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Correlates of health-related quality of life in type 2 diabetes

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Abstract *Aims/hypothesis:* We assessed the impact of medical comorbidities, depression, and treatment intensity on quality of life in a large primary care cohort of patients with type 2 diabetes. *Methods:* We used the Health Utilities Index-III, an instrument that measures health-related quality of life based on community preferences in units of health utility (scaled from 0=death to 1.0=perfect health), in 909 primary care patients with type 2 diabetes. Demographic and clinical correlates of health-related quality of life were assessed. *Results:* The median health utility score for this population was 0.70 (interquartile range 0.39–0.88). In univariate analyses, older age, female sex, low socioeconomic status, cardiovascular disease, microvascular complications, congestive heart failure, peripheral vascular disease, chronic lung disease, depression, insulin use and number of medications correlated with decreased quality of life, while obesity, hypertension and hypercholesterolaemia did not. In multiple regression analyses, microvascular complications, heart failure and depression were most strongly related to decreased health-related quality of life, independently of duration of diabetes; in these models, diabetes patients with depression had a utility of 0.59, while patients without symptomatic comorbidities did not have a significantly reduced quality of life. Treatment intensity remained a significant negative correlate of quality of life in multivariable models. *Conclusions/interpretation:* Patients with type 2 diabetes have a substantially decreased quality of life in association with symptomatic complications. The data suggest that treatment of depression and prevention of complications have the greatest potential to improve health-related quality of life in type 2 diabetes.

Keywords Adult diabetes · Chronic disease · Health-related quality of life

Abbreviations COPD: chronic obstructive pulmonary disease · HANDS: Harvard Department of Psychiatry/National Depression Screening Day Scale · HUI-3: Health Utilities Index Mark III · UKPDS: UK Prospective Diabetes Study

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Introduction

Diabetes results in life-threatening complications and reduced life expectancy, but only after many largely asymptomatic years during which patients must adhere to bothersome and difficult therapy. While the UK Prospective Diabetes Study (UKPDS) found that complications of diabetes affect quality of life more than overall treatment intensity [1], many patients find treatment itself burdensome [2, 3]. In addition, the prevalence of depression is substantially higher among patients with diabetes than those without diabetes [4]. Depression, in turn, decreases

quality of life [5, 6] and hinders treatment [7]. While there have been a number of studies of quality of life in patients with type 2 diabetes [1, 8–12], few have looked at a large primary care cohort while simultaneously accounting for multiple medical comorbidities, depression and treatment intensity.

To address these questions, we conducted a survey of over 900 primary care patients with type 2 diabetes using the Health Utilities Index Mark III (HUI-3) [13–15] to measure quality of life. The HUI-3 is a questionnaire that links patients' responses about their level of function in eight different health domains to previously defined health utilities derived from the general population. We estimated the utility associated with type 2 diabetes and determined the factors that contribute to diminished health-related quality of life, including clinical comorbidities, depression and treatment. We hypothesised that symptomatic comorbidities of diabetes would account for much of the decrement in health-related quality of life associated with diabetes.

Subjects and methods

Study population

We surveyed patients with diagnosed diabetes who were followed in one of two outpatient primary care medical clinics between December 2001 and July 2003: a community health centre in Revere (MA, USA), and a hospital-based primary care internal medicine practice in Boston (MA, USA). We generated lists of potentially eligible patients using billing claims for non-gestational diabetes (codes 250.00–250.90 in the International Classification of Diseases, 9th revision) over a 3-year period. Type 2 diabetes was confirmed by detailed chart review of the patient's medical record by trained research nurses. Diabetes was defined by adult-onset or obesity-associated diabetes diagnosis listed in the problem list, diabetes-specific medicine (e.g. sulfonylurea, metformin, insulin or equipment for insulin injection or home glucose monitoring) listed in the medication list, or diabetes diagnosis discussed in a progress note. Patients with clinical type 1 diabetes (defined by age of onset less than 40 years in conjunction with insulin treatment since diagnosis, designations of 'juvenile diabetes', or positive anti-islet cell antibodies when available) were excluded, and none was detected in the chart re-review. Eligible patients were diagnosed with diabetes before the intervention period, were alive at study completion, and received continuous care at their designated clinical site, with at least one visit in the first half and one in the second half of the study period. Patients with a terminal illness or cognitive impairment were excluded.

A total of 1,648 potential participants were mailed a letter co-signed by their primary care physican and the principal investigator (J. B. Meigs) describing the study. Of these, 18% either opted out from further contact or were initially excluded. The remainder (1,317 patients) were contacted by telephone in advance of a usual care clinic visit to arrange a meeting with a study staff member. Nine hundred and fifty-three patients (72.4%) provided informed consent and completed the study survey. Of those who did not participate, approximately one-third declined; one-quarter either did not arrive for their appointment, promised to complete the survey at home but did not, or could not be reached; and one-quarter were either not diabetic or excluded owing to illness or inability to participate. Limited chart data available on non-participants revealed that they had the same mean age as participants (66 years, p=0.6), similar Charlson comorbidity scores (2.7 vs 2.9, p=0.06), and a similar prevalence of depression (33 vs 36% p=0.2) and prescription of antidepressants (22 vs 21%, p=0.7). Non-participants were less likely to be white (72 vs 83% of participants, p<0.0001), less likely to speak English (87 vs 98%, p<0.0001), more likely to be receiving Medicaid (9 vs 6%, p=0.04), and less likely to have an HbA_{1c}<7% (39 vs 46%, p=0.01). Non-participants had higher blood pressure and were more likely to be on an antihypertensive medication (61 vs 54%, p=0.01) or aspirin (28 vs 20%). The final study population consisted of 909 patients with type 2 diabetes. The Massachusetts General Hospital Institutional Review Board approved the study.

Demographic and clinical covariates

Demographic data were derived from survey responses. Clinical data were collected from manual chart reviews, directly from the electronic medical record, from the hospital's central data repository (laboratory test dates and results), from billing claims (hospitalisations and hospital discharge diagnoses), and from administrative records (patient demographics and insurance status).

Comorbidities were determined based on medical record review of listed diagnoses. A condition, its synonyms, and/or its specific treatments were taken as indications of a given comorbidity. Microvascular complications were defined based on any one the following diagnoses, their synonyms, or their abbreviations on the problem list: neuropathy, amputation, foot ulcer, gastroparesis, diabetic diarrhoea, impotence, postural hypotension, nephropathy, renal failure, nephrotic syndrome, renal transplant, dialysis, microalbuminuria, renal insufficiency, retinopathy or photocoagulation. Microvascular complications were grouped because they do not occur independently, and numbers of patients with individual complications were too small to allow sufficient power to determine changes in quality of life. Because asymptomatic conditions may be less likely to affect quality of life, we also defined a subset of patients more likely to have symptomatic microvascular complications by excluding any patients identified solely by one or more potentially asymptomatic diagnoses (nephropathy, microalbuminuria, renal insufficiency, retinopathy, photocoagulation). Individual medications were identified based on chart review, whereas the total number of medications taken by an individual patient was derived from patient survey response. The mean number of prescribed medica-

tions was 5.5, with a range from 0–20. To minimise analytic effects of the skewed distribution we categorised the number of medications into ordinal categories (0–3, 4–6, 7–10 and >10 medications). BMI data were missing for 218 patients (24%); for these, BMI was imputed (as the mean of known BMI values) to avoid losing quality of life data from this subset. Seven hundred and seventy-two patients reported duration of diabetes; we imputed duration of diabetes by deriving the relationship of age, complications and insulin use to diabetes duration in those 772 patients, and using that formula to predict diabetes duration in the remainder. The mean duration (±SD) was 9.6±7.6 years before imputation and 9.6±7.3 years after imputation.

Survey instruments

Assessment of health utility Health-related quality of life is quantified by assigning a numeric utility between 0 and 1 to a given health state, where 0 represents the state of death and 1 represents optimal health. The Health Utilities Index Mark III (HUI-3) is a multi-attribute utility model developed to derive community perspective health utilities (i.e. the general population's assessment of the health-related quality of life associated with a particular disease or condition) from patient responses to a questionnaire. The HUI-3 is simpler to administer and complete than other utility assessment methods, such as the standard gamble or time trade-off [16–18]. In the HUI-3, patients answer 15 questions about their level of function to define eight health domains (vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain), each with five or six levels of impairment, ranging from none to severe impairment [13, 15]. Survey responses are coded into one level on each domain, corresponding to the preferences (i.e. utilities) of a reference population [14]. These values are then combined by multiplying weighted domain levels (W) according to the formula determined by validation of the HUI-3 model ($1.371\times W1\times W2\times W3\times W4\times W5\times W6\times W7\times W8)-0.371$) to derive a composite overall health utility score anchored between 0 and 1 [19], with negative values representing health states worse than death. Scores in individual domains determine the overall utility score, and inspection of the individual domains suggests those that make the greatest contribution to low utility. According to the validation of the HUI-3, increments of 0.03 unit of health utility represent a clinically significant difference in quality of life [20]; consequently, results have been rounded to the second decimal place in this analysis. The population distribution of health utility is typically left-skewed, with a small number of patients with very low quality of life. In addition, the HUI may be overweighted to the low end of the scale relative to the standard gamble method of determining health utility [17, 21]. Taking advantage of internal redundancy within the HUI-3 questionnaire, we used a validated method of inspection and logical deduction to impute HUI-3 data for 54 participants missing complete data on the HUI-3 [22]. The mean utility (±SD) was 0.61±0.32 before and 0.60±0.32 after imputation.

Assessment of depression We used the validated 10-item Harvard Department of Psychiatry/National Depression Screening Day Scale (HANDS) to assess depression. This scale is scored from 0–3 per item; a score of nine or greater has a 95% sensitivity for clinically significant levels of depression diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), and confirmed by structured clinical interview diagnosis [23]. While the questions on the HUI and the HANDS are different, the HUI queries pain and emotion, which are related to the symptoms of depression queried by the HANDS. To check for criterion contamination (i.e. overlap between the HANDS and HUI questionnaires on constructs related to mood), we repeated analyses of effects of depression using diagnosed depression derived from a problem list diagnosis or prescription of antidepressant medication.

Statistical analysis

We reported descriptive statistics with standard deviations. Because the estimates of health utility were left-skewed and because the Health Utilities Index tends to underestimate utility values derived from standard gambles, the median, rather than mean, values of utility associated with individual demographic and clinical covariates are reported. Wilcoxon-derived p values are reported for the difference in health utility between groups with and without the specified demographic and clinical covariates. The non-parametric Wilcoxon p values did not differ from p values derived by t tests, which assume underlying normality.

Despite the mild skew of health utilities, ordinary least squares and other multiple regression techniques that assume normality are robust to this problem and have been used in multiple publications using the HUI [24, 25]. We therefore used general linear modelling to determine the least-squares means of multi-category variables and in multivariable models. We forced age and sex into multivariable general linear models to determine the independent correlates of health-related quality of life using variables that were significant in univariate analysis. Sociodemographic variables that were not significant in multivariable models were dropped from the models. The normal probability plots of the residuals of the multivariable models revealed that the residuals were normally distributed. Because depression was such a strong predictor of quality of life, first-order interactions between depression and sex, heart failure, microvascular complications, low educational level, and the presence of severe obesity were tested. We used a significance level of 0.05 for exclusion of variables from the model. Analyses were conducted using the SAS statistical system (SAS Institute, Cary, NC, USA).

Results

Overall, patient health-related quality of life was moderately high. The mean utility of the group was 0.60±0.32, with a median of 0.70 and an interquartile range of 0.39–0.88. The 90th percentile was 0.97, but the 10th percentile was 0.07. The distributions of the individual HUI-3 domains (Table 1a) revealed that emotion, pain and impaired vision were the predominant drivers of low overall health utility in these patients. Overall health utility (derived from community measures) correlated well with patient self-reported health (Table 1b).

The demographic and clinical characteristics of the study population, along with health-related quality of life, measured in utility, are shown in Table 2. In univariate analysis, quality of life differed by sex, race, level of education and employment status, but not by clinic site. For instance, the median estimate of quality of life among women was 0.63, and among men, 0.75 ($p<0.0001$). The patients were elderly, and most were overweight or obese. One-third had CHD, one-half had microvascular complications, and one-fifth had depression. Patients with depression had the lowest health-related quality of life (median utility 0.28 vs 0.69 for those without depression, $p<0.0001$). The health-related quality of life was reduced in patients with CHD, stroke, microvascular complications, heart failure, chronic obstructive pulmonary disease (COPD) or depression, but not in those with hypertension, hyperlipidaemia, elevated blood pressure, current smoking or obesity, compared with patients without these conditions.

Table 1 Mean and median utilities according to HUI-3 domains and self-reported health status in 909 patients with type 2 diabetes

Health utilities index domain[a]			Domain utility	
			Mean	Median
Vision			0.91	0.95
Hearing			0.88	1.00
Speech			0.98	1.00
Ambulation			0.87	1.00
Dexterity			0.94	1.00
Emotion			0.88	0.91
Cognition			0.90	1.00
Pain			0.82	0.92
Self-reported health status			Overall utility	
	Number[b]	Percentage	Mean	Median
Excellent	116	22.0	0.85	0.92
Very good	268	29.9	0.75	0.79
Good	309	34.5	0.58	0.62
Fair	163	18.2	0.37	0.36
Poor	40	4.5	0.08	−0.04

[a]The overall health utility is a function of the component weighted levels of function on each of the domains according to the following formula determined by the initial validation of the HUI-3: $(1.371\times W1\times W2\times W3\times W4\times W5\times W6\times W7\times W8)-0.371$

[b]$n=896$ due to missing responses to the question on self-reported health status

Most patients were prescribed multiple medications, and about one-quarter were prescribed insulin with or without an oral hypoglycaemic. Increasing number of medications, insulin use and duration of diabetes were associated with decreased health utility in univariate analysis. This was an obese and elderly cohort (mean BMI was 31.3±6.7 kg/m^2). Metabolic and cardiac risk factor control was fair, with mean values of 7.45±1.46% for HbA_{1c}, 4.4±0.9 mmol/l (173±36.9 mg/dl) for total cholesterol, 1.2±0.3 mmol/l (44.5±13.4 mg/dl) for HDL and 2.5±0.8 mmol/l (94.7±29.7 mg/dl) for LDL; 58% of patients with blood pressure less than or equal to 130/80 mmHg. Utility was not correlated with level of glycaemic control or level of cholesterol ($p>0.3$).

The age- and sex-adjusted decrements in health-related quality of life associated with specific clinical variables and multivariable-adjusted median utilities are shown in Table 3. Table 3a shows the decrease in utility associated with each variable, adjusted only for age and sex. For example, microvascular complications alone were associated with a utility penalty of 0.12. After adjusting for the socioeconomic variables, multiple comorbidities and insulin use, shown in Table 3b, adjusted for all of the listed comorbidities and duration of diabetes, the penalty associated with comorbidities such as microvascular complications, heart failure, COPD and depression diminished to some degree, while CHD, stroke and insulin use were no longer independently associated with impairments in health-related quality of life. In the final multivariable model (Table 3c), microvascular complications, heart failure and number of medications were statistically and clinically significant correlates of decrement in overall health-related quality of life, but the presence of depression was the strongest correlate, decreasing utility by 0.37 when present. Model results were similar using depression identified by chart diagnosis rather than HANDS screen: the utility decrement associated with diagnosed depression was 0.14±0.02 ($p<0.0001$). Model results were also similar when microvascular complications that were less likely to be symptomatic were excluded from the analysis. After including number of medications in the model, CHD, COPD, stroke, insulin and duration of diabetes were no longer significant correlates of health-related quality of life, though the r^2 value (proportion of variance explained by the model) was not substantially improved. First-order interactions between depression and sex, heart failure, complications and educational level were not significant ($p>0.2$ for all).

Discussion

In this large, primary care clinic-based survey, we found that in the presence of specific comorbidities and complications, type 2 diabetes is associated with substantial decrements in health-related quality of life. Microvascular complications, heart failure, depression and a high number of medications were each strong independent correlates of decreased quality of life. Whereas a primary

Table 2 Median utilities of 909 primary care patients with type 2 diabetes according to demographic and clinical characteristics

	Number with specified characteristic	Percentage	Median utility for group with specified characteristic	*p* value[a]
Sample median	909		0.70	
Demographic characteristic				
Sex				
Female	444	49	0.63	
Male	465	51	0.75	<0.0001
Age, years (mean 66.3±12.5)				
<50	90	10	0.61	
50–59	181	20	0.62	
60–69	233	26	0.64	
70–79	274	30	0.60	
≥80	131	14	0.54	0.08
Race				
Non-Hispanic, white	744	83	0.69	
Non-white	153	17	0.75	0.1
Education				
Less than high school diploma	201	22	0.55	
High school diploma, its equivalent, or some time at college	496	55	0.70	
Four years of college or advanced degree	205	23	0.77	<0.0001
Employment				
Full-time	195	21	0.85	
Part-time	60	7	0.72	
Unemployed	118	13	0.42	
Retired	536	59	0.67	<0.0001
Marital status				
Married/living with partner	477	53	0.74	
Single	116	13	0.70	
Divorced/separated/widowed	306	34	0.64	<0.0001
Clinic site				
Hospital-based	550	61	0.70	
Community health centre	359	40	0.70	0.9
Clinical characteristic				
No complications[b]	217	24	0.84	<0.0001
CHD	316	35	0.58	<0.0001
Stroke	148	16	0.56	0.004
Peripheral vascular disease	130	14	0.58	0.001
Microvascular complications	441	49	0.61	<0.0001
Symptomatic microvascular complications	370	41	0.61	<0.0001
Hypertension	811	89	0.69	0.3
Heart failure	116	13	0.43	<0.0001
Hyperlipidaemia	684	75	0.70	0.5
COPD	156	17	0.56	<0.0001
Smoker	109	12	0.61	0.1
BMI, kg/m^2 (mean 31±7)				
Normal (<25)	150	17	0.64	
Overweight (25–29.9)	286	32	0.73	
Obese (≥30)	453	50	0.68	0.02
Depression[c]	156	13	0.28	<0.0001
Number of medications				
0–3	201	23	0.79	
4–6	322	37	0.75	

[a]Wilcoxon *p* value for difference in median utility between groups with and without the specified characteristic

[b]Patients without coronary artery disease, stroke, microvascular complications, heart failure, COPD or depression

[c]*n*=832 due to missing data from HANDS screening instrument

Table 2 (continued)

	Number with specified characteristic	Percentage	Median utility for group with specified characteristic	*p* value[a]
7–10	243	28	0.54	
>10	113	13	0.40	<0.0001
Hypoglycaemic medications				
Oral hypoglycaemic only	429	47	0.72	0.2
Insulin with or without oral hypoglycaemic	242	27	0.56	<0.0001
Metformin	174	19	0.65	0.05
Sulfonylurea	364	40	0.60	0.47
Duration of diabetes				
≤3 years	181	20	0.65	
4–6 years	191	21	0.66	
7–10 years	217	24	0.63	
≥11 years	320	35	0.52	<0.0001
Blood pressure≤130/80 mmHg	524	58	0.59	0.06

care patient with type 2 diabetes who lacked any of the variables specified in the model had a predicted overall health utility of 0.96±0.05, the presence of microvascular complications reduced predicted utility to 0.91, and if such a patient also had heart failure and depression, predicted utility dropped to 0.44. These estimates represent an improvement over prior estimates because of the setting and because of the degree of clinical detail, which allowed us to elucidate the determinants of quality of life.

The study was conducted in a usual care setting, had a very high response rate, and is one of the largest studies of health utility in primary care patients with type 2 diabetes in the US. This is also the first study to provide utility estimates adjusted for the presence of depression in addition to other demographic and clinical variables. While many studies have found that conditions such as hypertension, obesity and use of insulin [1, 9, 10] were correlated with decreased quality of life, we did not find these conditions to be significant after controlling for more symptomatic conditions and overall treatment intensity. Notably, other asymptomatic conditions, such as hyperlipidaemia, were not associated with decreased quality of life in this cohort. Poor glycaemic control, which is frequently symptomatic, was also not associated with decreased quality of life, consistent with recent findings in another population [26]. Symptomatic conditions such as heart failure [8] and macrovascular or microvascular complications [1, 8, 9, 27] of diabetes have consistently been shown to be associated with decreased health-related quality of life. Female gender [4, 9, 27] and indicators of low socioeconomic status [4, 27] have been identified as independent correlates of decreased health-related quality of life in other studies of patients with diabetes and in the general population [28]. The association of some of these conditions with decreased quality of life appears to be explained, in part, by the presence of complications and concurrent depression.

In the multivariable models, the number of medications was a strong correlate of decreased utility. As in other studies of health-related quality of life, people who take a large number of medications rate their health as poorer than those who do not [18]. This correlation may be due to reverse causality: sicker patients are prescribed more medications, but taking a large number of medications may decrease quality of life. A negative impact of medication on quality of life might be mediated by the effect of medication-taking behaviour, expense or side effects. The number of medications taken represents treatment intensity and correlates with severity of comorbid disease. After including this variable in model 3c (Table 3), some comorbidities and duration of diabetes were no longer significant, but the more symptomatic comorbidities remained significant correlates of health-related quality of life; the overall explanatory power of the model was not substantially improved. This suggests that while the number of medications is conceptually related to severity of comorbid disease, it is not completely collinear. We suspect that the strong correlation between number of medications and quality of life is partially related to severity of disease, but decreased quality of life may also be related to the burden of the medication regimen itself.

Insulin was not a statistically significant correlate of decreased quality of life in multivariable regression (p=0.7 after controlling for duration of diabetes), but was signif-

Table 3 Relationship of clinical variables to health-related quality of life in primary care patients with type 2 diabetes

	Model A: age- and sex-adjusted associations of individual variables with HRQOL			Model B: multiple regression with HRQOL, not including number of medications. n=827; R^2=0.36			Model C: multiple regression with HRQOL, including number of medications. n=808; R^2=0.39		
	Parameter estimate	Standard error	p value	Parameter estimate	Standard error	p value	Parameter estimate	Standard error	p value
Intercept	–			0.93	0.06		0.96	0.05	
Age	−0.002	0.0008	0.02	−0.002	0.001	0.05	−0.002	0.001	0.03
Female sex	−0.09	0.02	<0.0001	−0.05	0.02	0.01	−0.03	0.02	0.1
Education <12th grade[a]	−0.16	0.03	<0.0001	−0.08	0.03	0.003	−0.09	0.03	0.0007
Microvascular complications	−0.12	0.02	<0.0001	−0.06	0.02	0.002	−0.05	0.02	0.02
Heart failure	−0.24	0.03	<0.0001	−0.13	0.03	<0.0001	−0.10	0.03	0.001
Depression[b]	−0.42	0.02	<0.0001	−0.38	0.03	<0.0001	−0.37	0.02	<0.0001
CHD	−0.11	0.02	<0.0001	−0.04	0.02	0.08	−0.01	0.02	0.6
Stroke	−0.07	0.03	0.01	−0.02	0.02	0.4	−0.02	0.02	0.5
COPD	−0.11	0.03	<0.0001	−0.05	0.02	0.03	−0.03	0.06	0.3
Insulin	−0.10	0.03	<0.0001	−0.009	0.02	0.7	−0.006	0.02	0.8
7–10 medications	−0.17	0.03	<0.0001[c]	–			−0.10	0.02	0.0003
>10 medications	−0.29	0.04	<0.0001[c]	–			−0.19	0.03	<0.0001
Diabetes duration >10 years	−0.12	0.03	<0.0001[d]	−0.06	0.03	0.03	−0.04	0.03	0.1

Interpretation of age- and sex-adjusted models: the parameter represents the utility penalty incurred by an age- and sex-standardised patient with the specified clinical variable. For instance, the model estimates that heart failure in a patient with type 2 diabetes would decrease utility by 0.24

Interpretation of the multivariable models: the intercept represents the overall health utility of an individual (male) of the mean age of the population (66 years) without any of the conditions specified in the model. The parameter estimates represent the utility penalty incurred by an individual controlling for all other covariates in the model. For each condition, subtract the parameter estimate of the significant variable to determine health utility. For example, in model C, a patient with type 2 diabetes and heart failure alone would have a utility of 0.86; a patient with type 2 diabetes, heart failure, and depression would have a utility of 0.52

HRQOL Health-related quality of life

[a] n=902; [b] n=832; [c] n=879, compared with 0–3 medications; [d] n=909, compared with <3 years

icant in univariate analysis, and many studies have found that insulin use in association with complications is associated with decreased quality of life [9, 10]. The purported relationship of health-related quality of life to insulin use presents another dilemma of reverse causality. This has led some authors to suggest that delaying insulin therapy will improve quality of life [9], but these studies have not controlled for measures of severity of disease that are correlated with insulin use. In another large US population study in which multiple comorbidities were controlled for, insulin was not a significant predictor of decreased quality of life [8]. In keeping with the latter study and the UKPDS [1], we found that symptomatic conditions such as heart failure and microvascular complications were far more significant correlates of lower quality of life than unsymptomatic conditions. We conclude from this analysis that insulin has served as a proxy for sicker patients in studies that have not been able to control for these variables.

Depression is a well-recognised determinant of quality of life in diabetes [4, 10]. However, most prior estimates of health utility in type 2 diabetes have failed to account for depression, thus producing biased estimates of health utility. Patients with depression rate their quality of life lower than those with other chronic diseases [29]. Our models show that depression decreases health utility by 0.37–0.38, an estimate that is consistent with prior studies in other disease models [30, 31]. After including depression in our models, parameter estimates of the degree of disutility associated with heart failure and complications decreased, producing a less biased estimate of the independent effect of these comorbidities. Given that patients with depression are prone to rate their overall health as very poor, and that the prevalence of depression in patients with diabetes is high and correlated with comorbidities [32], our results highlight the importance of accounting for depression in any analysis of health-related quality of life in diabetes.

Estimates of mean utility in diabetes have ranged widely, from 0.69±0.39 in a study of 372 rural patients with type 2 diabetes in Alberta, Canada [12], to a mean of 0.89–0.90 in population surveys in Ontario [11, 33]. Our sample mean of 0.60±0.32 and median of 0.70 is in line with, but slightly lower than, results from other studies and represents a large

US primary care patient population. It may be on the low end of estimates due to the severity of illness in this population or due to the formula used to calculate the HUI-3, which is overweighted on the low end of the scale. The relationship between the absolute numbers and patient status can be gauged by inspecting the mean utilities associated with self-reported health status (Table 1b).

These estimates are comparable to those found in other patients with chronic illness surveyed with the HUI-3. For example, 103 British patients undergoing elective arthroplasty had a mean utility of 0.63 [21], 87 patients with claudication pre-revascularisation had a mean utility of 0.66 [34], and 679 patients with Alzheimer's disease and their caregivers had mean utilities of 0.22 and 0.87, respectively [35]. Our results are lower than those found in a recent population survey of 4,048 US adults (mean age 45), who had a mean utility of 0.81±0.01 on the HUI-3 [28].

In these studies and in ours, global utilities capture the impact of many of the evanescent symptoms associated with a given disease which can be hard to measure. For example, while symptoms of hyperglycaemia and hypoglycaemia may be transiently symptomatic and thus hard to measure as a specific comorbidity, the global utility can capture the sense of diminished well-being that may accompany such symptoms. It is also important to recognise that numeric utility estimates will vary according to population; consequently, sensitivity analysis should be employed when using utility estimates in cost-effectiveness models.

There are several limitations of our analysis. The lack of racial and ethnic heterogeneity restricted our ability to analyse these groups individually. Moreover, ethnic minorities and non-English speakers were less likely to participate in the study. Non-participants also had worse glycaemic and blood pressure control, but were more likely to be on a blood pressure medication or aspirin; the prevalence of depression and antidepressants were similar. Non-participants are likely to represent a sicker group who were nonetheless being treated for comorbidities. It is difficult to anticipate how these results would apply to that cohort, but it is likely that health utility would be lower in sicker patients who either could not participate or whose primary care doctors excluded them from the study, so the present results may underestimate the true impact of diabetes on quality of life. HUI-3 utilities represent community perspectives and may differ from those elicited directly from patients (for instance, using a standard gamble assessment), who may rate their quality of life higher than a community observer (with the exception of subjects with depression). While this should not affect the correlates of impaired quality of life, it is likely to affect the absolute utility values. Community-perspective utilities are useful for cost-effectiveness analysis and policy decisions, but patient utilities may be more useful for clinical decision-making [16]. In addition, an instrument that uses 15 questions to measure eight domains will necessarily fail to capture many disease-specific symptoms; while a generic instrument has the advantage of generalisability and comparability across studies, it will certainly miss many disease-specific subtleties.

In summary, in addition to providing more precise estimates of utilities that may be used in cost-effectiveness analysis, this study of responses to the HUI-3 questionnaire by 909 primary care patients with type 2 diabetes revealed important correlates of health-related quality of life. This is the first study to find that a patient with type 2 diabetes has minimal impairment in health-related quality of life in the absence of socioeconomic hardships, disease complications, or depression. Symptomatic conditions such as heart failure, microvascular complications, and treatment intensity (which may be a proxy for severity of disease) correlated with impaired quality of life. Based on these results, treating depression and preventing symptomatic complications have the greatest potential to improve health-related quality of life in patients with type 2 diabetes.

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Duality of interest We declare that we have no conflict of interest.

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