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PERSPECTIVES

Current Knowledge and Attitudes Concerning Cost-Effectiveness in Glaucoma Pharmacotherapy: A Glaucoma Specialists Focus Group Study

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Background: Rising healthcare costs motivate continued cost-reduction efforts. To help lower costs associated with open-angle glaucoma (OAG), a prevalent, progressive disease with substantial direct and indirect costs, clinicians need to understand the cost-effectiveness of intraocular pressure (IOP)-lowering pharmacotherapies. There is little published information on clinicians' knowledge and attitudes about cost-effectiveness in glaucoma treatment.

Purpose: This pilot focus group study aimed to explore clinician attitudes and perspectives around the costs and cost drivers of glaucoma therapy; the implementation of cost-effectiveness decisions; the clinical utility of cost-effectiveness studies; and the cost-effectiveness of available treatments.

Methods: Six US glaucoma specialists participated in two separate teleconferencing sessions (three participants each), managed by an independent, skilled moderator (also a glaucoma specialist) using a discussion guide. Participants reviewed recent publications (n=25) on health economics outcomes research in glaucoma prior to the sessions.

Results: Participants demonstrated a clear understanding of the economic burden of glaucoma therapy and identified medications, diagnostics, office visits, and treatment changes as key cost drivers. They considered cost-effectiveness an appropriate component of treatment decision-making but identified the need for additional data to inform these decisions. Participants indicated that there were only a few recent studies on health economics outcomes in glaucoma which evaluate parameters important to patient care, such as quality of life and medication adherence, and that longitudinal data were scant. In addition to efficacy, participants felt patient adherence and side-effect profile should be included in economic evaluations of glaucoma pharmacotherapy. Recently approved medications were evaluated in this context.

Conclusion: Clinicians deem treatment decisions based on cost-effectiveness data as clinically appropriate. Newer IOP-lowering therapies with potentially greater efficacy and favorable side-effect and adherence profiles may help optimize cost-effectiveness. Future studies should include: clinicians' perspectives; lack of commercial bias; analysis of long-term outcomes/costs; more comprehensive parameters; real-world (including quality-of-life) data; and a robust Markov model.

Keywords: open-angle glaucoma, ocular hypertension, cost-effectiveness, clinician knowledge and attitudes, focus group, prostaglandin analogs

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Introduction

Glaucoma, the leading cause of irreversible blindness globally, is increasing in prevalence due to rapid increase in the aging population.[1,2] An estimated 64.3 million people (aged 40 to 80 years) globally were affected by glaucoma in

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2013, and that number is expected to reach 76 million by 2020.[2] Open-angle glaucoma (OAG) accounts for more than 70% of all glaucoma cases.[3] The number of Americans living with OAG—which is a chronic, progressive disease—was estimated to be 2.7 million in 2011 and projected to reach 7.3 million in 2050, growing at a rate of 28% per decade.[4]

Glaucoma decreases health-related quality of life; the extent of the reduction is directly associated with the severity or stage of the disease.[5–7] Patients with glaucoma are faced with the difficult challenges of visual dysfunction in everyday life, such as reduced mobility and difficulty with reading. Among those with glaucoma, self-reported visual disability is associated with difficulty walking, falls, and depression. As the disease progresses, the psychological burden of vision loss increases.[8] Besides the affected individual, blindness and visual impairment from glaucoma also impact the families, the healthcare system, and society in general, creating a substantial socioeconomic burden.[7]

The annual medical cost of glaucoma and disorders of the optic nerve in the US was estimated at $6.1 billion in 2014 and projected to be as high as $12 billion by 2032 and $17.3 billion by 2050.[9] The true direct cost would be considerably higher if all patients with this heavily underdiagnosed disease were treated.[7,10] A retrospective cohort analysis of Medicare claims found that glaucoma patients with any degree of vision loss had 46.7% higher total costs compared with those without vision loss, with mean total annual medical costs increasing from $8157 for no vision loss to $18,670 for blindness.[11] A Markov model replicating health events over the remaining lifetime of a patient with newly diagnosed glaucoma on US Medicare claims data from 1999 to 2005 estimated that the average lifetime cost of care for people with primary OAG (POAG) was about $137 per patient per year, or $1688 greater than those without glaucoma.[12] Using a large, nationally representative sample of Medicare beneficiaries, a recent study found that patients with glaucoma incurred an additional $2903 annual total health care costs and $2599 higher non-outpatient costs (total health care costs with the exclusion of outpatient payments) compared with those without.[8]

The cost of glaucoma care in the US, then, is high and expected to become higher as the prevalence of the disease increases. In order to lower those costs, stakeholders—including clinicians—need to better understand the cost-effectiveness of IOP-lowering therapies. Cost-effectiveness data provide information about the costs of different interventions or treatment strategies relative to their performance, which can be helpful in identifying potential ways to reduce the economic burden of treatment. Over the past decade, research has begun to address cost-effectiveness in the treatment of OAG and ocular hypertension (OHT).[13–16]

While awareness of costs is of increasing importance, little is known about whether and how clinicians treating glaucoma patients use cost-effectiveness in clinical decision-making. We convened a small focus group of glaucoma specialists to learn more about their knowledge and attitudes regarding cost-effectiveness in the treatment of patients with OAG or OHT. The focus group method's main advantage is its qualitative nature, which is complementary to that of quantitative research and allows in-depth exploration of thoughts, attitudes, and opinions via open-ended questions. It is commonly used to gain original insights and perspectives, uncover opinion trends, deepen understanding, and develop new hypotheses or ideas for further research. The aim of this pilot focus group study was to: 1) explore clinician perspectives regarding the costs and cost drivers of glaucoma therapy; 2) explore clinician attitudes and experience regarding the implementation of cost-effective decisions when treating patients with OAG or ocular hypertension (OHT) and the clinical utility of cost-effectiveness studies; and 3) explore clinician views about the cost-effectiveness of available treatment strategies and modalities for OAG and OHT and identify potential opportunities to improve glaucoma pharmacotherapy and reduce costs.

Methods

A focus group was formed to include six academic glaucoma specialists recognized as leading experts in the field of glaucoma treatment. Two separate teleconference sessions, each with three participants and led by the same moderator (also a glaucoma specialist) were conducted.

A discussion guide was created and distributed beforehand to the participants in order to facilitate and focus the discussion sessions. The discussion guide comprised a mixture of standardized/ranked and open-ended questions, which were grouped under the following general topics: the cost of care, cost considerations, current medical glaucoma therapies, and health economics and outcomes research (HEOR)

(Figure 1). To help address the specific questions about HEOR in glaucoma, participants were asked to review the summaries of 25 recent publications on health economics of glaucoma therapies prior to the teleconferences (Table 1).

Sessions spanned 2 h to allow the moderator ample time to solicit responses from participants to standardized/ranked questions, and to allow for additional discussion around open-ended questions. Following the conclusion of the discussion sessions, responses of the participants to open-ended questions were summarized descriptively based on the teleconference transcripts. Where possible, ranked responses were tallied.

Because the discussions were based on existing published literature and general clinical experiences and no research was performed on human or animal subjects, human cell lines, or human tissues, this study did not require ethics committee approval.

- The Cost of Care
  - How do you define "cost"?
  - What are the major factors influencing the overall cost of glaucoma care?
- Cost Considerations
  - What are your considerations when selecting treatment for OAG or OHT? Are some factors more important than others? How would you rank these factors based on importance?
  - How does the cost of care factor in to your decision regarding what to prescribe to your OAG and OHT patients? What are your typical first-line medication choices? What is the rationale behind these choices? How important is the cost of care in determining which drug to prescribe first-line? Please rank from 1 to 5, with 1 being "not important" and 5 being "very important.
  - What are your typical second-line adjunct medication choices? How important is the cost of care in determining which drug to prescribe when modifying treatment? Please rank from 1 to 5, with 1 being "not important" and 5 being "very important."
- Current Medical Glaucoma Therapies
  - What do we know about the cost-effectiveness of different treatment strategies (medications, laser trabeculoplasty, and filtering surgery) for OAG?
  - From an economic standpoint, how do PGAs compare to other glaucoma medications as first-line choice or monotherapy? Do the available PGAs differ in terms of cost-effectiveness? Also, how do you decide whether to prescribe a branded or generic PGA? Do you have concerns about the efficacy of generics?
  - What is your approach to treatment modification during the course of treatment? What proportion of patients in your practice require a switch from their first-line prescription? What proportion of patients in your practice require more than one medication to achieve/maintain target IOP?
  - What are the cost implications of treatment changes in the management of glaucoma? How do medication changes (switches or adds) affect the cost of treatment?
  - What is needed in new glaucoma medications in order to maximize their cost-effectiveness?
  - What is the role of medication adherence in the costs of glaucoma care? How much does medication adherence affect the cost of glaucoma care?
  - What are the factors that contribute to the low adherence rate to glaucoma medications?
  - How much does the side-effect profile of an IOP-lowering drug affect adherence? Please rank your responses from 1 to 5, with 1 being "no influence" and 5 being "enormous influence." Feel free to answer this question in an open-ended way as well.
  - How important is it to improve adherence in the management of glaucoma? Please rank your responses from 1 to 5, with 1 being "not important" and 5 being "very important."
- HEOR Research
  - How much does HEOR research influence your thinking about IOP-lowering treatment? Please rank your responses from 1 to 5, with 1 being "no influence" and 5 being "enormous influence."
  - How useful do you think the HEOR research is that we presented to you? Looking at the HEOR in glaucoma, what do you find most compelling?
  - What do you consider to be the key limitations of HEOR in glaucoma?
  - How would you design an HEOR/cost-effectiveness study? What outcome measures would you look at?

Figure 1 Topics discussed in focus groups of glaucoma specialists.

Results

Costs and Cost Drivers in Glaucoma Therapy

Participants noted that medical costs, including the financial burden of glaucoma therapy, are rising. They asserted the need to reduce that cost so that it is possible for clinicians to continue to provide their patients the best care. When asked to define "cost," they noted that the economic implications of glaucoma extend well beyond the direct, short-term costs to the patient or health system. Some specifically stated that, apart from expenses for medical services including medications, office visits, diagnostic testing, and surgery, glaucoma also produces significant patient-based and societal costs in forms of productivity/income loss or expenses for assistance with daily living, ie, the long-term cost of vision loss.

Participants acknowledged that there are multiple cost drivers in glaucoma care. The drivers identified as having significant cost impact included medications, diagnostics, office visits, and treatment change (either switching medications or adding another agent, or advancement to laser or incisional surgery). Changes in treatment, the group noted, increase cost by adding office visits and patient time. Estimates of the contribution of medication cost to the overall cost of glaucoma care varied from 20% to 40% among the participants—and was perceived as a greater proportion of the cost relative to laser treatment and surgeries, especially among well-controlled patients.

Meanwhile, more than one participant noted that treatment costs are directly related to disease stage and the number of different treatments required. For OAG patients who are diagnosed and treated early, the greatest part of expenditure will most likely be on medication, these participants stated. However, they noted, for those patients who have more advanced disease when diagnosed, whose pressure is poorly controlled, and who require more interventions (multiple medications, even multiple surgeries), the overall cost will almost certainly be higher and likely be led by costs of surgical care and productivity losses.

Cost Considerations in Glaucoma Therapy

Participants acknowledged that patients' access to prescription medications is a major concern and influenced primarily by price and health insurance status. They stated that out-of-pocket cost to patients is an important consideration in their practice; indeed, a significant reason why

Table 1 Key HEOR Articles Identified Through Literature Search*

Lead Author,Year	Article Title
Berenson, 2011[52]	Cost-offset analysis: bimatoprost versus other prostaglandin analogues in open-angle glaucoma
Bernard, 2003[46]	Clinical and economic impacts of latanoprost 0.005% in first-line treatment of open-angle glaucoma and ocular hypertension in France
Bhosle, 2007[17]	Medication adherence and health care costs with the introduction of latanoprost therapy for glaucoma in a Medicare managed care population
Cantor, 2008[18]	Economic evaluation of medication, laser trabeculoplasty and filtering surgeries in treating patients with glaucoma in the US
Costagliola, 2003[19]	Assessing the cost-effectiveness of switching from a beta-blocker to latanoprost in the treatment of ocular hypertension
Day, 2004[47]	A persistency and economic analysis of latanoprost, bimatoprost, or beta-blockers in patients with open-angle glaucoma or ocular hypertension
De Natale, 2009[20]	Cost effectiveness of travoprost versus a fixed combination of latanoprost/timolol in patients with ocular hypertension or glaucoma: analysis based on the UK general practitioner research database
Denis, 2008[21]	Costs and persistence of alpha-2 adrenergic agonists versus carbonic anhydrase inhibitors, both associated with prostaglandin analogues, for glaucoma as recorded by The United Kingdom General Practitioner Research Database
Fiscella, 2006[22]	Estimated comparative costs of achieving a 20% reduction in intraocular pressure with bimatoprost or latanoprost in patients with glaucoma or ocular hypertension
Frenkel, 2007[23]	Pharmacoeconomic analysis of prostaglandin and prostamide therapy for patients with glaucoma or ocular hypertension
Fristrom, 2010[24]	A randomized, 36-month, post-marketing efficacy and tolerability study in Sweden and Finland of latanoprost versus non-prostaglandin therapy in patients with glaucoma or ocular hypertension
Goldberg, 2006[25]	Cost considerations in the medical management of glaucoma in the US: estimated yearly costs and cost effectiveness of bimatoprost compared with other medications
Holmstrom, 2006[26]	The cost-effectiveness of bimatoprost, latanoprost and timolol in treatment of primary open angle glaucoma in five European countries
Hommer, 2008[27]	A cost-effectiveness analysis of fixed-combination therapies in patients with open-angle glaucoma: a European perspective
Lachaine, 2008[16]	Prostaglandin analogues for ophthalmic use: a cost-effectiveness analysis
Noecker, 2006[28]	Cost-effectiveness of monotherapy treatment of glaucoma and ocular hypertension with the lipid class of medications
Orme, 2012[29]	Long-term medical management of primary open-angle glaucoma and ocular hypertension in the UK: optimizing cost-effectiveness and clinic resources by minimizing therapy switches
Payet 2008[30]	Assessment of the cost effectiveness of travoprost versus latanoprost as single agents for treatment of glaucoma in France
Prager, 2016[8]	Self-reported function, health resource use, and total health care costs among Medicare beneficiaries with glaucoma
Schmier, 2014[57]	Adjunctive therapy patterns in glaucoma patients using prostaglandin analogs
Seider, 2012[31]	Cost of selective laser trabeculoplasty vs topical medications for glaucoma
Stein, 2012[45]	Cost-effectiveness of medications compared with laser trabeculoplasty in patients with newly diagnosed open-angle glaucoma
Stewart, 2009[14,58]	Cost-effectiveness of latanoprost and timolol maleate for the treatment of glaucoma in Scandinavia and the United Kingdom, using a decision-analytic health economic model
van Gestel, 2012[48]	The long-term outcomes of four alternative treatment strategies for primary open-angle glaucoma
Wong, 2013[32]	An adherence based cost-consequence model comparing bimatoprost 0.01% to bimatoprost 0.03%

Notes: *A literature search was conducted in PubMed using the following search terms: cost-effectiveness; glaucoma medical treatment; health economics outcomes research glaucoma; glaucoma prostaglandin analogs cost-effectiveness; intraocular pressure-lowering glaucoma cost-effectiveness; open-angle glaucoma cost burden; open-angle glaucoma pharmacoeconomics; glaucoma care cost burden. The search was limited to English-language articles published within the past 15 years. Primary health economic research studies concerning medical glaucoma therapy, especially prostaglandin analogs (PGAs), and narrative or systematic review articles on glaucoma economics were identified, with priority given to those published more recently and/or involving some of our potential participants as authors and those that took place in the US and Europe. Selected references were reviewed by the focus group moderator to ensure that key publications have been taken into account.

a generic prostaglandin analog (PGA) is the first-choice monotherapy for the majority of their glaucoma patients is insurance coverage. They further noted that efficacy, ocular and/or systemic side effects, dosing convenience, and patient adherence are the main factors that influence treatment choices, first or second line. Patient preferences also play a role, with many patients holding strong preferences among available treatment options. Patient perceptions or attitudes about generic substitutions, for example, can vary widely. The participants stated that many of their patients simply opt for the least costly alternative, while others place the highest value on clinical outcomes and are therefore willing to pay or tolerate more adverse effects for therapies with greater efficacy.

Participants added that, in reality, clinicians are often unaware of medications' actual costs to patients. One noted that he prescribes mainly based on efficacy at least in part because it has become very difficult in the past few years to decipher the costs of medications charged at individual pharmacies.

Although the clinicians in this focus group generally do not view themselves as gatekeepers for the healthcare system, they were in agreement that cost is an important consideration in the management of glaucoma from the broader perspective of society. One of the participants specifically noted that, beyond a responsibility to patients, clinicians also have a responsibility to society. He pointed out that clinicians should keep in mind their obligation of being a good steward of societal dollars and healthcare resources when making treatment decisions.

Cost-Effectiveness of Current Medical Therapies

All participants agreed that PGAs, the most widely used first-line glaucoma medications, stand out as a cost-effective treatment among all available IOP-lowering medications. The drug class was described as efficacious (reaching a target IOP reduction of 30% most of the time), long-lasting in efficacy (which translates into less frequent visits and thus cost savings), safe (least number of systemic adverse events), time-tested (on the market more than 20 years), dosed conveniently at once daily, and reasonably priced in an era of generics. However, some participants cautioned that generics are not all created equal—their experiences indicate that the variability in efficacy and tolerability is significant between different generic brands.

Participants stated that first-line treatment with a PGA is efficacious in lowering IOP in the majority of patients with glaucoma and that only a small minority require an alternative therapy. However, they also noted that, from a longitudinal perspective, combination therapy is often necessary to achieve or maintain target IOP, and that medication switching due to reasons such as tachyphylaxis, side effects, and visual field progression is common despite treatment. One participant estimated that at least 80% of patients with moderate to advanced disease and possibly 20% of patients with early disease require adjunctive therapy. The general consensus among the clinicians was that newer agents with greater efficacy than current regimens are needed in order to better control the cost of glaucoma therapy. If most patients will require adjunctive therapy at some point—and if, as noted above, treatment changes increase the cost by adding office visits and patient time—then having better first- or second-line treatments should provide long-term cost savings.

The approach to adjunctive therapy varied among participants. The majority reported that they typically choose to add a second drug when PGA monotherapy is insufficient. Their add-on choices usually include a topical carbonic anhydrase inhibitor (CAI) or a beta-blocker. Some noted that they tend to switch medication when there is an inadequate initial response and may consider laser surgery earlier in some cases to avoid polypharmacy. While specific adjunctive intervention varies, the general consensus was that an optimal second-line therapy is still lacking. Two participants suggested that an alternative to adding a second drug is switching the initial PGA (typically generic latanoprost) to the NO-donating PGA latanoprostene bunod (LBN) 0.024%—the latter is as well tolerated and safe as latanoprost but has the potential to provide additional pressure-lowering.[33] Latanoprostene bunod was approved by the FDA in late 2017 and represents the first new PGA in more than 5 years, as well as the first NO-donating PGA.[34] One participant mentioned that he is considering the Rho kinase (ROCK) inhibitor netarsudil 0.02% as a second-line choice, another recently approved therapy, although it must be used in combination with another IOP-lowering medication, such as a PGA, in order to provide additional reductions in IOP over the standard of care; in addition, concerns about relatively high hyperemia rates exist with netarsudil.[35]

When asked what is needed in a new medication to make it cost-effective, participants responded that new drugs need to be significantly better than the current

options in one or several ways: efficacy, tolerability, safety, duration of action, or any combination thereof. In addition, participants asserted that adherence is an important consideration in determining whether a glaucoma medication is cost-effective. As one of them pointed out, no therapy can be cost-effective if the patient is non-adherent. Thus, a new medication may initially cost more, but if patients take it as prescribed, the increase in adherence may justify the cost over the long run. Participants emphasized that glaucoma is a chronic disease associated with low medication adherence in general and noted that improvement in adherence is critical for better management of the disease. Indeed, when asked to rank the importance of adherence improvement in the management of glaucoma on a rank scale of 1 to 5 (with 1 being "not important" and 5 being "very important"), the responses were 4 or 5. One participant remarked that adherence is one of the greatest unmet needs in glaucoma pharmacotherapy. Furthermore, participants viewed adherence as a multifactorial issue and identified the following factors as the main barriers to adherence in glaucoma therapy: side effects, number of drops, costs, and patient understanding of the disease.

The Utility of Cost-Effective Research

Participants were unanimous in their view that, overall, current cost-effectiveness research offers little clinical utility for the treatment of glaucoma or OHT. The group noted that published cost-effectiveness studies in the field of glaucoma have largely been geared towards insurers, payers, and pharmacy benefit managers, rather than doctors. They felt that few of the studies looked at parameters that are important to patient care and clinical practice, such as quality of life and medication adherence; and that longitudinal data are scant, with a dearth of evidence to determine what the most cost-effective treatment algorithm is over a patient's lifetime.

Responses to the ranking question "How much does HEOR research influence your thinking about IOP-lowering treatment?" were 1 to 2 (on a rank scale of 1 to 5, with 1 being "no influence" and 5 being "enormous influence.") indicating that the influence of current cost-effectiveness data on clinical decision-making is indeed minimal. Participants stated that the available data may be used to guide insurers and payers but would need to be more persuasive and better designed in order to guide clinicians. Several participants commented that they find being good stewards of resources for the health care system as a whole an important goal but difficult to achieve given the current knowledge base about cost-effectiveness and payer-based variability in drug pricing.

According to participants, desirable elements of future economic studies in glaucoma pharmacotherapy include: a clinician's perspective; an independent approach (ie, without commercial bias); analysis of long-term treatment outcomes and costs; a more comprehensive set of parameters, including stage of disease, treatment switch or addition, adherence, side effects associated with various therapies; real-world data related to clinical practice, including quality-of-life data; and a robust Markov model that allows assessment of all the costs.

Participants asserted that cost-effectiveness should be considered in the context of the patient's age and expected lifespan, and, if possible, it would be important to determine the incremental cost of every additional mm Hg of IOP reduction.

Discussion

The cost-effectiveness of care is becoming an increasingly important aspect of glaucoma therapy because of the growing patient population and associated cost increases. Some prior research has investigated the economic outcomes of various glaucoma treatments, but few if any past studies have sought to identify clinicians' views regarding cost-effectiveness and their attitudes and experience using cost-effective data in the treatment of glaucoma.

Participants in the present study displayed a consistent understanding of the economic impact of glaucoma and the need to reduce treatment costs. Their perception that medication use contributes substantially to costs is consistent with previous reports that prescription medication costs drive financial burden at all stages of glaucoma and are equal to or greater than all other charges.[36–40] There is also evidence in support of participants' impression that diagnostics are a significant cost driver. In a recent study among Medicare beneficiaries, diagnostic testing accounts for about one-third of glaucoma-related costs (excluding medication cost).[41]

There is abundant evidence from previous quantitative studies supporting participants' assertion that disease severity has a direct impact on the costs of glaucoma. According to a US study, annual direct medical costs for patients with early glaucoma, advanced glaucoma, and end-stage glaucoma averaged $623, $1915, and $2511, respectively.[36] European studies have reported similar findings. Resource utilization and direct medical costs increase as disease worsens, and medication costs ranged

from 42% to 56% of direct costs at each disease stage.[40] In a German cross-sectional study examining treatment costs of OHT and POAG, average total annual direct costs per patient were €226 for OHT, €423 for early POAG, €493 for moderate POAG, and €809 for advanced POAG.[42] Among patients with early glaucoma, medication costs comprise most of the cost of care.[39,42] For those with advanced disease, indirect costs such as costs for home health care and rehabilitation become predominant.[43,44]

The finding that many of the participants give considerable thought to cost—specifically fees charged to patients—in their prescribing decisions (in the context of ensuring efficacy) suggests that awareness of drug cost to patients is fairly high among prescribing clinicians. However, the results of the present study also suggest that some barriers exist to implementing cost-effectiveness decisions in the treatment of glaucoma. As the group noted, cost information for medications is often not readily accessible. This is not surprising, given that multiple middlemen (insurers, manufacturers, and pharmacy benefit managers) are involved in establishing drug prices. Without knowing what a drug's actual price is at the pharmacy, it is difficult for clinicians to base decisions on costs.

Additionally, clinical decision-making that aims to reduce cost requires the guidance of research showing the relative cost-effectiveness of therapeutics and treatment strategies, but such evidence is largely lacking in the literature. Based on their own experience and a review of select economic studies in the field, this group of glaucoma specialists was of the opinion that there is a shortage of solid, useful data on cost-effectiveness of glaucoma therapies in the present literature. Major questions—such as how cost-effective a particular medication is compared to other treatment modalities such as laser trabeculoplasty or surgery and which medication is most cost-effective in lowering IOP—still lack a definite answer, although some evidence exists suggesting that first-line PGA monotherapy provides greater value than laser trabeculoplasty assuming optimal medication adherence and is the more cost-effective treatment compared to other types of available glaucoma medications.[16,45–48] This highlights the need for unbiased, well-designed economic studies to establish the relative cost-effectiveness and impact on quality of life of the treatment regimens for OAG or OHT and to identify opportunities for further savings.

Since individual and societal economic burdens of glaucoma both increase with disease severity, early identification and effective treatment of patients may help reduce the overall costs.[7] In support of this concept, a French study modeling the lifetime treatment cost in glaucoma showed that initial treatment with the most effective drug would reduce medical and social costs.[49] Currently, PGAs are widely preferred as the first-line treatment for OAG or OHT. Highly effective in IOP-lowering and available in generic forms, PGAs are considered to be an overall cost-effective treatment option. Even so, as this group's clinical experience indicates, many patients do not achieve adequate IOP-lowering with available agents and require further interventions, increasing the cost of the disease. While cost-effectiveness information on the two latest additions to the treatment options for glaucoma—LBN and netarsudil—is currently lacking, there is clearly a need for more cost-effective IOP-lowering medications (Table 2).

In reality, prices for new medications are relatively high, but price alone does not determine whether or not a treatment is cost-effective. Any economic assessment of a new treatment must also take into account the other determinant of its cost-effectiveness: the clinical benefits it provides, which may translate to savings in other categories of care. As pointed out by participants of this study, a new medication can be cost-effective as long as it provides enough "added value" for which patients and the society are willing to pay.

One medication that participants discussed in this context was LBN 0.024%, the NO-donating PGA approved in late 2017 for lowering IOP in patients with OAG or OHT. LBN acts through its two metabolites—latanoprost acid and an NO-releasing moiety (butanediol mononitrate)—and lowers IOP by enhancing aqueous outflow through both the uveoscleral and trabecular meshwork pathways.[50] The new drug appears to have all the important therapeutic advantages of a first-line therapy: high IOP-lowering efficacy, once-daily dosing, negligible systemic side effects, and low rate of ocular hyperemia. In a pooled analysis of the pivotal clinical trials, it was more effective at lowering IOP than timolol 0.5% and safe and well tolerated.[51] Furthermore, LBN has been associated with an IOP reduction of 1 to 1.5 mm Hg greater than that of latanoprost 0.005% (Xalatan).[33]

An incremental improvement in efficacy, such as that reported with LBN, could be fairly significant from the cost-effectiveness standpoint. As mentioned, more

Table 2 Glaucoma Medications Approved in the US Since 2013

Medication	Drug Classification	Mechanism(s) of Action	Key Benefits
Netarsudil, 0.02%*	Rho kinase inhibitor	Increase trabecular outflow	-Negligible systemic side effects -Dosed once daily
Latanoprostene bunod, 0.024%	Nitric-oxide donating prostaglandin analog	Increase uveoscleral and trabecular outflow	-High IOP-lowering efficacy -Favorable ocular and systemic safety profile -Dosed once daily
Brinzolamide/ brimonidine, 1%/ 0.2%	Fixed combination (carbonic anhydrase inhibitor/alpha-adrenergic agonist)	Decrease aqueous production and increase uveoscleral outflow	-Possibly greater efficacy than either component used as monotherapy -Fewer daily drops than individual monotherapies -Improved adherence
Dorzolomide/ timolol PF, 2%/0.5%	Fixed combination (carbonic anhydrase inhibitor/beta-adrenergic antagonist)	Decrease aqueous production	-Preservative-free -Possibly greater efficacy than either component used as monotherapy -Fewer daily drops than individual monotherapies -Improved adherence

Note: *A fixed-dose combination of netarsudil 0.02% and latanoprost 0.005% has become available since the focus group was convened.

effective lowering of IOP and the resulting decrease in the risk of glaucoma progression itself could generate cost savings from reduced health care resource utilization. In a study using a cost-offset model to analyze the clinical and economic outcomes of PGAs, an extra 1 mm Hg of IOP reduction accounted for fewer cases of progression and increased cost savings on office visits, visual field tests, additional glaucoma medications, and surgeries over a 7-year period.[52] Further, when a monotherapy combines greater efficacy with a once-daily regimen and a tolerable side effect profile, treatment persistence may improve, with less likelihood of medication addition or switch and potentially better adherence. Poor adherence to topical therapy is a well-established challenge in the management of glaucoma patients.[53,54] According to the Glaucoma Adherence and Persistency Study, only 10% of patients are continuously persistent with IOP-lowering medications throughout a year, and, among the slightly more than half of patients who restart after a gap in refilling the prescription, nearly 80% will have at least another gap.[53] One possible barrier to adherence is the use of adjunctive agents, which is required within a year for adequate IOP control in about one-third of patients starting glaucoma therapy and has been shown to contribute to higher management costs.[55–57,59] Side effects of medications may also adversely impact adherence to therapy.[56,60]

Netarsudil 0.02%, another new topical therapy that is most recently available for reducing IOP in patients with glaucoma or OHT, is a Rho kinase (ROCK) inhibitor. Like LBN, netarsudil enhances trabecular outflow facility.[35] The drug is thought to also decrease aqueous production and episcleral venous pressure. Clinical trial data suggest that netarsudil is not as effective as the PGAs, and that more than half of patients experience conjunctival hyperemia.[35,61] As the most common side effect of topical ocular prostaglandins, hyperemia in glaucoma patients has been shown to be a major reason for medication changes and result in increased overall treatment costs.[59,62] Given that it is conveniently dosed once-daily and no associated systemic safety issues have been identified, however, netarsudil could be potentially a more cost-effective adjunctive option relative to the available alternatives.

Limitations of the present study include the small sample size (a single focus group of only six participants) and the lack of participant diversity with regard to demographics and/or professional backgrounds. In particular, the study included no input from comprehensive ophthalmologists or optometrists, who also manage glaucoma patients in everyday practice. All the participants were

glaucoma specialists, whose patients are more likely to have advanced disease and thus require special treatment considerations. Although the group discussions yielded meaningful data, the results may not be generalizable. The majority of this group of glaucoma specialists said that they discuss medication costs with their patients, for example, but research indicates that cost-related conversations between ophthalmologists and glaucoma patients are uncommon. In a recent study that analyzed 275 video-recorded glaucoma office visits at six different medical centers located in various geographic areas, only 87 visits involved a discussion of medication cost.[63]

In summary, the present study provides new data on glaucoma specialists' knowledge and attitudes about cost-effectiveness and cost-effectiveness research in glaucoma therapy. The results suggest that these clinicians support the incorporation of cost-effectiveness into treatment decisions for glaucoma patients and are willing to provide care proved to be cost-effective. A more robust evidence base is needed to derive clear practical guidelines for decisions based on cost-effectiveness. Newer IOP-lowering medications with the potential to provide clinically meaningful benefit, such as LBN 0.024% and netarsudil 0.02%, or a fixed-dose combination of netarsudil and latanoprost approved for marketing after this focus group convened, may be helpful in applying cost-effectiveness to the treatment of OAG or OHT.

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Disclosure

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