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## Prevalence and correlates of depressive disorders in people with Type 2 diabetes: results from the International Prevalence and Treatment of Diabetes and Depression (INTERPRETDD) study, a collaborative study carried out in 14 countries

### Journal Item

#### How to cite:

Lloyd, C. E.; Nouwen, A.; Sartorius, N.; Ahmed, H. U.; Alvarez, A.; Bahendeka, S.; Basangwa, D.; Boborov, A. E.; Boden, S.; Bulgari, V.; Burti, L.; Chaturvedi, S. K.; Cimino, L. C.; Gaebel, W.; de Girolamo, G.; Gondek, T. M.; Guinzbourg de Braude, M.; Guntupalli, A.; Heinze, M. G.; Ji, L.; Hong, X.; Khan, A.; Kiejna, A.; Kokoszka, A.; Kamala, T.; Lalic, N. M.; Lecic Tosevski, D.; Mankovsky, B.; Li, M.; Musau, A.; Mussig, K.; Ndetei, D.; Rabbani, G.; Srikanta, S. S.; Starostina, E. G.; Shevchuk, M.; Taj, R.; Vukovic, O.; Wolwer, W. and Xin, Y. (2018). Prevalence and correlates of depressive disorders in people with Type 2 diabetes: results from the International Prevalence and Treatment of Diabetes and Depression (INTERPRETDD) study, a collaborative study carried out in 14 countries. *Diabetic Medicine*, 35(6) pp. 760–769.

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Version: Accepted Manuscript

Link(s) to article on publisher's website:  
<http://dx.doi.org/doi:10.1111/dme.13611>

[oro.open.ac.uk](http://oro.open.ac.uk)

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Article type : Research Article

Title: Diabetic Medicine

Created by: Maria Davie

Email proofs to: Cathy.Lloyd@open.ac.uk

Article no.: DME-2017-00143

Article type: Research Article

Short title/*Authors running head*: Prevalence of depression in people with diabetes from 14 countries • C. E. Lloyd *et al.*

## **Research: Educational and Psychological Aspects**

**Prevalence and correlates of depressive disorders in people with Type 2 diabetes: results from the International Prevalence and Treatment of Diabetes and Depression (INTERPRET-DD) study, a collaborative study carried out in 14 countries**

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/dme.13611

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## **What's new?**

- Our study, unlike previous ones, used a standardized clinical interview to measure depressive disorders in people with diabetes in 14 countries.
- Although depressive disorders were frequently present in people with Type 2 diabetes, in most cases, these were neither diagnosed nor treated.
- We have identified particular factors associated with depressive disorders which could be considered when developing training for healthcare professionals in ways to identify and manage comorbid depression and diabetes.

## **Abstract**

**Aims** To assess the prevalence and management of depressive disorders in people with Type 2 diabetes in different countries.

**Methods** People with diabetes aged 18–65 years and treated in outpatient settings were recruited in 14 countries and underwent a psychiatric interview. Participants completed the Patient Health Questionnaire and the Problem Areas in Diabetes scale. Demographic and medical record data were collected.

**Results** A total of 2783 people with Type 2 diabetes (45.3% men, mean duration of diabetes 8.8 years) participated. Overall, 10.6% were diagnosed with current major depressive disorder and 17.0% reported moderate to severe levels of depressive symptomatology (Patient Health Questionnaire scores >9). Multivariable analyses showed that, after controlling for country, current major depressive disorder was significantly associated with gender (women) ( $P<0.0001$ ), a lower level of education ( $P<0.05$ ), doing less exercise ( $P<0.01$ ), higher levels of diabetes distress ( $P<0.0001$ ) and a previous diagnosis of major depressive disorder ( $P<0.0001$ ). The proportion of those with either current major depressive disorder or moderate to severe levels of depressive symptomatology who had a diagnosis or any treatment for their depression recorded in their medical records was extremely low and non-existent in many countries (0–29.6%)

**Conclusions** Our international study, the largest of this type ever undertaken, shows that people with diabetes frequently have depressive disorders and also significant levels of depressive symptoms. Our findings indicate that the identification and appropriate care for psychological and psychiatric problems is not the norm and suggest a lack of the comprehensive approach to diabetes management that is needed to improve clinical outcomes.

## Introduction

Worldwide, prevalence rates of both diabetes and mental health problems are increasing rapidly [1–4]. Studies indicate that depression and subthreshold depressive states are much more common and persistent in people with Type 2 diabetes than in those without [2,5,6]; however, in the past, most studies have not used both a psychiatric diagnostic interview and a validated diagnosis of Type 2 diabetes [4,6], which might have contributed to the

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differences in prevalence data reported. The use of a wide range of checklists rather than a clinical interview to diagnose depression makes the findings of these studies difficult to interpret and compare.

Depression is associated with less than optimal diabetes self-management, lower levels of physical activity and poorer control of diabetes, with a subsequent greater risk of poor microvascular and macrovascular outcomes, higher mortality rates and substantially increased healthcare costs [7,8].

There is evidence that depression can be treated successfully with both psychological and pharmacological interventions, but under-recognition of mental disorders is a significant barrier to successful care [9–11]. Translating the findings of previous studies into clinical practice remains a challenge, particularly when recommendations developed in one country are offered for use in different cultural and contextual settings, where resources are often lacking [11–13]. In addition, depression may overlap with the emotional distress associated with having and managing diabetes, leading to additional challenges to the provision of appropriate care [14].

This study was conducted under the auspices of the Dialogue on Diabetes and Depression (<http://diabetesanddepression.org/>), an international multidisciplinary group of academics and practitioners whose aim is to promote the importance of comorbid diabetes and depression, provide education and undertake research in this field. The main objective of the present study was to investigate the prevalence and treatment of depression in people with Type 2 diabetes in 14 countries. We have conducted a collaborative study using the same protocol in these countries which differ in level of socio-economic development, cultural setting and level of service development, using standardized ways of identifying depressive disorders. The present study is the first of its kind to use both a clinical interview as well as a



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screening instrument to detect clinical depression and depressive symptoms, and to also record the diagnoses of diabetes complications contained in medical records kept by leading centres of care for people with diabetes.

## Methods

A full description of the protocol used in the present study is provided in our earlier paper [15]. In brief, between September 2013 and May 2015 a sample of consecutive outpatient clinic attendees with Type 2 diabetes at each of the study sites was invited to participate in the study, with the aim of including 200 people with Type 2 diabetes in each country. Site investigators, recruited from leading centres of excellence in each country, included at least one psychiatrist and endocrinologist for each country. The treating physician/diabetologist in the diabetes clinic invited individuals to participate in the study. Diabetes clinics were based in either secondary or tertiary care centres, depending on the facilities available in each country. Written informed consent was obtained from all participants.

### Inclusion/exclusion criteria

Eligible study participants were adults (aged 18–65 years) with Type 2 diabetes [15] diagnosed at least 12 months before the point of contact attending their diabetes outpatient facilities. Individuals were excluded if they had been diagnosed with Type 2 diabetes for <12 months as it is usual to experience a period of adjustment when first diagnosed. Other exclusion criteria were: diagnosis of Type 1 diabetes; inability to complete the survey tools because of communication or cognitive difficulties; and any life-threatening or serious conditions (e.g. cancer, stroke in the last 6 months). Those currently admitted or planning an admission for inpatient care to a hospital (unless admitted for diabetes self-management)

were excluded because this group may have been receiving more intensive or different treatment for their diabetes and so were less comparable with those not admitted. Women who were pregnant or had given birth in the last 6 months were also excluded, as were those who had received a clinical diagnosis of dependency on alcohol or other substance (not tobacco) or a diagnosis of schizophrenia.

Prior to interview the site investigators completed an information form for each eligible individual. This form included information from medical records, such as age, duration of diabetes, family history of diabetes and presence/history of diabetes complications. The latter included cardiovascular disease, retinopathy, peripheral neuropathy, peripheral vascular disease and renal disease and associated disorders. Most recent measurements of blood pressure, HbA<sub>1c</sub>, height and weight were also recorded; however, because the timing of HbA<sub>1c</sub> measurements varied in terms of proximity to the clinical interviews they were not used in the data analysis. A diagnosis of current major depressive disorder (MDD) was made at interview so that the proximity of clinical records did not differ. Any documentation of prescribed medications for depression or other mental health problem in each individual's medical records was noted, as was any documented diagnosis or treatment of any psychiatric condition. Participants were asked if they lived in what they considered to be a rural or an urban area, and reported their highest level of education (defined as no formal, some/completed primary, some/completed secondary school, or higher education, which was defined as any college, postgraduate or professional training). Marital status was defined as married/cohabiting vs being single/widowed/divorced which, for our analyses, was dichotomized into living alone vs not living alone. Participants were also asked if they considered that they had a regular income.

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Each participant was asked to complete the Patient Health Questionnaire (PHQ-9) and the Problem Areas in Diabetes (PAID) scale. The PHQ-9 consists of nine items on a four-point Likert-type scale [17]. It has good sensitivity and specificity with regard to identifying cases of depression as well as being sensitive to change over time, and has been used in a number of different countries [17]. Moderate/severe depressive symptomatology was defined as PHQ-9 scores > 9, as this was a research study rather than clinical practice, in which a significant level of symptoms would usually be considered to be PHQ-9 scores >15 [11]. The PAID scale is a 20-item questionnaire which measures the extent of diabetes-related emotional distress [18]. Items include 'feeling overwhelmed with your diabetes' and 'feelings of guilt or anxiety when you get off track with your diabetes management'. Moderate/severe levels of diabetes-related distress are defined as scores (standardized to 100) >40 [18]. All questionnaires were completed using standard self-complete methods in the appropriate language, or assisted one-to-one collection, with the questions read out by the researcher and answered by the participant. Where no existing translation/cultural adaption of the questionnaire was available it was adapted using standard forward/back translation procedures. In addition, each country's investigators ensured the questionnaires were culturally applicable through their development over several iterative stages, involving discussion and testing by a range of healthcare professionals and people with Type 2 diabetes and focusing on the meaning of terms as well as language.

A psychiatric interview was subsequently conducted by a trained interviewer using the Mini International Neuropsychiatric Interview (V5 or V6 depending on current psychiatric practice at the study site) [19]. The Mini International Neuropsychiatric Interview has been widely used in a range of different populations, including those with serious illness, and in community surveys, and is a reliable diagnostic tool according to Diagnostic and Statistical

Manual of Mental Disorders 5th edition (DSM-V) criteria [20] as long as appropriate training is given. Individuals diagnosed with depression (or other psychiatric disorders such as anxiety disorders) were advised to consult their physician for further assessment and treatment. If any individual indicated suicidality (question 9 on the PHQ-9) the psychiatrist conducting the clinical interview initiated immediate appropriate care. Where required, all those collecting the data were trained in the use of the Mini International Neuropsychiatric Interview by the relevant senior staff. Depression was defined at interview as a current (within 2 weeks) diagnosis of MDD in accordance with the criteria given in the International Classification of Diseases 10 classification (and the corresponding criteria of MDDs in the DSM-IV). Previous MDD, lifetime (i.e. either current or previous MDD) and recurrent MDD (i.e. with both current and previous MDD) were also diagnosed at interview.

### **Ethical approval**

Prior to commencing the study, ethical approval was obtained in all study settings. Ethical approval also was obtained from the Open University, UK, where the data were stored for analysis.

### **Statistical analysis**

SPSS [23] was used to analyse the data. Descriptive statistics are reported, along with univariate (*t*-test, chi-squared test, Wilcoxon rank-sum test) analyses to examine the differences between those with and without current MDD and those with PHQ-9 scores above and below the threshold for moderate/severe depressive symptomatology (threshold >9). Missing data are indicated in the relevant tables for each country. Fewer than 3% of our data were missing, and could be regarded as missing completely at random for the predictors. After performing Little's missing-completely-at-random test (chi-squared=30.26,  $P=0.991$ ),

we imputed these missing data using hotdeck imputations [22] where a random draw from a subset of comparable cases by country, sex and education is imputed using the Bayesian bootstrap method of Rubin and Schenker [23].

We then used multivariable generalized estimating equations [24] with a binary logistic regression to examine risk factors for current MDD and PHQ-9 score >9 while controlling for country-specific effects. Only the variables that were significantly associated with MDD or moderate/severe depressive symptomatology in the bivariate analysis were included.

Estimations were calculated using an exchangeable working correlation structure. Predictor variables included demographic, anthropometric and diabetes-specific variables, and psychosocial variables. Having two models enabled us to compare the results for current MDD with moderate/severe depressive symptomatology.

## **Results**

### **Response rates**

A total of 2783 individuals with Type 2 diabetes agreed to participate in the study, a response rate of 92.3%. Response rates differed according to country of study, ranging from 64.7% (Ukraine) to 100% in Uganda, Mexico and India. Women were more likely to participate than men (93.7 vs 90.8%;  $P=0.003$ ). The main reason for not participating was being too busy to remain in the clinic to undergo the examination. Participants were younger than non-participants ( $53.54 \pm 9.20$  vs  $55.26 \pm 10.80$  years;  $P=0.010$ ), but diabetes duration was not significantly different between those who agreed to participate and those who did not. Those without a regular income were more likely to participate than those who did (97.1 vs 92.6%;  $P<0.0001$ ).

Table 1 provides the overall details of the participants; country-specific information is provided in Tables S1 and S2. Roughly equal proportions of men and women participated and the majority of participants (72.7%) were married or cohabiting. Only 7.4% had no formal education, 30.8% had a higher education level, and 16.8% had no regular income. In total, 50.8% of participants had one or more complications, with retinopathy and neuropathy being the most commonly diagnosed.

Overall, 10.6% of participants were diagnosed with current MDD at interview (Table 1) and 16.6% had lifetime MDD. Rates of current MDD differed widely among countries, ranging from 1% (Uganda) to 29.9% (Bangladesh; Table S2). Rates of lifetime MDD ranged from 1% (Uganda) to 32.5% (Russia). Similarly, the proportion of participants with a previous MDD was 10.5%, ranging from 0.5% (Uganda) to 21.0% (Russia). Recurrent MDD rates were much lower than this (4.6%; ranging from 0% in Uganda/Ukraine to 17.0% in Bangladesh). Nearly half (43.6%) of those with current MDD had a previous diagnosis of depression.

The proportion of individuals reporting moderate/severe depressive symptomatology (PHQ-9 scores >9) was higher than the current MDD diagnosis rate (17.0%; ranging from 1% in Uganda to 32.5% in Bangladesh). The majority (72.5%) of those with current MDD had moderate/severe depressive symptomatology. Overall, 12.8% of participants reported moderate/severe (scores >40) levels of diabetes-related distress (PAID scores).

### **Bivariate associations**

Those with current MDD were significantly more likely to be diagnosed with panic disorder than those without current MDD (14.7 vs 2.7; chi-squared (1) = 100.11,  $P < 0.0001$ ). Similarly those with current MDD were significantly more likely to have post-traumatic stress disorder

(7.2 vs 3.1%; chi-squared (1) = 12.69,  $P < 0.0001$ ) or generalized anxiety disorder (22.9 vs 4.6%; chi-squared(1) = 144.8,  $P < 0.0001$ ). There were also significant differences in the proportion of people with and without current MDD who also received a diagnosis of social anxiety disorder (8.9 vs 1.9%, respectively; chi-squared(1) = 51.07,  $P < 0.0001$ ) or psychotic disorder (1.0 vs 0.2%, respectively; chi-squared(1) = 5.0,  $P < 0.05$ ).

Those with moderate/severe depressive symptomatology were significantly more likely to be diagnosed with panic disorder than those with low scores (12.5 vs 2.2%; chi-squared (1) = 108.69,  $P < 0.0001$ ). Similarly those with moderate/severe depressive symptomatology were significantly more likely to have post-traumatic stress disorder (8.0 vs 2.4%; chi-squared (1) = 37.12,  $P < 0.0001$ ) or generalised anxiety disorder than those without (17.0 vs 4.4%; chi-squared (1) = 100.71,  $P < 0.0001$ ). There were also significant differences in the proportion of people with or without moderate/severe depressive symptomatology who also received a diagnosis of social anxiety disorder (5.4 vs 2.1%; chi-squared (1) = 16.36,  $P < 0.0001$ ) or psychotic disorder (1.1 vs 0.2%; chi-squared (1) = 9.51,  $P < 0.01$ ).

Overall, those with current MDD were significantly more likely to be women (women, 73.1% vs men, 26.9%; chi-squared (1) = 45.07,  $P < 0.0001$ ). Age and smoking preferences did not significantly differ between those with or without current MDD but longer duration of diabetes ( $z = -4.6$ , Prob  $> |z| < 0.0001$ ), less exercise ( $z = 4.11$ , Prob  $> |z| < 0.0001$ ), and lower education level ( $z = 2.6$ , Prob  $> |z| < 0.05$ ) did. Participants who were on insulin were twice as likely to have a current MDD diagnosis than those not taking insulin (14.5 vs 7.8%; chi-squared (1) = 32.7,  $P < 0.0001$ ), and had a greater BMI than those without current MDD ( $29.7 \pm 6.6$  vs  $28.8 \pm 6.0$  kg/m<sup>2</sup>;  $P < 0.05$ ).

Those with current MDD were significantly less likely to be married or cohabiting than those without current MDD (67.4 vs 73.3%; chi-squared (1) = 4.69,  $P < 0.05$ ), were more likely to report a lack of regular income (22.5 vs 16.5%; chi-squared (1) = 6.5,  $P < 0.01$ ) and were significantly more likely to be living in an urban rather than rural location (90.8 vs 84.4%; chi-squared (1) = 8.5,  $P < 0.01$ ).

Those with current MDD were significantly more likely to have a diagnosis of past MDD than those without current MDD (43.7 vs 6.8%; chi-squared (1) = 372.9,  $P < 0.001$ ).

Participants with current MDD were more likely to report moderate/severe levels of diabetes-related distress than those without current MDD (34.0 vs 10.7%; chi-squared (1) = 125.5,  $P < 0.001$ ). Overall, those with current MDD were significantly more likely to have nephropathy (16.0 vs 9.8%; chi-squared (1) = 10.23,  $P < 0.01$ ), neuropathy (47.2 vs 24.3%; chi-squared (1) = 69.4;  $P < 0.0001$ ) and stroke (9.6 vs 6.1%; chi-squared (1) = 5.15,  $P = 0.05$ ). The proportion of those individuals with current MDD significantly increased with the number of complications they had, from 6.5% of those without any complications to 15.5% of those with five or more complications ( $z = -7.3$ ,  $\text{Prob} > |z| < 0.001$ ).

Those with moderate/severe depressive symptomatology were more likely to be women (69.7%; chi-squared (1) = 51.1;  $P < 0.0001$ ). Age and smoking preferences did not significantly differ between those with or without moderate/severe depressive symptomatology, but longer duration of diabetes ( $z = -4.7$ ,  $\text{Prob} > |z| < 0.0001$ ), less exercise ( $z = 5.4$ ,  $\text{Prob} > |z| < 0.0001$ ), and less education ( $z = 4.9$ ,  $\text{Prob} > |z| < 0.0001$ ) did significantly differ between those with and without moderate/severe depressive symptomatology. Those taking insulin were significantly more likely to have moderate/severe depressive symptomatology than those not taking insulin (21.6 vs 13.7%, respectively; chi-squared (1) =



29.4,  $P < 0.0001$ ). In addition, BMI was significantly greater in those with moderate/severe depressive symptomatology ( $29.6 \pm 6.5$  vs  $28.7 \pm 6.0$ ,  $P < 0.01$ ). Those with moderate/severe depressive symptomatology were significantly less likely to be married or cohabiting than those without current MDD (68.0 vs 73.9%; chi-squared (1) = 6.8,  $P < 0.01$ ) and were more likely to report having no regular income (28.5 vs 14.9%; chi-squared (1) = 50.9,  $P < 0.0001$ ). There was no significant association between the likelihood of living in an urban vs a rural area according to PHQ-9 scores. Those with moderate/severe depressive symptomatology were much more likely to have a diagnosis of previous MDD than those with lower scores (46.1 vs 13.6%; chi-squared (1) = 194.0,  $P < 0.0001$ ). Participants with moderate/severe depressive symptomatology were more likely to report moderate/severe levels of diabetes-related distress than those without (35.8 vs 8.4%; chi-squared (1) = 255.9,  $P < 0.0001$ ).

Overall, those with moderate/severe depressive symptomatology were significantly more likely to have nephropathy (13.5 vs 9.9%; chi-squared (1) = 5.2,  $P < 0.05$ ) and neuropathy (43.5 vs 23.1%; chi-squared (1) = 80.9,  $P < 0.0001$ ) than those without. The proportion of those with moderate/severe depressive symptomatology significantly increased with the number of complications they had, from 12.0% of those without any complications to 23.6% of those with five or more complications  $Z = -7.5$  (Prob  $> |z| < 0.0001$ ).

### **Multivariable results**

As shown in Table 2, significant predictors of current MDD (controlling for country) were female gender, lower education level, insulin treatment, higher PAID scores, previous MDD, and less exercise. For current MDD, women had a statistically significant odds ratio of 1.96 vs men. Compared with participants who did not regularly exercise, those who exercised daily had a significantly lower risk of current MDD (odds ratio 0.88). Compared with PAID

scores  $\leq 40$ , participants with a score  $> 40$  had significantly higher odds of current MDD (2.88), while people with previous MDD had a statistically significant odds ratio of 7.46 of occurrence of current MDD compared with those without previous MDD. Higher education level significantly decreased the odds of MDD vs no education, whereas primary and secondary levels did not.

Similar associations were found in a separate model examining the variables associated with moderate/severe depressive symptomatology, with the exceptions of insulin treatment (only significant for the MDD model) and having fewer diabetes complications, which significantly decreased the odds of moderate/severe depressive symptomatology. Lack of a regular income increased the odds of having moderate/severe depressive symptomatology.

Between 0 and 37.5% of those with current MDD had any documentation of medications and between 0 and 20% had a diagnosis of a psychiatric disorder (including MDD) in their medical records (Table 3). Similarly, between 0 and 66.7% (two-thirds of cases) and 0 and 28.6% of those with recurrent MDD had either documentation of medications or a diagnosis in their medical records. Rates were similar in those with moderate/severe depressive symptomatology (Table 3). Even in those countries where there was some evidence of documented diagnoses/medications, very low rates were observed; for example, in Italy three out of eight people with current MDD had medications documented and only one in eight had a diagnosis documented. There was no significant difference in recording of medications between those with current (and no previous or recurrent) vs those with recurrent MDD (36.4 vs 63.6%; chi-squared (1) = 1.3,  $P=0.25$ ); however, those with recurrent MDD were significantly more likely to have a diagnosis of depression recorded in their medical records than those with current MDD (75.0 vs 25%; chi-squared (1) = 5.6,  $P<0.05$ ).

## Discussion

We observed substantial rates of mental health problems in the present study, with 10.6% of participants receiving a clinical diagnosis of current MDD and 17% reporting moderate/severe depressive symptomatology as measured by the PHQ-9. Furthermore, 16.6% had lifetime but only 4.6% had recurrent depression. Worryingly, the proportion of those with current MDD who had a diagnosis or treatment for their depression noted in their medical records was for the most part extremely low, and non-existent in many countries, suggesting a lack of joined-up care for those with comorbid diabetes and depression. Fewer than half (45.3%) of those with moderate/severe depressive symptomatology were diagnosed with current MDD at interview, suggesting that the former questionnaire may well identify individuals as being depressed who do not meet the criteria for diagnosis, or the perceptions of people with diabetes as to their difficulties in dealing with their diabetes.

The present INTERPRET-DD study was a collaborative study of the prevalence of depressive states that used the same protocol and was carried out at the same time in 14 different countries. It included almost 3000 people with a clinical diagnosis of Type 2 diabetes [15]. Overall our response rate was extremely high, most likely because of the place of recruitment (diabetes clinic) and the person doing the recruiting (the treating physician). However, the study has a number of limitations. Although the total number of study participants reached almost 3000, numbers in some countries were lower than in others and there were too few cases of MDD in many of the countries, which made it difficult to perform site-specific analyses, for example, comparing the socio-economic differences among countries. We cannot say for certain, therefore, that the different rates were not attributable to between-country characteristics. The data collected from participants' medical records were extensive, but, although participants were recruited at their usual clinic appointment, some information may have been missed when records were kept in more

than one place. The study was undertaken in specialist clinics where the case mix may be different from the wider diabetes population, therefore, there may be an overestimate of the risk of depression. Some countries may have less extensive medical records than others or may be less likely to document a diagnosis of a condition (either physical or mental) that in many cultures is often perceived as stigmatized and so is less likely to be acknowledged. Identifying symptoms of depression or distress using tools that were originally developed in Europe/North America may also be problematic despite their extensive development for use in other cultures [25]; for example, symptoms of distress may seem to be associated with the personal experience of physical illness and so not reported or identified as depression. Our results show that there is a significant difference between both diabetes distress (PAID score) and PHQ-9 scores according to the country of the study (Manova  $P < 0.0001$ ; Table S2, footnote). This may be attributable to different cultural experiences of symptoms; for example, in Uganda low rates may be related to the moderating effect of particular cultural practices where, when a person falls ill, the whole family and community are involved in care, in contrast to other countries where the focus is on the individual.

There may be different interpretations with regard to the variables 'regular income' and 'rural area', which may have limited our analysis when we included these variables. Nevertheless, we would argue that it is the participants' understanding of their life situation that is important, as is their reporting of whether they feel depressed or anxious about their diabetes.

In spite of the above-mentioned caveats, the major advantages of the present study are the large sample in 14 countries, which involved a clinical diagnosis of depression by specially trained interviewers using the same methods rather than solely relying on checklists to record depressive symptoms, and the use of standard methods for translating any questionnaires that had not been translated and validated before. The study took place in

each participant's usual place of care, where opportunities for identifying symptoms of depression and/or distress may exist.

In the present study, we confirmed previous findings from other countries in Europe that depressive disorders are common in people with diabetes. We identified differences in the prevalence of depressive symptoms, as well as the clinical diagnosis of depression among the countries. This may reflect differences in the acceptance/stigma (or indeed denial) of acknowledging symptoms of psychological and emotional distress in different cultural groups. The results of the present study showing significant multivariable associations of current MDD diagnosis with demographic and psychosocial variables are generally consistent with those of other cross-sectional studies carried out in the UK and USA using self-reported symptoms of depression. Although a somewhat similar pattern emerged when using a moderate/severe PHQ-9 score as the dependent variable, stronger associations were observed with income and complications, reflecting the importance of diabetes-related factors and wider life issues [26]. Although measures differ across studies, depression, whether assessed by self-reported symptoms or by diagnostic interviews, has been found to be strongly associated with gender, lower education level [26,27], physical inactivity [28] and previous depression [27]. Consistent with other studies, we found significant links between MDD and diabetes complications, although the latter was a stronger predictor in the moderate/severe depressive symptomatology model [29,30]. Mean age and BMI in the present study were comparable with data from other multinational studies such as the DAWN2 study [31]; however, the percentage of people treated with insulin was higher in the present study than in the DAWN2 study, which may be explained by the fact that participants in the latter study were stratified by type of treatment, while the present study only included participants from secondary care, who are more likely to be treated with insulin.

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Interestingly, we found that diabetes-related distress was a significant independent predictor of MDD and also moderate/severe depressive symptomatology. Recent research has shown that, although depressive symptoms and distress overlap to some extent, they are not interchangeable [16,32]. While it is sometimes difficult to distinguish between them, the present study indicates that the two measures assess distinct constructs, with many people reporting high levels of depressive symptoms who did not report significant levels of diabetes-related emotional distress.

There are now a number of national and international guidelines for supporting people with diabetes and mental health difficulties, and research into the psycho-emotional consequences of diabetes has been increasing in recent years [4,5,9,31–34]; however, although it has been acknowledged that mental disorders massively contribute to the numbers of years lost through disability [35], there remain barriers to access of services that would improve mental health, particularly in countries where resources are often unavailable. The situation is even worse when it comes to the comorbidity of mental and physical disorders, which is undoubtedly one of the major problems with regard to healthcare in the 21<sup>st</sup> century [35]. Based on our observations in the present study, the feasibility of using different therapies for the treatment of comorbid diabetes and depression rests on a number of factors. In particular the range of available treatments within each local context [15], the awareness of those caring for people with these two conditions, the acceptance of the need and preferences for treatment and the demonstrability of successful outcomes are all important factors that influence the applicability of different therapies in different settings. The countries involved in the INTERPRET-DD study have found that multi-disciplinary care and improved liaison between different specialties are key to improving care, but many countries still do not have national guidelines which can be implemented locally.

The present study draws attention to the magnitude and significance of comorbid depressive disorders and diabetes, both of which are of growing prevalence and public health significance. The burden of complications in association with MDD has important implications for both the individual with diabetes and also health services provision. Our finding that a previous MDD was predictive of current MDD underscores the need for better understanding of and monitoring and treatment for mental illness; however, mental health care is not likely to receive any attention until what are seen as more pressing needs for physical care are met. Although we determined the broad range of treatments available in each country before commencing data collection, we did not record any non-pharmacological treatments at baseline. Our follow-up study will rectify this, however, as the treatment journey for every person diagnosed at baseline will be recorded. We have found an almost non-existent recording of any symptoms of/medications prescribed for depression in the medical records of those to whom we gave a clinical diagnosis of MDD. This may be for a number of reasons, which require further investigation. Our research supports previous studies in which low recognition rates have also been observed [36,37]. Awareness of the importance of mental health problems is a first step towards improving care, but improved service provision is of major importance. Although better screening could be recommended, serious consideration must be given to the ethical quandary of identifying those who require psychological support where there is no treatment available to offer. Healthcare professionals may understandably be reluctant to make a diagnosis of depression (or indeed any other psychological problem) if care is not available.

Longitudinal studies are vital if we are to understand the impact of depression and other mental health problems on diabetes, its management and the development of other comorbidities.

## **Funding sources**

This study was carried out under the aegis of the Association for the Improvement of Mental Health Programmes (AIMH) and (supported by AIMH and the collaborating institutions). The meetings of the investigators and data entry were in part supported by unrestricted grants by Eli Lilly and Sanofi companies.

## **Competing interests**

Prof. Bobrov has received a research grant from Abbott, and fees for lectures from Lundbeck.

Dr Gaebel has received unrestricted funds from Janssen, Cilag, Aristo Pharma, Lilly Deutschland, Servier Deutschland, Sanofi, Aventis, Frankfurt am Main, Germany and Lundbeck International Neuroscience Foundation (LINF), Denmark. Prof. Kiejna has received personal fees (and non-financial support from) Eli Lilly and Sanofi companies. Prof. Kokoszka has received a research grant from Novo Nordisk, Poland. Prof. Lloyd has received travel expenses paid by unrestricted grants from Eli Lilly and Sanofi to attend the World Diabetes Congress and the American Psychiatric Association conference. The Association for the Improvement of Mental Health Programs, which sponsored this programme and financially supported tasks related to its management and data analysis, received unrestricted grants from Eli Lilly and SANOFI companies. Prof. Sartorius received travel support and fees from Janssen, Cilag, Lundbeck International Neuroscience Foundation, Servier: all outside the activities related to work on this study or on this paper. Dr Wölwer has received personal fees from Roche Pharma AG, outside the submitted work. All other authors had no competing interests.



## Acknowledgements

The authors thank the following: Argentina: Vera Olguita; Bangladesh: Chiranjeeb Biswas, Jalal Uddin, Manirul Islam, Tariqul Alam, Tanjina Hossain; Germany: Arne Herrnberger, Kaschoz Fariq, Julia Leuchtman, Anna Seeber, Lina Töws; India: Thummala Kamala; Italy: Andreone Nicola, Bani Moira, Bartoli Francesco, Bertolini Lorenzo, Bonfadini Silvia, Carretta Daniele, Claudio Luigi Ambrogio, Carrà Giuseppe, Castelnuovo Gianluca, Cimino Antonino, Clerici Massimo, Crocamo Cristina, Croci Marina, Diani Caterina, Dicembrini Ilaria, Fioravanti Giulia, Gamba Pierluigi, Girelli Angela, Invitti Cecilia, Mannucci Edoardo, Molinari Enrico, Paroli Antonio, Rocca Liliana, Rotella Francesco, Valentini Umberto, Zarra Emanuela, Zenari Luciano; Russia: Irina Agamamedova, Mikhail Antsiferov, Olga Boyarkina, Julia Karacheva, Olga Koteschkova, Valery Krasnov, Taisiya Nikitina, Maria Parpara, Dmitry Tsarenko, Marina Volodina; Poland: Edyta Sutkowska, Anna Krolicka, Marta Jakubczyk, Agnieszka Kazimierczyk, Agnieszka Misiołek, Przemysław Łukasiewicz; Serbia: Aleksandra Jotic, Nikola Jovanovic; Uganda: Anthony Makhoba; UK: Duncan Adam.

Special thanks also to Professor Pichet Udomratn, Prince of Songkla University, Thailand, and Dr Jos Twisk, Vu University Medical Centre, Amsterdam, the Netherlands for their support.

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### Supporting information

Additional Supporting Information may be found in the online version of this article:

**Table S1.** Demographic profile of the study population by country.

**Table S2.** Psychological profile of the study participants.

Table 1 Profile of INTERPRET-DD participants (total sample)

<b>Demographic profile</b>	
Men, <i>n</i> (%)	1261 (45.3)
Age, years	54.1 (9.1) <sup>5</sup>
Married/co-habiting, <i>n</i> (%)	2019 (72.5) <sup>5</sup>
Urban location, <i>n</i> (%)	2372 (85.4) <sup>4</sup>
Higher education, <i>n</i> (%)	856 (30.8) <sup>1</sup>
No regular income, <i>n</i> (%)	468 (16.8) <sup>2</sup>
Current smoker, <i>n</i> (%)	374 (13.5)
Exercise (at least weekly) , <i>n</i> (%)	1643 (59.0) <sup>18</sup>
<b>Diabetes specific and anthropometric profile</b>	
Diabetes duration, years	8.8 (6.7) <sup>78</sup>
BMI, kg/m <sup>2</sup>	28.86 (6.07) <sup>37</sup>
Insulin use, <i>n</i> (%)	1164 (41.8) <sup>9</sup>
Number of complications, <i>n</i> (%)	
0	1369 (49.2)
1	735 (26.4)
2	353 (12.7)
3	178 (6.4)
4	90 (3.2)
≥5	58 (2.1)
<b>Psychological profile</b>	
Current MDD	294 (10.6)
Previous MDD	297 (10.7) <sup>6</sup>
Recurrent MDD*	128 (4.6) <sup>6</sup>
Lifetime MDD*	463 (16.6) <sup>5</sup>
Moderate-severe depressive symptomatology (PHQ-9 >9)	466 (17.0) <sup>48</sup>
PAID (diabetes distress) score >40	352 (12.8) <sup>52</sup>

MDD, major depressive disorder; PAID, Problem Areas in Diabetes.

Values are mean (sd) except where indicated.

\*Lifetime MDD: current or previous MDD; recurrent MDD: both current and previous MDD.

Numbers in *italics* are the number of participants with missing data for that variable.

Country-specific rates are shown in Table S2.

Table 2 Demographic, anthropometric, diabetes-specific, lifestyle and psychosocial predictors of current major depressive disorder and moderate/severe depressive symptomatology, determined by generalised estimating equation logistic regression

Variables	Current MDD			Moderate/severe depressive symptomatology (PHQ-9 score >9)		
	Odds ratio	95% CI	<i>P</i>	Odds ratio	95% CI	<i>P</i>
Sex female vs male*	1.96	1.54; 2.51	<b>&lt;0.0001</b>	1.70	1.43; 2.02	<b>&lt;0.0001</b>
Marital status not married vs married*	0.97	0.76; 1.24	0.83	1.00	0.88; 1.14	0.99
Education level	0.81	0.68; 0.96	<b>0.01</b>	0.73	0.64; 0.83	<b>&lt;0.0001</b>
Regular family income no vs yes*	1.28	0.94; 1.74	0.12	1.99	1.43; 2.77	<b>&lt;0.0001</b>
Location of residence rural vs urban*	0.69	0.45; 1.05	0.08			
BMI	1.00	0.98; 1.02	0.96	1.01	0.98; 1.03	0.70
Duration of diabetes	1.03	0.98; 1.03	0.82	1.01	0.997; 1.03	0.11



Insulin treatment                      0.77            0.61; 0.97            **0.03**                      0.88            0.67; 1.15            0.36

no vs yes\*

Number of diabetes complications	1.18	0.98; 1.43	0.08	1.17	1.00; 1.35	<b>0.04</b>
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Exercise level	0.88	0.78; 0.98	<b>0.02</b>	0.88	0.82; 0.94	<b>&lt;0.0001</b>
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PAID score	2.88	1.99; 4.17	<b>&lt;0.0001</b>	5.59	3.54; 8.85	<b>&lt;0.0001</b>
high $\geq 40$ vs low $< 40$ *						

Previous MDD	7.46	4.26; 12.99	<b>&lt;0.0001</b>	3.97	2.68; 5.88	<b>&lt;0.0001</b>
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yes vs no\*

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MDD, major depressive disorder; PAID, Problem Areas in Diabetes; PHQ-9, Patient Health Questionnaire.

\*Denotes reference category;

Comparison of the two models to test if the odds ratio for one model falls outside the CI for the other model where the variables are significant in at least one model: the model is not significantly different except for previous MDD, PAID scores (significant in both the models but had odds ratio higher in one model than the CI) and family income (significantly associated only with moderate-severe depressive symptomatology with higher odds ratio for the moderate-severe depressive symptomatology model than the CIs of the first model).

Table 3 Number of recorded medications for depression or diagnosis of depression in those with diagnosed MDD (current and recurrent) and moderate/severe depressive symptomatology at interview

Country	Current MDD (diagnosed at interview)		Recurrent MDD (diagnosed at interview)		Moderate-severe depressive symptomatology (PHQ-9 score >9)	
	Number with medications documented	Number with a documented diagnosis	Number with medications documented	Number with a documented diagnosis	Number with medications documented	Number with a documented diagnosis
Argentina	0/16	0/16	0/10	2/10	0/18	2/18
Bangladesh	0/58	0/58	0/33	0/33	0/63	0/63
China	0/42	3/42	0/7	2/7	0/56	2/56
Germany	0/5	1/5	0/4	1/4	1/19	2/19
India	0/4	0/4	0/1	0/1	0/31	5/31
Italy	3/8	1/8	2/3	1/3	7/26	7/26
Kenya	0/5	0/5	0/0	0/0	2/22	0/22
Mexico	2/37	3/37	2/18	1/18	2/61	4/61
Pakistan	1/24	0/24	0/5	0/5	0/41	1/41
Poland	0/32	4/32	0/22	4/22	0/30	3/30
Russia	1/34	0/34	0/11	0/11	0/47	0/47
Serbia	4/19	2/19	3/13	1/13	4/27	3/27
Uganda	0/2	0/2	0/1	0/1	0/2	0/2
Ukraine	0/8	0/8	0/0	0/0	0/23	0/23
TOTAL	11/294	14/294	7/128	12/128	16/466	29/466

MDD, major depressive disorder; PHQ-9, Patient Health Questionnaire.

Medications documented: any documentation of prescribing medications for depression or other mental health problem in individual participant's medical records.

Documented diagnosis: any psychiatric condition reported as diagnosed or treated in individual participant's medical records.