

ONLINE FIRST

Cost-effectiveness of Medications Compared With Laser Trabeculoplasty in Patients With Newly Diagnosed Open-Angle Glaucoma

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Objective: To determine the most cost-effective treatment option for patients with newly diagnosed mild open-angle glaucoma: observation only, treatment with generic topical prostaglandin analogs (PGAs), or treatment with laser trabeculoplasty (LTP).

Methods: Using a Markov model with a 25-year horizon, we compared the incremental cost-effectiveness of treating newly diagnosed mild open-angle glaucoma with PGAs, LTP, or observation only.

Results: The incremental cost-effectiveness of LTP over no treatment is \$16 824 per quality-adjusted life year. By comparison, the incremental cost-effectiveness of PGAs over no treatment is \$14 179 per quality-adjusted life year, and they provide greater health-related quality of life rela-

tive to LTP. If PGAs are 25% less effective owing to poor patient adherence, LTP can confer greater value.

Conclusions: Prostaglandin analogs and LTP are both cost-effective options for the management of newly diagnosed mild open-angle glaucoma. Assuming optimal medication adherence, PGAs confer greater value compared with LTP. However, when assuming more realistic levels of medication adherence (making them 25% less effective than the documented effectiveness reported in clinical trials), at current prices for PGAs, LTP may be a more cost-effective alternative.

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OPEN-ANGLE GLAUCOMA (OAG) is one of the leading causes of irreversible vision loss in the United States, affecting more than 3 million individuals.¹ With the aging of the US population, the number of persons with OAG is expected to increase considerably in the coming decades.² Randomized clinical trials have demonstrated that decreasing intraocular pressure (IOP) can reduce the risk of persons with ocular hypertension developing OAG³ and can reduce the risk for disease progression in patients with mild,⁴ moderate,⁵ and severe glaucoma.⁶ Effective interventions for reducing IOP include the use of topical glaucoma medications, laser trabeculoplasty (LTP), and incisional glaucoma surgery.

*See also pages 506
and 529*

Several large, randomized clinical trials have been conducted to compare the effec-

tiveness of these different interventions for reducing IOP and preventing OAG progression. The Glaucoma Laser Trial (GLT) study randomized a group of patients to treatment with a topical β -blocker vs treatment with argon laser trabeculoplasty.⁷ This study found that during 9 years of follow-up, 34% of individuals in the group treated with medications experienced disease progression enough to require laser or incisional surgery, and 11% of patients in the group treated with argon laser trabeculoplasty progressed to require additional laser or incisional surgery. While this trial demonstrated that laser surgery is as effective, if not more effective, than treatment with topical glaucoma medications, according to a recent Cochrane review, little is known about whether the use of glaucoma medications or LTP is a more cost-effective treatment option for patients with newly diagnosed OAG.⁸

Glaucoma medications have long been the mainstay of treatment for OAG. During the past 2 decades, an array of different classes of glaucoma medications have become commercially available includ-

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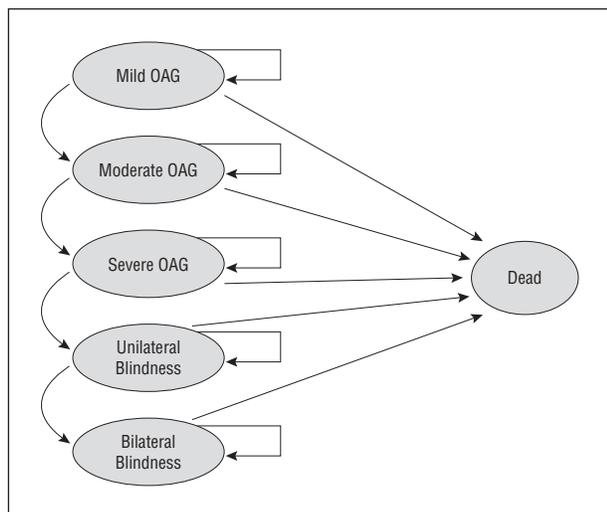


Figure 1. Markov model. OAG indicates open-angle glaucoma.

ing prostaglandin analogs (PGAs), β -blockers, α -agonists, carbonic anhydrase inhibitors, and miotics.⁹ Advantages of treatment with glaucoma medications as compared with other treatment modalities are that most medications especially the PGAs are well tolerated and have few serious adverse effects. Should a patient experience adverse effects from medication use, the adverse effects are often self-limiting on medication discontinuation. Patients often prefer glaucoma medications because they are less invasive than other treatment options. However, because OAG is a chronic condition, regular use of glaucoma medications can become quite costly over time.¹⁰ In addition, several studies have demonstrated that medication adherence is a major challenge for many patients with OAG.¹¹ Moreover, a subset of patients do not respond to certain classes of pressure-reducing medications.

Laser trabeculoplasty is a relatively quick, minimally invasive outpatient procedure performed in the clinic setting. It is effective in most patients with OAG, and studies have shown that it can reduce IOP by 20% to 35%.¹² If effective, LTP may reduce the long-term need for glaucoma medications and the costs and adverse effects associated with long-term medication use. Furthermore, LTP may be a more effective treatment strategy in patients who struggle with medication adherence. Disadvantages of LTP include higher upfront costs and the risk of complications including inflammation and a short-term elevation of IOP that, if left untreated, can lead to vision loss. Furthermore, there is a subset of patients who do not respond to LTP.¹³

Understanding whether one of these treatment options has greater incremental cost-effectiveness or confers a greater value relative to the other is important for many different stakeholders including health care policy makers, third-party payers, eye care providers, and most importantly, patients. With the dramatically increasing costs of health care in the United States,¹⁴ it is essential to find ways to curtail costs, ideally without sacrificing the quality of care provided.

The purpose of this study is to compare the incremental cost-effectiveness of PGAs vs LTP in the treat-

ment of individuals with newly diagnosed mild OAG. In addition, both of these treatment options will be compared with a control group of patients who are untreated to determine whether treatment of OAG (either using PGAs or LTP) is more cost-effective than following up patients with OAG without treatment.

METHODS

STUDY DESIGN

In this cost-effectiveness analysis, we compared treatment with PGAs, LTP, and observation only for patients with newly diagnosed OAG during a 25-year horizon. The target population was a hypothetical cohort of patients aged 60 years with mild OAG. Sixty years was chosen as the starting age for the analysis because OAG is more common among older individuals and studies have found this to be the average age for developing incident OAG.¹⁵ In sensitivity analyses, we explore the impact of changing these model parameters.

MARKOV MODEL

A Markov model is a mathematical method for quantifying the costs and health consequences of disease as patients transition through various disease stages over time.¹⁶⁻¹⁸ Such models can be useful in capturing the costs and benefits of treating chronic medical conditions such as glaucoma over time. In our Markov model, we assumed that each cycle through the model was 1-year long. In each cycle through the model, the costs and utilities were tabulated for each cohort. TreeAge Pro 2011 Health Care (TreeAge Software) was used to capture the total costs and utilities for each of the 3 cohorts during 25 years (approximate life expectancy for individuals aged 60 years).¹⁹ We modeled mortality using data obtained from US life tables.²⁰ We compared the incremental cost-effectiveness of each of the 3 interventions with one another in the base model to determine the cost-effectiveness of each of the 3 interventions. All costs were in 2010 US dollars and we assumed a 3% discounting rate per year.

HEALTH STATES

We considered 5 stages of disease: mild, moderate, and severe glaucoma, followed by unilateral and bilateral blindness. For this analysis, we defined mild glaucoma as glaucomatous damage with a mean deviation of -6 dB or less of visual field loss on standard automated perimetry. Moderate glaucoma was defined as glaucomatous damage with mean deviation of visual field loss of -6 to -12 dB on standard automated perimetry. Severe glaucoma was defined as mean deviation of -12 dB or worse on visual field testing. Unilateral blindness was defined as best-corrected visual acuity of less than 20/200 due to glaucoma in 1 eye, and bilateral blindness was defined as best-corrected visual acuity of less than 20/200 in both eyes caused by glaucoma.²¹

PROGRESSION FROM ONE HEALTH STATE TO ANOTHER

In the analysis, all patients started with mild glaucoma (**Figure 1**). Patients were assumed to progress from less severe disease states to more severe disease states. Once patients were in a more severe state, they could either remain in that state or continue to progress to the next more severe disease state.

For the untreated cohort, we determined disease progression from mild to moderate OAG based on data from the untreated group in the Early Manifest Glaucoma Trial.⁴ We used

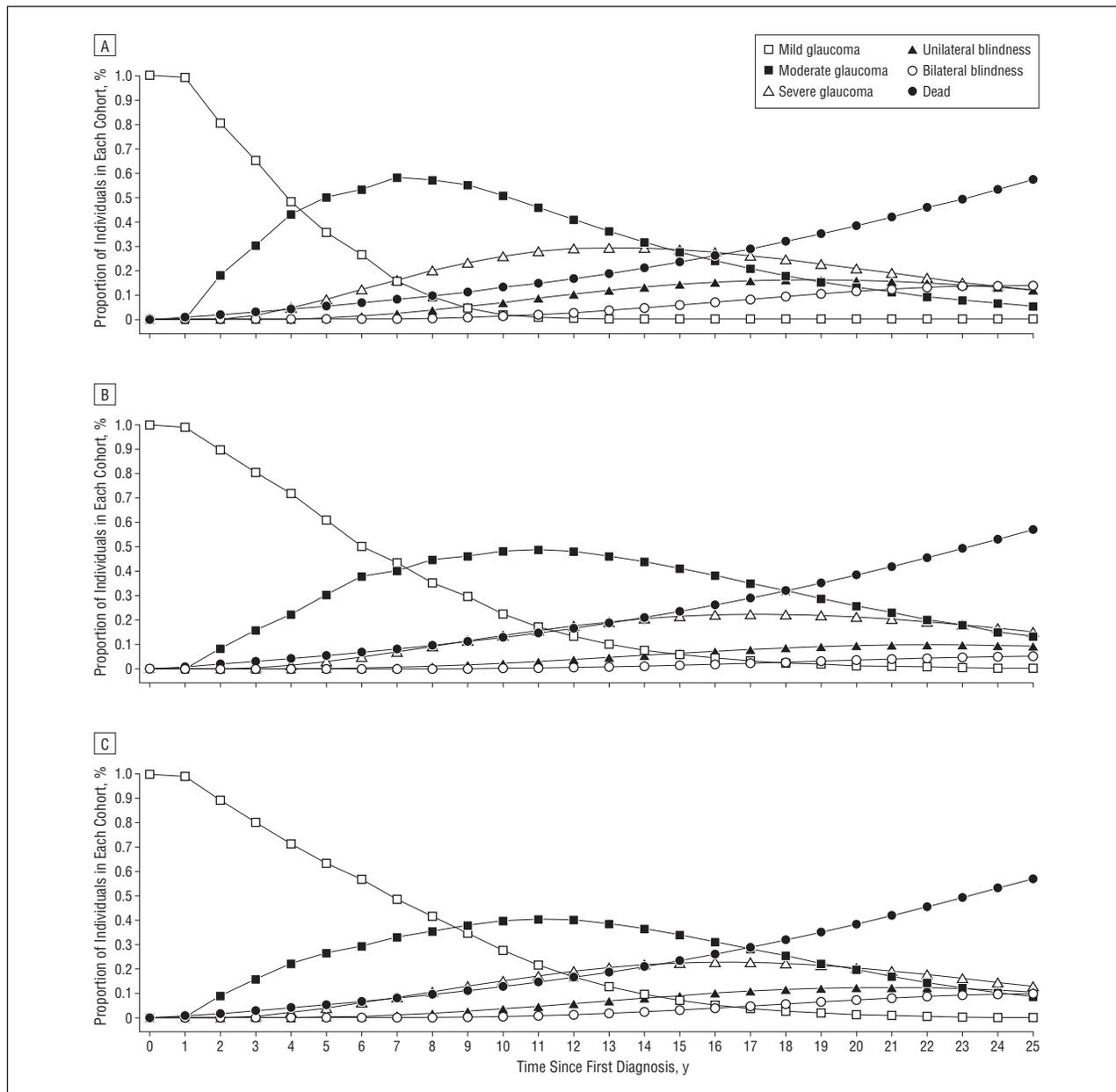


Figure 2. Markov tracings of glaucoma severity over time for the untreated cohort (A), the cohort treated with prostaglandin analogs (B), and the cohort treated with laser trabeculoplasty (C).

the progression rates from the GLT study to capture progression from mild to moderate OAG for the PGA and LTP cohorts. To determine the proportion of individuals in the medication and LTP treatment groups who progressed from less severe to more severe disease states, we reviewed the data from the GLT study, which captured on a year-by-year basis for both groups the proportion of individuals who required adjunctive glaucoma medical or surgical therapy because they were noted to have disease progression. At the time the GLT study was conducted, topical β -blockers were prescribed as initial therapy and adjunctive medications included pilocarpine hydrochloride and dipiveferin hydrochloride, both of which now have been nearly universally replaced with newer agents.⁷ Because phase 3 clinical trials report that PGAs are approximately 30% more effective at reducing IOP as compared with topical β -blockers²² and to enable us to make our study findings more applicable to medications that are commonly prescribed now, we assumed that

the medically treated group had a 30% reduced rate of disease progression relative to the rates of progression captured in the GLT study for the medication group. In sensitivity analyses, we tested the impact of varying the effectiveness of PGAs on the results of the analysis.

Once a patient was diagnosed with moderate OAG, we assumed a 10% rate of progression to more severe disease states per year for each of the 3 groups. Because few studies have tracked long-term disease progression of glaucoma, we varied the rate of progression to more severe disease states from 5% to 15% per year in sensitivity analyses.

MODEL VALIDATION

Using these assumptions, we generated Markov tracings for each of the 3 cohorts during 25 years (**Figure 2**). For the un-

Table 1. Costs and Utilities Used in the Model

	Model Input	Item	Value	Sensitivity Analysis Range	
Costs, \$ ^a	Medications (annual supply) ^b	Prostaglandin analogs	330	0-1000	
		α-Agonists	1242	0-1500	
		β-Blockers	435	0-500	
		Laser surgery	Laser trabeculoplasty	677	100-2000
		Incisional surgery	Trabeculectomy	2824	1000-4000
		Initial evaluation	Visit	190	100-200
			Diagnostic testing	207	100-300
		Follow-up evaluation	Visit	111	50-150
			Diagnostic testing	123	100-150
		Low vision services	Unilateral low vision	1000	500-4000
	Bilateral low vision		2000	1000-8000	
	Utilities	Adverse effects	Laser trabeculoplasty	1000	0-2000
			Glaucoma severity	Mild glaucoma	0.92
			Moderate glaucoma	0.89	0.7-0.95
		Severe glaucoma	0.86	0.6-0.9	
		Unilateral blindness	0.47	0.4-0.8	
		Bilateral Blindness	0.26	0.2-0.5	
Adverse effects		Laser trabeculoplasty	0.75	0.5-0.99	
		Effectiveness	Prostaglandin analogs	1.0	0.5-1.5
Other parameters			Laser trabeculoplasty	1.0	0.5-1.5
			Time horizon, y	25	9-30
		Age at OAG onset, y	60	40-80	
		Rate of OAG progression/y, %	10	5-15	

Abbreviation: OAG, open-angle glaucoma.

^aAll costs are in 2010 US dollars.

^bAll medication costs are for a 1-year supply.

treated cohort, these proportions were compared with findings from the St. Lucia study,²³ which assessed the natural history of untreated glaucoma and reported 16% of persons developed unilateral or bilateral blindness during 10 years. For both of the treated groups, we compared our cohorts to findings from Chen and colleagues,²⁴ who reported that 14% of patients treated for OAG experienced unilateral blindness and 4% of patients developed bilateral blindness from OAG during 15 years of follow-up. As Figure 2 demonstrates, we were able to achieve relatively similar rates of blindness in our Markov cohorts to those reported in these epidemiologic studies.

COSTS

Direct medical costs of glaucoma care were determined by using the 2010 average Medicare Fee Schedule for services.²⁵ Direct medical costs included costs of visits to eye care providers; ancillary glaucoma tests to monitor patients with OAG; and check for disease progression, as well as costs of medical, laser, and surgical interventions; costs of treating adverse effects caused by the laser; and costs of requiring low vision aids for individuals who have progressed to unilateral or bilateral blindness (**Table 1**).

COSTS OF VISITS AND DIAGNOSTIC TESTING

All patients receiving treatment incurred the cost of an initial office consultation (*Current Procedural Terminology* [CPT] code 99244), gonioscopy (CPT 92020), automated visual field testing (CPT 92083), scanning computerized imaging of the optic disc (CPT 92135), fundus photography (CPT 92250), and corneal pachymetry (CPT 76514). In the first year, individuals in all cohorts were assumed to incur costs for 2 follow-up examinations (CPT 92014), automated visual field testing, and scanning computerized imaging to determine whether they were

stable or progressing. In each cycle through the model, patients who were classified as stable continued to incur costs of biannual examinations, annual automated visual field testing, and annual scanning computerized imaging. In each cycle through the model, patients in each cohort who were classified as progressing incurred costs of ocular examinations 4 times in the following year, visual field testing twice in the following year, and annual scanning computerized imaging to capture more close monitoring of these patients.

COSTS OF MEDICAL AND SURGICAL INTERVENTIONS

Costs of glaucoma medications were obtained using average wholesale prices from the Red Book.²⁶ Since the average wholesale price for generic latanoprost has not yet been published, we determined the average annual charge for purchasing this product from 2 online pharmacies.^{27,28} In sensitivity analyses, we re-ran the model using the average wholesale price of a year supply of travaprost (a commonly prescribed PGA) of \$750. The proportion of individuals in the LTP and PGA groups requiring adjunctive medications each year was obtained from the GLT study. For those patients who required adjunctive medications, the cost of a year supply of 0.5% timolol was \$435 and a year supply of 0.1% brimonidine tartrate was \$1314 (Table 1). The costs of LTP and trabeculectomy were obtained from the 2010 average Medicare Fee Schedule for services using CPT codes 65855 and 66170, respectively. All individuals in the LTP cohort incurred the cost of LTP during the initial year in the model. Using information from the GLT study, depending on disease severity, 2% to 25% of the patients in the glaucoma medication cohort incurred the cost of LTP, 2% to 10% of patients in the glaucoma medication group incurred the cost of trabeculectomy, and 2% to 6% of patients in the LTP cohort incurred the cost of trabeculectomy each year.⁷

The proportion of patients who experience visually significant adverse effects following LTP is unknown as are the aver-

Table 2. Cost-effectiveness of Treating Newly Diagnosed Mild Open-Angle Glaucoma Using PGAs, LTP, or No Treatment

Intervention	Cost, \$	Incremental Costs, \$	Effectiveness, QALYs	Incremental Effectiveness, QALYs	Incremental Cost Effectiveness, \$/QALY
No treatment	2700		16.06		
LTP	13 788	11 088	16.71	0.65	16 824
PGAs	18 101	15 401	17.14	1.09	14 179

Abbreviations: LTP, laser trabeculoplasty; PGAs, prostaglandin analogs; QALY, quality-adjusted life year.

age costs associated with managing adverse effects following LTP. In the model, we assumed that 5% of patients who underwent LTP experienced adverse effects from the laser. While most adverse effects are transient and self-limiting, rarely one can experience sight-threatening complications from a marked elevation of IOP following the procedure. Because it is challenging to fully capture in the model the costs of managing these different adverse effects, we assumed the cost of managing adverse effects to be \$1000. This is likely an overestimation, but it covers the costs of medications used to treat adverse effects and incisional glaucoma surgery in the rare event this was necessary. In sensitivity analyses, we explored the impact of altering the proportion of patients developing adverse effects from LTP from 0% to 5% and the costs of managing adverse effects from LTP from \$0 to \$1000.

COST OF LOW VISION FROM GLAUCOMA

To capture the costs associated with need for low vision aids for unilateral blindness, we relied on findings of a study by Lee and colleagues,²⁹ who captured the costs associated with different stages of glaucoma. Based on this study, we assumed that the annual cost of low vision aids for unilateral blindness was \$1000 and \$2000 for bilateral blindness. These costs were varied in sensitivity analyses. Patients in all interventions including the untreated group incurred this cost if their disease progressed to blindness. Because indirect costs such as lost productivity associated with vision loss from OAG are difficult to measure and may be included in utility estimates, we did not incorporate indirect costs into the Markov model.

UTILITIES

Since glaucoma treatment is not known to improve length of life, the value of therapy is conferred by the quality-of-life improvement gained from reducing the chances of peripheral vision loss and ultimately central vision loss and blindness caused by OAG. Utility analysis quantifies health-related quality of life, with anchors of 1.00 (perfect vision permanently) to 0.00 (death). Lee and colleagues³⁰ quantified the utility values associated with different severities of glaucoma. These investigators determined that the utilities of OAG ranged from 0.92 for mild disease to 0.86 for severe damage. Brown and colleagues³¹ reported the utility score from unilateral blindness as 0.47 and for bilateral blindness as 0.26 (Table 1). Finally, for the subset of beneficiaries who experienced adverse effects from the laser procedure, we assigned them a utility score of 0.75. While this utility score likely overestimates the loss of utility for many transient self-limiting adverse effects of the laser, we feel it captures utility loss associated with some of the more severe adverse effects associated with the laser procedure. This parameter was also varied in sensitivity analyses.

SENSITIVITY ANALYSES

Several sensitivity analyses were performed to capture the known variability that exists in estimates of costs, utilities, and tran-

siting from one disease state to another. Table 1 shows the range of costs and utilities used when performing sensitivity analyses. An important factor that we varied in the sensitivity analyses was the effectiveness of the glaucoma medications. Because adherence with medical therapy is a known problem among individuals with OAG, by varying the effectiveness of the medications, we were able to determine how that factor influenced the results of the model. In addition, we conducted a 2-way sensitivity analysis, simultaneously varying the effectiveness of glaucoma medications and LTP. Other 1-way sensitivity analyses included restricting the time horizon to 9 years (the time frame of the actual GLT study) rather than extrapolating the results to 25 years, and increasing the utilities of mild, moderate, and severe OAG to be between 0.99 for mild disease and 0.90 for severe OAG because there is some evidence that even patients with advanced OAG experience little loss of health-related quality of life.²⁵ In sensitivity analyses, we also explored the impact of changing the age at onset of OAG and the proportion of patients in the LTP group who experienced adverse effects, as well as the costs and utilities of adverse effects from LTP.

RESULTS

BASE MODEL

During 25 years, the expected cost of untreated glaucoma for a single patient is \$2700, the long-term cost of undergoing LTP is \$13 788, and the cost of receiving PGAs is \$18 101. Compared with a patient with glaucoma who goes untreated, one who undergoes LTP accrues an additional \$11 088 in costs, and a patient treated with PGAs incurs an additional \$15 401 in costs. During this same period, the effectiveness for a patient with glaucoma in the untreated group is 16.06 quality-adjusted life years (QALYs), 16.71 QALYs for a patient who underwent LTP, and 17.14 QALYs for a patient who took PGAs. Compared with an untreated patient, a patient who received LTP had 0.65 more QALYs, and one who received PGAs had 1.09 more QALYs during the 25 years. The incremental cost-effectiveness of LTP over no treatment was \$16 824 per QALY. However, the incremental cost-effectiveness of PGAs over no treatment was \$14 179 per QALY, and PGAs provide greater health-related quality of life relative to LTP (**Table 2** and **Figure 3**).

SENSITIVITY ANALYSES

Sensitivity analyses were performed to determine whether the results of the Markov model would change by varying different model assumptions. A tornado diagram (eFigure, <http://www.archophthalmol.com>) helped identify spe-

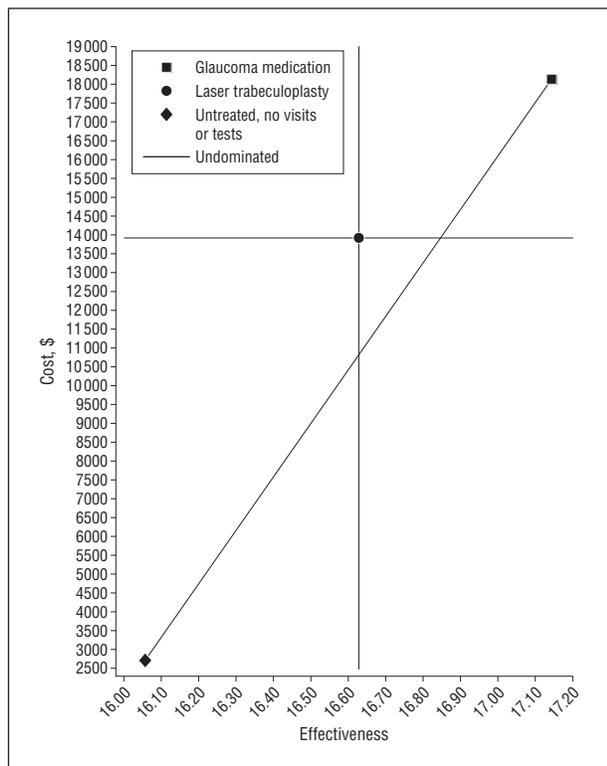


Figure 3. Cost-effectiveness plane comparing the effectiveness of glaucoma medications, laser trabeculoplasty, and no treatment.

cific inputs that could be altered to make treatment with PGAs more or less cost-effective relative to LTP. These inputs included the effectiveness of LTP and the effectiveness of PGAs.

Figure 4 shows a 2-way sensitivity analysis showing which treatment option would be preferred when simultaneously varying the effectiveness of both the LTP and PGAs relative to each other. Since prior studies have shown that many patients with OAG struggle with adherence to medication regimens and poorly adherent patients are more likely to experience disease progression, we examined lower effectiveness of PGAs. If PGAs are actually 25% less effective than the effectiveness reflected in the clinical trials owing to poor adherence, then LTP could be the preferred option. Likewise, if PGAs were as effective as in clinical trials but LTP were 20% or more effective than shown in the GLT study, then LTP could be the preferred option. If PGAs were 50% less effective owing to poor adherence and LTP is 17% less effective than estimates from the GLT study, observation only could actually confer the greater value.

Other model inputs were varied in the sensitivity analyses to determine whether they may affect the incremental cost-effectiveness of LTP vs treatment with PGAs (**Table 3**). Because some studies have reported that there is little impact of advanced OAG on health-related quality of life,³² we re-ran the models assuming utility scores of 0.99 to 0.90 for mild to advanced OAG and this had little impact on the findings generated in the base model. Varying the time horizon had an impact on cost-effectiveness of these therapies. When we re-ran our Markov model during a horizon of 9 years (the

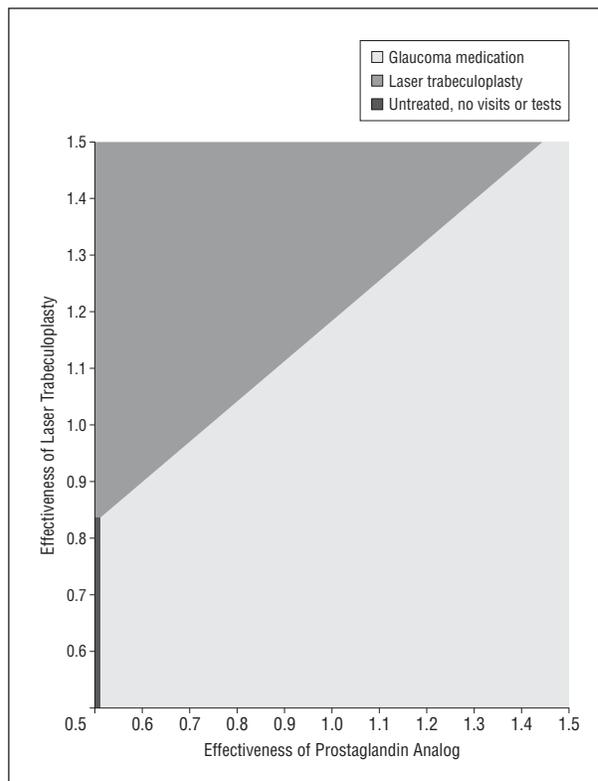


Figure 4. Two-way sensitivity analysis simultaneously varying the effectiveness of prostaglandin analogs and laser trabeculoplasty in a base model. Each axis captures the relative effectiveness of each intervention at delaying glaucoma progression. A value of 1.0 means the base case effectiveness as outlined in the article; higher values represent greater effectiveness and lower values represent reduced effectiveness (eg, a value of 0.75 means a 25% reduction in effectiveness). Each region represents the preferred intervention, assuming a willingness to pay \$100 000 per quality-adjusted life year.

actual length of follow-up of the GLT study) instead of the 25 years used in the base model, we found that LTP over no treatment is \$71 893 per QALY; however, compared with LTP, the incremental cost-effectiveness of PGAs is \$158 725 per QALY. This is likely because the treatments incur high upfront costs, but the potential benefits of treating glaucoma may not be realized within 9 years given that glaucoma tends to be a slowly progressing disease often taking more than 9 years to advance to a stage where it significantly reduces health-related quality of life. In addition, we were uncertain about the rates at which glaucoma progressed in individuals with and without treatment. In our base case, we had 10% of patients with untreated and treated glaucoma worsen each year from moderate OAG to more advanced disease states. However, in sensitivity analyses, we looked to see whether the results would change if only 5% worsened each year (slow progression) and if 15% worsened each year (fast progression). In both cases, the incremental cost-effectiveness ratios of PGAs and LTP were both less than \$50 000 per QALY, and treatment with PGAs had a more favorable incremental cost-effectiveness ratio and provided better health-related quality of life when compared to LTP. Finally, varying the proportion of patients who develop adverse effects from LTP to 0% and the cost of managing ad-

Table 3. Sensitivity Analyses

	Value	ICER LTP/QALY	ICER PGAs/QALY
Effectiveness of PGAs	0.5	16 824 ^a	Dominated by LTP ^b
	0.75	16 824 ^a	Dominated by LTP ^b
	1.0	16 824 ^c	14 179 ^a
	1.25	16 824 ^c	9621 ^a
	1.5	16 824 ^c	7266 ^a
Effectiveness of LTP	0.5	Dominated by no treatment ^b	14 179 ^a
	0.75	583 432 ^c	14 179 ^a
	1.0	16 824 ^c	14 179 ^a
	1.25	7750 ^a	Dominated by LTP ^b
	1.5	4750 ^a	Dominated by LTP ^b
Annual cost of PGAs, \$	0	15 928 ^c	9665 ^a
	250	16 607 ^c	13 085 ^a
	500	17 285 ^c	16 505 ^a
	750	17 964 ^{a,c}	22 950
	1000	18 643 ^a	30 600
	1500	19 322 ^a	38 250
Time horizon, y	9	71 893 ^a	158 725
	20	20 603 ^c	19 846 ^a
	25	16 824 ^c	14 179 ^a
	30	15 291 ^c	11 873 ^a
	40	14 872 ^c	12 037 ^a
Age at OAG onset, y	50	10 513 ^{a,c}	12 587
	60	9853 ^{a,c}	14 179
	70	21 547 ^c	19 536 ^a
	80	38 383 ^a	40 257
	90	55 219 ^a	71 083
	100	72 055 ^a	101 909
Utility for different severities of OAG	0.90/0.95/0.99 ^d	14 376 ^c	12 334 ^a
Annual rate of OAG progression, %	5	36 839 ^c	33 720 ^a
	10	16 824 ^c	14 179 ^a
	15	10 710 ^c	8969 ^a
	20	6 596 ^c	4660 ^a
Cost of adverse effects from LTP, \$	0	16 748 ^c	14 179 ^a
	800	16 809 ^c	14 179 ^a
	1600	16 870 ^c	14 179 ^a
	2400	16 931 ^c	14 179 ^a
Utility of adverse effects from LTP	0.50	17 149 ^c	14 179 ^a
	0.79	16 768 ^c	14 179 ^a
	0.89	16 645 ^c	14 179 ^a
	0.99	16 523 ^c	14 179 ^a
	1.00	16 400 ^c	14 179 ^a
Proportion of LTP patients who develop adverse effects, %	0	16 535	14 179 ^a
	2.5	16 824	14 179 ^a

Abbreviations: ICER, incremental cost-effectiveness ratio; LTP, laser trabeculoplasty; OAG, open-angle glaucoma; PGA, prostaglandin analog; QALY, quality-adjusted life year.

^aMost cost-effective treatment options.

^bA strategy is considered dominated if it is more costly and less effective than the alternative.

^cLaser trabeculoplasty strategy is dominated by PGA by extended dominance (lower QALYs at a higher cost per QALY).

^dUtilities for different severities of glaucoma: 0.90 for severe OAG, 0.95 for moderate OAG, and 0.99 for mild OAG.

verse effects from LTP to \$0 did not significantly impact the findings from the model.

COMMENT

In the 1980s, Eddy and Billings³³ published a report questioning the value of treating patients with glaucoma. In the report, they summarized the existing literature, which they found demonstrated little evidence that reducing IOP had any impact on glaucoma progression. Their report served as an impetus to the ophthalmological community to perform well-designed studies to assess the effectiveness of interventions for glaucoma. During the past 25 years, there have been several large, randomized clinical trials including the Ocular Hypertension Treatment Study, Early Manifest Glaucoma Trial, Collaborative Initial Glaucoma Treatment Study, and Advanced Glau-

coma Intervention Study that demonstrated that patients with all different severities of glaucoma, from patients with ocular hypertension to those with advanced glaucoma, benefit from reducing eye pressure.³⁻⁶ While these trials have provided strong evidence supporting the effectiveness of reducing eye pressure to prevent glaucoma progression, the next question for policy makers and third-party payers is whether these interventions are cost-effective. Rein and colleagues³⁴ assessed the incremental cost-effectiveness of screening for, identifying, and treating patients with primary OAG. They found that glaucoma treatment was highly cost-effective when assuming optimistic treatment efficacy (\$28 000 per QALY) and in line with other health interventions when incorporating the costs of diagnostic testing and assuming conservative treatment efficacy (\$46 000 per QALY).

The focus of our analysis was to perform a head-to-head comparison of the cost-effectiveness of the most commonly prescribed topical medication class, PGAs, vs LTP in the treatment of patients with newly diagnosed OAG. When using data generated from the GLT study, under the assumption that PGAs are 30% more effective than the medications that were available when the GLT study was conducted and that patients have excellent adherence to these agents, we find treatment with PGAs to be more cost-effective and to provide better health-related quality of life than LTP. However, assuming more realistic patterns of medication adherence, LTP could be a preferred treatment. If PGAs were 25% less effective or LTP was 20% more effective, then LTP could provide better value for health benefits than PGAs.

Problems with glaucoma medication adherence have been well documented in the literature.^{35,36} For PGAs to be effective, not only must patients acquire the medications but also remember to take them as prescribed and properly administer the drops into their eyes.^{37,38} Each of those steps is critical for these medications to be effective at reducing IOP, which can in turn help prevent glaucomatous progression. Studies have shown that poor medication adherence is associated with worsening glaucoma.^{35,37,39,40}

There are several study limitations that need to be acknowledged. These limitations can broadly be grouped into concerns about parameter values used in the model and limitations in how we accounted for LTP use. While we were able to obtain reasonable estimates of costs, utilities, and transition state probabilities for many of the variables included in the model from the literature, information on several parameters needed to be estimated since high-quality evidence is not available for all inputs. For all these assumptions, we were able to use sensitivity analyses to examine the impact of changing the assumptions on the findings (Table 3). The GLT study on which we relied to determine the likelihood of experiencing disease progression for the PGA and LTP groups only provided data for the first 9 years following treatment with 1 of these interventions. Because newly diagnosed 60-year-old patients with OAG live approximately 25 years on average, in the models we needed to extrapolate the findings from the GLT study for the remaining years. In the models, we assumed constant and equal progression rates from years 9 to 25 for those treated with medications or LTP. It is certainly possible that progression rates differ from years 9 to 25 among the groups. In sensitivity analyses, when we restrict our analyses to determining the incremental cost-effectiveness of PGAs vs LTP for only the first 9 years, we find that LTP may confer greater value. It is also unknown whether patients linearly progress from 1 severity level to another or whether rates of progression from mild to moderate disease occur more rapidly than from severe glaucoma to blindness. In our models, we used findings from GLT study and Early Manifest Glaucoma Trial to determine progression from mild to moderate glaucoma for the 3 groups. Then we assumed a 10% yearly rate of progression to more severe disease states. These assumptions appeared to match blindness outcomes observed in longer-term studies, and we found that small deviations from these pro-

gression rates do not affect the conclusions of the study. However, if these assumptions were further off from actual disease progression, this may affect the study results. More research is needed to understand longer-term glaucoma progression in untreated and treated patients.

Our study had limitations in how we accounted for LTP use (type of laser and frequency of treatment). The information on the effectiveness of medications and LTP were obtained from the GLT study, which was conducted 23 years ago. At that time, the only LTP unit commercially available was argon laser trabeculoplasty. Since then, selective laser trabeculoplasty became available. Several studies comparing argon laser trabeculoplasty with selective laser trabeculoplasty have reported these procedures to be equally as effective at reducing IOP; however, selective laser trabeculoplasty may have fewer risks for adverse effects.¹² It would be helpful to repeat such a cost-effectiveness analysis using the findings from the ongoing Selective Laser Trabeculoplasty Vs Topical Medical Therapy Study clinical trial, which have yet to be published. Additionally, in this analysis, we did not consider the role of repeat LTP before proceeding with other interventions in the model.

Finally, it is important to exercise care when generalizing these study findings to patients with other forms of glaucoma, those residing outside of the United States, those who are uninsured, and those living in communities who have no access to LTP as the variables may differ considerably from those used in the model for these groups.

CONCLUSION

Our findings highlight the importance of medication adherence in determining which intervention is most cost-effective. Identifying strategies to improve medication adherence will not only improve patient outcomes but also improve the cost-effectiveness of treating glaucoma with PGAs or other medications. Furthermore, if researchers can develop novel means of administering glaucoma medications (eg, intraocular injections) that reduce the need for adherence, assuming these medications are not overly costly, this too can improve the cost-effectiveness of caring for patients with OAG.

In conclusion, this study shows that generic PGAs and LTP can both be cost-effective options for managing patients with newly diagnosed mild OAG. Assuming optimal medication adherence, generic PGAs confer greater value compared with LTP. However, when assuming more realistic levels of medication adherence, at current prices for PGAs, LTP may be a more cost-effective alternative.

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