CLIN CARE/EDUCATION/NUTRITION/PSYCHOSOCIAL

High Prevalence of Depressive Symptoms in Patients With Type 1 and Type 2 Diabetes in Developing Countries: Results From the International Diabetes Management Practices Study

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OBJECTIVE

Depression is common in people with diabetes, but data from developing countries are scarce. We evaluated the prevalence and risk factors for depressive symptoms in patients with diabetes using data from the International Diabetes Management Practices Study (IDMPS).

RESEARCH DESIGN AND METHODS

IDMPS is an ongoing multinational, cross-sectional study investigating quality of care in patients with diabetes in real-world settings. Data from wave 5 (2011), including 21 countries, were analyzed using the 9-item Patient Health Questionnaire (PHQ-9) to evaluate depressive symptoms. Logistic regression analyses were conducted to identify risk factors of depressive symptoms.

RESULTS

Of 9,865 patients eligible for analysis, 2,280 had type 1 and 7,585 had type 2 diabetes (treatment: oral glucose-lowering drugs [OGLD] only, $n = 4,729$; OGLDs plus insulin, $n = 1,892$; insulin only, $n = 964$). Depressive symptoms (PHQ-9 score ≥ 5) were reported in 30.7% of those with type 1 diabetes. In patients with type 2 diabetes, the respective figures were 29.0% for OGLDs-only, 36.6% for OGLDs-plus-insulin, and 46.7% for insulin-only subgroups. Moderate depressive symptoms (PHQ-9 score 10–19) were observed in 8–16% of patients with type 1 or type 2 diabetes. Female sex, complications, and low socioeconomic status were independently associated with depressive symptoms. In type 1 diabetes and in the type 2 diabetes OGLDs-only group, depression was associated with poor glycemic control.

CONCLUSIONS

Depressive symptoms are common in patients with diabetes from developing countries, calling for routine screening, especially in high-risk groups, to reduce the double burden of diabetes and depression and their negative interaction.

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Patients with type 1 and type 2 diabetes both have a high prevalence of depressive symptoms, with ∼30% having depressive symptoms and 11% having major depression (1). A systematic review of studies predominantly from the U.S. and Europe reported the prevalence of depression was threefold higher in patients with type 1 diabetes and nearly twofold higher in patients with type 2 diabetes compared with the general population (2). A U.S. study also showed that poor glycemic control, female sex, and low levels of general education were independent risk factors for major depressive symptoms (3).

There is emerging evidence regarding the bidirectional association between depression and diabetes. In some studies, depression was associated with an increased risk of type 2 diabetes, whereas others showed that diabetes was a risk factor for depression (4,5). While the causal nature of this association remains uncertain, depression in people with diabetes may lead to poor treatment adherence, suboptimal glycemic control, increased risks of microvascular and macrovascular complications, and increased health care costs (6–9). Studies from the U.S. show that depression in people with diabetes is also associated with an increased risk of premature death, especially among older adults (10,11). For these reasons, the American Diabetes Association and the International Diabetes Federation recommend screening for depressive symptoms in people with diabetes at the initial visit (12,13). American Diabetes Association guidelines suggest screening should be performed at periodic intervals and when there is a change in disease, treatment, or life circumstance (13).

Most data documenting the diabetes–depression link are from high-income countries, yet almost 80% of people with diabetes reside in developing countries (14). Our aim was to address this knowledge gap by using data from the International Diabetes Management Practices Study (IDMPS) to estimate the frequency of depressive symptoms and associated risk factors in people with type 1 and type 2 diabetes living in developing countries. The IDMPS is an ongoing worldwide observational study program that describes patient profiles, management, and patterns of care over time in developing countries (15). Data for IDMPS have been collected in separate successive waves since 2005 and have provided new information on health care resource use and glycemic control and their associations with self-monitoring of blood glucose and patient education in people with diabetes living in developing countries (15–18). The present analysis explores the prevalence and associated risk factors of depressive symptoms in people with type 1 and type 2 diabetes by using data from the fifth wave of IDMPS, performed in 2011.

RESEARCH DESIGN AND METHODS

Study Design and Procedures

The IDMPS is an ongoing international, multicenter, observational study that has collected data from adult patients with type 1 or type 2 diabetes in distinct waves since 2005 (15). Each wave consists of a 2-week cross-sectional survey period when data on patient profiles and routine care practices were collected. The fifth wave of IDMPS was conducted in 2011 by 879 physicians in the following countries:

Africa: Algeria, Cameroon, Egypt, Morocco, Senegal, and Tunisia;
Eurasia: Georgia, Kazakhstan, Russia, Ukraine, and Uzbekistan;
Latin America: Argentina, Colombia, and Venezuela;
Middle East: Jordan, Lebanon, Kingdom of Saudi Arabia, and United Arab Emirates; and
South Asia: India, Pakistan; and Turkey.

Patients' demographic and socioeconomic characteristics, medical history, previous and current treatments, glycemic control, cardiovascular risk factors, diabetes-related complications, diabetes-related education, and mode of follow-up were collected in case report forms.

In addition, patients were asked to complete the 9-item Patient Health Questionnaire (PHQ-9) to evaluate depressive symptoms (19). The PHQ-9 is a brief screening questionnaire used for screening patients for depressive symptoms. Each of the nine criteria for depression of the DSM-IV are scored as "0" (not at all) to "3" (nearly every day). PHQ-9 scores of 5–9, 10–14, 15–19, and ≥20 are suggestive of mild, moderate, moderately severe, and severe depression, respectively (19). A PHQ-9 score of <5 represents no depression (19). The study was conducted in accordance with the relevant ethical standards and was approved by appropriate regulatory and ethics committees in all participating countries and investigational centers.

Sanofi researchers and staff coordinated and monitored the study in each participating country, assisting the local coordinators and investigators in collecting data.

Statistical Analysis

Physicians with experience of prescribing insulin therapy were selected randomly after stratification based on specialty. The number of participating physicians recruited was based on the country-specific estimated patient sample size required. Each physician recruited the first 10 patients with type 2 diabetes and first 5 patients with type 1 diabetes who presented during routine clinical practice in a 2-week period. The patient sample size of IDMPS wave 5 was determined on a country basis, based on the primary objective of IDMPS, which was to assess the therapeutic management of patients with type 2 diabetes over time. In addition to the primary objective, each wave of IDMPS has a particular focus. In wave 5, we aimed to analyze the pattern of depressive symptoms in patients with type 1 and type 2 diabetes, and the results are reported here.

SAS 9.2 software (SAS Institute, Cary, NC) was used for statistical analysis. Descriptive analyses were performed in patients with type 1 and type 2 diabetes. The latter group was further analyzed according to treatment-type subgroups: oral glucose-lowering drugs (OGLDs) only, OGLDs plus insulin, and insulin only. In wave 5 of IDMPS, use of glucagon-like 1 receptor agonists was captured; however, only very few patients (1.3%) used this class of drug. As such, when considering the type 2 diabetes therapy subgroups, these patients were included in the OGLD-only, OGLD-plus-insulin, or insulin-only therapy subgroups.

All data are expressed as mean ± SD or median (interquartile range), as appropriate. Depression was defined as a PHQ-9 score of ≥5, with subcategories defined as follows: mild, PHQ-9 score of 5–9; moderate, PHQ-9 score of 10–19; and severe, PHQ-9 score of 20–27. Univariate logistic regression analyses were conducted to identify risk factors for depression. Potential risk factors included

ethnicity, age, sex, living area, education level, health insurance, follow-up visit by a specialist, and specialty of the study physician. Other factors directly related to diabetes included disease duration, diabetes education, BMI, microvascular and macrovascular complications, self-management (self-monitoring of blood glucose and self-titration of insulin), insulin treatment, OGLD treatment, number of OGLDs, HbA_{1c} level, and fasting blood glucose level. Log-linearity was assessed for the quantitative variables. If the assumption of log-linearity was not met, the corresponding categorical variable was considered in the model. Variables significant at a P value of ≤ 0.20 were considered for multivariate logistic regression models. A backward approach was used to test each potential risk factor in the multivariate model adjusted on the country expressed as the odds ratio with 95% CI. A P value of ≤ 0.05 (two-tailed) was considered to be significant. Interactions between significant variables selected by the multivariate model were tested.

RESULTS

Complete PHQ-9 questionnaire data were collected from 9,865 eligible patients. Among them, 2,280 patients had type 1 diabetes, and 7,585 patients had type 2 diabetes, comprising 4,729 treated with OGLDs alone, 1,892 treated with OGLDs plus insulin, and 964 treated with insulin alone.

Patient Characteristics
Patients with type 2 diabetes were older than those with type 1 diabetes. Both groups had similar proportions of women (type 1 diabetes: 52.5%; type 2 diabetes subgroups: 52.0–54.9%). The mean ± SD disease duration was 11.8 ± 9.2 years in the type 1 diabetes group and ranged from 6.8 ± 6.1 to 12.6 ± 8.6 years in the type 2 diabetes subgroups. The proportion of patients with the last recorded HbA_{1c} <7% (<53 mmol/mol) was 22.6% in the type 1 diabetes group. Among those with type 2 diabetes, HbA_{1c} <7% (<53 mmol/mol) was recorded in 41.1% in the OGLD-only subgroup, in 16.5% in the OGLDs-plus-insulin subgroup, and in 18.5% in the insulin-only subgroup (Table 1). Obesity, hypertension, and dyslipidemia were more common in the type 2 diabetes

group than in the type 1 diabetes group. In the latter group, 46.8% and 9.1% of patients had microvascular and macrovascular complications, respectively. Among patients with type 2 diabetes, the respective corresponding figures were 36.8% and 16.0% in the OGLDs-only subgroup, 64.3% and 28.4% in the OGLDs-plus-insulin subgroup, and 77.0% and 44.7% in the insulin-only subgroup.

Depressive Symptoms
In the type 1 diabetes group, 30.7% (95% CI 28.8, 32.6) reported depressive symptoms (PHQ-9 score ≥ 5). Overall, 20.4% (95% CI 18.8, 22.2) of patients with type 1 diabetes reported mild symptoms (PHQ-9 score 5–9), 8.9% (95% CI 7.8, 10.1) reported moderate symptoms (PHQ-9 score 10–19), and 1.3% (95% CI 0.9, 1.9) reported severe symptoms (PHQ-9 score ≥ 20) (Fig. 1*A* and *B*). In patients with type 2 diabetes, 33.1% (95% CI 32.1, 34.2) reported depressive symptoms, 22.1% (95% CI 21.2, 23.0) reported mild symptoms, 9.9% (95% CI 9.3, 10.6) reported moderate symptoms, and 1.2% (95% CI 0.9, 1.4) reported severe symptoms (PHQ-9 score ≥ 20) (Fig. 1*A* and *B*). Higher proportions of insulin-treated patients with type 2 diabetes reported depressive symptoms compared with those treated with OGLDs only (36.6% [95% CI 34.5, 38.8] of patients receiving OGLDs plus insulin and 46.7% [95% CI 43.5, 49.9] of patients receiving insulin only vs. 29.0% [95% CI 27.7, 30.3] of patients receiving OGLDs only).

Eurasia had the highest proportion of patients reporting any depressive symptoms (PHQ-9 score ≥ 5) compared with Africa/Middle East, Latin America, or South Asia (Fig. 1*C*). In Eurasia and South Asia, respectively, ~20% of patients treated with insulin reported a high score (PHQ-9 score ≥ 10), suggestive of major depression (Supplementary Table 1).

In the whole study population, Caucasians, women, and patients with microvascular or macrovascular complications were more likely to have depressive symptoms (PHQ-9 score ≥ 5). For both the type 1 and type 2 diabetes groups, patients with depressive symptoms also had longer diabetes duration and were more likely to have poor glycemic control, hypertension, and dyslipidemia than those without depressive symptoms (PHQ-9 score <5). Among all groups,

except patients with type 2 diabetes receiving insulin only, depressive symptoms (PHQ-9 score <5) were more common in those with older age and lower education levels and were more likely to have obesity, hypertension, dyslipidemia, and poor glycemic control than those who did not have depressive symptoms. In the type 1 diabetes group, those living in a rural area or those not performing self-management behaviors were more likely to have depressive symptoms (PHQ-9 score ≥ 5). In patients with type 2 diabetes, depressive symptoms were more likely in those who were obese (Table 2).

Independent Risk Factors of Depressive Symptoms
After adjusting for confounders, among both the type 1 and type 2 diabetes groups, the presence of microvascular and macrovascular complications and female sex were independent risk factors for depressive symptoms (PHQ-9 score ≥ 5). For patients with type 1 diabetes, poor glycemic control and living in a rural area were further independent risk factors. Among patients with type 2 diabetes treated with OGLDs only, depressive symptoms (PHQ-9 score ≥ 5) were associated with poor glycemic control and older age. Among patients with type 2 diabetes treated with OGLDs plus insulin, depressive symptoms (PHQ-9 score ≥ 5) tended to be associated with low education level (Table 3).

CONCLUSIONS

The IDMPS aims to gather real-word data to identify knowledge and care gaps in order to inform health care decision makers to develop and implement strategies for optimizing diabetes care provision. In the fifth wave (2011), we focused on the diabetes–depression link and found a high prevalence of depressive symptoms in patients with type 1 or type 2 diabetes. We found 1 in 4 patients reported mild depressive symptoms (PHQ-9 score 5–9) and 1 in 10 reported moderately severe symptoms (PHQ-9 score 10–19). The highest prevalence of depressive symptoms (PHQ-9 score ≥ 5) was reported in insulin-treated patients with type 2 diabetes.

There were close associations between depressive symptoms (PHQ-9 score ≥ 5)

Table 1—Characteristics in patients with type 1 or type 2 diabetes

		Type 2 diabetes		
	Type 1 diabetes n = 2,280	OGLDs only n = 4,729	OGLDs + insulin n = 1,892	Insulin only n = 964
Age (years), mean (SD)	33.6 (12.9)	56.8 (11.3)	57.73 (10.46)	60.08 (11.52)
Females, n (%)	1,196 (52.5)	2,458 (52.0)	1,038 (54.9)	503 (52.2)
Ethnicity/race, n (%)				
White	1,098 (48.2)	1,470 (31.1)	776 (41.0)	442 (45.9)
Asian/Arab/Persian	358 (15.7)	1,414 (29.9)	415 (21.9)	148 (15.4)
South Asian	386 (16.9)	745 (15.8)	322 (17.0)	55 (5.7)
Native Latin	205 (9.0)	455 (9.6)	175 (9.2)	103 (10.7)
Black	57 (2.5)	319 (6.7)	73 (3.9)	113 (11.7)
Other	176 (7.7)	326 (6.9)	131 (6.9)	103 (10.7)
BMI (kg/m^2), n (%)				
≤25	1,499 (65.8)	1,059 (22.5)	361 (19.2)	240 (25.0)
25–30	599 (26.3)	1,974 (41.9)	731 (38.8)	390 (40.6)
>30	179 (7.9)	1,682 (35.7)	790 (42.0)	330 (34.4)
Education level, n (%)				
Illiterate/primary	298 (13.4)	1,548 (33.4)	660 (35.7)	306 (32.5)
Secondary	890 (40.1)	1,650 (35.6)	645 (34.9)	347 (36.9)
University/higher education	1,033 (46.5)	1,435 (31.0)	543 (29.4)	288 (30.6)
Health insurance, n (%)	1,361 (60.2)	2,930 (62.2)	1,207 (63.9)	513 (53.3)
Smoking habits, n (%)				
Former smoker	189 (8.3)	828 (17.5)	358 (18.9)	237 (24.6)
Current smoker	273 (12.0)	627 (13.3)	190 (10.0)	87 (9.0)
Hypertension, n (%)	461 (20.2)	2,881 (61.1)	1,382 (73.2)	717 (74.7)
Dyslipidemia, n (%)	477 (21.7)	2,813 (61.8)	1,255 (67.9)	598 (65.5)
Diabetes duration (years), mean (SD)	11.8 (9.2)	6.8 (6.1)	12.00 (7.4)	12.57 (8.6)
Microvascular complication, n (%)	1,041 (46.8)	1,674 (36.8)	1,217 (65.9)	722 (77.0)
Macrovascular complication, n (%)	202 (9.1)	730 (16.0)	525 (28.4)	419 (44.7)
Duration of insulin use (years), mean (SD)	11.08 (9.21)		3.26 (3.74)	4.70 (5.21)
Insulin treatment, n (%)				
Basal alone	125 (5.5)		944 (49.9)	143 (14.8)
Prandial alone	61 (2.7)		15 (0.8)	15 (1.6)
Basal + prandial	1,527 (67.2)		378 (20.0)	472 (49.0)
Premix alone	429 (18.9)		519 (27.4)	299 (31.0)
Others	132 (5.8)		36 (1.9)	34 (3.5)
OGLD treatment, n (%)				
Metformin alone	124 (5.4)	1,097 (23.2)	786 (41.6)	
Sulphonylureas alone	5 (0.2)	390 (8.2)	139 (7.4)	
Metformin + sulphonylureas	22 (1.0)	2,391 (50.6)	657 (34.7)	
Other	37 (1.6)	850 (18.0)	309 (16.3)	
HbA$_{1c}$ (%), mean (SD)	8.42 (2.03)	7.62 (1.73)	8.61 (1.93)	8.70 (2.07)
HbA$_{1c}$ (mmol/mol), mean (SD)	68.5 (22.2)	59.8 (18.9)	70.6 (21.1)	71.6 (22.6)
HbA$_{1c}$ <7% (<53 mmol/mol), n (%)	466 (22.6)	1,695 (41.1)	289 (16.5)	153 (18.5)
FBG ≤100 mg/dL, n (%)	409 (20.3)	604 (14.2)	202 (11.6)	102 (11.6)
Diabetes education received, n (%)	1,936 (85.2)	3,248 (69.1)	1,494 (79.5)	743 (77.6)
Self-management, n (%)	1,490 (70.4)	1 (0.5)	719 (41.9)	348 (39.5)

All values are calculated based on available data. FBG, fasting blood glucose.

and poor control of cardiovascular risk factors, including obesity, hypertension, dyslipidemia, and glycemic control. After adjusting for confounders, in both patients with type 1 or type 2 diabetes, we found female sex and the presence of microvascular or macrovascular complications were independent risk factors for depressive symptoms (PHQ-9 score ≥5). Living in rural areas (in patients with type 1 diabetes) and low educational levels (in patients with type 2 diabetes treated with OGLDs plus insulin) were also independent risk factors for depressive symptoms (PHQ-9 score ≥5). Poor glycemic control was a risk factor for depressive symptoms (PHQ-9 score ≥5) in patients with type 1 diabetes or type 2 diabetes treated with OGLDs only but not in insulin-treated patients with type 2 diabetes. Older age was an independent risk factor for depressive symptoms (PHQ-9 score ≥5), but only in patients with type 2 diabetes treated with OGLDs only.
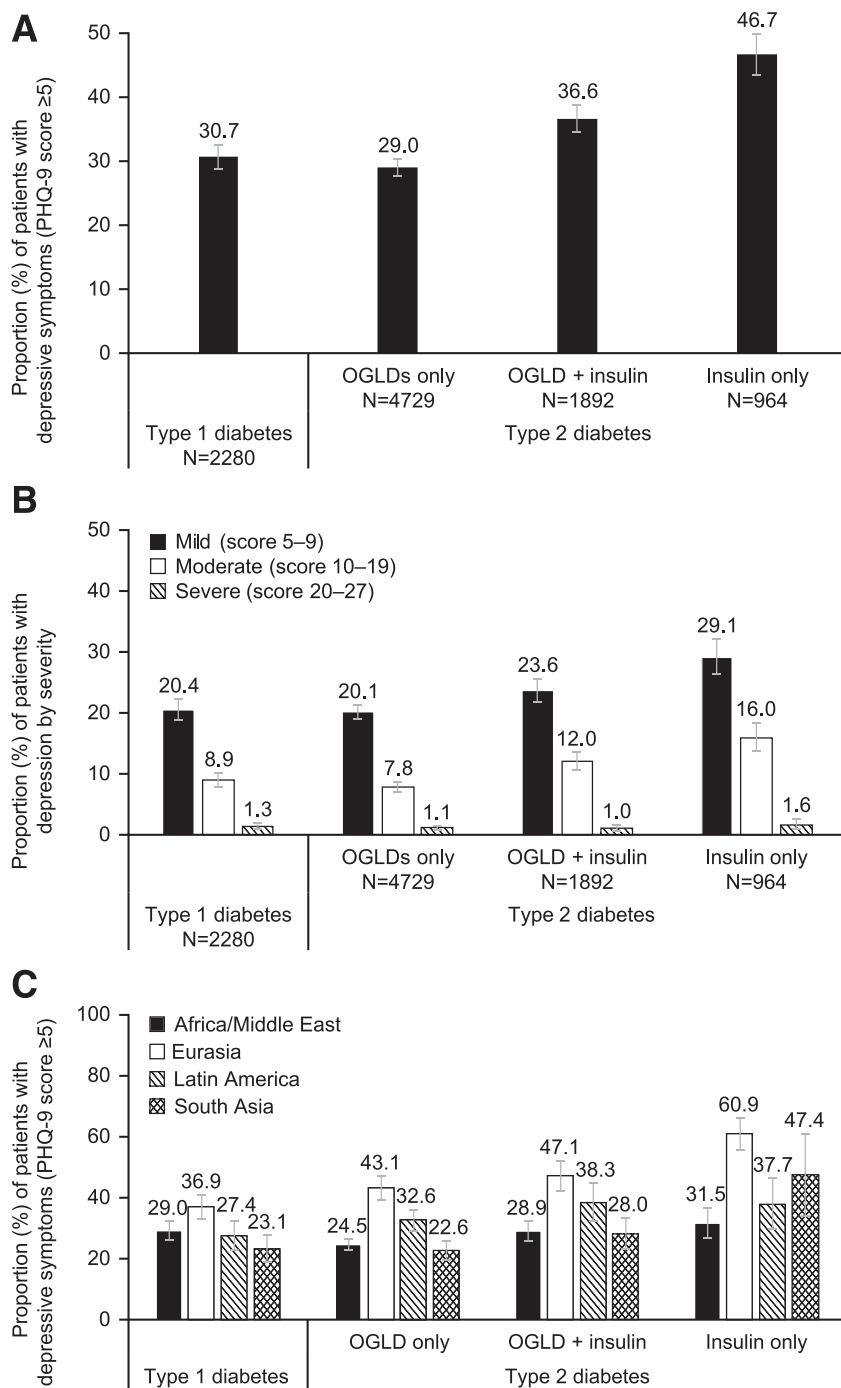
Figure 1—Proportion of patients reporting depressive symptoms overall (*A*), by severity (*B*), and by geographical region (*C*). Error bars indicate 95% CI values. Africa/Middle East: Algeria, Cameroon, Egypt, Jordan, Lebanon, Morocco, Kingdom of Saudi Arabia, Senegal, Tunisia, and United Arab Emirates; Eurasia: Georgia, Kazakhstan, Russia, Ukraine, and Uzbekistan; Latin America: Argentina, Colombia, and Venezuela; and South Asia: India and Pakistan. Turkey was included in the overall sample but was not included in the regional analyses.

from the U.S. and Saudi Arabia. In the U.S. study of 4,193 patients with type 1 or type 2 diabetes, 12% had major depression and 8.5% had minor depression (3). In the study from Saudi Arabia of 385 people with type 2 diabetes, 37.6% had depressive symptoms (PHQ-9 score ≥10), with 4.2% reporting severe depression (20).

In our analysis, poor glycemic control was an independent risk factor for depressive symptoms (PHQ-9 score ≥5) in both patients with type 1 or type 2 diabetes. Our results concurred with some (21–23) but not all studies (24). This may be due to multidimensional factors such as host factors, treatment regimens, health care systems, quality of care, and ongoing support that may influence glycemic control (15). Poor control of hypertension and dyslipidemia were also found to be associated with depressive symptoms in the univariate analysis. Poor cardiometabolic risk profile in patients with diabetes and depression may further increase their long-term risk of complications (25,26). Indeed, cross-sectionally, we found that microvascular and macrovascular complications were independently associated with depressive symptoms (PHQ-9 score ≥5). Results from a meta-analysis assessing comorbid depression and risk of cardiac events/mortality in people with diabetes also showed that the risk of cardiovascular mortality, coronary heart disease, and stroke was significantly elevated (*P* ≤ 0.001 for all) in people with diabetes and comorbid depression (27). In patients with depression and negative emotions, poor adherence to diet, physical activity, and medication may contribute to suboptimal risk factor control (28). While depressive symptoms may be a consequence of low self-esteem due to poor control and complications, depression itself may be a barrier to intensified interventions for glycemic control and prevention of complications. In a randomized clinical trial including 214 patients with type 2 diabetes and depression, multidisciplinary care significantly improved both emotional health and cardiometabolic risk factors compared with usual care (29).

In this analysis, women and patients from low socioeconomic backgrounds were at increased risk of depressive symptoms. Studies have shown that these same individuals were less likely to

Our findings are similar to a meta-analysis of 42 published studies involving 21,351 patients with type 1 or type 2 diabetes in which 31.0% of patients reported depressive symptoms and 11.4% had major depression. However, in this meta-analysis, minor depression was assessed using self-report scales, whereas major depressive disorder was measured using diagnostic interviews (1). Our results also align with population-based studies using the PHQ-9 questionnaire

Table 2—Characteristics of patients with or without depressive symptoms in patients with type 1 or type 2 diabetes

	Type 1 diabetes			Type 2 diabetes — OGLDs only			Type 2 diabetes — OGLDs + insulin			Type 2 diabetes — Insulin only		
	PHQ-9 <5 $n = 1{,}581$	PHQ-9 ≥5 $n = 699$	P	PHQ-9 <5 $n = 3{,}359$	PHQ-9 ≥5 $n = 1{,}370$	P	PHQ-9 <5 $n = 1{,}199$	PHQ-9 ≥5 $n = 693$	P	PHQ-9 <5 $n = 514$	PHQ-9 ≥5 $n = 450$	P
Ethnicity/race, n (%)			<0.001			<0.001			<0.001			<0.001
White	719 (45.5)	379 (54.2)		937 (27.9)	533 (38.9)		433 (36.1)	343 (49.5)		184 (35.8)	258 (57.3)	
South Asian	295 (18.7)	91 (13.0)		578 (17.2)	167 (12.2)		231 (19.3)	91 (13.1)		29 (5.6)	26 (5.8)	
Asian, Arab, Persian	261 (16.5)	97 (13.9)		1,049 (31.2)	365 (26.6)		289 (24.1)	126 (18.2)		91 (17.7)	57 (12.7)	
Other	306 (19.4)	132 (18.9)		795 (23.7)	305 (22.3)		246 (20.5)	133 (19.2)		210 (40.9)	109 (24.2)	
Age (years), mean (SD)	32.6 (12.4)	35.8 (13.7)	<0.001	56.2 (11.1)	58.2 (11.6)	<0.001	57.3 (10.5)	58.5 (10.4)	0.012	59.5 (11.5)	60.8 (11.6)	0.090
Females, n (%)	773 (48.9)	423 (60.5)	<0.001	1,615 (48.1)	843 (61.5)	<0.001	603 (50.3)	435 (62.8)	<0.001	238 (46.3)	265 (58.9)	<0.001
BMI (kg/m^2), n (%)			0.169			<0.001			<0.001			<0.001
≤25	1,046 (66.2)	453 (64.9)		795 (23.7)	264 (19.4)		246 (20.6)	115 (16.7)		151 (29.5)	89 (19.9)	
25–30	420 (26.6)	179 (25.6)		1,416 (42.2)	558 (40.9)		509 (42.6)	222 (32.3)		215 (42.0)	175 (39.1)	
>30	113 (7.2)	66 (9.5)		1,141 (34.0)	541 (39.7)		440 (36.8)	350 (50.9)		146 (28.5)	184 (41.1)	
Living area, n (%)			<0.001			0.289			0.036			0.852
Urban/suburban area	1,450 (92.2)	605 (86.6)		3,000 (89.6)	1,208 (88.5)		1,042 (87.0)	576 (83.5)		450 (88.6)	396 (88.2)	
Rural area	122 (7.8)	94 (13.4)		350 (10.4)	157 (11.5)		156 (13.0)	114 (16.5)		58 (11.4)	53 (11.8)	
Education level, n (%)			<0.001			<0.001			<0.001			0.322
Illiterate/primary	178 (11.5)	120 (17.9)		1,043 (31.7)	505 (37.7)		404 (34.3)	256 (38.3)		169 (33.7)	137 (31.2)	
Secondary	586 (37.8)	304 (45.4)		1,177 (35.7)	473 (35.3)		390 (33.1)	255 (38.1)		174 (34.7)	173 (39.4)	
University/higher education	787 (50.7)	246 (36.7)		1,073 (32.6)	362 (27.0)		385 (32.7)	158 (23.6)		159 (31.7)	129 (29.4)	
Time since diabetes diagnosis (years), mean (SD)	11.2 (9.1)	12.9 (9.5)	<0.001	6.6 (5.9)	7.3 (6.4)	<0.001	11.7 (7.3)	12.6 (7.41)	0.008	12.0 (8.6)	13.3 (8.5)	0.012
Time since diabetes diagnosis (years), n (%)			0.001			0.036			0.034			0.129
≤5	490 (31.0)	183 (26.2)		1,762 (52.5)	682 (49.8)		250 (20.9)	115 (16.6)		133 (25.9)	94 (20.9)	
5–10	379 (24.0)	143 (20.5)		880 (26.2)	349 (25.5)		337 (28.1)	186 (26.9)		115 (22.4)	97 (21.6)	
>10	712 (45.0)	372 (53.3)		714 (21.3)	338 (24.7)		612 (51.0)	391 (56.5)		266 (51.8)	259 (57.6)	
At least 1 microvascular complication, n (%)	630 (40.6)	411 (61.2)	<0.001	1,063 (32.8)	611 (46.6)	<0.001	703 (60.1)	514 (75.8)	<0.001	353 (71.6)	369 (84.6)	<0.001
At least 1 macrovascular complication, n (%)	101 (6.5)	101 (15.0)	<0.001	403 (12.4)	327 (24.9)	<0.001	261 (22.3)	264 (38.9)	<0.001	166 (33.7)	253 (58.0)	<0.001
Diabetes education, n (%)	1,351 (85.8)	585 (83.9)	0.239	2,359 (70.6)	889 (65.3)	<0.001	971 (81.5)	523 (76.0)	0.005	400 (78.4)	343 (76.7)	0.529
≥1 follow-up visits during the last 3 months, n (%)*	531 (36.3)	283 (44.0)	0.004	750 (24.8)	364 (29.4)	0.007	367 (33.9)	249 (38.8)	0.102	199 (43.0)	207 (49.9)	0.010
HbA$_{1c}$ <7% (<53 mmol/mol), n (%)	359 (24.9)	107 (17.2)	<0.001	1,264 (42.8)	431 (36.8)	<0.001	195 (17.6)	94 (14.7)	0.117	91 (21.0)	62 (15.7)	0.049
FBG ≤100 mg/dL, n (%)	301 (21.5)	108 (17.7)	0.053	459 (15.2)	145 (11.8)	0.004	141 (12.7)	61 (9.7)	0.056	60 (13.1)	42 (10.1)	0.167
Hypertension, n (%)	265 (16.8)	196 (28.0)	<0.001	1,968 (58.7)	913 (67.0)	<0.001	822 (68.7)	560 (80.9)	<0.001	344 (67.3)	373 (83.1)	<0.001
Dyslipidemia, n (%)	275 (17.9)	202 (30.2)	<0.001	1,985 (61.2)	828 (63.2)	0.205	768 (65.5)	487 (72.3)	0.003	297 (61.5)	301 (70.0)	0.007
Self-management, n (%)	1,064 (71.8)	426 (67.2)	0.032				448 (41.2)	271 (42.9)	0.483	179 (38.2)	169 (40.8)	0.435

FBG, fasting blood glucose. *Follow-up visit to an endocrinologist or diabetologist.

Table 3—Multivariate logistic regressions showing independent factors associated with depressive symptoms (PHQ-9 score ≥5)

Risk factors	Type 1 diabetes $n = 2,017^*$	Type 2 diabetes		
		OGLDs only $n = 3,993^*$	OGLDs + insulin $n = 1,804^*$	Insulin only $n = 929^*$
Macrovascular complication(s): yes vs. no	2.1 (1.4, 3.2)	1.7 (1.4, 2.1)	2.0 (1.5, 2.6)	2.4 (1.7, 3.4)
Microvascular complication(s): yes vs. no	2.5 (1.9, 3.2)	1.5 (1.2, 1.8)	1.8 (1.4, 2.4)	NS
HbA$_{1c}$: ≥7 vs. <7% (≥53 vs. <53 mmol/mol)	1.6 (1.2, 2.0)	1.3 (1.1, 1.5)	NS	NS
Sex: females vs. males	2.0 (1.6, 2.5)	2.1 (1.8, 2.5)	1.7 (1.4, 2.2)	2.1 (1.6, 2.9)
Living area: rural vs. urban/suburban	2.2 (1.5, 3.3)	NS	NS	NS
Age: >65 vs. ≤65 years old	NS	1.3 (1.1, 1.6)	NS	NS
Education level	NS	NS		NS
Illiterate/primary vs. university/higher			1.4 (1.0, 1.9)	
Secondary vs. university/higher			1.4 (1.1, 1.9)	

Data are presented as the odds ratio (95% CI). *Number of subjects included in the model.

achieve glycemic targets (30,31), raising the possibility that the co-occurrence of depressive symptoms might adversely affect self-management and glycemic control. In line with previous reports (32,33), this analysis found older age was associated with depressive symptoms, especially in patients with type 2 diabetes treated with OGLDs only. That said, older patients do not always present with the typical depressive symptoms, which may hinder the diagnosis of depression (34).

Living in a rural area was also a risk factor for development of depressive symptoms (PHQ-9 score ≥5) in patients with type 1 diabetes in our study. This may be due to scarcity of resources in such areas (e.g., less access to a diabetes care team/center, less contact with peers, less access to state-of-the-art self-monitoring) and potentially, poor knowledge about their disease, particularly for patients with type 1 diabetes.

Limitations
This is the first study measuring the prevalence of depressive symptoms using the same questionnaire and cutoff values in a large multinational population of patients with type 1 or type 2 diabetes living in developing countries. However, our results should be considered with caution. Observational studies are limited by selection bias and confounding factors. The lack of prospective and interventional data, a comparative group, and the cross-sectional nature of the study precludes assessment of causality, although these real-world data are applicable to a broader population (35). Differences in the size of relevant

treatment subgroups, for example, by region or country or treatment type, precluded any formal statistical analyses. We would also note that in cases where statistical analyses were conducted (e.g., univariate/multivariate logistic regression analyses for identification of risk factors for depression), differences in sample sizes between subgroups could have led to different statistical power to detect possible associations and may have had an impact on results. For example, larger populations were available for patients with type 1 diabetes and patients with type 2 diabetes treated with OGLDs only versus OGLDs plus insulin or insulin only.

The PHQ-9 questionnaire is a common tool used to identify depressive symptoms in primary care settings (19). In the International Diabetes Federation practice guidelines, PHQ scores were recommended for screening, followed by a full evaluation by a specialist as appropriate (12). The performance of different screening tools can vary with the PHQ-9 questionnaire, yielding a higher prevalence of depression, especially for severe depression, compared with other tools such as the Hospital Anxiety and Depression Scale (36). PHQ-9 response rates may also be influenced by patient education level (37). In this light, diagnostic interviews remain the gold standard for diagnosis of a depressive disorder, although they are time consuming and require qualified clinicians for their administration. In busy settings, even the administration of PHQ-9 may not be feasible. A recent meta-analysis found that a shortened version of the PHQ questionnaire, the PHQ-2 questionnaire,

which comprises two questions relating to "little interest or pleasure in doing things" and "feeling down, depressed, or hopeless," had similar validity to that of the PHQ-9 and may be useful in underresourced areas (38).

In conclusion, using real-world data collected from developing countries, we confirmed similarly high proportions of patients with type 1 or type 2 diabetes with mild (~20%) and moderate to severe (~10%) depressive symptoms as observed in developed countries, especially in women and those with low socioeconomic status as well as older individuals and those with poor cardiometabolic control and complications. These results add to the body of evidence that supports the need to perform routine screening for depressive symptoms in all patients with type 1 or type 2 diabetes. Support should be provided alongside multidisciplinary care to identify and alleviate sources of depression. Patients reporting major depressive symptoms should be referred for psychologic or psychiatric evaluation. This type of multidisciplinary approach may help to reduce the double burden of diabetes and depression.

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