Patient Perceptions of Quality of Life With Diabetes-Related Complications and Treatments

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OBJECTIVE — Understanding how individuals weigh the quality of life associated with complications and treatments is important in assessing the economic value of diabetes care and may provide insight into treatment adherence. We quantify patients' utilities (a measure of preference) for the full array of diabetes-related complications and treatments.

RESEARCH DESIGN AND METHODS — We conducted interviews with a multiethnic sample of 701 adult patients living with diabetes who were attending Chicago area clinics. We elicited utilities (ratings on a 0–1 scale, where 0 represents death and 1 represents perfect health) for hypothetical health states by using time-tradeoff questions. We evaluated 9 complication states (e.g., diabetic retinopathy and blindness) and 10 treatment states (e.g., intensive glucose control vs. conventional glucose control and comprehensive diabetes care [i.e., intensive control of multiple risk factors]).

RESULTS — End-stage complications had lower mean utilities than intermediate complications (e.g., blindness 0.38 [SD 0.35] vs. retinopathy 0.53 [0.36], $P < 0.01$), and end-stage complications had the lowest ratings among all health states. Intensive treatments had lower mean utilities than conventional treatments (e.g., intensive glucose control 0.67 [0.34] vs. conventional glucose control 0.76 [0.31], $P < 0.01$), and the lowest rated treatment state was comprehensive diabetes care (0.64 [0.34]). Patients rated comprehensive treatment states similarly to intermediate complication states.

CONCLUSIONS — End-stage complications have the greatest perceived burden on quality of life; however, comprehensive diabetes treatments also have significant negative quality-of-life effects. Acknowledging these effects of diabetes care will be important for future economic evaluations of novel drug combination therapies and innovations in drug delivery.

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Diabetes significantly increases an individual's risk of developing multiple microvascular and cardiovascular complications, and the risk of these complications can be significantly reduced with intensive and comprehensive diabetes care (1). Current recommendations for the ideal risk factor targets (e.g., A1C <7%) and specific therapies (e.g., prophylactic aspirin) for diabetes care reflect the findings of multiple clinical trials (2–4).

Although intensive and comprehensive diabetes care may generate significant health benefits, the current level of adoption of comprehensive diabetes care is incomplete. Quality-of-care studies indicate that there has been a steady rise in the proportion of patients taking beneficial medications such as aspirin and that there have been reductions in the proportion of patients with poor risk factor control (5). At the same time, large proportions of patients continue to have poor glycemic (20%), blood pressure (33%), and cholesterol control (40%) (5). These ongoing deficiencies have led to a large public investment in diabetes quality improvement programs (6).

The success of these quality improvement efforts depends, in part, on whether or not patients are willing to take the multiple medications that comprise comprehensive diabetes care. Patients' willingness to adopt this care is likely to be determined, in part, by their perceptions of the relative quality-of-life effects of complications and treatments (7,8). These perceptions are also critical for economic evaluations of quality improvement efforts and treatment innovations. The development of combination drugs such as the polypill, a proposed treatment combining an aspirin, a diuretic, an ACE inhibitor, a β-blocker, folic acid, and a statin, is motivated by the desire to simplify the treatment experience (9). Novel insulin delivery methods are intended to eliminate the discomfort associated with insulin injections (10). Whether these innovations will prove to be economically valuable depends on accurately accounting for the adverse quality-of-life effects of treatments and their downstream effects. Quality-of-life effects are reflected in medical cost-effectiveness analyses (CEAs) using quality-of-life weights called utilities. Utilities are quantitative measures of preference on a 0–1 scale, where 0 represents death and 1 represents life in perfect health (11).

Despite the importance of understanding the utilities for treatment and complication health states related to diabetes care, there have been no systematic efforts to directly elicit utilities for the full array of complications and treatments that patients may experience. As a result, important complication and treatment states have never been accounted for in prior CEAs, (12). The utilities for several intermediate microvascular complication states (e.g., diabetic neuropathy) are un-

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Abbreviations: CEA, cost-effectiveness analysis.

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

Table 1—*Demographics and clinical characteristics*

Age	63 ± 14
Male	42
Race/ethnicity	
African American	268 (38)
White	215 (31)
Latino	164 (23)
Health insurance	
Private	66
Medicare	46
Medicaid	18
Annual income ($)	
<10,000	20
10–25,000	26
25–50,000	34
>50,000	21
Duration of diabetes	9.9 ± 8.6
Self-reported comorbid conditions or complications	
Hypertension	74
Hypercholesterolemia	65
Eye disease	19
Kidney disease	8
Foot disease (peripheral neuropathy and amputation)	52
Heart disease	30
Stroke	11
Risk factor levels	
A1C	7.45 ± 1.62
A1C <7%	47
LDL cholesterol (mg/dl)	97 ± 34
LDL cholesterol <100 (mg/dl)	61
Systolic blood pressure (mmHg)	13 ± 18
Systolic blood pressure <130 mmHg	42
Diastolic blood pressure (mmHg)	74 ± 11
Diastolic blood pressure <80 mmHg	65
Mean number of medications	6 ± 4
Mean number of glucose-lowering medications	
Chart report	2 ± 1
Interview report	1 ± 1
Mean number of diabetes-related medications (including blood pressure, cholesterol, and aspirin)	
Chart report	4 ± 2
Interview report	4 ± 2
Glucose-lowering therapy	
Diet alone	
Chart report	14
Interview report	19
Oral medications alone	
Chart report	61
Interview report	58
Insulin and oral medications	
Chart report	11
Interview report	10
Insulin alone	
Chart report	14
Interview report	13
Aspirin	
Chart report	38
Interview report	40
Cholesterol-lowering drug	
Chart report	61
Interview report	57
Blood pressure–lowering drug	
Chart report	77
Interview report	73

Data are means ± SD, *n* (%), or %. *n* = 701.

known. Accounting for the effects of these states may influence CEA results because the incidences of intermediate complications are high compared with those of end-stage complications (3). Even more striking is the lack of accounting for the quality-of-life effects of treatments. We have previously found that accounting for the quality-of-life effects of treatments can alter the conclusions of CEA for intensive glucose control, and this may prove to be the case for comprehensive diabetes care (13). Thus, we set out to systematically collect, describe, and compare patients' utilities for the full range of complications and treatments related to diabetes.

RESEARCH DESIGN AND METHODS

— From May 2004 to May 2006, we conducted face-to-face interviews with patients without dementia who were aged ≥18 years, living with diabetes, and attending clinics affiliated with an academic medical center (University of Chicago, Chicago, IL) and physician offices affiliated with a suburban hospital (MacNeal Hospital, Berwyn, IL). Prospective subjects were initially identified through clinic scheduling software based on ICD-9 codes for diabetes (i.e., 250.xx). Randomly identified patients were sent study recruitment letters. Letters were followed by a telephone call. We performed a screening telephone mini-mental status examination and excluded patients with scores ≤17 (14). We successfully contacted 2,990 patients, and 2,398 of these patients were eligible for the study. A total of 910 patients (38% of eligible subjects) scheduled interviews, and 701 patients (29% of eligible subjects) completed interviews. The average of age of subjects who completed interviews did not differ from that of other eligible patients.

Interviews took ~1 h and were conducted by trained interviewers in English or Spanish. All Spanish interview materials were professionally translated and back translated. We elicited utilities using the time-tradeoff method (15). For each time-tradeoff elicitation, patients were given a description of a hypothetical health state and asked to consider life in that state. The text of all health state descriptions is included in an online appendix (available at http://dx.doi.org/10.2337/dc07-0499). The health state descriptions were based upon our prior study of diabetes-related health state utilities (13) and existing descriptions in the literature. Health state descriptions were

Table 2—*Complication utilities*

Complication	Mean	Median	Mode	SD	Skewness	Kurtosis
Angina	0.64	0.75	0.95	0.31	−0.65	−0.87
Mild stroke	0.70	0.85	0.95	0.31	−0.99	−0.36
Major stroke	0.31	0.26	0.05	0.31	0.90	−0.46
Diabetic neuropathy	0.66	0.85	0.95	0.34	−0.79	−0.87
Amputation	0.55	0.55	0.95	0.36	−0.25	−1.46
Diabetic retinopathy	0.53	0.50	0.05	0.36	−0.17	−1.53
Blindness	0.38	0.35	0.05	0.35	0.49	−1.26
Diabetic nephropathy	0.64	0.80	0.95	0.35	−0.72	−1.02
End-stage renal disease	0.35	0.25	0.05	0.33	0.66	−1.03

Data are *n*.

reviewed with the clinical faculty at the University of Chicago and pilot tested with patients. During the time-tradeoff elicitation, patients were asked to give their preference for 10 years in the health state of interest and a shorter period of time in perfect health. Using the ping-pong method, patients were asked a series of iterative questions where the time in perfect health was systematically altered by yearly increments and questioning was stopped, when the patient was indifferent between a given time choice. The point at which the patient was indifferent between the time choices was used to calculate the utility score (e.g., if 6 years of life in perfect health = 10 years with an amputation, the utility = 0.60). To minimize the effects of order response bias, the order of utility assessments was randomly allocated along two dimensions of the health states: *1*) complication states versus treatment states and *2*) severe/intensive states versus intermediate/conventional states.

The descriptions of several complication health states were based on previous descriptions of life with complications found in the utility literature (blindness [16], diabetic retinopathy [symptomatic] [16], end-stage renal disease on hemodialysis [17], amputation [18], and major and minor stroke [19]). When such descriptions were not available we developed health state descriptions based on clinical experience and from published descriptions of life with such complications (angina-stage II Canadian Heart Association [20], diabetic neuropathy [symptomatic] [18], and diabetic nephropathy [21]).

For each treatment state, we described the daily experience of treatments, the laboratory testing associated with treatments, and the likelihood of side effects. Patients were asked not to consider long-term effects of treatments on complications but to focus on the daily quality-of-life effects of treatments. We based our description of intensive and conventional glucose control on the treatment protocols and patient experiences of the U.K. Prospective Diabetes Study (UKPDS) (3). With intensive glucose control, patients were told that they would be more likely to be given multiple oral agents and insulin, that the frequency of major hypoglycemic episodes would be higher, and that the need for self-glucose of monitoring would be greater to achieve A1C <7% in comparison with conventional glucose control (A1C = 7.9%). Similarly, we used the UKPDS blood pressure trial protocols as the basis for descriptions of intensive and conventional blood pressure control (2). Patients were told that with intensive blood pressure control they would be more likely to be given three to four blood pressure agents compared with conventional blood pressure control. Descriptions for the remaining treatment states were based on data from the medical literature (e.g., aspirin [22] and cholesterol-lowering medication [23]).

We also queried patients about their perceptions of quality of life with comprehensive diabetes care, which we described as the combination of cholesterol-lowering medication, aspirin, intensive blood pressure control, intensive glucose control, diet, and exercise. This combination represented care that was both comprehensive in breadth but also intensive in terms of risk factor goals. We also asked patients about a state we called the comprehensive care with polypill state. This state was identical to the comprehensive diabetes care state except that the number of pills taken per day was reduced by the use of the polypill.

After utility elicitation, patients were asked about their overall health status, current medications, relationship with their physician, beliefs regarding medications, and willingness to take more medications. Medical records were abstracted for data on current medications, comorbidities (Charlson comorbidity index [24]), and risk factor levels. We performed a 10% rereview and found moderate to excellent agreement among abstractors. The intraclass correlation coefficient for A1C was 0.92. κ statistics for the presence of complications ranged from 0.59 to 0.79.

Statistical analysis

All analyses were performed using SAS statistical software (release 8.1; SAS Institute, Cary, NC). We describe the distribution of utilities using the mean, median, mode, SD, skewness, and kurtosis provide graphical illustration of the distributions of utility scores. Paired *t* tests were used to compare multiple health state utilities ascertained from the same individuals. Wilcoxon's rank-sum tests were used for comparisons of utilities across subgroups.

RESULTS — The mean age of subjects was 63 years; 42% were men, 38% were black, and 24% were Latino (Table 1). The mean duration of diabetes was 9.9 years and the mean Charlson comorbidity index was 2.64 (24). Of the patients, 23% had experienced a microvascular complication, and 30% reported having cardiovascular complications. In comparison with nationally reported risk factors levels, study subjects had lower mean glucose and cholesterol levels but similar blood pressure levels (5). The majority (61%) used oral diabetes medications alone, 25% used insulin as part of their therapy, and 14% used no medications for glucose control.

Patient utilities for diabetes-related complications

Among the complication state utilities, each end-stage complication had a lower mean utility than its intermediate complication counterpart (e.g., major stroke 0.31 vs. minor stroke 0.70, $P < 0.01$) (Table 2). The complication state with the lowest mean utility was major stroke (0.31). Study patients rated complication utilities for, angina, diabetic neuropathy, and mild kidney disease similarly. In addition, diabetic retinopathy utilities were equivalent to amputation ratings.

Table 3—*Treatment utilities*

Treatment	Mean	Median	Mode	SD	Skewness	Kurtosis
Conventional glucose control	0.76	0.95	0.95	0.31	−1.46	0.68
Intensive glucose control	0.67	0.85	0.95	0.34	−0.88	−0.77
Conventional blood pressure control	0.77	0.95	0.95	0.30	−1.52	0.88
Intensive blood pressure control	0.73	0.90	0.95	0.32	−1.22	0.03
Aspirin	0.80	0.95	0.95	0.29	−1.78	1.80
Cholesterol-lowering drug	0.78	0.95	0.95	0.29	−1.60	1.19
Comprehensive diabetes care	0.64	0.75	0.95	0.34	−0.67	−1.03
Comprehensive care with polypill	0.66	0.85	0.95	0.34	−0.81	−0.83
Diet	0.88	0.95	1.0	0.24	−2.67	6.17
Exercise	0.89	1.0	1.0	0.23	−2.86	7.34

Data are *n*.

Patient utilities for diabetes-related treatments

Each intensive treatment state had a lower mean utility than its conventional counterpart (e.g., intensive glucose control 0.67 vs. conventional glucose control 0.76, $P < 0.01$) (Table 3). The individual diabetes-related treatment with the lowest mean utility rating was intensive glucose control (0.67) and the comprehensive diabetes care treatment state was the lowest rated treatment state overall (0.64). The highest rated treatment states were life with diet and exercise therapy. The comprehensive care with polypill state had a mean utility (0.66) that was slightly higher but not significantly different from that of comprehensive diabetes care. Among treatment utilities, conventional glucose control was rated similar to conventional blood pressure control, as was cholesterol-lowering medication and conventional blood pressure control. The intensive glucose control and comprehensive care with polypill states were rated equally, and diet therapy was equivalent to exercise therapy.

Comparisons of complication and treatment utilities

Mean utilities for the comprehensive diabetes care and the comprehensive care with polypill were not statistically different from the mean utilities for angina, diabetic neuropathy, and diabetic nephropathy ($P > 0.04$). The mean utility for intensive glucose control was not significantly different from that for diabetic neuropathy. All other comparisons were significantly different ($P < 0.01$).

Heterogeneity of health state utilities

Each health state had significant variation in scores as reflected in large SDs (0.23–0.36) and ranges of observed values (Tables 2 and 3). Many health state utility distributions had a trimodal distribution with variation in weighting 0, 0.5, and 1. For complication states, the end-stage complications had especially heavy left-sided tails near 0, indicated by a positive skewness value. Between 12 and 50% of patients were willing to give up 8 of 10 years in perfect health to avoid life with complications. For treatment states, the mode of all utility distributions was ≥0.95, and distributions tended to have a right-sided deviation, with less prominent left-sided tails, indicated by a negative skewness value. Between 10 and 18% of patients were willing to give up 8 of 10 years of life in perfect health to avoid life with treatments.

Impact of experience on health state utilities

Patients with existing complications had a general tendency to rate life with those complications higher than those without complications. This was only statistically significant for major stroke (0.42 vs. 0.31), diabetic neuropathy (0.70 vs. 0.64), and diabetic retinopathy (0.61 vs. 0.53). In a similar fashion, patients who were taking specific medications had a general tendency to give higher utilities for related treatment states than patients not taking those medications. This was only statistically significant for intensive glucose control (0.76 vs. 0.66) and aspirin (0.84 vs. 0.81). The overall hierarchy of health states was not different among patients with complications/medications and those without them.

CONCLUSIONS — Patients with diabetes perceive significant differences in the quality-of-life effects of complications and treatments related to their condition. On average, patients rated life with complications, especially end-stage complications, as significantly lower than that of life with treatments. However, we also found that patients perceived comprehensive diabetes care as having significant negative effects on quality of life, and these effects were equivalent to life with several intermediate complications. This quality-of-life burden appeared to arise from the prospect of multiple daily insulin injections rather than the prospect of multiple oral agents. This is implied by the facts that the treatment states with the lowest ratings each included multiple daily injections of insulin and that the utilities for comprehensive diabetes care and comprehensive care with polypill were not significantly different.

It is important to note that these differences in mean utilities are directly influenced by the heterogeneity in patient utilities and that this heterogeneity varied by complications and treatments. For complication states, it was common to see a heavy left-sided tail for end-stage complications. For treatment states, the majority of patients actually rated life with treatments as being close to perfect health, indicating that treatments were not burdensome. At the same time, an important minority of patients (10–18%) gave ratings indicating that they perceived life with treatments as being a significant burden on quality of life. Our observation that there is significant heterogeneity in patient treatment preferences highlights the importance of incorporating a shared decision-making approach into everyday diabetes care. Acknowledging individual patient treatment preferences may be one of the keys to translating findings from clinical trial populations to general patient populations (8).

These utility values may be used in future cost-effectiveness analyses of diabetes care. This study provides directly elicited utilities from a single population of adult patients living with type 2 diabetes. It provides an additional source of utility data that may have particular advantages when one is comparing alternative diagnostic or treatment options (11). Indirect methods of utility elicitation (e.g., EuroQoL) (25,26) have a primary advantage of ease of administration; however, they may be relatively insensitive to important differences for particular treatment decisions. Directly eliciting utilities for specific health states provides a more theoretically sound (11) and sensitive approach to detecting differences in pa-

tients' preferences regarding different health states. The primary limitation of direct elicitation methods is the challenge of collecting such data; however, this study was performed to overcome this limitation. This study also provides utilities for complications and treatments that have not been considered previously in analyses, and accounting for these utilities may shift the balance of CEA results (13). A major insight that has not been extensively studied in previous CEAs of chronic diseases is that any negative quality-of-life effect of treatment can outweigh its benefits over a population. Failure to acknowledge the quality-of-life effects of current treatments may lead to an overestimation of the benefits of ongoing quality improvement efforts and an underestimation of the benefits of treatment innovations (10). It is important to note that these utilities represent patient-derived utilities and that there may still be a need to collect these health state utilities from the general population to accurately reflect the societal perspective in base case CEAs (11). CEAs of diabetes care have tended to rely on utilities that are available in the literature, and these have tended to be patient derived (26).

Several limitations of this study should be considered when these results are interpreted. The preferences of this particular patient population may not be representative of those of all patients living with diabetes. All of our patients had an established relationship with a provider, and they may represent a group of patients more adherent to treatment than those in the general population. However, our study sample is ethnically and economically diverse. Our results are also limited by the fact that the validity of utility measurements cannot be directly assessed because there is no gold standard for measuring preferences. However, our patient population had significant experience with the various described health states, the order of our utility results has face validity, and our complication utilities are similar to those collected by the time-tradeoff method (27). Another limitation of the study is that we did not formally assess the reliability of the utility ratings over time. Our comparisons of patients with and without experiences with complications and medications provide some insight into how these utilities might change over time. Finally, our utility ratings are influenced by the specific descriptions of health states provided during the survey.

This study has important implications for current policies and programs that are designed to enhance the quality of chronic disease management. Many of these programs essentially encourage patients to add more medications to their treatment regimen. In the near future, the results of the Action to Control Cardiovascular Risk in Diabetes trial may actually lead to even lower risk factor goals that will require even greater use of medications to achieve them. Our study results show that taking multiple medications on a routine basis represents a significant burden for many patients. Our study helps elucidate what facets of medication taking concern patients and provides a starting point from which we can think about how to overcome these concerns with patients. Quality of life related to treatments will be likely to improve if we can simplify or modify current treatments through treatment innovations. Without such technological innovations, we may still be able to allay patient concerns by educating patients very early in their disease about the true nature of optimal diabetes care, by incorporating their preferences into treatment decisions, and by acknowledging patient preferences and quality-of-life concerns in public health efforts to improve the quality of diabetes care.

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