THE BURDEN OF AGE-RELATED MACULAR DEGENERATION: A VALUE-BASED MEDICINE ANALYSIS

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ABSTRACT

Purpose: To assess the quality-of-life loss and the macroeconomic financial consequences associated with age-related macular degeneration (ARMD).

Methods: Time tradeoff utility analysis was performed to assess the quality-of-life diminution caused by ARMD (both dry and neovascular) in cohorts consisting of (1) patients with ARMD, (2) ophthalmologists asked to assume they had various degrees of severity of ARMD, (3) healthcare providers asked to assume they had various degrees of severity of ARMD, and (4) participants from the general community asked to assume they had various degrees of severity of ARMD. ARMD was classified according to vision in the better-seeing eye as (1) mild: 20/20 to 20/40, (2) moderate: 20/50 to 20/100, (3) severe: ≤20/200, or (4) very severe: ≤20/800.

Results: Mild ARMD caused a 17% decrement in the quality of life of the average patient, similar to that encountered with moderate cardiac angina or symptomatic human immunodeficiency virus syndrome. Moderate ARMD caused a 32% decrease in the average patient's quality of life, similar to that associated with severe cardiac angina or a fractured hip. Severe ARMD caused a 53% decrease in quality, more than that of dialysis, and very severe ARMD caused a 60% decrease in the average ARMD patient's quality of life, similar to that encountered with end-stage prostate cancer or a catastrophic stroke that leaves a person bedridden, incontinent, and requiring constant nursing care. Patients with varying degrees of severity of ARMD were found to have quality-of-life impairment ranging from 96% to 750% greater than that estimated by treating ophthalmologists for the same condition.
An economic analysis based upon losses to the gross domestic product suggests that ARMD has approximately a $30 billion annual negative impact. The return on investment is therefore potentially high for both treatment with current ARMD therapies and the research costs invested in the development of new ARMD treatment modalities.

Conclusions: ARMD is a major public health problem that has a devastating effect upon patients and marked adverse financial consequences for the economy.

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INTRODUCTION

Age-related macular degeneration (ARMD) is the leading cause of legal blindness in the older population in the United States today.[1] In addition to the considerable deleterious effect it has upon the quality of life,[2-4] ARMD has adverse financial consequences upon the overall economy of the United States. To date, little study has been devoted to comparing the adverse effects of ARMD with those of other diseases.[2-4]

There are two forms of ARMD: (1) dry, or atrophic, and (2) wet, or neovascular. According to the International Age-Related Maculopathy Epidemiological Study Group,[5] the fundus appearance of *dry macular degeneration* is characterized by the presence of geographic atrophy, drusen, and areas of retinal pigment epithelial hyperplasia. Typically, dry ARMD occurs in an eye prior to development of the wet form.

The onset of *wet macular degeneration* (also called *exudative macular degeneration* or *neovascular macular degeneration*) is heralded by the appearance of subretinal blood, hard exudates, and/or subretinal fluid in the macula occurring secondary to choroidal neovascularization. Development of the wet variant of ARMD is usually accompanied by visual loss that progresses over weeks to months and longer.[2] The majority of eyes that progress to legal blindness (20/200 or worse visual acuity) have the wet variant. Although ARMD is the leading cause of legal blindness in the older population in the United States,[6] the etiology is unknown.

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PREVALENCE

The prevalence of ARMD increases with advancing age.[1,6] Overall, 1.47% of people over 40 years of age, or approximately 1.75 million people in the United States, have *advanced macular degeneration* (the neovascular variant and/or geographic atrophy variant). Among this group, approximately 1.25 million have the neovascular (wet) variant of macular degeneration (Table 1).[1,6] The number of cases of wet macular degeneration in the United States is expected to rise to 1.875 million by the year 2020.[6]

It should be noted that many ophthalmologists in clinical practice consider the presence of macular drusen to be an early form of dry ARMD. Using that definition, 7 million people in the United States with macular drusen measuring 125 μm or more in diameter could be considered to have dry ARMD.[6]

TABLE 1. PREVALENCE OF AGE-RELATED MACULAR DEGENERATION (ARMD) IN THE UNITED STATES

AGE (YEARS)	NEOVASCULAR ARMD	GEOGRAPHIC ATROPHY ARMD*	DRUSEN (125 μm OR LARGER)
40-49	20,000	NA	51,000
50-54	40,000	27,000	519,000
55-59	36,000	25,000	534,000
60-64	41,000	31,000	585,000
65-69	60,000	46,000	709,000
70-74	101,000	80,000	906,000
75-79	154,000	132,000	1,049,000
80+	734,000	632,000	2,154,000

NA = not applicable.

*Geographic atrophy is an area of retinal pigment epithelial depigmentation at least 175 μm in diameter. Note that some cases can have neovascular ARMD in one eye and geographic atrophy in the fellow eye.

Adapted from Bird, et al.[5]

INCIDENCE

Data from the Beaver Dam Eye Study,[1] a longitudinal cross-sectional study of people living in Beaver Dam, Wisconsin, reveal that among a group aged 43 to 86 years, the incidence of early (mild) ARMD is 12.1% over a 10-year period, or 1.21% per year. Nonetheless, among people aged 75 years or older, the incidence rises to 36.7% over a 10-year period, or 3.67% per year. The incidence of late (advanced) ARMD is 2.1% over a 10-year period in the 43- to 86-year-old group and 9.5% over a 10-year period in the group aged 75 years or older. These numbers are summarized in Table 2.

TABLE 2. INCIDENCE OF AGE-RELATED MACULAR DEGENERATION (ARMD) OVER A 10-YEAR PERIOD FROM THE BEAVER DAM STUDY

AGE GROUP (YEARS)	10-YEAR INCIDENCE OF EARLY ARMD (%)	10-YEAR INCIDENCE OF LATE ARMD (%)
43 to 54	4.1	0.1
55 to 64	10.7	1.0
65 to 74	23.6	4.4
75+	36.7	9.5
Overall	12.1	2.1

Adapted from Klein et al.[1]

Extrapolation of data from the Beaver Dam Eye Study[1] and the Eye Diseases Prevalence Research Group[6] suggests that 1.6 million new cases of dry macular degeneration and 153,000 new cases of wet macular degeneration associated with ARMD develop in the United States each year.

The relevance, or burden, of a disease from the public health perspective depends upon the incidence of the disease, the impact of the disease upon the lives of people it affects, and the cost impact. In essence, both the human burden and the economic burden give the best profile of the total burden of a disease and its public health relevance.

From the incidence viewpoint, it is already clear that ARMD is a major public health problem. The effect of ARMD upon an individual, or the human burden, can best be demonstrated using evidence-based medicine data integrated with value-based medicine methodology, whereas the economic disease impact can be assessed by multiple methods, one of which is measuring the effect of the disease upon the gross domestic product (GDP).

The objectives of this manuscript are to assess the relevance of ARMD as a public health dilemma by (1) comparing the patient-perceived quality of life associated with ARMD with quality-of-life estimates obtained from surrogate respondents asked to presume they had ARMD; (2) comparing the patient-perceived quality of life associated with ARMD with the quality of life associated with other diseases; and (3) quantifying the adverse macroeconomic effect of ARMD upon the economy of the United States.

METHODS

REVIEW OF VALUE-BASED MEDICINE CONCEPTS

Evidence-based medicine is the practice of medicine based upon the highest level of scientific evidence available. There are five levels of interventional studies, as shown in Table 3.[7] Level 1, the randomized clinical trial, represents the highest level of evidence. Level 1 data from clinical trials are the most reproducible and allow clinicians and patients to have the greatest confidence in the repeated outcomes of their treatments. It is preferable to use Level 1 data in value-based analyses that evaluate interventions. For the evaluation of quality of life, such as the case herein, cross-sectional data are reasonable.

TABLE 3. FIVE LEVELS OF INTERVENTIONAL EVIDENCE

LEVEL OF EVIDENCE	INTERVENTIONAL STUDY
Level 1	Randomized clinical trial with low type 1 error (≤0.05) and low type 2 error (≤20%) or meta-analysis
Level 2	Randomized clinical trial with high type 1 error (>0.05) and/or high type 2 error (>0.20)
Level 3	Uncontrolled, nonrandomized clinical trial (treatment group compared to no treatment group without randomization)
Level 4	Intervention on a series of patients with no comparison group
Level 5	Interventional case report

Adapted from Sharma.[7]

Although the data gleaned from clinical trials are invaluable, the primary evidence-based outcomes of clinical trials (eg, number of deaths, number of strokes, 3 lines of visual loss) often overlook important quality-of-life variables associated with a disease and interventions employed to treat that disease. In particular, the data do not present a mechanism by which the adverse effects associated with an intervention can be factored into the clinical value equation. Just as important, evidence-based data alone generally do not allow a comparison of the value conferred by dissimilar interventions across different specialties.

VALUE-BASED MEDICINE

Value-based medicine is the practice of medicine based upon the *value* conferred by interventions. This *value* is derived from evidence-based data that are converted to value-based data. As well as allowing a comparison of data from disparate interventions, value-based medicine also permits data from evidence-based clinical trials to be used in healthcare economic analyses. Of note is the fact that a value-based analysis is only as good as the underlying evidence-based data utilized in that analysis.

WHAT IS VALUE?

The value of a healthcare intervention is measured by quantifying the improvement it confers in (1) length of life and/or (2) the patient-perceived quality of life. Every intervention must deliver one or both, or it should be discarded from the therapeutic armamentarium. Most ophthalmologic interventions do not confer an improvement in length of life; the conferred value is therefore generally measured by quantifying the improvement in patient-perceived quality of life.

The improvement in length of life for most interventions can be gleaned from data in the evidence-based literature, but measuring the improvement in quality of life gained from an intervention is more difficult. It can, however, be objectively determined using

health-related quality-of-life instruments.

HEALTH-RELATED QUALITY-OF-LIFE INSTRUMENTS

There are numerous health-related quality-of-life instruments in use, including the Medical Outcomes Study Short-Form-36 (SF-36),[8] the Quality of Well-Being Scale,[9] and the Activities of Daily Living (ADL) Scale.[10] For ophthalmologic diseases, the most popular instruments are the 14-item Visual Function (VF-14)[11] and the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25).[12]

FUNCTION-BASED INSTRUMENTS

The majority of the health-related quality-of-life instruments in use are *function-based*, meaning that they evaluate entities such as physical function, social function, visual function, and psychological function.[13] But by essentially evaluating function, they can miss important additional aspects that compose quality of life, such as caregiver status, the welfare of dependants, economic distress, and fear of the future.[13] In addition, most function-based instruments are not applicable to diseases encountered across all specialties in healthcare. This is especially so for ophthalmologic instruments such as the VF-14 and the NEI VFQ-25, which are used only to evaluate ocular diseases. Function-based instrument results, in contrast to those of preference-based instruments, are generally not used in healthcare economic analyses.[13]

PREFERENCE-BASED INSTRUMENTS

Preference-based instruments require a patient to indicate a preference for the desirability of a health state (state of health). The term *health state* is often synonymous with *disease*, but it also includes the states of perfect health, death, and combinations of diseases.

There are two basic types of preference-based instruments: (1) rating scales and (2) utility analysis. Rating scales typically ask a person to rate his or her health on a scale ranging from 0 (death) to normal health (100), although other anchors, such as the poorest possible health and the best possible health, have also been used. Rating scales have been criticized for poorer reliability (reproducibility) than utility analysis, and also create patient comprehension difficulties when the lower anchor of death is used and the disease under evaluation is not lethal (as is the case with many ophthalmic, otolaryngologic, dermatologic, and plastic surgical conditions).[13,14]

UTILITY ANALYSIS

Utility analysis is the health-related quality-of-life instrument preferred by most healthcare economic researchers to objectively measure the quality of life improvement conferred by medical interventions.[13,15,16] There are four basic variants: (1) time tradeoff utility analysis, (2) standard gamble utility analysis, (3) willingness-to-pay utility analysis, and (4) multi-attribute instruments such as the EuroQol and the Health Utilities Index.[13] The time tradeoff method is among the most reproducible[13,14] of the group and has excellent construct validity (meaning that the instrument measures what it is intended to measure, in this instance the health-related quality of life associated with a disease).[13] Those with an in-depth interest in utility analysis are referred to other writings for additional information.[13,15,16]

With the time tradeoff utility analysis variant used in the current study, a respondent is first asked how long he or she theoretically expects to live. The person is next asked what is the *maximum* amount of that time—if any—he or she would be willing to trade for a return to normal health during the years that remain. The utility value associated with the disease is then calculated by subtracting the proportion of time traded from 1.0. For example, if a person with ARMD expects to live for 10 additional years and is willing to trade 3 of those years to be rid of the ARMD, the resultant utility value associated with the condition is **0.70** (1.00 – 0.30). If the same patient is willing to trade 6 of 10 remaining years to be rid of ARMD, the resultant utility value is **0.40 (**1.00 – 0.60**).**

Utility analysis values obtained from a large number of patients typically have a narrow 95% confidence interval, meaning the *mean* utility value associated with a disease has a 95% chance of falling within that narrow range if the study was to be repeated.[17-21] Narrow confidence intervals give clinicians assurance that the results of a study are reproducible.

OPHTHALMIC UTILITY VALUES

Ophthalmic utility values have been previously shown to most highly correlate with visual acuity in the better-seeing eye, rather than the underlying cause of visual loss.[4,13] A list of ophthalmic utility values previously obtained from patients with varied visual conditions is shown in Table 4. Noteworthy is the fact that normal 20/20 visual acuity in each eye *permanently* is associated with a utility value of 1.00. Patients with ocular disease (eg, ARMD, diabetic retinopathy, glaucoma) and no visual loss (20/20 visual acuity bilaterally) have a utility value of 0.97 because of the fear that vision will be lost in the future. When the visual acuity is 20/20 in one eye and 20/40 or worse in the second eye, the associated utility value is 0.92. As the vision in the better-seeing eye decreases, so does the utility value. No perception of light bilaterally is associated with a utility value of 0.26, and death, the lower anchor of the scale, is associated with a utility value of 0.00

IMPROVEMENT IN QUALITY OF LIFE GAINED FROM AN INTERVENTION

Just as utility analysis measures the quality of life associated with a health state, it can also measure the improvement in the quality of life conferred by an intervention. Using the above example, assuming that pretreatment ARMD is associated with a visual acuity of 20/400 (utility value = 0.54) and posttreatment ARMD is associated with a visual acuity of 20/40 (utility value = 0.80), the

improvement in utility value gained from the intervention is **+0.26**. The improvement in quality of life (value) in this instance is **48%** (0.26/0.54).

TABLE 4. TIME TRADEOFF UTILITY VALUES ASSOCIATED WITH VISUAL ACUITY LEVELS IN THE BETTER-SEEING EYE

VISUAL ACUITY	UTILITY VALUE
20/20 in each eye permanently	1.00
20/20 (20/20 to 20/25 in the other eye)	0.97
20/20 (≤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 (20/800)	0.52
Hand motions	0.35
Light perception	0.35
No light perception	0.26
Death	0.00

Adapted from Brown MM, et al.[4]

TOTAL VALUE GAINED FROM AN INTERVENTION

Once the utility value improvement gained from an intervention is ascertained, the total value conferred to a patient can be calculated. The total value gained is measured by using the outcome of the *quality-adjusted life-year* (QALY).

People accrue QALYs with time. If a patient's utility value remains unchanged for a period of time, the formula for the number of QALYs accrued during that time is:

Utility value × time (years)

Thus, a person in perfect health with a utility value of 1.0 accrues **1.0 QALY** during 1 year. If a person with ARMD lives at a utility value of 0.8 for 1 year, that person accrues **0.8 QALY** over the year. A person with a utility value of 0.8 who lives for 20 years accrues **16.0** (0.8 × 20) **QALYs** during that time. The 16.0 QALYs represent the total *value* of the person's life accrued during that time.

The formula to measure the total value gained from an intervention in QALYs is the sum of:

(utility value gain from intervention) × (duration of treatment benefit in years)

+

(posttreatment utility value) × (additional years of life gained from the intervention)

For the great majority of ophthalmologic interventions, no additional years of life are gained. The value conferred by ophthalmologic interventions is therefore generally calculated by multiplying the utility value gain conferred by an intervention by the duration of treatment benefit. Assuming that treatment for macular degeneration improves a person's utility value from 0.54 to 0.80 for 20 years, the total QALY gain is 5.2 (0.26 × 20 years). For a nonocular intervention, such as a carotid endarterectomy that improves the utility from 0.70 to 0.90 and adds 2 more years to an expected 5-year life expectancy, the gain in value is 2.8 QALYS [(0.2 × 5 years) + (0.9 × 2 years)].

Conversely, the value loss in a patient's life incurred from a disease can also be measured. For example, if a person develops permanent, moderate macular degeneration and drops to an ocular utility value of 0.60 from 1.00, this person experiences a 40%

diminution in quality of life. This can alternatively be looked at as a 40% decrement in the person's remaining value of life.

SOURCE OF UTILITY VALUES

A primary tenet of value-based medicine is the principle that *patient-based utility values* should be utilized in quality-of-life analyses and healthcare economic analyses.[13] It has been demonstrated repeatedly that the utility values of surrogate respondents often differ considerably from those of patients for the same disease.[3,4,17,20,21] Measures of quality of life other than utility analysis have also shown a considerable difference between the perceptions of patients who have lived with a disease and treating physicians asked to estimate the quality of life associated with that disease.[22-25] Patient-based utility values are generally the *criterion*, or gold standard, for the quality-of-life measures used in value-based medicine, because patients who live with a disease on a firsthand basis are those best qualified to assess the quality of life associated with that disease.[4,13,21,22]

STUDY DESIGN

The study herein was approved by the Wills Eye Hospital Institutional Review Board. The quality of life of patients with ARMD and that of patients with other diseases are addressed, as is the loss to the GDP from ARMD.

For the purpose of evaluating the quality of life associated with ARMD in this study, primary data from previous studies[2,3,22] were re-analyzed. Time tradeoff utility analysis data were gathered from 82 consecutive subjects with ARMD,[2] as well as 142 community members,[3] 62 nonophthalmologist clinicians,[3] and 46 ophthalmologists who treat patients with ARMD.[22] Included in the nonophthalmologist clinician group were residents and medical students, and included within the ophthalmologist group were attending physicians and residents. Subjects in the community, the nonophthalmologist clinician group, and the ophthalmologist group were all asked to assume that they had mild, moderate, or severe ARMD. The criteria for the visual strata are as listed below for the medical personnel (ophthalmologists and nonophthalmic physicians), whereas the community participants were given scenarios of mild, moderate, and severe visual loss, rather than the actual Snellen visual acuities.

Subjects were classified as having *mild ARMD (group 1)* if they had a visual acuity of 20/20 to 20/40 in the better-seeing eye, *moderate ARMD (group 2)* if they had a visual acuity of 20/50 to 20/100 in the better-seeing eye, and *severe ARMD (group 3)* if the acuity was 20/200 or worse in the better-seeing eye. Data on patients with *very severe ARMD (group 4),* with a visual acuity of 20/800 or less in the better-seeing eye, were also available, but only for the ARMD patient group and the ophthalmologist group.

The means of the utility value groups were compared with one-way analysis of variance, and post hoc testing was performed using the least significant difference test for comparisons. Significance was presumed to occur at the $P = .05$ level.

In addition to the patient quality of life, an analysis was undertaken on the macroeconomic burden of ARMD. This analysis did not include aspects such as disability payments or caregiver payments, but rather was based on the annual loss in the US GDP occurring as a result of ARMD. The GDP reflects the total income (wages, rents, income, and profits) produced in the United States on a yearly basis and thus reflects the patient loss in salary incurred by ARMD.

RESULTS

THE QUALITY-OF-LIFE BURDEN OF ARMD

The time tradeoff utility analysis results are shown in Table 5. They demonstrate significant differences between the mean ARMD utility values of the patient cohort and those of the community, nonophthalmologist clinician, and patient cohorts, respectively ($P < .001$).

Especially dramatic are the differences between the group of patients with ARMD and the group of ophthalmologists who treat ARMD. For *mild ARMD* (visual acuity 20/20 to 20/40 in the better-seeing eye), the mean patient utility value was 0.83, which was 750% worse than the mean estimate from ophthalmologists (utility value of 0.98) who treat patients with ARMD. Overall, the condition produced a 17% decrement in the average ARMD patient's remaining quality of life, whereas the ophthalmologists estimated a mean 2% quality-of-life decrement for the same condition.

For *moderate ARMD* (visual acuity 20/50 to 20/100 in the better-seeing eye), the mean patient utility value was 0.68, which was 191% worse than the treating ophthalmologists' mean estimate (utility value = 0.89). Patients in this group experienced a mean 32% loss in quality of life from the condition.

For *severe ARMD* (visual acuity ≤20/200 in the better-seeing eye), the mean patient utility value was 0.47, which was 96% worse than the treating ophthalmologists' mean estimate (utility value = 0.73). Patients in this group experienced a mean 53% diminution in quality of life from the condition.

For *very severe ARMD* (visual acuity ≤20/800 in the better-seeing eye), the mean patient utility value was 0.40, which was 97% worse than the treating ophthalmologists' mean estimate (utility value = 0.67). Patients in this group experienced a 60% loss in quality of life from the condition.

Although the ophthalmologist mean utility value was closer to the mean patient value for the very severe cases of ARMD than were the community and the nonophthalmologist mean utility values, the disparity compared with the mean patient utility value was still remarkable. The average ophthalmologist asked to assess the quality of life associated with very severe ARMD was willing to trade approximately 3.3 of every 10 remaining years for a return to normal vision, whereas the average patient with very severe ARMD was willing to trade 6.1 of every 10 remaining years for the same result.

TABLE 5. UTILITY VALUES OF PATIENTS WITH AGE-RELATED MACULAR DEGENERATION (ARMD) AND RESPONDENT GROUPS

ARMD GROUPINGS*	UTILITY VALUE (SD; 95% CI)				*P* VALUE
	PATIENTS WITH ARMD†[2,3] (N = 82)	COMMUNITY[3] (N = 142)	CLINICIANS[3] (N = 62)	OPHTHALMOLOGISTS[22] (N = 46)	
Mild (20/20 to 20/40)	0.83 (.19; .77–.89) (n = 42)	0.96 (.06; .95–.97) (n = 142)	0.93 (.10; .90–.96) (n = 62)	0.98 (.03; .97–.99) (n = 46)	<.001*
Moderate (20/50 to 20/100)	0.68 (.21; .59–.77) (n = 22)	0.92 (.10; .90–.94) (n = 142)	0.88 (.12; .85–.91) (n = 62)	0.89 (.10; .86–.92) (n = 46)	<.001*
Severe (20/200 or worse)	0.47 (.18; .39–.55) (n = 18)	0.86 (.15; .84–.88) (n = 142)	0.82 (.14; .78–.86) (n = 62)	0.73 (.19; .68–.78) (n = 46)	<.001*
Very severe (≤20/800)	0.40 (.13; .31–.49) (n = 8)	NA	NA	0.67 (.18; .62–.72) (n = 46)	<.001*

ARMD = age-related macular degeneration; NA = not available.
*Snellen visual acuity ranges for the better-seeing eye are listed below the Mild, Moderate, Severe, and Very severe groupings.
†The patient values are significantly different from those of the community, clinician, and ophthalmologist groups in all categorical ARMD groupings, by one-way analysis of variance (*P* <.0001.)

QUALITY OF LIFE ASSOCIATED WITH ARMD VERSUS QUALITY OF LIFE ASSOCIATED WITH OTHER DISEASES

Utility analysis has an advantage over other health-related quality-of-life instruments in that it can effectively compare the quality of life associated with any health state and the quality-of-life improvement conferred by any healthcare intervention. For the comparison to be valid, however, the utility values must be obtained from the same respondent group (patients) using the same methodology of utility analysis (time tradeoff).[4,13]

Patient-based time tradeoff utility values associated with systemic diseases and different levels of severity of ARMD are shown in Table 6. For the purpose of clarity, the utility values listed are divided into three groups: (1) 0.75 to 1.00: mild to moderate changes, (2) 0.50 to 0.74: moderate to severe changes, and (3) <0.50: severe to very severe changes.

In group 1,[23-31] *mild ARMD (mean utility value = 0.83)* is associated with a greater quality-of-life decrement than that encountered with cancer (average among several types),[25] a mild stroke,[27] impotence,[28] or gout.[29] The quality of life associated with it is similar to that associated with having a vertebral fracture[26] or symptomatic HIV syndrome[23] and very close to that of moderate angina.[30]

In group 2,[32-34] *moderate ARMD (mean utility value = 0.68)* is associated with a quality of life similar to that following a moderate stroke,[27] after which a patient requires considerable help with daily functions. The quality of life is also similar to that associated with AIDS.[23]

In group 3, *severe ARMD (mean utility value = 0.47)* is associated with a quality of life similar to that of a patient with total renal failure on home dialysis.[33]

In group 4,[35-37] patients with the *very severe macular degeneration (utility value = 0.39)*, the associated quality of life is comparable to that encountered with a severe stroke that causes a person to be bedridden, incontinent, and in need of constant nursing care.[27] Another comparable condition is advanced prostate cancer with uncontrollable pain.[31] Thus, the quality of life associated with very severe ARMD is on a par with some of the most harsh health states imaginable.

THE ECONOMIC BURDEN OF ARMD

The GDP can be calculated by adding the income of wages, rents, interest, and profits received by all factors in the production of all goods and services produced in the United States during a calendar year.[38] A loss of wages due to the sequelae of ARMD will consequently result in a diminution of the GDP. Thus, a major component of the macroeconomic burden of ARMD is the amount by which it decreases the GDP.

TABLE 6. PATIENT-BASED, TIME TRADEOFF UTILITY VALUES ASSOCIATED WITH AGE-RELATED MACULAR DEGENERATION (ARMD) AND SYSTEMIC HEALTH STATES

CONDITION	TTO UTILITY VALUE
GROUP 1	
HIV, asymptomatic	0.94[23]
Status post–myocardial infarction, no symptoms	0.93[24]
Cancer, all	0.92[25]
Osteoporosis	0.91[26]
Stroke, mild (able to perform usual activities)	0.90[27]
Impotence	0.85[28]
Gout	0.86[29]
ARMD, mild*	**0.83***
Vertebral fracture	0.82[26]
HIV, symptomatic	0.82[23]
Angina, moderate	0.80[30]
Status post–myocardial infarction, some residual angina and congestive heart failure	0.78[24]
Prostate cancer (no pain; normal bladder, bowel, and sexual function)	0.78[31]
GROUP 2	
Claudication, severe	0.74[32]
Prostate cancer (pain controlled; ± bladder bowel, and sexual function, ± energy ± depression)	0.72[31]
AIDS	0.70[23]
Stroke, moderate (requiring some help, but able to walk without assistance)	0.69[27]
ARMD, moderate*	**0.68***
Fractured hip	0.63[26]
Tuberculosis, hospitalized	0.60[33]
Angina, severe	0.58[30]
Ulcerative colitis, requiring surgery	0.58[34]
GROUP 3	
Dialysis, home	0.56[33]
ARMD, severe*	**0.47***
GROUP 4	
ARMD, very severe*	**0.39***
Prostate cancer, advanced (uncontrolled pain; bladder, bowel and sexual function abnormal; depression, severe fatigue)	0.35[31]
Stroke, severe (bedridden, incontinent, and requiring constant care, at 6 months)	0.34[27]
Total blindness (NLP OU)	0.26[35]
Stroke, severe, with aphasia	0.26[36]
Stroke, severe, total paralysis (at 10 years)	0.20[37]

AIDS = acquired immunodeficiency syndrome; ARMD = age-related macular degeneration; HIV = human immunodeficiency virus; NLP = no light perception; TTO = time tradeoff.
***Bold** indicates current study.

THE ECONOMIC BURDEN OF NEOVASCULAR ARMD

People with visual loss from ARMD experience considerable difficulty in obtaining employment. Data from the Bureau of Labor and Statistics provide a wealth of information in this arena.[39] The employment rate for those with ARMD and severe visual limitation, such as encountered with advanced ARMD (neovascular and/or geographic atrophy[5]), is 30.6%, whereas the employment rate for people with mild visual limitation is 44.1%. The comparable employment rate for unaffected people aged 16 to 63 years is 78.2%.[39] People with neovascular ARMD are considered to have severe visual loss for the purpose of the economic calculations presented herein.

In addition to having difficulty finding employment, people with severe visual limitation (advanced ARMD) have decreased earnings compared with those who have no disabilities. The 1997 mean wage for a person with no disabilities was $31,182, whereas that for a person with mild visual loss was $21,804, or 30% less ($9,378) than that for a person with no disabilities. In the same year, the average wage for a person with severe visual loss, such as associated with advanced ARMD, was $19,326, or 38% less ($11,856) than that for a person with no disabilities.[39]

Incorporating the above data with the assumptions that 10% of the 36 million Medicare population (65 years and older) have full-time employment[40,41] and 2.9% of this group have neovascular ARMD (Table 1), the annual loss from the GDP caused by neovascular ARMD and the consequent reduction in salary is **$1.238 billion** ($11,856 × 36 million × 10% × 2.9%). Conservatively, it is likely that another 5% of remaining seniors with neovascular ARMD would be in the labor market if they did not have severe visual loss.[40,41] This latter subgroup accounts for an additional **$1.628 million** ($31,182 × 36 million × 5% × 2.9%) loss from the GDP. The sequelae of neovascular ARMD therefore account for a combined **$2.866** billion GDP loss in the Medicare population.

Among the 137,000 people under the age of 65 years with neovascular ARMD (Table 1), the loss in salary is calculated by considering the percentage of the workforce unable to obtain a job due to severe visual loss (78.2% – 30.6% = **47.6%**) and the salary decrease ($11,856) attributed to 30.6% of employed people with severe visual loss. The loss to the GDP in this group is therefore (47.6% × 137,000 × $31,182) + (30.6% × 137,000 × $11,856) = $2.033 billion + $0.497 billion = **$2.530 billion**.

The total yearly loss to the GDP due to lost wages from neovascular ARMD among all affected people is therefore $2.866 billion + $2.530 billion = **$5.396 billion**. Other costs, as yet poorly quantified, such as transportation costs, caregiver costs, and injury costs, make the overall economic burden from ARMD higher yet. A summary of the adverse economic sequelae occurring as a result of ARMD is shown in Table 7.

TABLE 7. YEARLY ECONOMIC LOSS TO THE GROSS DOMESTIC PRODUCT (GDP) IN THE UNITED STATES FROM THE SEQUELAE OF AGE-RELATED MACULAR DEGENERATION (ARMD)

CATEGORY	PATIENT ≥65 YEARS OLD	PATIENTS <65 YEARS OLD
A. WET (NEOVASCULAR) ARMD		
Per capita salary loss for those employed	$11,856	$11,856
People employed	104,400	41,922
Total salary reduction loss	$1.237 billion	$497 million
Jobs lost from neovascular ARMD	52,200	65,212
Average job salary	$31,182	$31,182
Total salary loss	$1.628 billion	$2.033 billion
Subtotal all losses	$2.866 billion	$2.530 billion
Total GDP loss from wet ARMD = $5.396 billion		
B. DRY ARMD		
Per capita salary loss for those employed	$9,378	$9,378
Employed with mild visual loss	240,900	548,824
Total salary reduction loss	$2.259 billion	$5.147 billion
Jobs lost from dry ARMD and mild visual loss	120,450	424,375
Average job salary	$31,182	$31,182
Total salary loss	$3.756 billion	$13.233 billion
Subtotal all losses	$6.015 billion	$18.380 billion
Total GDP loss from dry ARMD = $24.395 billion		
TOTAL GDP LOSS FROM WET + DRY ARMD = $29.791 BILLION		

Data from references 1, 6, and 39 through 42.

THE ECONOMIC BURDEN OF DRY ARMD

If the assumption is made that half of the 7.3 million people with dry ARMD and drusen greater than 125 μm across (Table 1) also have mild visual limitation,[39,42] the additional loss to the GDP can be calculated in a manner similar to that for neovascular macular degeneration

Among the 2,489,000 people under the age of 65 years with dry ARMD (Table 1), the loss in salary is calculated by considering the percentage of the workforce unable to obtain a job due to mild visual loss (78.2% – 44.1% = **34.1%**) and the salary decrease ($9,378) attributed to 44.1% of employed people with severe visual loss. The loss to the GDP in this group is therefore (0.5 × 34.1% × 2,489,000 × $31,182) + (0.5 × 44.1% × 2,489,000 × $9,378) = $13.233 billion + $5.147 billion = **$18.380 billion**.

Among the 4,818,000 people with dry ARMD aged 65 years or older (Table 1), the loss in salary is calculated by considering the percentage of the workforce unable to obtain a job due to mild visual loss (78.2 – 44.1 = **34.1%**) and the salary decrease ($9,378) attributed to 44.1% of employed people with severe visual loss. The loss to the GDP in this group is therefore (0.5 × 0.1 × 34.1% × 4,818,000 × $31,182) + (0.5 × 0.1 × 44.1% × 2,489,000 × $9,378) = $3.756 billion + $2.259 billion = **$6.015 billion**.

The total GDP loss from dry ARMD, assuming that 50% with dry ARMD have mild visual loss, is $18.380 billion + $6.015 billion = **$24.395 billion**.

THE COMBINED ECONOMIC BURDEN OF NEOVASCULAR AND DRY ARMD

When the $24.395 billion GDP loss from dry ARMD is combined with the loss of $5.396 billion from neovascular ARMD, the total loss to the GDP from both forms of ARMD is $29.791 billion. The annual GDP of the United States for 2003 was $10.988 trillion.[43] The potential loss of close to $30 billion, while only 0.27% of the GDP, is nonetheless a formidable sum. Not only does ARMD cause substantial human loss of quality of life, but its economic consequences in a population that grows older every year are severe.

DISCUSSION

The data herein suggest that ARMD has a considerable adverse effect upon quality of life. They also suggest that this adverse effect is considerably underestimated by physicians, by the general community, and by ophthalmologists who actually treat patients with ARMD. Although ophthalmologists dramatically underestimated the quality-of-life loss associated with macular degeneration, treating physicians in other specialties have also underestimated the degree of patient quality-of-life impairment caused by diseases they treat.[44-46] The phenomenon appears to be widespread and reinforces the concept that patient-based values should be used to calculate the value of interventions and to calculate the cost-utility associated with interventions.[13]

Of note, 30% of persons with ARMD also have clinical depression.[47] This can contribute to the low utility values encountered with ARMD, especially among persons with the more severe types of ARMD. Although it is not the intention of this paper to discuss the treatment of ARMD, clinicians should not lose sight of the fact that, in addition to treatment to preserve vision, treatment ofdepression in those with ARMD can result in a considerable improvement in quality of life.[47]

As is the case with any study, the current study has shortcomings. The fact that community participants may not understand the disability associated with decreased vision should be considered. Nonetheless, the underestimations suggest that society overall underappreciates the quality-of-life loss sustained by ARMD patients.

A detailed description of the therapeutic modalities currently used to treat ARMD[48-52] is beyond the scope of this article. (For details on current treatments, please see references 48 through 52.) However, laser therapy[52] for extrafoveal choroidal neovascularization with neovascular ARMD and photodynamic therapy[51] for subfoveal choroidal neovascularization with neovascular ARMD are both cost-effective modalities that provide a great deal of value to patients. Each of these modalities is considerably more cost-effective than treatment for systemic arterial hypertension, one of the most common healthcare interventions in the United States.[51,52]

The needs to apply current ARMD therapies properly[42,48-52] and pursue the discovery of more effective ARMD therapies are great. The education of patients and the public regarding the severely debilitating nature of ARMD will hopefully stimulate awareness among affected patients that treatments are available and more effective when the disease is caught at earlier stages.[48-52] Whereas value-based medicine data can be difficult to navigate, the percent improvement in quality of life conferred by an intervention is a concept that most people understand. This percent improvement in quality of life can be even more germane when interventions can also be compared across disparate specialties. Knowing the percentage improvement conferred in quality of life will likely help patients to better appreciate the value of interventions they are undertaking or considering to undertake.

Of great importance is the fact that value-based medicine will differentiate the *value* and the *cost-utility* (dollars spent for this value) among all interventions utilized for the treatment of ARMD when evidence-based clinical data alone do not allow this form of differentiation.[13] Both clinicians and patients will readily realize which treatments provide the most value, thus empowering both physicians and patients in an era of considerable marketing outside the medical arena.

The improvements in quality of life for US citizens and the financial gains for the country conferred by current and future therapies for ARMD are immense.[51,52] The effect upon GDP discussed herein, although it takes into account wages lost from ARMD, does not include disability payments, healthcare costs, caregiver costs, transportation costs, and family caregiver costs (if they prevent earning a salary). Thus, the numbers presented herein are lower than if these other costs were included.

In summary, the substantial public health burden of ARMD includes both its adverse effects upon quality of life and upon the economy. ARMD causes a marked decrease in quality of life, the diminution of which is underestimated by multiple sectors of

society, including physicians who regularly care for ARMD patients. The adverse effect of ARMD upon the GDP is also considerable. Interventions that improve the morbidity caused by ARMD have the potential to greatly benefit the quality of life of individual patients[51,52] as well as the overall economic well-being of the country.

REFERENCES

1. Klein R, Klein BEK, Tomany SC, et al. Ten-year incidence and progression of age-related maculopathy: the Beaver Dam Eye Study. *Ophthalmology* 2002;109:1767-1779.
2. Brown GC, Brown MM, Sharma S, et al. Utility values associated with age-related macular degeneration. *Arch Ophthalmol* 2000;118:47-51.
3. Stein JD, Brown MM, Brown GC, et al. Quality of life with macular degeneration. Perceptions of patients, clinicians and community members. *Br J Ophthalmol* 2003;87:8-12.
4. Brown MM, Brown GC, Sharma S, et al. Health care economic analyses and value-based medicine. *Surv Ophthalmol* 2003;48:204-223.
5. Bird AC, Bressler NM, Bressler SM, et al. An international classification and grading system for age-related maculopathy and age-related macular degeneration: the International ARM Epidemiological Study Group. *Surv Ophthalmol* 1995;39:367-374.
6. Friedman DS, O'Colmain BJ, Munoz B, et al. Eye Diseases Prevalence Research Group. Prevalence of age-related macular degeneration in the United States. *Arch Ophthalmol* 2004;122:564-572.
7. Sharma S. Levels of evidence and interventional ophthalmology. *Can J Ophthalmol* 1997;32:359-362.
8. RAND Corporation. RAND 36-Item Health Survey 1.0. Available at: www.rand.org/health/surveys/sf36item. Accessed July 4, 2004.
9. Kaplan RM, Ganiats TG, Sieber WJ, et al. The Quality of Well-Being Scale: Critical similarities and differences with the SF-36. *Int J Qual Health Care* 1998;10:509-520.
10. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969;9:179-186.
11. Steinberg EP, Tielsch JM, Schein OD, et. al. The VF-14. An index of functional impairment in patients with cataract. *Arch Ophthalmol* 1994;112:630-638.
12. Mangione CM, Lee PP, Gutierrez PR, et al. National Eye Institute Visual Function Questionnaire Field Test Investigators. Development of the 25-item National Eye Institute Visual Function Questionnaire. *Arch Ophthalmol* 2001;119:1050-1058.
13. Brown MM, Brown GC, Sharma S. *Evidence-Based to Value-Based Medicine.* Chicago: AMA Press; 2005.
14. Froberg DG, Kane RL. Methodology for measuring health state preferences. II. Scaling methods. *J Clin Epidemiol* 1989b;42:459-471.
15. Gold MR, Patrick DL, Torrance GW, et al. Identifying and valuing outcomes. In Gold MR, Siegel JE, Russell LB, et al, eds. *Cost-Effectiveness in Health and Medicine*. New York: Oxford University Press; 1996:82-134.
16. Drummond MF, O'Brien B, Stoddart GL, et al. *Methods for the Economic Evaluation of Health Care Programmes.* Oxford, England: Oxford University Press; 2000:139-199.
17. Brown GC, Brown MM, Sharma S, et al. Quality-of-life associated with diabetes mellitus in an adult population. *J Diabet Complications* 2000;14:18-24.
18. Brown MM, Brown GC, Sharma S, et al. Quality-of-life associated with unilateral and bilateral good vision. *Ophthalmology* 2001;108:643-647.
19. Brown MM, Brown GC, Sharma S, et al. Quality of life associated with visual loss. Time tradeoff utility analysis comparison with systemic health states *Ophthalmology* 2003;110:1076-1081.
20. Landy J, Stein JD, Brown GC, et al. Patient, community and clinician perceptions of the quality of life associated with diabetes mellitus. *Med Sci Monit* 2002;8:543-548.
21. Stein J, Brown GC, Brown MM, et al. The quality of life of patients with hypertension. *J Clin Hypertens* 2002;4:181-188.
22. Brown GC, Brown MM, Sharma S. Difference between ophthalmologist and patient perceptions of quality-of-life associated with age-related macular degeneration. *Can J Ophthalmol* 2000;35:27-32.
23. Tengs TO, Lin TH. A meta-analysis of utility estimates for HIV/AIDS. *Med Decis Making* 2002;22:475-481.
24. Kuntz TM, Tsevat J, Goldman L, et al. Cost-effectiveness of routine coronary angiography after acute myocardial infarction. *Circulation* 1996;94:957-965.
25. O'Leary JF, Fairclough DL, Jankowski MK, et al. Comparison of time-tradeoff utilities and rating scale values of cancer patients and their relatives. Evidence for a possible plateau relationship. *Med Decis Making* 1995;15:132-137.
26. Tosteson AN, Gabriel SE, Grove MR, et al. Impact of hip and vertebral fractures on quality-adjusted life years. *Osteoporos Int* 2001;12:1042-1049.
27. Duncan PW, Lai SM, Keighley J. Defining post-stroke recovery: implications for design and interpretation of drug trials. *Neuropharmacology* 2000;39:835-841.
28. Krahn MD, Mahoney JE, Eckman MH, et al. Screening for prostate cancer. A decision analytic view. *JAMA* 1994;272:773-780.
29. Fryback DG, Dasbach EJ, Klein R, et al. The Beaver Dam Health Outcomes Study: initial catalog of health-state quality factors. *Med Decis Making* 1993;13:89-102.
30. Miyamoto JM, Eraker SA. Parameter estimates for a QALY utility model. *Med Decis Making* 1985;5:191-213.

31. Chapman GB, Elstwin AS, Kuzel TM, et al. Prostate cancer patients' utilities for health states. How it looks depends on where you stand. *Med Decis Making* 1998;18:278-286.
32. Bosch JL, Hunink MG. The relationship between descriptive and valuational quality-of-life measures in patients with intermittent claudication. *Med Decis Making* 1996;16:217-225.
33. Sackett DL, Torrance GW. The utility of different health states as perceived by the general public. *J Chronic Dis* 1978;31:697-704.
34. McLeod RS, Churchill DN, Lock AM, et al. Quality of life of patients with ulcerative colitis preoperatively and postoperatively. *Gastroenterology* 1991;101:1307-1313.
35. Brown MM, Brown GC, Sharma S, et al. Utility values associated with blindness in an adult population. *Br J Ophthalmol* 2001;85:327-331.
36. Samsa GP, Matchar DB, Goldstein I, et al. Utilities for major stroke: results from a survey of preferences among persons at increased risk for stroke. *Am Heart J* 1998;136:703-713.
37. Tengs TO, Yu M, Luistro E. Health-related quality of life after stroke. A comprehensive review. *Stroke* 2001;32:964-972.
38. Case KE, Fair RC. *Principles of Economics.* 4th ed. Upper Saddle River, NJ: Prentice Hall; 1996:1-165, 571-592.
39. Data on Disability and Unemployment. Bureau of Labor and Statistics. Available at: http://www.bls.gov. Accessed July 10, 2004
40. Access Update. Massachusetts elderly and prescription drug coverage. Available at: http://www.mass.gov/dhcfp/pages/pdf/access1.pdf. Accessed July 11, 2004.
41. Houser M. Seniors' role critical in today's business world. *Pittsburgh Tribune-Review*. February 23, 2003.
42. Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report No. 8. *Arch Ophthalmol* 2001;119:1417-1436.
43. Gross Domestic Product. Availaable at: http://www.bea.doc.gov/bea/dn/nipaweb/TableView.asp?SelectedTable=5&FirstYear=2003&LastYear=2004&Freq=Qtr. Accessed July 10, 2004.
44. Lunde IM. Patients' perceptions. A shift in medical perspective. *Scand J Prim Health Care* 1993;11:98-104.
45. Rothwell PM, McDowell Z, Wong CK, et al. Doctors and patients don't agree. Cross sectional study of patients' and doctors' perceptions and assessments of disability in multiple sclerosis. *Br Med J* 1997;314:1580-1583.
46. Schrader GD. Subjective and objective assessments of medical comorbidity in chronic depression. *Psychother Psychosom* 1997;666:258-260.
47. Casten RJ, Rovner BW, Tasman W. Age-related macular degeneration and depression: a review of recent research. *Curr Opin Ophthalmol* 2004;15:181-183.
48. Macular Photocoagulation Study Group. Argon laser photocoagulation for neovascular maculopathy: five-year results from randomized clinical trials. *Arch Ophthalmol* 1991;109:1109-1114.
49. Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: two-year results of 2 randomized clinical reports. TAP report 2. *Arch Ophthalmol* 2001;119:198-207.
50. Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Verteporfin therapy for subfoveal choroidal neovascularization in age-related macular degeneration. Three-year results of an open-label extension of 2 randomized clinical trials—TAP report No. 5. *Arch Ophthalmol* 2002;120:1307-1314.
51. Brown GC, Brown MM, Roth Z, et al. The cost-utility of photodynamic therapy in eyes with neovascular age-related macular degeneration. A reappraisal with 5-year data. *Am J Ophthalmol* (in press).
52. Busbee B, Brown MM, Brown GC, et al. A cost-utility analysis of laser photocoagulation for extrafoveal choroidal neovascularization. *Retina* 2003;23:279-287.

PEER DISCUSSION

DR FREDERICK L FERRIS III. Dr Brown and the co-authors of this manuscript have used a "time tradeoff utility analysis" to assess the economic and personal burdens associated with age-related macular degeneration (AMD). This approach may be particularly important for those making decisions on the cost of AMD treatments or research.

Using quality of life questionnaires, such as the NEI-VFQ[1], it has been documented that persons with AMD have a reduction in their quality of life even when they still have good visual acuity in the fellow eye.[2-4] However, although there is a definite decrease in quality of life as assessed by these questionnaires, it is difficult define the economic effect of AMD on patients or compare its morbidity with other diseases. Dr Brown and his co-authors have provided a service to ophthalmology by utilizing time tradeoff utility analysis to calculate utility adjusted quality of life years, a method that allows for both economic and relative value assessment of disease morbidity. Some of their findings are expected, while others are perhaps a surprise.

The degree of difference between patients and their caregivers, or the community, in the utility assessment related to various levels of visual acuity in the better-seeing eye is somewhat surprising. The surprise is not that there is a difference, but rather that the difference is as large as it appears in this analysis. It is especially important to note that ophthalmologists caring for patients with AMD seem to under-value the degree of impact AMD has on their patients.

Another, perhaps surprising, result is the comparison of utility trade-off for AMD with other diseases. At every level of visual

function loss associated with AMD the comparison with other diseases seems dramatic. For example, even developing mild AMD is viewed as worse than a diagnosis of cancer; and developing severe AMD is equivalent to total renal failure or dialysis, while very severe AMD is equivalent to a debilitating stroke or prostate cancer with uncontrollable pain. Thus, from a patient perspective, very severe AMD is comparable to the most debilitating conditions imaginable.

The economic analysis, presented by Brown and colleagues, is one of the first that provides a scientifically based comparison of AMD with other major diseases. This is important because those who make decisions on how much to pay for research, and those who make decisions regarding spending for health care delivery will increasingly be using such analyses to support their decisions. Many economic approaches significantly under-value the impact of AMD, because it is largely a disease of persons who are retired. Estimates of the economic impact of AMD, in the analysis by Brown and colleagues, include many factors other than simply lost income, but are driven by the multiple assumptions needed for such analyses. It may be useful to give a range to these estimates by doing a sensitivity analysis, using ranges for the various assumptions. However, the assumptions in the analyses presented seem conservative and underscore both the personal and economic importance of finding ways to prevent AMD and its visual consequences. Dr Brown and his colleagues have made an important contribution to the field and hopefully they will continue this important work and others will replicate their analyses.

REFERENCES

1. Mangione CM, Lee PP, Gutierrez PR et al. National Eye Institute Visual Function Questionnaire Field Test Investigators. Development of the 25-item National Eye Institute Visual Function Questionnaire. *Arch Ophthalmol* 2001; 119:1050 –1058.
2. Williams RA, Brody BL, Thomas RG et al. The psychosocial impact of macular degeneration. *Arch Ophthalmol* 1998; 116:514–520
3. DeCarlo DK, Scilley K, Wells J, Owsley C. Driving habits and health-related quality of life in patients with age-related maculopathy. *Optom Vis Sci* 2003; 80:207–213.
4. Berdeaux GH, Nordmann JP, Colin E, Arnould B. Vision-related Quality of Life in Patients Suffering From Age-related Macular Degeneration, *Am J Ophthalmol* 2005; 139:271-279

DR RICHARD L. LINDSTROM. How do you factor that into the evaluation, when a therapy improves both the quality of life and also the length of life?

DR M EDWARD WILSON. You indicated that with mild, moderate and severe, and more severe AMD, that the values were stable. Do the values change when a group of those patients has a good experience with vision rehabilitation? Even at stable vision acuity, can you measure the value of well-done vision rehabilitation with a medical provider and occupational therapist and such?

DR ELIAS I. TRABOULSI. Have you factored the presence of co-morbidities into your analysis? In young adults in whom we are studying the effect of strabismus, and who are healthy otherwise, the responses are going to be different than older people in whom you are studying the effects of macular degeneration. Some of these latter may be perfectly healthy and willing to trade a lot whereas others are sick and may not be willing to trade anything because they have more important problems. Co-morbidities may affect the results. And have you analyzed your data by comparing these groups?

DR DOUGLAS R. ANDERSON. There are a number of things that are a bit fuzzy, and I wonder whether sensitivity analysis may have a place. For example, a person who has lost visual acuity early or never had visual acuity from the time of infancy and has had a happy upbringing, may be fairly content and therefore give a different answer concerning what he would give to have restoration of vision than would a person who had vision for much of his life, and then lost it. To say that a visual acuity of 2/200 has a certain utility, or utility loss, is not the same for all diseases or for all types of people. In part it is because of the time of onset of the disability but also some of these disabilities are associated with other visual features. For example, consider the person with glaucoma, who has 2/200 acuity in his better eye and also has a tremendous loss of visual field. In macular degeneration, there is loss of contrast at different spacial frequencies that may affect the ability to recognize faces; his sense of loss may be only partly related to his able to read letters, which is how we measure visual acuity. With cataracts you have the problem of glare interfering with the ability to see even if you can see small letters in a dark room, and thus have a good visual acuity recorded in the medical record. So, I would be troubled with using acuity, for example, as something that would be standard across diseases, as a utility measure.

It is wonderful thing to try to evaluate the quality of the care that we're delivering and trying to determine whether it really makes any difference to our patients' lives, or alternatively whether it reveals that something we are doing doesn't really improve the quality of life. The instruments are still a bit crude and difficult and the visually related instruments seem to supplement and complement those that are broad disease-related, so that you can equate angina with macular degeneration. But even within eye diseases, it seems as if there has to be some distinction of those instruments that are specific-to-specific diseases, or even the time of onset.

DR STEVEN E. FELDON. Some of these scores do not pass the common-sense test. Does someone who has 2/200 vision compare himself or herself to individuals who are bed-ridden for the rest of their lives, in terms of the utility score? I don't think that's true. I would like to see some sort of forced choice test, such as simply saying "would you rather have 2/200 vision, or would you rather be bedridden, or in a wheelchair, or a quadriplegic", and have that kind of forced choice to make, so we can get a true idea of what the value is. On a theoretical basis, in the abstract, I think you can trade a lot of things. But when it comes down to visualizing yourself having to use telescopes or reading aides versus being unable to perform the minimum things that are necessary to take care of yourself, I just don't think they match up.

DR J. BRONWYN BATEMAN. These questions are really for Drs Melissa Brown and Frederick Ferris. These instruments seem like they are going to help medicine tremendously. But I am wondering about the average American, and how they see our government spending healthcare dollars money. This study may help ophthalmology get a bigger 'piece of the healthcare pie', but how might we influence our representatives to put more money into the healthcare pot? I would be curious what those in Washington think about how we might get more money into the healthcare pie.

DR TRAVIS A. MEREDITH. I was struck by the disconnect and distinction between what physicians thought was happening with the patients, and what the patients thought and what their values were. The study showed a distinctive difference between the patients' perception of the interaction, or the value of the disease management, and the physicians' perception. Another study has just been completed by Dr Hartnett (Hartnett ME, Key IJ, Loyacano NM et al. Perceived Barriers to Diabetic Eye Care: Qualitative Study of Patients & Doctors. *Arch Ophthalmol* 2005; 123: 387-391) at our institution with a similar result. When she was at Louisiana State University, she used a focus group methodology, and looked at barriers to why people weren't getting screened for diabetic retinopathy. She questioned providers and patients. If you rank order the perceptions of the patients, in terms of what the barriers were, and you rank order the perceptions of the doctors, it was an inverse correlation. There is a rich area here for us to better understand what our patients think they need and are getting from us. It's remarkable that in two very common diseases, diabetes and macular degeneration, the two participants in the interaction understand things so differently.

DR GARY C. BROWN. In regard to Dr. Ferris' comment, we believe that the NEI-VFQ is a very valuable instrument. Certainly it is complementary to utility analysis. We learn so much more when we use the two together rather than using one alone. We never do just utility analysis alone. We look at other issues to find out what bothers people the most.

In response to Dr Lindstrom's question, with value-based medicine we incorporate the improvement in length of life, as well as the improvement in quality of life. We incorporate all benefits and all adverse effects. There is nothing that you could imagine in any treatment equation that cannot be incorporated with value-based medicine.

I do not know the answer to Dr Wilson's question regarding value change with visual rehabilitation. I suspect that there is, but nobody, to my knowledge, has currently performed that study.

Dr Traboulsi asked about co-morbidities. The Panel on Cost-Effectiveness in Health and Medicine really had a difficult problem when they met about ten years ago with the Department of Public Health. They had such a problem that they did not even address it. For example, take someone like Mr X who has had a kidney transplant and Guillan Barre syndrome. Is cataract surgery in this person as valuable as cataract surgery in somebody who is otherwise healthy? I think the cataract surgery in Mr X is just as valuable as in someone who has normal health. It is paternalistic to say that his quality of life doesn't really merit the same type of care. Also, when we looked at co-morbidities, they did not affect the utility. Most importantly it is illegal to have any system put into public policy that might use co-morbidities to discriminate against a patient. Consider the Americans with Disabilities Act of 1991; if we were to discriminate against people who are disabled, which essentially is saying people who have co-morbidities, and decide that they do not deserve to have intervention, this would not get past the first court. We want to have value-based medicine incorporated into public policy, rather than just used as an academic exercise. We should also not discriminate against people on the basis of age. That is why we perform something called reference case analyses

Dr Anderson mentioned visual loss is different in different diseases. We've considered that situation and have been unable to show that. Dr Melissa Brown's paper (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) was able to demonstrate that the degree of visual loss, i.e. the visual acuity, correlates with the same utility in diabetic retinopathy versus macular degeneration. It seems to be more so the degree of loss, rather than the underlying disease, that is associated with the utility. As far as visual fields, we've been able to create a nice glaucoma model. We looked at about 300 patients with glaucoma, and to date, we have been unable to show that diminishing visual field really diminishes quality of life, using this particular instrument. Now, we do need more people with those 10-degree fields. When people lose half their field, their quality of life, or at least they've told us, is still quite good.

In response to Dr Feldon's question, most stroke patients think that they are going to get better. When they give up hope totally, that's when the utility score hits bottom. The people with macular degeneration seem to be in bad shape. Rather than look at this and say, "No, we can't assimilate these two things together," we should listen to what the patients say. Because the patients, we believe, understand the diseases much better than those of us who have not lived in that health state.

In regard to Dr Bateman question, we would love to see this incorporated into public policy. We think it would make it a lot more rational sense than our current lack of quality standards.

Dr Meredith noted the disparity between the quality of life perceptions between ophthalmologists and patients. This has also been demonstrated for neurologists, rheumatologists, and psychiatrists. Physicians in all specialties do not have a very good appreciation, in many instances, of the quality of life loss incurred by the diseases we treat.