

# The comparative effectiveness and cost-effectiveness of vitreoretinal interventions

Melissa M. Brown<sup>a,b,c</sup>, Gary C. Brown<sup>a,d,e</sup>, Heidi C. Brown<sup>a</sup>, Blair Irwin<sup>a</sup> and Kathryn S. Brown<sup>a</sup>

<sup>a</sup>Center for Value-Based Medicine, Flourtown,

<sup>b</sup>Department of Ophthalmology, University of Pennsylvania, Philadelphia, <sup>c</sup>Leonard Davis Institute of Health Economics, University of Pennsylvania, Philadelphia, <sup>d</sup>Retina Service, Wills Eye Institute, Jefferson Medical College, Philadelphia and

<sup>e</sup>Eye Research Institute, Philadelphia, Pennsylvania, USA

Correspondence to Melissa M. Brown, MD, BSN, MN, MBA, Director, Center for Value-Based Medicine, Box 335, Flourtown, PA 19031, USA  
E-mail: mbrown@valuebasedmedicine.com

**Current Opinion in Ophthalmology** 2008, 19:202–207

## Purpose of review

The comparative effectiveness of medical interventions has recently been emphasized in the literature, typically for interventions in a similar class. Value-based medicine, the practice of medicine based on the value (improvement in quality of life and/or length of life) conferred by medical interventions, allows a measure of comparative effectiveness of interventions across all of health care, no matter how disparate. This report discusses recent comparative effectiveness studies in the vitreoretinal literature.

## Recent findings

Vitreoretinal interventions have good to excellent comparative effectiveness compared with commonly utilized interventions across health care, such as treatment for osteoporosis and hyperlipidemia. They also tend to be cost-effective when an upper limit of \$100 000/quality-adjusted life-year is utilized.

## Summary

Value can be measured using either or both of two outcomes – the quality-adjusted life-year gain and/or the percentage improvement in value – both of which allow for an evaluation of comparative effectiveness, which can be compared on the same scale for every intervention. This value can also be integrated with costs using the outcome of dollars expended per quality-adjusted life-year (\$/quality-adjusted life-year, or the cost-utility ratio), which allows a comparison of cost-effectiveness across all interventions. The majority of vitreoretinal interventions confer considerable value and are cost-effective.

## Keywords

comparative effectiveness, cost-effectiveness, value-based medicine, vitreoretinal interventions

Curr Opin Ophthalmol 19:202–207  
© 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins  
1040-8738

## Introduction

Value-based medicine is the practice of medicine based upon the value (improvement in quality of life and/or length of life) conferred by medical interventions [1–3,4<sup>••</sup>]. As such, value integrates all of the benefits and adverse events associated with an intervention into the most probable outcome. This value outcome can be measured using the quality-adjusted life-year (QALY) and/or the percentage improvement in value, both of which allow for evaluations of comparative effectiveness across all interventions. The value can also be integrated with associated costs using the outcome of dollars expended per QALY (\$/QALY, or the cost-utility ratio); this allows a measure of cost-effectiveness that can be compared across all interventions [5–18].

## Comparative effectiveness

Most comparative effectiveness studies compare the benefit of medical interventions in the same class using

common outcomes [19–21]. For example, an exhaustive comparative effectiveness analysis of treatments for osteoporosis uses the major outcomes of vertebral fracture, hip fracture, and/or other fractures (wrist, humerus, radius, ulna, and so forth) [21]. The analysis takes into account the best evidence-based medicine data from randomized clinical trials and meta-analyses. It also considers what are judged by a group of experts to be the most important adverse events associated with treatment, for instance upper gastrointestinal perforations, ulcers and bleeds, acute coronary syndrome, breast cancer, and others.

Evidence-based medicine comparative effectiveness analyses, despite extensive, superlative literature investigations, encounter four major problems [1]. First, they fail to incorporate all benefits, all adverse events, and the incidences of all adverse events associated with an intervention into a single numeric. Second, they fail to take into account quality of life issues, which are critically important in assessing both benefits and adverse events. Third, their outcomes are generally not comparable

across specialties. As an example, it is difficult to ascertain whether bone fractures are more or less incapacitating than vitreous hemorrhage in diabetic retinopathy. Finally, their outcomes are difficult to incorporate into economic analyses.

Value-based medicine comparative effectiveness analyses overcome each of the above inadequacies [1–3,4\*\*]. The same extensive, evidence-based literature searches, analyses of randomized clinical trials, and meta-analyses can be used, but they are taken to the higher level of value-based medicine. In contrast to the outcomes of evidence-based medicine comparative effectiveness analysis, the value-based medicine comparative effectiveness outcomes of QALY gain, value gain, and cost-utility integrate all benefits and adverse events (and their respective incidences) into a single numeric. They also take into account all beneficial and adverse quality of life issues, and can be compared across all specialties and interventions, no matter how disparate. Finally, they encompass the most sophisticated form of health care economic analysis, namely cost-utility analysis.

A description of value-based medicine analyses follows.

### Quality-of-life measured by utility analysis

The length of life gain conferred by an intervention can often be determined from the literature, but the quality of life improvement is more difficult to ascertain. Utility analysis, however, can objectively measure the quality of life associated with a disease or health state. (The terms ‘disease’ and ‘health state’ are most often used interchangeably; a disease, however, typically connotes one health problem, whereas a health state can refer to a single health problem or a combination of problems [1]. For example, age-related macular degeneration is a disease, whereas a health state might refer to the overall health of a patient with hypertension in conjunction with osteoarthritis and cataracts.)

Utility analysis quantifies quality of life along a scale from 0.00 (death) to 1.00 (normal health, or normal bilateral

**Table 1 Time tradeoff utilities associated with visual acuity in the better-seeing eye**

Visual acuity	Utility
20/20 in each eye permanently	1.00
20/20 (20/20–20/25 in the other eye)	0.97
20/20 ( $\leq$ 20/40 in the other eye)	0.92
20/25	0.87
20/30	0.84
20/40	0.80
20/50	0.77
20/70	0.74
20/100	0.67
20/200	0.66
20/300	0.63
20/400	0.54
Counting fingers	0.52
Hand motions	0.35
Light perception	0.35
No light perception	0.26
Death	0.00

Adapted from Brown *et al.* [3].

vision, permanently). As the vision in the better-seeing eye decreases, the corresponding utility decreases (Table 1) [3]. The reason why ‘permanently’ is specified is illustrated by the fact that patients with normal 20/20 vision in each eye permanently have a utility of 1.00, whereas those with ocular disease, such as diabetic retinopathy, and 20/20 vision bilaterally have an associated utility of 0.97 [3]. The latter occurs predominantly because patients with eye disease worry about the possibility that their vision will be diminished or lost in the future [1,3].

Utility analysis can thus quantify the improvement in quality of life conferred by an intervention [22–28]. For example, if the vision in the better-seeing eye improves from 20/100 to 20/40, then the corresponding utility (Table 1) increases from 0.67 to 0.80—a utility gain of 0.13.

Value-based medicine analyses utilize time tradeoff utilities from patients, because utilities obtained from patients with a disease can differ dramatically from those obtained from surrogate respondents (Table 2) [29]. A list of utilities associated with nonocular health states is

**Table 2 Utilities of respondent groups for age-related macular degeneration**

Categorical ARMD groupings	Study subjects				P value (n = 46)
	Patients [2,3] (n = 82)	Community [3] (n = 142)	Clinicians [3] (n = 62)	Ophthalmologists [22]	
Mild ARMD (20/20–20/40)	0.83	0.96	0.93	0.98	<0.0001 <sup>a</sup>
Moderate ARMD (20/50–20/100)	0.68	0.92	0.88	0.89	<0.0001 <sup>a</sup>
Severe ARMD (20/200 or worse)	0.47	0.86	0.82	0.73	<0.0001 <sup>a</sup>
Very severe ARMD (<20/800)	0.40	NA	NA	0.67	<0.0001 <sup>a</sup>

Snellen visual acuity ranges for the better seeing eye are listed below the mild age-related macular degeneration (ARMD), moderate ARMD, severe ARMD, and very severe ARMD groupings.

<sup>a</sup> The patient average utilities differ significantly from those of the community, clinician, and ophthalmologist groups in all categorical ARMD groupings (analysis of variance,  $P < 0.0001$ ). Adapted from Brown *et al.* [29].

**Table 3 Patient-based time tradeoff utilities associated with multiple conditions**

Condition	TTO utility value
<b>Group 1</b>	
HIV, asymptomatic	0.94
S/P myocardial infarction, no symptoms	0.93
Cancer, all	0.92
Osteoporosis	0.91
Stroke, mild (able to perform usual activities)	0.90
Impotence	0.85
Gout	0.86
ARMD, mild	0.83
Vertebral fracture	0.82
HIV, symptomatic	0.82
Angina, moderate	0.80
S/P myocardial infarction, some residual angina and congestive heart failure	0.78
Prostate cancer (no pain; normal bladder, bowel and sexual function)	0.78
<b>Group 2</b>	
Claudication, severe	0.74
Prostate cancer (pain controlled; + normal bladder, bowel and sexual function + normal energy + presence of depression)	0.72
AIDS	0.70
Stroke, moderate (requiring some help, but able to walk without assistance)	0.69
ARMD, moderate	0.68
Fractured hip	0.63
Tuberculosis hospitalized	0.60
Angina, severe	0.58
Ulcerative colitis, requiring surgery	0.58
Dialysis, home	0.56
<b>Group 3</b>	
ARMD, severe	0.47
ARMD, very severe	0.40
Prostate cancer, advanced (uncontrolled pain; bladder, bowel and sexual function abnormal, depression, severe fatigue)	0.35
Stroke, severe (bedridden, incontinent and requiring constant care, at 6 months)	0.34
Total blindness (NLP OU)	0.26
Stroke, severe, with aphasia	0.26
Stroke, severe, total paralysis (at 10 years)	0.20

Group 1 includes health states associated with a utility  $>0.75$ , group 2 includes health states associated with a utility  $<0.75$  and  $>0.50$ , and group 3 includes health states associated with a utility  $\leq 0.50$ . ARMD, age-related macular degeneration; NLP, no light perception; ou, bilaterally; s/p, status post; TTO, time tradeoff. Adapted from Brown *et al.* [30].

shown in Table 3 [30], as are patient macular degeneration utilities.

The time tradeoff methodology of utility analysis has been described in detail elsewhere [22–28]. In essence, it presents the theoretical scenario of trading a proportion of theoretical future time of life in return for normal health during those years that remain after the trade. The utility is then calculated by subtracting the proportion of years traded from 1.0. As an example, if a person with 20/40 vision in the better eye is willing to trade 4 of 20 remaining years so that he or she would live the 16 remaining years with normal bilateral vision, then the utility associated with the 20/40 vision is  $(1.0 - 4/20) = 0.80$ .

## Value

The value conferred by an intervention is ascertained by multiplying its conferred utility gain by the duration of treatment benefit (in years), with the outcome measured in QALYs. For example, an intervention that improves vision from 20/100 to 20/40 for 20 years until death confers  $0.13$  utility gain  $\times 20$  years = 2.6 QALYs accrued. Value, as used in value-based medicine, does not connote money or obtaining a tangible good or service for a lesser price, but is rather the net patient benefit conferred by an intervention [1].

Length of life gain can also be integrated into the therapeutic equation. For example, if the above intervention also increases life expectancy by 2 years, then the total resultant QALY gain equals the sum of the 2.6 QALYs accrued due to quality of life improvement and the 1.6 QALYs accrued from living 2 years longer at a utility of 0.80. The total QALY gain is 4.2 QALYs =  $[(0.13 \times 20) + (0.80 \times 2)]$ . Needless to say, however, ophthalmic interventions rarely increase the length of life.

### Quality-adjusted life-year and percentage gain in value

Use of the QALY allows for the most sophisticated variant of comparative effectiveness, because this outcome can be compared for interventions across all of health care [1,5,6]. Alternatively, the outcome of percentage gain in value can also be used in the same fashion, with the same degree of comparative effectiveness sophistication. Percentage gain in value, similar to the QALY, takes into account both improvement in quality of life and/or length of life. As an example, the conferred value of the statins, which decrease cardiac ischemic events and stroke, thus improving length of life and quality of life, can be compared side by side with the conferred value of a pars plana vitrectomy, which improves vision, and thus quality of life, in a patient with diabetic retinopathy and vitreous hemorrhage.

### Value is critical

A critical pillar of value-based medicine is the dictum that a patient deserves the intervention that confers the greatest value. Only if the conferred value is similar for comparator interventions is it reasonable to differentiate on the basis of cost and select the intervention that is less expensive.

### Reference case

Of note is the fact that value-based medicine analyses typically assess the conferred value gained by the reference case, or the case of the average patient with a disease [1]. For example, the reference case age for neovascular age-related macular degeneration is approximately 74–75 years [31\*\*]. Using a reference cases analysis greatly decreases any bias against age for the methodology.

### Disability-adjusted life-year

One additional outcome, the disability-adjusted life-year (DALY), should be addressed. The DALY, the favored outcome by the World Health Organization, is similar to the QALY but it gives greater weight (value) to those in middle age, theoretically the most productive time of life [32]. The authors herein are not proponents of the DALY and believe that the DALY will not gain favor in the USA, because it is biased, and accrues less value, for those who are very young or who are older.

### Vitreoretinal interventions

The value-based medicine analyses of most vitreoretinal interventions reported are based upon randomized clinical trials. A list is provided in Table 4 [7–11,15,16, 31<sup>\*\*</sup>,33,34<sup>\*</sup>].

### Comparative effectiveness

It is of note that the majority of vitreoretinal interventions confer greater value, and thus have better comparative effectiveness, than two commonly prescribed drug groups, namely the biphosphonates for osteoporosis and the statins for hyperlipidemia. In the case of the statins, the vitreoretinal interventions confer greater value despite the fact that the statins decrease the incidence of myocardial infarction and stroke, thus decreasing both the disability and death associated with these events. It can thus be seen that both interventions that

improve length of life and quality of life can be compared using the same outcome.

### Cost-effectiveness

Standards for cost-utility analysis outcomes are not formally established by any agency in the USA at the current time. Nonetheless, most researchers in the USA consider interventions costing less than \$50 000/QALY to be very cost-effective [35], whereas those that cost more than \$100 000/QALY are not considered to be cost-effective [1,36]. It can readily be seen that vitreoretinal interventions are cost-effective when an upper cost-utility ratio of \$100 000/QALY is used (Table 4).

### UK National Institute for Health and Clinical Excellence

In the UK, the National Institute for Health and Clinical Excellence has established standards and advises the National Health Service regarding which drugs, devices, and other interventions are cost-effective and should or should not be used [37]. Interventions costing less than £20 000/QALY (about US\$40 000/QALY) are generally accepted as cost-effective, whereas those that cost more than £30 000/QALY (about US\$60 000/QALY) are only accepted as cost-effective for increasingly strong reasons [37].

The World Health Organization has suggested that interventions costing less than 1 × gross domestic product (GDP) per capita for a DALY (~\$40 000/QALY in the

**Table 4** Interventional comparative effectiveness

Intervention	QALY gain <sup>a</sup>	Value gain	2006 US\$/QALY
Biphosphonates ( <i>n</i> = 4, osteoporosis)	0.009 <sup>b</sup>	1.0% <sup>b</sup>	\$152 000 <sup>b</sup>
Retinal detachment repair (PVR), silicone oil	0.261	2.7%	\$45 304
Amblyopia therapy [10]	0.786	3.6%	\$2710
Statins ( <i>n</i> = 8, hyperlipidemia)	0.500 <sup>b</sup>	4.0% <sup>b</sup>	\$69 300 <sup>b</sup>
Laser, subfoveal CNVM	0.246	4.4%	\$8179
Vitrectomy, diabetic vitreous hemorrhage [8]	0.759	5.1%	\$2269
Laser, branch vein macular edema [15]	0.542	5.1%	\$3466
Subfoveal CNVM, all types, pegaptanib [31 <sup>**</sup> ]	0.363	5.9%	\$66 978
Calcium channel blockers ( <i>n</i> = 5, hypertension)	0.057/year <sup>b</sup>	6.3% <sup>b</sup>	\$10 218 <sup>b</sup>
Laser, extrafoveal CNVM [16]	0.513	8.1%	\$5985
PDT, classic subfoveal CNVM [31 <sup>**</sup> ]	0.491	8.1%	\$31 544
Proton pump inhibitors ( <i>n</i> = 5, GERD)	0.089/year <sup>b</sup>	11.0% <sup>b</sup>	\$17 909 <sup>b</sup>
Cataract extraction, second eye [11]	0.920	12.7%	\$2 972
Macular pucker surgery [33]	0.930	12.9%	\$4680
Threshold ROP, laser [7]	7.854	14.7%	\$239
Ranibizumab, occult/minimally classic CNVM [34 <sup>*</sup> ]	1.039	15.8%	\$50 691
Cataract extraction, first eye [9]	1.250	20.8%	\$2 262
SSRIs ( <i>n</i> = 5, depression)	0.140/year <sup>b</sup>	25.6% <sup>b</sup>	\$5750 <sup>b</sup>

Comparative effectiveness is measured in quality-adjusted life-year (QALY) gain and percentage gain in value. The cost-utility (\$/QALY) is also listed. Values for the nonocular interventions were calculated as follows. The value of the biphosphonates was calculated by utilizing the underlying evidence-based outcome of reduction in hip and/or spine fractures. The value of the statins was calculated by utilizing the underlying evidence-based outcome of reduction in cardiac events and/or stroke. The value of the calcium channel blockers was calculated by utilizing the underlying evidence-based outcome of reduction in cardiac events, stroke, and/or renal failure. The value of the proton pump inhibitors was calculated by utilizing the underlying evidence-based outcome of reduction in the symptoms of gastroesophageal reflux disease (GERD). The value of the selective serotonin reuptake inhibitors (SSRIs) was calculated by assessing the underlying evidence-based outcome of reduction in depression.

<sup>a</sup>The QALY accrual is for the duration of benefit for the reference case, unless the QALY accrual is shown per year of treatment.

<sup>b</sup>These interventional data are from internal files held at the Center for Value-Based Medicine (Flourtown, Pennsylvania, USA).

<sup>c</sup>Recalculated from the reference listed. CNVM, choroidal neovascular membrane; PDT, photodynamic therapy with verteporfin; PVR, proliferative vitreoretinopathy; ROP, retinopathy of prematurity.

USA) are very cost-effective, whereas those costing  $1 \times \text{GDP}$  per capita to  $3 \times \text{GDP}$  per capita for a DALY (about \$40 000–\$120 000/QALY) are cost-effective, and those costing more than  $3 \times \text{GDP}$  per capita for a DALY ( $> \$120\,000/\text{QALY}$ ) are not cost-effective [32]. By this definition, vitreoretinal interventions again appear to be cost-effective.

Of note is the fact that we [1] and other authors [6] refer to an economic analysis performed with the outcome of  $\$/\text{QALY}$  as a cost-utility analysis, whereas others [5] refer to this as a cost-effectiveness analysis. We believe that, for the sake of clarity, cost-effectiveness should refer to a study with an outcome other than  $\$/\text{QALY}$ , such as cost per life-year or cost per year of good vision gained.

### Cost-effectiveness without conferred value is insufficient

Comparing the cost-effectiveness of interventions without knowing their conferred value can provide misleading information. For example, the cost-utility associated with the treatment of subfoveal choroidal neovascularization is \$8179, whereas that associated with treatment of the same disease by intravitreal ranibizumab is \$50 691. Nonetheless, subfoveal laser therapy should virtually never be substituted for ranibizumab therapy because laser therapy, despite being more cost-effective, confers a 4.4% improvement in quality of life whereas ranibizumab therapy confers a 15.8% improvement in quality of life. From this example, it is evident that when comparing two or more interventions, it is critically important to know both the comparative effectiveness (conferred value) and cost-effectiveness. The cost-effectiveness alone is insufficient.

### Conclusion

In summary, vitreoretinal interventions deliver considerable value compared with other commonly utilized interventions across health care. They are also typically cost-effective. It is anticipated that, as additional vitreoretinal interventions become available, most will also be cost-effective. The reason for this is that people place an extraordinary degree of importance on their vision, especially when the vision is already diminished or threatened.

### References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 265–267).

- 1 Brown MM, Brown GC, Sharma S. Evidence-based to value-based medicine. Chicago, Illinois, USA: AMA Press; 2005. pp. 1–324.
- 2 Brown GC, Brown MM, Sharma S, *et al.* Value-based medicine and ophthalmology. An appraisal of cost-utility analyses. *Trans Am Ophthalmol Soc* 2004; 102:177–185.
- 3 Brown MM, Brown GC, Sharma S, Landy J. Healthcare economic analyses and value-based medicine. *Surv Ophthalmol* 2003; 48:204–223.
- 4 Brown MM, Brown GC, Sharma S. Value-based medicine. A paradigm for quality pharmaceutical care. *Drug Benefit Trends* 2006; 18:285–289. This paper demonstrates the power of the value-based medicine comparative effectiveness and cost-effectiveness tools in improving quality of care, in this instance pharmaceutical care, while reducing costs.
- 5 Gold MR, Patrick DL, Torrance GW, *et al.* Identifying and valuing outcomes. In: Gold ME, Siegel JE, Russell LB, Weinstein MC, editors. *Cost-effectiveness in health and medicine*. New York, New York, USA: Oxford University Press; 1996. pp. 82–134.
- 6 Drummond MF, O'Brien B, Stoddart GL, Torrance GW. *Methods for the economic evaluation of healthcare programmes*, 2nd ed. Toronto, Canada: Oxford University Press; 2000. pp. 1–3005.
- 7 Brown GC, Brown MM, Sharma S, *et al.* Cost-effectiveness of therapy for threshold retinopathy of prematurity. *Pediatrics* 1999; 104:e47.
- 8 Sharma S, Hollands H, Brown GC, *et al.* The cost-effectiveness of early vitrectomy for the treatment of vitreous hemorrhage in diabetic retinopathy. *Curr Opin Ophthalmol* 2001; 12:230–234.
- 9 Busbee B, Brown MM, Brown GC, Sharma S. Incremental cost-effectiveness of initial cataract surgery. *Ophthalmology* 2002; 109:606–612.
- 10 Membreno J, Brown MM, Brown GC, *et al.* A cost-utility analysis of therapy for amblyopia. *Ophthalmology* 2002; 109:2265–2271.
- 11 Busbee B, Brown MM, Brown GC, Sharma S. A cost-utility analysis of cataract surgery in the second eye. *Ophthalmology* 2003; 110:2310–2317.
- 12 Sharma S, Brown GC, Brown MM, *et al.* The cost-effectiveness of grid laser photocoagulation for the treatment of diabetic macular edema: Results of a patient-based cost-utility analysis. *Curr Opin Ophthalmol* 2000; 11:175–179.
- 13 Brown GC, Brown MM, Sharma S, *et al.* Incremental cost-effectiveness of laser photocoagulation for choroidal neovascularization associated with histoplasmosis. *Retina* 2000; 20:331–337.
- 14 Brown GC, Brown MM, Sharma S. Incremental cost-effectiveness of laser therapy for subfoveal choroidal neovascularization. *Ophthalmology* 2000; 107:1374–1380.
- 15 Brown GC, Brown MM, Sharma S, *et al.* Incremental cost-effectiveness of therapeutic interventions for branch retinal vein occlusion. *Ophthalmic Epidemiol* 2002; 9:1–10.
- 16 Busbee B, Brown MM, Brown GC, Sharma S. A cost-utility analysis of laser photocoagulation for extrafoveal choroidal neovascularization. *Retina* 2003; 23:279–287.
- 17 Brown GC, Brown MM, Sharma S, Busbee B. A cost-utility analysis of interventions for proliferative vitreoretinopathy. *Am J Ophthalmol* 2002; 133:365–372.
- 18 Brown GC, Brown MM. Is prophylactic PRP in ischemic CRVO a good idea? *Rev Ophthalmol* 2000; 7:106, 106–111.
- 19 Balk E, Raman G, Chung M, *et al.* Comparative effectiveness review number 5. Comparative effectiveness management strategies for renal artery stenosis. Rockville, Maryland, USA: Agency for Health-Related Quality (AHRQ); 2006.
- 20 Bolen S, Wilson L, Vassy J, *et al.* Comparative effectiveness review number 8. Comparative effectiveness and safety of oral diabetes medications with type 2 diabetes. Rockville, Maryland, USA: Agency for Health-Related Quality (AHRQ); 2007.
- 21 MacLean C, Alexander A, Carter J, *et al.* Comparative effectiveness review number 12. Comparative effectiveness of treatments to prevent fractures in men and women with low bone density or osteoporosis. Rockville, Maryland, USA: Agency for Health-Related Quality (AHRQ); 2007.
- 22 Brown GC. Vision and quality of life. *Trans Am Ophthalmol Soc* 1999; 97:473–512.
- 23 Brown MM, Brown GC, Sharma S, Landy J. Quality of life with visual acuity loss from diabetic retinopathy and age-related macular degeneration. *Arch Ophthalmol* 2002; 120:481–484.
- 24 Brown GC, Brown MM, Sharma S, Kistler J. Utility values associated with age-related macular degeneration. *Arch Ophthalmol* 2000; 118:47–51.
- 25 Brown MM, Brown GC, Sharma S, Shah G. Utility values and diabetic retinopathy. *Am J Ophthalmol* 1999; 128:324–330.
- 26 Brown MM, Brown GC, Sharma S, *et al.* Utility values associated with blindness in an adult population. *Br J Ophthalmol* 2001; 85:327–331.
- 27 Brown GC, Brown MM, Sharma S, *et al.* The reproducibility of ophthalmic utility values. *Trans Am Ophthalmol Soc* 2001; 99:71–76.

- 28** Sharma S, Brown GC, Brown MM, *et al.* Validity of the time trade-off and standard gamble methods of utility assessment in retinal patients. *Br J Ophthalmol* 2002; 86:493–496.
- 29** Brown GC, Brown MM, Sharma S, *et al.* The burden of age-related macular degeneration. A value-based analysis. *Trans Am Ophthalmol Soc* 2005; 103:180–193.
- 30** Brown MM, Brown GC, Sharma S, *et al.* The burden of age-related macular degeneration: a value-based analysis. *Curr Opin Ophthalmol* 2006; 17:257–266.
- 31** Brown GC, Brown MM, Brown HC, *et al.* A value-based medicine comparison of interventions for subfoveal neovascular macular degeneration. *Ophthalmology* 2007; 114:1170–1178.
- An article which compares then cost-utility of different vitreoretinal interventions.
- 32** World Health Organization. The World Health Report 2002: reducing risks, promoting healthy life. Geneva, Switzerland: World Health Organization; 2002. <http://www.who.int/whr/2002/en/index.html> [Accessed 28 February 2008].
- 33** Gupta O, Brown GC, Brown MM. A value-based medicine cost-utility analysis of idiopathic epiretinal membrane surgery. *Am J Ophthalmol* 2008 (in press).
- 34** Brown MM, Brown GC, Brown HC, Peet J. A value-based medicine analysis of ranibizumab for the treatment of subfoveal neovascular macular degeneration. *Ophthalmology* 2008 [Epub ahead of print].
- This is an example of comparative effectiveness and cost-effectiveness performed using value-based medicine principles.
- 35** Heudebert GR, Centor RM, Klapow JC, *et al.* What is heartburn worth? A cost-utility analysis of management strategies. *J Gen Intern Med* 2000; 15:175–182.
- 36** Laupacis A, Feeny D, Detsky AS, Tugwell PX. How attractive does a new technology have to be to warrant adoption and utilization. Tentative guidelines for using clinical and economic evaluations. *Can Med Assoc J* 1992; 146:473–481.
- 37** National Institute for Health and Clinical Excellence (NICE). Incorporating health economics in guidelines and assessing resource impact. In: The guidelines manual. London, UK: NICE; 2007. <http://www.nice.org.uk/niceMedia/pdf/GuidelinesManualChapter8.pdf> [Accessed 28 February 2008].