Glaucoma Therapy Delivers Great Patient and Financial Value

The cost-utility analysis associated with glaucoma therapy.

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This is the third and final installment in a three-part primer on Value-Based Medicine (VBM; Center for Value-Based Medicine) as it applies to glaucoma care. As stated in earlier installments, health care reimbursement will be about proving the value of what we physicians do, not just performing a test or a procedure. The thorough explanations of VBM by Drs. Brown and colleagues are an excellent guide to this new terminology. Most of us are unfamiliar with the terms, much less the concepts they represent. As physicians, our future depends on proving that what we do is not only based on evidence but patient oriented, cost-effective, and ultimately of great value to society. I thank these authors for bringing this timely topic into focus, and I urge my colleagues to read over all three installments again. The information will allow us to improve legislative chambers, not just anterior chambers.

—Ronald L. Fellman, MD, section editor

As noted in earlier installments in this series, a model for assessing the comparative effectiveness and cost-effectiveness of open-angle glaucoma (OAG) therapy was presented at the American Academy of Ophthalmology Annual Meeting in New Orleans in November 2013.[1] The model showed that glaucoma therapy provides great benefit to patients by maintaining their vision, thus considerably improving their quality of life.[1] Glaucoma therapy was also noted to be highly cost-effective, yielding a large financial return on investment (ROI) to patients and insurers and increasing the overall wealth of the nation.

The first article in this series dealt with the patient value gain from ophthalmic interventions,[2] while the second discussed the costs associated with health care interventions.[3] The third and final installment presents an overview of the entire VBM cost-utility analysis model for the treatment of glaucoma using topical latanoprost 0.005%. Although latanoprost therapy is the intervention of interest, this model can be applied to virtually any glaucoma intervention. Comparable models can be applied to interventions across all of medicine.

WHY THE NEED?

As noted in earlier installments, Comparative Effectiveness Review No. 59 from the Agency for Healthcare Research and Quality did not find evidence that screening for OAG decreased vision impairment.[4] Comparative Effectiveness Review No. 60 on glaucoma therapy stated, "Although it is logical to presume that slowing glaucoma damage would lead to preservation of vision-related quality of life and reduction in visual impairment, this link has not been demonstrated in the research literature."[5]

Such a statement in a report sponsored by a government agency could affect the decisions of predominantly nonophthalmologists who allocate medical resources. We therefore thought it important to perform a VBM cost-utility analysis comparing glaucoma therapy to no therapy using the best available evidence-based data and a transparent model logical to providers, patients, and decision makers.

VALUE-BASED MEDICINE

Overview

VBM is the practice of medicine based on the patient value gain and financial value gain delivered by health care interventions.[6-12] It uses a standardized cost-utility analysis instrument, with "standardization" as the key

concept. Because more than 27 million possible inputs (different utilities, utility respondents, cost bases, cost perspectives, time frames, discount rates, currencies, years, etc.) can go into a cost-utility analysis, any differing one might invalidate a comparison of one cost-utility analysis with another.[13] There are also 56,000 different ways to initiate glaucoma therapy,[14] but a VBM cost-utility analysis can tell which is the best for which patient.[6] VBM cost-utility analyses can be compared for interventions across all of ophthalmology as well as interventions across all specialties in medicine. The same outcomes are used, no matter the specialty.[6]

Patient Value Gain

Patient value gain in a VBM cost-utility analysis starts with the highest level of interventional evidence available, preferably level 1 clinical trials or meta-analyses.[15] It uses patients' preferences (time trade-off utilities) to assess quality of life gain and amalgamates this with length of life gain to quantify patient value gain in terms of quality-adjusted life-year (QALY) gain and percent value gain. QALY gain is calculated by multiplying (utility gain) × (years of benefit). For most ophthalmic interventions, there is no gain in length of life, as is also the case for latanoprost therapy. The percent value gain is therefore equivalent to the percent improvement in quality of life.

Financial Value Gain

Financial value gain includes cost-effectiveness and the financial ROI. Average national Medicare costs are integrated with patient value gain in QALYs to arrive at the cost-utility ratio, or cost-effectiveness, in terms of $/QALY (dollars expended per QALY gained). In the United States, most consider interventions costing less than $100,000/QALY to be cost-effective, although the World Health Organization considers interventions costing less than $150,000 to be cost-effective.[6]

Direct medical costs (providers, facilities, drugs, etc.) are used to calculate the third-party insurer, cost perspective cost-utility ratio. The societal cost-perspective cost-utility ratio is also desirable, however, because it includes direct medical costs, direct nonmedical costs (caregivers, transportation, residence, etc.), and indirect medical costs (loss of salary, retraining, etc.) precluded by an intervention. The ROI, or the dollars returned to society (patients, commercial insurers, Medicare, Medicaid, Gross Domestic Product, etc.) for the direct medical costs expended, is typically greater when the societal cost perspective is used.[10]

Benefits of VBM Cost-Utility Analysis

VBM cost-utility analyses are theoretically superior to evidence-based medicine analytic comparative effectiveness analyses[6] in that VBM analyses

- integrate patient quality of life preferences (time trade-off utilities)[2]
- incorporate adverse events and their incidences into patient value gain, often with decision analysis[2]
- can directly compare disparate interventions across all specialties in medicine using the same outcomes[2,3]
- integrate costs expended and saved with patient benefit (patient value gain)[10]

NATURAL HISTORY OF UNTREATED GLAUCOMA

We are unaware of randomized clinical trials in which untreated glaucoma patients were observed prospectively to end-stage glaucoma. Nonetheless, the innovative work of Jay and Murdoch[16] on the long-term natural progression of untreated glaucoma patients showed that an IOP of 23 mm Hg in an eye with glaucoma causes progression to end-stage disease in 14.4 years, whereas an IOP of 28 mm Hg does the same in 6.5 years. Decreasing the IOP to 17 mm Hg (average resultant IOP with latanoprost therapy[17]) from 25 mm Hg (average IOP of patients entering many OAG treatment trials[17]) prolongs the time of good central vision from 11.2 to 24.9 years, a gain of 13.7 years of good central vision.[16] Because the average, newly discovered, OAG patient is a 63-year-old with a life expectancy of 21 years, good central vision is maintained with therapy for the rest of his or her life.[18] Thus, lowering the IOP gives the average patient with OAG an additional 9.8 years of good vision until death.

PATIENT VALUE GAIN

Quality of Life

The quality of life associated with a health state can be quantified with time trade-off utility analysis using a scale with anchors of 1.00 (perfect health permanently or 20/20 visual acuity in each eye permanently) to 0.00 (death).[19,20] Ocular utilities correlate most highly with vision in the better-seeing eye, decreasing as the central vision decreases (Table 1).[19,20] The utility associated with end-stage glaucoma and bilateral count fingers vision is 0.52, whereas that associated with 0.005% latanoprost therapy—integrating all drug-related adverse events and their incidences with decision analysis—is 0.9529. Bilateral progression to end-stage glaucoma at a mean time of 11.2 years after an average IOP of 25 mm Hg converts the average utility of an untreated person to 0.52. The utility difference is between the latanoprost-treated, glaucoma patient utility and the untreated glaucoma patient utility (0.9529 - 0.52 =) 0.4329 with therapy from year 11.2 after diagnosis to the end of year 21 at death. The average, untreated glaucoma patient thus lives with

TABLE 1. TIME TRADE-OFF VISION UTILITIES	
Visual Acuity in the Better-Seeing Eye (unless otherwise noted)	**Time Trade-off Utility**
20/20 OU permanently	1.00
20/20 OU with an ocular disease	0.97
20/20, < 20/40 in fellow eye	0.92
20/25	0.87
20/30	0.84
20/40	0.80
20/50	0.78
20/70	0.72
20/100	0.69
20/200	0.62
20/800 (CF)	0.52
HM - LP	0.35
NLP OU	0.26
Death	0.00
Abbreviations: OU, both eyes; CF, counts fingers; HM, hand motions; LP, light perception; NLP, no light perception.	

bilateral end-stage disease (count fingers vision) for the last 9.8 years of his or her life.

If we assume patients with glaucoma who were not treated did not know they had the disease, their utility during the first 11.2 years of the 21-year life expectancy is 1.00 (Table 1) versus 0.9529 in the latanoprost treatment group. This results in a mean utility loss with treatment of (0.9529 - 1.00 =) -0.0471 during the first 11.2 years of life after discovery of the glaucoma.

Visual Fields

To date, mild to moderate visual field loss has not been convincingly shown to diminish quality of life.[21-23] Nonetheless, visual field loss can be readily integrated into a VBM cost-utility model when field loss is shown to decrease quality of life.

Total Patient Value Gain

The gain of 9.8 years of good vision with glaucoma therapy can be translated into total patient value gain by multiplying (utility gain, or 0.4329) × (time of benefit in years, or 9.8 years) to derive the QALY gain. Nonetheless, the loss from latanoprost therapy during the first 11.2 years in treated patients is (-0.0471 × 11.2 =) -0.4557 QALY. This must be subtracted from the QALY gain from latanoprost therapy. It should also be noted that all QALY gains (losses) herein are discounted, typically at 3% annually, as is the case for all costs.[6] Taking these parameters into account, latanoprost therapy confers a gain of 2.229 QALYs (Table 2).

People accrue QALYs by living at a certain utility level. The total patient QALYs accrued over 21 years by a patient with glaucoma on latanoprost therapy is 15.129. The total QALYs accrued by a patient with glaucoma who does not realize that he or she has glaucoma until reaching bilateral end-stage disease is 12.900 over 21 years. The overall QALY gain from therapy is therefore (15.129 - 12.900 =) 2.229 QALYs. This equates to a (2.229/12.900 =) 17.3% value gain from latanoprost therapy versus no therapy. The 2.229 QALY gain equates to a (2.229/12.900 =) 17.3% improvement in quality of life for latanoprost therapy (Table 2).

A comparison of the patient value gain associated with other ophthalmic and nonophthalmic interventions is shown in Table 3. Latanoprost confers its great patient value by preventing for the last 9.8 years of the average patient's life blindness that would occur without therapy.

FINANCIAL VALUE GAIN

Financial value gain integrates the direct medical costs expended for bilateral latanoprost treatment with those gained from the costs made unnecessary by the therapy (Table 2). The 21-year, direct ophthalmic medical costs (drug, physician, and testing) total was $17,110. Within this number is the assumption that 20% of latanoprost drops are wasted during administration.[24] Integrating all

TABLE 2. COST-UTILITY ANALYSIS OF LATANOPROST THERAPY FOR OPEN-ANGLE GLAUCOMA VERSUS NO THERAPY IN THE AVERAGE PATIENT WITH A 21-YEAR LIFE EXPECTANCY

Parameter	Result
Utility with latanoprost therapy	0.9529
Utility with no therapy for first 11.2 years in untreated glaucoma patients who do not know they have glaucoma	1.00
Utility with bilateral end-stage glaucoma for 9.8 years prior to death	0.52
Patient value gain	2.229 QALYs
Patient value gain	17.3% quality of life improvement
Direct ophthalmic medical costs expended for bilateral glaucoma therapy over 21 years	$17,110
Costs accruing against direct ophthalmic medical costs[a]	($500,693)
Net total cost (total financial value gain over the 21-year model)	($483,582)
Third-party insurer cost-utility ratio	($17,110/2.229 =) $7,676/QALY
Societal cost-utility ratio	[($483,582/2.229 =)] ($216,931/QALY)
21-year financial ROI referent to ophthalmic direct medical costs	2,826%
Annual ROI	18.2%

Abbreviations: QALY, quality-adjusted life-year; ROI, return on investment.
Note: Patient value and financial value gains over the 21-year model (the life expectancy of the average new glaucoma patient diagnosed at age 63 years) associated with the use of topical latanoprost 0.005% in each eye for open-angle glaucoma.
[a]The negative costs of decreased trauma, decreased depression, decreased nursing home admissions, decreased caregiver costs, decreased job loss, and so forth. All costs are in 2014 US real dollars.
( ) = negative costs accruing against the ophthalmic direct medical costs of glaucoma therapy.

21-year costs (societal costs) includes ophthalmic direct medical costs expended of $17,110; nonophthalmic direct medical costs saved from decreased depression, trauma, and nursing home admissions (-$121,395)[25]; direct nonmedical costs saved from fewer caregiver services (-$368,877)[26]; and indirect medical costs saved by preventing salary losses (-$10,421).[27] Overall, latanoprost therapy accrues a net gain of $483,582 per capita to patients, insurers, and society over and above the $17,110 ophthalmic direct medical costs expended. This results in a 21-year financial ROI of 2,826%, which equates to an 18.2% annual ROI during each of the 21 years.

COST-EFFECTIVENESS

The third-party insurer, cost perspective (direct ophthalmic medical costs an insurer should pay) cost-utility ratio (CUR) is ($17,110/2.229 QALYs =) $7,676/QALY. The societal cost perspective, CUR, including all costs expended and gained, is (-$483,582/2.229 QALYs =) -$216,931/QALY. A negative CUR indicates that the overall societal costs returned to as a result of an intervention exceed the direct medical costs expended for that intervention. There is thus a financial gain to society, predominantly to patients.[10]

Using the conventional upper limit of cost-effectiveness in the United States of $100,000/QALY,[6] it is evident that the third-party insurer cost perspective, CUR for latanoprost therapy for OAG, is very cost-effective at $7,676/QALY. With the societal cost perspective, CUR, the cost-effectiveness is extraordinary, providing a considerable financial ROI to society for the ophthalmic direct medical costs expended (Table 2).

CONCLUSION

The analysis herein addresses important issues concerning glaucoma therapy with latanoprost, including the features with which the therapy is associated: a substantial improvement in quality of life due to the vision

TABLE 3. THE COST-UTILITY (COST-EFFECTIVENESS) OF INTERVENTIONS ACROSS MEDICINE COMPARED TO OPEN-ANGLE GLAUCOMA THERAPY WITH TOPICAL LATANOPROST 0.005% (IN 2014 US REAL DOLLARS)

Intervention	Patient Value Gain (%)	Third-Party Insurer Cost-Utility Ratio ($/QALY)
Warfarin versus aspirin, atrial fibrillation, 65-year-old low-risk cohort	0.15	$768,202
Statin therapy, low potency, low cardiovascular risk	1.5	$32,0489
Statin therapy, high potency, low cardiovascular risk	2.7	$22,434
Hypertension, β-adrenergic blockers	6.3 – 9.1	$2,850 - $30,540
Cataract surgery, second eye	12.7	$3,403
Ranibizumab, neovascular age-related macular degeneration	15.8	$49,377
Open-angle glaucoma therapy, latanoprost, 0.005%	17.8	$7,676
Cataract surgery, first eye	20.8	$1,636
Depression therapy, selective serotonin reuptake inhibitors	20-24	$1,275 - $12,866
Cochlear implant, child, profound deafness	29.3	$15,542

$/QALY = cost-utility ratio = dollars expended per quality-adjusted life-year gained. The patient value gain in percent is equivalent to the patient preference-based (utility-based) comparative effectiveness.

loss it prevents, highly favorable cost-effectiveness, and considerable dollars returned to society for the ophthalmic direct medical dollars expended.

Included among the important elements of this cost-utility model are the following features:

1. Jay and Murdoch[16] demonstrated that increased IOP in untreated glaucoma patients leads to progressive vision loss and end-stage glaucoma.
2. Higher IOP increases the rapidity of vision loss that occurs in association with end-stage glaucoma.[16]
3. End-stage glaucoma is associated with a visual acuity of approximately 20/800.[16]
4. Vision loss is typically bilateral with OAG.[28]
5. Glaucoma therapy improves quality of life considerably by prolonging the time of good vision. The gain in quality of life can be measured with patient-based, time trade-off utilities.[6]
6. The comparative effectiveness (patient value gain = patient quality of life gain = 17.3%) associated with latanoprost therapy for OAG compares favorably with interventions across ophthalmology and medicine (Table 3).[6-10]
7. Glaucoma therapy with latanoprost is very cost-effective, with a third-party insurer cost perspective, CUR of $7,676/QALY and a societal cost perspective, CUR of (-$216,931)/QALY.
8. Glaucoma therapy with latanoprost provides a large financial value gain (ROI of 2,826% over 21 years, or 18.2% annually) for the direct ophthalmic medical costs expended.
9. This VBM, glaucoma cost-utility (cost-effectiveness) model is standardized and can be compared with VBM cost-utility models across all ophthalmic and medical interventions.[6-10]

Although the Agency for Healthcare Research and Quality Comparative Effectiveness Reviews[2,3] cast doubt on the effectiveness of glaucoma therapy, our VBM cost-utility model strongly indicates a different clinical

scenario. Glaucoma therapy yields superb comparative effectiveness by preventing the vision loss associated with untreated glaucoma; greatly improves patients' quality of life; returns considerable dollars to patients, insurers and society; and has excellent cost-effectiveness referent to interventions across medicine.

We are certain that VBM cost-utility analysis will eventually play a major role in the delivery of health care in the United States for two reasons. First, it allows identification of the therapies that confer the greatest patient value (benefit), thus allowing higher-quality patient care. Second, it demonstrates which comparator interventions that provide similar patient value are less expensive. This feature is estimated to have the potential to save hundreds of billions of dollars over years in the US health care system.[6] Such a system of cost-utility analysis has been highly successful in the United Kingdom to date and is becoming increasingly popular across the globe. We believe physicians must play an active role in the creation of a VBM information system for physicians and patients, rather than leave its development solely in the hands of those who may not be directly involved in the clinical care of patients. ■

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