Introduction

Healthcare economic analyses have appeared with increased frequency in the more recent healthcare literature [1**]. It behooves the clinician to have a working knowledge and familiarity of these analyses since they often accurately reflect the patient value conferred by interventions more so than just evidence-based data alone. Additionally, these analyses, especially cost-utility analysis, are appropriately beginning to play a role in the actual delivery of healthcare and healthcare policy [2*].

Types of healthcare economic analyses

There are essentially four basic types of healthcare economic analyses:

1. Cost-minimization analysis
2. Cost-benefit analysis
3. Cost-effectiveness analysis
4. Cost-utility analysis

We will discuss each of these and their applications in order and address examples of each. In particular, we will emphasize cost-utility analysis, the most sophisticated and clinically useful form of healthcare economic analysis.

Cost-minimization analysis

Cost-minimization analysis compares two interventions of identical effectiveness to determine which one is less costly [1**]. It is the least commonly used of the healthcare economic analyses [3].

A major drawback to the performance of a cost-minimization analysis is the fact that two interventions are not often directly comparable. For example, a comparison of cholecystectomy performed by conventional surgery and by laparoscopic surgery compares two seemingly alike interventions until it becomes apparent with closer scrutiny that the discomfort associated with the interventions, as well as the complications, rehabilitation, use of medicines, and so forth can be quite different.

A good example of an appropriate cost-minimization analysis is the study by Cresswell et al. [4]. These authors noted that cataract surgery performed in a center in which only cataract surgery is performed is less expensive than cataract surgery performed in a center in which all forms of ophthalmic surgery are performed. In this instance, the interventions under study are exactly the same.

Cost-benefit analysis

Cost-benefit analysis compares the dollars expended for an intervention with the dollars saved as a result of the...
intervention \[1^{**}\]. For example, the costs expended treating infants with threshold retinopathy of prematurity with laser therapy can be compared with the disability costs obviated by the prevention of blindness, as well as the greater contribution of sighted individuals (with generally higher income than blind individuals) to the Gross Domestic Product (GDP). The GDP is the sum of all goods produced in the United States annually. As such, the salaries of individuals are included in the GDP.

Cost-benefit analysis as described above is generally well understood. It is particularly useful in demonstrating savings associated with healthcare policy decisions.

**Cost-effectiveness analysis**

Cost-effectiveness analysis measures the dollars expended in return for a particular benefit \[1^{**}\]. The benefit is often measured in terms of years of life (life-years) gained, but can also be measured in vision-years saved, disability-free years, years of good vision, strokes averted, myocardial infarctions averted, and so forth.

An excellent example of cost-effectiveness analyses is the paper by Tengs et al. \[5\], which describes the cost effectiveness, in terms of cost per year of life saved, for 500 life-saving interventions. Cost-effectiveness analyses reveal that the approximate, mean 2004 US dollar cost expended to gain a year of life for different classes of interventions as in Table 1.

Examples of medical therapy include immunizations, blood pressure treatment, cancer screening, and so forth. Injury reduction controls include speed limit laws, seat belt regulations, and the use of motorcycle helmets, while toxin controls include the prevention of radiation emissions, asbestos regulations, and limits on lead levels in water.

Of importance is the fact that some researchers consider the realm of cost-effectiveness analysis to include the costs expended for value, as measured in quality-adjusted life-years (QALYs) \[6\]. Other researchers \[7\], including the authors herein \[1^{**}\], believed that a healthcare economic analysis that uses the QALY outcome should be routinely referred to as cost-utility analysis.

**Cost-utility analysis**

Cost-utility analysis measures the dollars expended in return for the value gained. Value is measured in terms of the improvement in length of life and/or quality of life, and is measured using the outcome of the quality-adjusted life year. Cost-utility analysis is the main instrument used in value-based medicine, the practice of medicine based upon the patient-perceived value conferred by healthcare interventions.

### Quality of life

Measuring the improvement in length of life conferred by an intervention can generally be gleaned from a review of clinical trials in the peer-reviewed literature, but quantifying the improvement in quality of life is more difficult. The improvement in quality of life can, however, be objectively measured using utility analysis \[8-15\].

By convention, utility analysis measures quality of life on a scale from 0.0 (death) to 1.0 (perfect health or perfect vision for ophthalmic interventions). There are three basic variants of utility analysis: (1) time tradeoff; (2) standard gamble and (3) willingness-to-pay. Data suggest that the time tradeoff method is the most reproducible \[1^{**}\]. A time tradeoff utility value is typically calculated by asking a person how long they expect to live and subtracting the proportion of time traded, if any from 1.0. For example, the average person with 20/200 vision in the better-seeing eye is willing to trade about one of three years remaining in return for perfect vision. The resultant utility value is therefore \(1.0 - \frac{1}{3} = 0.67\). Of note is the fact that ocular utility values most closely correlate with the vision in the better-seeing eye, rather than the underlying cause of visual loss \[7,8\]. It is the authors’ belief that the time tradeoff data should be assessed from the patient perspective and in sufficient numbers to allow for narrow confidence intervals.

### Value

Utility analysis measures the quality of life associated with a health state and can quantify the improvement in quality of life conferred by an intervention. For example if a patient with a bilateral diabetic vitreous hemorrhage and 20/200 vision OU (utility value of 0.67) undergoes a vitrectomy and the vision improves to 20/20 (utility value of 0.92) there is a gain of 0.25 utility points, or a 37% improvement in quality of life. Multiplying this improvement by the duration of benefit in years yields the number of QALYs gained. For example, if the duration of benefit is 8 years, the QALY gain = \(8 \times 0.25 = 2.0\). The improvement in length of life, which is not usually the case with ophthalmic interventions is integrated by adding the product of (the number of years gained) \(\times\) (the utility value). Thus, if the ophthalmic intervention theoretically added two years of life as well as improving quality, the added value conferred would also include \(2 \times 0.92 = 1.84\) QALYs.
The value conferred by an intervention can be compared with that conferred by any other intervention. Thus, the value of all interventions in healthcare, within ophthalmology and outside the field, can be compared using the same outcome. Since it incorporates quality of life variables often ignored in the primary outcomes of evidence-based clinical trials, the practice of value-based medicine allows for higher quality of care than evidence-based data alone [1**]. In this regard, decision analysis is a tool that, combined with utility analysis, allows for the incorporation of all benefits and all adverse effects of an intervention into the value-based medicine therapeutic equation [1**].

Cost-utility
Once the value of an intervention is calculated, the cost can be incorporated to arrive at the cost-utility. For example, if the 2.0 QALY gain from cataract surgery is associated with an incremental (extra cost occurring due to the intervention) cost of $2000, the cost per quality-adjusted life-year, or $/QALY, is $2000/2, or $1000/QALY.

By convention, interventions that cost less than $100,000/QALY are considered cost effective [16], while those costing less than $50,000 are especially cost effective [17]. (Note that with cost-utility analysis that interventions are still referred to as cost-effective, rather than cost-utilitarian.) Nonetheless, this upper limit is an arbitrary number and, as more interventions are studied, the cost-utility will likely be measured in standard deviations from the mean.

A list of the cost-utility of ophthalmologic interventions is shown in Table 2. Non-ophthalmologic interventions have also been inserted into the table for reference. The great majority of ophthalmologic interventions are cost effective, in large part secondary to the great value that patients place upon good vision and interventions that can maintain or restore good vision [18,19-30**].

What's important?
Both the value and the cost-utility of an intervention are important, and both should be assessed when evaluating an intervention. From the patient perspective, the desired intervention should be the one that provides the greatest value. For example, if laser therapy for subfoveal choroidal neovascularization associated with age-related macular degeneration (ARMD) is very cost effective at $5298/QALY (Table 2) and a pharmacologic therapy for ARMD has a cost-utility of $35,000 one might naturally assume that laser therapy is preferred. This is not necessarily the case. If laser therapy confers 0.3 QALY but pharmacologic therapy confers 0.3 QALY, the pharmacologic treatment is the strategy of choice. The pharmacologic treatment may be less cost effective in an absolute measure, but if it confers greater value it should be the preferred strategy. It is at this point that the finances of the healthcare system evaluating the intervention may become relevant. In the US measures falling within the 'very cost-effective' range (<$50,000/QALY) relative to all medical interventions should be viewed as important therapies available within our medical armamentarium. As the use of cost-utility analyses becomes more common and relevant in determining quality standards of care, it is imperative that the analyses be performed using standardized measures of quality of life and calculation of costs as well as the

<table>
<thead>
<tr>
<th>Intervention</th>
<th>$/QALY gained</th>
</tr>
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<tbody>
<tr>
<td>Laser therapy for threshold retinopathy of prematurity [18]</td>
<td>793</td>
</tr>
<tr>
<td>H. pylori eradication for dyspepsia [2*]</td>
<td>1,427</td>
</tr>
<tr>
<td>Cryotherapy for threshold retinopathy of prematurity [18]</td>
<td>2,088</td>
</tr>
<tr>
<td>Vitrectomy for vitreous hemorrhage in type 1 diabetics [19]</td>
<td>2,098</td>
</tr>
<tr>
<td>Initial cataract surgery [20]</td>
<td>2,155</td>
</tr>
<tr>
<td>Treatment of amblyopia [21]</td>
<td>2,463</td>
</tr>
<tr>
<td>Second eye cataract surgery [22]</td>
<td>2,945</td>
</tr>
<tr>
<td>Laser therapy for diabetic macular edema [23]</td>
<td>3,406</td>
</tr>
<tr>
<td>Laser therapy for extrafoveal choroidal neovascularization with histoplasmosis [24]</td>
<td>4,662</td>
</tr>
<tr>
<td>Laser therapy for subfoveal choroidal neovascularization associated with ARMD [25]</td>
<td>5,298</td>
</tr>
<tr>
<td>Drug maintenance for recurrent depression [2*]</td>
<td>6,588</td>
</tr>
<tr>
<td>Laser therapy for macular edema associated with branch retinal vein occlusion [26]</td>
<td>7,021</td>
</tr>
<tr>
<td>Cochlear implant in children [2*]</td>
<td>10,520</td>
</tr>
<tr>
<td>Laser therapy for extrafoveal choroidal neovascularization associated with ARMD [27]</td>
<td>13,061</td>
</tr>
<tr>
<td>Laser therapy to prevent neovascular glaucoma with very ischemic central retinal vein occlusion [28]</td>
<td>17,147</td>
</tr>
<tr>
<td>Computerized tomography (CT) for equivocal neurological symptoms</td>
<td>24,733</td>
</tr>
<tr>
<td>Radiation therapy after conservative surgery for early-stage breast cancer [2*]</td>
<td>33,264</td>
</tr>
<tr>
<td>Surgery for PVR, silicone oil (no previous vitrectomy) [29]</td>
<td>40,252</td>
</tr>
<tr>
<td>Chemoprophylaxis after occupational HIV exposure [2*]</td>
<td>44,051</td>
</tr>
<tr>
<td>Treating mildly symptomatic Herpes zoster [2*]</td>
<td>53,873</td>
</tr>
<tr>
<td>70-year old</td>
<td>53,873</td>
</tr>
<tr>
<td>40-year old</td>
<td>118,069</td>
</tr>
<tr>
<td>Magnetic resonance imaging for equivocal neurologic symptoms [2*]</td>
<td>123,935</td>
</tr>
<tr>
<td>Treatment (anterior chamber paracentesis + Carbogen [30] therapy) for central retinal artery occlusion</td>
<td>7,15 million</td>
</tr>
</tbody>
</table>
Value-based medicine is the practice of medicine based on the utility of any interventions in healthcare, no matter how frequently in the literature. Cost-utility analysis, the most sophisticated of the healthcare economic analyses, assesses both the value conferred by an intervention and the dollars expended for that value. Thus the value and the cost-utility of any interventions in healthcare, no matter how disparate, can be compared using the same outcomes. Value-based medicine is the practice of medicine based upon the patient value conferred by interventions. It also integrates the cost paid for value. The practice of value-based medicine improves quality of care by identifying those interventions that provide the most value, and also allows healthcare savings by identifying interventions that confer superior value for lesser cost.

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

A comprehensive review of all of the ophthalmic cost-utility analyses in the literature to date.