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The association between antidepressant use and glycemic control in the Southern Community Cohort Study (SCCS)

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Abstract

Introduction—Among people with diabetes, comorbid depression has been associated with suboptimal health outcomes. However, the independent impact of antidepressant use on glycemic control (A1C) has not been well understood.

Research Design and Methods—The Southern Community Cohort Study collected self-reported antidepressant use and measured continuous A1C in a sample of racially diverse adults with and without diabetes who visited community health clinics serving low-income families in the southeastern United States (N = 2445). Crude and adjusted linear regression models were used to examine the relationships between using specific antidepressant subclasses and continuous A1C.

Results—Although use of any single antidepressant subclass was not a significant predictor of A1C level, there was a significant association between using multiple antidepressant subclasses and higher A1C, specifically among individuals with diabetes (standardized effect size = .12, p = .04).

Conclusion—Among adults with diabetes, the use of multiple antidepressant subclasses may be a risk factor for suboptimal glycemic control. Prospective studies are needed to confirm the direction of this observation, as the present study was limited by a cross-sectional design and small sample size.

Keywords

Diabetes; Antidepressants; A1C; Glycemic control; Drug interaction

1. Introduction

1.1. Depression and Diabetes

A number of studies have observed that depression, a disorder characterized by “lowering of mood, reduction of energy, and decrease in activity” (World Health Organization, 2015) can

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lead to both an increased risk for and worsening of type 2 diabetes, a disease of impaired insulin sensitivity and/or production (Diabetes Association, 2010). Specifically, experiencing depressive symptoms is associated with an increased risk of developing type 2 diabetes (Carnethon, Jacobs, Sidney, & Liu, 2003; Eaton, Armenian, Gallo, Pratt, & Ford, 1996; Mezuk, Eaton, Albrecht, & Golden, 2008), as well as hyperglycemia (Lustman et al., 2000), a higher incidence of complications (de Groot, Anderson, Freedland, Clouse, & Lustman, 2001), disability (Egede, 2004), and increased mortality (Lin et al., 2009) among people with a diabetes diagnosis. Furthermore, among people with diabetes, the presence of more severe depressive symptoms is associated with having worse diabetes treatment adherence and increased healthcare costs (Ciechanowski, Katon, & Russo, 2000; Egede, Zheng, & Simpson, 2002).

Among adults in the United States, approximately 17% have had major depressive disorder at some point in their lives (Kessler, Chiu, Demler, Merikangas, & Walters, 2005), 9.3% currently have diabetes (Centers for Disease Control and Prevention, 2014), and an estimated 17% of those with diabetes have comorbid depression (Li, Ford, Strine, & Mokdad, 2008). Given the high prevalence of depression and diabetes, the serious consequences of comorbid depression and diabetes, and increasing trends in antidepressant use (Mojtabai & Olfson, 2014), it is important to explore the role of antidepressant use on the risk of type 2 diabetes and the worsening of glycemic control. While the literature has generally established depression as a risk factor for diabetes and poorer glycemic control, the literature is less clear on the independent impact of antidepressant medications on these outcomes. It is important to disentangle the independent effect antidepressants may have on glucose levels from the disorders they are used to treat. A number of studies have observed a direct relationship between other psychotropic agents, namely antipsychotics, and an increased risk for a number of cardiometabolic effects, including diabetes (Nielsen, Skadhede, & Correll, 2010; Ulcickas Yood et al., 2011). However, the presence of any risk or benefit to glycemic control, as measured by A1C, or glycated hemoglobin, associated with antidepressant use has not been well-established.

1.2. A1C

A1C tests measure average glucose levels over roughly the past three months, with glucose levels over the past month contributing most to the measure (Goldstein et al., 2004). An A1C test result of lower than 5.7% is considered normal, while 5.7% through 6.4% indicates prediabetes, and 6.5% or higher is used to diagnose diabetes (Diabetes Association, 2010). A1C tests are widely used to monitor glycemic control among individuals with diagnosed diabetes as part of a comprehensive treatment and self-care regimen. Research has indicated that maintaining A1C levels below 7% can reduce the risk of associated health complications among individuals with diabetes (National Institute of Diabetes and Digestive and Kidney Diseases, 2014). In addition, an elevated A1C can also indicate an increased risk for serious cardiovascular outcomes, such as heart failure and atherosclerosis among individuals without diabetes (Matsushita et al., 2010; Vitelli et al., 1997).

1.3. Antidepressants and A1C

Antidepressants are a class of drugs that treat depression by altering levels of monoamine neurotransmitters, primarily serotonin and norepinephrine, available in synapses between nerve cells (Mann, 2005). Researchers have conducted a number of studies to determine the potential effects of antidepressant use on glucose-related variables and results have varied widely. For example, a recent large cross-sectional analysis of population-based data (Mojtabai, 2013) did not observe use of any antidepressant subclass to be associated with A1C or glucose levels among individuals not diagnosed with diabetes. Other observations suggest that the impact of antidepressant use on glucose levels may vary by medication subclass and diabetes diagnosis. In a review, Deuschle (2013) observed that use of selective serotonin reuptake inhibitors (SSRIs) improved glycemic control while use of tricyclic antidepressants (TCAs) worsened glycemic control among individuals with diabetes, and use of SSRIs reduced the risk of developing diabetes for individuals without diabetes. In another review, Hennings, Schaaf, & Fulda (2012) concluded that, among individuals both with and without diabetes, use of SSRIs or monoamine-oxidase inhibitors (MAOIs) improved glucose homeostasis while use of antidepressants that act on norepinephrine worsened glucose homeostasis. They also observed that using serotonin-norepinephrine reuptake inhibitors (SNRIs) had no effect on glucose, and the evidence for any effect of using bupropion, which primarily inhibits dopamine reuptake, was unclear. Furthermore, according to this review, SSRIs may have an especially beneficial effect among individuals with diabetes. On the other hand, Kivimäki et al. (2010)) and Pan, Sun et al. (2012) observed that use of SSRIs or TCAs was associated with an increased risk of subsequent diabetes among individuals without the condition in separate prospective studies.

The aim of the current study was to determine whether antidepressant use was associated with A1C among a sample of racially diverse adults with and without diabetes who visited community health clinics serving low-income families in the southeastern United States as part of the Southern Community Cohort Study (SCCS). Because both having a low income and residing in the southeastern region are associated with elevated prevalence of diabetes and depression (Anonymous, 2009a; Anonymous, 2010; Pratt & Brody, 2014; Robbins, Vaccarino, Zhang, & Kasl, 2001), research in this less well-studied population may be more sensitive to observing a relationship between antidepressant use and A1C, if one exists.

2. Research design and methods

2.1. Participants

The SCCS investigates health disparities between African-Americans and non-Hispanic-Whites living in the southern United States, with a focus on disparities relating to cancer. The study enrolled about 85,000 individuals aged between 40 and 79 years who visited community health clinics serving low-income individuals in twelve states (Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, Virginia, West Virginia) between 2002 and 2009 (Anonymous, 2009b; Signorello et al., 2005). Participants responded to a comprehensive set of structured interview items to collect demographic information, health history, medication usage, and

other self-reported data. About half of those interviewed in community health clinics gave a blood sample at the time of enrollment.

Blood was separated and stored at −80°C at Vanderbilt University (Signorello et al., 2005). While the SCCS enrolled nearly 85,000 patients, A1C information is available for 2508 of these patients as part of two separate sub-studies, a breast cancer study (N = 1737) and a pilot biomarker study (N = 781). A1C in both samples was quantified in the Clinical Chemistry laboratories in Vanderbilt University Medical Center with the Bio-Rad Variant II Hemoglobin Testing System (HPLC) according to manufacturer's protocol. The limit of quantification was 3.1% and the coefficients of variation were between 4.0% and 5.1%. A1C from the pilot biomarker sample was measured in 2004. This sample was stratified by race, sex, smoking status, and BMI to ensure an even distribution of these covariates (Zhang et al., 2008). A1C from the breast cancer study data was measured in 2008 from two stratified samples; the entire sample was stratified by race and BMI, while one subsample within this study was also stratified by smoking status and another on menopausal status (Cohen et al., 2012). When A1C for an individual was available from both samples (N = 10) pilot biomarker A1C was used. Total sample size with complete data was 2445. Sample characteristics are listed in Table 1. The Vanderbilt Institutional Review Board approved the SCCS, and the SCCS's internal review board approved this sub-study.

2.2. Variables

The outcome of interest in the present study is continuous A1C. The exposure of interest, antidepressant use, was self-reported in the SCCS baseline questionnaire. Following the methods of Mojtabai (2013), Deuschle (2013), and Hennings et al. (2012), antidepressants were grouped by subclass; categories included only serotonin-norepinephrine reuptake inhibitors (SNRIs), only selective serotonin reuptake inhibitors (SSRIs), only tricyclic antidepressants (TCAs), only other subclasses (tetracyclic antidepressants, serotonin reuptake inhibitors, serotonin antagonist and reuptake inhibitors, or bupropion), multiple subclasses, and no antidepressant use.

Covariates included gender (man or woman), race (African-American or White), age category (40–49 years, 50–64 years, 65 years and older), education level (less than high school, high school, more than high school), smoking status (current smoker or non-smoker), CESD-10 score category, a measure of depressive symptom experience within the last week (none, mild, moderate, or severe depressive symptoms), body mass index (BMI) category (b25 kg/m^2, 25–29 kg/m^2, ≥30 kg/m^2), and diabetes status (never diagnosed or ever diagnosed with either type 1 or type 2 diabetes, excluding diagnoses received during pregnancy). Because having received a depression diagnosis was associated with CESD-10 score and was not significantly associated with the outcome, it was left out of the adjusted models. Furthermore, a large proportion of those who indicated current moderate (46%) or severe (29%) depressive symptoms indicated never having received a depression diagnosis, and we expected that depression symptomology would play a more important role in confounding a relationship between antidepressant use and A1C. Individuals who indicated having been diagnosed with sickle-cell anemia (N = 8) were excluded from analyses because of the disease's effect on biasing A1C test results (Mongia et al., 2008).

The CESD-10 measures depressive symptoms, and was derived from a longer depression inventory originally developed in the 1970s (Radloff, 1977). The shorter, 10-item version provides a similarly reliable and valid assessment of depressive symptom experience (Andresen, Malmgren, Carter, & Patrick, 1994). Items address emotional experiences, sleep quality, and motivation over the past week, with response options corresponding with the frequency with which they occurred (rarely, some of the time, a moderate amount of time, or most or all of the time). The scores of 10, 15, and 20 were used to define the lower cut-off points for mild, moderate, and severe depression, respectively, based on the methods of Osborn (Osborn et al., 2011), who previously studied depression and diabetes in the SCCS population.

2.3. Statistical analyses

SAS Studio 3.2 software (Research Triangle, NC, 2012–2014) was used to run all analyses. Sixty-three participants were missing information for at least one variable. Complete case analysis was used, resulting in $N = 2445$. Preliminary analyses included univariate frequencies and percentages and mean A1C for the entire sample and each diabetes stratum. Bivariate analyses were performed to assess the distribution of continuous A1C and antidepressant use by each predictor variable. ANOVA and chi-square tests were used to assess the statistical significance of bivariate relationships. The association between antidepressant subclass use and A1C was analyzed in crude and adjusted least-squares linear regression models. Five models were run. Once a variable was added in it was not removed from subsequent models. The first was the crude model, the second adjusted for demographic variables (age category, sex, race, and education level), the third additionally adjusted for smoking status, the fourth added CESD-10 score, and the final adjusted for BMI category in addition to all other variables to assess whether the association between antidepressant medication use and continuous A1C would be independent of BMI. Because the interaction term between subclass use and diabetes status was significant in the full linear model, models were stratified by whether participants reported ever having received a diabetes diagnosis. Diagnostics were performed to assess linear model fit. Continuous A1C was log-transformed in an attempt to normalize the distribution of errors (Bland & Altman, 1996). F statistics were used to test the association between antidepressant use and A1C. The nominal false-positive rate was set at .05 for all analyses; although results were not adjusted for multiple comparisons, we will state that those corresponding to a p-value less than .05 are “significant”.

3. Results

3.1. Sample characteristics

Sample characteristics are presented in Table 1 for the total sample and stratified by self-reported diabetes diagnosis. The sample was predominantly composed of women between the ages of 40 and 50 years. The sample was roughly half African-American and half non-Hispanic White. About one-third of the sample consisted of current smokers, the majority had a BMI classification of overweight (BMI 25.0–29.9 kg/m^2) or obese (BMI ≥30.0 kg/m^2), and about 20% indicated having been diagnosed with diabetes. About 80% ($N = 376$) of the 462 individuals in the diabetes stratum were on at least one diabetes medication.

About half of the sample indicated some level of current depressive symptoms, and about 20% indicated current use of an antidepressant medication. The most commonly used antidepressant subclass was SSRIs, and the most commonly used antidepressant medication was Zoloft® (Sertraline), followed by Paxil® (Paroxetine) and Prozac® (Fluoxetine). The mean A1C was 5.96% (standard deviation .87) among individuals without a diabetes diagnosis and 8.71% (standard deviation 2.57) among individuals with diagnosed diabetes. The median A1C for the entire sample was 6.0%.

3.2. Unadjusted associations

Antidepressant use was significantly associated with sex ($p < .0001$), age ($p = .0165$), race ($p < .0001$), depression diagnosis ($p < .0001$), CESD-10 score category ($p < .0001$), and BMI ($p = .0431$). Women (20% vs. 10%), non-Hispanic Whites (18% vs. 10%), and those under 65 (19% vs. 8%) were more likely to use antidepressant medications. Almost 85% of individuals taking any antidepressant medication indicated having received a depression diagnosis at some point, compared with less than 20% of those not taking antidepressants. Those on antidepressants also tended to be more likely to report experiencing moderate to severe depressive symptoms. Furthermore, those in a higher BMI category were more likely to use antidepressants (20% vs 14%). A1C was significantly associated with sex ($p < .0019$), age ($p < .0001$), race ($p < .0001$), education level ($p = .0001$), smoking status ($p < .0001$), BMI ($p < .0001$), and diabetes status ($p < .0001$) (Table 2). Women, older individuals, African-Americans, and those who did not complete high school tended to have higher A1C. Those in a higher BMI category, individuals with a diabetes diagnosis and individuals who were non-smokers also tended to have a higher A1C (Table 2).

Mean A1C among individuals with diabetes was 7.38 (1.72) among SNRI users, 8.49 (2.62) among SSRI users, 7.13 (1.31) among TCA users, 9.25 (2.84) among users of other antidepressants, 10.50 (2.74) among those using multiple antidepressant subclasses, and 8.74 (2.56) among those not using antidepressants.

3.3. Model results

Model results are listed in Table 3. In the crude model, antidepressant use significantly predicted A1C only among participants without a diabetes diagnosis ($F = 2.29$, p-value = .04); in the non-diabetes strata, participants who reported taking antidepressants in the other subclass category, which included primarily bupropion and trazodone, had a significantly lower A1C than participants who did not use antidepressants at all (standardized effect estimate = −.05, standard deviation = .02). However, this relationship did not persist after adjustment for other variables. There was a small statistically-significant association observed between use of SNRIs and higher A1C among those without diabetes in two of the adjusted models. Among participants with diabetes, those taking antidepressants from multiple subclasses tended to have a higher A1C value compared to participants not taking any antidepressant medication (standardized effect estimate = .12, standard deviation = .09). This effect on log A1C translates into an A1C effect of 1.26%. This relationship persisted after adding all covariates to the model, including demographics, smoking status, depressive symptoms (CESD-10 category) and BMI category (full adjusted model $F = 2.37$, p-value = .

04). No other significant associations were consistently observed among participants with diabetes.

4. Conclusions

In this study, we examined the relationship between antidepressant use and A1C among a sample of racially diverse adults who visited community health clinics serving low-income families in the southeastern United States. We observed a significant association between the use of multiple antidepressant subclasses and increased A1C among individuals with diabetes. As far as the authors are aware, this is a novel observation, as literature on the effects of antidepressant polypharmacy on A1C among persons with diabetes is sparse. We observed no consistent association between antidepressant use and A1C among individuals without diabetes. Furthermore, no association between using a single antidepressant subclass and A1C was observed among those with diabetes. This study generally supports the observations of Mojtabai (2013) who observed no cross-sectional association between antidepressant use and A1C level in a nationally-representative sample of individuals without diabetes. This study also extended Mojtabai's research with the inclusion of individuals with and without diabetes, and the inclusion of a multiple-subclass exposure category.

This study is not the first to observe a relationship between using antidepressants from multiple subclasses and worse diabetes outcomes. A nested case–control study performed in a Canadian cohort observed that those who were prescribed SSRIs and TCAs were at an increased risk for a subsequent diabetes diagnosis compared to those who used TCAs alone (Brown, Majumdar, & Johnson, 2008). Additionally, previous research has observed other medication interactions involving antidepressants that worsened outcomes among persons with diabetes. A study by Tatonetti et al. (2011) observed that those with diabetes who used the SSRI Paroxetine combined with Prevastatin, a cholesterol-lowering medication, experienced increases in random blood glucose tests, though this effect was not seen among those who only used one of these medications. Furthermore, previous research has observed that combination therapy does not improve outcomes more than the use of one antidepressant among persons with comorbid medical conditions (Morris et al., 2012), suggesting that further research on the safety and effectiveness of antidepressant polypharmacy among individuals with diabetes is needed.

This significant observation in the present study should be interpreted cautiously, however, as the number of individuals with diabetes taking antidepressants from multiple subclasses was small ($N = 10$). Furthermore, those with diabetes taking antidepressants from multiple subclasses likely represent an already less healthy population compared with those not taking antidepressants, which may not have been completely controlled for in the present study's set of confounders, especially because several important covariates were categorized to improve model fit, including age, CESD-10 score, and BMI. While exploratory analyses that controlled for frequency of glucose testing and frequency of taking diabetes medications as instructed in addition to all other covariates in the full model within the strata of individuals with a diagnosis of diabetes did not result in meaningfully different associations between use of multiple antidepressant subclasses and A1C, other diabetes self-care

practices (e.g., diet and physical activity), which may have differed between exposure groups, were not accounted for. Other limitations include the cross-sectional study design, the fact that important differences in antidepressant medication usage such as length of use, dose, and adherence were not taken into account, and the reliance on self-reported exposure data, which is subject to social desirability and recall bias. While use of self-reported diabetes diagnosis may be considered a limitation, a previous SCCS validation study was able to confirm 96% of self-reported diabetes cases using medical records or elevated A1C levels (Signorello, Hargreaves, & Blot, 2010). This study did not differentiate between type 1 and type 2 diabetes. However, because the majority of diabetes diagnoses are type 2, it is expected that the observations of the current study largely reflect the relationship between antidepressant use and A1C among individuals with type 2 diabetes. Because the sample was drawn from a low-income clinic population primarily composed of women younger than 50, results may not generalize to men or healthier, higher-income, or older populations.

Though the current observational study had several limitations and should be viewed as exploratory and preliminary, this study also had several strengths. This study included a population with relatively high rates of antidepressant use and diagnosed diabetes, which was expected to increase power. Additionally, analyses were stratified by diabetes status and included A1C as an outcome rather than self-reported diabetes diagnosis, which was expected to both increase power and reduce the impact of detection bias. It has been hypothesized that different patterns in outpatient visits may account for the relationship between antidepressant use and A1C (Mojtabai, 2013). This explanation is unlikely to have caused the association observed in the current study for two reasons. First, because the sample was drawn from clinic participants and not the general population, all respondents were current treatment-seekers and had access to clinical care. Second, an association with A1C was not consistently observed among individuals taking a single antidepressant as would be expected if detection bias were solely responsible for the observed association. Because antipsychotic use, a known risk factor for increased A1C, was reported in three out of the ten individuals with diabetes using multiple subclasses of antidepressants, a sensitivity analysis was performed that removed all individuals who reported using an antipsychotic (N = 47), which did not significantly change the observed relationship between using antidepressants from multiple subclasses and having worse A1C.

Though possibly due to residual confounding or chance, the observed association between using antidepressants from multiple subclasses and A1C among individuals with diabetes may also indicate that using antidepressants from multiple subclasses worsens glucose control among individuals with an already impaired insulin response. The literature on the potential impact of interactions between antidepressants from multiple subclasses on glucose or A1C among those with diabetes is sparse. It is difficult to disentangle the glycemic effects of depression and its treatment in an observational study, especially the one with a small sample size, even after controlling for level of current self-reported symptoms, so our results should be interpreted cautiously. Therefore, future trials comparing monotherapy with the use of multiple antidepressants should measure A1C in evaluating the incidence of adverse effects. Future studies should also examine the pathway through which antidepressants subclasses may interact with each other to interfere with the action of diabetes medications

or directly increase A1C levels, as the mechanism behind this association is unclear. Quantifying the impact of antidepressant polypharmacy on common chronic disease outcomes is especially important as the use of more than one antidepressant has increased over time (Glezer, Byatt, Cook, & Rothschild, 2009).

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Table 1

SCCS sample characteristics.

Variable	Category	Overall		Diabetes		No diabetes	
		N	%	*N*	%	*N*	%
Sex	Woman	2072	84.74	399	86.36	1673	84.37
	Man	373	15.26	63	13.64	310	15.63
Age category	40-49 years	1354	55.38	184	39.83	1170	59
	50-65 years	894	36.56	222	48.05	672	33.89
	>65 years	197	8.06	56	12.12	141	7.11
Race	White	1205	49.28	192	41.56	1013	51.08
	African-American	1240	50.72	270	58.44	970	48.92
Education	Less than high school	776	31.74	169	36.58	607	30.61
	High school	849	34.72	162	35.06	687	34.64
	More than high school	820	33.54	131	28.35	689	34.75
Smoking status	Non-smoker	1497	61.23	339	73.38	1158	58.4
	Smoker	948	38.77	123	26.62	825	41.6
BMI	Under 25 kg/m^2	643	26.3	55	11.9	588	29.65
	25 to 29 kg/m^2	650	26.58	98	21.21	552	27.84
	30 kg/m^2 or higher	1152	47.12	309	66.88	843	42.51
Depression diagnosis	No	1684	68.88	297	64.29	1387	69.94
	Yes	761	31.12	165	35.71	596	30.06
CESD-10 score category	No depression	1335	54.6	239	51.73	1096	55.27
	Mild depression	582	23.8	111	24.03	471	23.75
	Moderate depression	331	13.54	70	15.15	261	13.16
	Severe depression	197	8.06	42	9.09	155	7.82
Diabetes status	No diagnosis	1983	81.1				
	Diagnosis	462	18.9				
Antidepressant subclass	SNRI	26	1.06	6	1.3	20	1.01
	SSRI	296	12.11	61	13.2	235	11.85
	TCA	36	1.47	7	1.52	29	1.46
	Other	53	2.17	8	1.73	45	2.27
	Multiple	40	1.64	10	2.16	30	1.51
	None	1994	81.55	370	80.09	1624	81.9
A1C category	<5.7% (<39 mmol/mol)	673	27.53	25	5.41	648	32.68
	5.7%-6.4% (39-46 mmol/mol)	1094	44.74	59	12.77	1035	52.19
	>6.4% (>46 mmol/mol)	678	27.73	378	81.82	300	15.13

Diabetes status based on self-report diagnosis.

Table 2

Mean A1C by predictor category.

Variable	Category	Mean (SD) A1C (%)	Mean (SD) A1C (mmol/mol)	*F* value (*p*-value)
Sex	Woman	6.51 (1.72)	48 (18.8)	9.71 (.0019)
	Man	6.30 (1.85)	45 (20.2)	
Age Category	40-49 years	6.28 (1.66)	45 (18.2)	30.57 (<.0001)
	50-65 years	6.72 (1.87)	50 (20.4)	
	> 65 years	6.75 (1.45)	50 (15.9)	
Race	White	6.25 (1.52)	45 (16.7)	55.02 (<.0001)
	African-American	6.70 (1.90)	50 (20.8)	
Education	Less than high school	6.66 (1.86)	49 (20.3)	9.02 (.0001)
	High school	6.45 (1.71)	47 (18.7)	
	More than high school	6.34 (1.64)	46 (17.9)	
Smoking status	Non-smokers	6.59 (1.82)	49 (19.9)	19.74 (<.0001)
	Smokers	6.31 (1.59)	45 (17.4)	
BMI	Under 25 kg/m^2	6.03 (1.41)	42 (15.4)	65.61 (<.0001)
	25 to 29 kg/m^2	6.34 (1.65)	46 (18.1)	
	30 kg/m^2 or higher	6.81 (1.88)	51 (20.5)	
Depression diagnosis	No	6.50 (1.79)	48 (19.6)	.33 (.5634)
	Yes	6.44 (1.62)	47 (17.7)	
CESD-10 score category	No depression	6.43 (1.66)	47 (18.1)	.71 (.5458)
	Mild depression	6.53 (1.78)	48 (19.5)	
	Moderate depression	6.53 (1.87)	48 (20.5)	
	Severe depression	6.57 (1.90)	48 (20.8)	
Diabetes status	No diagnosis	5.96 (0.87)	42 (9.6)	1757.47 (<.0001)
	Diagnosis	8.71 (2.57)	72 (28.1)	
Antidepressant subclass	SNRI	6.55 (1.60)	48 (17.5)	1.21 (.2995)
	SSRI	6.41 (1.67)	47 (18.2)	
	TCA	6.20 (0.82)	44 (9.0)	
	Other	6.25 (1.72)	45 (18.8)	
	Multiple	7.00 (2.47)	53 (27.0)	
	None	6.49 (1.75)	47 (19.1)	
Sickle cell	Yes	6.01 (0.75)	42 (8.2)	
	No	6.48 (1.74)	47 (19.0)	
	Overall	6.48 (1.74)	47 (19.0)	

ANOVA performed using log A1C. Individuals with sickle-cell anemia diagnosis excluded from models.

Table 3

Standardized intercept and subclass coefficients with standard errors in crude and adjusted linear models stratified by diabetes status.

Variables added to model	Diabetes	Intercept	SNRI	SSRI	TCA	Other	Multiple	Subclass *F*-statistic (*p*-value)
Subclass	Yes	0 (0.01)	−0.06 (0.11)	−0.04 (0.04)	−0.08 (0.10)	0.03 (0.10)	**0.10 (0.09)**	2.14 (0.06)
Subclass	No	0 (0.00)	0.03 (0.03)	−0.04 (0.01)	0.01 (0.02)	**−0.05 (0.02)**	−0.02 (0.02)	2.29 (0.04)
Age category, gender, race, education	Yes	0 (0.05)	−0.05 (0.11)	−0.03 (0.04)	−0.08 (0.10)	0.03 (0.10)	**0.12 (0.09)**	2.33 (0.04)
Age category, gender, race, education	No	0 (0.01)	**0.04 (0.03)**	−0.02 (0.01)	0.02 (0.02)	−0.03 (0.02)	−0.00 (0.02)	1.61 (0.15)
Smoking status	Yes	0 (0.06)	−0.05(0.11)	−0.02 (0.04)	−0.08 (0.10)	0.03 (0.10)	**0.12 (0.09)**	2.38 (0.04)
Smoking status	No	0 (0.01)	0.04 (0.03)	−0.02 (0.01)	0.02 (0.02)	−0.04 (0.02)	−0.00 (0.02)	1.59 (0.16)
CESD-10 score category	Yes	0 (0.07)	−0.05 (0.11)	−0.03 (0.04)	−0.07 (0.11)	0.03 (0.10)	**0.12 (0.09)**	2.36 (0.04)
CESD-10 score category	No	0 (0.02)	0.04 (0.03)	−0.02 (0.01)	0.01 (0.02)	−0.04 (0.02)	−0.01 (0.02)	1.61 (0.15)
BMI category	Yes	0 (0.08)	−0.05 (0.11)	−0.03 (0.04)	−0.08 (0.11)	0.03 (0.10)	**0.12 (0.09)**	2.37 (0.04)
BMI category	No	0 (0.02)	**0.04 (0.03)**	−0.03 (0.01)	0.01 (0.02)	−0.04 (0.02)	−0.01 (0.02)	2.00 (0.08)

Once variable was added in it was not removed from subsequent models. Model outcome is log (A1C). No subclass is referent category. Highlighted cells associated with significant t-test at alpha = .05.