A systematic review and meta-analysis to compare the prevalence of depression between people with and without Type 1 and Type 2 diabetes

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Declaration of interests
We declare no competing interests

Research in context

What is already known?

- Inconsistencies have been reported in the prevalence of depression in those with Type 1 and Type 2 diabetes. Previous systematic reviews also included studies with small numbers of participants or without adequate control subjects.

What has this study found?

- The prevalence of depression was significantly higher in people with Type 1 and Type 2 diabetes compared with those without diabetes.
- The prevalence of depression in people with diabetes did not significantly differ between methods of depression assessment.
- Prevalence of depression in people with diabetes was higher in studies set in specialist care, compared to those set in the community or primary care, and higher in low- and middle-income countries compared to countries with high income economies.

What are the implications of the study?

- Effective chronic disease management is vital, including screening and managing depression in specialist care settings. **'**Diabetes distress' and 'depression' should be distinguished, and appropriate and targeted-patient centred interventions should be used accordingly.

Abstract

Aims

Diabetes can significantly impact quality of life and mental health. However, inconsistencies have been reported in the prevalence of depression in those with Type 1 and Type 2 diabetes, and those without. Systematic reviews also included studies without adequate control subjects. We update existing literature, by comparing depression prevalence between individuals with and without Type 1 and Type 2 diabetes.

Methods

A systematic review and meta-analysis. We searched MEDLINE, EMBASE and PSYCHINFO, from January 1985 to August 2021. Studies were excluded if they failed to have an adequate control group, specified type of diabetes, or reported depression prevalence by type of diabetes.

Results

44 studies were selected for inclusion. The prevalence of depression was significantly higher in people with Type 1 (22% vs 13%, OR = 2.10 (95% CI: 1.23,3.52)), or Type 2 diabetes (19% vs 11%, OR = 1.76 (1.55,2.01)) compared to those without diabetes. There was no association between study effect size and mean age or gender. Findings did not significantly differ between

methods of depression assessment. Prevalence of depression in people with diabetes was higher in studies carried out in specialist care (36%, OR = 3.14 (2.12,4.63)) compared to those in community or primary care (12%, OR= 1.51 (1.35,1.70) and in low- and middle-income countries (OR = 2.58 (1.91, 3.50) compared to countries with high income economies (OR= 1.59 (1.39, 1.82)).

Conclusions
Depression prevalence remains significant in those with type 1 and type 2 diabetes. Effective chronic disease management in people with diabetes is important, particularly screening and managing depression and diabetes distress in specialist care settings.

Keywords: Co-morbidity, depression, depressive symptoms, prevalence, Type 1 diabetes mellitus, Type 2 diabetes mellitus, diabetes distress

Abbreviations: PHQ: Patient Health Questionnaire, CES-D: Center for Epidemiological Studies-Depression, DIS: Diagnostic Interview Schedule.

INTRODUCTION

Diabetes is a major health challenge, affecting nearly 415 million people globally. This is expected to increase to 642 million by 2040, predominately due to the prevalence of sedentary lifestyles and increasing rates of obesity (1). Managing diabetes is important, as it can have significant impacts on functioning and quality of life, negatively impacting mental health (2).

The prevalence of depression in people with Type 1 and Type 2 diabetes has been the subject of many studies and existing systematic reviews (2-7), from which the key findings were the prevalence of depression was significantly higher in people with Type 1 and Type 2 diabetes compared to those without.

Epidemiological data suggests a bidirectional relationship between diabetes and depression, however conflicting evidence exists on the role of different factors that may modulate this relationship (8). Depression is associated with unhealthy behaviours, such as a poor diet and sedentary lifestyle, increased activity of the hypothalamus pituitary adrenal axis, and increased levels of stress hormones and pro-inflammatory cytokines (9). This may affect insulin resistance and subsequent development of Type 2 diabetes (10). Depressive co-morbidity can result in serious consequences, such as poor glycemic control, poor adherence to medical treatment, and higher rates of cardiac events and cardiac mortality (11). Children and adolescents with Type 1 diabetes may also be at an increased risk for depression (12), though this remains controversial as what is considered as depression may be attributed to diabetes distress, resulting from diabetes and its management (such as fears of complications, and diabetes burnout as a result of the demands of self-care) (13). Reduced self-esteem and adjustment to this chronic disease may play a role in developing depressive symptoms (14).

Existing systematic reviews have methodological limitations, including the review of a relatively small set of studies reflecting good quality literature when determining the prevalence of depression (15-17), failure to distinguish between type 1 and type 2 diabetes, which differ significantly in the nature and onset of complications (18) or failing to include adequate control subjects increasing recruitment bias (19).

Inconsistencies have also been reported in the prevalence of depression in diabetes , compared to those without, due to varying diagnostic techniques for measuring depression. Elevated scores on self-report measures, such as the Patient Health Questionnaire (PHQ), may reflect diabetes distress or depressive symptoms, rather than meeting diagnostic criteria for depression on the basis of a structured clinical interview (20).

We aim to update the literature by comparing the prevalence of depression in people with and without Type 1 and Type 2 diabetes, excluding studies if they failed to have an adequate control group, specified type of diabetes, or reported depression prevalence by type of diabetes. We also compared prevalence by methods of screening used to ascertain depression, study setting, and economic status of the country where the study was conducted.

METHODS

Search strategy and selection criteria

We conducted this systematic review and meta-analysis following a protocol registered in the PROSPERO International prospective register of systematic reviews (identification No. CRD42020179241) and have reported our findings in accordance with MOOSE guidelines. We searched MEDLINE, EMBASE and PSYCHINFO, for all articles containing the keywords 'depression', 'depressive disorder', 'major depressive disorder' and 'dysthymic disorder' in combination with 'diabetes mellitus' or 'Type 1 diabetes mellitus' or 'Type 2 diabetes mellitus' (titles and abstract). The computer-based searches combined free text and medical subject headings and combination of key words related to depression and diabetes, with results restricted to English language publications. We also searched reference lists of selected studies and relevant reviews for additional publications. We contacted authors of relevant articles for full report of their unpublished studies. Studies published from January 1985 to August 2021 were included to ensure a relatively consistent diabetes diagnostic criteria was used, and to avoid the earlier WHO 1985 guidelines definition. No separate ethical approval was required for the conduct of this study, as any necessary ethical approval was obtained for each of the individual studies contributing data to the meta-analysis.

Observational, cross-sectional studies were chosen as these enable the strength of relationships between exposures and outcomes to be determined (21). Studies were included if at baseline participants were identified as either having diabetes or no diabetes (control group), and the prevalence of depression was reported in both groups. An adequate control group must not include partners, first-degree relatives or patients exclusively with other chronic conditions such as hypertension or osteoporosis (22). Studies were excluded if they failed to specify type of diabetes, or report prevalence of depressive symptoms by type of diabetes.

Studies were limited to those involving at least 50 people with either Type 1 diabetes (including children or adolescents) or Type 2 diabetes (adults > 18 years only), and at least 50 people within a matched or unmatched control group (without diabetes). Studies were included regardless of whether self-report (interview or questionnaire) or doctor verification (such as measuring fasting blood glucose) was used to assess a diagnosis of diabetes. Previous studies have established the reliability of self-reports as comparable to measures of doctor-diagnosed diabetes (23).

Articles were included if either self-report depression rating scales (such as the CES-D: Center for Epidemiological Studies-Depression or PHQ-9: Patient Health Questionnaire-9), clinician administered diagnostic interviews (such as the DIS: Diagnostic Interview Schedule) or doctor diagnosis (defined in this study as ascertaining depression from medical records) were used to identify depression. It is important to consider that scores on these assessment methods, particularly screening instruments such as the PHQ, may reflect depressive symptoms or diabetes distress syndrome, rather than meeting the criteria for clinically relevant depression (13). Therefore, we compared prevalences by different methods used to assess depression or depressive symptoms.

The titles and abstracts of all articles identified by the broad literature search were assessed independently by two reviewers (AF and HS). Studies that did not meet the inclusion criteria were discarded. Full text of selected articles were retrieved and assessed to determine if they met the inclusion criteria. Of the studies that met the inclusion criteria, one author (AF) initially conducted the data extraction using a standardised data collection form and a second author (HS) independently checked the extracted data with that in the original articles. Any disagreements with data extraction and screening were resolved by discussion with a third reviewer (KK). Data were extracted on the following characteristics: article title, author, journal, publication date, country, setting, race, sample size (with diabetes and without diabetes-control), gender, mean age, assessment method of diabetes and depression, prevalence of depression with and without diabetes, odds ratio (for depression in people with diabetes compared to those without diabetes), confounders adjusted for. Studies were also classified by the economic status of the country in which they were conducted, i.e. high or medium/low income economy, as reported by the World Bank (24).

Data analysis

Prevalences and odds ratios for depression in people with and without diabetes were pooled across included studies using random effects meta-analyses to allow for between study heterogeneity. Prevalences were pooled separately by gender, type of diabetes (type 1, type 2), study setting (community, primary care, or specialist care), economic status of country, diabetes diagnosis (self-report or medical records), and type of depression assessment (self-reported, diagnostic interview, or doctor diagnosed). Where an adjusted odds ratio was reported for risk of depression in people with and without diabetes, this was utilised in the meta-analysis. If a number of adjusted odds ratios were reported, the ratio adjusted for the most variables was used. Where an odds ratio was not reported, this and a standard error were calculated from

numbers reported with depression in each group (25). Odds ratios were pooled across all studies, and then by study setting, gender, depression diagnosis method, and type of diabetes.

Although many studies had matched age and gender controls, some studies included control groups which were not matched on any clinical or demographic characteristics. We therefore included adjusted odds ratios for age and gender in the meta-analysis where these were reported.

Between study heterogeneity was assessed using the I-squared statistic (26) and explored through sub-group analyses and meta-regression models using study level estimates for mean age, and percentage of the study population who were female. A funnel plot and Begg's test were carried out to assess for publication bias (27).

All studies included underwent quality assessment using the Newcastle-Ottawa scale (NOS), which has been validated (28) and recommended by the Cochrane collaboration (29). The cohort NOS assessed studies on three subscales including the selection of participants, the comparability of exposure group and non-exposed group, and the ascertainment of the outcomes (28). Four, two and three stars were scored for those three domains, respectively.
The modified NOS scale for cross-sectional studies has 7 items for three subscales (4 items for selection, 1 item for comparability, and 2 items for outcome) with a maximum score of ten (2 points for validated depression scale, 2 points for comparability and 2 points for linked records in the outcome section) (30). As suggested by previous reviews, a score greater than five suggests fair study quality or higher for both cohort and cross-sectional scales (31, 32). To increase inter-rater reliability, one author (SA) performed the quality assessment and two authors (AA and CG) reviewed the quality assessment, with disagreements being resolved by consensus. A sensitivity analyses was also carried out, removing studies that did not score highly on the quality assessment, i.e. those that scored less than 5 out of 10. .

RESULTS

A total of 978 potentially relevant citations were retrieved from electronic database searches, and reference lists of selected studies and relevant reviews, from which 89 articles were selected for full text review. Of these, 45 full texts were excluded (figure 1). 4 studies were excluded as control groups involved less than 50 participants. 5 studies were excluded as they used spouses or first-degree relatives of patients with diabetes as control subjects. 32 studies were excluded as the type of diabetes in patients could not be ascertained from the text. 4 studies did not report the cross-sectional prevalence of depression. In total, 44 studies were selected for inclusion in the systematic review, 4 for Type 1 diabetes only, 37 for Type 2 diabetes only, and 3 for both Type 1 and Type 2 diabetes (where prevalence was reported separately for each diabetes type), and all reported data that enabled them to be included in a meta-analysis (Supplementary table 1).

<figure 1>

Twenty-seven studies were assessed using the scale for cohort studies and seventeen studies were assessed using the scale for cross-sectional studies. The twenty-seven cohort studies were assessed using a nine-star scale NOS scale; five studies received an eight to nine star score, 15 studies received a six to seven star score, and seven studies received a score of 5 or less. The NOS cohort scores indicate that the majority of the studies had minimal bias present (31). . The seventeen cross-sectional studies were assessed out of a ten-star modified for cross-sectional studies (30). Sixteen out of the seventeen cross-sectional studies received a rating of five stars or more out of ten, suggesting satisfactory to very good study quality (32). The quality assessment scores for each study can be found in Supplementary Tables 2 and 3.

In total there were 1,007,234 people in the meta-analysis, 2,453 of whom had Type 1 diabetes, 117,924 with Type 2 diabetes, and 886,857 people who had no diabetes (control group). 16 studies reported the prevalence of depression was higher in those with Type 2 diabetes and co-morbidities, such as hypertension and coronary heart disease (CHD). 22 studies reported adjusted prevalences for potential confounders such as co-morbid disease, age, gender and body weight.

The majority of studies (16 studies) were conducted in Europe (e.g. Germany, Italy, Ireland, Finland, UK), and the USA (9 studies), with 3 studies conducted in the Middle East (Iran, Kuwait and Iraq), 4 from the Far East (China and Taiwan), 6 from South Asia (India and Bangladesh) and the remaining in Australia, Canada, and Mexico. 7 studies stated the ethnic background of the participants. One described participants as Mexicans (33), one as an Indian population (34), one as a Chinese population (35). 5 studies reported a mixed sample, which included Black, Caucasian, Chinese, Hispanic, West Indian or Asian individuals (36-40). These studies did not report prevalences separately by ethnic group.

The prevalence of diagnosed depression or elevated depressive symptoms was significantly higher in people with either Type 1 or Type 2 diabetes compared with those without diabetes , p <0.001. This finding was consistent when rates were determined by gender, type of diabetes, method of diabetes and depression assessment, and study setting (table 1). The overall prevalence of depression was 22% in people with Type 1 diabetes, and 13% without Type 1 diabetes ($p < 0.001$), and 19% in people with Type 2 diabetes, and 11% without Type 2 diabetes ($p = 0.005$).

<table 1>

The results of the meta-analysis are shown in figure 2, separated by type of diabetes. A fitted random effects meta-analysis was conducted using data from 7 studies. This analysis included data for 2,453 people with Type 1 diabetes. The odds ratio for diagnosed depression (or elevated depressive symptoms) was significantly increased in people with Type 1 diabetes compared to those without diabetes (OR = 2.10 (1.23, 3.52) , $p < 0.001$). The I^2 value was 78.9%, indicating substantial heterogeneity between study results (table 1).

<figure 2 >

A fitted random effects meta-analysis was also conducted using data from 40 studies, which compared the association between depression in people with Type 2 diabetes, compared with those without diabetes. This analysis included data for 117,924 people with Type 2 diabetes. The odds ratio for diagnosed depression (or elevated depressive symptoms) was significantly increased in people with Type 2 diabetes compared with those without diabetes (OR = 1.76 (1.55, 2.01) , $p = 0.005$). The I^2 value was 89.6%, indicating substantial heterogeneity between study results.

Study heterogeneity was explored using meta-regression and sub-group analyses. Meta-regression analysis showed that the study effect size was not associated with mean age (p= 0.150) or the percentage of females (p = 0.603) in the study cohort. 24 studies reported the prevalence of depression separately for men and women. The pooled prevalence of diagnosed depression (or elevated depressive symptoms) did not differ significantly between men and women in either the control or diabetes study arms, despite estimated depression being higher in women for both. In women with diabetes, depression was estimated as 26% and in men with diabetes as 18%, p= 0.291. In the control groups the pooled prevalence of depression was estimated as 14% in women and 9% in men, p= 0.144 (table 2). The pooled odds ratio showed a statistically significant difference in the odds of depression for both men (OR = 1.82 (1.36, 2.43) I^2 = 79.5), and women (OR = 1.80 (1.42, 2.30), I^2 = 89.5), compared to those without diabetes. There was no significant difference between these odds ratios (p = 0.894*)*.

23 studies identified depression cases by self-report questionnaire, 17 using diagnostic interviews and 4 by examination of medical records held by general practitioners. 10 studies identified diabetes through self-report, and 34 studies through examining medical history. Figure 2 shows a forest plot for the meta-analysis of depression in people with and without diabetes, by method of depression assessment. The prevalence of depression in people with diabetes was not significantly higher when diagnosed depression (or elevated depressive symptoms) was self-reported (25%), and ascertained from diagnostic interviews (16%) rather than doctor diagnosed (7%), and the estimated odds comparing risk of depression in people with diabetes and those without was not significantly higher; OR = 1.92 (1.60, 2.32), I^2 = 83.8 for self-reported depression, OR = 2.08 (1.64, 2.64), I^2 = 85.0 for diagnostic interviews, and OR = 1.22 (1.07, 1.38), I^2 = 83.9 for doctor diagnosed depression. Sub-group analyses by mode of diabetes diagnosis found similar estimated pooled odds ratios in those using self-report, compared to those using medical history (table 1).

14 studies were conducted in a specialist setting, and 30 studies were conducted in community or primary-care settings. Figure 2 shows a forest plot for the meta-analysis of depression in people with and without diabetes, by study setting. The prevalence of diagnosed depression (or elevated depressive symptoms) in people with diabetes was significantly higher in studies set in specialist care, compared to those set in the community or primary care (36% vs 12%), and the estimated odds ratio for risk of depression with diabetes compared to those without also

differed significantly between the two subgroups; community or primary care settings (OR = 1.51 (1.35, 1.70) vs specialist care (OR = 3.14 (2.12, 4.63), $p<0.001$).

Sub-group analyses were also carried out by economic status of the country where the study was conducted. 15 studies were conducted in countries classified as having a medium or low-income economy, and 29 in countries classified as having a high-income economy. The impact of diabetes on depression was found to be significantly greater ($p<0.010$) in the low- and middle-income countries compared to countries with high income economies (OR = 2.58 (1.91, 3.50) and 1.59 (1.39, 1.82) respectively).

Sensitivity analysis removing studies that did not score highly on the NOS scale showed similar results as to when all studies were meta-analysed; 7 studies removed from the analysis and 37 studies meta-analysed, the pooled odds ratios for risk of depression in participants with diabetes compared to those without was OR = 1.79 (1.56, 2.06, $p<0.001$). Funnel plots and tests did not suggest evidence of publication bias (Begg's test, $p = 0.199$) (Supplementary figure 1).

DISCUSSION

In this systematic review and meta-analysis we compared depression prevalence between individuals with and without Type 1 and Type 2 diabetes. The prevalence of diagnosed depression or elevated depressive symptoms was significantly higher in people with Type 1 diabetes compared with those without (OR = 2.10, 95% CI: 1.23, 3.52), and in Type 2 diabetes compared to those without (OR = 1.76, 95% CI: 1.55, 2.01). Our findings are consistent with previous reviews on this topic (2-6, 15, 41). Analyses also indicated no significant difference in the prevalence of depression between males and females with and without diabetes, contrary to previous findings (15, 41). Although we included a larger number of studies compared to previous meta-analyses, the power to detect any gender differences may be low, as we only had aggregate data available to assess this.

The overall prevalence of depression in people with Type 1 diabetes was 22% and Type 2 diabetes was 19%, suggesting that approximately 1 in 5 people with diabetes are likely to experience depression, or elevated depressive symptoms. This may be associated with adverse outcomes, including impaired functioning and quality of life, poorer adherence to medical treatment and glycemic control, and increased risk of diabetes complications (3). Furthermore, people with diabetes are more likely to experience suicidal ideations and attempt suicide (42).

The prevalence of depression in people with diabetes did not significantly differ between methods of depression assessment, although again this may be due to lack of power associated with meta-analysis studies where only aggregate data is available. However, it is still important to consider the extent to which different assessment measures may identify a broader spectrum of depressive disorders (e.g. dysthymic disorder, or minor or subsyndromal depression), somatic complaints reflecting diabetes rather than depression severity (43) or symptoms that reflect comorbid psychiatric illness, such as anxiety or diabetes distress (41). 'Diabetes distress' and 'depression' should be distinguished, particularly as the overlap between symptomatology may be quite large, relating to poor self-management behaviour, and

emotional distress (44). Therefore, appropriate and targeted-patient centred interventions should be used accordingly (45).

Fisher et al. (13) found an unexpectedly low rate of depression in people with Type 1 diabetes, and a high rate of false-positives when using the PHQ-8 compared to using a structured interview. They concluded that people with Type 1 diabetes may be at an increased risk of emotional distress and poor adjustment to this chronic disease (14), and fear of diabetes complications (3), rather than being caused by underlying psychopathology. Further longitudinal, prospective studies may provide further insight into the nature of the relationship between depression and Type 1 and Type 2 diabetes, including lifetime prevalence of experiencing depression.

Several studies (39), (45-47) found no significant association between diabetes and depression after adjusting for comorbid diseases, such as coronary disease, stroke and peripheral arterial disease. Comorbidities can result in depression in people with diabetes due to functional limitations affecting quality of life or fearing future outcomes (45). Studies have also reported that undiagnosed diabetes is not related to increased depressive symptomology, concluding intense diabetes management and treatment regimens may result in elevated depressive symptoms or 'diabetes distress' (48).

Other studies (49, 50) found a significant relationship between diabetes and elevated depressive symptoms after comorbid diseases were controlled for, suggesting the possible influences of other psychosocial factors (e.g. exposure to external stressors and socio-economic status) and/or potential pathophysiologic mechanisms, and increased levels of stress hormones and pro-inflammatory cytokines which may affect insulin resistance (9).

The prevalence of depression was significantly higher in specialist care settings, compared to community and primary care studies. Although research undertaken in specialist care settings may be exposed to biases of case selection and referral, which may overestimate the prevalence of depression, patients referred to hospital are more likely to have later or more severe disease than those seen in primary care (51). This may result in poorer cardiometabolic outcomes associated with diabetes. It is vital that depression should be screened for and managed in specialist care settings.

The impact of diabetes on depression was significantly greater in low- and middle-income countries compared to countries with high income economies (52) . Contributing factors may include under-developed health systems and social support networks, including limited access to, and associated stigma of using mental health services (52, 53). By 2030, it is projected that around 82.5% of people with diabetes will live in developing countries (54). Focus on both diabetes and depression prevention is therefore imperative. Clinicians must be aware of the increased risk of depressive symptoms in people with Type 1 and Type 2 diabetes. The under recognition and undertreatment of depression in primary care practice needs to be addressed (55). Routine screening of depressive symptoms or diabetes distress should be considered, and timely psychiatric consultation to enhance care of this group of patients. Collaboration between primary care and specialist clinicians may be required, which may include integrated clinical

care and self-management programmes (53, 56). Effective chronic disease management and continuity of care is also vital to ensure that comorbidities are actively managed, risk factors are controlled, and to improve adherence to medical treatments.

A review on the strengths and limitations of treatments of depression in diabetes is important. Although research has advanced in identifying treatments, more effective treatments are still required for better long-term psychological and physical benefits (57). Those with comorbid depression or diabetes distress and diabetes may be less likely to adhere to lifestyle changes and medication treatment, compared to those who have diabetes without depression (58). Therefore, more focus may be required on targeted, individualised behavioural interventions addressing these psychosocial factors affecting adherence (58).

Strengths and limitations

The main strength of this analysis is the comprehensive search strategy which yielded several published studies on the topic. Overall, this review involved 2,453 people with Type 1 diabetes and 117,924 with Type 2 diabetes. Formal tests demonstrated no evidence of publication bias. We also report data by how diabetes and depression were assessed.

Although results indicated significant heterogeneity, we accounted for some of this when conducting subgroup analysis by type of diabetes, method of depression assessment and study setting. As the studies included were observational, study level confounding factors, not corrected for, could have affected the results and conclusions we are drawing from this meta-analysis. Due to a lack of information regarding potential moderating factors in some studies, it was not possible to conduct any multivariate analysis, or take all the main confounding variables into account when determining prevalences (including the use of antidepressants which may be associated with an increased diabetes risk (59). Furthermore, we could not analyse the relationship between diabetes and depression according to other comorbidities, as we would need individual patient data. Another limitation was we could not assess temporal trends in depression prevalence in people with and without diabetes, due to large variabilities in the study designs and assessment methods.

Cross-sectional studies were included in this meta-analysis, making it difficult to determine the causality or temporality of the association between diabetes and depression. However, one study (60) found evidence for a bidirectional relationship between diabetes and depression, with a stronger relationship between depression and incidence of diabetes, compared to diabetes and incidence of depression. Some longitudinal studies were included, including Aarts (61) who found people with diabetes are more likely to develop depression. ~~Some researchers (62) have previously highlighted the need for further prospective longitudinal research to further understand the complex aetiology of depression in Type 1 and Type 2 diabetes~~. Similarly, a recent meta-analysis of longitudinal studies conducted by (63) found that diabetes is an independent risk factor for depression, although they acknowledged the need for further prospective longitudinal research, with better designed cohort studies, to further understand the complex aetiology of depression in Type 1 and Type 2 diabetes.

Combining data from studies with differing measures of depression is another limitation, although we compared studies which reported clinically diagnosed depression compared to those using a self-reported measure. In large data sets clinical interviews are prohibitively expensive, and may therefore be a limitation in future studies. Future studies should consider diabetes-related distress as a core construct when considering the link between diabetes and depression (44).

Conclusion

Depression prevalence remains significant in those with type 1 and type 2 diabetes, affecting one out of every five people with diabetes. This depression prevalence is twice as high as in people without diabetes. It is also higher in people with diabetes treated in specialised care or in people living in low- and middle-income countries. Effective chronic disease management in people with diabetes is important, particularly screening and managing depression and diabetes distress in specialist care settings

Contributors

AF took the lead in writing the manuscript and conducted the data search and extraction. HS acted as second reviewer. CLG performed the statistical analysis, designed the figures, and aided in interpreting the results and worked on the manuscript. SA performed quality assessment of the studies included in the systematic review and checked data extraction. KK conceived the original idea and supervised the findings of the work. SS, MJD , WHP, and KK contributed to the discussion and reviewed the manuscript.

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***Table 1*: Pooled prevalence and odds of depression in people with and without diabetes, for all studies and by sub-groups**

	Number of studies	Prevalence of depression in participants with diabetes % (95% CI)	I-squared (%)	Prevalence of depression in participants without diabetes % (95% CI)	I-squared (%)	Pooled odds ratio for risk of depression in participants with diabetes compared to those without (95% CI), p-value	I-squared (%)	Comparison of odds ratios between sub-groups (p-value)
All studies	44	19 (15, 23)	99.6	10 (8, 13)	99.9	1.86 (1.63, 2.12), <0.001	90.1	-
Sex								
Men	11	18 (12, 26)	98.7	9 (6, 13)	98.3	1.82 (1.36, 2.43), <0.001	79.5	Reference
Women	13	26 (15, 37)	99.5	14 (8, 22)	99.9	1.80 (1.42, 2.30), <0.001	89.5	0.894
Diabetes type								
Type 1	7	22 (5, 46)	99.1	13 (5, 23)	99.9	2.10 (1.23, 3.52), <0.001	78.9	Reference
Type 2	40	19 (16, 23)	99.6	11 (8, 14)	99.9	1.76 (1.55, 2.01), 0.005	89.6	0.461
Depression assessment								
Self-report	23	25 (17, 34)	99.0	14 (12, 17)	99.3	1.92 (1.60, 2.32), <0.001	83.8	Reference
Diagnostic interview	17	16 (10, 22)	99.2	7 (4, 10)	99.8	2.08 (1.64, 2.64), <0.001	85.0	0.684
Doctor diagnosed *(ascertaining depression from medical records)*	4	7 (2, 14)	99.9	5 (2, 10)	99.8	1.22 (1.07, 1.38), 0.003	83.9	0.099
Diabetes assessment								
Self-report	10	13 (5, 25)	99.8	10 (4, 18)	99.9	1.52 (1.30, 1.77), <0.001	90.7	Reference
Medical history	34	21 (17, 25)	99.5	10 (8, 13)	99.5	2.05 (1.74, 2.43), <0.001	79.7	0.070
Setting								
Community and primary care	30	12 (9, 16)	99.6	8 (6, 11)	99.9	1.51 (1.35, 1.70), <0.001	84.8	Reference
Specialist Care	14	36 (23, 50)	98.6	16 (11, 23)	98.1	3.14 (2.12, 4.63), <0.001	89.7	<0.001
*High income economy country**								
Yes	29	16 (12, 20)	99.5	10 (8, 12)	99.7	1.59 (1.39, 1.82)	87.5	Reference
No	15	25 (17, 35)	99.6	11 (8, 15)	99.8	2.58 (1.91, 3.50)	91.5	0.010

*As classified by the World Bank

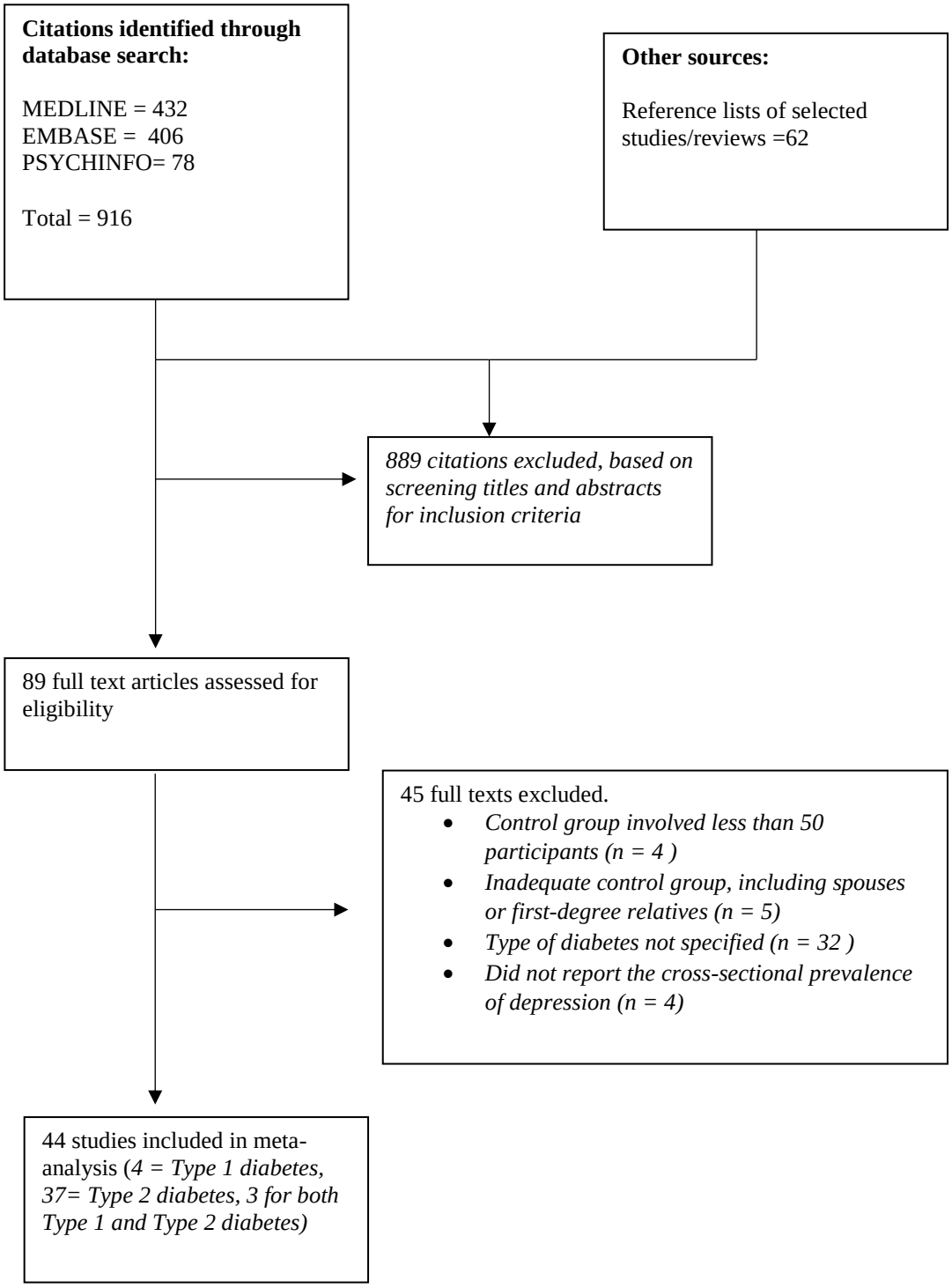

Figure 1*:* Flow chart summarising studies selected for review

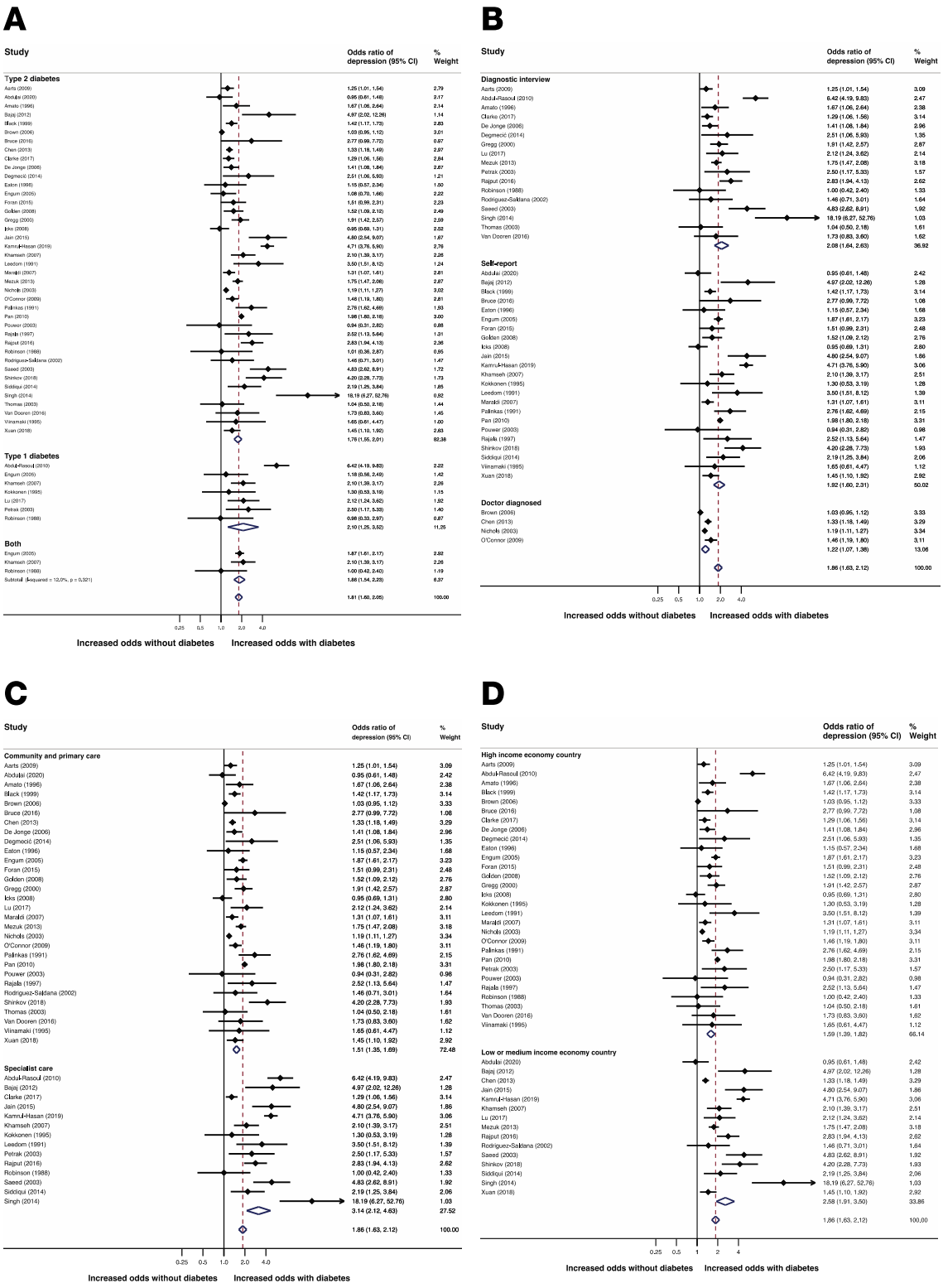

Figure 2- Forest plot for odds of diagnosed depression in individuals with and without diabetes. **Panel A** . by type of diabetes. **Panel B.** by method of depression assessment. **Panel C.** by study setting. **Panel D.** by economic status of country where study was conducted

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