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Quality of life, health status and clinical outcomes in Type 2 diabetes patients

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Abstract

This study examines relationships between patient reported outcomes (PROs) and clinical outcomes in Type 2 diabetes mellitus (T2DM). Patients at the outpatient clinics of a university hospital completed measures of generic health status (SF-12), diabetes-specific quality of life (Audit of Diabetes Dependent Quality of Life – ADDQoL), and depressive symptoms (Center for Epidemiologic Studies Depression – CES-D). Patient reported data were merged with a retrospective collection of clinical and utilization data, including HbA1C, from electronic medical records. A Charlson comorbidity score, diabetes complications score, BMI, and total number of ER and hospital visits were calculated. Usable response rate was 44.3% (n = 385). Patients were dichotomized into glycemic control levels based on the ADA recommended A1C level < 7.0, vs. ≥ 7.0. The ADDQoL, PCS-12, and MCS-12 scores were separately examined as dependent variables using hierarchical regression models, with glycemic control as the primary explanatory variable, and controlling for demographics and clinical variables including comorbidities and complications. Glycemic control was not a significant predictor in any regression model. Obesity was a significant predictor leading to poorer PCS-12 and MCS-12 scores, while depressive symptoms significantly resulted in lower PCS-12, MCS-12 and ADDQoL scores. These and other factors related to self-management behaviors may contribute to a greater understanding of how to intervene with patients with T2DM. The use of such PROs alongside biomedical measures such as A1C is recommended.

Key words: Depression, Diabetes mellitus – type 2, HbA1C, Obesity, Quality of life

Abbreviations: A1C – HbA1C; ADA – American Diabetes Association; ADDQoL – Audit of Diabetes Dependent Quality of Life; ANOVA – Analysis of Variance; BMI – Body Mass Index; CES-D – Center for Epidemiologic Studies-Depression; DCCT – Diabetes Control and Complications Trial; EMR – Electronic Medical Records; ER – Emergency Room; HRQoL – Health-Related Quality of Life; ICD-9 – International Classification of Diseases 9th revision; MCS-12 – Mental Component Summary-12; PRO – Patient Reported Outcomes; PCS-12 – Physical Component Summary-12; QoL – Quality of Life; SF-12 – Medical Outcomes Study Short-Form 12; UKPDS – United Kingdom Prospective Diabetes Study

Introduction

There is increasing appreciation of the need to measure patient-reported outcomes (PROs), or the patient's perspective on health, disease, and medical treatments and their quality of life (QoL) [1]. In diabetes care, comprehensive assessments of the impact of glucose control regimens on health and QoL are recommended rather than only emphasizing strict glycemic control [2]. Rubin and

Peyrot [3] emphasize the importance of performing multidimensional assessments of QoL in diabetes patients by including both generic and disease-specific instruments.

Glycemic control is one of the major objectives in the clinical management of diabetes. However, the complexity of regimens aimed at achieving better glycemic control may impact patients' QoL. Longitudinal studies like the Diabetes Control and Complications Trial (DCCT) [4] and the United Kingdom Prospective Diabetes Study (UKPDS) [5] both reported no differences in PROs between patients undergoing conventional treatment versus intensive treatment aimed at achieving better glycemic control [6, 7].

Previous studies have produced inconsistent findings regarding the relationship between glycemic control and patient-reported outcomes including health status and QoL. Some correlational studies indicate that better glycemic control, assessed using a long-term measure of glycemic control such as HbA1C (A1C), is variously associated with lower emotional distress [8], better well- being [9], better health status [10], worse health status [11], and better QoL [12]. Other studies report no association with health status [13, 14]. These studies included patients with Type 1 diabetes mellitus only [12], Type 2 diabetes mellitus (T2DM) only [11, 13, 14], or both [9, 10, 15]. These results can be viewed in light of Bradley's [15, 16] suggestion that health status instruments that broadly measure aspects of physical and mental functioning, and other specific body functions and symptoms important in diabetes research should not be confused with instruments measuring the QoL of individuals.

Obesity and depression are two conditions that are increasingly being studied for their influence on the prevalence of T2DM, as well as their appropriate management in patients. Obesity is a risk factor for T2DM as well as its associated comorbidities [17, 18], and has been found to lead to reduced health status [19, 20]. Depression in diabetes patients has been reported to be associated with diminished adherence to diet and medication regimen [21] and also to increased risk of diabetes-related complications [22]. Hence, there is increased interest in studying the impact of depressive symptoms in patients with diabetes [23]. It has been suggested that the strength of the relationship between depressive symptoms and health status is greater among patients with elevated glycemic levels compared with those with lower glycemic levels [24]. There is need for further research studying the impact of both these conditions on both the health status and QoL of patients with T2DM.

Rationale for the study

Existing evidence varies in its conclusions about the nature of association between glycemic control and QoL. The American Diabetes Association's (ADA) clinical practice recommendation suggests that providers should adjust therapeutic management plans for patients to achieve the goal of having A1C below 7.0 [25]; this recommendation was derived from longitudinal studies like the DCCT [4] and the UKPDS [5] which suggested that patients in this tight glycemic control range had substantially reduced risk of diabetes complications. In addition, average daily glucose readings were correlated with A1C levels to delineate and categorize levels of glycemic non-control for those with A1C above 7.0 [26]. By descriptively characterizing patients into levels of increased risk for complications, these control categories are useful in making treatment and intervention decisions, and can be evaluated for their relationship with QoL and health status.

Although there is increasing interest in the association between obesity/depression and T2DM, there is little research on its impact on scores of QoL instruments used in T2DM. Clinical diagnosis has been reported to underestimate the presence of depression in diabetes patients as compared to self-reported questionnaires [27]. Hence, research is needed to probe the relative impact on QoL of these factors in T2DM, also taking into account the complexities of other relevant medical history and sociodemographic factors.

The objectives of the current study were:

(1) To assess the relationships between health status (SF-12), QoL (ADDQoL), and glycemic control in patients with T2DM
(2) To study the impact of obesity and depressive symptoms on scores on health status and QoL among patients with T2DM

(3) To identify the association of glycemic control, obesity and depressive symptoms with health status and QoL in a multivariate framework of sociodemographic and medical history factors.

Methods

Data collection

WVU Institutional Review Board approval was obtained for the study protocol. This was a cross-sectional study in a cohort of persons with T2DM. The study participants were a convenience sample of persons receiving care at the West Virginia University (WVU) Diabetes Institute. The WVU Hospitals' Office of Medical Staff Affairs (OMSA) served as a coordinator for identifying patients with T2DM from an electronic medical record (EMR) database.

The protocol of the present study did not include taking a separate measurement of A1C for each participating patient, but relied on available EMR. Hence, only those patients who had an A1C performed anytime in the previous 90–120 days prior to the assessment of PROs were eligible to participate in the study. A cover letter signed by the patient's provider, along with a questionnaire booklet, was mailed to the 989 adult patients with T2DM identified using the above criteria. Reminder post cards were sent to each participant two weeks after the initial mailing.

Study variables

In the study, three categories of variables were collected: patient reported measures (health status, QoL, and depressive symptoms), demographic variables, and medical history variables.

Patient-reported measures

Health status was measured using the Medical Outcomes Study Short-Form 12 (SF-12) [28, 29]. This instrument is a 12-item version of the widely used SF-36, and was found to reproduce scores on the original SF-36 with considerable accuracy yet with less respondent burden [28]. The SF-12 contains 12 questions covering eight domains of health status [28]. Responses to the SF-12 were coded as per instructions in the user's manual to yield the Physical Component Score-12 (PCS-12, or physical health status), and the Mental Component Score (MCS-12, or mental health status). The PCS-12 and MCS-12 scores range from 0 to 100, where 0 represents poorest health status [29].

Among diabetes-specific QoL measures, the Audit of Diabetes Dependent Quality of Life (ADDQoL) is an individualized instrument designed to measure individuals' perceptions of the impact of diabetes on their QoL [30, 31]. The instrument has been described as an index measuring QoL in diabetes patients, distinguishing it from other measures of health status or well-being [32]. The ADDQoL has been recommended for use in QoL assessments in both Type 1 and Type 2 diabetes patients, and described as a brief and recent instrument generated with patient input, with good reliability, internal and external construct validity [33, 34]. In answering the ADDQoL, respondents indicate the impact of their diabetes on those applicable among 18 items (three of which already have a 'not applicable' option) representing domains of life, and also rate how important those domains are in their life. The resulting weighted impact scores for domains are divided by the number of applicable domains to generate a single final ADDQoL average weighted impact score that ranges from -9 to $+9$, where more negative scores indicate more negative impact of diabetes on QoL [30, 31].

The Center for Epidemiologic Studies Depression Scale (CES-D) was used to identify the presence of persistent depressive symptoms in our sample. The CES-D, originally developed by Radloff [35], consists of 20 questions measuring the frequency with which respondents experience depression-related symptoms. The instrument has been reported to have good reliability [36] and has been reported to be used in diabetes populations [3]. On a large community sample, it was found that persons with a score of 16 or greater on the CES-D had clinically significant symptoms of depression [37]. The CES-D is not intended to be used alone as a clinical diagnostic tool, but can be used to identify patients with depressive symptoms who should be evaluated clinically by qualified providers.

Clinical and socio-demographic variables

Reviewing relationships between QoL and factors such as duration of diabetes, diabetes-related complications, diabetes treatment regimen, glycemic

control, and demographic variables, Rubin and Peyrot [3] recommend controlling for these factors in studies assessing QoL in patients with diabetes. Other variables which have exhibited significant association with outcomes in T2DM include co-morbid illnesses [11, 38, 39], and use of medical services. These were also collected and analyzed in this study.

The following demographic information was collected from patient self-report: age category, gender, marital status, education, and type of insurance. Information on duration of diabetes and type of diabetes treatment (including insulin use) were additionally obtained by self-report since these variables were not available to the researchers via EMR.

Patient reported data were merged with a retrospective collection of clinical and utilization data via the patient's EMR, with the assistance of our coordinators at OMSA. The following variables were included: A1C (most recent value as well as an average of a patient's values from the past 1 year), Body Mass Index (BMI, the most common method of tracking weight problems and obesity among adults), and International Classification of Diseases, Ninth Revision (ICD-9) codes resulting from all outpatient visits, emergency room (ER) visits and hospitalizations in the past 1 year.

The ICD-9 diagnosis codes were used to calculate the following: (1) a Charlson comorbidity score, based on the original Charlson Index [40] consisting of a list of 19 medical conditions, with each condition having a weight assigned from one to six (a version for use with administrative claims data [41], was used in this study); (2) the number of diabetes complications, indicating the presence of up to four diabetes-related complications (renal, ophthalmic, neurological, and peripheral circulatory); and (3) the total number of emergency room (ER) visits and total number of hospitalizations overall in the past 1 year, not just those related to diabetes.

Statistical analyses

Correlations tested the association between SF-12 and ADDQoL scores, and A1C levels directly. Cohen's [42] conventions were used to interpret the results: any correlation greater than 0.5 is large, 0.5–0.3 is moderate, 0.29–0.1 is small, and anything smaller than 0.1 is insubstantial.

Some of the medical history variables were categorized using a clinical rationale in order to assist in meaningfully interpreting the results. Respondents were dichotomized into two groups representing level of glycemic control: one group that had A1Cs below 7.0 and the second group that had A1Cs equal to or above 7.0, based on ADA's clinical practice recommendation [25]. BMI values were categorized as underweight, normal, overweight, or obese, using the CDC classification [43]. On this basis, a dichotomous variable was also calculated classifying patients as obese (BMI $>=30$) or not obese. Another dichotomous variable representing presence or absence of depressive symptoms was created on the basis of the cut-off ($>=16$) suggested for CES-D scores [37]; this cut-off was confirmed as suitable to distinguish between those having depressive symptoms from those not having such symptoms [44]. In a large epidemiologic study, this categorization was used to assess the impact of depressive symptoms in patients with diabetes [45].

T-tests were used to identify any significant differences in SF-12, ADDQoL, and CES-D scores between patients dichotomized on the basis of glycemic control, obesity status, and depressive symptomology. Chi-square tests were used to assess the independence between categories based on obesity and depressive symptoms.

Hierarchical multiple regression models were employed to identify significant predictors of ADDQoL average weighted impact scores, PCS-12 scores and MCS-12 scores, respectively, in three separate models. In the base model for each dependent variable (Model A), the explanatory variables were demographic variables (age group, gender, marital status, education, insurance type) and medical history variables (glycemic control category, insulin use status, diabetes duration, diabetes complication score, Charlson comorbidity score, number of hospitalizations in the past year, and number of ER visits in the past year). The added influence of obesity and depressive symptoms was then analyzed by introducing these variables (dichotomized) to the above-mentioned set of variables. Obesity was first added to the list of predictors in Model A (Model B), and then both obesity and depressive symptoms were added to Model A (Model C).

Prior to analyzing the regression models using these predictor variables, tests were employed that

indicated that the inclusion of all above-mentioned variables did not introduce statistically significant multicollinearity. Minimum sample sizes corresponding to 50 + 8*number of predictors [46] or 15 subjects per predictor [47] have been recommended to build power in multivariate regression models. All statistical analyses were performed using SPSS (version 10.0).

Results

Overview

Demographic variables

There were 385 usable responses, leading to a usable response rate of 44.3%. The distribution of the respondents by the various demographic variables is depicted in Table 1.

Medical history variables

Table 2 summarizes the clinical variables for respondents in terms of their glycemic control category, BMI, diabetes treatment level and type, and medical services (ER and hospitalization) utilization. Approximately 42% of respondents with T2DM used insulin.

The mean self-reported duration of diabetes was 10.20 years (±9.10). Mean of most recent A1C for the respondents was 7.20 (±1.40) among the 360 respondents for whom the value was available. The mean of respondents' A1C (average A1C) over the previous year was 7.24 (±1.30) among the 384 respondents for whom the average A1C could be calculated. Paired samples *t*-test revealed that there was no significant difference between respondents' most recent A1C value and the average A1C value. The proportion of respondents with A1C level above the ADA guidelines, using recent A1C and average of A1C values in the past year, was calculated to be 49% and 53%, respectively.

Mean BMI for the respondents was 33.5 (±8.10), which falls in the obese category (BMI≥30), with 62% of the respondents being clinically obese. The mean Charlson score was 1.18 (±2.56) and ranged between 0 (no co-morbidity as per Charlson description) and 22. About 49% of respondents had at least one complication related to diabetes. About 28% respondents had at least

Table 1. Demographics summary

Variable	*N* (%)
Age	
< 50 years	75 (19.4%)
50–59 years	107 (27.8%)
60–69 years	100 (26.0%)
≥70 years	102 (26.5%)
Gender	
Male	165 (42.9%)
Female	220 (57.1%)
Marital status	
Single	47 (12.2%)
Married/with partner	238 (61.8%)
Divorced/separated	36 (9.4%)
Widowed	59 (15.3%)
Race	
White	361 (93.8%)
Black	14 (3.6%)
Asian	4 (1.0%)
Education	
High school or less	200 (51.9%)
Some college/vocational	85 (22.1%)
College degree and beyond	93 (2.2%)
Insurance	
No insurance	28 (7.3%)
State/Federal insurance	223 (57.9%)
Private insurance/managed care	121 (31.4%)

Table 2. Medical history summary

Variable	*N* (%)
Glycemic control	
Excellent control (A1C ≤ 7.0)	210 (54.5%)
Good control (A1C 7.1–9.0)	133 (34.5%)
Marginal control (A1C 9.1–10.0)	28 (7.3%)
Poor control (A1C > 10.0)	13 (3.4%)
Weight status	
Underweight (BMI < 18.5)	2 (0.5%)
Normal (BMI 18.5–24.9)	44 (11.4%)
Overweight (BMI 25.0–29.9)	89 (23.1%)
Obese (BMI > 30.0)	239 (62.1%)
Treatment	
Diet and exercise only	29 (7.5%)
Oral medications only	189 (49.1%)
Insulin only	36 (9.4%)
Oral medications and insulin	122 (31.7%)
Emergency room utilization	
No emergency room visits	278 (72.2%)
At least one emergency room visit	107 (27.8%)
Hospitalizations	
No hospitalizations	307 (79.7%)
At least one hospitalization	78 (20.3%)

one ER visit in the past year and 21% had at least one hospitalization for any health condition, not just related to diabetes.

QoL, health status, and depressive symptoms

A total of 377 ADDQoL average weighted impact scores and 348 PCS-12 and MCS-12 scores were calculable. The mean weighted impact ADDQoL score was -1.95 (± 1.76), indicating an overall negative impact of diabetes on QoL in the patients participating in the study. The mean PCS score was 45.54 (± 12.30), while the mean MCS score was 38.44 (± 13.1). The mean CES-D score was 17.23 (± 11.85). Thirty-nine percent of the respondents were found to have depressive symptoms (CES-D score ≥ 16). However, only 8.3% of respondents had an actual clinical diagnosis of depression in their EMR.

Reliability and validity of the instruments in the present study was found to be adequate and has been described elsewhere [48]. A summary of the reliability and validity of the ADDQoL is provided here. The recommended one-factor structure of the ADDQoL was analyzed for internal consistency using Cronbach's alpha. The alpha coefficient obtained was 0.92. Construct validity of the measures was studied by analyzing differences in scores between sub-groups based on diabetes treatment type. *T*-tests revealed significantly lower average weighted ADDQoL scores ($p < 0.001$) in the insulin-treated group compared to the non-insulin treated group. Further analyses using the ADDQoL revealed that the insulin treated group had significantly poorer scores on the general QoL item, on the overall item about the impact of diabetes on QoL, as well as on the average weighted impact ADDQoL score, as shown in Fig. 1.

The ADDQoL showed low correlations with the PCS-12, MCS-12 and CES-D, although the magnitude of the correlations with the latter two were relatively greater and comparable (see Table 3).

Relationships with A1C

Spearman's correlation coefficients (r) between the ADDQoL average weighted score and A1C were low ($r = -0.20$ with recent A1C, $r = -0.19$ with average A1C). Correlations between A1C (recent or average) and PCS-12 and MCS-12 scores were insubstantial (see Table 3). Those respondents with A1C level within ADA guidelines (A1C < 7.0) had significantly higher ADDQoL scores than those with A1C levels above ADA guidelines (A1C $\geq$ 7.0) ($p = 0.001$). There were no significant differences in PCS-12 and MCS-12 scores on the basis of glycemic control.

Obesity and depressive symptoms

Patients who were obese had significantly lower PCS-12 scores ($p < 0.001$) as well as MCS-12 scores ($p = 0.001$), compared with those who were not obese. ADDQoL average weighted impact scores did not differentiate between obese and non-obese patients, although the overview item on present QoL detected poorer QoL in the obese patients

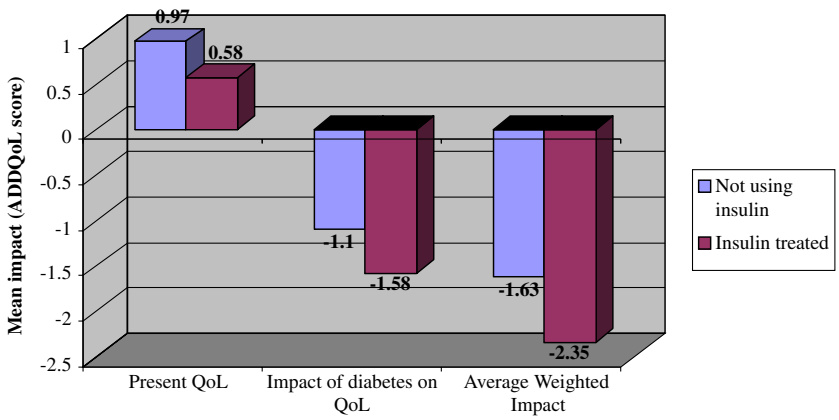

Figure 1. Impact of diabetes on QoL, by insulin use.

Table 3. Correlations[a] among the ADDQoL, PCS-12, MCS-12 and relevant clinical variables

	1	2	3	4	5
1 ADDQoL (average weighted impact score)	1.0	0.199** (n = 343)	0.291** (n = 343)	−0.283** (n = 314)	−0.185** (n = 376)
2 PCS-12 score		1.0	0.078 (n = 348)	−0.262* (n = 294)	−0.047 (n = 347)
3 MCS-12 score			1.0	−0.777** (n = 294)	−0.083 (n = 347)
4 CES-D score				1.0	0.106 (n = 319)
5 A1C (average of values in past year)					1.0

[a] Spearman's correlations are reported in this table.
* Correlation is significant at the 0.01 level.
** Correlation is significant at the 0.001 level.

($p = 0.001$). *T*-tests revealed that those with depressive symptoms (CES-D score ≥ 16) had significantly poorer PCS-12 scores ($p < 0.001$), MCS-12 scores ($p < 0.001$), as well as ADDQoL scores ($p < 0.001$). These results are reported in Table 4.

About 55% of the obese respondents had depressive symptoms (CES-D score ≥ 16) as compared to 33% among those who were not obese (χ^2 [1, 310] = 14.3, $p < 0.001$). In the group with depressive symptoms, *t*-tests revealed significantly greater Charlson comorbidity scores ($p = 0.029$), diabetes complication scores ($p = 0.041$), as well as a greater number of hospitalizations ($p < 0.001$) and ER visits ($p < 0.001$) in the past year.

Predictors of QoL in a multivariate framework

Since we found no significant difference between the most recent A1C value and the average of A1C values in the past year for the study participants, the regression analyses were conducted using the average A1C values.

Glycemic control was not a significant predictor of ADDQoL, PCS-12 or MCS-12 scores in any of the regression models (A, B and C). The inclusion of obesity significantly added to the proportion of variance explained only in the models predicting PCS-12 and MCS-12 scores, while depressive symptoms significantly added to the proportion of variance explained in all models, especially the one predicting MCS-12 scores (see Table 5).

In Model C (see Table 6), the factors associated with higher PCS-12 scores (indicating better physical health status) included having a college degree ($p = 0.001$), not being obese ($p = 0.007$), not having any hospitalizations in the past year ($p = 0.007$), and not having depressive symptoms ($p = 0.021$). Not having depressive symptoms ($p < 0.001$) and older age ($p = 0.017$) were the only factors that significantly explained higher MCS-12 scores (indicating better mental health status), while some of the factors associated with higher ADDQoL scores (indicating lesser impact of diabetes on QoL) were being female ($p = 0.017$), older age ($p = 0.043$) and not having depressive symptoms ($p < 0.001$).

Discussion

The DCCT and the UKPDS researchers concede the possibility that the instruments used in their respective studies lacked the sensitivity to detect QoL differences between groups [6, 7]. Importantly, the interpretation of QoL results from the UKPDS and other studies have been questioned due to the choice of instruments used [16, 49]. In designing and interpreting studies to assess the relationship between glycemic control and QoL, as well as the influence of obesity and depressive symptoms in T2DM, it is necessary to discuss the instruments used to measure these variables.

Reviews of existing QoL instruments and other patient-reported measures used in diabetes, with added commentary on their psychometric properties are available [33, 34]. While the ADDQoL measures individuals' perceptions of the impact of diabetes on their QoL, the SF-12 is a generic measure of health status. The brevity and satisfactory psychometric properties of these instruments render them suitable for our objectives of assessing QoL and health status with generic and disease-specific perspectives as recommended in the literature [6]. There are currently no published

Table 4. Mean scores on the ADDQoL, PCS-12, and MCS-12, and significance of sub-group differences

Variable	ADDQoL average weighted impact score[a]		SF-12 PCS Score[b]		SF-12 MCS Score[b]	
	Mean (SD)	*p* Value	Mean (SD)	*p* Value	Mean (SD)	*p* Value
Glycemic control (average A1C)						
In control (A1C < 7.0)	−1.65 (±1.68)	$t(374) = 3.13$, $p = 0.002$	39.40 (±13.17)	$t(345) = 1.26$, $p = 0.209$	46.82 (±12.24)	$t(345) = 1.81$, $p = 0.072$
Not controlled (A1C≥7.0)	−0.21 (±1.80)		37.63 (±13.02)		44.44 (±12.22)	
BMI						
Not obese (BMI < 3)	−1.88 (±1.80)	$t(364) = 0.604$, $p = 0.546$	42.06 (±12.29)	$t(335) = 4.02$, $p < 0.001$	48.03 (±10.56)	$t(335) = 3.23$, $p = 0.001$
Obese (BMI > 30)	−1.99 (±1.76)		36.36 (±12.94)		43.85 (±12.90)	
CES-D						
Depressive symptoms (score≥16)	−2.44 (±1.97)	$t(312) = 4.68$, $p < 0.001$	34.66 (±12.87)	$t(292) = 5.15$, $p < 0.001$	37.48 (±10.85)	$t(292) = 14.98$, $p < 0.001$
No depressive symptoms (score < 16)	−1.51 (±1.45)		42.12 (±11.96)		53.83 (±7.76)	

[a] Score ranges from −9 to +9, where more negative scores indicate more negative impact of diabetes on QoL.
[b] Scores range from 0 to 100, where 0 represents poorest health status; greater the score, better the physical (PCS-12) or mental (MCS-12) health status.

studies that use both the SF-12 and the ADDQoL; another study used the SF-36 in combination with the ADDQoL [50]. The present study, in our knowledge, is the first to use the two instruments in combination, to assess the effects of glycemic control, obesity and depressive symptoms on QoL and health status of patients with T2DM.

Glycemic control

An A1C provides a generally accurate and reliable method to routinely measure the relative level of diabetes control. Jenkinson [51] suggested that patients' perspectives can differ from what biomedical measures may indicate in terms of their disease status. Univariate analyses indicated that the ADDQoL indicated better QoL among those with A1Cs within the ADA suggested level of glycemic control [A1C < 7.0], with the SF-12 being unable to make this distinction. Correlation results of the study, however, demonstrate that A1C has a weak relationship with both QoL and health status. This indicates that an A1C test alone is a poor indicator of patients' views on the current quality of their lives and health.

This result also agrees with previous suggestions that the lack of association between glycemic control and health status may contribute to inadequate adherence to complex diabetic regimens [13]. The present study sample consisted of patients whose mean A1C was 7.2, which is close to the ADA recommended level. Therefore, because of this reason, it is possible that patients did not perceive an impact on their QoL and health status as related to present health states. Additionally, with the sample being predominantly comprised of older patients (more than 52% were aged 60 or older) and those with experience in dealing with the disease (the mean duration of diabetes was 10 years), there are possible issues of adaptation and acceptance of health concerns.

One of the highlights of this study is the use of multivariate regression analyses probing the impact of medical history and socio-demographic variables on QoL and health status. All of our regression analyses had more than 15 subjects per predictor, and satisfied suggested criteria for statistical power [46, 47]. Results from our hierarchical regression models indicated that variables such as the Charlson comorbidity index and most

Table 5. Summary of the block-wise entry of predictors in the hierarchical regression models predicting PCS-12, MCS-12, and ADDQoL scores

Model	R^2	Adjusted R^2	R^2 Change	F Change	Sig. F change	Model F statistic	Sig. model F statistic
Dependent variable: ADDQoL average weighted impact score							
1[a]	0.13	0.08	0.13	2.83	0.001	2.83	0.001
2[b]	0.14	0.09	0.01	2.14	0.145	2.79	0.001
3[c]	0.18	0.13	0.04	13.09	< 0.001	3.61	< 0.001
Dependent variable: PCS-12 score							
1[a]	0.24	0.19	0.24	5.39	< 0.001	5.39	< 0.001
2[b]	0.27	0.23	0.03	10.97	0.001	6.01	< 0.001
3[c]	0.29	0.24	0.02	5.40	0.021	6.08	< 0.001
Dependent variable: MCS-12 score							
1[a]	0.09	0.04	0.09	1.68	0.067	1.68	0.067
2[b]	0.11	0.06	0.02	6.01	0.015	2.02	0.017
3[c]	0.46	0.42	0.35	140.96	< 0.001	12.46	< 0.001

[a] Predictors: Diabetes duration, Diabetes Complications Score, A1C category, Insulin use status, Charlson Comorbidity Score, Number of ER visits, Number of hospital visits, Private Insurance, Government insurance, Gender, Education, Marital status, Age.
[b] Predictors: Predictors in 'A' and also Obesity Status.
[c] Predictors: Predictors in 'A' and also Obesity Status and Depressive symptoms.

of the diabetes severity indicator variables (A1C, insulin use, diabetes complications score) did not significantly influence ADDQoL, PCS-12, or MCS-12 scores. While the Charlson index has an advantage in weighting different disease conditions, it may not account for all conditions comorbid to diabetes that may also influence QoL, like depression. The results from our cross-sectional study indicate that the disease severity variables considered, notably glycemic control, do not influence the present QoL of patients with T2DM. It is likely that this relationship is being influenced by other factors, an understanding of which will help formulate a treatment regimen that can not only optimize metabolic parameters but also QoL and health status.

Obesity and depressive symptoms

This study was designed to understand also the role of some these 'other' factors. We obtained interesting results from our regression models which examined the influence of obesity and depression. In the present study, 62% of respondents were found to be clinically obese; another 23% were overweight. When examining the association of obesity with the SF-12 health status measure, regression models showed non-obese respondents as having significantly higher PCS-12 and MCS-12 scores (Model B), after controlling for other factors.

The impact on PCS-12 scores could be as a result of the direct influence of the mobility and related issues and the indirect physical functioning issues that obese individuals face. The impact of obesity on MCS-12 scores as seen in our sample assumes importance in view of the increasingly studied relationship between depression and diabetes. A significantly greater proportion of obese people were found to have depressive symptoms than non-obese people in our study. This suggests that obese individuals experience a range of psychosocial issues that impair their mental health status, although the causal nature of this relationship cannot be established here.

A major objective of management of T2DM is to minimize deterioration in psychological well-being due to diabetes treatments while avoiding debilitating complications in the long run. In the study, nearly 40% of respondents exhibited depressive symptoms (CES-D score ≥ 16); responses to the CES-D may be influenced by any frustrations or difficulty patients may encounter in the management of their diabetes. Controlling for other factors including obesity (Model C), ADDQoL, PCS-12 and MCS-12 scores were significantly influenced by the presence of depressive symptoms. The ADDQoL seems well-placed to substantiate this measurement because the scores were not affected in the presence of factors such as obesity. In a previous study, ADDQoL scores were not

Table 6. Results of the hierarchical regression models

Dependent variable and predictor variables	Model A[a]		Model B[b]		Model C[c]	
	Std. β[d]	*p*-Value	Std. β	*p*-Value	Std. β	*p*-Value
ADDQoL score	*F(13,245) = 2.83, p = 0.001*		*F(14,244) = 2.79, p = 0.001*		*F(15,243) =3.61, p < 0.001*	
A1C (above ADA guideline)	−0.070	*0.274*	−0.065	*0.312*	−0.066	*0.294*
Insulin user	−0.083	*0.255*	−0.080	*0.268*	−0.074	*0.299*
Diabetes duration	−0.130	*0.072*	−0.134	*0.063*	−0.121	*0.086*
Diabetes complications score	−0.046	*0.474*	−0.042	*0.507*	−0.035	*0.572*
Charlson comorbidity score	0.069	*0.293*	0.073	*0.268*	0.074	*0.247*
Number of ER visits	−0.126	*0.062*	−0.132*	*0.050*	−0.110	*0.096*
Number of hospital visits	−0.047	*0.495*	−0.051	*0.454*	−0.011	*0.875*
Govt. insurance	−0.034	*0.775*	−0.016	*0.890*	−0.014	*0.902*
Private insurance	0.098	*0.396*	0.112	*0.331*	0.105	*0.353*
Age (60 years or older)	0.171*	*0.013*	0.161*	*0.019*	0.137*	*0.043*
Gender (Female)	0.113	*0.072*	0.123	*0.051*	0.148*	*0.017*
Marital status (with partner)	−0.008	*0.895*	−0.024	*0.708*	−0.023	*0.709*
Education (College educated)	0.112	*0.076*	0.106	*0.092*	0.074	*0.229*
Obese			−0.091	*0.145*	−0.040	*0.522*
Depressive symptoms					−0.231*	*< 0.001*
PCS-12 score	*F(13,226) = 5.39, p < 0.001*		*F(14,225) = 6.01, p < 0.001*		*F(15,224) = 6.08, p < 0.001*	
A1C (above ADA guideline)	0.016	*0.800*	0.021	*0.735*	0.019	*0.750*
Insulin user	−0.116	*0.106*	−0.111	*0.114*	−0.107	*0.121*
Diabetes duration	−0.126	*0.078*	−0.133	*0.057*	−0.127	*0.066*
Diabetes complications score	−0.017	*0.782*	−0.008	*0.897*	−0.005	*0.940*
Charlson comorbidity score	−0.022	*0.732*	−0.011	*0.859*	−0.015	*0.808*
Number of ER visits	0.028	*0.675*	0.016	*0.807*	0.026	*0.681*
Number of hospital visits	−0.195*	*0.004*	−0.205*	*0.002*	−0.179*	*0.007*
Govt. insurance	0.088	*0.447*	0.126	*0.266*	0.127	*0.259*
Private insurance	0.174	*0.119*	0.208	*0.059*	0.198	*0.070*
Age (60 years or older)	−0.119	*0.075*	−0.144*	*0.029*	−0.158*	*0.016*
Gender (Female)	−0.067	*0.270*	−0.043	*0.472*	−0.034	*0.567*
Marital status (with partner)	0.101	*0.102*	0.070	*0.251*	0.069	*0.252*
Education (College educated)	0.228*	*< 0.001*	0.220*	*< 0.001*	0.195*	*0.001*
Obese			−0.197*	*0.001*	−0.164*	*0.007*
Depressive symptoms					−0.144*	*0.021*
MCS-12 score						
A1C (above ADA guideline)	−0.046	*0.502*	−0.042	*0.535*	−0.048	*0.366*
Insulin user	0.016	*0.839*	0.020	*0.797*	0.034	*0.572*
Diabetes duration	−0.011	*0.886*	−0.017	*0.828*	0.008	*0.890*
Diabetes complications score	−0.008	*0.908*	0.000	*0.998*	0.015	*0.782*
Charlson comorbidity score	0.021	*0.767*	0.030	*0.669*	0.012	*0.827*
Number of ER visits	−0.090	*0.210*	−0.100	*0.161*	−0.053	*0.346*
Number of hospital visits	−0.087	*0.237*	−0.095	*0.193*	0.023	*0.696*
Govt. insurance	0.071	*0.572*	0.103	*0.412*	0.106	*0.284*
Private insurance	0.148	*0.227*	0.175	*0.150*	0.129	*0.175*
Age (60 years or older)	0.220*	*0.003*	0.200*	*0.006*	0.138*	*0.017*
Gender (Female)	0.010	*0.881*	0.029	*0.656*	0.070	*0.179*
Marital status (with partner)	0.058	*0.386*	0.033	*0.623*	0.030	*0.572*
Education (College educated)	0.070	*0.290*	0.064	*0.334*	−0.046	*0.379*
Obese			−0.161*	*0.015*	−0.014	*0.794*
Depressive symptoms					−0.643*	*< 0.001*

[a] Predictors in Model A: diabetes duration, diabetes complications score, A1C category, insulin use status, charlson comorbidity score, number of ER visits, number of hospital visits, private insurance, government insurance, gender, education, marital status, age.
[b] Predictors in Model B: Predictors in 'A' and also obesity status.
[c] Predictors in Model C: Predictors in 'A' and also obesity status and depressive symptoms.
[d] Standardized beta
* Significant at 0.05 level.

influenced by self-reported non-diabetic comorbidity, but SF-36 scores were [51].

In the hierarchical regression models used in the study, the same given set of predictors was able to explain a greater proportion of variance in PCS-12 scores as compared to ADDQoL scores (24% vs. 13% in Model C). This may be since the SF-12 taps into problems that impair physical health status due to the high prevalence of obesity in our sample of patients with T2DM. Adding CES-D scores to the model explaining MCS-12 scores (Model C) added to its explanatory power to a large extent (35%), indicating the role played by depressive symptoms in explaining mental health status. This can be expected in light of the high correlation between scores on the CES-D and the MCS-12.

The formulation of the SF-12 and the ADDQoL may reflect in these results. The process of item generation for QoL instruments is iterative; it uses a combination of theory, primary data collection, and statistical analyses. Hence, the ADDQoL as it is available today consists of life domains that are often found to be impacted by diabetes that can be important for patients' QoL. On the other hand, the SF-12 measures the impact on various aspects of life that reflect the physical status (physical functioning, role limitations due to physical health problems, bodily pain, general health) and mental status (vitality, social functioning, role limitations due to emotional problems, and mental health) of individuals. In the present study, ADDQoL average weighted impact scores showed a low correlation with PCS-12 and MCS-12 scores, suggesting that the instruments provide assessments from a different, possibly complementary perspective.

Study limitations

All measurements in the study were planned and implemented to protect the integrity of study results, but there were potential limitations inherent in the study design. The study employed a cross-sectional design that has limited capability in identifying any causal relationships between glycemic control and PROs. The non-response analysis that we were able to conduct was limited to differences in A1C. There were no significant differences in recent A1C values between the two groups. However, non-responders had significantly higher average A1C values [7.4($\pm$1.56)] than responders [7.2($\pm$1.40] ($p = 0.041$). The clinical significance of this difference was not ascertained, but it appears that those with better average A1C values responded to our survey.

Due to differences in the extent to which questionnaires were completed, we were able to calculate 377 ADDQoL average weighted scores and 348 PCS-12 and MCS-12 scores, using guidelines available from the scoring manuals of these instruments. To maintain uniformity, we did not employ imputation techniques to replace missing data in both the ADDQoL and the SF-12. Given that 94% of our respondents were white, and were recruited into the study at a convenience site, the generalizability of the study findings may be limited. The study may be influenced by errors in coding the data in the EMR. On the other hand, this eliminated threats to validity from the recall bias associated with patient reported data. Also, the ER visit and hospitalization data used in this study included data pertaining to care received only at WVU.

Despite accounting for socio-demographic and medical history variables, the proportion of total variance in QoL and health status accounted for by those variables in the regression models was low. Future studies could additionally obtain information on the duration of insulin usage in patients with T2DM. Other psychosocial indicators – including variables describing the engagement of patients in diabetes self-management behaviors, and the coping styles that patients embrace in facing their diabetes – could contribute to a greater understanding of the QoL and health status of patients with T2DM. In addition, examining their associations may contribute to an understanding of how to intervene with patients with T2DM to help facilitate self-management.

Conclusion

The current study supports the utility of employing the ADDQoL and the SF-12 in combination in populations with T2DM. The results of the study suggest that the A1C has a weak relationship with QoL, suggesting that the two important outcomes are not directly related. The presence of depressive symptoms in T2DM is associated with significantly

poorer QoL and health status. While QoL scores were not affected by obesity, the condition was significantly associated with impaired physical health status.

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