Cost-effectiveness of Treating Ocular Hypertension

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Purpose: To assess the cost-effectiveness of treating ocular hypertension (OHT) in the United States.

Design: A Markov model was constructed to perform a cost-effectiveness analysis.

Participants: Patients with OHT.

Methods: The health states considered were stable OHT and glaucoma. Practice patterns for the model were derived from the Ocular Hypertension Treatment Study (OHTS), and transition probabilities were derived from previous literature. Specific unit costs used for medications, patient visits, and diagnostic and therapeutic procedures were obtained from Blue Cross/Blue Shield. The time horizon was 5 years. Costs were discounted at 3% per annum.

Main Outcome Measure: Long-term cost effectiveness of treating OHT to prevent the development of glaucoma.

Results: The incremental cost-effectiveness ratio (ICER) for all OHT patients to prevent 1 case from progressing to primary open-angle glaucoma was $89 072. However, the minimally cost-effective ICER level after adjustment for risk factors identified by multivariate analysis in the OHTS were: 20 years above the average of 56 years, ICER of $45 155; 4 mmHg above the average pressure of 25 mmHg, ICER of $46 748; 40 μm less than the average central corneal thickness of 573 μm, ICER of $36 683; and a vertical cup-to-disc ratio of 0.2 wider than the average of 0.4, ICER of $35 633.

Conclusions: Based on the results and practice patterns of the OHTS, treating all OHT patients seems not to be cost-effective. However, treating selective OHT patients with risk factors identified in the OHTS, for example, advancing age, higher pressures, thinner central corneal thickness, and wider vertical cup-to-disc ratios, does seem to be cost-effective for preventing the onset of glaucomatous damage. *Ophthalmology 2008; 115:94–98 © 2008 by the American Academy of Ophthalmology.*

The Ocular Hypertension Treatment Study (OHTS) was developed to determine if the treatment of elevated intraocular pressure in ocular hypertension was an effective means of preventing primary open-angle glaucoma.[1] Importantly, this trial showed that a 20% reduction in intraocular pressure limited progression to 4.4%, whereas those who received no treatment had a progression rate of 9.5%. This trial also identified risk factors, by multivariate regression analysis, for progression to glaucoma: higher intraocular pressure, older age, thinner cornea, and wider vertical cup-to-disc ratio.[1]

However, the OHTS did not answer the question of whether treating ocular hypertension is cost-effective, either in the general public or in specific subpopulations based on the identified risk factors, for prevention of glaucoma development. The purpose of this study was to assess the long-term cost effectiveness of ocular hypertension treatment to prevent progression to primary open-angle glaucoma by use of a Markov decision-analytic health model.

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Patients and Methods

Procedures

A Markov model was created to assess cost-effectiveness in association with the quality of life gained (quality-adjusted life years).[2] This type of model has the advantage of analyzing medical situations when the treatment outcomes and costs may be dissimilar among several therapeutic options. The model allows determination of cost per unit of benefit of treatment. The unit of benefit chosen for ocular hypertension was the prevention of disease progression to glaucoma as defined by the onset of optic nerve head damage (rim thinning, saucerization, or nerve fiber layer hemorrhage) or the development of visual field damage (i.e., nasal step, or arcuate, paracentral, or Seidel's scotoma).[3–5] The time horizon for the model was 5 years.

Markov Model: Medical Aspects

The Markov model was developed using TreeAge Pro 2006 Healthcare software (TreeAge Software, Inc., Williamstown, MA). The model analyzed the cost-effectiveness of beginning treatment

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for ocular hypertension patients or not treating them. The potential of developing glaucomatous optic disc or visual field loss over 5 years was based on OHTS results.[1]

Few published data exist regarding a quality-of-life weighted utility for glaucoma or ocular hypertension. Therefore, the present weights were based, with a slight modification, on different levels of visual acuity published by Tengs and Wallace,[6] using 0.9 for none, 0.68 for mild (the first progressed state), and 0.57 for moderate (the second progressed state) visual loss.

Frequency of visits and procedures, as well as indications for laser and conventional therapy, were based generally on the OHTS, because this study reflected, but may not have imitated completely, routine clinical practice.[1] This trial assumed that at the first examination, each patient would undergo gonioscopy and a corneal thickness measurement, with 1 comprehensive and 1 noncomprehensive visit annually, refraction and visual field testing at each visit, and disc photography once yearly.

The model was created with the cycle stage set as 1 year. Patients in the model were placed into either a treatment or no treatment health state, where they remained for the first 2 years of the model. At the third year of the model, progression was presumed to occur by the percentages found in OHTS. Although progression could occur at any time within 5 years for ocular hypertension, for simplification, it was assumed that progression occurred at 3 years, the median point of the model.

For the treatment arm, patients in the first 2 1-year cycles were assumed to use 1 medication. In the third year, the percent of progression was 4.4% based on the OHTS results.[1] Three health states were defined in the third year: first, the nonprogressed group (95.6%), who then were administered 1.4 medications, assuming that more medication would be needed over time to control the ocular hypertension.[1,7]

In contrast, 4.4% of treated patients were presumed to progress according to the OHTS results, for whom the second and third health states were defined: patients who had 1 medication added or 2 medications added to control their newly diagnosed glaucoma. These 2 health states were populated in a 3:1 ratio to approximate the ratio of patients who were prescribed 2 versus 3 or more medications in the OHTS (39.7% of patients were prescribed 2 or more medications and 9.3% were prescribed 3 or more medicines by the end of the trial).

Patients who progressed to primary open-angle glaucoma were presumed to have early disease and to remain stable for 2 years until the fifth year. At this time, progression was assumed to occur again, based on the incidence found in the Early Manifest Glaucoma Trial (EMGT).[8] The EMGT indicated that 45% (9% per year) of patients with early glaucoma progressed over 5 years. Consequently, we assumed an 18% progression from the third to the fifth year (9% multiplied by 2 years). Progression was limited to the fifth year for simplification.

Based on the EMGT, the early glaucoma patients who were using 2 medications were divided into 2 health states: a stable group of 82% who remained using 2 medications and an unstable group of 18% who were administered a third medication. Also based on the EMGT results, the early glaucoma patients who were taking 3 medications were divided into 2 health states: 82% remained stable with 3 medications until the end of the model and 18% who progressed and were presumed to require argon laser trabeculoplasty. The 1.4 average number of medicines in the nonprogressed group and the additional medications in the progressed group by the fifth year (either 2 or 3 medications, depending on if they had progressed once or twice as described above) approximated for our model the 1.47 average number of medicines at the end of OHTS.[1]

Patients in the no treatment group remained with no treatment for the first 2 years. Based on the OHTS results, at the third year, similar health states were changed as in the treatment group: 90.5% did not progress and remained without treatment until the end of the model, and 9.5% progressed. Because these patients now had primary open-angle glaucoma, they were assumed to need the same level of therapy as patients in the treatment group. Consequently, the health states were similar from this point forward, as described above. Because of the early onset of glaucoma in these patients, it was assumed that no trabeculectomy surgery would have been performed and that no patient would have become blind throughout the course of this model.

Markov Model: Economic Aspects

The Markov model was completed with cost information for visits and procedures from the Blue Cross/Blue Shield directory from the state of South Carolina. These cost figures are shown Table 1. Only direct medical costs were considered (i.e., cost of visits, procedures, and therapy). Full out-of-pocket prices for medicine costs were used, which were determined from 3 separate pharmacies in each of 6 distinct geographic areas within the United States. Because it was not specified with which medications patients would be treated, an average price was calculated using latanoprost, bimatoprost, travoprost, generic timolol, and brimonidine. Cost results were discounted per annum at 3%.

The incremental cost-effectiveness ratio (ICER) was determined for the ocular hypertensive study population as a whole to prevent progression to primary open-angle glaucoma. The ICERs then were adjusted by the risk factors found by multivariate analysis in the OHTS, including progressively: advancing age, higher intraocular pressures, thinner central corneal thickness, and wider vertical cup-to-disc ratio. This was performed by using the risk ratios (RRs) from the OHTS and multiplying the RR by 9.5% progression rate for the untreated group.[1] Further adjustments were made again by multiplying the RR by the adjusted previous progression rate. All 4 risk factors were modified to the extent that would be common in clinical practice above the approximate average values found in the OHTS.

Markov Model Sensitivity Analysis

For the sensitivity testing, 1-way analyses were performed for costs including: argon laser trabeculoplasty, the number of medications used over 5 years, and follow-up visits. In each case, the cost was changed by ±10%.

Table 1. Unit Costs of Procedures

Treatment Options	Cost
Comprehensive visit	$109
Central corneal thickness	$28
Follow-up visit	$57
Gonioscopy	$36
Intraocular pressure	$35
Optic disc imaging	$82
Refraction	$20
Annual cost of glaucoma medication	$492
Automated visual field	$76

Table 2. Cost Effectiveness Results from the Markov Model

Strategy	Subcategory		Cost	Efficacy (Quality-Adjusted Life Years)	Cost/Efficacy	Incremental Cost Effectiveness Ratios
Baseline		No treatment	$2467	4.45	$554	
		Treatment	$5001	4.48	$1116	$89 072
Age	Plus 1 decade	No treatment	$2539	4.44	$572	
		Treatment	$5001	4.48	$1116	$62 756
	Plus 2 decades	No treatment	$2629	4.43	$594	
		Treatment	$5001	4.48	$1116	$45 155
Intraocular pressure	Plus 1 mmHg	No treatment	$2498	4.45	$562	
		Treatment	$5001	4.48	$1116	$75 676
	Plus 2 mmHg	No treatment	$2536	4.44	$571	
		Treatment	$5001	4.48	$1116	$63 696
	Plus 3 mmHg	No treatment	$2574	4.44	$580	
		Treatment	$5001	4.48	$1116	$54 755
	Plus 4 mmHg	No treatment	$2620	4.43	$592	
		Treatment	$5001	4.48	$1116	$46 748
	Plus 5 mmHg	No treatment	$2669	4.42	$604	
		Treatment	$5001	4.48	$1116	$40 157
Cup-to-disc ratio	Plus 0.5	No treatment	$2570	4.44	$579	
		Treatment	$5001	4.48	$1116	$55 431
	Plus 0.6	No treatment	$2708	4.42	$613	
		Treatment	$5001	4.48	$1116	$35 633
	Plus 0.7	No treatment	$2890	4.39	$659	
		Treatment	$5001	4.48	$1116	$23 061
	Plus 0.8	No treatment	$3130	4.35	$719	
		Treatment	$5001	4.48	$1116	$14 677
Corneal thickness	Plus 40 μm	No treatment	$2698	4.42	$611	
		Treatment	$5001	4.48	$1116	$36 683
	Plus 80 μm	No treatment	$3099	4.36	$711	
		Treatment	$5001	4.48	$1116	$15 567

Results

General Analysis

The ICER for the complete population of ocular hypertension patients from OHTS, regardless of risk factors, was $89 072. This indicates the cost of preventing 1 patient from progressing to primary open-angle glaucoma if all ocular hypertensive patients received treatment by the OHTS guidelines.

Analysis by Risk Factor

The adjustments made to the ICER by the risk factors are shown in Table 2 for each RR. This table presents risk factors as described by the OHTS and the ICER value associated with advancing risk by increasing age, intraocular pressure, cup-to-disc ratio, and corneal thickness. By the National Institute for Clinical Excellence (NICE) standard, when the ICER reaches $50 000 or less, treatment generally is thought to be cost-effective at that level of risk.[9]

The ICER for all patients with ocular hypertension to prevent 1 from progressing to primary open-angle glaucoma fell below the generally accepted $50 000 level by the following adjustments[9]: 20 years or more above the average age of 56 years (76 years); 4 mmHg or more above the average pressure of 25 mmHg (29 mmHg); 40 μm or more below the average central corneal thickness of 573 μm (533 μm); and 0.2 vertical cup-to-disc ratio or wider than the average ratio of 0.4 (0.6 ratio).

Markov Model Sensitivity Analysis

The sensitivity testing results are shown in Table 3. This table includes economic sensitivity testing for the durability of the Markov model, which includes $\pm$10% change in cost and the associated ICER levels. A $\pm$10% change of price in argon laser trabeculoplasty, cost of medication, or cost of a noncomprehensive follow-up visit altered the ICER by $10 000 or less.

Discussion

This study showed that the ICER to prevent 1 patient with ocular hypertension from progressing to primary open-angle glaucoma based on the results of the OHTS was $89 072 for the treatment of every patient with ocular hypertension with an ocular hypotensive medication. Although controversial, the NICE stated that if an ICER generally is lower than $50 000, the strategy could be considered effective and a specific resource allocation could be made available.[9] The ICER in this study for the treatment of all ocular hypertension patients seemed to be somewhat above the NICE definition.

However, by using risk factors found in the OHTS by multivariate regression analysis and by adjusting the ICER level, subgroups were found within the ocular hypertensive population that appeared cost-effective to treat using the approximate midpoint of the NICE definition ($50 000): 20 years or more above the average of 56 years (76 years); 4 mmHg or more above the average pressure of 25 mmHg (29 mmHg); 40 μm or less below the average central corneal thickness of 573 μm (533 μm); and 0.2 vertical cup-to-disc ratio or wider than the average ratio of 0.4 (0.6 ratio). Allowing for a less strict definition of cost-effectiveness to the limit of the upper range of the NICE definition

Table 3. Sensitivity Testing

Strategy	Subcategory		Cost	Efficacy (Quality-Adjusted Life Years)	Cost/Efficacy	Incremental Cost Effectiveness Ratios
Argon laser trabeculoplasty	−10%	No treatment	$2467	4.45	$554	
		Treatment	$5001	4.48	$1116	$89 076
	+10%	No treatment	$2467	4.45	$554	
		Treatment	$5001	4.48	$1116	$89 067
Cost of medications	−10%	No treatment	$2437	4.45	$548	
		Treatment	$4728	4.48	$1055	$80 533
	+10%	No treatment	$2497	4.45	$561	
		Treatment	$5274	4.48	$1177	$97 612
Noncomprehensive visit	−10%	No treatment	$2436	4.45	$547	
		Treatment	$4960	4.48	$1107	$88 717
	+10%	No treatment	$2498	4.45	$561	
		Treatment	$5042	4.48	$1126	$89 427

($59 223), patients with a pressure 3 mmHg above the average (28 mmHg) and a 0.5 cup-to-disc ratio also would be included. The fact that the 4 risk factors found by multivariate regression in OHTS were associated with more cost-effective treatment of ocular hypertension is not surprising because each of these risk factors previously has been shown to be associated with a greater incidence of progression to glaucoma from ocular hypertension.[10–16]

Kymes et al[17] recently evaluated the cost-effectiveness of treating ocular hypertension using a Markov model, also based on the OHTS. Similar to the present study, they found it was not cost-effective to treat all ocular hypertensive patients, but it seemed reasonable to treat selected patients. Their study differed from the current one, however, by basing the cost-effectiveness of treatment on the percent annual risk of developing glaucoma. Specifically, they indicated that in patients with more than a 2% annual risk for glaucoma, or an intraocular pressure of more than 24 mmHg, treatment likely would be cost-effective. In contrast, in the current study, ICER levels were evaluated based on progressively more severe specific clinical findings derived from risk factors described in the OHTS.

Clinical decisions based on cost-effectiveness must be considered in relative terms that allow for medical judgment in assessing the need for treatment. Such situations may include, but would not necessarily be limited to, patients who have more than 1 risk factor or those with other potential risk factors described in previous studies (e.g., cardiovascular disease, diabetes, family history of glaucoma). Such situations were not taken into account in this model. Therefore, physicians should not base their clinical decisions solely on pharmacoeconomic data. Such decisions may lead to clinical error because they would fail to account for all clinical factors that would be assessed by clinical judgment and which could not be included in even a detailed pharmacoeconomic model.

In contrast to a pharmacoeconomic model, a medical approach to the treatment of ocular hypertension based on the OHTS was reported previously by Medeiros et al.[18] The authors developed a risk calculator for assessing who should be treated to prevent progression to glaucoma based on the results of the OHTS and the presence of the 4 multivariate risk factors described in this study.

Despite the importance of the OHTS in helping us understand the usefulness of treating ocular hypertension, caution is warranted in drawing treatment guidelines based on a medical or economic basis that are too strict. Any treatment guidelines or risks were derived from slightly more than 1600 patients participating in this trial. In contrast, treatment guidelines for common diseases in internal medicine-based specialties (e.g., asthma, systemic hypertension) frequently are formulated from metaanalyses derived from multiple trials that sum to more than 10 000 patients.[19,20]

Although it would be difficult to achieve such a sample size for ocular hypertension, efforts should be made to expand the evaluable database of patients from which treatment indications and risk factors are determined, especially from more diverse geographic and ethnic backgrounds. Such data may cause adjustments to the accepted risk factors, or to treatment algorithms, for ocular hypertension.

Risk factors for ocular hypertension described in past epidemiologic studies have not been completely consistent with those found in the OHTS. Of note are cardiovascular disease, diabetes, and family history, which were not identified as risk factors for glaucoma in the OHTS, but which have been noted in multiple past studies evaluating ocular hypertension.[21,22] Accordingly, future research may concentrate on further clarifying treatment indications, risk factors, and their associated costs for ocular hypertension. In addition, future randomized trials also may concentrate on clinical outcomes of specific glaucoma medications in high-risk patients. These data, then, may be pooled into a metaanalysis that could better support or adjust findings from individual trials.

Sensitivity testing for argon laser trabeculoplasty, cost of medications, or a noncomprehensive follow-up visit showed that adjusting the cost of each of these by ±10% did not bring the ICER level for progression to glaucoma close to $50 000. The findings from the sensitivity tests suggest that the model is not overly dependent on cost fluctuations, which helps to confirm that treating all patients with ocular hypertension is not cost efficient. However, the authors cannot explain the lack of sensitivity to changes in the direct diagnostic treatment costs.

These results suggest that, based on the results and practice patterns of the OHTS, treating all ocular hypertension patients seems not to be cost-effective. However, treating selective ocular hypertension patients with risk factors identified in the OHTS—advancing age, higher pressures, thinner central corneal thickness, and wider vertical cup-to-disc ratios—does seem to be cost-effective to prevent the onset of glaucomatous damage.

This model had several limitations. The time horizon of the model was limited to 5 years. Ocular hypertension demands long treatment, and future analyses may include a longer time analysis. In addition, this model did not include indirect costs, which may influence the overall disease financial burden. In the future, improved assumptions may improve a Markov analysis such as: quality-of-life weighted utilities specific to glaucoma, data derived from additional prospective long-term trials that may include results derived from clinical examination schedules, and unmasked treatment regimens for ocular hypertension that may be found in routine clinical practice.

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