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Prognostic Utility of a Self-Reported Depression Questionnaire versus Clinician-Based Assessment on Renal Outcomes

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Abstract

Background—The prognostic utility of self-administered depression scales in CKD independent of a clinician-based Major Depressive Disorder (MDD) diagnosis is not clearly established, nor the optimal cutoff scores for predicting outcomes. The overlap between symptoms of depression and chronic disease raises the question of whether a cut-off score on a depression scale can be substituted for a time-consuming diagnostic interview to prognosticate risk.

Methods—The Quick Inventory of Depression Symptomatology Self-Report (QIDS-SR₁₆) was administered to 266 consecutive outpatients with non-dialysis CKD, followed prospectively for 12 months for an *a priori* composite outcome of death or dialysis or hospitalization. Association of QIDS-SR₁₆ best cut-off score, determined by receiver/responder operating characteristics curves, with outcomes was investigated using survival analysis. The effect modification of an interview-based clinician MDD diagnosis on this association was ascertained.

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Results—There were 126 composite events. A QIDS-SR₁₆ cutoff 8 had the best prognostic accuracy, HR =1.77 (1.24–2.53), $p=0.002$. This cutoff remained significantly associated with outcomes even after controlling for comorbidities, eGFR, hemoglobin and serum albumin, adjusted HR (aHR) =1.80 (1.23–2.62), $p=0.002$, and performed similarly to a clinician-based MDD diagnosis [aHR =1.72 (1.14, 2.68)]. Adjustment for MDD conferred the association of QIDS-SR₁₆ with outcomes no longer significant.

Conclusions—QIDS-SR₁₆ cutoff 8 adds to the prognostic information available to practicing nephrologists during routine clinic visits from comorbidities and laboratory data. This cutoff score performs similarly to a clinician diagnosis of MDD and provides a feasible and time-saving alternative to an interview-based MDD diagnosis for determining prognosis in CKD patients.

Keywords

Depression; chronic kidney disease; outcomes; survival; hospitalization; prognosis

INTRODUCTION

Depression is more prevalent among patients with chronic diseases such as chronic kidney disease (CKD) as compared to the general population [1, 2]. We reported that 20% of CKD patients experience Major Depressive Disorder (MDD) [2], greater than the proportion with depression reported for other chronic diseases, such as diabetes mellitus [3], coronary artery disease [4] or congestive heart failure [5]. Higher scores on self-administered depressive symptom scales are independently associated with greater morbidity and mortality among dialysis-dependent [6–10] and non-dialysis CKD patients [11–14]. We have previously shown that when MDD is present based on a structured clinician interview, non-dialysis CKD patients are at nearly twice the risk of initiating dialysis, dying, or being hospitalized at 12 months, as compared to when MDD is absent [11]. However, it has not been clearly established whether the association of depressive symptoms, as ascertained by self-report questionnaires, with outcomes is *independent* of a MDD diagnosis and whether regardless of a MDD, these scales have prognostic utility for outcomes in CKD patients. Most importantly, clinical practice would be made far more efficient if we could identify a threshold on an easily-administered self-report scale that might offer nearly identical prognostic information at less cost and time than it would take to establish MDD diagnosis using a clinician-based interview.

In addition to depression, patients with chronic diseases, such as CKD, also report many physical symptoms, such as low energy, poor appetite, sleep disturbance, and psychomotor agitation or retardation [15]. Importantly, a large burden of such symptoms is associated with medical comorbidities [16] and impaired health-related quality of life [17]. There is some overlap between these symptoms of depression and those of chronic disease, which may confound the assessment of depression in this group of patients, as well as overestimate the association of depression with clinical outcomes [18]. A recent meta-analysis found that self-report depression scales may overestimate the presence of MDD as compared with the clinician-administered interviews in patients with CKD and End-Stage Renal Disease (ESRD) [18]. Although somatic symptoms were reported to increase risk of adverse outcomes in patients with cardiovascular disease (CVD) [15, 19], it is not entirely evident

whether it is these symptoms that confer increased risk in CKD patients or the actual presence of a MDD. It remains unclear whether association of depressive symptoms on self-report scales with outcomes is independent of MDD, or is attenuated after adjusting for MDD.

We chose to evaluate the 16-item Quick Inventory of Depressive Symptomatology-Self Report scale (QIDS-SR₁₆) in this regard (see supplement) because: 1) it is in the public domain and short and easy for practitioners to use [20]; 2) it evaluates the same 9 criterion symptom domains that define a major depressive episode for a diagnosis of MDD in both the fourth and fifth editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) [21, 22]; 3) we previously validated the QIDS-SR₁₆ against a DSM-based interview for diagnosis of MDD among non-dialysis CKD patients [23]; 4) and, finally, a clinician-based version of the QIDS is currently being used as the primary outcome measure in 2 ongoing large randomized controlled trials of depression treatment in non-dialysis CKD [24] and ESRD patients [25].

We sought to investigate 1) whether higher QIDS-SR₁₆ scores are associated with adverse outcomes in patients with non-dialysis CKD, independent of estimated glomerular filtration rate (eGFR) and medical comorbidities; 2) the best prognostic cutoff score on the QIDS-SR₁₆ using receiver/responder operating characteristics (ROC) curve analysis; 3) whether the diagnosis of MDD based on a clinical interview confers any additional prognostic information. We hypothesized that baseline QIDS-SR₁₆ score would be associated with death, hospitalization, or progression to ESRD and dialysis at 12 months in patients with non-dialysis CKD, even after adjusting for cardiovascular (CV) comorbidities and other risk factors that were shown to predict poor outcomes in this high risk group. We also hypothesized that adjustment for MDD would attenuate the association and would not provide additional prognostic information beyond that provided by the QIDS-SR₁₆ [26].

SUBJECTS AND METHODS

Study Design, Setting & Participants

It is a prospective observational study of outpatients with CKD, and was approved by the Institutional Review Board in accordance with ethical standards and Helsinki Declaration of 1975, as revised in 2000. Patients were approached consecutively for participation during presentation for a routine CKD clinic visit at the Dallas Veterans Affairs Medical Center. Written informed consent was obtained prior to enrollment. Patients were eligible if they had stages 2–5 non-dialysis CKD for at least 3 months, defined as an eGFR <90 mL/min/1.73 m². To be categorized as CKD, other evidence of kidney disease apparent by either pathology of kidney on biopsy or markers of kidney damage on urinary studies or imaging [27] had to be present for at least 3 months if eGFR was 60–89 mL/min/1.73m². Patients on dialysis, kidney transplant recipients and those who could not sign consent were excluded.

Clinical Covariates

Computerized medical records and patient interviews were used to collect demographic and clinical data. Use of insulin or oral hypoglycemic medication or documentation of diabetes

mellitus on the medical chart was used to define diabetes mellitus. CVD was defined as the presence of coronary artery disease, congestive heart failure, cerebrovascular or peripheral vascular disease. The number of medical comorbidities other than diabetes or CVD was also recorded. Drug and alcohol abuse (current or past) was noted as present if self-reported or documented in the medical record. Baseline laboratory data were recorded at enrollment. The 4-variable *Modification of Diet for Renal Disease Study* formula was used to calculate eGFR [28].

Assessments of Depression

QIDS-SR₁₆ was administered to all participants at enrollment by research personnel blinded to medical records. QIDS-SR₁₆ takes 5 to 10 minutes to complete. Total score ranges from 0 to 27 with higher scores indicating higher depression severity. It assesses each of the 9-criterion symptom domains used by DSM IV to define MDD [26, 29]. We previously validated the QIDS-SR₁₆ as a screening tool for MDD in patients with CKD [23]. For the formal diagnosis of a current MDD, the Mini International Neuropsychiatric Interview (MINI), a DSM IV-based validated structured interview that has also been used in CKD patients, was administered to all of the participants by trained assessors who were blinded to the patients' past medical history and to the QIDS-SR₁₆ score [23, 30–31]. This interview takes 30 to 60 minutes to administer, and assessors have to be trained in its administration. If a current MDD was diagnosed by MINI, the patient and their primary care provider were informed, and the patient was offered either treatment with a selective serotonin reuptake inhibitor or an increase in dose if already receiving an antidepressant medication.

Outcome Measures

The *a priori* primary outcome was a composite of the occurrence of one or more of the following events: 1) progression to ESRD (i.e., initiation of chronic hemodialysis, peritoneal dialysis or kidney transplantation) or 2) death or 3) hospitalization from any cause. Participants were prospectively followed for 12 months. Events were adjudicated by 2 members of the research team blinded to depression scores at pre-specified time-points, 6 and 12 months after enrollment. Each event was determined by first searching the medical records and then confirmed by direct patient contact. The participants were also asked about any hospitalizations or events that may have occurred at outside facilities, and subsequently, outside medical records were obtained to confirm the events and dates.

Statistical Analysis

Logistic regression and ROC curve analysis was used to derive the optimal QIDS-SR₁₆ cutoff score with the best prognostic accuracy for the composite outcome, based on the Kraemer's quality index [32]. Positive and negative likelihood ratios were estimated using the method of Simel [33]. Variables were compared based on the derived cutoff [23]. Student's *t*-test or one-way ANOVA was used for comparing continuous, and chi-square or Fisher's exact test for categorical variables. Kaplan-Meier curves estimated time to events, which was compared among groups using Log-rank statistics. Censorship took place at first event, last follow-up, or 12 months if the participant was alive, not hospitalized or initiated on dialysis. Complete case analysis was used when data were missing for included covariates. Four patients were excluded from the survival analyses for the composite event

and hospitalization because of missing time data. Multivariable Cox Proportional hazards models were constructed to investigate the independent associations of total and cutoff score with the composite outcome. Candidate independent variables were included in the models only if clinically relevant and significantly associated with the composite, with a retention p -value <0.05 . MDD was entered into the multivariable models to investigate whether MDD would attenuate the association of QIDS-SR₁₆ with outcomes. Finally, a sensitivity analysis was performed to investigate whether treatment of MDD would make a difference in the association of QIDS-SR₁₆ with outcomes. "Treatment" was defined as either the prescription of a new antidepressant medication or increasing the dose of an already prescribed antidepressant. All statistical tests were two-sided, conducted at the nominal significance level of 0.05. Statistical analyses were performed using SAS 9.3 (SAS, Inc., Cary, NC) software.

RESULTS

Baseline Characteristics

The flowchart of the number of participants that were enrolled and completed follow-up is described in Figure 1. Mean age ($n=266$) was 64 ± 12 years (range 25–89 years), and 2 were women. One hundred and fifty patients (56.4%) were white, 99 (37.2%) were African American, and 17 (6.4%) were of other races. Diabetes mellitus was present in 55.8% and hypertension in 97.0%. Mean eGFR was 31.6 ± 16.7 mL/min/1.73 m². The frequencies of CKD stages 2, 3, 4, and 5 were 17 (6.4%), 101 (38.0%), 109 (41.0%), and 39 (14.6%), respectively. The mean QIDS-SR₁₆ score was 7.1 ± 4.9 and median (interquartile range) was 6.0 (3.0–10.0), with a range of 0 to 21.0. Of the cohort, 56 (21.0%) met diagnosis for a current MDD.

Optimal QIDS-SR₁₆ Cutoff Score

The optimal QIDS-SR₁₆ cutoff score with the best prognostic accuracy for the composite outcome was 8, with a positive likelihood ratio (LR) of 1.67, 95% CI (0.23 – 11.97) and a negative LR of 0.75 (0.62 – 0.90). Of the 266 participants with a completed QIDS-SR₁₆, 98 (37%) scored ≥ 8 and 168 (63%) <8 . There was a high degree of overlap between the presence of a MDD and a QIDS score of 8 or more: 96% of subjects with an MDD also had a QIDS-SR₁₆ ≥ 8 and 79% of subjects without a MDD had a QIDS-SR₁₆ <8 . Participants with a QIDS-SR₁₆ ≥ 8 (vs. <8) were younger ($p=0.02$), and fewer of them were employed ($p=0.01$) (Table 1). Stages of CKD and presence of hypertension and CVD did not differ among groups. A higher proportion of those with QIDS-SR₁₆ ≥ 8 vs. <8 had a history of drug or alcohol abuse ($p=0.03$), history of depression ($p<0.0001$), or were receiving antidepressant medications ($p<0.0001$). Laboratory values did not differ among groups (Table 1).

Association of QIDS-SR₁₆ with Outcomes

There were 126 composite events, with 37 instances of progression to dialysis, 18 deaths, and 115 instances of at least one hospitalization. Kaplan-Meier estimate of participants experiencing a composite event was greater among those who scored ≥ 8 vs. <8 on the QIDS-SR₁₆ (59.8% vs. 41.0%, $p=0.001$). A significantly higher percentage of those with

QIDS-SR₁₆ ≥ 8 vs. <8 progressed to dialysis (20.2% vs. 11.0%, $p=0.045$). Similarly, a higher percentage of those with QIDS-SR₁₆ ≥ 8 died (11.8% vs. 4.3% if <8, $p=0.021$). Percentage of hospitalizations were 56.2% among participants with score ≥ 8 and 38.3% if score <8, $p=0.003$. Event-free mean survival time, defined as the time to death, dialysis, or first hospitalization, was 221.8 days, 95% CI (194.1–249.5 days) if score ≥ 8 and was significantly longer if score <8 at 279.1 days (260.6–297.6 days), $p=0.001$ (Figure 2).

A QIDS-SR₁₆ cutoff score of ≥ 8 was significantly associated with the composite outcome measure, unadjusted hazard ratio (HR) 1.77 (95% CI: 1.24–2.53). Other variables that were associated significantly with the composite outcome in univariate analyses are included in Table 2.

In multivariable analysis, the association of QIDS-SR₁₆ score ≥ 8 with the composite outcome measure remained significant even after controlling for age, race, eGFR, serum albumin, hemoglobin, CPP, diabetes mellitus, CVD, other medical comorbidities and drug or alcohol abuse, HR 1.80 (1.23–2.62) (Table 3). In the multivariable model, other covariates associated with the composite outcome included younger age, white race, presence of diabetes, and lower baseline eGFR, hemoglobin, and albumin (Table 4). Importantly, the magnitude of risk of QIDS-SR₁₆ ≥ 8 for the composite was, in fact, higher than that of diabetes, CVD, or comorbid illness in both univariate and multivariable models (Tables 2 and 4).

Taken continuously, each unit (point) increase in the total QIDS-SR₁₆ score was also associated with a 5% higher risk of progression to dialysis, hospitalization and death, HR 1.05 (95% CI: 1.02–1.09), which remained statistically significant even in the adjusted model (Table 3). Controlling for antidepressant treatment (defined as either prescribing a new antidepressant medication or increasing the dose of an already prescribed antidepressant after a MDD was diagnosed) did not significantly change the association between QIDS-SR₁₆ and outcomes (Table 3). However, adjustment for the diagnosis of a MDD attenuated these associations so that the correlations were no longer significant (Table 3). The hazard ratios for the associations of MDD with outcomes were similar to that of the QIDS-SR₁₆ cutoff of 8 in both unadjusted and adjusted models (Table 3).

DISCUSSION

We report three important new findings: 1) the total score on a validated and easily administered self-report scale that tests the 9 symptom criterion domains of depression, the QIDS-SR₁₆, is independently associated with clinically important outcomes in consecutively recruited participants with non-dialysis CKD, independent of medical comorbidities, eGFR, hemoglobin and serum albumin; 2) the optimal cutoff score on this scale with the best prognostic utility is ≥ 8; 3) the hazard ratios for the associations of MDD with outcomes are similar to that of the QIDS-SR₁₆ cutoff of 8 and controlling for MDD presence attenuates the association of QIDS-SR₁₆ with outcomes. Therefore, the QIDS-SR₁₆ may provide a feasible and time-saving alternative to a MDD diagnosis based on a clinician-conducted interview for determining prognosis in CKD patients.

Our finding of a direct and independent association between total QIDS-SR₁₆ score and clinically important outcomes in CKD patients confirms findings from previous studies using other self-report depression scales. Importantly, it extends prior findings to establish that severe depressive symptoms are associated with poorer outcomes even *after controlling* for both comorbid illnesses common in CKD patients (such as diabetes and CVD) and other factors associated with poor outcomes in CKD (such as eGFR, serum albumin and CPP). Tsai, *et al.* reported a 3% increase in the risk of death or dialysis initiation per unit increase in baseline Beck Depression Inventory II (BDI-II) score in pre-dialysis Taiwanese CKD patients [13]. The analyses were not adjusted for CVD and other comorbidities, and 10% of participants were lost to follow-up. Kellerman, *et al.* reported 3% increase in mortality per unit increase in baseline BDI-II score in CKD patients with baseline serum creatinine concentrations 4.85 mg/dL [14]. Again, there was no adjustment for comorbidities and eGFR. In addition, the sample was 90% Caucasian, which is not representative of the U.S. CKD population. A secondary analysis of the *African American Study of Kidney Disease* cohort reported an important association between the total BDI-II score and CV outcomes [12], but did not reveal a significant association with renal outcomes or all-cause mortality. Inclusion of only African Americans, lack of diabetes as a comorbid condition, and use of another symptom scale may have influenced these differential findings. Clearly, we confirm and extend findings on the BDI-II and establish QIDS-SR₁₆ as a valid tool for assessing depression symptom severity and prognosticating outcomes in non-dialysis CKD patients, independent of comorbidities. We believe that the QIDS-SR₁₆ has some advantages as a useful screening tool in CKD as it has fewer items than the BDI, rates only the elements that define an episode of MDD, and is in the public domain for individual users who are not charging for the test [20].

We also show that controlling for MDD presence renders the association between QIDS-SR₁₆ scores and adverse outcomes no longer significant. This result was expected and confirms the potential of using the QIDS-SR₁₆ as an alternative to interview-based MDD diagnosis for prognosticating outcomes. The well-known overlap between the physical symptoms of depression and those of chronic diseases raises the question of whether it is the presence of comorbid illness or MDD that confers the increased risk. Given that symptoms reported by patients with chronic illness, such as fatigue, decreased concentration, sleep disturbance, and appetite changes, overlap with physical symptoms of depression, it has been proposed that presence of such symptoms on self-report questionnaires may confound and, perhaps, inflate the association between depressive affect and poor outcomes [6]. Previous studies that reported association of BDI-II with outcomes demonstrate conflicting results on whether the somatic or the cognitive component of the scale drives most of the association. Although a cross-sectional study of 460 dialysis-dependent patients reported that the *somatic* subgroup of the BDI-II explains 81% of the variance in the best-fitted model for depressive symptom severity [34], Kimmel *et al.* reported that not only the time-varying total score, but also the cognitive subgroup of the BDI-II was associated with mortality in 295 dialysis-dependent participants [8]. For this reason, we adjusted our analyses for the diagnosis of MDD to see if controlling for this factor affects the association between QIDS-SR₁₆ and outcomes. We observed that although the association was independent of presence of diabetes mellitus and other comorbid illnesses, and it remained significant even after

controlling for eGFR, serum albumin, CPP and hemoglobin, it was attenuated and lost its statistical significance after MDD was introduced into the models. This finding supports the hypothesis that the presence of a diagnosis of depression, and not just physical symptoms of depressive affect, confers increased risk.

Finally, we identify an optimal threshold on the QIDS-SR₁₆ for prognosticating outcomes in non-dialysis CKD patients, providing a feasible alternative to a structured interview needed to establish MDD presence, which requires significantly more clinician time and training to administer. Several studies reported a correlation between total scores on self-reported depression questionnaires and adverse outcomes, including CV events [12], incident ESRD [13, 35] and hospitalization [6] and a few showed that pre-specified BDI or PHQ-9 thresholds correlated with such outcomes [8, 12, 35]. Fischer, *et al.* used *previously validated* BDI-II thresholds (11 and 14) as a substitute for depression diagnosis in CKD patients and found that the incidence of CV death/hospitalization was significantly greater for participants with baseline scores of 11 or 14 [12]. Yu, *et al.* reported a 1.85-higher hazard of incident ESRD in diabetic patients with baseline PHQ scores 10 (threshold for MDD) vs. <10 [35]. However, these studies used pre-specified thresholds that were previously validated for *depression diagnosis*, and did not set out *a priori* to identify the best prognostic cutoff score for *outcomes* using ROC analysis, as we report here.

Using a structured, clinician-administered interview, we previously validated a QIDS-SR₁₆ cutoff score of 10 to have the best diagnostic accuracy as a screening tool for a MDD in patients with CKD [23]. Now we establish that a cutoff of 8 has the best prognostic accuracy for predicting outcomes. This may suggest that patients with significant depressive symptoms that do not quite hit the DSM thresholds for MDD may be still at substantial risk for poorer outcomes. For example, one paper found the optimal QIDS-SR₁₆ cutoff for minor depression to be in the general population [36], which is below the threshold of 10 for MDD. In addition, several mechanisms have been proposed and investigated to explain the association of depressive symptoms with poor outcomes including non-adherence to prescribed medications, underlying alterations in inflammation and the immune system, enhanced hypothalamic-pituitary axis activity, and increased platelet aggregation [37].

This report has several limitations. Generalizability is limited as the sample was predominantly male Veterans, although our higher percentage of diabetics as compared to previous studies makes our data more representative of the U.S. CKD population [12, 13]. Larger studies that include more women may be needed to confirm the findings. In addition, our analysis did not adjust for time-varying covariates during the observation period, such as changing eGFR or repeated measures of depression. Whether repeated QIDS-SR₁₆ measurements would add to the prognostic value of a single measurement was not studied.

In conclusion, the QIDS-SR₁₆ was independently associated with important clinical outcomes in patients with non-dialysis CKD, but controlling for the presence of a MDD diagnosis attenuated this association. As such, the QIDS-SR₁₆ may be a valid construct that not only can be used as a tool to quickly identify and refer patients at risk for MDD, but also an efficient alternative to a structured, clinician-based interview in non-dialysis CKD patients that adds to the prognostic information otherwise available from the general

nephrology perspective. Future studies should determine whether or not depression treatment impacts morbidity and mortality in this high risk population.

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Figure 1. Flow diagram of participants

MINI, Mini International Neuropsychiatric Interview; QIDS-SR₁₆: Quick Inventory of Depression Symptomatology Self-Report Scale.

Figure 2. Kaplan-Meier survival curve for time to first event based on QIDS-SR₁₆ cutoff score QIDS-SR₁₆, Quick Inventory of Depression Symptomatology Self-Report Scale; Composite event: death, hospitalization, or initiation of renal replacement therapy (peritoneal or hemodialysis). Four participants were missing time data for hospitalization and were excluded from the survival analyses for composite event and hospitalization.

Table 1Baseline Characteristics by QIDS-SR₁₆ Cutoff Score

Variable	QIDS-SR ₁₆ <8 (N =168)	QIDS-SR ₁₆ ≥ 8 (N =98)
Demographic Variables		
Age (y), mean (SD)	65.7 (11.7)	62.3 (12.2) [†]
Men (vs. women), %	99.4	99.0
Race, %		
White	58.9	52.0
African American	35.1	40.8
Other	6.0	7.1
High school or higher education, %	62.7	53.2
Married, %	68.3	65.3
Employed, %	24.1	11.2 [†]
Clinical Variables		
Chronic Kidney Disease, %		
Stage 2	6.6	6.1
Stage 3	39.3	35.7
Stage 4	40.5	41.8
Stage 5	13.7	16.3
Diabetes mellitus, %	53.9	59.2
Hypertension, %	97.6	95.9
Cardiovascular disease, %	61.3	65.3
Other comorbid illnesses ²		
Mean (SD)	1.5 (0.8)	1.7 (0.7)
Median (IQR)	1.0 (1.0–2.0)	2.0 (1.0–2.0)
History of drug or alcohol abuse, %	24.7	37.8 [†]
History of depression, %	12.7	44.8 [†]
Use of antidepressant medication, %	12.5	32.7 [†]
Laboratory Values, mean (SD)		
Hemoglobin (g/dL)	12.4 (2.0)	12.5 (1.9)
Ca x Phos Product (mg ² /dL ²)	36.0 (8.7)	37.6 (8.8)
Albumin (g/dL)	4.0 (0.4)	4.0 (0.6)
Creatinine (mg/dL)	3.1 (2.0)	3.5 (3.0)
Blood urea nitrogen (mg/dL)	42.0 (19.6)	42.6 (22.1)
Estimated GFR (mL/min/1.73m ²)	31.9 (16.5)	31.0 (17.1)

QIDS-SR₁₆: 16-Item Quick Inventory of Depression Symptomatology Self-Report Scale

Conversion factors for units: serum creatinine in mg/dL to mol/L, × 88.4; serum urea nitrogen in mg/dL to mmol/L, × 0.357.

¹ Cardiovascular disease refers to coronary artery disease, congestive heart failure, cerebrovascular disease or peripheral vascular disease.

²Other comorbid illnesses refers to the number of medical comorbidities other than diabetes or cardiovascular disease.

[†]*P*-value <0.05 for comparison between QIDS-SR₁₆ <8 vs. QIDS-SR₁₆ ≥ 8

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Table 2

Univariate Cox Proportional Hazards Estimates for the Composite Outcome

Variable	Hazard Ratio (95% CI)	P-value
Demographic Variables		
Age, per year increase	0.99 (0.98–1.00)	0.17
Race (White vs. African American and other)	1.07 (0.75–1.54)	0.70
High school or higher education	1.02 (0.71–1.47)	0.91
Married	0.92 (0.63–1.34)	0.66
Employed	0.98 (0.62–1.55)	0.94
Clinical Variables		
Diabetes mellitus	1.48 (1.02–2.14)	0.04
Hypertension	0.94 (0.35–2.54)	0.90
Cardiovascular disease	1.22 (0.83–1.78)	0.31
Other comorbid illnesses, per unit increase	1.42 (1.14–1.78)	0.01
History of drug or alcohol abuse	1.54 (1.06–2.24)	0.02
History of depression	1.70 (1.16–2.50)	0.01
Use of antidepressant medication	1.71 (1.14–2.56)	0.01
Laboratory Values		
Hemoglobin, per unit decrease	1.19 (1.06–1.34)	<0.001
Ca x Phos Product, per unit increase	1.04 (1.02–1.06)	<0.001
Albumin, per unit decrease	2.09 (1.40–3.10)	<0.001
Creatinine, per unit increase	1.10 (1.06–1.14)	<0.001
Blood urea nitrogen, per unit increase	1.02 (1.01–1.03)	<0.001
Estimated GFR, per unit decrease	1.02 (1.01–1.04)	<0.001

Table 3Cox Proportional Hazards Models for Composite Outcome Based on QIDS-SR₁₆ and MDD

Variable	Hazard Ratio (95% CI)			
	Unadjusted	Adjusted ¹	Adjusted + MDD ²	Adjusted + Treatment ³
QIDS-SR ₁₆ Score, per unit increase	1.05 (1.02–1.09)	1.05 (1.01–1.09)	1.03 (0.97–1.08)	1.05 (1.01–1.09)
QIDS-SR ₁₆ Cutoff ≥ 8	1.77 (1.24–2.53)	1.80 (1.23–2.62)	1.61 (0.98–2.64)	1.82 (1.22–2.70)
MDD Presence	1.82 (1.22–2.72)	1.75 (1.14–2.68)		1.89 (1.15–3.10)

QIDS-SR₁₆: 16-Item Quick Inventory of Depression Symptomatology Self-Report Scale; MDD: Major Depressive Disorder

¹ Adjusted for age, race, eGFR (estimated glomerular filtration rate), diabetes mellitus, cardiovascular disease, other comorbidities, drug or alcohol use, serum albumin, hemoglobin, and calcium x phosphorus product.

² Adjusted for all covariates in number 1, plus the presence of a current Major Depressive Disorder.

³ Adjusted for all covariates in number 1, plus if antidepressant medication was initiated or if the dose of an existing antidepressant was increased for a Major Depressive Disorder.

Table 4

Multivariable Model: Adjusted Hazard Ratios for Individual Covariates

Variable	Hazard Ratio (95% CI)	P-value
QIDS-SR ₁₆ Cutoff = 8	1.80 (1.23–2.62)	0.01
Age, per year increase	0.98 (0.96–1.00)	0.05
Race (White vs. African American and other)	1.58 (1.06–2.36)	0.02
Estimated GFR, per unit decrease	1.04 (1.02–1.05)	0.01
Diabetes mellitus	1.33 (0.90–1.97)	0.16
Cardiovascular disease	1.13 (0.75–1.71)	0.55
Other comorbid illnesses, per unit increase	1.29 (0.99–1.69)	0.06
History of drug or alcohol abuse	1.05 (0.69–1.59)	0.82
Hemoglobin, per unit decrease	1.37 (1.24–1.51)	0.01
Albumin, per unit decrease	3.03 (2.17–4.24)	<0.001
Ca x Phos Product, per unit increase	1.01 (0.98–1.03)	0.49