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Original Research Article

Health-related quality of life and psychological distress among patients with type 2 diabetes using semaglutide

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ABSTRACT

Background: Semaglutide is increasingly used for type 2 diabetes mellitus (T2DM), but its real-world association with health-related quality of life (HRQoL) and psychological wellbeing remains underexplored in Saudi Arabia. The study aims to assess HRQoL and psychological distress among patients with T2DM according to current semaglutide use.
Methods: This analytical cross-sectional study included 349 adults with T2DM attending outpatient diabetic clinics in Taif, Saudi Arabia, between September 2025 and February 2026. HRQoL was assessed using the Arabic EQ-5D-5L, including EQ-5D-5L index and EQ-VAS scores, while psychological distress was assessed using the Arabic PHQ-4. Adjusted regression models examined associations between semaglutide use and study outcomes.
Results: Among 349 participants, 145 were semaglutide users and 204 were non-users. Semaglutide use was not significantly associated with EQ-VAS score (B=-0.091, 95% CI: -2.259 to 2.078, p=0.935) or EQ-5D-5L index score (B=-0.030, 95% CI: -0.062 to 0.003, p=0.072). However, semaglutide use was associated with higher odds of pain/discomfort (OR=2.610, 95% CI: 1.385-4.917, p=0.003), anxiety/depression (OR=2.175, 95% CI: 1.213-3.899, p=0.009), and any psychological distress (OR=2.929, 95% CI: 1.503–5.710, p=0.002).
Conclusions: Semaglutide use was not associated with better overall HRQoL, but was associated with higher odds of pain/discomfort and psychological distress. Longitudinal studies are needed to clarify whether these associations reflect treatment effects, baseline patient complexity, or unmeasured clinical factors.

Keywords: Diabetes mellitus type 2, Health related quality of life, Semaglutide

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a major public health burden worldwide and remains particularly important in Saudi Arabia. The International Diabetes Federation estimated 5.34 million adults in Saudi Arabia had diabetes in 2024, with an adult prevalence of 23.1%, placing the country among the countries with a high diabetes burden globally.[1] T2DM causes long-term microvascular and macrovascular complications, impacting daily functioning, emotional well-being, treatment burden, and HRQoL. Therefore, modern diabetes care focuses on person-centered assessment and treatment, including outcomes that reflect patients' lived experiences, in addition to biomedical indicators like HbA1c and body weight.[2]

HRQoL is especially relevant in T2DM because patients often live with the condition for many years while managing medications, lifestyle modification, monitoring requirements, comorbidities, and fear of complications.[3]

Patient-reported outcome measures provide information beyond clinical records. The EQ-5D-5L, a widely used generic HRQoL instrument, assesses five broad health dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.[4] This structure is useful in diabetes research as it provides an overall health assessment and a domain-level understanding of daily life's most affected aspects. Evidence supports the EQ-5D-5L's validity in diabetes populations, reflecting general health, psychological symptoms, and diabetes-related quality of life.[5,6]

The EQ-5D-5L calculates an index score, a preference-based summary value for health status. This converts patients' reported health states into a single utility score for comparison across groups, diseases, and healthcare settings. Country-specific value sets are recommended due to varying preferences for health states across populations and cultural contexts.[7] The development of a Saudi EQ-5D-5L value set is therefore particularly relevant for local research, as it allows HRQoL estimates to reflect societal preferences in Saudi Arabia rather than relying on value sets from other countries.[8]

The EQ visual analogue scale (EQ-VAS) complements the EQ-5D-5L index score by capturing the patient's own rating of their health on the day of assessment. Unlike the index score, which is derived from responses to the five EQ-5D-5L domains and population-based preferences, the EQ-VAS directly reflects self-perceived health. This distinction is important because patients' perceptions may be influenced by confidence in treatment, perceived disease control, symptom burden, psychological wellbeing, and expectations of improvement. For example, a patient may rate their overall health positively because they feel their diabetes is being actively managed, even if they continue to experience specific symptoms such as pain, discomfort, or anxiety. Therefore, using both EQ-5D-5L index scores and EQ-VAS provides a more complete assessment of HRQoL than either measure alone.[4,9]

Psychological wellbeing is another important component of diabetes care. Depression and anxiety are common among patients with diabetes and are associated with poorer self-care, reduced medication adherence, worse perceived health, and lower HRQoL.[10,11] The patient health questionnaire-4 (PHQ-4) is an ultra-brief screening tool that combines two items assessing anxiety and two items assessing depressive symptoms, making it practical for use in clinical and research settings.[12,13] Including psychological distress alongside HRQoL measures is therefore important because physical health status and mental wellbeing may influence each other in patients with chronic diseases such as T2DM.

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), including semaglutide, are important therapeutic options for T2DM due to their benefits in glycemic control, weight reduction, and cardiometabolic risk. Semaglutide has shown efficacy in major clinical trials, reducing HbA1c, body weight, and improving cardiovascular outcomes in patients with high cardiovascular risk.[2,14] In addition to metabolic outcomes, some evidence suggests that semaglutide may improve patient-reported outcomes and HRQoL when added to standard care, although much of this evidence comes from clinical trial populations rather than routine clinical settings.[15]

Despite the growing use of semaglutide, real-world evidence on its association with HRQoL and psychological wellbeing is limited, especially in Saudi Arabia and the Middle East. This gap is significant because clinical trial effects may not reflect patient experiences in everyday practice, where patients vary in age, comorbidities, treatment duration, adherence, tolerability, expectations, and access to care.

Therefore, this study assessed HRQoL and psychological distress among patients with T2DM in an outpatient diabetes center in Taif, Saudi Arabia, comparing semaglutide users and non-users. The study compared EQ-5D-5L index scores, EQ-VAS scores, EQ-5D-5L domain-level problems, and PHQ-4 psychological distress, adjusting for sociodemographic and clinical characteristics.

METHODS

Study design and setting

This analytical cross-sectional study was conducted at the outpatient clinics of a diabetic center in Taif, Saudi Arabia. Data were collected between September 1, 2025 and February 28, 2026.

Study population and sampling

The study included adult patients with confirmed T2DM attending outpatient diabetic clinics. Convenience sampling recruited 349 patients, including 204 non-users and 145 current users of semaglutide.

Participants were classified into two groups based on semaglutide exposure: current users and non-users. Although semaglutide dose and duration of use were collected, they were not included in the final analysis because the primary exposure of interest was current semaglutide use as a binary variable.

Eligibility criteria

Eligible participants were adults aged 18 years or older with confirmed T2DM who were willing to complete the study questionnaire. Patients were excluded if they had type 1 diabetes mellitus, severe psychiatric disorders, cognitive impairment, concurrent use of other GLP-1 receptor agonists, were undergoing dialysis, or had significant medical conditions that could interfere with the study outcomes.

Data collection and study variables

Data were collected using a structured Arabic questionnaire and relevant clinical information from patient files and participant reports. The questionnaire assessed sociodemographic and clinical variables, including age, gender, marital status, education, occupation, duration of T2DM, semaglutide use, and HbA1c level. Standardized patient-reported outcome measures assessed HRQoL and psychological distress. Completed questionnaires were checked, coded, and entered for analysis. Some clinical variables were supplemented from medical records.

Assessment of HRQoL

HRQoL was assessed using the Arabic version of the EQ-5D-5L.[4] This instrument evaluates five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each measured on five response levels ranging from no problems to extreme problems.[16] Participants also rated their overall health status using the EQ-VAS, which ranges from 0 to 100, with higher scores indicating better self-rated health.[16]

EQ-5D-5L index scores were calculated using the Saudi Arabian value set.[8] For descriptive and regression analyses of the EQ-5D-5L domains, responses were dichotomized into "no problems" and "any problems" because of sparse cell counts across the original five response levels.

Assessment of psychological distress

Psychological distress was assessed using the Arabic version of the PHQ-4, an ultra-brief screening tool for anxiety and depression.[12,17] The PHQ-4 consists of four items, each scored from 0 to 3, yielding a total score ranging from 0 to 12.[12] Scores were categorized as normal (0-2), mild distress (3-5), moderate distress (6-8), and severe distress (9-12).

For adjusted regression analysis, PHQ-4 was further dichotomized into no distress versus any distress to improve model stability and address sparse observations in higher severity categories.

Statistical analysis

Data were entered and analyzed using IBM SPSS Statistics version 30.0. Categorical variables were summarized as frequencies and percentages, whereas continuous variables were summarized using mean and standard deviation or median and interquartile range (IQR), as appropriate.

Baseline categorical characteristics were compared between semaglutide users and non-users using the chi-square test. For ordinal baseline variables with sparse cell counts, categories were combined where appropriate and linear-by-linear association was used to assess trend.

For unadjusted comparisons of HRQoL outcomes, independent-samples t test was used to compare EQ-VAS scores, whereas Mann-Whitney U test was used for EQ-5D-5L index scores because index score was not normally distributed. Dichotomized EQ-5D-5L domains were compared using chi-square test. PHQ-4 categories were also compared between 2 groups using chi-square test.

To examine adjusted associations, multiple linear regression models were fitted for EQ-VAS score and EQ-5D-5L index score. Although the EQ-5D-5L index score was non-normally distributed in univariate analysis, linear regression was used because model residuals were judged to be approximately normally distributed. For dichotomized EQ-5D-5L domains and dichotomized PHQ-4 distress status, binary logistic regression models were applied. Ordinal regression was initially explored for these outcomes; however, due to sparse distributions across categories and unstable model diagnostics, binary models were used instead.

All multivariable models included the same covariates: age group, gender, marital status, duration of T2DM, occupational status, educational level, HbA1c level, and semaglutide use. Results from linear regression were reported as regression coefficients (B) with 95% CIs, and results from logistic regression were reported as adjusted odds ratios (ORs) with 95% CIs. A 2-sided $p<0.05$ was considered statistically significant.

Missing data

Participants with missing data relevant to a specific analysis were excluded from that analysis. No data imputation was performed.

Ethical considerations

Ethical approval was obtained from the research ethics committee, and verbal informed consent was obtained from all participants before enrollment. Confidentiality was maintained, and all data were used solely for research.

RESULTS

Participant characteristics

A total of 349 patients with type 2 diabetes mellitus were included in the analysis, of whom 204 were non-users of semaglutide and 145 were current users. Baseline sociodemographic and clinical characteristics are summarized in Table 1. Semaglutide users were significantly younger than non-users, with a greater proportion in the 41-50 years and 51-60 years age groups, whereas non-users were more commonly aged >61 years ($p<0.001$). A significant linear trend was also observed across age categories ($p<0.001$).

Gender distribution differed significantly between the groups, with males accounting for a higher proportion of

semaglutide users than non-users (77.9% vs 57.8%, p<0.001). Educational level and occupational status also differed significantly, as semaglutide users were more likely to have a higher educational level (73.1% vs 31.9%, p<0.001) and to be employed (38.6% vs 11.3%, p<0.001). Duration of T2DM was shorter among semaglutide users, while longer disease duration was more common among non-users; a significant linear trend was observed across duration categories (p=0.001). HbA1c category also differed significantly between the groups (p=0.003), whereas marital status did not (p=0.129).

Unadjusted comparison of EQ-5D-5L outcomes

Unadjusted EQ-5D-5L outcomes are presented in Table 2. Mean EQ-VAS scores were similar between semaglutide users and non-users (91.917±9.453 vs 91.226±8.583, p=0.477). Likewise, median EQ-5D-5L index scores did not differ significantly between the two groups (0.976 [IQR 0.099] vs 0.961 [IQR 0.109], p=0.771).

Significant between-group differences were observed for mobility, self-care, and anxiety/depression. Semaglutide users were less likely than non-users to report mobility problems (24.8% vs 35.3%, p=0.037) and self-care problems (4.8% vs 12.3%, p=0.018). In contrast, semaglutide users were more likely to report problems in the anxiety/depression domain (32.4% vs 22.1%, p=0.030). Differences in usual activities (p=0.056) and pain/discomfort (p=0.169) were not statistically significant.

Unadjusted comparison of psychological distress

PHQ-4 psychological distress categories are reported in Table 3. Their distribution differed significantly between semaglutide users and non-users (p=0.011). A higher proportion of non-users had normal PHQ-4 scores compared with semaglutide users (88.2% vs 75.0%), whereas mild distress was more common among semaglutide users (22.9% vs 10.8%). Moderate and severe distress were uncommon in both groups.

Adjusted associations With HRQoL and psychological distress

Adjusted regression analyses are presented in Tables 4 and 5. In the multivariable linear regression models (Table 4), semaglutide use was not significantly associated with EQ-VAS score (B=-0.091, 95% CI: -2.259 to 2.078, p=0.935) or EQ-5D-5L index score (B=-0.030, 95% CI: -0.062 to 0.003, p=0.072) after adjustment for age group, gender, marital status, duration of T2DM, occupational status, educational level, and HbA1c level.

In the adjusted binary logistic regression analyses of the dichotomized EQ-5D-5L domains (Table 5), semaglutide use was not significantly associated with mobility (OR=1.464, 95% CI: 0.809-2.651, p=0.208), self-care (OR=0.975, 95% CI: 0.297-3.196, p=0.966), or usual activities (OR=1.326, 95% CI: 0.685-2.567, p=0.402). However, semaglutide use was significantly associated with higher odds of reporting pain/discomfort (OR=2.610, 95% CI: 1.385-4.917, p=0.003) and anxiety/depression (OR=2.175, 95% CI: 1.213-3.899, p=0.009).

For psychological distress, the adjusted binary logistic regression model (Table 5) showed that semaglutide use was significantly associated with higher odds of any distress on the PHQ-4 (OR=2.929, 95% CI: 1.503-5.710, p=0.002).

Table 1: Baseline sociodemographic and clinical characteristics of participants by semaglutide use.

Characteristics		Do not use semaglutide, (n=204)	Use semaglutide, (n=145)	Total, (n=349)	P value
Age group (in years)	18-30	0 (0.0)	6 (4.1)	6 (100.0)	<0.001* Linear-by-linear association <0.001
	31-40	0 (0.0)	14 (9.7)	14 (100.0)	
	41-50	26 (12.7)	43 (29.7)	69 (100.0)	
	51-60	69 (33.8)	52 (35.9)	121 (100.0)	
	More than 61	109 (53.4)	30 (20.7)	139 (100.0)	
Gender	Female	86 (42.2)	32 (22.1)	118 (100.0)	<0.001
	Male	118 (57.8)	113 (77.9)	231 (100.0)	
Marital status	Single	36 (17.6)	17 (11.7)	53 (100.0)	0.129
	Married	168 (82.4)	128 (88.3)	296 (100.0)	
Educational level	Low (no education, primary school, middle school)	139 (68.1)	39 (26.9)	178 (100.0)	<0.001
	High (high school, undergraduate, postgraduate)	65 (31.9)	106 (73.1)	171 (100.0)	
Occupational status	Not working	88 (43.1)	27 (18.6)	114 (100.0)	<0.001
	Employed	23 (11.3)	56 (38.6)	79 (100.0)	
	Retired	93 (45.6)	62 (42.8)	154 (100.0)	

Continued.

Characteristics		Do not use semaglutide, (n=204)	Use semaglutide, (n=145)	Total, (n=349)	P value
Duration of T2DM	Less than a year	2 (1.0)	7 (4.8)	9 (100.0)	<0.001* Linear-by-linear association 0.001
	1-5 years	29 (14.2)	41 (28.3)	70 (100.0)	
	6-10 years	52 (25.5)	38 (26.2)	90 (100.0)	
	More than 10 years	121 (59.3)	59 (40.7)	180 (100.0)	
Current HbA1c level	Less than 6.5	48 (23.5)	61 (42.1)	109 (100.0)	0.003
	6.5-7.5	80 (39.2)	37 (25.5)	117 (100.0)	
	7.6-8.5	34 (16.7)	26 (17.9)	60 (100.0)	
	More than 8.5	28 (13.7)	13 (9.0)	41 (100.0)	
	Unknown	14 (6.9)	8 (5.5)	22 (100.0)	

*Data are presented as n (%). Group differences were assessed using the chi-square test. For ordinal variables with sparse cell counts, categories were combined where appropriate and linear-by-linear association was used. Percentages are column percentages.

Table 2: Unadjusted comparison of EQ-5D-5L outcomes between semaglutide users and non-users.

Variables		Do not use semaglutide, (n=204)	Use semaglutide, (n=145)	P value
EQ-VAS score (mean±SD)		91.226±8.583	91.917±9.453	0.477
EQ-5D index score (median, IQR)		0.961, 0.109	0.976, 0.099	0.771
Mobility	No problems	132 (64.7)	109 (75.2)	0.037
	Any problems	72 (35.3)	36 (24.8)	
Self-care	No problems	179 (87.7)	138 (95.2)	0.018
	Any problems	25 (12.3)	7 (4.8)	
Usual activity	No problems	148 (72.5)	118 (81.4)	0.056
	Any problems	56 (27.5)	27 (18.6)	
Pain/discomfort	No problems	162 (79.4)	106 (73.1)	0.169
	Any problems	42 (20.6)	39 (26.9)	
Anxiety/depression	No problems	159 (77.9)	98 (67.6)	0.030
	Any problems	45 (22.1)	47 (32.4)	

*Data are presented as mean±standard deviation, median (interquartile range), or n (%), as appropriate. EQ-VAS scores were compared using the independent-samples t test, and EQ-5D-5L index scores were compared using the Mann-Whitney U test. EQ-5D-5L domain responses were dichotomized into “no problems” and “any problems” and compared using the chi-square test. Percentages are column percentages.

Table 3: Unadjusted comparison of PHQ-4 psychological distress categories between semaglutide users and non-users.

PHQ-4 category	Do not use semaglutide, (n=204)	Use semaglutide, (n=145)	P value
Normal	180 (88.2)	108 (75.0)	0.011
Mild	22 (10.8)	33 (22.9)	
Moderate	2 (1.0)	2 (1.4)	
Severe	0 (0.0)	1 (0.7)	

*Data are presented as n (%). Group differences were assessed using the chi-square test. PHQ-4 categories were defined as normal (0-2), mild distress (3-5), moderate distress (6-8), and severe distress (9-12). Percentages are column percentages.

Table 4: Adjusted linear regression models for EQ-VAS and EQ-5D-5L index score.

Outcomes	Adjusted regression coefficient for semaglutide use (B)	95% CI	P value
EQ-VAS score	-0.091	-2.259-2.078	0.935
EQ-5D-5L index score	-0.030	-0.062-0.003	0.072

*Multiple linear regression models were used to examine the association of semaglutide use with EQ-VAS and EQ-5D-5L index score after adjustment for age group, gender, marital status, duration of type 2 diabetes mellitus, occupational status, educational level, and HbA1c level. Results are presented as regression coefficients (B) with 95% confidence intervals.

Table 5: Adjusted binary logistic regression models for dichotomized EQ-5D-5L domains and dichotomized PHQ-4 score.

EQ-5D-5L domain	Adjusted odds ratio for semaglutide use	95% CI	P value
Mobility	1.464	0.809-2.651	0.208
Self-care	0.975	0.297-3.196	0.966
Usual activity	1.326	0.685-2.567	0.402
Pain/discomfort	2.610	1.385-4.917	0.003
Anxiety/depression	2.175	1.213-3.899	0.009
PHQ-4 categories			
No distress vs. any distress	2.929	1.503-5.710	0.002

*Binary logistic regression models were used for dichotomized EQ-5D-5L domains and PHQ-4 distress status. Models were adjusted for age group, gender, marital status, duration of T2DM, occupational status, educational level, and HbA1c level. B: regression coefficient; CI: confidence interval; HRQoL: health-related quality of life; OR: odds ratio; PHQ-4: Patient Health Questionnaire-4; T2DM: type 2 diabetes mellitus.

DISCUSSION

This cross-sectional study assessed HRQoL and psychological distress among patients with T2DM based on semaglutide use. Semaglutide use was not significantly associated with overall self-rated health (EQ-VAS or EQ-5D-5L index) after adjusting for age, gender, marital status, diabetes duration, occupational status, education, and HbA1c. However, it was significantly associated with higher odds of reporting problems in pain/discomfort and anxiety/depression domains (EQ-5D-5L) and any psychological distress (PHQ-4). These findings suggest that overall HRQoL measures may not fully capture domain-specific differences among semaglutide users.

The lack of a significant adjusted association between semaglutide use and overall EQ-VAS or EQ-5D-5L index score should be interpreted cautiously. Previous clinical trial evidence suggests semaglutide may improve HRQoL in patients with T2DM at high cardiovascular risk when added to standard care. In the SUSTAIN 6 patient-reported outcomes analysis, semaglutide was associated with improvements in several short form-36 domains and component scores compared with placebo.[15] However, clinical trial findings may not directly translate to routine practice because trial participants are selected using strict eligibility criteria and are followed under structured monitoring conditions. In contrast, this study reflects a real-world outpatient population in which semaglutide users and non-users differed significantly in age, gender, education, employment, diabetes duration, and HbA1c. Therefore, the absence of a significant adjusted difference in overall HRQoL should not be interpreted as evidence that semaglutide has no effect on patient wellbeing, but rather that current semaglutide use was not independently associated with better global HRQoL in this cross-sectional clinical sample.

The EQ-VAS finding deserves attention as it reflects patients' subjective health ratings on assessment day. In this study, EQ-VAS scores were high and similar between semaglutide users and non-users, suggesting comparable self-perceived health. This may indicate semaglutide use didn't significantly impact global self-perceived health. However, EQ-VAS is influenced by symptoms, expectations, adaptation to chronic illness, treatment effectiveness, and confidence in disease control.[18] A patient receiving a newer or more intensive therapy may feel reassured that their diabetes is being actively managed, even while experiencing specific symptoms such as pain, discomfort, or anxiety. This may explain why global EQ-VAS scores were similar despite significant domain-level differences. This interpretation is consistent with the conceptual distinction between EQ-VAS, which reflects self-rated health, and EQ-5D utility scores, which are derived from reported health states and population-based preferences.[19]

The domain-level findings provide a more nuanced interpretation of the results. In unadjusted analysis, semaglutide users reported fewer mobility and self-care problems than non-users, but these differences were no longer significant after adjustment. This suggests that the apparent unadjusted advantage may have been partly explained by baseline differences between groups. Semaglutide users in this sample were generally younger and had shorter diabetes duration, both of which may improve physical functioning. Previous HRQoL research in T2DM shows that diabetes-related quality of life is influenced by age, complications, comorbidities, and psychological health.[20] Therefore, the loss of significance after adjustment supports the importance of accounting for baseline differences when interpreting HRQoL outcomes in observational studies.

In contrast, semaglutide use remained significantly associated with higher odds of pain/discomfort after adjustment. This finding may appear unexpected because semaglutide is often associated with weight reduction and improved metabolic outcomes, which could theoretically improve physical function.[21] However, in real-world practice, patients prescribed semaglutide may represent a clinically different subgroup. They may be more likely to have obesity, weight-related functional limitations, cardiometabolic risk, or more complex diabetes management needs, even if these factors were not fully

captured in the adjusted model. Obesity is strongly associated with musculoskeletal pain, impaired mobility, osteoarthritis, fatigue, and lower physical HRQoL, and recent evidence continues to support the relationship between excess weight and pain burden.[22,23] Therefore, the higher odds of pain/discomfort among semaglutide users may reflect underlying obesity-related or cardiometabolic burden that influenced semaglutide prescribing, rather than a direct adverse effect of semaglutide itself.

Another possible explanation is that the broad EQ-5D-5L pain/discomfort domain doesn't identify the source of discomfort. Participants may report pain/discomfort due to musculoskeletal pain, diabetic neuropathy, obesity-related symptoms, gastrointestinal symptoms, or other conditions. This is relevant because gastrointestinal adverse effects are common with semaglutide; the Ozempic prescribing information lists nausea, vomiting, diarrhea, abdominal pain, and constipation among the most common adverse reactions.[24] Since the present study did not include BMI, weight change, diabetes complications, adverse effects, treatment tolerability, or other diabetes medications in the final adjusted models, the mechanism behind the pain/discomfort association cannot be determined. Future studies should investigate the relationship between pain/discomfort among semaglutide users and baseline obesity, diabetic complications, medication adverse effects, and the changes in weight and the metabolic control.

Semaglutide use is clinically important because it's associated with higher odds of anxiety/depression problems and PHQ-4 psychological distress. Depression and anxiety are common among T2DM patients, and they're linked to poorer HRQoL, impaired self-care, reduced adherence, and less favorable glycemic outcomes.[11,25] However, this study cannot determine whether psychological distress preceded semaglutide use or developed after treatment initiation. Semaglutide users may have had greater weight-related concerns, higher expectations of treatment, more complex disease experiences, or other psychosocial stressors that were not measured. Therefore, the observed association should be interpreted as a signal requiring further investigation, not as evidence that semaglutide causes psychological distress.

This distinction is important because current regulatory evidence does not support a causal link between GLP-1 receptor agonists and suicidal thoughts or actions. The U.S. Food and Drug Administration reported in its preliminary evaluation that available evidence did not show that GLP-1 receptor agonists cause suicidal thoughts or actions, although monitoring has continued.[26] Therefore, the psychological distress findings in this study are better interpreted in the context of patient complexity, chronic disease burden, obesity-related concerns, and unmeasured confounding rather than as a direct psychiatric medication effect.

Overall, the findings emphasize the value of assessing both global HRQoL scores and individual HRQoL domains. Although EQ-VAS and EQ-5D-5L index scores did not differ significantly between groups, domain-level analysis identified important differences in pain/discomfort and anxiety/depression. Similar patterns have been observed in diabetes HRQoL research, where pain/discomfort and anxiety/depression are often among the most commonly affected EQ-5D domains in patients with T2DM.[20] This suggests that global HRQoL scores may mask clinically relevant problems in specific areas of patient wellbeing. For clinicians, this is important because patients may report generally good overall health while still experiencing pain, discomfort, emotional distress, or treatment-related concerns that require targeted assessment.

The present findings also help position this study within the broader semaglutide literature. Clinical trials have generally emphasized semaglutide's benefits on HbA1c, body weight, cardiovascular outcomes, and in some studies HRQoL.[15,27] Real-world HRQoL outcomes may vary due to differences in baseline obesity, treatment duration, adherence, adverse effects, comorbidities, psychological status, and therapy expectations. This study provides local evidence from Saudi Arabia showing that semaglutide use wasn't associated with better global HRQoL, but with specific discomfort and psychological distress domains. This suggests that semaglutide-related patient experience may not be fully understood through overall HRQoL scores alone.

This study used standardized patient-reported outcome measures, including the EQ-5D-5L and PHQ-4, and calculated EQ-5D-5L index scores using the Saudi Arabian value set. It examined both overall HRQoL and domain-specific outcomes, providing a detailed understanding of patient experience. Adjusted analyses accounted for relevant sociodemographic and clinical variables, including age, gender, marital status, duration of diabetes, occupational status, educational level, and HbA1c.

Limitations

Several limitations exist. The cross-sectional design prevents causal inference and doesn't assess HRQoL changes before and after semaglutide initiation. Convenience sampling from a single diabetes center limits generalizability to other Saudi or regional populations. Semaglutide dose and duration were collected but not included in the final analysis, preventing dose-response or duration-related effects. Important clinical factors like BMI, weight change, diabetes complications, medication adherence, adverse effects, treatment satisfaction, and concurrent diabetes medications were excluded from the adjusted models, potentially causing residual confounding. Finally, dichotomizing EQ-5D-5L domains and PHQ-4 distress improved model stability but reduced the detail from the original ordinal responses.

CONCLUSION

In this cross-sectional study of T2DM patients, semaglutide use wasn't linked to better overall HRQoL, but users reported higher odds of pain, anxiety, depression, and psychological distress. Global HRQoL measures may not fully capture patient experience, especially with obesity, comorbidities, treatment expectations, or psychosocial concerns. Incorporating patient-reported outcomes can help identify areas needing clinical attention. Future studies in Saudi patients with T2DM should assess HRQoL before and after semaglutide initiation, considering BMI, weight change, dose, duration, adverse effects, complications, adherence, and satisfaction.

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REFERENCES

1. International Diabetes Federation. Saudi Arabia. Available at: https://idf.org/our-network/regions-and-members/middle-east-and-north-africa/members/saudi-arabia/. Accessed on 26 April 2026.
2. American Diabetes Association. American Diabetes Association releases Standards of Care in Diabetes-2026. Available at: https://diabetes.org/newsroom/press-releases/american-diabetes-association-releases-standards-care-diabetes-2026. Accessed on 26 April 2026.
3. ElSayed NA, McCoy RG, Aleppo G, Bajaj M, Balapattabi K, Beverly EA, et al. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Care in Diabetes-2025. Diabetes Care. 2025;48(1):S59-85.
4. EuroQol Research Foundation. EQ-5D-5L User Guide. Rotterdam, the Netherlands; 2019. Available at: https://euroqol.org/wp-content/uploads/2023/11/EQ-5D-5LUserguide-23-07.pdf. Accessed on 26 April 2026.
5. Bilbao-González A, González-Sáenz de Tejada M, Ferrer M, Ramallo-Fariña Y, Paja-Fano M, García-Forero C, et al. Psychometric properties of the EQ-5D-5L in diabetes mellitus patients in Spain. J Patient Rep Outcomes. 2025;9(1):60.
6. Jankowska A, Młyńczak K, Golicki D. Validity of EQ-5D-5L health-related quality of life questionnaire in self-reported diabetes: evidence from a general population survey. Health Qual Life Outcomes. 2021;19(1):138.
7. EuroQol Research Foundation. Value sets for scoring the EQ-5D. Available at: https://euroqol.org/information-and-support/resources/value-sets/. Accessed on 26 April 2026.
8. Al-jedai A, Almudaiheem H, Al-Salamah T, Aldosari M, Almutairi AR, Almogbel Y, et al. Valuation of EQ-5D-5L in the Kingdom of Saudi Arabia: A National Representative Study. Value in Health. 2024;27(5):552-61.
9. Al Sayah F, Jin X, Short H, McClure NS, Ohinmaa A, Johnson JA. A Systematic Literature Review of Important and Meaningful Differences in the EQ-5D Index and Visual Analog Scale Scores. Value in Health. 2025;28(3):470-6.
10. Yang K, Fang Y, He J, Li J. Prevalence and risk factors of depression in patients with diabetes mellitus: a systematic review and meta-analysis. Front Endocrinol (Lausanne). 2025;16:1660478.
11. Alwhaibi M. Depression, Anxiety, and Health-Related Quality of Life in Adults with Type 2 Diabetes. J Clin Med. 2024;13(20):6028.
12. Kroenke K, Spitzer RL, Williams JBW, Lowe B. An Ultra-Brief Screening Scale for Anxiety and Depression: The PHQ-4. Psychosomatics. 2009;50(6):613-21.
13. Ghaheri A, Omani-Samani R, Sepidarkish M, Hosseini M, Maroufizadeh S. The Four-item Patient Health Questionnaire for Anxiety and Depression: A Validation Study in Infertile Patients. Int J Fertil Steril. 2020;14(3):234-9.
14. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, et al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Eng J Med. 2016;375(19):1834-44.
15. Jódar E, Michelsen M, Polonsky W, Réa R, Sandberg A, Vilsbøll T, et al. Semaglutide improves health-related quality of life versus placebo when added to standard of care in patients with type 2 diabetes at high cardiovascular risk. Diabetes Obes Metab. 2020;22(8):133-47.
16. Bekairy AM, Bustami RT, Almotairi M, Jarab A, Katheri AM, Aldebasi TM, et al. Validity and reliability of the Arabic version of the the EuroQOL (EQ-5D). A study from Saudi Arabia. Int J Health Sci (Qassim). 2018;12(2):16-20.
17. AlHadi AN, AlAteeq DA, Al-Sharif E, Bawazeer HM, Alanazi H, AlShomrani AT, et al. An arabic translation, reliability, and validation of Patient Health Questionnaire in a Saudi sample. Ann Gen Psychiatry. 2017;16(1):32.
18. Ernstsson O, Burström K, Heintz E, Mølsted Alvesson H. Reporting and valuing one's own health: a think aloud study using EQ-5D-5L, EQ VAS and a time trade-off question among patients with a chronic condition. Health Qual Life Outcomes. 2020;18(1):388.
19. Bilbao-González A, González-Sáenz de Tejada M, Ferrer M, Ramallo-Fariña Y, Paja-Fano M, García-Forero C, et al. Psychometric properties of the EQ-5D-5L in diabetes mellitus patients in Spain. J Patient Rep Outcomes. 2025;9(1):60.
20. Amaama LA, Osei GN, Okyere P, Opoku VO, Yankey TJ, Attoh T, et al. Health-related quality of life of type 2 diabetes mellitus patients: A cross-sectional study in

the cape coast metropolis. Health Sci Rep. 2024;7(2):e1937.
21. Rubino D, Bjorner JB, Rathor N, Sharma AM, von Huth Smith L, Wharton S, et al. Effect of semaglutide 2.4 mg on physical functioning and weight- and health-related quality of life in adults with overweight or obesity: Patient-reported outcomes from the 1-4 trials. Diabetes Obes Metab. 2024;26(7):2945-55.
22. Menoth Mohan D, Al Anouti F, Kohli N, Khalaf K. Association of obesity with musculoskeletal health and functional mobility in females-a systematic review. Int J Obes. 2025;49(11):2184-205.
23. Garcia MM, Corrales P, Huerta MÁ, Czachorowski MJ, López-Miranda V, Medina-Gómez G, et al. Adults with excess weight or obesity, but not with overweight, report greater pain intensities than individuals with normal weight: a systematic review and meta-analysis. Front Endocrinol (Lausanne). 2024;15:1340465.
24. Novo Nordisk. Ozempic prescribing information. 2025. Available at: https://www.ozempic.com/prescribing-information.html. Accessed on 26 April 2026.
25. Wojujutari Ajele K, Sunday Idemudia E. The role of depression and diabetes distress in glycemic control: A meta-analysis. Diabetes Res Clin Pract. 2025;221:112014.
26. U.S. Food and Drug Administration. Update on FDA's ongoing evaluation of reports of suicidal thoughts or actions in patients taking a certain type of medicines approved for type 2 diabetes and obesity. 2024. Available at: https://www.fda.gov/drugs/drug-safety-communications/update-fdas-ongoing-evaluation-reports-suicidal-thoughts-or-actions-patients-taking-certain-type. Accessed on 26 April 2026.
27. Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, et al. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. N Eng J Med. 2023;389(24):2221-32.

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