Table 1. Statements in the 2005 American Academy of Ophthalmology primary open angle glaucoma Preferred Practice Pattern translated into clinical questions

Statements in the 2005 AAO POAG PPP (ordered as in PPP)*	Restated clinical questions and question number
"The IOP can be lowered by medical treatment, or by laser, filtering, or cyclodestructive surgery (alone or in combination). The choice of initial therapy depends on numerous considerations, and discussion of treatment with the patient should include appropriate options. [A: III] In many instances, topical medications constitute effective initial therapy. [56] [A:I]	**1.** Is medical therapy an effective initial treatment in lowering IOP in patients with POAG? **9.** Does discussion of the treatment options for lowering IOP (medical, laser, filtering or cyclodestructive surgery) affect the patient's choice of initial therapy?
The prostaglandin analogs and the beta adrenergic antagonists are the most frequently used eye drops for lowering IOP in patients with glaucoma.	**2.** Are prostaglandin analog eye-drops effective in lowering IOP in patients with POAG? **3.** Are beta-adrenergic antagonist eye-drops effective in lowering IOP in patients with POAG?
Agents less frequently used include alpha$_2$ adrenergic agonists, topical and oral carbonic anhydrase inhibitors, and parasympathomimetics.	**4.** Are alpha2 adrenergic agonist eye-drops effective in lowering IOP in patients with POAG? **5.** Are topical and oral carbonic anhydrase inhibitors effective in lowering IOP in patients with POAG? **6.** Are parasympathomimetic eye-drops effective in lowering IOP in patients with POAG?
To determine the effectiveness of topical therapy, it is necessary to distinguish between the therapeutic impact of an agent on IOP and ordinary background fluctuations of IOP. It may be useful to begin by treating only eye and comparing the relative change of the IOP in the two eyes at follow-up visits. However, because the two eyes of an individual may not respond equally to the same medication, and because of the possibility of asymmetric spontaneous fluctuations and the potential for contralateral effect monocular topical medications, [143] it is an acceptable alternative to compare the effect in one eye relative to multiple baseline measurements. [144]	**8.** Is treating one eye initially, and comparing it to the other initially untreated eye, a useful way of determining the pressure lowering efficacy of a topical ocular hypotensive agent?
If a drug fails to reduce IOP, it should be replaced with an alternative agent until effective medical treatment is established. [A:III] If a single medication is effective in lowering IOP but the target pressure is not reached, combination therapy or switching to an alternative therapy may be appropriate. The patient and the ophthalmologist may decide that it is impractical or impossible to use multiple medicines simultaneously and then it is important to consider alternative approaches (see subsections on surgical procedures).	**7.** Is combination medication effective in lowering IOP in patients with POAG?
The ophthalmologist should discuss the benefits and risks of medical treatment with the patient. [B:III]	**10.** Does discussion of the benefits and harms of medical treatment with patients affect patient satisfaction?
The ophthalmologist should assess the patient who is being treated with glaucoma medication for local and systemic side effects, toxicity, and possible interactions with other medications. [A:III] The ophthalmologist must be prepared to recognize potential life-threatening adverse reactions. [A:III]	**11.** Does routine assessment help reduce systemic side effects, toxicity, and possible interactions of glaucoma medication?
To reduce systemic absorption, patient should be educated about eyelid closure or nasolacrimal occlusion when applying topical medications. [145] [B:II]	**12.** Does patient education about eyelid closure or nasolacrimal occlusion help reduce systemic absorption when applying topical medications?
Adequate treatment of glaucoma requires a high level of adherence to therapy. Frequently this is not achieved; studies indicate relatively poor adherence to therapy in one-third or more of patients, depending on the mediations used. [146, 147] Repeated instruction in proper techniques for using medication may improve adherence to therapy. [145.148.149]	**13.** Are interventions (e.g., repeated instruction, patient education) effective for improving adherence to medical therapy and efficacy of medical therapy in patients with POAG?

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At each examination, medication dosage and frequency of use should be recorded. Adherence to the therapeutic regimen and the patient's responses to recommendations for therapeutic alternatives or diagnostic procedures should be discussed. [A:III] Cost may be a factor in adherence, especially when multiple medications are used. [149] Patient education and informed participation in treatment decisions may improve adherence[149] and overall effectiveness of glaucoma management.	
Laser trabeculoplasty is an appropriate initial therapeutic alternative. [56 [A:I]] Laser trabeculoplasty increases aqueous outflow and provides a clinically significant reduction of IOP in more than 75% of initial treatments of previously unoperated eyes.[56,58]	**14.** Is laser trabeculoplasty an effective initial treatment in lowering IOP in patients with POAG?
Selective laser trabeculoplasty is a form of pulsed green laser anterior-chamber angle treatment that, in the short term, appears to be as effective as other trabeculoplasty techniques in lowering IOP.[150]	**15.** What is the relative effectiveness of selective laser trabeculoplasty compared with other trabeculoplasty techniques in lowering IOP in patients with POAG?
Laser trabeculectomy is an alternative for patients who cannot or will not use medications reliably due to cost, memory problems, difficulty with instillation, or intolerance to the medication.	**16.** Is laser trabeculectomy effective in patients with POAG who cannot or will not use medications reliably?
The amount of medical treatment required for glaucoma is occasionally reduced after trabeculoplasty.[58]	**17.** Is laser trabeculoplasty effective in reducing the amount of medical treatment required in patients with POAG?
Results from long-term studies indicate that 30% to more than 50% of eyes require additional surgical treatment within 5 years after laser trabeculoplasty.[58,151-154] For eyes that have failed to maintain a previously adequate response, repeat laser trabeculoplasty has a low long-term rate of success, with failure occurring in nearly 90% of these eyes by 2 years.[155-159] After previous applications to the full circumference of the anterior-chamber angle, repeat laser trabeculoplasty is almost never successful in eyes that have not had a reduction in IOP for at least a year following the first laser surgery.[158] Compared with initial laser trabeculoplasty, there is an increased risk after repeat laser trabeculoplasty of problems and complications, such as IOP spikes.[155,156,159,160]	**18.** Is repeat laser trabeculoplasty effective and safe in lowering IOP in patients with POAG who have not responded adequately to the first laser surgery?
The ophthalmologist who performs the surgery must ensure that the patient receives adequate postoperative care.[161 [A:III]] The plan for care prior to and after laser trabeculoplasty should include the following elements: • At least one preoperative evaluation and IOP measurement by the surgeon.[161 [A:III]] • Informed consent prior to surgery.[162,163 [A:III]] (Ethical or legal statement) • At least one IOP check within 30 to 120 minutes of surgery.[164 [A:I]] • 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.[151,165-167 [A:III]]	**19.** Does preoperative care (e.g., preoperative evaluation, IOP measurement, informed consent) result in better outcomes in patients scheduled to undergo laser trabeculoplasty? **20.** Does postoperative care (e.g., IOP check within 30-120 minutes of surgery, follow-up examination within 6 weeks of surgery) result in better outcomes in patients who undergo laser trabeculoplasty?
Medications that are not being used chronically may be used perioperatively to avert temporary IOP elevations, particularly in those patients with severe disease.[164,168,169]	**21.** Are perioperative medications (not being used chronically) effective in preventing temporary IOP elevations in patients who undergo laser trabeculoplasty?
Filtering surgery is effective at lowering IOP and may sometimes be an appropriate initial therapeutic alternative instead of medications or laser trabeculoplasty. [44,45,139,140 [A:I]] Filtering surgery provides an alternative path for the escape of aqueous humor, and it often reduces IOP and the need for medical treatment. The best estimate of the failure rate of filtering surgery alone or combined with medical therapy in a previously unoperated eye comes from the Advanced Glaucoma Intervention Study.[58] The 10-year results indicate about 30% failure in African American patients and 20% failure in Caucasian American patients. [58]	**22.** Is filtering surgery an effective and safe (initial) treatment in lowering the IOP in patients with POAG?

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Furthermore, filtering surgery increases the likelihood that phakic eyes will undergo cataract surgery.[105,173,174]	
While long-term control is often achieved, many patients will require further therapy or a re-operation, which carries a higher failure rate.[58,170-172]	**23.** Are one or more repeat filtering surgeries effective and safe for POAG patients with failed response to an initial filtering procedure?
In eyes that have undergone previous cataract surgery involving the conjunctiva, the success rate of initial glaucoma surgery is reduced.[57]	**24.** Is filtering surgery effective in eyes that have undergone previous cataract surgery involving the conjunctiva?
Antifibrotic agents may be used intraoperatively and postoperatively to reduce the subconjunctival scarring after filtration surgery that can result in failure of the operation. The use of intraoperative mitomycin C reduces the risk of surgical failure both in eyes at high risk of surgical failure[175,176] and in eyes that have not undergone previous surgery.[176-179] Some studies have demonstrated a benefit of intraoperative 5-fluorouracil[180,181] and others have not.[182] The use of postoperative injections of 5-fluorouracil also reduces the likelihood of surgical failure in both high-risk eyes[57,183-185] and eyes that have not undergone previous surgery.[185-187] The use of an antifibrotic agent carries with it an increased likelihood of bleb-related complications such as hypotony,[188-190] hypotony maculopathy,[188] late-onset bleb leak,[185,191] and late-onset infection[192,193] that must be weighed against the benefits when deciding whether or not to use these agents. These complications may be even more common in primary filtering surgery of phakic patients.[194-196]	**25.** Is intraoperative mitomycin C effective and safe in improving the success rate of primary and repeat filtering surgery? **26.** Is intraoperative 5-fluorouracil effective and safe in improving the success rate of primary and repeat filtering surgery? **27.** Is postoperative mitomycin C effective and safe in improving the success rate of primary and repeat filtering surgery? **28.** Is postoperative 5-fluorouracil effective and safe in improving the success rate of primary and repeat filtering surgery?
Nonpenetrating glaucoma surgery is being used as an alternative to trabeculectomy in selected patients by some surgeons. (Not a recommendation) The two main types of nonpenetrating glaucoma surgery are viscocanalostomy and nonpenetrating deep sclerectomy. (Not a recommendation) The rationale for nonpenetrating glaucoma surgery is that by avoiding a continuous passageway from the anterior chamber to the subconjunctival space, the incidence of bleb-related problems and hypotony can be reduced. The nonpenetrating procedures have a higher degree of surgical difficulty compared with trabeculectomy and require special instrumentation. (Not a recommendation) Randomized clinical trials comparing viscocanalostomy with trabeculectomy generally suggest both greater IOP reduction and more complications with trabeculectomy than with viscocanalostomy.[197-201] One randomized clinical trial found that trabeculectomy was more effective than nonpenetrating deep sclerectomy at lowering IOP,[202] and one found that the two surgeries were equally effective.[203] The precise role of nonpenetrating surgery in the surgical management of glaucoma remains to be determined. (Not a recommendation)	**29.** Is viscocanalostomy effective in lowering IOP in patients with POAG? **30.** Is nonpenetrating deep sclerectomy effective and safe in lowering IOP in patients with POAG? **31.** What is the relative effectiveness of viscocanalostomy compared with trabeculectomy in lowering IOP in patients with POAG? **32.** What is the relative effectiveness of nonpenetrating deep sclerectomy compared with trabeculectomy in lowering IOP in patients with POAG?
The use of drainage devices (such as those described by Molteno,[204] Ahmed,[205] Krupin,[206] Baerveldt,[207] and others) is generally reserved for patients who have failed filtering surgery with antimetabolites or for patients whose conjunctiva is so scarred from previous surgery that filtering surgery with antimetabolites is at high risk for failure.	**33.** Is use of drainage devices effective and safe in management of POAG among patients with failed filtering surgery/scarred conjunctiva/poor prognosis of filtration surgery?
Patients who require filtration surgery and who also have cataract may benefit from simultaneous cataract and glaucoma surgery, as may glaucoma patients with a visually significant cataract and severe, but well-controlled, glaucoma. Generally, combined cataract and glaucoma surgery is not as effective as glaucoma surgery alone in lowering intraocular pressure,[208,209] so patients who require filtration surgery who also have mild cataract may be better served by filtration surgery alone and cataract surgery later.[B:III]	**34.** Is sequential filtration and cataract surgery more effective than combined procedures in lowering IOP in patients with POAG and cataract?
The use of mitomycin C, but not 5-flurouracil, results in lower IOP in combined procedures.[176,208,209]	**35.** Is mitomycin C effective in lowering IOP in combined glaucoma and cataract procedures?

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Separating the cataract and glaucoma incisions results in lower IOP than a one-site combined procedure, but the differences in outcomes are small.[208,209]	**36.** Are combined glaucoma and cataract procedures with separate incisions more effective than a one-site incision?
Cataract surgery alone sometimes results in a modest reduction of IOP.[210]	**37.** Is cataract surgery alone effective in lowering IOP in patients with POAG and cataract?
The plan for care before filtering surgery should include the following elements: • At least one preoperative evaluation by the surgeon.[161 [A:III]] • Informed consent prior to surgery.[163 [A:III]] (Ethical or legal statement)	**38.** Does preoperative care (e.g., preoperative evaluation, informed consent) by the surgeon result in better outcomes in patients scheduled to undergo filtering surgery?
• The ophthalmologist who performs the surgery must ensure that the patient receives adequate postoperative care, which includes the following:[161 [A:III]] • Use of topical corticosteroids in the postoperative period, unless contraindicated.[211,212 [A:II]] • Follow-up evaluation on the first postoperative day (12 to 36 hours after surgery) by the surgeon and at least once from the second to the tenth postoperative day to evaluate visual acuity, IOP, and status of the anterior segment.[213-218 [A:II]] • In the absence of complications, additional postoperative visits during a 6-week period to evaluate visual acuity, IOP, and status of the anterior segment.[213-218 [A:III]] • 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 formation.[213-218 [A:III]] • Additional treatments as necessary, including surgical procedures to correct a flat anterior chamber, repair bleb leaks, perform bleb massage, perform suture lysis, or perform bleb needling or other surgical revisions of the bleb to maximize the chances for a successful long-term result.[[A:III]] • A discussion between the surgeon and the patient to explain that filtration surgery places the eye at risk for endophthalmitis for the duration of the patient's life, and that the patient must regard the symptoms of pain and decreased vision and the signs of redness and discharge as a medical emergency that requires medical attention. (Ethical or legal statement)	**39.** Does postoperative care (e.g., topical corticosteroids,bleb leaks repair, bleb massage, suture lysis,etc) result in better outcomes in patients who undergo filtering surgery? **40.** Does the use of topical corticosteroids in the postoperative period improve patient outcomes? **41.** Do additional surgical procedures such as flat anterior chamber correction, bleb leaks repair, bleb massage, suture lysis, and bleb needling improve the long-term result for patients who undergone filtering surgery?
Cyclodestructive procedures reduce the rate of aqueous production. In recent years, cyclodestructive procedures are more commonly performed using a transscleral laser delivery system but they can also be performed endoscopically.[219] (Not a recommendation) Because cyclodestructive procedures have been associated with subsequent decrease of visual acuity,[220,221] and, rarely, cases of sympathetic ophthalmia,[222,223] they are often reserved for eyes with reduced visual acuity and patients who are poor candidates for incisional surgery. A small case series with follow-up of at least 13 months showed good preservation of visual acuity in most eyes after laser cyclophotocoagulation.[224] Disadvantages of cyclodestructive procedures include postoperative inflammation and the necessity for additional steps of treatment weeks or months later.[225] Cyclodestructive procedures have advantages over filtration surgery that include technical ease, rapid recovery, reduced postoperative care, and reduced likelihood of the complications of bleeding and infection. The advantages and disadvantages of a cyclodestructive procedure compared with a filtration operation or a tube shunt procedure should be discussed with patients who are poor surgical candidates, have limited visual potential, or have	**42.** Are cyclodestuctive procedures effective and safe in the treatment of POAG patients who are poor incisional surgical candidate, have limited visual potential, or have undergone multiple previous glaucoma operations?

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undergone multiple previous glaucoma operations.[A:III] (Ethical or legal statement)	
The indications for adjusting therapy are as follows:[A:III] • Target IOP is not achieved. • A patient has progressive optic nerve damage despite achieving the target IOP. The validity of the diagnosis and target pressure should be reassessed.[A:III] Additional evaluation may reveal conditions that are contributing to the progression of damage and serving as a justification to escalate therapy. These evaluations include obtaining diurnal IOP measurements, repeating the central corneal thickness measurement to verify a thin cornea or a change in corneal thickness after refractive surgery, or seeking evidence of unrecognized low ocular perfusion pressure.[10] A neurologic evaluation also may be considered. • Patient is intolerant of the prescribed medical regimen. (Ethical or legal statement) • Patient does not adhere to the prescribed medical regimen. (Ethical or legal statement) • Contraindications to individual medicines develop. (Ethical or legal statement) • Stable optic nerve status and low IOP occurs for a prolonged period in a patient on pressure-lowering medications. 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 or visual field change.[232, 233 [A:III]] Upward adjustment of target pressure should be considered if the patient has been stable and if the patient either requires (because of side effects) or desires less medication.[B:III] The ophthalmologist should plan a follow-up visit in 2 to 8 weeks to assess the response and side effects from washout of the old medication or onset of maximum effect of the new medication.[A:III]"	**43.** Do the recommended indications (i.e., target IOP not achieved, etc.) for adjusting therapy improve outcomes in patient with POAG? **44.** In patients with stable optic nerve status and low IOP, is discontinuation of medication (or upward adjustment of IOP) effective and safe in terms of disease progression? **45.** What is the optimal interval for follow-up visit to assess the response and side effects from washout of the old medication and onset of maximum effect of the new medication?

* Statements, including the reference number, ratings of importance and ratings of strength of evidence, are reproduced with permission from the American Academy of Ophthalmology Glaucoma Panel. Preferred Practice Pattern® Guidelines. Primary Open-Angle Glaucoma. San Francisco, CA: American Academy of Ophthalmology; 2005.

The ratings of importance are divided into three levels:
Level A, most important
Level B, moderately important
Level C, relevant but not critical

The ratings of strength of evidence are divided into three levels:
Level I: evidence obtained from at least one properly conducted, well-designed randomized controlled trial, or meta-analyses of randomized controlled trials.
Level II: evidence obtained from well-designed controlled trials without randomization; well-designed cohort or case-control analytic studies, preferably from more than one center, or multiple-time series with or without the intervention.
Level III: evidence obtained from descriptive studies, case reports, or reports of expert committees/organizations (e.g., PPP panel consensus with external peer review).

AAO American Academy of Ophthalmology
POAG Primary Open Angle Glaucoma
PPPs Preferred Practice Patterns
IOP Intraocular Pressure

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