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ORIGINAL RESEARCH

Depressive symptoms and adherence to cardiometabolic therapies across phases of treatment among adults with diabetes: the Diabetes Study of Northern California (DISTANCE)

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Objective: Among adults with diabetes, depression is associated with poorer adherence to cardiometabolic medications in ongoing users; however, it is unknown whether this extends to early adherence among patients newly prescribed these medications. This study examined whether depressive symptoms among adults with diabetes newly prescribed cardiometabolic medications are associated with early and long-term nonadherence.

Patients and methods: An observational follow-up of 4,018 adults with type 2 diabetes who completed a survey in 2006 and were newly prescribed oral antihyperglycemic, antihypertensive, or lipid-lowering agents within the following year at Kaiser Permanente Northern California was conducted. Depressive symptoms were examined based on Patient Health Questionnaire-8 scores. Pharmacy utilization data were used to identify nonadherence by using validated methods: early nonadherence (medication never dispensed or dispensed once and never refilled) and long-term nonadherence (new prescription medication gap [NPMG]: percentage of time without medication supply). These analyses were conducted in 2016.

Results: Patients with moderate-to-severe depressive symptoms had poorer adherence than nondepressed patients (8.3% more patients with early nonadherence, P=0.01; 4.9% patients with longer NPMG, P=0.002; 7.8% more patients with overall nonadherence [medication gap >20%], P=0.03). After adjustment for confounders, the models remained statistically significant for new NPMG (3.7% difference, P=0.02). There was a graded association between greater depression severity and nonadherence for all the models (test of trend, P<0.05).

Conclusion: Depressive symptoms were associated with modest differences in early and long-term adherence to newly prescribed cardiometabolic medications in diabetes patients. Interventions targeting adherence among adults with diabetes and depression need to address both initiation and maintenance of medication use.

Keywords: medication adherence, depression, diabetes mellitus, type 2 diabetes, Patient Health Questionnaire-8, PHQ-8, antihypertensive, hypoglycemic, hypolipidemic agents, pharmacoepidemiology, observational cohort study

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Introduction

Medication nonadherence is a modifiable contributor to morbidity and mortality associated with chronic conditions, such as diabetes and cardiovascular disease, and thus serves as a potential target for tertiary preventive interventions.[1] The societal burden of medication nonadherence is substantial; in the USA, nonadherence has been estimated to account for 125,000 annual deaths, a major proportion of

preventable hospitalizations, and to carry economic costs between $100 and $300 billion each year.[2] Past research to identify risk factors for medication nonadherence has focused on nonadherence among ongoing (prevalent) medication users,[3,4] termed secondary nonadherence. However, studies on secondary nonadherence underestimate overall medication nonadherence because they systematically exclude people who are nonadherent in the earliest phases of treatment, that is, those who never fill a medication prescription or those who fill an initial prescription but never refill it.[5–7] Nonadherence at this early phase is important because such individuals do not go on to become ongoing users of the medication and therefore do not receive the potential benefits of treatment as a prevention of premature morbidity and mortality. Recent methodological innovations allow the characterization of adherence in new prescription cohorts (patient cohorts in which baseline is the date of first medication prescribed), thus enabling researchers to more comprehensively evaluate the public health burden and correlates of nonadherence over the entire course of treatment.[6]

Depression, which is common among people with chronic diseases including diabetes,[8–13] has been identified as a risk factor for secondary medication nonadherence among adults with diabetes.[14–16] In a recent systematic review, depression and out-of-pocket costs were among the few patient-, treatment-, and system-level factors that demonstrated consistent, significant associations with adherence to diabetes medications across multiple studies employing differing methods.[4] Although reasons for the association between depression and secondary adherence are not fully established, related research has found that, among people with diabetes, those with comorbid depression have poorer self-care in multiple domains than nondepressed counterparts.[14] Depression has negative effects on cognitive and affective functioning that may serve as barriers to participation in self-care broadly and medication adherence specifically. For example, depression negatively affects motivation and executive functioning and includes psychological effects such as hopelessness, helplessness, poor self-efficacy, and feelings of low self-worth, all of which may interfere with activities needed for effective self-care.

It is not known whether the well-established association between depression and secondary medication adherence extends to early nonadherence. This knowledge is important for understanding the overall public health impact of depression, which may be underestimated in the literature on secondary adherence. The present study examined whether depressive symptoms among adults with type 2 diabetes were associated with initiation and maintenance of newly prescribed cardiometabolic therapies. It is hypothesized that patients with greater depressive symptom severity would have poorer early and long-term adherence than those without depressive symptoms.

Patients and methods

Setting and study population

Kaiser Permanente Northern California (KPNC) is a large integrated health care delivery system serving ~30% of the catchment population of Northern California. The KPNC membership is ethnically diverse and sociodemographically similar to the population of the region, except for the extreme tails of the income distribution.[17] The Diabetes Study of Northern California (DISTANCE) surveyed an ethnically stratified, random sample of adult (aged 30–75 years) health plan members from the KPNC Diabetes Registry in 2005–2006. The methods employed to construct the KPNC Diabetes Registry and the DISTANCE sample have been previously described in detail.[18] There were no additional exclusion criteria for the survey. The overall eligibility-adjusted response rate was 62%, yielding a final sample of 20,188 participants.[18] Participants completed a written survey (33.1%), a web-based survey (15.2%) in English, or a computer-assisted telephone interview (51.7%) in English, Spanish, Cantonese, Mandarin, or Tagalog. The KPNC Institutional Review Board (IRB) approved this study. The requirement that informed consent be obtained from study participants was waived by the IRB; answering any survey questions constituted consent.

The present study examined medication nonadherence in patients with type 2 diabetes during a period of 24 months following a new prescription order for any of three types of common cardiometabolic medications: oral antihyperglycemic agents, antihypertensive agents, and lipid-lowering agents. This study identified the 4,018 DISTANCE survey respondents who: 1) had a new prescription (index prescription) for an oral antihyperglycemic agent (n=1,481), an antihypertensive agent (n=1,620), or a lipid-lowering agent (n=917; refer Table S1 for complete medication list) within 1 year following survey completion, 2) were not previously dispensed the same medication in the 2 years preceding the index prescription date, 3) had continuous pharmacy benefits for at least 2 years before and after the index prescription date, and 4) completed the survey items assessing depressive symptoms (refer Figure S1 for details of cohort creation).

Exposure

Depressive symptoms were assessed by using the Patient Health Questionnaire (PHQ) that asks about the presence

of depressive symptoms over the past 2 weeks.[19,20] The PHQ has been widely validated as a measure for detecting the presence of clinically significant depressive disorders and is brief, easy to administer, and available in numerous languages.[20–24] A diagnostic meta-analysis found a sensitivity of 0.80 and specificity of 0.92 for the detection of major depressive disorder.[25] The present study used the PHQ-8 that is most commonly used for survey research given the inability to respond appropriately and in a timely fashion to positive suicidal ideation when administered via a written survey. (The PHQ-9 includes an additional item assessing thoughts of death or self-harm and is therefore more frequently employed in the clinical setting).[19,20] Past research has demonstrated that scores of the PHQ-8 and PHQ-9 are highly correlated (rs≥0.997), both measures have similar operating characteristics, and identical scoring cut-points can be used.[19,20] The PHQ-8 is scored from 0 to 24 and based on established cut-points; depressive symptom severity was coded as "none" (score 0–4), "mild" (score 5–9), or "moderate/severe" (score ≧10).[20,23]

Outcomes

Pharmacy prescribing and dispensing data for the index prescriptions were used to calculate several indicators of nonadherence. Although pharmacy utilization is a distinct behavior from medication-taking, prior research has established the validity of this method.[6,26] Early nonadherence was defined as either no dispensing of the index prescription within 60 days of the date it was ordered or the dispensing of the index prescription once but no additional dispensing of that medication (ie, no refill) within the period defined by the number of days' supply of medication dispensed plus a 90-day grace period. A continuous and comprehensive measure of nonadherence, new prescription medication gap (NPMG), was also calculated. This measure provides an estimate of the percentage of time without a supply (ie, gaps) of the index prescription during the 24 months after the initial order.[6] NPMG is calculated by using the daily dosage of medication prescribed, the number of pills dispensed, and dispensing dates over 24 months to estimate gaps in medication supply. By using NPMG, the patients were categorized as "nonadherent" overall if they lacked medication supply for at least 20% of the time (ie, NPMG >20%). For patients who had more than one new prescription, only adherence to the first medication prescribed for any of the three indications was assessed. For patients whose dispensing data indicated a switch from the index prescription to an alternate medication within the same drug class between 3 months prior and 1 month after the discontinuation date, the discontinuation of the index prescription was considered to be clinically recognized rather than an indicator of nonadherence. In such instances, follow-up as of the date of switch to the alternate medication was censored.

Covariates

Participants self-reported sociodemographic information (ie, age; gender; race/ethnicity: white, African–American, Latino, Asian–American, Filipino, or other/unknown/multiracial; marital status: married/partnered, single/separated/divorced/widowed) and a history of any of the following: myocardial infarction, cerebrovascular accident, coronary artery disease (as indicated by coronary artery bypass surgery or angioplasty), lower extremity amputation, or renal failure requiring dialysis or transplantation. Missing survey data on diabetes complications were imputed using data on complications obtained from the electronic medical record.

Data analysis

Modified Poisson regression models were specified to estimate the relative risk (RR) of nonadherence for those with mild or moderate/severe depressive symptoms compared with those with none,[27] and modified least squares regression[28] was employed to generate the predicted probability for each measure of nonadherence for each depressive symptom category. To assess whether nonadherence was greater among those with higher depression symptom severity, a Cochran–Armitage test for trend was applied to the predicted probabilities from the unadjusted and adjusted models for dichotomous outcomes (ie, adherent vs nonadherent). A generalized linear regression model was specified to evaluate the relationship between depressive symptom category and the percentage of time without pill supply (continuous NPMG). A directed acyclic graph (DAG) depicting hypothesized causal relationships and temporal ordering between the exposure (depressive symptom category) and outcomes of interest (measures of adherence) was constructed (refer Figure S2, for the graph and its interpretation).[29,30] Then, established DAG rules were used to determine the subset of covariates (potentially confounding variables) required in adjusted models to estimate the unbiased direct effect of depressive symptoms on medication adherence. In accordance with the findings from the present DAG analysis, each model was adjusted by including age, gender, race/ethnicity, marital status, and diabetes complications as covariates (described in Covariates section). All the models were expansion-weighted to accommodate the race/ethnicity-stratified

sampling design (nonproportional sampling fractions) of the original DISTANCE survey and further weighted for survey nonresponse by using the Horvitz–Thompson method.[31] Analyses were completed in 2016.

Results

Among 4,018 patients who were prescribed a new cardiometabolic medication, 2,573 (64.0%) patients were categorized as having no depressive symptoms, and the remaining 1,445 (36.0%) were categorized as having mild (935, 23.3%) or moderate/severe (510, 12.7%) depressive symptoms. Depressive symptoms were significantly associated with younger age, female gender, low educational attainment, race/ethnicity (particularly Latinos), unmarried status, the history of diabetes complications, and number of medications (Table 1).

Overall, early nonadherence was common, with 27.9% of patients either never filling or never refilling their newly prescribed cardiometabolic medication. Over the course of 2 years following a new prescription, on average, patients were lacking medications for 194 days (ie, NPMG =27%), and 39.3% of patients were categorized overall as nonadherent (ie, NPMG >20%).

Associations between depressive symptoms and nonadherence

Nonadherence to cardiometabolic medications was greater among patients with moderate/severe depressive symptoms than patients with no depressive symptoms. This pattern held for all indicators of nonadherence (Table 2). There was an 8.3% increase in early nonadherence (RR =1.33, P=0.006), a 7.8% increase in overall nonadherence (NPMG >20%; RR =1.22, P=0.02), and 4.9% greater days without pill supply (NPMG; P=0.002). The point estimates changed only minimally after adjustment for age, gender, race/ethnicity, marital status, and diabetes complications. Only the model for NPMG specified as a continuous variable remained statistically significant after adjustment (3.7% greater days without supply among patients with moderate/severe depressive symptoms than patients with no depressive symptoms; P=0.02). However, the Cochran–Armitage test for trend consistently demonstrated that nonadherence increased significantly as depressive symptoms increased with and without adjustment (early nonadherence: P<0.0001 [unadjusted] and P=0.0028 [adjusted]; and overall nonadherence [NPMG >20%]: P=0.0002 [unadjusted] and P=0.0118 [adjusted]). Similarly, the linear regression model also demonstrated a significant

Table 1 Demographic and clinical characteristics by depressive symptom category (n=4,018)

	Depressive symptom severity			*P*-value
	None	Mild	Moderate/severe	
Total	2,573 (64)	935 (23)	510 (13)	
Age (years)				<0.0001
30–45	239 (9.3)	114 (12.2)	55 (10.8)	
46–61	1,117 (43.4)	459 (49.1)	254 (49.8)	
62–77	1,217 (47.3)	362 (38.7)	201 (39.4)	
Gender				<0.0001
Male	1,414 (55.0)	416 (44.5)	172 (33.7)	
Female	1,159 (45.0)	519 (55.5)	338 (66.3)	
Race/ethnicity				0.0042
African–American	542 (21.1)	195 (20.9)	110 (21.6)	
Asian–American	357 (13.9)	85 (9.1)	28 (5.5)	
Filipino	270 (10.5)	98 (10.5)	51 (10.0)	
Latino	435 (16.9)	186 (19.9)	106 (20.8)	
Other/unknown/multiracial	387 (15.0)	144 (15.4)	92 (18.0)	
Caucasian	582 (22.6)	227 (24.3)	123 (24.1)	
Marital status (n=3,989)				<0.0001
Single, separated, divorced, or widowed	706 (27.6)	311 (33.4)	179 (35.7)	
Married or partnered	1,852 (72.4)	619 (66.6)	322 (64.3)	
Education (n=3,958)				<0.0001
Less than high school graduate	314 (12.4)	141 (15.3)	97 (19.3)	
High school graduate or greater	2,220 (87.6)	779 (84.7)	407 (80.8)	
Any diabetes complication	487 (18.9)	210 (22.5)	158 (31.0)	<0.0001
Number of chronic medications, mean (SD)	5.6 (2.9)	6.3 (3.3)	7.3 (3.9)	<0.0001

Notes: None: PHQ-8 =0–4; mild: PHQ-8 =5–9; moderate/severe: PHQ-8 ≧10. Values are presented as n (%) in table unless otherwise indicated.
Abbreviations: PHQ, Patient Health Questionnaire; SD, standard deviation.

Table 2 Association between depressive symptom severity and cardiometabolic medication adherence for 4,018 adults with type 2 diabetes

	Trend test *P*-value[b]	Depressive symptom severity				
		None, PHQ =0–4	Mild, PHQ =5–9		Moderate/severe, PHQ ≥10	
		Estimated %	Estimated % difference (95% CI)	RR (95% CI)	Estimated % difference (95% CI)	RR (95% CI)
Early nonadherence						
Unadjusted	<0.0001	25.2	+4.4 (−0.5, +9.3)	1.18 (0.99, 1.40)	+8.3 (+2.0, +14.6)	1.33 (1.09, 1.62)
Adjusted[a]	0.003	25.9	+2.9 (−2.0, +7.9)	1.12 (0.94, 1.33)	+5.3 (−1.1, +11.8)	1.20 (0.97, 1.48)
Overall nonadherence (NPMG >20%)						
Unadjusted	0.0002	36.0	+3.9 (−1.6, +9.5)	1.11 (0.96, 1.28)	+7.8 (+0.8, +14.7)	1.22 (1.03, 1.44)
Adjusted[a]	0.012	36.7	+2.0 (−3.5, +7.4)	1.06 (0.92, 1.22)	+5.2 (−1.8, +12.1)	1.14 (0.96, 1.35)
NPMG						
Unadjusted	0.0007	24.9	+2.5 (+0.1, +5.0)	n/a	+4.9 (+1.8, +8.0)	n/a
Adjusted[a]	0.019	25.3	+1.3 (−1.1, +3.7)	n/a	+3.7 (+0.6, +6.8)	n/a

Notes: Results are reported as the estimated percentage of individuals (early nonadherence, overall nonadherence [NPMG >20%]) or the NPMG (estimated percentage of days without medication supply over 24 months). [a]Due to missing covariates, adjusted models have n=3,989. Models are adjusted for age, gender, race/ethnicity, marital status, and diabetes complications. [b]For categorical outcomes (early nonadherence, overall nonadherence [NPMG >20%]), the *P*-value reported is from the Cochran–Armitage test for trend; for the continuous outcome (NPMG), the *P*-value reported is for the linear trend based on a linear regression model.
Abbreviations: CI, confidence interval; n/a, not applicable; NPMG, new prescription medication gap; PHQ, Patient Health Questionnaire; RR, relative risk.

linear trend between depression and nonadherence (NPMG: *P*=0.0007 [unadjusted] and *P*=0.019 [adjusted]).

Discussion

Among adults with diabetes, associations between depressive symptom severity and adherence to cardiometabolic medications were modest for indicators of both early and long-term adherence over 24 months, which extends prior research focused on secondary adherence.[14,15] These findings are relevant because initiating and maintaining long-term adherence are important for optimal control of cardiometabolic risk factors and for prevention of associated diabetes complications and mortality.

The 5% greater rate of early nonadherence among patients with depressive symptoms is clinically significant, given these patients never become ongoing medication users. A graded pattern was observed between greater depressive symptom severity and poorer adherence. The finding from the present study differs from prior research in hypertensive patients from the same source population (KPNC) which did not detect an association between depression and early nonpersistence to antihypertensive medications.[32] Unlike the prior study that classified depression based on electronic medical records (ie, clinically recognized depression), the present study classified depression based on direct assessment of patient-reported symptoms using the PHQ-8. Thus, the present sample was not limited to people whose depression was clinically recognized.[9,33] This expanded exposure definition may explain the difference in findings and supports the value of patient-reported outcome measures and the use of dimensional measures for studies of mental disorders such as depression. The findings are consistent with prior research reporting that the association between depression and nonadherence is not limited to those with probable major depression.[34] Diabetes distress has also been associated with nonadherence; however, it is believed diabetes distress is unlikely to explain the association between depression and nonadherence. Prior research has found that the association between diabetes distress and adherence does not persist after depressive symptoms are accounted for, whereas in that study depression was independently associated with adherence after diabetes distress was taken into account.[35]

Whereas early nonadherence reflects discrete behaviors at two specific points in time, NPMG is an aggregate indicator that reflects the cumulative effect of repeated utilization (or lack thereof) over a period of 24 months. This difference may be informative for tertiary prevention efforts, namely, the development of interventions to address suboptimal medication adherence among adults with depressive symptoms. The present findings suggest that medication adherence interventions for people with comorbid depression may need to be applied both at the initiation of treatment and on an ongoing basis to sustain adherence over time.

Limitations

Some study limitations should be considered. Patterns of adherence were examined for a limited set of cardiometabolic medication classes and indications, and only the first

new prescription was included within a medication class. Thus, the study findings may not generalize to other patient populations, multiple prescriptions within therapeutic classes, ongoing use of medications, or other types of medications. The estimates of nonadherence based on pharmacy utilization data are conservative, given that it is unknown whether any medications dispensed were actually consumed because medication-taking and prescription filling are distinct behaviors. Research indicates that the use of pharmacy utilization measures of adherence results in lesser effects for depression than when self-report adherence measures are used;[16] therefore, the results from the present study represent conservative estimates of the true effects of depression. Nevertheless, these findings are based on objective measures of utilization according to the methods that have been previously validated,[6] thus avoiding concerns of recall bias or social desirability associated with retrospective, self-reported medication adherence.

In this study, depressive symptoms were assessed at a single point in time that preceded a new prescription by no more than 1 year and based on self-report (using the PHQ-8). Although depressive symptoms fluctuate over time, evidence suggests that depression is often recurrent and chronic among adults with diabetes[36] and often not clinically recognized.[9,33] The presence of consistent associations between depressive symptoms and adherence over the long term supports the enduring nature of the risk for nonadherence associated with depressive symptoms and suggests that these findings may be conservative because the observed associations may have been attenuated by the small delay between the measurement of depressive symptoms and adherence in some participants. A minority of individuals who scored in the moderate/severe range on the PHQ-8 likely would not have met criteria for major depression or another clinically significant depressive disorder and may instead have a related condition such as an anxiety disorder or diabetes distress that presents with substantial comorbid depressive symptomatology. This is not viewed as a limitation because the present findings generalize to a broader group of people, those with at least one PHQ-8 score of 10 or greater, who can be identified easily in routine practice settings. Moreover, using PHQ scores to identify patients at an increased risk for nonadherence is consistent with recommendations from a recent issue brief from the Office of the National Coordinator for Health Information Technology to develop predictive analytics based on electronic medical record data to enable targeted interventions.[37] The present study found a significant, graded relationship between depressive symptom severity and nonadherence for all measures, which affirms the utility of depressive symptoms as a dimensional construct in understanding its association with adherence, regardless of the extent that symptoms overlap with related constructs such as diabetes distress. Because all participants in this study were insured and received services via KPNC, which includes integrated pharmacy services, results may not generalize to disadvantaged patient populations or safety net health care settings. Although the large sample was ethnically and socioeconomically diverse, the findings may not reflect patterns in settings where access to care differs across social groups. Although initial data collection occurred in 2005–2006, depression identification, care, and adherence remain persistent clinical challenges.[2,38] However, it is not believed that the overall relationship between depression and adherence would change substantively over time.

Conclusion

Clinicians treating patients with type 2 diabetes who prescribe new cardiometabolic therapies should be aware that those with depression are more likely to have elevated rates of nonadherence both initially and over the long term. However, it is likewise important to note that the differences attributable to depression were modest compared to the baseline high rate of nonadherence in the overall sample. Patients with type 2 diabetes and depression experience a disproportionately high burden of premature morbidity and mortality.[39–42] The small increased probability of nonadherence among patients with type 2 diabetes and comorbid depression should not deter clinicians from initiating cardiometabolic therapies. Rather, such treatments should be offered alongside care for depression, and interventions to address adherence should be delivered longitudinally to target the barriers that depressed patients face to maintaining adherence. Promising interventions, such as the routine assessment of medication adherence, exploration of barriers and problem-solving, and use of motivational interviewing to facilitate behavior change,[43–45] may need to be offered when medications are initiated and implemented repeatedly in a routine clinical practice. Although recognition of depression and appropriate treatment are necessary for improving depression outcomes, these alone may be insufficient to improve self-care and outcomes for people with type 2 diabetes.[46] To optimally treat patients with comorbid type 2 diabetes and depression and prevent diabetes complications, clinicians should pair interventions that address depressive symptoms with interventions that directly target diabetes self-care, including sustained medication adherence.[44,47] Future research should examine the effectiveness of such paired interventions for people with comorbid diabetes and depression on adherence and clinical

outcomes and evaluate interventions both at the time of initial medication prescription and over the long term.

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Disclosure

The authors report no conflicts of interest in this work.

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Supplementary materials

Table S1 Classification of cardiometabolic medications

Therapeutic category	Medication name(s)
Oral antihyperglycemic agent	Glimepiride
	Glipidize
	Glyburide
	Metformin
	Tolazamide
	Tolbutamide
Antihypertensive agent	Amlodipine
	Atenolol
	Benazepril
	Bisoprolol
	Bumetanide
	Captopril
	Carvedilol
	Chlorthalidone
	Diltiazem
	Enalapril
	Ethacrynic
	Felodipine
	Furosemide
	Hydrochlorothiazide
	Indapamide
	Labetalol
	Lisinopril
	Losartan
	Metolazone
	Metoprolol
	Nadolol
	Nifedipine
	Propranolol
	Ramipril
	Spironolactone
	Spironolactone/hydrochlorothiazide
	Torsemide
	Triamterene/hydrochlorothiazide
	Valsartan
	Verapamil
Lipid-lowering agent	Atorvastatin
	Fluvastatin
	Pravastatin
	Simvastatin

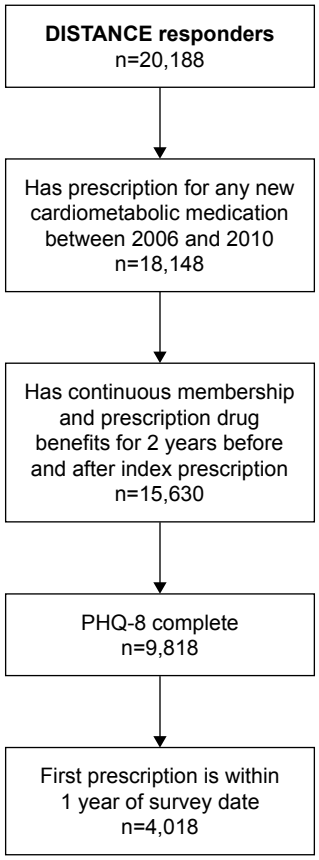

Figure S1 Flowchart of new cardiometabolic medication user cohort.
Abbreviations: DISTANCE, the Diabetes Study of Northern California; PHQ, Patient Health Questionnaire.

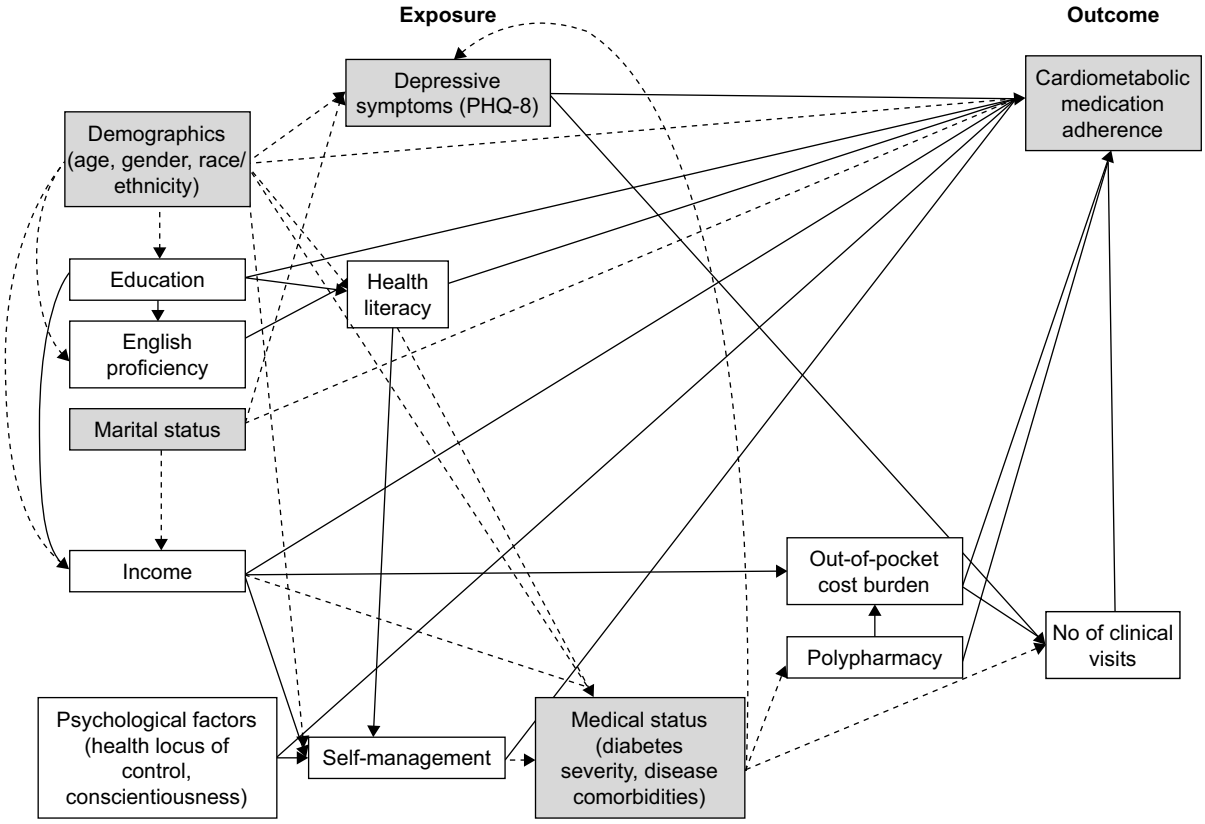

Figure S2 DAG demonstrating covariate selection.

Notes: Shaded box: variable included in multivariate analyses; white box: variable excluded as potential confounder and therefore not included in multivariate analyses; solid arrow: causal pathways that do not confound the association between depressive symptoms and cardiometabolic medication adherence; dotted arrow: causal pathways that potentially confound the association between depressive symptoms and cardiometabolic medication adherence in unadjusted analyses but are no longer confounders in multivariate models that include the variables identified in the shaded boxes. The DAG was constructed to illustrate the hypothesized causal relationships and time ordering between variables associated with depressive symptoms and cardiometabolic medication adherence. All of the variables represented were available in the DISTANCE data set. Analysis of the DAG followed an established process to identify which of these variables were potential confounders of the association between depressive symptoms and adherence.[1] This analysis revealed that adjustments for the variables in the shaded boxes (age, gender, race/ethnicity, marital status, and diabetes complications) were necessary and sufficient to address potential confounding variables, whereas variables in the white boxes were excluded as covariates because they did not function as potential confounders. Causal pathways illustrated by the gray dotted arrows are accounted for by adjustment of the identified covariates, and therefore, these relationships do not confound the association between depressive symptoms and adherence. This includes all variables with casual links to the independent variable, depressive symptoms. The remaining causal relationships (solid arrows) do not function as confounders and therefore do not require adjustment. This is visualized in the graph because variables that are causally associated with the dependent variable (variables in white boxes that have solid arrows to adherence) are not causally associated with the independent variable (these variables do not have solid arrows terminating at depressive symptoms).

Abbreviations: DAG, directed acyclic graph; DISTANCE, the Diabetes Study of Northern California; PHQ, Patient Health Questionnaire.

Reference

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