with standard trabeculectomy in the surgical treatment of glaucoma. *Ophthalmic Surg Lasers Imaging* 2011;42:453-9.
652. Seider MI, Rofagha S, Lin SC, Stamper RL. Resident-performed Ex-PRESS shunt implantation versus trabeculectomy. *J Glaucoma* 2012;21:469-74.
653. de Jong L, Lafuma A, Aguade AS, Berdeaux G. Five-year extension of a clinical trial comparing the Ex-PRESS glaucoma filtration device and trabeculectomy in primary open-angle glaucoma. *Clin Ophthalmol* 2011;5:527-33.
654. Wagschal LD, Trope GE, Jinapriya D, et al. Prospective randomized study comparing Ex-PRESS to trabeculectomy: 1-year results. *J Glaucoma* In press.
655. Netland PA, Sarkisian SR, Jr., Moster MR, et al. Randomized, prospective, comparative trial of Ex-PRESS glaucoma filtration device versus trabeculectomy (XVT study). *Am J Ophthalmol* 2014;157:433-40.
656. Park J, Rittiphairoj T, Wang X, et al. Device-modified trabeculectomy for glaucoma. *Cochrane Database Syst Rev* 2023;3:CD010472.
657. Arimura S, Miyake S, Iwasaki K, et al. Randomised clinical trial for postoperative complications after Ex-PRESS implantation versus trabeculectomy with 2-year follow-up. *Sci Rep* 2018;8:16168.
658. Patel HY, Wagschal LD, Trope GE, Buys YM. Economic analysis of the Ex-PRESS miniature glaucoma device versus trabeculectomy. *J Glaucoma* 2014;23:385-90.
659. Arora KS, Robin AL, Corcoran KJ, et al. Use of various glaucoma surgeries and procedures in Medicare beneficiaries from 1994 to 2012. *Ophthalmology* 2015;122:1615-24.
660. Tseng VL, Coleman AL, Chang MY, Caprioli J. Aqueous shunts for glaucoma. *Cochrane Database Syst Rev* 2017;7:CD004918.
661. Bluestein EC, Stewart WC. Trabeculectomy with 5-fluorouracil vs single-plate Molteno implantation. *Ophthalmic Surg* 1993;24:669-73.
662. Tran DH, Souza C, Ang MJ, et al. Comparison of long-term surgical success of Ahmed valve implant versus trabeculectomy in open-angle glaucoma. *Br J Ophthalmol* 2009;93:1504-9.
663. Wilson MR, Mendis U, Paliwal A, Haynatzka V. Long-term follow-up of primary glaucoma surgery with Ahmed glaucoma valve implant versus trabeculectomy. *Am J Ophthalmol* 2003;136:464-70.
664. Gedde SJ, Schiffman JC, Feuer WJ, et al. Treatment outcomes in the tube versus trabeculectomy (TVT) study after five years of follow-up. *Am J Ophthalmol* 2012;153:789-803 e2.
665. Gedde SJ, Herndon LW, Brandt JD, et al. Postoperative complications in the tube versus trabeculectomy (TVT) study during five years of follow-up. *Am J Ophthalmol* 2012;153:804-14.
666. Saheb H, Gedde SJ, Schiffman JC, et al. Outcomes of glaucoma reoperations in the tube versus trabeculectomy (TVT) study. *Am J Ophthalmol* 2014;157:1179-89 e2.
667. Swaminathan SS, Jammal AA, Kornmann HL, et al. Visual field outcomes in the tube versus trabeculectomy study. *Ophthalmology* 2020;127:1162-9.
668. Kotecha A, Feuer WJ, Barton K, et al. Quality of life in the tube versus trabeculectomy study. *Am J Ophthalmol* 2017;176:228-35.
669. Gedde SJ, Feuer WJ, Lim KS, et al. Treatment outcomes in the primary tube versus trabeculectomy study after 5 years of follow-up. *Ophthalmology* 2022;129:1344-56.
670. Gedde SJ, Feuer WJ, Lim KS, et al. Postoperative complications in the primary tube versus trabeculectomy study during 5 years of follow-up. *Ophthalmology* 2022;129:1357-67.
671. Coulon SJ, Vanner EA, Gedde SJ, Primary Tube Versus Trabeculectomy Study Group. Outcomes of glaucoma reoperations in the primary tube versus trabeculectomy study. *Ophthalmol Glaucoma* 2023;6:422-31.
672. Swaminathan SS, Jammal AA, Medeiros FA, et al. Visual field outcomes in the primary tube versus trabeculectomy study. *Ophthalmology* 2024;131:1157-63.

673. Ayyala RS, Zurakowski D, Monshizadeh R, et al. Comparison of double-plate Molteno and Ahmed glaucoma valve in patients with advanced uncontrolled glaucoma. *Ophthalmic Surg Lasers* 2002;33:94-101.
674. Goulet RJ, 3rd, Phan AD, Cantor LB, WuDunn D. Efficacy of the Ahmed s2 glaucoma valve compared with the Baerveldt 250-mm2 glaucoma implant. *Ophthalmology* 2008;115:1141-7.
675. Siegner SW, Netland PA, Urban RC, Jr., et al. Clinical experience with the Baerveldt glaucoma drainage implant. *Ophthalmology* 1995;102:1298-307.
676. Tsai JC, Johnson CC, Kammer JA, Dietrich MS. The Ahmed shunt versus the Baerveldt shunt for refractory glaucoma II: Longer-term outcomes from a single surgeon. *Ophthalmology* 2006;113:913-7.
677. Sidoti PA, Dunphy TR, Baerveldt G, et al. Experience with the Baerveldt glaucoma implant in treating neovascular glaucoma. *Ophthalmology* 1995;102:1107-18.
678. Heuer DK, Lloyd MA, Abrams DA, et al. Which is better? One or two?: A randomized clinical trial of single-plate versus double-plate molteno implantation for glaucomas in aphakia and pseudophakia. *Ophthalmology* 1992;99:1512-9.
679. Britt MT, LaBree LD, Lloyd MA, et al. Randomized clinical trial of the 350-mm2 versus the 500-mm2 Baerveldt implant: Longer term results: Is bigger better? *Ophthalmology* 1999;106:2312-8.
680. Nassiri N, Kamali G, Rahnavardi M, et al. Ahmed glaucoma valve and single-plate molteno implants in treatment of refractory glaucoma: A comparative study. *Am J Ophthalmol* 2010;149:893-902.
681. Christakis PG, Kalenak JW, Tsai JC, et al. The Ahmed versus Baerveldt study: Five-year treatment outcomes. *Ophthalmology* 2016;123:2093-102.
682. Budenz DL, Barton K, Gedde SJ, et al. Five-year treatment outcomes in the Ahmed Baerveldt comparison study. *Ophthalmology* 2015;122:308-16.
683. Christakis PG, Zhang D, Budenz DL, et al. Five-year pooled data analysis of the Ahmed Baerveldt comparison study and the Ahmed versus Baerveldt study. *Am J Ophthalmol* 2017;176:118-26.
684. Bowden EC, Choudhury A, Gedde SJ, et al. Risk factors for failure of tube shunt surgery: A pooled data analysis. *Am J Ophthalmol* 2022;240:217-24.
685. Albis-Donado O, Gil-Carrasco F, Romero-Quijada R, Thomas R. Evaluation of Ahmed glaucoma valve implantation through a needle-generated scleral tunnel in Mexican children with glaucoma. *Indian J Ophthalmol* 2010;58:365-73.
686. Gil-Carrasco F. Tunnelization technique for Ahmed glaucoma valve implantation. *Revista Mexicana de Oftalmologia* 2013;87:191-4.
687. Kang JJ, Ritterband DC, Atallah RT, et al. Clinical outcomes of descemet stripping endothelial keratoplasty in eyes with glaucoma drainage devices. *J Glaucoma* 2019;28:601-5.
688. The fluorouracil filtering surgery study group. Five-year follow-up of the fluorouracil filtering surgery study. *Am J Ophthalmol* 1996;121:349-66.
689. Musch DC, Gillespie BW, Niziol LM, et al. Intraocular pressure control and long-term visual field loss in the Collaborative Initial Glaucoma Treatment Study. *Ophthalmology* 2011;118:1766-73.
690. Islamaj E, Wubbels RJ, de Waard PWT. Primary Baerveldt versus trabeculectomy study after 5 years of follow-up. *Acta Ophthalmol* 2020;98:400-7.
691. Yazdani S, Doozandeh A, Pakravan M, et al. Adjunctive triamcinolone acetone for Ahmed glaucoma valve implantation: A randomized clinical trial. *Eur J Ophthalmol* 2017;27:411-6.
692. Ates H, Uretmen O, Andac K, Azarsiz SS. Deep sclerectomy with a nonabsorbable implant (T-Flux): Preliminary results. *Can J Ophthalmol* 2003;38:482-8.
693. Dahan E, Ravinet E, Ben-Simon GJ, Mermoud A. Comparison of the efficacy and longevity of nonpenetrating glaucoma surgery with and without a new, nonabsorbable hydrophilic implant. *Ophthalmic Surg Lasers Imaging* 2003;34:457-63.
694. Ravinet E, Bovey E, Mermoud A. T-Flux implant versus Healon GV in deep sclerectomy. *J Glaucoma* 2004;13:46-50.
695. Chiselita D. Non-penetrating deep sclerectomy versus trabeculectomy in primary open-angle glaucoma surgery. *Eye* 2001;15:197-201.
696. El Sayyad F, Helal M, El-Kholify H, et al. Nonpenetrating deep sclerectomy versus trabeculectomy in bilateral primary open-angle glaucoma. *Ophthalmology* 2000;107:1671-4.
697. Ambresin A, Shaarawy T, Mermoud A. Deep sclerectomy with collagen implant in one eye compared with trabeculectomy in the other eye of the same patient. *J Glaucoma* 2002;11:214-20.
698. Mermoud A, Schnyder CC, Sickenberg M, et al. Comparison of deep sclerectomy with collagen implant and trabeculectomy in open-angle glaucoma. *J Cataract Refract Surg* 1999;25:323-31.
699. Cillino S, Di Pace F, Casuccio A, et al. Deep sclerectomy versus punch trabeculectomy with or without phacoemulsification: A randomized clinical trial. *J Glaucoma* 2004;13:500-6.

700. Carassa RG, Bettin P, Fiori M, Brancato R. Viscocanalostomy versus trabeculectomy in white adults affected by open-angle glaucoma: A 2-year randomized, controlled trial. *Ophthalmology* 2003;110:882-7.
701. Luke C, Dietlein TS, Jacobi PC, et al. A prospective randomized trial of viscocanalostomy versus trabeculectomy in open-angle glaucoma: A 1-year follow-up study. *J Glaucoma* 2002;11:294-9.
702. O'Brart DP, Rowlands E, Islam N, Noury AM. A randomised, prospective study comparing trabeculectomy augmented with antimetabolites with a viscocanalostomy technique for the management of open angle glaucoma uncontrolled by medical therapy. *Br J Ophthalmol* 2002;86:748-54.
703. Jonescu-Cuypers C, Jacobi P, Konen W, Krieglstein G. Primary viscocanalostomy versus trabeculectomy in white patients with open-angle glaucoma: A randomized clinical trial. *Ophthalmology* 2001;108:254-8.
704. Gilmour DF, Manners TD, Devonport H, et al. Viscocanalostomy versus trabeculectomy for primary open angle glaucoma: 4-year prospective randomized clinical trial. *Eye (Lond)* 2009;23:1802-7.
705. Wishart MS, Dages E. Seven-year follow-up of combined cataract extraction and viscocanalostomy. *J Cataract Refract Surg* 2006;32:2043-9.
706. Park M, Hayashi K, Takahashi H, et al. Phaco-viscocanalostomy versus phaco-trabeculectomy: A middle-term study. *J Glaucoma* 2006;15:456-61.
707. Yalvac IS, Sahin M, Eksioglu U, et al. Primary viscocanalostomy versus trabeculectomy for primary open-angle glaucoma: Three-year prospective randomized clinical trial. *J Cataract Refract Surg* 2004;30:2050-7.
708. Eldaly MA, Bunce C, Elsheikha OZ, Wormald R. Non-penetrating filtration surgery versus trabeculectomy for open-angle glaucoma. *Cochrane Database Syst Rev* 2014:CD007059.
709. Lewis RA, von Wolff K, Tetz M, et al. Canaloplasty: Three-year results of circumferential viscodilation and tensioning of Schlemm canal using a microcatheter to treat open-angle glaucoma. *J Cataract Refract Surg* 2011;37:682-90.
710. Ayyala RS, Chaudhry AL, Okogbaa CB, Zurakowski D. Comparison of surgical outcomes between canaloplasty and trabeculectomy at 12 months' follow-up. *Ophthalmology* 2011;118:2427-33.
711. Matlach J, Dhillon C, Hain J, et al. Trabeculectomy versus canaloplasty (TVC study) in the treatment of patients with open-angle glaucoma: A prospective randomized clinical trial. *Acta Ophthalmol* 2015;93:753-61.
712. Meyer SJ. Diathermy cauterization of ciliary body for glaucoma. *Am J Ophthalmol* 1948;31:1504-6.
713. Pastor SA, Singh K, Lee DA, et al. Cyclophotocoagulation: A report by the American Academy of Ophthalmology. *Ophthalmology* 2001;108:2130-8.
714. Lin SC. Endoscopic and transscleral cyclophotocoagulation for the treatment of refractory glaucoma. *J Glaucoma* 2008;17:238-47.
715. Egbert PR, Fiadoyor S, Budenz DL, et al. Diode laser transscleral cyclophotocoagulation as a primary surgical treatment for primary open-angle glaucoma. *Arch Ophthalmol* 2001;119:345-50.
716. Ansari E, Gandhewar J. Long-term efficacy and visual acuity following transscleral diode laser photocoagulation in cases of refractory and non-refractory glaucoma. *Eye (Lond)* 2007;21:936-40.
717. Rotchford AP, Jayasawal R, Madhusudhan S, et al. Transscleral diode laser cycloablation in patients with good vision. *Br J Ophthalmol* 2010;94:1180-3.
718. Zhekov I, Janjua R, Shahid H, et al. A retrospective analysis of long-term outcomes following a single episode of transscleral cyclodiode laser treatment in patients with glaucoma. *BMJ Open* 2013;3.
719. Kramp K, Vick HP, Guthoff R. Transscleral diode laser contact cyclophotocoagulation in the treatment of different glaucomas, also as primary surgery. *Graefes Arch Clin Exp Ophthalmol* 2002;240:698-703.
720. Grueb M, Rohrbach JM, Bartz-Schmidt KU, Schlote T. Transscleral diode laser cyclophotocoagulation as primary and secondary surgical treatment in primary open-angle and pseudoexfoliative glaucoma. Long-term clinical outcomes. *Graefes Arch Clin Exp Ophthalmol* 2006;244:1293-9.
721. Lai JS, Tham CC, Chan JC, Lam DS. Diode laser transscleral cyclophotocoagulation as primary surgical treatment for medically uncontrolled chronic angle closure glaucoma: Long-term clinical outcomes. *J Glaucoma* 2005;14:114-9.
722. Kelada M, Normando EM, Cordeiro FM, et al. Cyclodiode vs micropulse transscleral laser treatment. *Eye (Lond)* 2024;38:1477-84.
723. Douglas E, Gaasterland M. Diode laser cyclophotocoagulation. *Glaucoma Today* 2009.
724. Duerr ER, Sayed MS, Moster S, et al. Transscleral diode laser cyclophotocoagulation: A comparison of slow coagulation and standard coagulation techniques. *Ophthalmol Glaucoma* 2018;1:115-22.
725. Sheheitli H, Persad PJ, Feuer WJ, et al. Treatment outcomes of primary transscleral cyclophotocoagulation. *Ophthalmol Glaucoma* 2021;4:472-81.
726. Khodeiry MM, Sheheitli H, Sayed MS, et al. Treatment outcomes of slow coagulation transscleral cyclophotocoagulation in pseudophakic patients with medically uncontrolled glaucoma. *Am J Ophthalmol* 2021;229:90-9.

727. Hwang YH, Lee S, Kim M, Choi J. Comparison of treatment outcomes between slow coagulation transscleral cyclophotocoagulation and micropulse transscleral laser treatment. *Sci Rep* 2024;14:23944.
728. Khodeiry MM, Lauter AJ, Sayed MS, et al. Primary slow-coagulation transscleral cyclophotocoagulation laser treatment for medically recalcitrant neovascular glaucoma. *Br J Ophthalmol* 2023;107:671-6.
729. Aquino MC, Barton K, Tan AM, et al. Micropulse versus continuous wave transscleral diode cyclophotocoagulation in refractory glaucoma: A randomized exploratory study. *Clin Exp Ophthalmol* 2015;43:40-6.
730. Ma A, Yu SWY, Wong JKW. Micropulse laser for the treatment of glaucoma: A literature review. *Surv Ophthalmol* 2019;64:486-97.
731. Ling Q, Cai Z, Zhang X, Duan X. The efficacy and safety of micropulse transscleral laser treatment in glaucoma: A systematic review and meta-analysis. *BMC Ophthalmol* 2023;23:263.
732. Pantcheva MB, Kahook MY, Schuman JS, Noecker RJ. Comparison of acute structural and histopathological changes in human autopsy eyes after endoscopic cyclophotocoagulation and trans-scleral cyclophotocoagulation. *Br J Ophthalmol* 2007;91:248-52.
733. Lin SC, Chen MJ, Lin MS, et al. Vascular effects on ciliary tissue from endoscopic versus trans-scleral cyclophotocoagulation. *Br J Ophthalmol* 2006;90:496-500.
734. Chen J, Cohn RA, Lin SC, et al. Endoscopic photocoagulation of the ciliary body for treatment of refractory glaucomas. *Am J Ophthalmol* 1997;124:787-96.
735. Kahook MY, Lathrop KL, Noecker RJ. One-site versus two-site endoscopic cyclophotocoagulation. *J Glaucoma* 2007;16:527-30.
736. Murthy GJ, Murthy PR, Murthy KR, Kulkarni VV. A study of the efficacy of endoscopic cyclophotocoagulation for the treatment of refractory glaucomas. *Indian J Ophthalmol* 2009;57:127-32.
737. Ahmad S, Wallace DJ, Herndon LW. Phthisis after endoscopic cyclophotocoagulation. *Ophthalmic Surg Lasers Imaging* 2008;39:407-8.
738. Uram M. Ophthalmic laser microendoscope ciliary process ablation in the management of neovascular glaucoma. *Ophthalmology* 1992;99:1823-8.
739. Gayton JL, Van Der Karr M, Sanders V. Combined cataract and glaucoma surgery: Trabeculectomy versus endoscopic laser cycloablation. *J Cataract Refract Surg* 1999;25:1214-9.
740. Lima FE, Magacho L, Carvalho DM, et al. A prospective, comparative study between endoscopic cyclophotocoagulation and the Ahmed drainage implant in refractory glaucoma. *J Glaucoma* 2004;13:233-7.
741. Chen MF, Kim CH, Coleman AL. Cyclodestructive procedures for refractory glaucoma. *Cochrane Database Syst Rev* 2019;3:CD012223.
742. Toth M, Shah A, Hu K, et al. Endoscopic cyclophotocoagulation (ECP) for open angle glaucoma and primary angle closure. *Cochrane Database Syst Rev* 2019;2:CD012741.
743. Brizido M, Rodrigues PF, Almeida AC, Abegao Pinto L. Cataract surgery and IOP: A systematic review of randomised controlled trials. *Graefes Arch Clin Exp Ophthalmol* 2023;261:1257-66.
744. Jampel HD, Friedman DS, Lubomski LH, et al. Effect of technique on intraocular pressure after combined cataract and glaucoma surgery: An evidence-based review. *Ophthalmology* 2002;109:2215-24; quiz 25, 31.
745. Buys YM, Chipman ML, Zack B, et al. Prospective randomized comparison of one- versus two-site phacotrabeculectomy two-year results. *Ophthalmology* 2008;115:1130-3.
746. Cotran PR, Roh S, McGwin G. Randomized comparison of 1-site and 2-site phacotrabeculectomy with 3-year follow-up. *Ophthalmology* 2008;115:447-54 e1.
747. Gdih GA, Yuen D, Yan P, et al. Meta-analysis of 1- versus 2-site phacotrabeculectomy. *Ophthalmology* 2011;118:71-6.
748. Rebolleda G, Munoz-Negrete FJ. Phacoemulsification in eyes with functioning filtering blebs: A prospective study. *Ophthalmology* 2002;109:2248-55.
749. Ehrnrooth P, Lehto I, Puska P, Laatikainen L. Phacoemulsification in trabeculectomized eyes. *Acta Ophthalmol Scand* 2005;83:561-6.
750. Longo A, Uva MG, Reibaldi A, et al. Long-term effect of phacoemulsification on trabeculectomy function. *Eye (Lond)* 2015;29:1347-52.
751. Zhang ML, Hirunyachote P, Jampel H. Combined surgery versus cataract surgery alone for eyes with cataract and glaucoma. *Cochrane Database Syst Rev* 2015:CD008671.
752. Muallem MS, Nelson GA, Osmanovic S, et al. Predicted refraction versus refraction outcome in cataract surgery after trabeculectomy. *J Glaucoma* 2009;18:284-7.
753. Yeh OL, Bojikian KD, Slabaugh MA, Chen PP. Refractive outcome of cataract surgery in eyes with prior trabeculectomy: Risk factors for postoperative myopia. *J Glaucoma* 2017;26:65-70.

754. Zhang N, Tsai PL, Catoira-Boyle YP, et al. The effect of prior trabeculectomy on refractive outcomes of cataract surgery. *Am J Ophthalmol* 2013;155:858-63.
755. Teichman JC, Ahmed, II. Intraocular lens choices for patients with glaucoma. *Curr Opin Ophthalmol* 2010;21:135-43.
756. Aychoua N, Junoy Montolio FG, Jansonius NM. Influence of multifocal intraocular lenses on standard automated perimetry test results. *JAMA Ophthalmol* 2013;131:481-5.
757. Jonsen A, Siegler M, Winslade W. Clinical ethics: A practical approach to ethical decisions in clinical medicine. 3rd ed. Summit, PA: *McGraw-Hill, Inc., Health Professions Division*, 1992; 40-3.
758. Roth SM, Spaeth GL, Starita RJ, et al. The effects of postoperative corticosteroids on trabeculectomy and the clinical course of glaucoma: Five-year follow-up study. *Ophthalmic Surg* 1991;22:724-9.
759. Starita RJ, Fellman RL, Spaeth GL, et al. Short- and long-term effects of postoperative corticosteroids on trabeculectomy. *Ophthalmology* 1985;92:938-46.
760. Stewart WC, Shields MB. Management of anterior chamber depth after trabeculectomy. *Am J Ophthalmol* 1988;106:41-4.
761. Fiore PM, Richter CU, Arzeno G, et al. The effect of anterior chamber depth on endothelial cell count after filtration surgery. *Arch Ophthalmol* 1989;107:1609-11.
762. Phillips CI, Clark CV, Levy AM. Posterior synechiae after glaucoma operations: Aggravation by shallow anterior chamber and pilocarpine. *Br J Ophthalmol* 1987;71:428-32.
763. Brubaker RF, Pederson JE. Ciliochoroidal detachment. *Surv Ophthalmol* 1983;27:281-9.
764. Gressel MG, Parrish RK, 2nd, Heuer DK. Delayed nonexpulsive suprachoroidal hemorrhage. *Arch Ophthalmol* 1984;102:1757-60.
765. Ruderman JM, Harbin TS, Jr., Campbell DG. Postoperative suprachoroidal hemorrhage following filtration procedures. *Arch Ophthalmol* 1986;104:201-5.
766. Radhakrishnan S, Quigley HA, Jampel HD, et al. Outcomes of surgical bleb revision for complications of trabeculectomy. *Ophthalmology* 2009;116:1713-8.
767. Sharan S, Trope GE, Chipman M, Buys YM. Late-onset bleb infections: Prevalence and risk factors. *Can J Ophthalmol* 2009;44:279-83.
768. Ferguson TJ, Samuelson TW, Herndon L, et al. Negative pressure application by the ocular pressure adjusting pump to lower intraocular pressure in normal-tension glaucoma: HERCULES study. *Am J Ophthalmol* 2025;275:121-34.
769. Coleman AL, Stone KL, Kodjebacheva G, et al. Glaucoma risk and the consumption of fruits and vegetables among older women in the study of osteoporotic fractures. *Am J Ophthalmol* 2008;145:1081-9.
770. West AL, Oren GA, Moroi SE. Evidence for the use of nutritional supplements and herbal medicines in common eye diseases. *Am J Ophthalmol* 2006;141:157-66.
771. Gunasekera V, Ernst E, Ezra DG. Systematic internet-based review of complementary and alternative medicine for glaucoma. *Ophthalmology* 2008;115:435-9 e2.
772. Loskutova E, O'Brien C, Loskutov I, Loughman J. Nutritional supplementation in the treatment of glaucoma: A systematic review. *Surv Ophthalmol* 2019;64:195-216.
773. Jampel H. American Glaucoma Society position statement: Marijuana and the treatment of glaucoma. *J Glaucoma* 2010;19:75-6.
774. Kim J, Aschard H, Kang JH, et al. Intraocular pressure, glaucoma, and dietary caffeine consumption: A gene-diet interaction study from the UK Biobank. *Ophthalmology* 2021;128:866-76.
775. Tseng V, Yu F, Coleman AL. Exercise intensity and risk of glaucoma in the National Health and Nutrition Examination Survey. American Academy of Ophthalmology New Orleans, USA2017.
776. Wu BQ, Kuo HT, Hsu AY, et al. The clinical efficacy of different relaxation exercises on intraocular pressure reduction: A meta-analysis. *J Clin Med* 2024;13.
777. De Moraes CG, John SWM, Williams PA, et al. Nicotinamide and pyruvate for neuroenhancement in open-angle glaucoma: A phase 2 randomized clinical trial. *JAMA Ophthalmol* 2022;140:11-8.
778. Shukla AG, Cioffi GA, John SWM, et al. American Glaucoma Society-American Academy of Ophthalmology position statement on nicotinamide use for glaucoma neuroprotection. *Ophthalmol Glaucoma* 2025;8:112-6.
779. Shukla AG, Cioffi GA, Liebmann JM. Drug-induced liver injury during a glaucoma neuroprotection clinical trial. *J Glaucoma* 2024;33:e58-e9.
780. Herndon LW, Weizer JS, Stinnett SS. Central corneal thickness as a risk factor for advanced glaucoma damage. *Arch Ophthalmol* 2004;122:17-21.
781. Hjortdal JO, Moller-Pedersen T, Ivarsen A, Ehlers N. Corneal power, thickness, and stiffness: Results of a prospective randomized controlled trial of PRK and LASIK for myopia. *J Cataract Refract Surg* 2005;31:21-9.

782. Mudie LI, LaBarre S, Varadaraj V, et al. The iCare home (TA022) study: Performance of an intraocular pressure measuring device for self-tonometry by glaucoma patients. *Ophthalmology* 2016;123:1675-84.
783. Mansouri K, Shaarawy T. Continuous intraocular pressure monitoring with a wireless ocular telemetry sensor: Initial clinical experience in patients with open angle glaucoma. *Br J Ophthalmol* 2011;95:627-9.
784. Mansouri K, Weinreb RN. Meeting an unmet need in glaucoma: Continuous 24-h monitoring of intraocular pressure. *Expert Rev Med Devices* 2012;9:225-31.
785. Mansouri K, Gillmann K. Intereye symmetry of 24-hour intraocular pressure-related patterns in untreated glaucoma patients using a contact lens sensor. *J Glaucoma* 2020.
786. Hjortdal JO, Jensen PK. In vitro measurement of corneal strain, thickness, and curvature using digital image processing. *Acta Ophthalmol Scand* 1995;73:5-11.
787. Zeyen TG, Caprioli J. Progression of disc and field damage in early glaucoma. *Arch Ophthalmol* 1993;111:62-5.
788. Caprioli J, Prum B, Zeyen T. Comparison of methods to evaluate the optic nerve head and nerve fiber layer for glaucomatous change. *Am J Ophthalmol* 1996;121:659-67.
789. Airaksinen PJ, Tuulonen A, Alanko HI. Rate and pattern of neuroretinal rim area decrease in ocular hypertension and glaucoma. *Arch Ophthalmol* 1992;110:206-10.
790. Bradley C, Hou K, Herbert P, et al. Evidence-based guidelines for the number of peripapillary OCT scans needed to detect glaucoma worsening. *Ophthalmology* 2023;130:39-47.
791. Dong ZM, Wollstein G, Schuman JS. Clinical utility of optical coherence tomography in glaucoma. *Invest Ophthalmol Vis Sci* 2016;57:OCT556-67.
792. Scuderi G, Fragiotta S, Scuderi L, et al. Ganglion cell complex analysis in glaucoma patients: What can it tell us? *Eye Brain* 2020;12:33-44.
793. Chang RT, Knight OJ, Feuer WJ, Budenz DL. Sensitivity and specificity of time-domain versus spectral-domain optical coherence tomography in diagnosing early to moderate glaucoma. *Ophthalmology* 2009;116:2294-9.
794. Lederer DE, Schuman JS, Hertzmark E, et al. Analysis of macular volume in normal and glaucomatous eyes using optical coherence tomography. *Am J Ophthalmol* 2003;135:838-43.
795. Smith SD, Katz J, Quigley HA. Analysis of progressive change in automated visual fields in glaucoma. *Invest Ophthalmol Vis Sci* 1996;37:1419-28.
796. Katz J, Tielsch JM, Quigley HA, Sommer A. Automated perimetry detects visual field loss before manual Goldmann perimetry. *Ophthalmology* 1995;102:21-6.
797. Heijl A, Asman P. A clinical study of perimetric probability maps. *Arch Ophthalmol* 1989;107:199-203.
798. Jay JL, Murdoch JR. The rate of visual field loss in untreated primary open angle glaucoma. *Br J Ophthalmol* 1993;77:176-8.
799. Melchior B, De Moraes CG, Paula JS, et al. Frequency of optical coherence tomography testing to detect progression in glaucoma. *J Glaucoma* 2022;31:854-9.
800. Mohammadzadeh V, Fatehi N, Yarmohammadi A, et al. Macular imaging with optical coherence tomography in glaucoma. *Surv Ophthalmol* 2020;65:597-638.
801. Sabouri S, Haem E, Masoumpour M, et al. Frequency of visual fields needed to detect glaucoma progression: A computer simulation using linear mixed effects model. *J Glaucoma* 2023;32:355-60.
802. Medeiros FA, Malek DA, Tseng H, et al. Short-term detection of fast progressors in glaucoma: The fast progression assessment through clustered evaluation (Fast-PACE) study. *Ophthalmology* 2024;131:645-57.
803. Melchior B, De Moraes CG, Paula JS, et al. What is the optimal frequency of visual field testing to detect rapid progression among hypertensive eyes? *J Glaucoma* 2023;32:721-4.
804. Gardiner SK, Crabb DP. Frequency of testing for detecting visual field progression. *Br J Ophthalmol* 2002;86:560-4.
805. Viswanathan AC, Hitchings RA, Fitzke FW. How often do patients need visual field tests? *Graefes Arch Clin Exp Ophthalmol* 1997;235:563-8.
806. Crabb DP, Garway-Heath DF. Intervals between visual field tests when monitoring the glaucomatous patient: Wait-and-see approach. *Invest Ophthalmol Vis Sci* 2012;53:2770-6.
807. Chauhan BC, Mikelberg FS, Balazsi AG, et al. Canadian Glaucoma Study: 2. Risk factors for the progression of open-angle glaucoma. *Arch Ophthalmol* 2008;126:1030-6.
808. Rabiolo A, Montesano G, Crabb DP, et al. Relationship between intraocular pressure fluctuation and visual field progression rates in the United Kingdom Glaucoma Treatment Study. *Ophthalmology* 2024;131:902-13.
809. Kim JH, Rabiolo A, Morales E, et al. Risk factors for fast visual field progression in glaucoma. *Am J Ophthalmol* 2019;207:268-78.
810. Kwon YH, Kim YI, Pereira ML, et al. Rate of optic disc cup progression in treated primary open-angle glaucoma. *J Glaucoma* 2003;12:409-16.

811. Martus P, Stroux A, Budde WM, et al. Predictive factors for progressive optic nerve damage in various types of chronic open-angle glaucoma. *Am J Ophthalmol* 2005;139:999-1009.
812. Nouri-Mahdavi K, Hoffman D, Gaasterland D, Caprioli J. Prediction of visual field progression in glaucoma. *Invest Ophthalmol Vis Sci* 2004;45:4346-51.
813. Daugeliene L, Yamamoto T, Kitazawa Y. Risk factors for visual field damage progression in normal-tension glaucoma eyes. *Graefes Arch Clin Exp Ophthalmol* 1999;237:105-8.
814. Suh MH, Park KH, Kim H, et al. Glaucoma progression after the first-detected optic disc hemorrhage by optical coherence tomography. *J Glaucoma* 2012;21:358-66.
815. Kernstock C, Dietzsch J, Januschowski K, et al. Optical coherence tomography shows progressive local nerve fiber loss after disc hemorrhages in glaucoma patients. *Graefes Arch Clin Exp Ophthalmol* 2012;250:583-7.
816. Wang YX, Hu LN, Yang H, et al. Frequency and associated factors of structural progression of open-angle glaucoma in the Beijing Eye Study. *Br J Ophthalmol* 2012;96:811-5.
817. De Moraes CG, Liebmann JM, Park SC, et al. Optic disc progression and rates of visual field change in treated glaucoma. *Acta Ophthalmol* 2013;91:e86-91.
818. Kim JM, Kyung H, Azarbod P, et al. Disc haemorrhage is associated with the fast component, but not the slow component, of visual field decay rate in glaucoma. *Br J Ophthalmol* 2014;98:1555-9.
819. Komori S, Ishida K, Yamamoto T. Results of long-term monitoring of normal-tension glaucoma patients receiving medical therapy: Results of an 18-year follow-up. *Graefes Arch Clin Exp Ophthalmol* In press.
820. Tezel G, Siegmund KD, Trinkaus K, et al. Clinical factors associated with progression of glaucomatous optic disc damage in treated patients. *Arch Ophthalmol* 2001;119:813-8.
821. Stewart WC, Kolker AE, Sharpe ED, et al. Factors associated with long-term progression or stability in primary open-angle glaucoma. *Am J Ophthalmol* 2000;130:274-9.
822. Jonas JB, Martus P, Horn FK, et al. Predictive factors of the optic nerve head for development or progression of glaucomatous visual field loss. *Invest Ophthalmol Vis Sci* 2004;45:2613-8.
823. Brandt JD. Corneal thickness in glaucoma screening, diagnosis, and management. *Curr Opin Ophthalmol* 2004;15:85-9.
824. Papadia M, Sofianos C, Iester M, et al. Corneal thickness and visual field damage in glaucoma patients. *Eye (Lond)* 2007;21:943-7.
825. Rossi GC, Pasinetti GM, Scudeller L, et al. Do adherence rates and glaucomatous visual field progression correlate? *Eur J Ophthalmol* 2011;21:410-4.
826. Stewart WC, Chorak RP, Hunt HH, Sethuraman G. Factors associated with visual loss in patients with advanced glaucomatous changes in the optic nerve head. *Am J Ophthalmol* 1993;116:176-81.
827. Granstrom PA. Progression of visual field defects in glaucoma. Relation to compliance with pilocarpine therapy. *Arch Ophthalmol* 1985;103:529-31.
828. Newman-Casey PA, Niziol LM, Gillespie BW, et al. The association between medication adherence and visual field progression in the collaborative initial glaucoma treatment study. *Ophthalmology* 2020.
829. Kass MA, Kolker AE, Becker B. Prognostic factors in glaucomatous visual field loss. *Arch Ophthalmol* 1976;94:1274-6.
830. Chen PP, Bhandari A. Fellow eye prognosis in patients with severe visual field loss in 1 eye from chronic open-angle glaucoma. *Arch Ophthalmol* 2000;118:473-8.
831. Chen PP. Correlation of visual field progression between eyes in patients with open-angle glaucoma. *Ophthalmology* 2002;109:2093-9.
832. Fontana L, Armas R, Garway-Heath DF, et al. Clinical factors influencing the visual prognosis of the fellow eyes of normal tension glaucoma patients with unilateral field loss. *Br J Ophthalmol* 1999;83:1002-5.
833. Jonas JB, Stroux A, Velten I, et al. Central corneal thickness correlated with glaucoma damage and rate of progression. *Invest Ophthalmol Vis Sci* 2005;46:1269-74.
834. Vogel R, Crick RP, Mills KB, et al. Effect of timolol versus pilocarpine on visual field progression in patients with primary open-angle glaucoma. *Ophthalmology* 1992;99:1505-11.
835. Coleman AL, Caprioli J. The logic behind target intraocular pressure. *Am J Ophthalmol* 2009;147:379-80.
836. Damji KF, Behki R, Wang L. Canadian perspectives in glaucoma management: Setting target intraocular pressure range. *Can J Ophthalmol* 2003;38:189-97.
837. European Glaucoma Society. Terminology and guidelines for glaucoma. 4th ed. Savona, Italy:Editrice dogma s.R.L.; 2014:138. .
838. Lim MC, Shiba DR, Clark IJ, et al. Personality type of the glaucoma patient. *J Glaucoma* 2007;16:649-54.
839. Odberg T, Jakobsen JE, Hultgren SJ, Halseide R. The impact of glaucoma on the quality of life of patients in Norway. II. Patient response correlated to objective data. *Acta Ophthalmol Scand* 2001;79:121-4.

840. Lundmark PO, Trope GE, Shapiro CM, Flanagan JG. Depressive symptomatology in tertiary-care glaucoma patients. *Can J Ophthalmol* 2009;44:198-204.
841. Mabuchi F, Yoshimura K, Kashiwagi K, et al. High prevalence of anxiety and depression in patients with primary open-angle glaucoma. *J Glaucoma* 2008;17:552-7.
842. Skalicky S, Goldberg I. Depression and quality of life in patients with glaucoma: A cross-sectional analysis using the geriatric depression scale-15, assessment of function related to vision, and the glaucoma quality of life-15. *J Glaucoma* 2008;17:546-51.
843. Juzych MS, Randhawa S, Shukairy A, et al. Functional health literacy in patients with glaucoma in urban settings. *Arch Ophthalmol* 2008;126:718-24.
844. Kass MA, Hodapp E, Gordon M, et al. Part I. Patient administration of eyedrops: Interview. *Ann Ophthalmol* 1982;14:775-9.
845. Chamberlain NN, McKinney JK, Yang L, et al. Analysis of legal verbiage in state legislation for insurer coverage of early eyedrop refills in the United States. *Ophthalmol Glaucoma* 2024.
846. Sherwood MB, Garcia-Siekavizza A, Meltzer MI, et al. Glaucoma's impact on quality of life and its relation to clinical indicators: A pilot study. *Ophthalmology* 1998;105:561-6.
847. Hein JC, Tauber J, Shrivastava A. Refractive surgery for the glaucoma suspect. *Curr Opin Ophthalmol* 2023;34:290-5.
848. Cameron BD, Saffra NA, Strominger MB. Laser in situ keratomileusis-induced optic neuropathy. *Ophthalmology* 2001;108:660-5.
849. Lyle WA, Jin GJ, Jin Y. Interface fluid after laser in situ keratomileusis. *J Refract Surg* 2003;19:455-9.
850. Galal A, Artola A, Belda J, et al. Interface corneal edema secondary to steroid-induced elevation of intraocular pressure simulating diffuse lamellar keratitis. *J Refract Surg* 2006;22:441-7.
851. Hamilton DR, Manche EE, Rich LF, Maloney RK. Steroid-induced glaucoma after laser in situ keratomileusis associated with interface fluid. *Ophthalmology* 2002;109:659-65.
852. Hong ASY, Ang BCH, Dorairaj E, Dorairaj S. Premium intraocular lenses in glaucoma-a systematic review. *Bioengineering (Basel)* 2023;10.
853. Jackson ML, Virgili G, Shepherd JD, et al. Vision rehabilitation Preferred Practice Pattern®. *Ophthalmology* 2023;130:P271-P335.
854. Ramulu PY, Mihailovic A, E JY, et al. Environmental features contributing to falls in persons with vision impairment: The role of home lighting and home hazards. *Am J Ophthalmol* 2021;230:207-15.
855. Sotimehin AE, Yonge AV, Mihailovic A, et al. Locations, circumstances, and outcomes of falls in patients with glaucoma. *Am J Ophthalmol* 2018;192:131-41.
856. Center for Vision and Population Health. Vision loss and mental health: Key takeaways from an interprofessional task force. <https://preventblindness.org/wp-content/uploads/2023/05/mental-health-issue-brief.pdf> Accessed September 6, 2025.
857. Varma R, Lee PP, Goldberg I, Kotak S. An assessment of the health and economic burdens of glaucoma. *Am J Ophthalmol* 2011;152:515-22.
858. Ramulu P. Glaucoma and disability: Which tasks are affected, and at what stage of disease? *Curr Opin Ophthalmol* 2009;20:92-8.
859. Haymes SA, Leblanc RP, Nicoleta MT, et al. Risk of falls and motor vehicle collisions in glaucoma. *Invest Ophthalmol Vis Sci* 2007;48:1149-55.
860. McKean-Cowdin R, Varma R, Wu J, et al. Severity of visual field loss and health-related quality of life. *Am J Ophthalmol* 2007;143:1013-23.
861. Rein DB, Zhang P, Wirth KE, et al. The economic burden of major adult visual disorders in the United States. *Arch Ophthalmol* 2006;124:1754-60.
862. Kymes SM, Plotzke MR, Li JZ, et al. The increased cost of medical services for people diagnosed with primary open-angle glaucoma: A decision analytic approach. *Am J Ophthalmol* 2010;150:74-81.
863. Real JP, Lafuente MC, Palma SD, Tartara LI. Direct costs of glaucoma: Relationship between cost and severity of the disease. *Chronic Illn* 2020;16:266-74.
864. Lee PP, Walt JG, Doyle JJ, et al. A multicenter, retrospective pilot study of resource use and costs associated with severity of disease in glaucoma. *Arch Ophthalmol* 2006;124:12-9.
865. Lindblom B, Nordmann JP, Sellem E, et al. A multicentre, retrospective study of resource utilization and costs associated with glaucoma management in france and sweden. *Acta Ophthalmol Scand* 2006;84:74-83.
866. Poulsen PB, Buchholz P, Walt JG, et al. Cost-analysis of glaucoma-related blindness in Europe. *International Congress Series* 2005;1292:262-6.
867. Thygesen J, Aagren M, Arnavielle S, et al. Late-stage, primary open-angle glaucoma in Europe: Social and health care maintenance costs and quality of life of patients from 4 countries. *Curr Med Res Opin* 2008;24:1763-70.

868. Rathi S, Andrews C, Greenfield DS, Stein JD. A comparison of resource use and costs of caring for patients with exfoliation syndrome glaucoma versus primary open-angle glaucoma. *Am J Ophthalmol* 2019;200:100-9.
869. Rein DB, Wittenborn JS, Lee PP, et al. The cost-effectiveness of routine office-based identification and subsequent medical treatment of primary open-angle glaucoma in the United States. *Ophthalmology* 2009;116:823-32.
870. Stein JD, Kim DD, Peck WW, et al. Cost-effectiveness of medications compared with laser trabeculoplasty in patients with newly diagnosed open-angle glaucoma. *Arch Ophthalmol* 2012;130:497-505.
871. Toteberg-Harms M, Berlin MS, Meier-Gibbons F. Increasing healthcare costs: Can we influence the costs of glaucoma care? *Curr Opin Ophthalmol* 2017;28:127-32.
872. Newman-Casey PA, Salman M, Lee PP, Gatwood JD. Cost-utility analysis of glaucoma medication adherence. *Ophthalmology* 2020;127:589-98.
873. Hung A, Williams AM, Newman-Casey PA, et al. Cost-utility analysis of a medication adherence-enhancing educational intervention for glaucoma. *Ophthalmol Glaucoma* 2023;6:395-404.
874. Williams AM, Theophanous C, Muir KW, et al. Within-trial cost-effectiveness of an adherence-enhancing educational intervention for glaucoma. *Am J Ophthalmol* 2022;244:216-27.
875. King AJ, Fernie G, Hudson J, et al. Primary trabeculectomy versus primary glaucoma eye drops for newly diagnosed advanced glaucoma: TAGS RCT. *Health Technol Assess* 2021;25:1-158.
876. Kaplan RI, De Moraes CG, Cioffi GA, et al. Comparative cost-effectiveness of the Baerveldt implant, trabeculectomy with mitomycin, and medical treatment. *JAMA Ophthalmol* 2015;133:560-7.
877. Elhusseiny AM, Yannuzzi NA, Khodeiry MM, et al. Cost-analysis of surgical intraocular pressure management in glaucoma. *J Glaucoma* 2021;30:947-51.
878. Agrawal P, Bradshaw SE. Systematic literature review of clinical and economic outcomes of micro-invasive glaucoma surgery (MIGS) in primary open-angle glaucoma. *Ophthalmol Ther* 2018;7:49-73.
879. Ahmed Ik I, Hussein I, Saheb H, et al. Cost-effectiveness analysis of Hydrus microstent for patients with mild to moderate primary open-angle glaucoma in Canada. *Ophthalmol Glaucoma* 2025.
880. Nieland K, Labbe A, Schweitzer C, et al. A cost-effectiveness analysis of iStent inject combined with phacoemulsification cataract surgery in patients with mild-to-moderate open-angle glaucoma in France. *PLoS One* 2021;16:e0252130.
881. Healey PR, Tilden D, Jackson D, Aghajanian L. A cost-utility analysis of trabecular bypass devices versus usual care for patients with open-angle glaucoma. *Pharmacoecon Open* 2022;6:355-65.
882. Fea AM, Cattel F, Gandolfi S, et al. Cost-utility analysis of trabecular micro-bypass stents (TBS) in patients with mild-to-moderate open-angle glaucoma in Italy. *BMC Health Serv Res* 2021;21:824.
883. Sood S, Heilenbach N, Sanchez V, et al. Cost-effectiveness analysis of minimally invasive trabecular meshwork stents with phacoemulsification. *Ophthalmol Glaucoma* 2022;5:284-96.