Comparative Effectiveness of Eye Drops vs. Laser Trabeculoplasty

Final Report

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**Topic:** Comparative Effectiveness of Eye Drops vs. Laser Trabeculoplasty

**Overall Comparative Research Question:** What is the comparative effectiveness of eye drops versus laser trabeculoplasty to reduce excess morbidity from open-angle glaucoma in black and Hispanic individuals?

1. **Contributors**

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2. **Introduction**

Glaucoma is a chronic, progressive eye disease characterized by optic nerve damage and visual field loss. Glaucoma is classified into two broad categories: open-angle glaucoma (OAG) and angle-closure glaucoma; more than 80% of cases are OAG. Glaucoma can progress without causing symptoms until the disease is quite advanced, leading to visual impairment and blindness. The second leading cause of blindness worldwide after cataracts, glaucoma’s risk factors include older age, family history of glaucoma, elevated intraocular pressure (IOP), type 2 diabetes mellitus, and black race or Hispanic ethnicity. Several trials have shown that treatments reducing IOP—medications, laser therapy, and incisional surgery—can slow the progression of glaucoma. This topic brief focuses on medications and laser therapy, two treatments that physicians can deliver in an outpatient setting and that do not carry the surgical risks of infection and bleeding. Medical therapy with eye drops typically has been the first-line treatment for glaucoma, although a growing body of evidence suggests that laser trabeculoplasty, an office-based procedure that does not involve making an incision in the eye, can also be used as initial therapy, particularly if a patient struggles with adherence to daily medications. Thus, glaucoma treatment is a topic ripe for comparative effectiveness research—research that compares the benefits and harms of two efficacious treatment options to help physicians and patients make clinical decisions best suited for individual patients.

Glaucoma is characterized by a striking health disparity; black and Hispanic individuals are more likely to have the disease than white individuals, and the onset of blindness starts 10 years earlier in black individuals. In terms of the impact of health disparities on treatment, data on current treatments of eye drops and laser trabeculoplasty are sparse. Older studies that compared surgery with medications or laser therapy demonstrated that black and white individuals with medically uncontrolled OAG have different outcomes. For example, in the Advanced Glaucoma Intervention Study, vision was better preserved in black participants randomized to laser therapy compared with those randomized to surgery; in contrast, white participants undergoing surgery had better visual outcomes. However, more recent comparative effectiveness research has not examined how the effectiveness of current first-line treatment options used in practice—laser trabeculoplasty or eye drops—varies by racial or ethnic subgroups. In this brief, we review the burden of glaucoma, the current evidence base for glaucoma treatment, ongoing studies, and opportunities for new comparative effectiveness research.
3. **Patient Centeredness**

In the face of clinical uncertainty, patient-centered care becomes essential to the management of disease.\(^1\) Both medical and laser therapy are associated with slowing progression of disease.\(^2\) However, some patients may not opt for medical therapy because of the side effects and costs of daily medication.\(^3\) The need for retreatment 5 to 10 years after laser therapy may pose a concern for other patients.\(^4\) Patients can also find lifelong adherence to a chronic medication burdensome for several reasons. Patients with deteriorating vision from glaucoma may be unable to self-administer medications, or patients may struggle to comply with complex dosing schedules.\(^5\) Accordingly, some experts suggest laser therapy as first-line treatment for patients who have difficulties with adherence.\(^6\) Strong patient–provider communication and patient education can support decision making about a therapy that promotes improved patient outcomes and takes into consideration patients’ preferences.\(^7\) Patients and doctors should make treatment decisions in the context of the patient’s age, preferences, and degree of ocular damage.\(^8\) Furthermore, as discussed in the sections below, the impact of the disease and effect of treatment may vary by racial and ethnic subgroups, emphasizing the importance of patient-centered care.

4. **Burden of the Condition**

Glaucoma affects an estimated 2.9 million individuals in the United States; over half (54.3%) are unaware that they have the disease.\(^9\) The projected prevalence of OAG is expected to rise to 7.32 million by 2050.\(^1\) Glaucoma is the second leading cause of blindness worldwide.\(^2\) Furthermore, glaucoma can have a profound effect on a patient’s quality of life (QOL). As visual loss progresses, glaucoma patients can struggle with activities of daily living like walking, reading, and driving,\(^3\) although even patients early in disease can report reduced QOL.\(^4\)

As noted above, glaucoma disproportionately affects black and Hispanic individuals. Studies using the National Health and Nutrition Survey (NHANES) estimate the prevalence of glaucoma in black individuals at 3.7% compared with 2% for white individuals.\(^5\) Black individuals have roughly 4.4 times greater odds of having undiagnosed and untreated glaucoma than white individuals.\(^6\) Although rates of blindness increase with age for all individuals, studies show that the onset of blindness starts 10 years earlier for black individuals.\(^7\) Glaucoma is the leading cause of blindness in black individuals in the United States,\(^8\) whereas age-related macular degeneration is the leading cause for white individuals.\(^9\)

Estimates for glaucoma prevalence in Hispanic individuals range from 1.9% to 4.7%, and some studies report prevalence comparable with blacks.\(^10\) Hispanic individuals have 2.5 times greater odds of undiagnosed and untreated glaucoma than non-Hispanic whites in an NHANES study.\(^11\) In a study of the National Health Interview Survey, Dominicans and Central and South Americans were among the understudied racial and ethnic groups with high rates of self-reported visual impairment.\(^12\) Accounting for future demographic shifts, Hispanic men are predicted to be the largest demographic group with OAG in 2050.\(^13\)

Few studies compare prevalence of glaucoma across racial and ethnic groups.\(^14\) Furthermore, we do not have a clear understanding of the factors that underlie these observed health disparities; the reasons are likely multifactorial and include biologic and social determinants of health.
Advances in genetics research have led to the identification of several genetic variants associated with glaucoma. The African Descent and Glaucoma Evaluation Study (ADAGES) has identified anatomic differences in the eyes of black and white participants and was the first study powered to assess performance on several visual field-test variables. Whether these findings are associated with early onset of disease or more rapidly progressive disease remains to be seen.

Some studies have shown that black and Hispanic patients are less likely to be seen by an eye care provider and are less likely to undergo monitoring once diagnosed with glaucoma even when they have insurance. These patients also have lower rates of medical and surgical treatment than white patients. Patient factors such as poor understanding of disease, mistrust of the medical community, limited financial resources, and poor adherence to therapy also serve as barriers to diagnosis and treatment of glaucoma. Studies of patient–physician communication found that although patient education could improve adherence to medical therapy for glaucoma, providers were less likely to educate black patients about glaucoma than white patients.

5. Evidence Gaps

We identified evidence gaps primarily through a review of peer-reviewed primary studies and systematic reviews and supplemented our understanding through conversations with three key informants. Our key informants are clinical investigators and practicing ophthalmologists with appointments at major academic centers in the United States. They have led glaucoma studies with funding from multiple sources, including the Centers for Disease Control and Prevention, the National Eye Institute, and industry. (Appendix A lists our key informants.)

5.1 Literature Review

The mainstay of glaucoma treatment is reducing IOP, which can be achieved through medications (eye drops), laser therapy, or incisional surgery. Eye drops and laser therapy are provided in outpatient settings. The major classes of eye drops are prostaglandin analogues (e.g., latanoprost, travoprost), beta adrenergic antagonists (e.g., timolol, beta-blockers), carbonic anhydrase inhibitors (e.g., acetazolamide, dorzolamide), alpha2 adrenergic agonists, and combination treatments. Prostaglandins lower IOP more than other classes of medications and are currently used as first-line therapy. Laser therapies include argon laser trabeculoplasty (ALT) and more recently selective laser trabeculoplasty (SLT). The effectiveness of laser therapy decreases over 5 years of follow-up. Incisional surgeries, such as trabeculectomy, achieve the greatest reduction of IOP with longer lasting results compared with medical or laser therapy. However, incisional surgery carries the rare risk of intraocular infection and bleeding not present with medical or laser therapy and is outside the scope of the literature review for this topic brief.

We performed a systematic search using the populations, interventions, comparators, outcomes, timing, and setting (PICOTS) framework in Table 1 (Appendix B lists the search strategy). We identified five comparative effectiveness systematic reviews. Three reviews included the same primary studies, so we selected the review that included a meta-analysis to discuss below. The remaining primary studies we identified from title and abstract review were (1) included in one of the aforementioned systematic reviews, (2) protocols for ongoing studies discussed in Section 7, or (3) exclusions for wrong comparator, primarily older eye drops that are no longer used in clinical practice or no active comparator. We describe two major trials excluded for no active comparator below.
The Collaborative Normal Tension Glaucoma Study compared any treatment to reduce IOP (eye drops, laser therapy, or incisional surgery) with observation; likewise, the Early Manifest Glaucoma Trial compared a combination of laser therapy and eye drops with observation only. Both of these studies reported a 50% reduction in the progression of glaucoma, finding that even small changes in IOP can slow the progression of glaucoma. According to one key informant, the striking benefit of treatment observed in these seminal studies shifted the treatment paradigm away from observation to providing some form of IOP-lowering treatment when glaucoma is diagnosed. Thus, we did not include studies with an inactive comparator in our literature review.

Table 1. Eligibility Criteria for Studies on the Comparative Effectiveness of Laser Therapy versus Medical Therapy for Glaucoma

<table>
<thead>
<tr>
<th>PICOTS</th>
<th>Population: Adults &gt;40 years with OAG</th>
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<tbody>
<tr>
<td>Intervention</td>
<td>Laser trabeculoplasty or combination laser and medical therapy</td>
</tr>
<tr>
<td>Comparator</td>
<td>Medical therapy (eye drops)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Final health outcomes: Reduced visual impairment, patient-reported outcomes</td>
</tr>
<tr>
<td></td>
<td>Intermediate health outcomes: Reduced IOP, visual field loss, optic nerve damage</td>
</tr>
<tr>
<td></td>
<td>Harms: Adverse effects of eye drops or laser trabeculoplasty</td>
</tr>
<tr>
<td>Time frames</td>
<td>All</td>
</tr>
<tr>
<td>Setting</td>
<td>Outpatient settings</td>
</tr>
<tr>
<td>Study designs</td>
<td>Randomized controlled trials (RCTs)</td>
</tr>
</tbody>
</table>

IOP = intraocular pressure; OAG = open-angle glaucoma; RCT = randomized controlled trial.

5.1.1 Systematic Review: “Laser Trabeculoplasty for Open-Angle Glaucoma” (Rolim de Moura et al., 2007)

A Cochrane meta-analysis of three trials comparing ALT with medications reported that ALT reduced the chance of uncontrolled IOP at 6 months and 24 months (pooled relative risk [RR] 0.80, 95% confidence interval [CI] 0.71 to 0.91, I²=0%). The review found a lower but not statistically significant difference in the risk of visual field progression for ALT when compared with medications at the 2-year follow-up (RR 0.70, 95% CI 0.42 to 1.16, I² 0%). The review also reported no differences in optic nerve deterioration. Two older studies from the 1980s evaluated the effectiveness of ALT combined with medications in patients already using medications; patients receiving combined ALT and medications were less likely to fail therapy than those on medications alone. The review did not pool results because of the underlying heterogeneity of interventions. In terms of harms, two studies reported adverse effects of peripheral anterior synechiae in the ALT-treated patients (pooled RR 11.15, 95% CI 5.63 to 22.09, I²=0%) compared with medications. The primary outcomes of this review were all intermediate visual outcomes (failure to control IOP, failure to stabilize visual field progression, and failure to stabilize optic disc deterioration); authors found no evidence for outcomes related to visual impairment or vision-related QOL.

5.1.2 Systematic Review: “Treatment for Glaucoma: Comparative Effectiveness” (Boland et al., 2012)

Boland and associates, in a review for the Agency of Healthcare Research and Quality, examined the effect of medical, laser, and surgical treatments for OAG on intermediate and final visual health outcomes including harms. They report intermediate visual outcomes from Rolim de Moura et al. and three additional primary studies in which laser therapy and medication groups did not differ significantly in the change in IOP, visual field loss, and optic nerve deterioration. Regarding harms,
laser therapy did not carry the risk of ocular discomfort associated with medications. The reviewers identified no evidence regarding visual impairment outcomes.

5.1.3 Meta-analysis of SLT versus Topical Medication in the Treatment of OAG (Li et al., 2015)

A systematic review and meta-analysis by Li and associates included five studies comparing SLT with medications. Of these, three studies compared SLT with prostaglandin eye drops (current first-line therapy) and two studies compared SLT with medications from several classes. In the four studies that reported percent IOP reduction (IOPR\%) between the SLT and medication groups, the pooled results showed no significant difference between the two groups (weighted mean difference in IOPR\%=-1.90, 95\% CI -5\% to 1.1\%, \(I^2=0\%\)). The results were robust to sensitivity analyses of study type (RCT only) and medication comparator (prostaglandin only). Li and associates also found no significant difference in success rates between the two therapies, although the definition of success varied by study. Three studies reported adverse events, but the review did not pool the results. The reviewers did not report on visual impairment outcomes.

5.1.4 Summary of Systematic Reviews

In summary, the studies reviewed by Rolim de Moura and associates show that ALT or ALT in combination with medications reduces the risk of some intermediate visual health outcomes in glaucoma compared with medications alone. In comparison, results from Boland et al. and Li et al. show no significant differences in outcomes between medications and laser therapy. This difference may be due to the use of older eye drops in the studies of the Cochrane Review by Rolim de Moura et al., which are not as effective as first-line medical therapy typically used today (e.g., prostaglandins). None of the reviews reported race or ethnicity subgroup analyses for studies comparing laser therapy with medications.

5.2 Limitations

The authors of these reviews and our key informants highlighted several limitations in the body of evidence for glaucoma treatments.

5.2.1 Limitations in Comparative Effectiveness Research

Reviewers and key informants agreed that the number of studies that adequately compare two or more treatments over time is insufficient to draw conclusions about the comparative effectiveness of most currently used therapies. Much of the evidence comparing laser therapy with medical therapy relies on trials that used older medication therapies that do not have the improved clinical effectiveness or milder side effect profile of current first-line treatment with prostaglandins. Glaucoma research would also benefit from more rigorous study design, standardized diagnostic criteria for glaucoma and severity of disease, and standardized reporting of outcomes using the World Glaucoma Association guidelines.

5.2.2 Limited Research on Racial Disparities in Glaucoma Treatment

Evidence for racial disparities in glaucoma treatment comes from older studies that were excluded from our review for wrong intervention (e.g., surgery). The Advanced Glaucoma Study (2000–2004) and the Collaborative Initial Glaucoma Treatment Study (CIGTS) (2001) compared incisional surgery with laser therapy and medications, respectively. Both studies found that black participants had
worse outcomes than white participants who had surgery first.\textsuperscript{6,14} No studies on the differential impact of treatment on racial subgroups have been published since these two studies. Key informants and reviewers proposed additional RCTs to understand racial differences in response to laser therapy compared with medications.\textsuperscript{17}

5.2.3 Limited Reporting of Patient-Centered Outcomes

Most studies report intermediate outcomes but are not long enough to measure outcomes that ultimately matter to patients—visual impairment, vision-related QOL, or pragmatic outcomes like delaying the need for surgery.\textsuperscript{17,51} The minimal QOL data from treatment trials come from the CIGTS and Early Manifest Glaucoma trials, which were excluded from our review because they used surgery as a major intervention. Although ophthalmologic examination may show optic nerve deterioration, the patient may not have any disability in activities of daily living for years,\textsuperscript{65} thus emphasizing the need for data on patients’ experience of treatment to better tailor glaucoma management.

The challenges of measuring QOL in glaucoma lie in the chronic, indolent nature of the disease. The most commonly used measure is the National Eye Institute Visual Function Questionnaire (NEI-VFQ-25), which is not specific to glaucoma and may not capture the slow progressive changes in function in glaucoma as compared with, say, cataract disease. Some have suggested modifying the NEI-VFQ-25 to make it more glaucoma specific.\textsuperscript{66} Two key informants recommended developing better glaucoma-sensitive QOL measures.

6. Guidelines

Table 2 lists professional health organizations that offer guidelines for glaucoma management. In general, these guidelines recommend medications as first-line therapy, but none give a definitive recommendation.

<table>
<thead>
<tr>
<th>Organization, Year</th>
<th>Recommendations</th>
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<tr>
<td>American Academy of Ophthalmology, 2016\textsuperscript{22}</td>
<td>Medical treatment is the most common initial intervention. Laser trabeculoplasty can be considered as initial therapy in some specific patients or as an alternative for patients for whom adherence will be difficult.</td>
</tr>
<tr>
<td>American Academy of Family Physicians, 2016\textsuperscript{67}</td>
<td>Early treatment of patients with glaucoma is recommended to reduce the risk of visual field progression.</td>
</tr>
<tr>
<td>American Glaucoma Society, 2016\textsuperscript{68}</td>
<td>Treatment should be based on the therapy with the best chance of lowering the patient’s IOP.</td>
</tr>
<tr>
<td>Canadian Ophthalmological Society, 2009\textsuperscript{69}</td>
<td>The overarching aims of glaucoma management are to preserve visual function and maintain or enhance overall health-related QOL. This is achieved through a careful process of observing and monitoring visual function and providing patient education and support and medical, laser, or surgical intervention, as appropriate.</td>
</tr>
<tr>
<td>American Optometric Association, 2010\textsuperscript{70}</td>
<td>In the choice of a specific form of treatment or the decision to alter or provide additional therapy, the overriding consideration must be the risk or benefit to the patient. All forms of treatment for glaucoma have potential harms for the patient. The clinician must evaluate the possible impact of the treatment from a social, psychological, financial, and convenience standpoint.</td>
</tr>
</tbody>
</table>

IOP = intraocular pressure; OAG = open-angle glaucoma; QOL = quality of life.

7. Ongoing Research

We captured ongoing glaucoma research in our primary literature search and by searching ClinicalTrials.gov,\textsuperscript{71} NIHRePORTER,\textsuperscript{72} and HRSProj,\textsuperscript{73} and National Institutes of Health funding.\textsuperscript{74} We
found four active comparative effectiveness treatment trials for glaucoma, summarized in Table 3. All of these studies compare SLT to eye drops, specifically first-line medical therapy of prostaglandins or any topical medication. All studies assess intermediate ocular outcomes, including IOP reduction, visual field progression, and optic nerve deterioration; two are powered to examine health-related QOL as primary outcomes. The first study is conducted in an African population, although study protocols or descriptions did not include a subgroup analysis by race or ethnicity for any of the studies in Table 3.

Additionally, we identified a number of projects funded by the National Eye Institute aiming to identify genetic markers associated with OAG in blacks and Mexican Americans, as well as a few studies on aspects of glaucoma management in these subgroups (i.e., adherence in blacks with glaucoma).

### Table 3. Ongoing Studies Comparing Laser Therapy with Medications

<table>
<thead>
<tr>
<th>Study (Clinical Trial Identifier)</th>
<th>Funding Agency</th>
<th>Location</th>
<th>Population; Size</th>
<th>Investigations</th>
<th>Outcomes</th>
<th>Status as of 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Glaucoma Treatment Trial in Kenya and South Africa—SLT vs. Medication (NCT02774811)</td>
<td>University College, London</td>
<td>UK, South Africa, Kenya</td>
<td>18 years or older, men and women, glaucoma, black African; 400</td>
<td>Multicenter RCT of SLT versus prostaglandin analogue therapy</td>
<td>IOP reduction</td>
<td>Recruiting</td>
</tr>
<tr>
<td>A Comparison of Bimatoprost SR to Selective Laser Trabeculoplasty in Patients With Open-Angle Glaucoma or Ocular Hypertension (NCT02636946)</td>
<td>Allergan</td>
<td>US</td>
<td>18 years or older, men and women with OAG; 160</td>
<td>RCT of SLT versus Bimatoprost SR</td>
<td>IOP reduction</td>
<td>Recruiting</td>
</tr>
<tr>
<td>Laser-1st versus Drops-1st for Glaucoma and Ocular Hypertension Trial (LiGHT) (ISRCTN32038223)</td>
<td>National Institutes of Health, Research Health Technology Assessment Panel</td>
<td>UK</td>
<td>18 years or older, men and women newly diagnosed with OAG; 718</td>
<td>Multicenter RCT of SLT versus eye drops (any drug)</td>
<td>Health-related QOL measures, Glaucoma-specific QOL measures, IOP reduction, Visual field progression, Optic nerve progression, Adverse effects, Adherence, Cost-effectiveness</td>
<td>Complete, results not published</td>
</tr>
<tr>
<td>The Glaucoma Initial Treatment Study (GITS) (ACTRN12611000720910)</td>
<td>Australian National Health and Medical Research Council</td>
<td>Australia</td>
<td>18 years or older, newly diagnosed men and women, primary OAG or pseudo-exfoliation glaucoma; 400</td>
<td>Multicenter RCT of SLT versus eye drops (any drug)</td>
<td>Health-related QOL measures, Glaucoma-specific QOL measures, IOP reduction, Visual field progression, Optic nerve progression, Adverse effects, Cost-effectiveness</td>
<td>Recruiting</td>
</tr>
</tbody>
</table>

IOP = intraocular pressure; OAG = open-angle glaucoma; QOL = quality of life; RCT = randomized controlled trial; SLT = selective laser trabeculoplasty; UK = United Kingdom; US = United States.
8. **Likelihood of Implementation of Research Results in Practice**

Our key informants did not identify practice-level barriers to implementation of comparative effectiveness research on laser therapy versus eye drops. Although laser therapy is widely available in ophthalmologic practices, provider-level and patient-level factors are barriers to its implementation. One key informant noted that even after the trials of the 1980s and 1990s suggested comparable efficacy of medications and laser therapy, laser therapy experienced limited uptake, even among patients who may struggle with adherence to chronic treatment with eye drops. Another key informant noted general clinical inertia to adopting new research.\(^{36}\) However, as discussed above, comparative effectiveness research on laser trabeculoplasty and currently used eye drops is limited. Additionally, comparative effectiveness research on racial differences in treatment is nearly nonexistent. Further research in these areas can support provider–patient medical decision making.

Our key informants indicated a need for broader research into the contextual factors influencing racial disparities. One informant noted the multiple ongoing glaucoma genetics studies funded by the National Eye Institute, but he also pointed to the limited research in understanding and overcoming barriers to accessing glaucoma care for black and Hispanic populations. Studies examining the reasons for racial disparities could facilitate implementation of comparative effectiveness research and help reduce health disparities. For example, the Philadelphia Glaucoma Detection and Treatment study is a community-based intervention where educational workshops, screening, and treatment are offered on site in underserved communities, in settings like churches and community centers. Twenty percent of participants had suspected OAG and 9% received a diagnosis.\(^{87}\) Among newly diagnosed OAG patients who attended a workshop that presented laser therapy and medications as first-line therapies, 20% chose laser therapy over medications for initial treatment.\(^{87}\) This uptake was much higher than expected, according to one of our key informants, indicating the role for improved patient education. Project EQUALITY (Eye Care Quality and Accessibility Improvement in the Community), another community-based intervention offering educational workshops, showed some improvement in knowledge\(^{88}\) and offers glaucoma screening and treatment through community-based optometrists with ophthalmology telemedicine support (results not yet available).

All key informants also noted the importance of patient-reported outcomes in supporting implementation of research findings: information about patient experience and QOL with different procedures could better guide medical decision making and facilitate implementation of comparative effectiveness research.

9. **Durability of Information**

In the last few decades, research advances have solidified the practice paradigm of lowering IOP to slow the progression of visual loss in glaucoma, using medical therapy, laser trabeculoplasty, or incisional surgery. Our key informants did not anticipate new medical therapies that would make the use of laser therapy or surgery obsolete. Even if a new medication came to market with better efficacy and fewer side effects, adherence to medications for a chronic condition would remain an issue.

*Minimally invasive glaucoma surgeries* (MIGS) is an umbrella term applied to newly developed surgical techniques using micro devices that aim to achieve the same IOP-lowering effects of surgery without the less-than-ideal risk profile. Most studies of MIGS are of limited quality and duration and lack
study standardization, cost-effectiveness data, and information on ideal patient selection.\textsuperscript{89} Furthermore, many of these surgeries have been performed in patients with concurrent cataract surgery; MIGS may be the more appropriate procedure in patients already undergoing surgery.\textsuperscript{89} Our key informants had differing views on the future role of MIGS, particularly in racial and ethnic subgroup populations. One downside of laser therapy is that the IOP-lowering effects generally dissipate after 5 years.\textsuperscript{20} One key informant suggested that if the promise of MIGS were realized—lower risk compared with surgery and more durable reduction in IOP compared with laser therapy—then it would be important to incorporate MIGS into future comparative effectiveness research. However, two other key informants emphasized that incisional surgery, even minimally invasive surgery, still carries the risk of intraocular infection, bleeding, and possible blindness that medical and laser therapy do not and that the latter two will remain mainstays of initial treatment for glaucoma. Moreover, even if MIGS do show comparable efficacy to laser or medical therapy, black patients may not benefit compared with white patients as observed with past comparative effectiveness research on surgical treatment of glaucoma.\textsuperscript{6,14}

10. Potential Research Questions

The evidence gaps identified by our evidence review (Section 5) are not adequately addressed by ongoing research (Section 7). We highlight comparative effectiveness research areas in which PCORI can offer funding opportunities for impactful research for glaucoma treatments.

1) *What is the comparative effectiveness of laser therapy versus eye drops on patient-centered outcomes of visual impairment and quality of life?*

Longer studies are required to study visual impairment, and further work in patient-reported outcomes for glaucoma could help address this question. Studies will need to address patient-level, provider-level, and system-level barriers to treatment that may help facilitate implementation of comparative effectiveness research for high-risk populations.

2) *What is the comparative effectiveness of laser therapy versus eye drops for black and Hispanic individuals?*

More comparative effectiveness studies are needed for all patients, but future studies should be powered to measure differences in racial and ethnic subgroups. Studies will need to address patient-level, provider-level, and system-level barriers to treatment that may help facilitate implementation of comparative effectiveness research for high-risk populations.

11. Conclusion

Untreated, glaucoma silently leads to visual impairment and blindness. Black and Hispanic individuals are disproportionately affected. Future comparative effectiveness research in glaucoma may fill evidence gaps by focusing on patient-centered outcomes, outcomes by racial and ethnic subgroups, and strategies for addressing barriers to treatment that can lead to a reduction in disparities.
References


Appendix A: Key Informant Information

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Appendix B. Search Strategy

B1. Search strategy for primary literature review.

PubMed – 232 records

Embase – 58 records (29 records with duplicates removed)
Web of Science - 122 records (93 records with duplicates removed)

#3 122 #2 OR #1

#2 72 TITLE: (glaucoma* AND ("eye drop**" OR eyedrop* OR "ophthalmic drop**" OR "eye solution**" OR "ophthalmic solution**" OR ((topical* OR ophthalmic*) AND (drop* OR solution* OR administ*)) OR "prostaglandin analog**" OR "synthetic prostaglandin**" OR Latanoprost OR Travoprost OR Tafluprost OR Unoprostone OR bimatoprost OR "β-Adrenergic blocker**" OR "beta adrenergic blocker**" OR "Adrenergic beta-Antagonist**" OR Timolol OR Levobunolol OR Carteolol OR Metipranolol OR betaxolol OR "Adrenergic alpha-Agonist**" OR "α-Adrenergic agonist**" OR "alpha Adrenergic agonist**" OR Brimonidine OR apraclonidine OR "Carbonic anhydrase Inhibitor**" OR Dorzolamide OR Brinzolamide OR acetazolamide OR "Cholinergic agonist**" OR Pilocarpine OR carbachol)) AND TOPIC: ((laser* OR trabeculoplasty)) AND LANGUAGE: (English) Indexes=SCI-EXPANDED, SSCI, CPCI-S, CPCI-SSH Timespan=1990-2016

#1 59 TITLE: (glaucoma* AND (laser* OR trabeculoplasty)) AND TOPIC: ("eye drop**" OR eyedrop* OR "ophthalmic drop**" OR "eye solution**" OR "ophthalmic solution**" OR ((topical* OR ophthalmic*) NEAR/2 (drop* OR solution* OR administ*)) OR "prostaglandin analog**" OR "synthetic prostaglandin**" OR Latanoprost OR Travoprost OR Tafluprost OR Unoprostone OR bimatoprost OR "β-Adrenergic blocker**" OR "beta adrenergic blocker**" OR "Adrenergic beta-Antagonist**" OR Timolol OR Levobunolol OR Carteolol OR Metipranolol OR betaxolol OR "Adrenergic alpha-Agonist**" OR "α-Adrenergic agonist**" OR "alpha Adrenergic agonist**" OR Brimonidine OR apraclonidine OR "Carbonic anhydrase Inhibitor**" OR Dorzolamide OR Brinzolamide OR acetazolamide OR "Cholinergic agonist**" OR Pilocarpine OR carbachol)) AND LANGUAGE: (English) Indexes=SCI-EXPANDED, SSCI, CPCI-S, CPCI-SSH Timespan=1990-2016

Cochrane Library - 123 records (42 records with duplicates removed)

#1 glaucoma*:ti or glaucoma*:kw Publication Year from 1990 to 2016 3627
#2 laser* or trabeculoplasty:ti or laser* or trabeculoplasty:kw Publication Year from 1990 to 2016 8752
#3 "eye drop**" or eyedrop* or "ophthalmic drop**" or "eye solution**" or "ophthalmic solution**" or ((topical* or ophthalmic*) and (drop* or solution* or administ*)) or "prostaglandin analog**" or "synthetic prostaglandin**" or Latanoprost or Travoprost or Tafluprost or Unoprostone or bimatoprost or "β-Adrenergic blocker**" or "beta adrenergic blocker**" or "Adrenergic beta-Antagonist**" or Timolol or Levobunolol or Carteolol or Metipranolol or betaxolol or "Adrenergic alpha-Agonist**" or "α-Adrenergic agonist**" or "alpha Adrenergic agonist**" or Brimonidine or apraclonidine or "Carbonic anhydrase Inhibitor**" or Dorzolamide or Brinzolamide or acetazolamide or "Cholinergic agonist**" or Pilocarpine or carbachol:ti or "eye drop**" or eyedrop* or "ophthalmic drop**" or "eye solution**" or "ophthalmic solution**" or ((topical* or ophthalmic*) and (drop* or solution* or administ*)) or "prostaglandin analog**" or "synthetic prostaglandin**" or Latanoprost or Travoprost or Tafluprost or Unoprostone or bimatoprost or "β-Adrenergic blocker**" or "beta adrenergic blocker**" or "Adrenergic beta-Antagonist**" or Timolol or Levobunolol or Carteolol or Metipranolol or betaxolol or "Adrenergic alpha-Agonist**" or "α-Adrenergic agonist**" or "alpha Adrenergic agonist**" or Brimonidine or apraclonidine or "Carbonic anhydrase Inhibitor**" or Dorzolamide or Brinzolamide or acetazolamide or "Cholinergic agonist**" or Pilocarpine or carbachol:kw Publication Year from 1990 to 2016 16108

B. Search strategy for ongoing research studies.

Search terms: "trabeculoplasty" WITH Condition: glaucoma; "Medical therapy AND trabeculoplasty" WITH Condition: Glaucoma