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The Association Between Depressive Symptoms Access to Diabetes Care and Glycemic Control in Five MiddleIncome Countries

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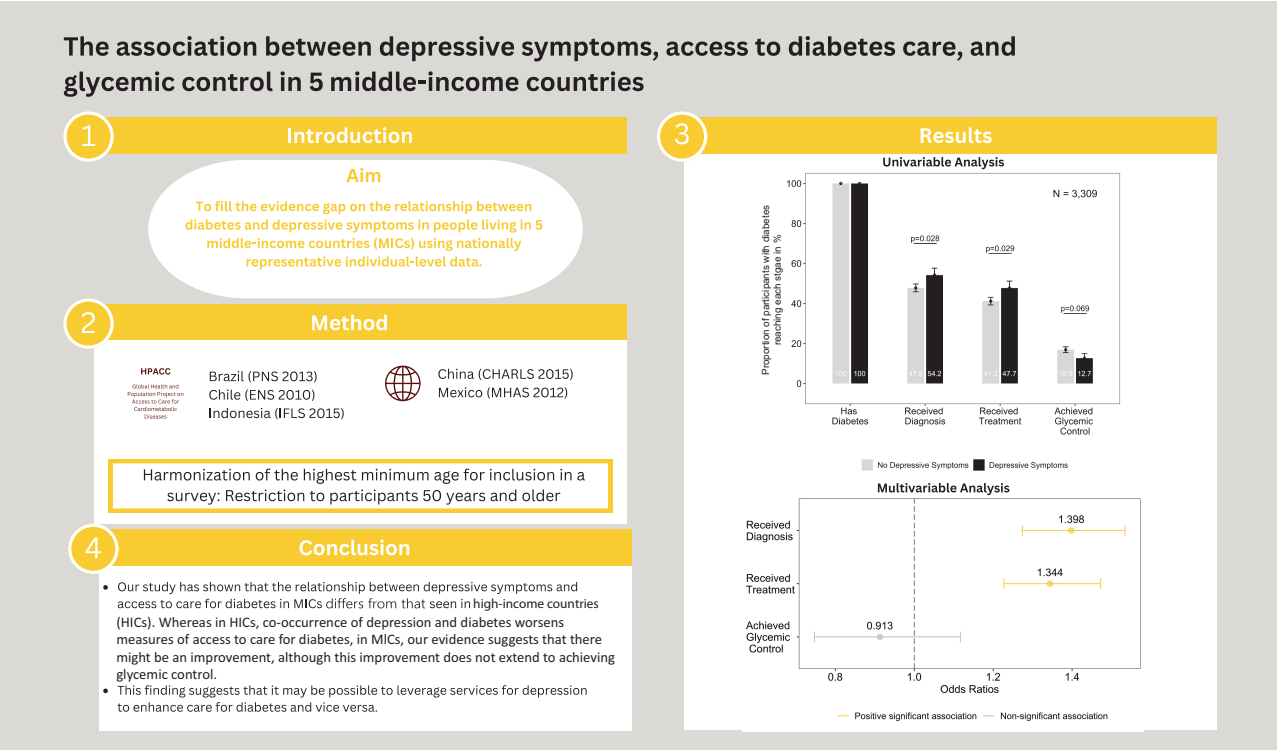
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Diabetes Care
American Diabetes Association

The Association Between Depressive Symptoms, Access to Diabetes Care, and Glycemic Control in Five Middle-Income Countries

Lena Merkel, Felix Teufel, Deborah Carvalho Malta, Michaela Theilmann, Maja-Emilia Marcus, David Flood, Pascal Geldsetzer, Jennifer Manne-Goehler, Frank Petrak, Sebastian Vollmer, and Justine Davies

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ARTICLE HIGHLIGHTS

- **Why did we undertake this study?**
  In middle-income countries, limited research has examined the relationship between depressive symptoms and diabetes care outcomes relevant to glycemic control. Our study contributes to filling this knowledge gap.
- **What is the specific question we wanted to answer?**
  We wanted to describe the differences in diabetes care outcomes and glycemic control in people with and without coincidental depressive symptoms living across five middle-income countries.
- **What did we find?**
  We found that individuals with diabetes and depressed mood were more likely to be diagnosed with diabetes and receive treatment compared with those without depressed mood.
- **What are the implications of our findings?**
  Our findings contrast with results from high-income countries and imply the potential for reciprocal enhancement of diabetes and depression care through integrated services.

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The Association Between Depressive Symptoms, Access to Diabetes Care, and Glycemic Control in Five Middle-Income Countries

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OBJECTIVE

The relationship between depression, diabetes, and access to diabetes care is established in high-income countries (HICs) but not in middle-income countries (MICs), where contexts and health systems differ and may impact this relationship. In this study, we investigate access to diabetes care for individuals with and without depressive symptoms in MICs.

RESEARCH DESIGN AND METHODS

We analyzed pooled data from nationally representative household surveys across Brazil, Chile, China, Indonesia, and Mexico. Validated survey tools Center for Epidemiologic Studies Depression Scale Revised, Composite International Diagnostic Interview, Short Form, and Patient Health Questionnaire identified participants with depressive symptoms. Diabetes, defined per World Health Organization Package of Essential Noncommunicable Disease Interventions guidelines, included self-reported medication use and biochemical data. The primary focus was on tracking diabetes care progression through the stages of diagnosis, treatment, and glycemic control. Descriptive and multivariable logistic regression analyses, accounting for gender, age, education, and BMI, examined diabetes prevalence and care continuum progression.

RESULTS

The pooled sample included 18,301 individuals aged 50 years and above; 3,309 (18.1%) had diabetes, and 3,934 (21.5%) exhibited depressive symptoms. Diabetes prevalence was insignificantly higher among those with depressive symptoms (28.9%) compared with those without (23.8%, $P = 0.071$). Co-occurrence of diabetes and depression was associated with increased odds of diabetes detection (odds ratio [OR] 1.398, $P < 0.001$) and treatment (OR 1.344, $P < 0.001$), but not with higher odds of glycemic control (OR 0.913, $P = 0.377$).

CONCLUSIONS

In MICs, individuals aged 50 years and older with diabetes and depression showed heightened diabetes identification and treatment probabilities, unlike patterns seen in HICs. This underscores the unique interplay of these conditions in different income settings.

Over the past few decades, diabetes has become increasingly prevalent and is now ranked eighth in the Global Burden of Disease cause of disability-adjusted life years (1). As a leading risk factor for cardiovascular disease, it is imperative to understand

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ORIGINAL ARTICLE

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individual, societal, economic, and disease-related factors associated with diabetes prevalence and access to care to limit its impact. This is especially important in middle-income countries (MICs) where rapid demographic, epidemiological and socioeconomic shifts are associated with an increasingly large burden of diabetes that health systems have struggled to cope with (1). Understanding of associations with diabetes and barriers to quality clinical care in MICs has increased in recent years (1–4). However, beyond behavioral factors and socioeconomic status, knowledge of other disease-level associations with diabetes and receipt of clinical care is limited (5,6).

In high-income countries (HICs), depression and diabetes are intertwined. As early as the 17th century, the anatomist Thomas Willis established the connection between diabetes and emotional distress (7,8). Now, data from several HICs show a well-recognized bidirectional relationship between depression and diabetes, with depression being more prevalent in people with diabetes and vice versa. Additionally, substantial evidence indicates a strong association between depression and suboptimal care outcomes for individuals with diabetes, notably in relation to the incidence of complications and health care utilization. Moreover, depression correlates with higher mortality rates and adverse psychosocial outcomes, such as diabetes distress, diminished quality of life, and reduced adherence to diabetes treatment regimens (9–11).

Multiple causal mechanisms have been proposed to explain the co-occurrence of diabetes and depression. For example, diabetes and depression share common biological mechanisms as well as environmental and lifestyle risk factors. As such, they may interact in a way that exacerbates each other's outcomes (9). Diabetes also increases the risk of depression due to the psychological burden of diabetes management, so-called diabetes distress (11). Moreover, depression heightens the likelihood of developing diabetes, potentially stemming from the side effects of antidepressant medications (in relation to type 2 diabetes), as well as poor diet regimens and low levels of physical activity (12–14). The adverse impacts of depression on the effectiveness of diabetes care have been postulated to be related to factors such as nonadherence to treatment regimens (15), low levels of physical activity (16), and decreased quality of life (17,18).

Despite existing evidence gaps, the importance of poor mental health, including depression, has been increasingly recognized in MICs (19). Mental health is also viewed as an integral part of global health and sustainable development (20). However, despite increasing knowledge of the burden of diabetes or depression in MICs, much less is known about the relationship between depression and diabetes, with the few studies of this relationship being small and clinic based, in geographically limited areas, and with a focus on comorbidity as an outcome (21–24). To our knowledge, there has not yet been a study examining the association of depression with care outcomes for people with diabetes in MIC settings.

Our study aims to use nationally representative individual-level data from large, population-based surveys to describe differences in diabetes care outcomes and glycemic control in people with and without coincidental depressive symptoms living across five MICs. Additionally, we explore the effect of antidepressant use on this relationship.

RESEARCH DESIGN AND METHODS

Data Sources

We first constructed an individual participant-level, cross-sectional data set from nationally representative household surveys from the Global Health and Population Project on Access to Care for Cardiometabolic diseases (HPACC) data set (25). We limited this data set to surveys that used a validated screening tool for depressive symptoms. Eligible surveys had to include a diabetes biomarker (fasting or random glucose or the glycated hemoglobin A1c [HbA_{1c}]) and data on diabetes-related care outcomes for testing and treatment. We then supplemented the surveys available from HPACC with additional nationally representative surveys with individual participant data conducted in a MIC after 2008. For this step, we did a systematic search in online databases including the World Health Organization (WHO) Noncommunicable Disease Microdata Repository, the Evaluation Global Health Data Exchange of the Institute for Health Metrics, the Gateway to Global Aging, and the Demographic and Health Surveys Program to identify additional surveys that met the inclusion criteria. Data were locked for analysis in February 2023.

Variable Definitions

Presence of diabetes was defined using biochemical evidence of diabetes, as measured in the survey and based on definitions provided in the WHO Package of Essential Noncommunicable Disease Interventions (WHO PEN) guidelines, and self-reported use of glucose-lowering oral medication or insulin injections. As in previous work, this method was considered more reliable than using self-reports of diabetes status, which were also not available in all surveys. For biochemical evidence of diabetes, we used fasting plasma glucose of 7.0 mmol/L or higher, random plasma glucose of 11.1 mmol/L or higher, or an HbA_{1c} measure of 6.5% or higher. In countries with both fasting plasma glucose and HbA_{1c} measurements available, we used the latter as the preferred biomarker value, as detailed in previous manuscripts (3,25). In countries with only the capillary glucose measure available, we multiplied the capillary measures by 1.11 to produce plasma equivalents (Supplementary Material 1) (26).

The stages of the care continuum were defined using the care cascade approach in line with previous work (3,24,27). The first stage was defined as being diagnosed, among those identified as having diabetes as specified above. Being diagnosed was based on self-reported receipt of diagnosis ("received diagnosis") (28). The second stage was defined as self-reported use of glucose-lowering medication (either oral medication or insulin injections) among those who had received a diagnosis ("received treatment"). The third stage was defined as having achieved glycemic control consistent with the WHO PEN guidelines ("achieved glycemic control") among those who were treated. We define glycemic control as plasma glucose levels lower than 10.1 mmol/L and HbA_{1c} lower than 7%. An overview of the questions used to construct the cascade is provided in Supplementary Material 2.

The presence of clinically relevant depressive symptoms was defined by threshold scores relevant to the respective screening module included in the country survey, using the following tools and cut points: the Center for Epidemiologic Studies Depression Scale Revised (CESD-R) with 10 and 9 items and cut points of 10/30 and 5/9, respectively (29) (Supplementary

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Material 3 and 4); the Major Depressive Episodes screening module of the Composite International Diagnostic Interview, Short Form (CIDI-SF, Supplementary Material 5), which evaluated symptoms based on affirmative answers to at least one screening question and, at a minimum, additional five symptoms (30); and the Patient Health Questionnaire (PHQ-9, Supplementary Material 6) with a cut point of 10/27 (31). All depression tools and cut point scores have been validated in the respective countries (for references and further details, see Supplementary Material 7). To indicate the presence of depressive symptoms, we constructed a dichotomous variable indicating whether an individual was above the threshold of the respective screening tool. We set the variable to missing if participants did not answer all questions of the screening tool. We used additional information on self-reported antidepressant use among respondents in our exploratory analysis. Since these data were only available for a subset of countries, we could not control for antidepressant use in our main analysis.

In addition to our predictors of interest, we included individual-level risk factors that are recognized to affect both diabetes and depression. Sociodemographic risk factors were age as continuous variable and sex as dichotomous variable. Socioeconomic status was indicated by educational attainment categorized as no schooling, primary education, and secondary or above. BMI was categorized as underweight ($<$18.5 kg/m^2), normal (18.5 to $<$25.0 kg/m^2), overweight (25.0 to $<$30.0 kg/m^2), or obese ($\geq$30.0 kg/m^2).

Statistical Analysis

We performed a complete case analysis. We first described the relationship between depressive symptoms and our outcome variables in univariable analyses. We reported the 95% exact (Clopper-Pearson) CIs and the *P* value of the χ^2 test statistic for comparisons. To further explore relationships and reduce potential confounding, we conducted multivariable logistic regression analysis with individual-level predictors and country-level fixed effects (using country dummy variables) to control for unobserved heterogeneity across countries. We used survey weights and rescaled them such that each country is weighted equally. SEs were clustered at the country level. All estimates were reported as odds ratios (ORs) and accounted for the multistaged probabilistic sampling method by using sampling weights. The analysis was done in *R* (version 4.2.1).

Because of differences in the age inclusion criteria across surveys, we restricted our main sample to participants of 50 years and older, corresponding to the highest minimum age for inclusion in a survey. We additionally did a sensitivity analysis using a lower age threshold.

To further understand the findings in our main analysis, we conducted additional analyses. First, we compared the prevalence of depressive symptoms among individuals with diabetes reaching each care cascade stage compared with those who did not reach this stage. Second, to understand whether our results were affected by severity of depression, we repeated the univariable analysis further disaggregating by the severity of depressive symptoms for each included individual. Two different methods were used for this purpose. Given that PHQ-9 allows cutoff scores to estimate severity of depression, we first used these validated cut points for the severity of depressive symptoms in countries where this survey was used (31). Furthermore, we calculated and harmonized quintiles across the range of total depression screening tool scores in all countries. Third, we repeated the main analysis with only those individuals identified with elevated markers of diabetic control.

Sensitivity Analyses

To test the validity of our results, we conducted multiple sensitivity analyses. First, we limited our sample to surveys with a minimum age of 18 years and above. Second, we conducted a sensitivity analysis considering lifestyle advice received—both diabetes-specific and general cardiovascular risk reduction advice—in our treatment stage. In a third sensitivity analysis, we used a threshold HbA_{1c} measure of lower than 8% for the definition of the last cascade step, because our sample included people 65 years and older, for which a less stringent threshold for glycemic control is sometimes recommended (32). In a fourth sensitivity analysis, we examined whether symptomatic hyperglycemia confounded our results. To do this, we first entered glycemia (HbA_{1c} or plasma glucose levels) as an independent variable into the model, either as a continuous variable for countries where it was available, or as harmonized quintiles of these variables across all countries. Second, we entered an interaction term between glycemia and depressive symptoms.

Exploratory Analysis

To explore whether the association found in the analyses was affected by antidepressant use by depressed individuals, we conducted an exploratory analysis. For this, we compared the diabetes prevalence and the care cascade outcomes in depressed participants with and without self-reported antidepressant use.

The data set is available from the HPACC upon request (https://www.hpaccproject.org).

RESULTS

Study Population

Our final cross-sectional data set comprised data from Brazil, Chile, China, Indonesia, and Mexico, five major transitioning MICs, which together account for more than a quarter of the world population. Moreover, all five countries are either currently or projected to be among the eight leading countries in terms of diabetes prevalence (33). Details of the surveys and sample sizes are given in Supplementary Material 8 and 9. Additional information on the biomarker data used to define diabetes status and missingness in our outcome variables of interest is provided in Supplementary Material 9. Of the four depression screening instruments used, the CESD-R-10 was used in China and Indonesia (n = 11,539), the PHQ-9 in Brazil (n = 3,128), the CIDI-SF in Chile (n = 2,065), and the CESD-9 in Mexico (n = 1,571).

We included 18,301 individuals of 50 years and older of which 3,309 (18.1%, 95% CI 17.5–18.6) had diabetes and 3,934 (21.5%, 95% CI 20.9–22.1) had depressive symptoms (Table 1 and Supplementary Material 10). In the countries included in the main analysis, diabetes prevalence ranged from 12.2% (95% CI 10.9–13.6) in Indonesia to 38.4% (95% CI 36.0–41.0) in Mexico. The prevalence of depressive symptoms was lowest in Brazil (9.9%, 95% CI 8.9–11.0) and highest in Mexico (35.6%, 95% CI 33.2–38.0).

Diabetes Prevalence and Depressive Symptoms

Diabetes prevalence was not significantly higher among participants with depressive

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Table 1—Participant characteristics

Characteristics	Total
Total sample, *n* (%)	18,301 (100%)
Age (years), mean (SD)	62.59 (8.89)
Sex, *n* (%)	
Male	8,317 (45.4%)
Female	9,984 (54.6%)
Educational attainment, *n* (%)	
No formal schooling	4,017 (22.0%)
Primary school	8,374 (45.9%)
Secondary school or above	5,859 (32.1%)
BMI*, *n* (%)	
Underweight	914 (5.1%)
Normal weight	8,401 (46.5%)
Overweight	5,996 (33.2%)
Obese	2,737 (15.2%)
Has depressive symptoms† (as per screening tool), *n* (%)	
No	14,367 (78.5%)
Yes	3,934 (21.5%)
Uses antidepressants‡, *n* (%)	
No	2,148 (84.3%)
Yes	399 (15.7%)
Has diabetes§ (as per study definition), *n* (%)	
No	14,992 (81.9%)
Yes	3,309 (18.1%)

*BMI was categorized as underweight ($<$18.5 kg/m^2), normal (18.5 to $<$25.0 kg/m^2), overweight (25.0 to $<$30.0 kg/m^2), or obese ($\geq$30.0 kg/m^2). †Depressive symptoms were defined based on the threshold scores of the screening modules: *1*) CESD-R–10 (threshold: 10/30), *2*) CESD-9 (threshold: 5/9), *3*) Major Depressive Episodes CIDI-SF (threshold: one screening symptom and a minimum of five additional symptoms), or *4*) PHQ-9 (threshold: 10/27). ‡Antidepressant use was defined as self-reported use of an unspecified antidepressant medication. §Diabetes was defined as any of the following: *1*) self-reported use of glucose-lowering oral medications or insulin injections, *2*) fasting plasma glucose $\geq$7.0 mmol/L, *3*) random plasma glucose $\geq$11.1 mmol/L, or *4*) HbA_{1c} measure $\geq$6.5%.

symptoms (28.9%, 95% CI 27.4–30.3) compared with those without (23.8%, 95% CI 23.12–24.6, *P* for difference = 0.071); the relationship became less significant when including other variables in the model (*P* = 0.594) (Supplementary Material 11).

Diabetes Care Outcomes and Depressive Symptoms

Considering care outcomes for diabetes, in univariable testing, a higher percentage of participants with diabetes and depressive symptoms had their diabetes diagnosed (54.2%, 95% CI 50.8–57.7) than those without depressive symptoms (47.8%, 95% CI 45.8–49.7, *P* for difference = 0.028). Similarly, among those diagnosed, 47.7% (95% CI 44.3–51.2) of participants with depressive symptoms and diabetes had received treatment compared with 41.2% (95% CI 39.2–43.1) without (*P* for difference = 0.029). Fewer (12.7%, 95% CI 10.4–15.0) participants with depressive symptoms than those without (16.9%, 95% CI 15.4–18.4) achieved glycemic control (*P* for difference = 0.069), although this was not statistically significant (Fig. 1). The associations found in the univariable analysis were similar across countries (Supplementary Material 12).

In the multivariable regression model, depressive symptoms remained associated with an increase in the probability of receiving a diagnosis and treatment of diabetes (Fig. 2 and Table 2). Among those with diabetes, the probability of receiving a diagnosis of diabetes was almost 40% higher in people with depressive symptoms compared with those without (OR 1.398, $P < 0.001$). Similarly, the odds of receiving diabetes treatment among those diagnosed were 34.4% (OR 1.344, $P < 0.001$) higher for individuals with diabetes and depressive symptoms compared with those without. There was no significant difference in the odds of achieving glycemic control in those with diabetes and depressive symptoms compared with those without (OR 0.913, *P* = 0.377). The results were similar when conducting multivariable analysis by country (Supplementary Material 13).

The prevalence of depressive symptoms in people with diabetes was marginally, but significantly higher for those who had been diagnosed with diabetes (26.7%, 95% CI 24.5–28.9 compared with 22.4%, 95% CI 20.4–24.3) than those who had not received a diagnosis (*P* for difference = 0.004) (Supplementary Material 14). For the treatment stage, 27.6% (95% CI 25.2–30.0) of individuals who reached this stage had depressive symptoms compared with 22.3% (95% CI 20.5–24.1) in those who did not reach this stage (*P* for difference $<$0.001). Prevalence of depressive symptoms was lower in participants who achieved glycemic control (22.4%, 95% CI 19.0–25.9) compared with those who did not, but this was not significant (24.8%, 95% CI 23.2–26.4, *P* for difference = 0.228).

When analyzing by depression severity levels using the PHQ-9 score (Brazil) or depression score quintiles (all countries), findings for those with at least moderate depression were similar to our main analysis (Supplementary Material 15 and 16). In both analyses, we found that a higher proportion of individuals with at least moderate depression were diagnosed and treated, but did not achieve glycemic control, compared with those without clinically relevant symptoms. Limiting the analysis to people with uncontrolled diabetes did not substantially affect the results (Supplementary Material 17).

Sensitivity Analysis

Results from sensitivity analyses were similar to those in the main analysis.

In a subset of Brazil, Chile, and Indonesia (*n* = 1,723) of individuals aged 18 years and older, there were no significant differences in univariable analysis between participants with and without depressive symptoms for each cascade stage (Supplementary Material 18). Multivariable regression in this sample showed that depression was significantly associated with diabetes prevalence (OR 1.277, *P* = 0.006), diagnosis (OR 1.471, *P* = 0.027), and treatment (OR 1.548, *P* = 0.006) (Supplementary Material 19).

Including lifestyle advice in treatment definition increased treated individuals by 97; but, multivariable analysis results

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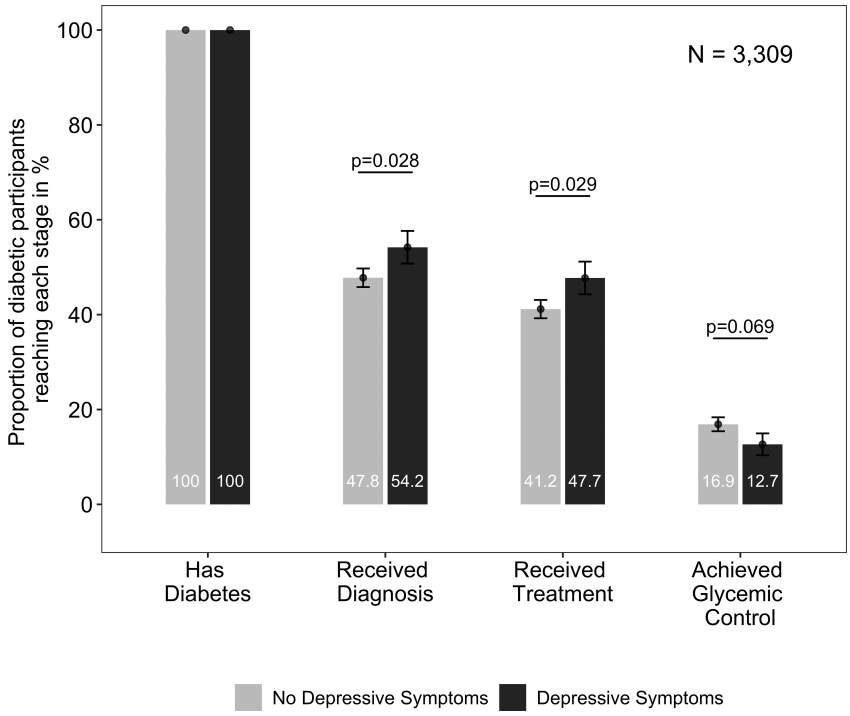


Figure 1—Univariable analysis: diabetes care outcomes. Shown are the proportion of people with diabetes who progress through the diabetes care cascade for respondents with and without depressive symptoms. The first bars are set to 100% and thus represent the whole sample (n = 3,209) who have diabetes, of which 808 had depressive symptoms and 2,501 did not. Diagnosis was received by 417 with and 1,145 without depressive symptoms. Treatment was received by 366 with and 959 without depressive symptoms. Glycemic control was achieved by 127 with and 439 without depressive symptoms. Results are unadjusted for confounding variables and rescaled using survey weights.

remained consistent (Supplementary Material 20). Raising the HbA_{1c} threshold for glycemic control resulted in 188 more individuals achieving glycemic control; sensitivity analysis showed similar multivariable results (Supplementary Material 20).

While the level of hyperglycemia was significantly associated with diagnosis and treatment or diabetes, it did not affect the directionality or scale of the association between depressive symptoms and these outcome variables. The findings hold for both variable specifications, continuous measures of both HbA_{1c} and plasma glucose levels, and harmonized quintiles of glycemic control (Supplementary Material 21–23). The interaction between level of glycemia and depressive symptoms had no effect on outcomes (Supplementary Material 24 and 25).

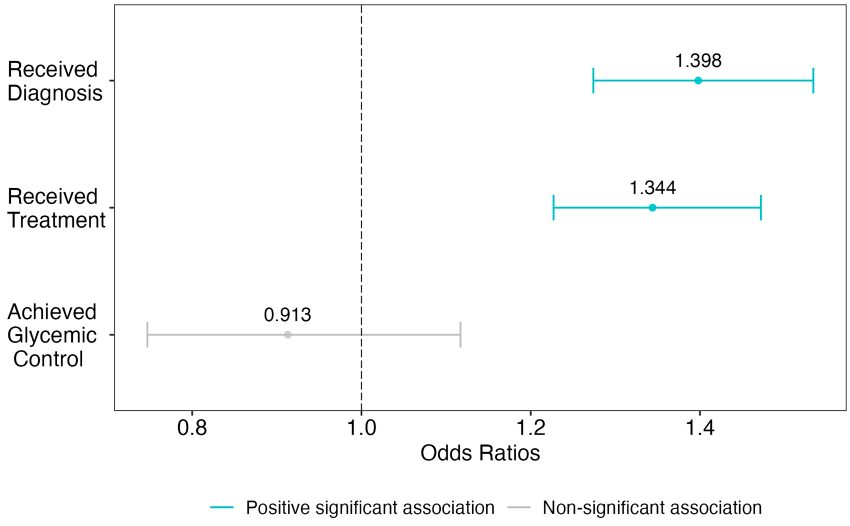


Figure 2—Multivariable analysis: depressive symptoms and diabetes care outcomes. Shown are point estimates and 95% exact CIs for the explanatory variable depressive symptoms on the diabetes care outcomes, receipt of diagnosis, receipt of treatment, and achievement of glycemic control. Coefficients are expressed as ORs. The x-axis is log transformed.

Exploratory Analysis

Exploration of the role of antidepressant use on the care outcomes was done in 108 participants of 50 years and older with depressive symptoms and diabetes from Brazil, Chile, and China. Of these participants, 36 used an antidepressant, and 72 did not. We found no significant difference in progress through the cascade among participants who used antidepressants compared with those who did not (P for difference = 0.406) (Supplementary Material 26).

CONCLUSIONS

Our study provides understanding of the implications of depressive symptoms for individuals with diabetes in MICs and, to the best of our knowledge, is the first study to explore the relationship between depressive symptoms and care outcomes for people with diabetes across multiple countries using a large representative sample.

Our analyses show that, in individuals aged 50 years and above living across five MICs, the co-occurrence of diabetes and depression is linked to higher odds of diabetes detection and treatment, but not to increased likelihood of achieving glycemic control. These patterns hold when analyzed by individual country. Our results are supported by our sensitivity analysis, which indicates a stronger association with increasing severity of depression. Our findings are consistent with the idea of a detection effect, where patients interacting with the health care system for one condition might receive more regular screening for the other (34). The association being lost at the cascade stage of achieving control might be explained by the fact that depression is associated with unsatisfactory self-care and nonadherence to treatment, which may adversely affect diabetes management, as demonstrated in HICs (16–18). Our study contrast with previous research in low- and middle-income countries using population-based data. For example, a study in Zanzibar

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Table 2—Multivariable regression results

	1		2		3	
	Received diagnosis		Received treatment		Achieved glycemic control	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
N	3,255		3,255		3,255	
Depressive symptoms						
No	1 (ref)		1 (ref)		1 (ref)	
Yes	1.398 (1.274, 1.534)	<0.001	1.344 (1.227, 1.472)	<0.001	0.913 (0.747, 1.117)	0.377
Sex						
Male	1 (ref)		1 (ref)		1 (ref)	
Female	1.341 (1.262, 1.425)	<0.001	1.369 (1.260, 1.487)	<0.001	0.960 (0.736, 1.252)	0.762
Age (cont.)	1.003 (0.990, 1.016)	0.687	1.008 (0.998, 1.018)	0.136	1.015 (1.000, 1.030)	0.057
Educational attainment						
No formal schooling	1 (ref)		1 (ref)		1 (ref)	
Primary school	1.083 (0.760, 1.542)	0.659	1.020 (0.782, 1.331)	0.884	1.122 (0.902, 1.396)	0.302
Secondary school or above	1.246 (0.715, 2.172)	0.438	1.267 (0.793, 2.024)	0.322	1.562 (1.434, 1.700)	<0.001
BMI						
Underweight	0.553 (0.236, 1.296)	0.173	0.707 (0.302, 1.655)	0.425	0.473 (0.252, 0.888)	0.020
Normal weight	1 (ref)		1 (ref)		1 (ref)	
Overweight	0.829 (0.738, 0.932)	0.002	0.858 (0.739, 0.997)	0.046	1.139 (0.822, 1.578)	0.435
Obese	0.574 (0.459, 0.717)	<0.001	0.601 (0.507, 0.712)	<0.001	0.980 (0.858, 1.120)	0.767

Regression results of multivariable logistic regression analysis with individual-level predictors and country-level fixed effects (using country dummy variables). Observations are weighted using survey weights. We report OR and the 95% CIs. Ref, reference category.

found no link between mental illness and diabetes. While the same study showed no association of mental illness with hypertension care stages, it lacked power to analyze diabetes cases (24). Another study in South Africa also found no significant link between mental illness and diabetes care progression (35). The differences may be explained by the small sample sizes and the differences in income levels, with Zanzibar being low income.

Our findings contrast with prospective cohort and cross-sectional studies done in HICs where individuals with diabetes and depression perform worse in care outcomes compared with those without depression (17,18,36). This difference may be explained by higher diabetes detection rates in HICs (although there are various socioeconomic statuses and indicators of vulnerability [37]). In MIC settings, where health systems are underresourced, fewer people with diabetes are detected. In this context, it could be hypothesized that individuals may be more cognizant of experiencing depressive symptoms than diabetes symptoms and thus more frequently visit health practitioners with depression and have their diabetes detected as a second condition. Although, it is recognized that, in many MICs, depression is underdiagnosed, depression is characterized by a diminished sense of emotional well-being, and directly and perceptibly impacts an individual's quality of life (18). This could make it more likely that affected individuals will make their condition visible within the health care system, whereas, in contrast, diabetes is likely to be asymptomatic for long durations.

Given that the surveys used in our study relied on self-reported symptoms of depression, we considered that our results might contrast with studies done in HICs because of respondents in surveys reporting milder depression than is seen in HIC studies, which often use health system records (17,18,36). Social desirability or ascertainment bias could lead to respondents with severe depression either not taking part in the survey or minimizing their symptoms of depression, biasing our sample toward reporting less severe depression that seen in HIC studies. However, from an analysis of the distribution of depressive symptoms, it was clear that our sample did contain participants reporting severe depression, and, from our sensitivity analyses, it can be seen that, in those with severe depression, the associations were the same as those seen in the main sample.

We also considered that our results might be because of people who have knowledge of their diabetes suffering from depression as a result (11). This would result in a greater prevalence of depressive symptoms in people who have been diagnosed with—and potentially put on treatment of—diabetes than those with diabetes who had not reached these cascade steps. That prevalence of depressive symptoms was lower in those who achieved glycemic control versus those who were not lends some support to this hypothesis, as people with diabetes who are controlled may have fewer depressive symptoms than people who are not controlled. But the directionality can be only fully explored in longitudinal studies, which are lacking in MICs at the present time.

In the additional exploratory analysis, we investigated the potential role of antidepressant use for the association between diabetes and depression. Our results give an indication that individuals with diabetes and depressive symptoms who used antidepressants received a diagnosis and treatment, as well as achieving glycemic control, as has been suggested in previous studies (38,39). But, as these differences are not statistically significant, we cannot draw firm conclusions from this exploratory analysis.

Our findings indicate that it is imperative to integrate mental health care into that for noncommunicable diseases, particularly in MICs where the prevalence of

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diabetes and depression is high. Adopting a health care platform approach that integrates care for individuals across multiple diseases, as South Africa has planned for in their Ideal Clinics, rather than being confined to disease silos, could represent a promising approach for improving the management of co-occurring diabetes and depression.

Limitations

This study has limitations to consider when interpreting the findings. First, the small number of countries included in our study highlights the need for more comprehensive data on chronic diseases and mental health in low- and middle-income countries. Separate consideration of chronic diseases and mental health in most surveys limits data availability for studying their associations. Although the number of surveys collecting harmonized data on noncommunicable disease epidemiology and mental health is increasing, the current data set remains limited in size. Our results, therefore, are not representative of all MICs globally but include the largest group on this topic, to our knowledge.

The study's predictors and outcomes are limited by the available measures' accuracy, reliability, and differences in recall period. Additionally, we defined diabetes status and glycemic control based on a biomarker point estimate that could be impacted by the quality of blood sample collection and laboratory testing; however, this is similar to what is done in other epidemiology studies and the only available clinical data in many MICs. Finally, we could not differentiate between diabetes type 1 and type 2. Given the higher prevalence of type 2 diabetes in general populations and a median age of 61 years, most participants likely had type 2 diabetes (40).

The use of complete case analysis may have introduced selection or information bias. While we used individual weights to account for the missingness in the diabetes biomarker data, we assumed noninformative missingness in the depression screening tools. However, missingness in the screening tools was overall low (median = 0.3%).

Finally, the use of screening tools for depressive symptoms may lead to an overestimation of depression rates. Furthermore, some researchers have argued that existing screening tools for depression are not suitable to detect depression in patients with diabetes, because of the possibility of diverging phenotypes (9,10). For example, in individuals with diabetes, depressive symptoms and diabetes-related distress are not clearly delineated concepts (11). Consequently, various clinical profiles of depression exist based on blurred definitions and the severity of symptoms. This limitation may be exacerbated by the fact that we harmonized different screening tools.

Conclusion

Differences in findings between MIC and HIC suggest that porting solutions based on findings in HIC may not be appropriate in MIC settings. The positive associations between having depressive symptoms and access to care for diabetes lends further support for integration of care for mental health conditions into existing and developing health care systems for diabetes care.

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