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## The Association of Lower Urinary Tract Symptoms, Depression and Suicidal Ideation: Data from the 2005–2006 and 2007–2008 National Health and Nutrition Examination Survey

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### Abstract

**Purpose**—We examine the association among depression, suicidal ideation and self-reported lower urinary tract symptoms using a large, cross-sectional, population based study.

**Materials and Methods**—The study included 2,890 men from the 2005–2006 or 2007–2008 cycles of the NHANES (National Health and Nutrition Examination Survey) who were 40 years old or older. Men were asked if they experienced nocturia, urinary hesitancy and/or incomplete bladder emptying. The PHQ-9 (Patient Health Questionnaire-9) was used to determine the likelihood of clinical depression and suicidal ideation.

**Results**—The prevalence of lower urinary tract symptoms was 33.7% and 10.3% for men reporting 1 and 2 or more symptoms, respectively. Moderate to severe depression (PHQ-9 score 10 or greater) and suicidal ideation were reported by 181 (6.3%) and 105 (3.6%) men, respectively. Men reporting moderate to severe depression (compared to those reporting minimal depression) had a higher odds of reporting lower urinary tract symptoms (adjusted odds ratio [AOR] 5.09, 95% CI 3.17–8.17 for PHQ-9 score 5 to 9 and AOR 7.62, 95% CI 3.90–14.87 for PHQ-9 score 10 or greater;  $p$  trend <0.0001). More lower urinary tract symptoms were associated with a significantly higher odds of moderate to severe depression (AOR 3.09, 95% CI 1.86–5.15 for 1 symptom and AOR 8.06, 95% CI 4.18–15.53 for 2 or more symptoms,  $p$  trend <0.0001) and a higher odds of suicidal ideation (AOR 1.70, 95% CI 0.85–3.42 and AOR 2.71, 95% CI 1.40–5.25, respectively,  $p$  trend = 0.004).

**Conclusions**—A significant relationship was observed between lower urinary tract symptoms and depression/suicidal ideation. While the pathophysiology of the relationship and its significance in clinical practice remain unclear, clinicians may consider screening men with severe lower urinary tract symptoms for depression.

### Keywords

lower urinary tract symptoms; depression; suicide

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Lower urinary tract symptoms are a common and costly problem with more than half of the male population experiencing at least 1 urinary symptom costing billions annually to treat.<sup>1,2</sup> A condition commonly associated with LUTS is depression.<sup>3-8</sup>

Depression is the most common mental illness<sup>9</sup> and in some patients it leads to suicide. Each year suicide claims more than 1 million lives worldwide and approximately 1 of every 10,000 Americans.<sup>10</sup> While depression is more common in women, men are 3 times more likely to commit suicide.<sup>11</sup>

To our knowledge the relation between LUTS and suicidal ideation has not been studied. If an association between LUTS and suicidal ideation exists, the findings would have important implications for the clinician who treats patients with LUTS who appear depressed or report depression. Thus, we examined the association between depression and LUTS in men as well as the relation between suicidal ideation and LUTS in men. We hypothesized that depression and suicidal ideation would be associated with more urinary symptoms and that higher depression scores would be positively associated with reported LUTS.

## METHODS

### NHANES 2005-2006 and 2007-2008

The NHANES is a cross-sectional health survey conducted by the National Center for Health Statistics, a division of the Centers for Disease Control and Prevention. The NHANES uses a complex, stratified, multistage, probability cluster design to provide estimates of the health status of the United States population by selecting a nationally representative sample of civilian, noninstitutionalized people. The National Center for Health Statistics Ethics Review Board approved the protocol and all participants provided written informed consent.

### Study Population

We included men 40 years old or older who underwent at-home interviews and physical examinations at a mobile examination center. Lifestyle data (eg smoking history, type and frequency of leisure time physical activity etc) were assessed during the interview and dietary data (eg alcoholic beverage consumption) were collected using a food frequency questionnaire during the interview. Trained interviewers asked about LUTS, mental health and suicidal ideation. We excluded all men from analysis who were younger than 40 years at participation (6,670), those who reported a history of prostate cancer (141) and those missing data on LUTS or depression (475), leaving 2,890 eligible participants.

### Lower Urinary Tract Symptoms

Several questions to assess LUTS were asked of all men 40 years old or older, including 1) how many times per night do you usually get up to urinate? (bothersome nocturia,<sup>12</sup> defined as waking at least twice per night to urinate), 2) after urinating, does your bladder feel empty? (yes/no, incomplete emptying) and 3) do you usually have trouble starting to urinate? (yes/no, hesitancy). LUTS status was categorized as 0, 1, or 2 or more symptoms.

Our main LUTS outcome included men reporting at least 2 of 3 lower urinary tract symptoms. We also examined individual LUTS domains (nocturia, hesitancy and incomplete emptying) as outcomes.

### Depression

Depression status was assessed using the Patient Health Questionnaire-9 instrument, a self-administered validated module for major depression.<sup>13</sup> The PHQ-9 consists of 9 questions and is scored from 0 to 27. Depression scores were categorized into 3 groups of minimal (less than 5), mild (5 to 9) and moderate to severe (10 or greater). A PHQ-9 score of 10 or greater was used as the threshold for identifying the outcome of major depression (sensitivity 88% and specificity 88%).<sup>13</sup>

### Suicidal Ideation

The PHQ-9 addresses suicidal ideation with the single question, “Over the last 2 weeks, how often have you been bothered by thoughts that you would be better off dead or of hurting yourself in some way?” Any suicidal ideation in the last 2 weeks was considered an affirmative response for this variable. This variable was previously validated to identify outpatients at increased risk for suicide attempt or death.<sup>14</sup>

### Statistical Analysis

Those participants without LUTS were compared across categories of demographic indicators, lifestyle and mental health characteristics to those who had LUTS (2 or more symptoms). We also compared those with minimal (0 to 4) and moderate to severe (10 or greater) PHQ-9 depression scores.

Logistic regression modeling was used to calculate the OR and 95% CI of reporting the outcome (dependent variable) of LUTS (2 or more symptoms), and the individual symptoms of nocturia, incomplete bladder emptying and urinary hesitancy. When evaluating depression and suicidal ideation as the primary exposure, multivariate models were adjusted for age in years, income-to-poverty ratio (continuous), BMI (less than 25, 25 to 29, 30 kg/m<sup>2</sup> or greater), alcohol intake (intake less than once per week vs more than once per week), physical activity (any vigorous or moderate recreational activity, yes/no), current smoking (yes/no) and comorbidities (continuous score that assigned 1 point for each for cancer, coronary heart disease, stroke, hypertension and diabetes). Additional adjustment for place of birth (United States vs foreign born), race (nonHispanic white, non-Hispanic black, Hispanic, other), education (less than high school, high school graduate/some college, college graduate), health insurance (yes/no) and income (categories) did not affect the main estimates, and were left out of the final models. We considered models adjusted for sleep apnea (yes/no), psychotherapeutic agents (yes/no), mental health care visit in the last year (yes/no), emotional support (yes/no), financial support (yes/no) and the number of close friends (continuous), and retained only those variables that changed the main estimates by more than 10%.

We also used logistic regression to calculate ORs and 95% CIs of reporting the outcome (dependent variable) of moderate to severe depression (PHQ-9 score 10 or greater) and

suicidal ideation. With LUTS and the individual lower urinary tract symptoms as the primary exposure, we adjusted models for income-to-poverty ratio, BMI, alcohol intake, physical activity, current smoking and comorbidities. Additional adjustment for the other variables previously described did not affect the main estimates and, thus, they were excluded from the multivariate models.

We used sample weights that took into account the specific probabilities of selection for the individual domains that were oversampled, nonresponse, and differences between the demographic characteristics of the sample and the total United States population. All analyses were performed using SAS® version 9.3 and results with a 2-sided  $p < 0.05$  were considered statistically significant.

## RESULTS

Mean (SE) participant age was 55.9 years (0.38). The LUTS reported by the cohort are displayed in the figure. The prevalence of LUTS was 33.7% and 10.3% for men reporting 1 and 2 or more symptoms, respectively. Nocturia was the most common symptom reported (35.8%), followed by incomplete emptying (10.9%) and hesitancy (9.2%). Moderate to severe depression (PHQ-9 score 10 or greater) and suicidal ideation were reported by 181 (6.3%) and 105 (3.6%) men, respectively.

When categorized by LUTS status, men with LUTS (2 or more urinary symptoms) were more likely to be older, to have less formal education and income, to have diabetes and hypertension, to exercise less, to consume less alcohol and to take psychotherapeutic agents (see supplementary table, <http://jurology.com/>). Compared to men without depression, those with depression were more likely to be younger, to have less education than a college degree and to smoke, and were less likely to exercise and to consume alcohol on a weekly basis (data not shown).

### Outcome: LUTS (hesitancy, incomplete bladder emptying, nocturia)

With LUTS (2 or more symptoms) as the outcome, men reporting moderate to severe depression (compared to those reporting minimal depression) had a higher odds of reporting LUTS (AOR 5.09, 95% CI 3.17–8.17 for PHQ-9 score 5 to 9 and AOR 7.62, 95% CI 3.90–14.87 for PHQ-9 score 10 or greater;  $p$  trend  $< 0.0001$ , tables 1 and 2). When examining each individual lower urinary tract symptom as an outcome (hesitancy, incomplete bladder emptying, nocturia), having depression led to an increased risk of reporting each lower urinary tract symptom, with estimates increasing with worsening depression ( $p$  trend  $< 0.0001$ ). Patients with suicidal ideation were also more likely to report the outcome of LUTS (AOR 3.47, 95% CI 1.94–6.20). Those with suicidal ideation were more likely to report the outcome of nocturia (AOR 2.41, 95% CI 1.60–3.62) but other LUTS did not reach statistical significance after adjustment.

### Outcome: Depression and Suicidal Ideation

When examining depression and suicidal ideation as the outcome, men with more urinary symptoms had an increased risk of reporting moderate to severe depression (score 10 or greater) and suicidal ideation (table 3). A significant trend was observed with increasing

severity of LUTS which were associated with a significantly higher odds of moderate to severe depression (AOR 3.09, 95% CI 1.86–5.15 for 1 symptom and AOR 8.06, 95% CI 4.18–15.53 for 2 or more symptoms;  $p$  trend <0.0001) and a higher odds of suicidal ideation (AOR 1.70, 95% CI 0.85–3.42 and AOR 2.71, 95% CI 1.40–5.25, respectively,  $p$  trend = 0.004). Each individual lower urinary tract symptom analyzed increased the risk of reporting the outcome of moderate to severe depression, while only nocturia increased the odds of reporting the outcome of suicidal ideation.

## DISCUSSION

In this cross-sectional study of men 40 years old or older, those with more lower urinary tract symptoms were more likely to have depression and suicidal ideation. We also found that men with greater depression scores were more likely to have LUTS. We modeled LUTS and depression and suicidal ideation as the outcome as well as the predictor after considering possible mechanisms that may account for the direction of the relationship.

Cross-sectional studies support an association between depression and LUTS,<sup>4,7,15–18</sup> and a prospective study revealed a positive association between mental illness and incident nocturia.<sup>3</sup> Psychological as well as physiological mechanisms may explain this relationship. Chronic lower urinary tract symptoms reduce quality of life, and can lead to embarrassment, social anxiety, demoralization and poor self-esteem.<sup>19,20</sup> For men, having LUTS may carry a stigma of weakness and aging as perceived by the patient, his partner, family and friends.<sup>18</sup> Nocturia can lead to daytime drowsiness, an inability to concentrate and decreased motivation to perform activities. All of these consequences could place one at increased risk for the development of depression.

On the other hand, depressed patients may report worse subjective symptoms scores and bother due to the tendency of depressed patients to catastrophize symptoms.<sup>21,22</sup> Steers et al postulate that an underlying defect in serotonin (5-HT) synthesis may promote depression and abnormal voiding in some patients, noting that “by virtue of altered synthesis, handling or actions of 5-HT, patients genomically predisposed to depression may also be at risk for the development of idiopathic detrusor overactivity, [overactive bladder] and LUTS.”<sup>6</sup> Evidence for this hypothesis is bolstered by numerous animal models examining micturition with and without 5-HT and its metabolites.<sup>6</sup> Increased adrenergic tone and the hypothalamic-pituitary axis have similarly been proposed as mediating depressive symptoms and LUTS.<sup>5,6</sup> In this regard experiments suggest that stress induced depression or anxiety is associated with the corticotropin releasing factor pathway, which also has a role in micturition.<sup>23</sup> Inflammation has been noted to be central in the pathogenesis of depression<sup>24</sup> and LUTS.<sup>4</sup> Depressed patients frequently have increased C-reactive protein, tumor necrosis factor-alpha and interleukin-6.<sup>24</sup>

Regardless of the selected outcome we found increasing significant trends with higher depression scores and more lower urinary tract symptoms. Our findings regarding LUTS and depression in a well classified cohort representative of American men are consistent with previously published results.<sup>3–8,16–18</sup> However, this is the first study to show that LUTS in men are associated with suicidal ideation.

The public health implications of the relationship between LUTS and suicide are unknown. Macaulay et al asked 211 women, “generally how troubled are you by your bladder problems?” with 25% reporting that their urinary symptoms “make life not worth living.”<sup>25</sup> Others have studied suicide risk in primary care patients with major physical diseases. In a case-control study cancer, coronary heart disease, stroke, chronic obstructive pulmonary disease and osteoporosis were all associated with successful suicide. However, when models were adjusted for clinical depression, no increased risk was found, suggesting that depression may act as a mediator between disease and suicide.<sup>26</sup> Similarly noncancer pain conditions such as back pain, migraine, fibromyalgia and psychogenic pain have been associated with risk of suicide.<sup>27</sup> After adjustment for concomitant psychiatric conditions, associations between pain conditions and suicide were reduced while some remained significant.

The strong association of LUTS and depression demonstrated here and previously,<sup>3–8,16–18</sup> and the possible association between LUTS and suicide, raise the question of whether to perform depression screening in men with LUTS.<sup>6</sup> Steers et al suggested administering the Hospital Anxiety and Depression Scale,<sup>28</sup> a 14-item validated instrument, to urology patients.<sup>6</sup> The authors contend that failure to assess and manage symptoms of emotional distress could lead to poor communication and patient dissatisfaction with treatment outcomes, and may put patients at risk for progression of their emotional illness. A potential obstacle to this approach is the inherent time constraint of an office visit, which could make widespread implementation of such screening low. The application of screening to those at highest risk for depression (ie those with severe LUTS) may be most effective by identifying those who need help while also being time efficient.

The USPSTF (U.S. Preventive Services Task Force) examined the role of depression screening in healthy primary care patients, analogous to screening all urology patients.<sup>29</sup> They recommend against routinely screening adults for depression when staff assisted depression care supports are not in place. The USPSTF does not specifically address the benefit of screening in a specialty clinic for depression. Despite the potential sequelae of screening such as false-positive results, cost and adverse effects to patients who are incorrectly identified as being depressed, they found no harm in depression screening.

This study should be considered within its limitations. Because it is a cross-sectional study we cannot make statements regarding causality. This study also lacked a validated urinary symptom score and only assessed 3 urinary symptoms. The questions regarding LUTS addressed their presence and not the degree of bother. It could be inferred that men who are bothered by LUTS would have greater distress and, in turn, depression and suicidal ideation, thus leading to an underestimation of the association between LUTS and depression and suicidal ideation in this analysis. It is possible that important confounding variables were not included in our multivariate models, which could spuriously influence our risk estimates. Despite these limitations, the NHANES provides a unique and representative sample of the entire United States population. In men 40 years old or older we were able to demonstrate that severe LUTS and depression are associated, and that the most negative sequela of severe depression, suicidal ideation, appears to be associated with LUTS.

## CONCLUSIONS

A significant association was observed between LUTS and depression/suicidal ideation. For men reporting severe LUTS, practitioners may consider screening for depression and, when appropriate, discuss mental health referral. Further research is needed to determine whether such screening would benefit patients.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Abbreviations and Acronyms

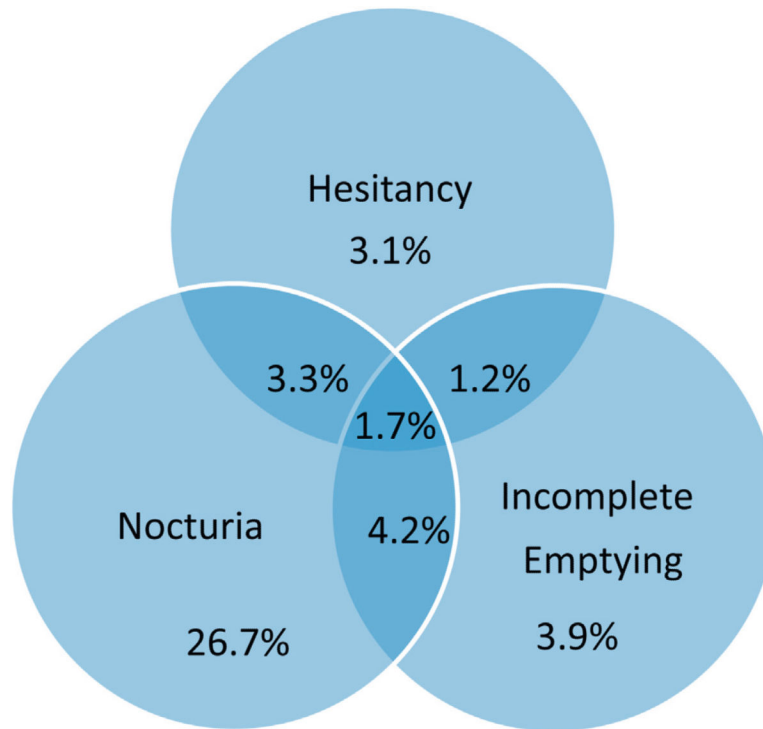
<b>BMI</b>	body mass index
<b>LUTS</b>	lower urinary tract symptoms

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Venn diagram of LUTS distribution in study population showing percentage reporting hesitancy, nocturia and incomplete emptying symptoms of 1,272 patients with LUTS from total cohort (2,890).

**Table 1**

Association between PHQ-9 depression score and LUTS

	PHQ-9 Categories		
	0-4	5-9	10-27
LUTS (2 or more symptoms):*	186	61	50
Age adjusted OR (95% CI) <sup>†</sup>	1.00	6.12 (3.98, 9.42)	11.61 (6.83, 19.73)
Multivariate adjusted OR (95% CI) <sup>‡</sup>	1.00	5.09 (3.17, 8.17)	7.62 (3.90, 14.87)
Urinary hesitancy:	177	53	37
Age adjusted OR (95% CI) <sup>†</sup>	1.00	2.61 (1.70, 4.02)	4.25 (2.57, 7.00)
Multivariate adjusted OR (95% CI) <sup>‡</sup>	1.00	2.54 (1.63, 3.97)	3.69 (2.07, 6.56)
Incomplete bladder emptying:	221	52	42
Age adjusted OR (95% CI) <sup>†</sup>	1.00	2.73 (1.89, 3.95)	3.46 (2.00, 5.98)
Multivariate adjusted OR (95% CI) <sup>‡</sup>	1.00	2.60 (1.77, 3.81)	2.95 (1.51, 5.75)
Nocturia:	759	170	106
Age adjusted OR (95% CI) <sup>†</sup>	1.00	3.09 (2.31, 4.15)	5.01 (3.37, 7.45)
Multivariate adjusted OR (95% CI) <sup>‡</sup>	1.00	2.81 (2.11, 3.73)	3.82 (2.46, 5.92)

All values p trend &lt;0.0001.

\* Reported at least 2 of 3 LUTS (trouble starting to urinate, incomplete bladder emptying and nocturia defined as 2 or more voids per night). This analysis included only those men with no LUTS or 2 or more LUTS reported.

<sup>†</sup> Adjusted for age in years, using sampling weights.

<sup>‡</sup> Adjusted for age in years, income-to-poverty ratio (continuous), BMI (less than 25, 25 to 29, 30 kg/m<sup>2</sup> or greater), alcohol intake (less than once vs more than once per week), physical activity (any vigorous or moderate recreational activity, yes/no), current smoking (yes/no) and comorbidity score (continuous, comprised of cancer yes/no, coronary heart disease yes/no, stroke yes/no, hypertension yes/no and diabetes – yes if currently using insulin or oral diabetes medications, or if their doctor told them that they were diabetic/no), using sampling weights.

**Table 2**

## Association between suicidal ideation and LUTS

	No Suicidal Ideation Reported	Yes Suicidal Ideation Reported
LUTS (2 or more symptoms): *	271	26
Age adjusted OR (95% CI) <sup>†</sup>	1.00	5.77 (3.04, 10.93)
Multivariate adjusted OR (95% CI) <sup>‡</sup>	1.00	3.47 (1.94, 6.20)
Urinary hesitancy:	250	17
Age adjusted OR (95% CI) <sup>†</sup>	1.00	2.28 (1.18, 4.40)
Multivariate adjusted OR (95% CI) <sup>‡, §</sup>	1.00	1.68 (0.87, 3.26)
Incomplete bladder emptying:	293	22
Age adjusted OR (95% CI) <sup>†</sup>	1.00	2.25 (1.26, 4.00)
Multivariate adjusted OR (95% CI) <sup>‡</sup>	1.00	1.62 (0.84, 3.12)
Nocturia:	974	61
Age adjusted OR (95% CI) <sup>†</sup>	1.00	3.48 (2.22, 5.45)
Multivariate adjusted OR (95% CI) <sup>‡</sup>	1.00	2.41 (1.60, 3.62)

\* Reported at least 2 of 3 LUTS (trouble starting to urinate, incomplete bladder emptying and nocturia defined as 2 or more voids per night). This analysis included only those men with no LUTS or 2 or more LUTS reported.

<sup>†</sup> Adjusted for age in years, using sampling weights.

<sup>‡</sup> Adjusted for age in years, income-to-poverty ratio (continuous), BMI (less than 25, 25 to 29, 30 kg/m<sup>2</sup> or greater), alcohol intake (less than once vs more than once per week), physical activity (any vigorous or moderate recreational activity, yes/no), current smoking (yes/no) and comorbidity score (continuous, comprised of cancer yes/no, coronary heart disease yes/no, stroke yes/no, hypertension yes/no and diabetes – yes if currently using insulin or oral diabetes, or if their doctor told them that they were diabetic/no), using sampling weights.

<sup>§</sup> Additionally adjusted for mental health care visit in the last year (yes/no).

**Table 3**

Association between LUTS, and depression and suicidal ideation

	Moderate-Severe Depression <sup>*</sup>			Suicidal Ideation		
	Events	Age Adjusted <sup>†</sup>	Multivariate Adjusted <sup>‡</sup>	Events	Age Adjusted <sup>†</sup>	Multivariate Adjusted <sup>‡</sup>
		OR (95% CI)	OR (95% CI)		OR (95% CI)	OR (95% CI)
LUTS status:						
No LUTS	60	1.00	1.00	39	1.00	1.00
1 Symptom	71	4.18 (2.64, 6.62)	3.09 (1.86, 5.15)	40	2.58 (1.32, 5.05)	1.70 (0.85, 3.42) <sup>§</sup>
2 or More symptoms	50	13.43 (7.46, 24.17)	8.06 (4.18, 15.53)	26	5.53 (2.73, 11.22)	2.71 (1.40, 5.25) <sup>§</sup>
p Trend <sup>*</sup>		<0.0001	<0.0001		<0.0001	0.004
Urinary hesitancy:						
No	144	1.00	1.00	88	1.00	1.00
Yes	37	4.17 (2.54, 6.85)	3.46 (1.94, 6.17)	17	2.26 (1.17, 4.38)	1.53 (0.79, 2.97) <sup>§</sup>
Incomplete bladder emptying:						
No	139	1.00	1.00	83	1.00	1.00
Yes	42	3.54 (2.03, 6.17)	2.58 (1.22, 5.43)	22	2.25 (1.26, 4.00)	1.59 (0.79, 3.17)
Nocturia:						
No	75	1.00	1.00	44	1.00	1.00
Yes	106	5.32 (3.50, 8.10)	3.68 (2.31, 5.87)	61	3.48 (2.20, 5.49)	2.23 (1.50, 3.30)

Symptoms of LUTS reported included trouble starting to urinate, incomplete bladder emptying and nocturia defined as 2 or more voids per night.

<sup>\*</sup> A total of 2,550 individuals were included in the analysis comparing those with minimal scores (less than 5) to those with moderate to severe depression scores (10 or greater). A total of 2,431 individuals were included in the analysis comparing those with minimal scores (less than 5) to those with moderately severe to severe depression scores (15 or greater).

<sup>†</sup> Adjusted for age in years, using sampling weights.

<sup>‡</sup> Adjusted for age in years, income-to-poverty ratio (continuous), BMI (less than 25, 25 to 29, 30 kg/m<sup>2</sup> or greater), alcohol intake (less than once vs more than once per week), physical activity (any vigorous or moderate recreational activity, yes/no), current smoking (yes/no) and comorbidity score (continuous, comprised of cancer yes/no, coronary heart disease yes/no, stroke yes/no, hypertension yes/no and diabetes – yes if currently using insulin or oral diabetes medications, or if their doctor told them that they were diabetic/no), using sampling weights.

<sup>§</sup> Additionally adjusted for mental health care visit in the last year (yes/no).