Assessing the Impact of Visual Acuity on Quality of Life in Individuals With Type 2 Diabetes Using the Short Form-36

PHILIP M. CLARKE, PHD[1,2,3]
JUDIT SIMON, MD[2]
CAROLE A. CULL, PHD[1]
RURY R. HOLMAN, FRCP[1]

OBJECTIVE — We sought to ascertain quality-of-life measures and utility values associated with visual acuity in type 2 diabetes.

RESEARCH DESIGN AND METHODS — The Medical Outcome Study Short Form with 36 items (SF-36) was administered to 4,051 individuals with type 2 diabetes who were enrolled in the Lipids in Diabetes Study, and their best attainable vision was determined using an Early Treatment of Diabetic Retinopathy Study chart, expressed as a LogMAR score. Eight domain scores and a utility value representing an overall quality-of-life score were calculated using predefined algorithms. The associations between quality of life measured and best-eye visual acuity were assessed graphically and by regression analysis.

RESULTS — All eight SF-36 domain scores were negatively associated with reduced visual acuity. The impact of lower levels of visual acuity ranged from a decline of 1.3 units for a 0.1-LogMAR increase for physical functioning and 0.6 units in mental health. Regression analysis indicated a negative association ($P < 0.001$) between utility and reduced visual acuity after controlling for sex, BMI, smoking status, and history of diabetes complications. Patients whose LogMAR scores equated to legally blind had, on average, 0.054 (95% CI 0.034–0.074) lower utility compared with patients with normal visual acuity.

CONCLUSIONS — Reduced visual acuity is negatively associated with quality of life. The utility scores estimated here should inform studies quantifying the burden of diabetes and those evaluating potential therapies for treating or preventing diabetic eye diseases.

Diabetes Care 29:1506–1511, 2006

Diabetes is associated with an increased risk of visual impairment (1) and is the leading cause of blindness in individuals between the ages of 20 and 74 years in the U.S. (2). Blindness can result from cataract, glaucoma, and diabetic maculopathy or retinopathy. Some 80% of patients with type 2 diabetes for ≥15 years have retinopathy, 5% of whom have sight-threatening diabetic retinopathy (2).

Early detection and treatment of diabetic retinopathy with retinal photocoagulation can minimize further visual loss (3), and improved glycemic and blood pressure control have been shown to reduce the risk of diabetic retinopathy (4). The range of therapies for preventing or treating eye-related diseases in individuals with diabetes is expanding, and many new treatments are under development (5). Improvements to health-related quality of life (HRQOL) are likely to be the principle outcome of interventions to prevent or treat vision loss. In regard to economic evaluation of these interventions, cost-utility analysis is generally regarded as the preferred method of evaluation, as it measures outcomes in quality-adjusted life-years (6) with health status valued on a scale where 1.0 implies perfect health and 0.0 is equivalent to death.

Utilities for health states can be derived directly using a variety of methods such as standard gamble or time trade off (5), but these require detailed personal interviews to produce reliable utility values. An alternative approach is to use generic quality-of-life instruments such as the Medical Outcome Study Short Form with 36 items (SF-36) (7) and then convert item responses into health state utility values using predefined algorithms such as that based on the Short Form with six dimensions (SF-6D) (8). The SF-36 summarizes HRQOL using multi-item scales measuring eight health concepts, such as physical functioning and mental health, that can provide insight into how visual loss impacts on different aspects of quality of life.

We have used the SF-36 to evaluate the relationships between visual acuity and quality of life in a wide population of individuals from the U.K. with established type 2 diabetes at the time they were enrolled into the Lipids in Diabetes Study (LDS) (9).

RESEARCH DESIGN AND METHODS

— Between April 1999 and July 2001, the LDS recruited patients aged 40–75; those included were recruited from hospital-based diabetes clinics or local general practitioner registers of individuals with diabetes. Patients had clinically diagnosed type 2 diabetes for ≥6 months, were not thought to have clinically significant cardiovascular disease, and had LDL cholesterol between ≥1.5 and <4.1 mmol/l and plasma triglycerides <4.5 mmol/l. Exclusion criteria included clinical evidence of cardiovascular disease, prior lipid-lowering therapy, impaired renal function, hepatic insufficiency, myopathy or serum creatinine >150 μmol/l, and untreated cholelithiasis. The study design and protocol

From the [1]Diabetes Trials Unit, Oxford Centre for Diabetes, Endocrinology and Metabolism, Churchill Hospital, Oxford, U.K.; the [2]Health Economics Research Centre, Division of Public Health and Primary Care, University of Oxford, Oxford, U.K.; and the [3]School of Public Health, University of Sydney, New South Wales, Australia.

Address correspondence and reprint requests to Dr. Philip Clarke, Health Economics Research Centre, Old Road Campus, University of Oxford, Headington, Oxford OX3 7LF, U.K. E-mail: philip.clarke@dphpc.ox.ac.uk.

Received for publication 4 November 2005 and accepted in revised form 19 March 2006.

Abbreviations: HRQOL, health-related quality of life; LDS, Lipids in Diabetes Study; SF-36, Medical Outcome Study Short Form with 36 items; SF-6D, Short Form with six dimensions.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

DOI: 10.2337/dc05-2150. Clinical trial reg. no. ISRCTN 22144829.

amendments, which conform to the guidelines of the Declarations of Helsinki, were approved by the Central Oxford Research Ethics Committee and by the equivalent committees at each center. All patients gave informed witnessed consent.

Information on demographic and clinical characteristics such as height, weight, blood pressure, and smoking status were collected together with information on preexisting medical conditions. Biochemical measurements were undertaken by a central laboratory, with samples couriered overnight at 4°C to Oxford, and included HbA_{1c} (A1C) and total and HDL cholesterol. Corrected visual acuity in both eyes of all patients was measured at entry using Early Treatment of Diabetic Retinopathy Study charts. Patients were asked to sit 4 m from a well-illuminated chart and to use their usual spectacles or a pinhole, as necessary, to obtain the best visual acuity at the retina. This was measured as a LogMAR score ranging from −0.3 to 1.0, with normal vision (20/20 Snellen acuity) corresponding to a LogMAR score of 0.0 and legal blindness (20/200 Snellen acuity in the U.S.) corresponding to a LogMAR value of 1.0 (i.e., 10 times or 1 log unit worse than 20/20) (10). A member of the clinic staff assisted some patients with poor visual acuity to complete the quality-of-life questionnaire, taking care to avoid any interpretation of either questions or answers.

Table 1—*Patient characteristics* (n = *4,051*)

Male (%)	65
Ethnicity (%)	
Caucasian	90
Afro-Caribbean	4
Indian Asian	4
Other	2
Age (years)	61.6 ± 8.6
Diabetes duration (years)	6 (3, 11)
BMI (kg/m^2)	30.5 ± 5.9
Systolic blood pressure (mmHg)	143 ± 19
A1C (%)	8.2 ± 1.5
Total cholesterol (mmol/l)	4.9 ± 0.8
HDL cholesterol (mmol/l)	1.2 ± 0.3
Smoking (%)	
Never	38
Ex	47
Current	15
History of diabetes complications (%)	3
LogMAR scores (best/worst eye) (%)	
≤0	58/33
>0 and ≤0.5	41/50
>0.5	1/7
SF-36 domain scores	
Physical functioning	74.7 ± 25.8
Role physical	78.9 ± 25.7
Role emotional	86.2 ± 21.9
Social functioning	84.9 ± 22.1
Mental health	77.2 ± 17.1
Energy	59.7 ± 19.6
Bodily pain	71.6 ± 25.7
General health	65.5 ± 20.3
Utility score	0.76 ± 0.11

Data are means ± 1 SD or median (25th, 75th percentile) unless otherwise indicated.

Quality-of-life and utility assessment

Quality of life was assessed using SF-36 version 2, a 36-item self-administered questionnaire that measures health in terms of eight multi-item scales: physical functioning, role limitations due to physical problems or role physical, role limitations due to emotional problems or role emotional, social functioning, mental health, energy/vitality, bodily pain, and general health perception (for a description of each scale, see ref. 7). For each scale, the relevant item scores are coded, summed, and transformed onto a scale from 0 (worst possible health state measured by the questionnaire) to 100 (best possible health state). Scores for scales with missing items were imputed according to the procedures prescribed by the developers (11).

Since the SF-36 health survey is not designed to provide a single overall quality-of-life index score, we have used a recently developed algorithm for calculating utility values using the SF-6D, which is derived by collapsing the SF-36 into six dimensions (8). Utility values are measures of quality of life that also reflect societal preferences for individual health states. The Brazier algorithm is based on a regression equation that is estimated using a sample of 249 health states that were valued using the standard gamble approach by 611 individuals from the general U.K. population in face-to-face interviews. The highest possible utility value with this algorithm is 1.0, representing full health, and the lowest possible utility value is 0.296. Using this method, an overall utility score was calculated for each person in the study.

Statistical analyses

Analyses are based on the 4,051 (of 4,191 total) patients with the requisite data available.

Graphical analysis

The means of the eight SF-36 domain scores and the utility value by category of visual acuity in the better eye were estimated using a regression model. Better-eye values were used, as previous studies (12–14) have demonstrated a closer association with HRQOL changes than worst-eye visual acuity. Categories represent 0.1-LogMAR score increments, except for the highest category, LogMAR >0.5, which is the range in which a patient is likely to be unable to drive a car. To allow for potential confounding factors, we estimated a model that adjusted for male sex, Caucasian ethnicity, age at diagnosis (60–69 years), duration of diabetes (5–10 years), absence of smoking, BMI (25–30 kg/m^2), A1C <7%, systolic blood pressure ≥140 and <160 mmHg, and having a history of no previous major diabetes-related complications (any of amputation, congestive heart failure, nonacute ischemic heart disease, or stroke). These parameters were chosen to reflect the most common categories of characteristics for participants in the study, that is, the mean age, systolic blood pressure, and A1C; the median duration of diabetes; and the modal ethnic group, sex, BMI, smoking status, and complication status.

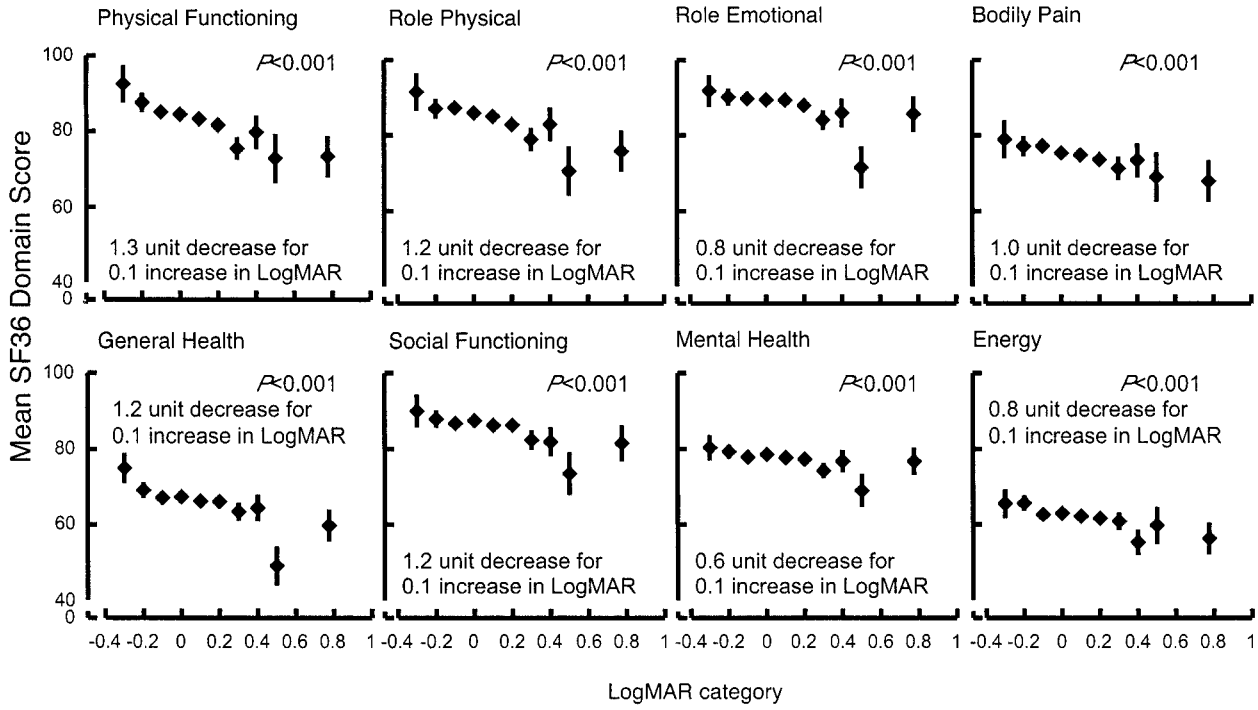

Figure 1—*Associations between SF-36 domains and LogMAR score categories in the better eye.*

The estimated model was used to predict mean LogMAR scores for individuals in these reference categories. We also estimated the association between LogMAR score as a continuous variable and report the marginal effect of a 0.1-unit change in value. While some domains of the SF-36 are subject to ceiling effects that arise when a significant proportion of respondents are rated at the maximum score, we used *t* tests to examine the association with levels of visual acuity, as previous studies have demonstrated its applicability in this context (15).

Regression analysis

As the strength of association between visual acuity and utility may vary over the LogMAR scale, a linear spline regression was used in the main statistical analysis, as it allows the slope of the regression line to vary for different levels of visual acuity. The regression model estimated the association between utility and the LogMAR score in the best and worst eye, adjusting for age, duration of diabetes, sex, BMI, smoking status, and history of complications. To examine potential threshold effects, we use a spline function with a knot at LogMAR score of zero to allow the association to vary between normal vision or better (LogMAR $\leq$0) and worse-than-normal vision (LogMAR $>$0) in both eyes. Stepwise regression with backwards selection using a P value <0.05 was used to determine the final model.

RESULTS — Patients had a mean (±SD) age of 61.6 ± 8.6 years, 65% were male, and median duration of diagnosed diabetes was 6 (interquartile range 8) years (Table 1). Mean A1C was 8.2 ± 1.5% and mean systolic blood pressure 143 ± 19 mmHg. Fifty-eight percent of patients had a LogMAR score ≤0.0 indicating normal or better-than-normal corrected vision. Mean SF-36 domain scores ranged from 86.2 ± 21.9 for role emotional to 59.7 ± 19.6 for energy and vitality. No systematic differences were observed across the eight domains when compared with the general population derived from the 1996 Health Survey for England (16) for those aged 55–64 years. The mean score for four of the domains in the study population were significantly higher (role physical, role emotional, social functioning, and mental health) than the general population and two were significantly lower (energy/vitality and bodily pain) with the maximum difference being 5.3 (95% CI 4.2–6.3) for role emotional.

For most SF-36 version 2 domains, there was a negative association between the domain scores and LogMAR category (Fig. 1) that persisted after adjustment for potential confounders. The impact of reduced visual acuity differs by domain with, for example, a 0.1-LogMAR increment associated with a 1.3-unit decline in the physical functioning domain and a 0.6-unit decline in the mental health domain. The mean utility score by LogMAR category shows little association with utility for those with normal or better-than-normal vision but a decline in mean utility for the higher LogMAR categories.

Adjusted regression models of the association between utility and LogMAR scores (Table 2 and Fig. 2) show that only best-eye–corrected visual acuity levels, which are worse than normal vision, are associated with lower levels of utility (the model assumes a linear decline over this range). Patients whose LogMAR scores equated to being legally blind had, on average, 0.054 (95% CI 0.034–0.074) lower utility compared with patients with normal or better-than-normal visual acuity. This indicates that a loss of acuity of this magnitude in the better eye is associated with 7% lower utility scores for the average patient.

CONCLUSIONS — We report here a small but statistically independent association between SF-36 domain and derived utility scores with visual acuity levels in U.K. patients with established type 2 diabetes. These results indicate that a reduced visual acuity can have an impact on

Table 2—*Regression model associations between SF-6D–derived utility values and LogMAR scores*

	Initial model		Final model	
Variables	Coefficient ± SE	*P* value	Coefficient ± SE	*P* value
Constant	0.858 ± 0.011	<0.001	0.850 ± 0.010	<0.001
Female	−0.026 ± 0.004	<0.001	−0.024 ± 0.004	<0.001
Duration of diabetes (years)*				
<5	0.001 ± 0.004	0.854		
≥10 and <15	−0.007 ± 0.005	0.198		
≥15 and <20	−0.004 ± 0.007	0.529		
≥20	−0.016 ± 0.009	0.061		
Age (years)†				
≥40 and <50	0.004 ± 0.006	0.460		
≥60 and <70	0.001 ± 0.004	0.871		
≥70	0.000 ± 0.006	0.969		
History of complications‡	−0.052 ± 0.010	<0.001	−0.065 ± 0.014	<0.001
Ex-smoker	−0.006 ± 0.004	0.141		
Current smoker	−0.020 ± 0.005	<0.001	−0.016 ± 0.005	0.001
BMI	−0.002 ± 0.000	<0.001	−0.002 ± 0.000	<0.001
Visual acuity				
LogMAR ≤0 (better eye)	0.000 ± 0.041	0.996		
LogMAR >0 (better eye)	−0.054 ± 0.018	0.003	−0.054 ± 0.010	<0.001
LogMAR ≤0 (worse eye)	−0.007 ± 0.062	0.914		
LogMAR >0 (worse eye)	−0.005 ± 0.009	0.617		
Adjusted R^2	0.04		0.04	

*Base category, ≥5 and <10 years; †base category, ≥50 and <60 years; ‡one of amputation, congestive heart failure, nonacute ischemic heart disease, or stroke.

all of the quality-of-life measures assessed, as there were negative associations for all eight SF-36 scores and the SF-36–derived utility score after adjusting for potential confounders. These results were seen for visual acuity levels, as assessed in the better eye, with those patients whose visual acuity was below normal having a continuous negative association between their LogMAR and utility scores. The difference in utility scores between those with normal vision and those with LogMAR scores equating to legally blind was similar to the impact of having a previous major diabetes-related complication and would appear to be large enough to be regarded as a clinically important difference in HRQOL (17). These findings are in contrast to previous studies (involving <500 subjects) that have not shown an association between visual acuity and most SF-36 domains in individuals with type 2 diabetes (18,19).

There have been three recent studies (20–23) using algorithms to derive utility values from generic HRQOL instruments such as the EQ-5D (24). Clarke et al. (20) assessed health utility scores by surveying a sample of the U.K. Prospective Diabetes Study patients using the EQ-5D and then, using the U.K. tariff values to assign utilities, found that blindness in one eye reduced overall utility by 0.074 (95% CI 0.025–0.124). Coffey et al. (21) used a self-administered quality–of–well-being index to assess the HRQOL of 1,256 individuals with type 2 diabetes attending specialty clinics at a university medical center. They found that blindness in one eye reduced utility by 0.043 (0.021–0.065) and loss of vision in both eyes by 0.17 (0.148–0.192). Finally, based on data from the CODE-2 study (25), Bagust and Beale (22) found that loss of sight in one or both eyes reduced utility by 0.057 (0.014–0.100).

This study has shown the estimated impact that loss of sight has on utility when it has been derived from the SF-36 and is of a similar magnitude to previous estimates using other instruments. It also demonstrates a negative association between utility and the LogMAR scores when vision is below the normal range, suggesting that any degree of impaired vision in the better eye may have an impact on utility. While the association between visual acuity in the better eye and the SF-6D utility value was highly significant ($P < 0.001$), the adjusted R^2 for the overall equation was 0.04. This is consistent with several previous studies (20,22) that indicate that while eye-related complications are associated with lower scores, the regression models explain only a relatively small proportion of the variation in utility scores (with previous R^2 ranging between 0.04 and 0.21).

Several studies (12–14) have also directly elicited utilities from diabetic patients who have varying levels of visual loss by using either the standard gamble or time trade-off techniques. This involves dividing patients into groups based on their best corrected vision and eliciting the patients willingness to trade either in terms of accepting a risk of death (in the case of standard gamble) or to sacrifice years of their remaining life (in the case of time trade off) to return to perfectly normal vision in both eyes. These studies have generally shown a greater variation in utility values by levels of visual acuity than reported here. For example, a recent study (14) showed average utility was 0.90 (0.83–0.97) for patients with near-normal vision, while it was 0.71 (0.58–0.84) for those with best-corrected visual acuity of LogMAR 1.0–1.3. This suggests a stronger negative association between visual acuity and utility when they are directly elicited from patients rather than indirectly from the SF-6D. An important question for future research is the degree to which SF-6D fully captures the effect of lower visual acuity on HRQOL. The SF-36, unlike some other generic instruments (e.g., Health Utility Index [23]), does not have a domain representing vi-

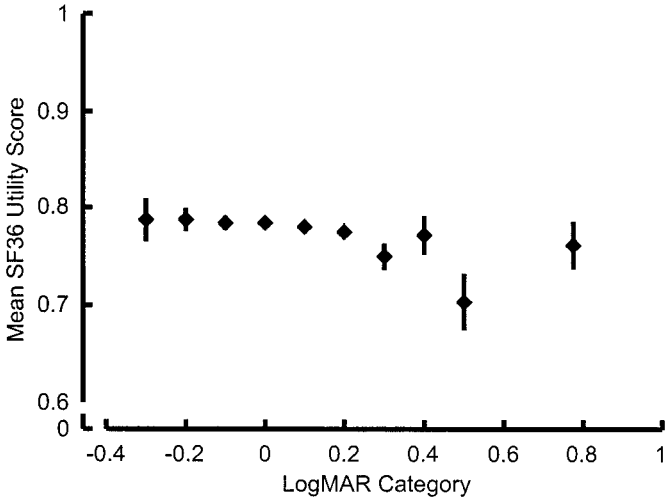

Figure 2— *Association between SF-36–derived utility score and LogMAR score categories in the better eye.*

sion. Testing the validity of utilities derived using the SF-6D by comparing these with directly elicited values for various levels of acuity would be an advantage.

In this study, we have used HRQOL and visual acuity information provided by the patients on only one occasion; therefore, our measures of impact on quality of life should be interpreted as differences across the population rather than change in an individual's HRQOL following a decline in visual acuity. There is also a need to examine how changes in visual acuity impact responses to the SF-36 and how adaptation following vision loss can impact measures of HRQOL. This is particularly relevant in the context of its use as an outcome measure in major randomized controlled trials, such as ADOPT (A Diabetes Outcome Progression Trial) (26), especially since a recent study (27) found a deterioration in the mean SF-36 scores in a population that showed improved clinical outcomes.

This study has demonstrated that reduced visual acuity affects many aspects of HRQOL, as measured by the SF-36. Unlike previous studies, we have found negative associations between visual acuity and all eight domains of the SF-36. The estimates of association between visual acuity and utility will facilitate in capturing the burden of diabetes, as it allows outcomes to be quantified in measures such as quality-adjusted life-years. They can also be used to inform health economic evaluations of interventions designed to treat or prevent diabetic eye disease.

Acknowledgments— The LDS was supported by an unrestricted educational grant from Bayer (to R.R.H.). P.M.C. was partly supported by a National Health and Medical Research Council Program Grant (211205). J.S. holds a Research Scientist in Evidence Synthesis Award from the U.K. Department of Health.

We thank Irene Stratton for assistance with the derivation of the ETDRS (Early Treatment of Diabetic Retinopathy Study) scores. The participation of the LDS patients and staff is appreciated.

References

1. Sinclair AJ, Bayer AJ, Girling AJ, Woodhouse KW: Older adults, diabetes mellitus and visual acuity: a community-based case-control study. *Age Ageing* 29:335–339, 2000
2. Klein R, Klein BEK: Vision disorders in diabetes. In *Diabetes in America*. 2nd ed. Harris MI, Cowie CC, Stern MP, Boyko EJ, Reiber GE, Bennett PH, Eds. Washington, DC, U.S. Govt. Printing Office, 1995
3. Early Treatment Diabetic Retinopathy Study Research Group: Early photocoagulation for diabetic retinopathy: ETDRS report number 9. *Ophthalmology* 98 (Suppl. 5):766–785, 1991
4. Stratton IM, Kohner EM, Aldington SJ, Turner RC, Holman RR, Manley SE, Matthews DR: Risk factors for incidence and progression of retinopathy in type II diabetes over 6 years from diagnosis (UKPDS 50). *Diabetologia* 44:156–163, 2001
5. Aiello LM: Perspectives on diabetic retinopathy. *Am J Ophthalmol* 136:122–135, 2003
6. Johannesson M: Theory and methods of economic evaluation of health care. 4:1–245, 1996
7. Ware JE Jr, Sherbourne CD: The MOS 36-item short-form health survey (SF-36). I. conceptual framework and item selection. *Med Care* 30:473–483,1992
8. Brazier J, Roberts J, Deverill M: The estimation of a preference-based measure of health from the SF-36. *J Health Econ* 21: 271–292, 2002
9. Neil A, Wheeler F, Cull C, Manley S, Keenan J, Holman R: Combination statin and fibrate therapy in type 2 diabetes: results from the Lipids in Diabetes Study (Abstract). *Diabetes* 52 (Suppl. 1):A74, 2003
10. Holladay JT: Visual acuity measurements. *J Cataract Refract Surg* 30:287–290, 2004
11. Ware JE, Snow KK, Kosinski M, Gandek B: *SF-36 Health Survey: Manual and Interpretation Guide*. Lincoln, RI, QualityMetric, 2000
12. Brown MM, Brown GC, Sharma S, Landy J, Bakal J: Quality of life with visual acuity loss from diabetic retinopathy and age-related macular degeneration. *Arch Ophthalmol* 120:481–484, 2002
13. Brown MM, Brown GC, Sharma S, Shah G: Utility values and diabetic retinopathy. *Am J Ophthalmol* 128:324–330, 1999
14. Sharma S, Brown GC, Brown MM, Shah GK, Snow K: Converting visual acuity to utilities. *Can J Opthalmol* 35:267–272, 2000
15. Sullivan LM, D'Agostino RB: Robustness of the *t* test applied to data distorted from normality by floor effects. *J Dent Res* 71: 1938–1943, 1992
16. Prescott-Clarke P, Primatesta P (Eds.): *Health Survey for England 96. Volume 1: Findings*. London, The Stationery Office, 1998
17. Walters SJ, Brazier JE: What is the relationship between the minimally important difference and health state utility values? The case of the SF-6D. *Health Qual Life Outcomes* 1:4, 2003
18. Greenfield S, Rogers W, Mangotich M, Carney MF, Tarlov AR: Outcomes of patients with hypertension and non-insulin dependent diabetes mellitus treated by different systems and specialties: results from the medical outcomes study. *JAMA* 274:1436–1444, 1995
19. Lee PP, Whitcup SM, Hays RD, Spritzer K, Javitt J: The relationship between visual acuity and functioning and well-being among diabetics. *Qual Life Res* 4:319–323, 1995
20. Clarke P, Gray A, Holman R: Estimating utility values for health states of type 2 diabetic patients using the EQ-5D (UKPDS 62). *Med Decis Making* 22:340–349, 2002
21. Coffey JT, Brandle M, Zhou H, Marriott D, Burke R, Tabaei BP, Engelgau MM, Kaplan RM, Herman WH: Valuing health-related quality of life in diabetes. *Diabetes Care* 25:2238–2243, 2002
22. Bagust A, Beale S: Modelling EuroQol health-related utility values for diabetic complications for CODE-2 data. *Health*

Econ 14:217–230, 2005
23. Feeny D, Furlong W, Boyle M, Torrance GW: Multi-attribute health status classification systems: Health Utilities Index. *Pharmacoeconomics* 7:490–502, 1995
24. EuroQol Group: EuroQol: a new facility for the measurement of health-related quality of life. *Health Policy* 16:199–208, 1990
25. Massi-Benedetti M, the CODE-2 Advisory Board: The cost of diabetes type II in Europe. *Diabetologia* 45:51–54, 2002
26. Viberti G, Kahn SE, Greene DA, Herman WH, Zinman B, Holman RR, Haffner SM, Levy D, Lachin JM, Berry RA, Heise MA, Jones NP, Freed MI: A Diabetes Outcome Progression Trial (ADOPT): an international multicenter study of the comparative efficacy of rosiglitazone, glyburide, and metformin in recently diagnosed type 2 diabetes. *Diabetes Care* 25:1737–1743, 2002
27. Hill-Briggs F, Gary TL, Baptiste-Roberts K, Brancati FL: Thirty-six-item short-form outcomes following a randomized controlled trial in type 2 diabetes (Letter). *Diabetes Care* 28:443–444, 2005