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Glycemia and the quality of well-being in patients with diabetes

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Abstract

Objectives: To investigate the cross-sectional relationships among self-reported frequencies of symptomatic hyperglycemia and hypoglycemia, HbA1c, and symptoms in the Quality of Well-Being Self-Administered (QWB-SA), and to examine the associations among these measures of glycemia and health-utility scores. *Methods*: The study group included 1522 patients with diabetes who attended University of Michigan Health System clinics. Published studies were reviewed to identify symptoms in the QWB-SA that might be associated with measures of glycemia. Linear-regression analyses were performed to evaluate the strength of the associations among the frequency of self-reported measures of glycemia, QWB-SA symptoms, and QWB-SA-derived health-utility scores. *Results*: Frequency of hyperglycemic symptoms was associated with 3% of the variance in the QWB-SA-derived health-utility score in type-1 diabetes and with 5% of the variance in type-2 diabetes. Frequency of hypoglycemic symptoms was not associated with the QWB-SA-derived health-utility score in type-1 diabetes but was associated with 1% of the variance in type-2 diabetes. HbA1c levels were not significantly associated with QWB-SA-derived health-utility scores. After controlling for age, gender, and complications, frequency of hyperglycemic symptoms was significantly associated with QWB-SA-derived health-utility scores in type-1 and type-2 diabetes. *Conclusions*: Reported frequency of hyperglycemic symptoms is associated with symptoms included in the QWB-SA and with QWB-SA-derived health-utility scores. The QWB-SA may be an appropriate measure to assess the health burden of hyperglycemia.

Key words: Clinical economics, Cost-effectiveness, Diabetes mellitus, Health utilities, Hemoglobin A1c, Hyperglycemia, Hypoglycemia, Quality-adjusted life-years

Introduction

In recent years, the relationship between glycemic control and quality of life (QoL) has been studied in patients with diabetes by applying disease-specific and generic QoL instruments. Studies that used disease-specific instruments have reported associations between glycemic control and QoL [1, 2] as have some studies that used generic instruments [3, 4]. To date, however, only one study has employed multiattribute utility models or assessed the relationship between glycemic control and health-utility scores [5]. Since the Self-Administered Quality of Well-Being questionnaire (QWB-SA) contains questions about symptoms that potentially reflect changes in glycemia, we used the QWB-SA to explore the relationship between measures of glycemia, assessed as self-reported frequencies of symptomatic hyperglycemia and hypoglycemia, and HbA1c, and health-utility scores.

Previously, we have shown that major diabetes complications are associated with lower health-utility scores [6]. Our current study involved four questions: first, which symptoms in the QWB-SA are most strongly associated with measures of

glycemia (self-reported frequencies of symptomatic hyperglycemia and hypoglycemia, and HbA1c) in patients with diabetes? Second, is the QWB-SA-derived health-utility score associated with measures of glycemia in diabetic patients? Third, to what extent does the QWB-SA-derived health-utility score in diabetic patients vary with age, gender and complications. Fourth, is the QWB-SA-derived health-utility score associated with measures of glycemia in diabetic patients when age, gender and complications are also considered?

Methods

The QWB-SA was developed in 1996 as a self-administered, scanable version of the Quality of Wellbeing Index (QWB), a previously validated measure of preference-based general health status [7, 8] that has been used in populations with a variety of diseases [1, 9, 11–18]. The QWB-SA assesses symptoms (acute and chronic) and functioning (self-care, mobility, physical activity, and social activity) to provide a health-utility score as a summary measure of QoL [9, 10]. The worst symptom for each of the four domains for each day (yesterday, two days ago, three days ago) enters into the scoring system. The symptoms and reported levels of functioning are weighted by the preferences of an independent sample of judges. Using this system, it is possible to place the general health status of any individual on the continuum between death and optimal functioning. The QWB-SA has been shown to be highly correlated with and to retain the psychometric properties of the QWB [12].

The protocol was reviewed and approved by the University of Michigan Institutional Review Board and all patients provided written informed consent. We estimated that to detect a clinically meaningful difference of 0.025 in the QWB-derived health-utility score [19] with 90% power and $\alpha = 0.05$, we would need to study approximately 600 patients with type-1 diabetes and 600 patients with type-2 diabetes. The study group included 1522 patients: 634 with type-1 diabetes and 888 with type-2 diabetes who attended endocrinology, diabetes, and ophthalmology clinics at the University of Michigan Health System between June 29, 1998 and March 15, 2001 and had HbA1c measurements on the day of the visit. All patients were $\geqslant 18$ years of age, able to give informed consent, and able to either self-administer the questionnaires or, if visually impaired, to respond to a research assistant reading the questionnaires.

The questionnaires used were the Diabetes Staging Questionnaire (DSQ) and the QWB-SA. The DSQ was adapted from two instruments available from the Michigan Diabetes Research and Training Center, the Diabetes Care Profile (DCP) and the Diabetes Medical History (DMH). The DCP is a validated instrument [20, 21] which includes questions about demographics, age at onset of diabetes, frequency of hyperglycemic and hypoglycemic symptoms, and limits on performing activities of daily living due to diabetes. Frequency of symptomatic hyperglycemia was self-reported as the number of times in the past month the patient experienced high blood sugar with symptoms such as thirst, dry mouth and skin, increased sugar in the urine, less appetite, nausea or fatigue. Frequency of symptomatic hypoglycemia was self-reported as the number of times in the past month the patient experienced a low blood-sugar reaction with symptoms such as sweating, weakness, anxiety, trembling, hunger or headache. The DCP subscale on control problems, which included questions on the frequency of hyperglycemic and hypoglycemic symptoms, is reliable (Cronbach's $\alpha = 0.86$) and correlated with glycosylated hemoglobin level ($r = 0.21$, $p < 0.01$) [21]. The subscale on control problems is also significantly associated with the Centers for Epidemiologic Studies depression scale ($r = 0.34$, $p \leqslant 0.01$) [21]. Type-1 diabetes was defined as diabetes with onset before 30 years of age with current insulin treatment. Type-2 diabetes was defined as diabetes with onset at 30 years of age or older with diet, oral agent or insulin treatment, or diabetes with onset before 30 years of age without current insulin treatment. HbA1c was measured using capillary blood and a Bayer DCA 2000 analyzer (Bayer, Elkhart, Indiana). Quality control procedures included daily assays on standard normal and abnormal control samples containing a stable lyophilized hemolysate of human blood. Patient samples were not run until acceptable quality control results were achieved. Coefficients of variation were $< 5\%$ (STAT Technologies, Golden Valley, Minnesota).

Correlation of DCA readings and high performance liquid chromotography (HPLC) measures of HbA1c is 0.99.

Descriptive statistics were obtained for all variables using medians and minimums and maximums for continuous variables, and frequencies and proportions for categorical variables. Statistical significance of differences between groups was assessed with the Wilcoxon rank sum test for continuous variables and the Cochran–Mantel–Haenszel χ^2 test for categorical variables (Table 1).

To identify which symptoms in the QWB-SA were most strongly associated with measures of glycemia, we reviewed published studies relating symptoms to glycemic control. Grootenhuis et al. [22] developed a Diabetes Symptom Checklist for type-2 Diabetes (DSC-Type 2) that included symptoms related to hyperglycemia and hypoglycemia. Testa and Simonson also provided a list of symptoms affected by improved glycemic control [23]. Based on these studies, we selected 14 symptoms (8 hyperglycemic, 9 hypoglycemic, and 3 shared symptoms) from the QWB-SA questionnaire. The responses to these 14 symptom questions from the QWB-SA were compared with the self-reported frequency of hyperglycemia and hypoglycemia and with HbA1c values. Each measure of glycemia was divided into five groups. For the frequency of hyperglycemic and hypoglycemic symptoms reported within the past month, categories were 0 times, 1–4 times, 5–8 times, 9–12 times, and over 12 times. HbA1c values were distributed into 5 equal groups that differed by type of diabetes, varying from less than 7.0% to more than 9.6%.

The relationship between individual QWB-SA symptoms and measures of glycemia (reported frequency of hyperglycemia and hypoglycemia, and measured HbA1c categories) were assessed with one-way analysis of variance using general linear models (Table 2). Relationships among health-utility scores and measures of glycemia were assessed with one-way analysis of variance using general linear models (Figure 1) and simple linear regression analysis (Table 3, panel A). To further evaluate the strength of the associations between the QWB-SA-derived utility scores and the predictor variables, multiple linear regression analysis was performed (Table 3, panel B). For both types of diabetes, linear regression models

Table 1. Characteristics and comparison of study group by type of diabetes

Characteristics	Type-1 diabetes	Type-2 diabetes
Total number	634	888
Age, median (min.–max.), years	33 (18–78)	56 (18–88)*
Female gender (%)	54	48**
White (%)	86	74***
BMI, median (min.–max.), kg/m^2	25 (15–70)	31 (16–66)
Duration of diabetes, median (min.–max.), years	19 (0–77)	9 (0–61)*
Diabetes treatment (%), insulin/OHA/diet	100/0/0	54/39/7*
>4 Hyperglycemic episodes per month (%)	22	25
>4 Hypoglycemic episodes per month (%)	13	8***
HbA1c, median (min.–max.)	8.3 (4.7–14.1)	8.0 (4.1–14.0)**
Retinopathy (%)	38	22*
Nephropathy (%)	26	19*
Renal transplant (%)	4	1*
Neuropathy (%)	30	45*
Amputation (%)	2	2
Hypertension (%)	33	59*
Hypercholesterolemia (%)	29	60*
Smoker (%)	24	13*
Stroke (%)	2	3
Limitations due to heart disease (%)	9	27*
Peripheral vascular disease (%)	11	16***

BMI = body mass index [weight (kg)/height (m^2)], OHA = oral hypoglycemic agents; HbA1c = glycosylated hemoglobin.
* $p < 0.001$, ** $p < 0.05$, *** $p < 0.01$, statistically significance difference type-1 vs. type-2 diabetes patients.

Table 2. Relationship between QWB-SA symptoms and measures of glycemia

	Type-1 diabetes		Type-2 diabetes	
	R^2	p-Value*	R^2	p-Value*
Frequency of hyperglycemic symptoms				
Current general fatigue, tiredness, weakness	0.052	0.0001	0.051	0.0001
Loss of bladder control, frequent night-time urination, difficulty with urination	0.036	0.0001	0.051	0.0001
Loss of appetite, over-eating	0.030	0.005	0.035	0.0001
Current unwanted weight gain or loss	0.025	0.01	0.011	0.10
Headache	0.015	0.19	0.032	0.0009
Genital pain, itching, burning, abnormal discharge, pelvic cramping, abnormal bleeding	0.009	0.26	0.039	0.002
Upset stomach, abdominal pain, nausea, heartburn or vomiting	0.009	0.33	0.029	0.002
Frequency of hypoglycemic symptoms				
Headache	0.023	0.005	0.020	0.002
Fever, chills or sweats	0.013	0.06	0.031	0.02
Spells of feeling nervous or shaky	0.009	0.18	0.064	0.0001
Current general fatigue, tiredness, weakness	0.004	0.41	0.013	0.03
Excessive anxiety or worry	0.002	0.86	0.019	0.003
HbA1c level				
Genital pain, itching, burning, abnormal discharge/bleeding, pelvic cramping	0.023	0.0008	0.002	0.78
Loss of bladder control, frequent night-time urination, difficulty with urination	0.021	0.02	0.014	0.02
Fever, chills or sweats	0.017	0.03	0.006	0.30

* The coefficients of determinations (R^2) and p-values were generated from the analysis of variance using general linear models and show the degree of general association between the measures of glycemia and QWB-SA symptoms. The measures of glycemia were modeled as categorical variables.

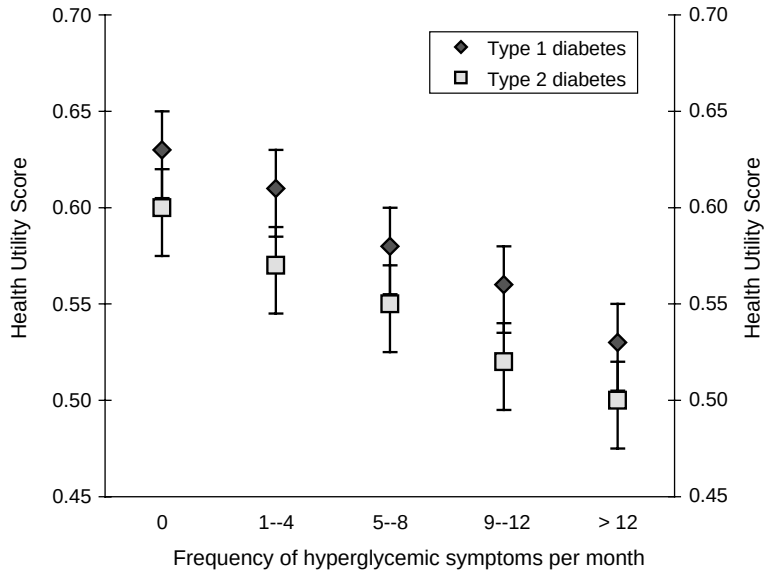

Figure 1. Frequency of self-reported hyperglycemic symptoms and mean (95% CIs) total QWB-SA-derived health utility scores in type-1 and type-2 diabetic patients.

Table 3. Overall QWB-SA score, regression coefficient, and correlation coefficient by type of diabetes and (A) measures of glycemia, (B) sex and complications controlling for age, (C) frequency of hyperglycemic symptoms, sex, and complications controlling for age

Mean QWB-SA score	Type-1 diabetes (0.63)		Type-2 diabetes (0.60)	
	Regression coefficient (SE)	Correlation coefficient	Regression coefficient (SE)	Correlation coefficient
Panel A				
Frequency of hyperglycemic symptoms by group (0, 1–4, 5–8, 9–12, 12+)	−0.025 (0.005)*	−0.184*	−0.026 (0.004)*	0.220*
Frequency of hypoglycemic symptoms by group (0, 1–4, 5–8, 9+)	−0.010 (0.006)	−0.060	−0.019 (0.006)*	0.001*
HbA1c level by group	−0.006 (0.004)	−0.066	−0.004 (0.003)	−0.042
Panel B				
Female gender	−0.044 (0.012)*	−0.148*	−0.027 (0.001)**	−0.098**
Neuropathy	−0.074 (0.013)*	−0.207*	−0.072 (0.010)*	−0.240*
Amputation	–	–	−0.114 (0.034)*	−0.112*
Blindness	−0.128 (0.016)*	−0.302*	−0.109 (0.012)*	−0.295*
Hypertension	−0.060 (0.014)*	−0.164*	−0.022 (0.010)***	−0.073***
Stroke	−0.115 (0.045)	−0.097*	−0.087 (0.028)*	−0.102**
Peripheral vascular disease	−0.080 (0.019)*	−0.163*	−0.112 (0.014)*	−0.271*
Limitations due to heart disease	–	−0.060	−0.027 (0.011)***	−0.074***
Panel C				
Frequency of hyperglycemic symptoms by group (0, 1–4, 5–8, 9–12, 12+)	−0.020 (0.005)*	−0.177*	−0.018 (0.003)*	−0.181*
Female gender	−0.040 (0.012)*	−0.136*	−0.031 (0.010)*	−0.110*
Neuropathy	−0.068 (0.014)*	−0.196*	−0.077 (0.010)*	−0.256*
Amputation	–	–	−0.131 (0.034)*	−0.135*
Blindness	−0.132 (0.016)*	−0.312*	−0.109 (0.012)*	−0.306*
Hypertension	−0.056 (0.014)*	−0.165*	−0.014 (0.010)	−0.486
Stroke	−0.121 (0.045)**	−0.108*	−0.082 (0.027)**	−0.107**
Peripheral vascular disease	−0.080 (0.020)*	−0.161*	−0.101 (0.014)*	−0.246*
Limitations due to heart disease	–	–	−0.026 (0.012)***	−0.079***

SE = Standard error of the coefficient; – = not computed.
*$p < 0.001$, **$p < 0.01$, ***$p < 0.05$.

were developed and fitted to the data using the forward stepwise selection procedure with the QWB-SA-derived utility scores as the dependent variable and age, sex, duration of diabetes and the complications of diabetes as independent covariates. Once the influence of age, gender, duration of diabetes, and diabetic complications was determined, the influence of frequency of hyperglycemic and hypoglycemic symptoms and HbA1c on the QWB-SA-derived utility score was evaluated by forcing individual measures of glycemia into these stepwise-selected linear regression models (Table 3, panel C).

Because the QWB-SA-derived health-utility scores varied from 0 to 1.0, and were not normally distributed, we empirically transformed them using arcsin ($\sin^{-1}$) in the linear analysis (both Pearson correlations and linear regressions) presented in Table 3 [24, 25]. Interaction terms between independent variables were also considered. None of the interaction effects were statistically significant. The coefficient of determination (R^2) was used as a quantitative measure of how well the independent variables explain the outcome. For the multiple linear regression models, adjusted R^2 was used to control for the number of independent variables in the equation. Pearson correlation analysis and partial correlation analysis were performed to assess the strength of the relationship between the outcome variable (QWB-SA-derived utility score) and the independent variables in the linear regression models. A p-value < 0.05 was

defined as statistically significant. All statistical analyses were performed using SAS software version 6.12 (SAS Institute, Cary, North Carolina).

Results

Table 1 describes the clinical and demographic characteristics of the patients by type of diabetes. In general, patients with type-1 diabetes were more likely to be younger, female, white, and to have longer duration of diabetes than patients with type-2 diabetes. More than one-half of patients with type-2 diabetes were treated with insulin. Frequency of more than four hyperglycemic episodes in the past month did not differ among patients with type-1 and type-2 diabetes. However, 13% of type-1 diabetic patients experienced more than four hypoglycemic episodes in the past month compared to 8% of patients with type-2 diabetes. The median HbA1c was significantly higher for type-1 diabetic patients. Retinopathy, laser treatment, nephropathy, renal transplant, and smoking were more common in patients with type-1 diabetes. Patients with type-2 diabetes were more likely to have neuropathy, hypertension, hypercholesterolemia, and limitations due to heart disease and peripheral vascular disease.

Table 2 presents the relationship among QWB-SA symptoms and the frequency of self-reported hyperglycemic and hypoglycemic symptoms over the past month, and HbA1c. In both type-1 and -2 diabetic patients, QWB-SA symptoms related to lack of energy, headache, appetite and abnormal urination were positively associated with the self-reported frequency of hyperglycemia. Headache was positively associated with self-reported frequency of hypoglycemia. Abnormal urination was positively associated with HbA1c. Among patients with type-1 diabetes, weight changes were positively associated with the self-reported frequency of hyperglycemia, and sweating and genital symptoms were positively associated with HbA1c. Among patients with type-2 diabetes, upper gastrointestinal discomfort and genital problems were positively associated with the self-reported frequency of hyperglycemia. Lack of energy, anxiety, nervousness and sweating were positively associated with the self-reported frequency of hypoglycemia. In patients with type-2 diabetes, symptoms were for the most part associated with measures of glycemia *per se* and not with specific diabetes treatments (data not shown).

Figure 1 presents the frequency of self-reported hyperglycemic symptoms per month and mean total QWB-SA-derived health-utility scores by type of diabetes. Mean (95% CI) QWB-SA-derived health-utility scores for type-1 and type-2 diabetes patients with no hyperglycemic symptoms were 0.63 (0.61–0.65) and 0.60 (0.57–0.63), with 1–4 hyperglycemic symptoms were 0.61 (0.58–0.63) and 0.57 (0.55–0.59), with 5–8 hyperglycemic symptoms were 0.58 (0.56–0.60) and 0.55 (0.52–0.58), with 9–12 hyperglycemic symptoms were 0.56 (0.54–0.57) and 0.52 (0.49–0.55), and with >12 hyperglycemic symptoms were 0.53 (0.50–0.55) and 0.50 (0.47–0.53), respectively. In both type-1 and type-2 diabetic, patients with more frequent hyperglycemic symptoms had lower health-utility scores ($p = 0.003$ and $p = 0.0001$ respectively). Hyperglycemic symptoms were associated with 3% of the variance in the utility score in type-1 diabetic patients ($R^2 = 0.03$, $p = 0.0001$), and with 5% of the variance in type-2 diabetic patients ($R^2 = 0.05$, $p = 0.0001$) (Table 3, panel A). Hyperglycemic symptoms were negatively correlated with QWB-SA-derived utility scores in type-1 diabetic patients (correlation $= -0.184$, $p = 0.0001$) and type-2 diabetic patients (correlation $= -0.220$, $p = 0.0001$). Compared to patients with no episodes of hyperglycemic symptoms, frequency of hyperglycemic symptoms was associated with a reduction in health-utility score of 0.025, 0.050, 0.075, and 0.10 in type-1 diabetic patients and 0.026, 0.052, 0.078, and 0.104 in type-2 diabetes patients with 1–4, 5–8, 9–12, and 12+ episodes of hyperglycemic symptoms over the past month.

Frequency of self-reported hypoglycemic symptoms was not significantly related to the QWB-SA-derived utility score in type-1 diabetic patients ($p = 0.66$) but was inversely related to the total QWB-SA-derived utility score in type-2 diabetic patients ($p = 0.004$). Hypoglycemic symptoms were associated with 0.4% of the variance in the QWB-SA derived utility score in type-1 diabetic patients ($R^2 = 0.004$, $p = 0.13$), and with 1% of the variance in type-2 diabetic patients ($R^2 = 0.01$,

$p = 0.001$). Hypoglycemic symptoms were not significantly correlated with QWB-SA-derived utility scores in type-1 diabetic patients (correlation $= -0.060$, $p = 0.13$) and only weakly negatively correlated with the utility score in type-2 diabetic patients (correlation $= -0.113$, $p = 0.001$). Compared to patients with no episodes of hypoglycemic symptoms, frequency of hypoglycemic symptoms was associated with a reduction in health-utility score of 0.019, 0.038, 0.057, and 0.076 in type-2 diabetic patients with 1–4, 5–8, 9–12, and 12+ episodes of hypoglycemic symptoms over the past month.

HbA1c was not significantly associated with the QWB-SA-derived utility score in type-1 or type-2 diabetic patients.

Gender differences and presence vs. absence of complications were responsible for 34% of the variance in the utility score in the patients with type-1 diabetes (adjusted $R^2 = 0.34$, $p = 0.0001$) and 32% of the variance in type-2 diabetic patients (adjusted $R^2 = 0.32$, $p = 0.0001$) (Table 3, panel B). When we forced measures of glycemia into the multivariable models after including gender and complications, frequency of hyperglycemic symptoms was negatively associated with the QWB-SA-derived utility score and was responsible for 3% of the variance in the utility score in patients with both type-1 and type-2 diabetes (partial $R^2 = 0.03$, $p = 0.0001$) (Table 3, panel C). Frequency of hyperglycemic symptoms was negatively correlated with QWB-SA-derived utility score in type-1 diabetic patients (partial correlation $= -0.177$, $p = 0.0001$) and type-2 diabetic patients (partial correlation $= -0.181$, $p = 0.0001$). Compared to patients with no episodes of hyperglycemic symptoms, frequency of hyperglycemic symptoms was associated with a reduction in health-utility score of 0.020, 0.040, 0.060, and 0.080 in type-1 diabetic patients and 0.018, 0.036, 0.054, and 0.072 in type-2 diabetes patients with 1–4, 5–8, 9–12, and 12+ episodes of hyperglycemic symptoms over the past month. Neither frequency of hypoglycemic symptoms nor HbA1c level was significantly associated with the health-utility score. (For type-1 diabetic patients, hypoglycemia, partial $R^2 = -0.04$, $p = 0.37$; HbA1c, partial $R^2 = -0.05$, $p = 0.25$; for type-2 diabetic patients, hypoglycemia, partial $R^2 = -0.05$, $p = 0.14$; HbA1c, partial $R^2 = -0.02$, $p = 0.55$.)

Discussion

QoL may be assessed using disease-specific and generic instruments. Disease-specific instruments focus on symptoms, function, and disability specific to particular diseases. Their disadvantage is that they are not comprehensive and cannot be used to compare QoL across different disease states. Generic instruments are designed for use in diverse disease states and across populations, but may not reflect small but clinically important disease-specific symptoms or changes in function [1, 20, 26].

The goal of our study was to determine the cross-sectional relationships among self-reported frequencies of symptomatic hyperglycemia and hypoglycemia and measured HbA1c and symptoms in the QWB-SA, and to assess the associations among these measures of glycemia in diabetic patients and health-utility scores. To our knowledge, this is the first study that has assessed the association between measures of glycemia and health utilities in type-1 and type-2 diabetic patients.

We demonstrated that the QWB-SA includes symptoms that are associated with measures of glycemia. QWB-SA symptoms related to lack of energy, headache, altered appetite, and abnormal urination were positively associated with the self-reported frequency of hyperglycemic symptoms in both type-1 and type-2 diabetic patients. In both type-1 and type-2 diabetic patients, headache was positively associated with frequency of hypoglycemic symptoms and urinary symptoms were associated with HbA1c levels.

The QWB-SA-derived health-utility score was negatively associated with the self-reported frequency of hyperglycemic symptoms in both type-1 and type-2 diabetic patients and the frequency of hyperglycemic symptoms explained 3–5% of the variance in the utility score (Table 3, panel A). These results confirm studies showing a relationship between self-reported frequency of hyperglycemia and reduced treatment satisfaction as assessed by a disease-specific questionnaire [27]. The QWB-SA-derived health-utility score was also negatively associated with the frequency of hypoglycemic symptoms in type-2 diabetic patients, but explained less than 1% of the variance. Another study has shown a weak association between the

frequency of hypoglycemic reactions and the physical role subscale of the SF-36 in patients with type-1 diabetes [3].

We found no association between QWB-SA-derived health-utility scores and HbA1c. Several other studies that employed the SF-20 and SF-36 have also not demonstrated associations between QoL and HbA1c [2, 20, 28–30]. In contrast, a study that assessed QoL with a diabetes-specific measure [27], two studies that assessed QoL with the SF-36 and SWEDQUAL instruments [3, 4], and a study that assessed QoL with the EQ-5D [5] demonstrated relationships between QoL and HbA1c. The lack of association in our study may be explained in part by the generally good glycemic control and narrow range of HbA1c levels observed (fewer than 10% of patients with diabetes had HbA1c levels $> 11\%$).

Our results are consistent with other studies that have demonstrated lower health-utility scores in women with diabetes [6, 31–33] and worse QoL in the presence of complications [6, 20, 33, 34]. However, even with inclusion of gender and diabetic complications in the model, frequency of hyperglycemic symptoms was associated with lower health-utility scores. The magnitude of the differences in health-utility scores in patients with and without hyperglycemic symptoms was small compared to the magnitude of the differences in patients with and without diabetic complications and may be clinically less important. However, having > 4 episodes of hyperglycemic symptoms over the past month was associated with clinically meaningful reductions in health-utility scores of 0.036–0.072 in patients with type-2 diabetes and 0.040–0.080 in patients with type-1 diabetes. The lack of a significant association between hypoglycemia and QWB-SA-derived health-utility scores might be explained by the fact that hypoglycemia is an infrequent, brief, and usually self-limited event that might affect QoL less than persistent hyperglycemia.

Our study has some limitations. First, because we analyzed self-reported measures of glycemia, recall bias may be present. Second, because our study was cross-sectional, we cannot establish a temporal relationship between exposure and outcome. Finally, the association between the frequency of hyperglycemic or hypoglycemic symptoms and QWB-SA symptoms (Table 2) might be confounded by depressive symptoms. Despite these limitations, we found a clinically meaningful negative association between self-reported frequency of hyperglycemic symptoms in type-1 and type-2 diabetic patients and QWB-SA-derived health-utility scores. The association existed for frequency of hyperglycemic symptoms alone and for frequency of hyperglycemic symptoms after adjusting for gender and diabetic complications. We also found a small negative association between the frequency of hypoglycemic symptoms in type-2 diabetes patients and health-utility scores, but no association with HbA1c. These results suggest that the QWB-SA-derived health-utility score may be an appropriate measure to assess the health burden of hyperglycemia. Prospective studies that include repeated measurements of both health-utility scores and glycemia are needed.

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