

The prevalence of diabetes-specific emotional distress in people with Type 2 diabetes: a systematic review and meta-analysis

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Conflicts of interest

None declared

Abstract

Aims

Psychological comorbidity, such as depression and/or diabetes-specific emotional distress (DSD), is widespread in people with Type 2 diabetes (Type 2 DM) and is associated with poorer treatment outcomes. While extensive research into the prevalence of depression has been conducted, the same attention has not been given to DSD. The aim of this systematic review was to determine the overall prevalence of DSD in people with Type 2 DM.

Methods

Seven databases were searched to identify potentially relevant studies; eligible studies (adult population (>18 years) with Type 2 DM and an outcome measure of DSD) were selected and appraised independently by two reviewers. Multiple **fixed and random-effect** meta-analyses were performed to synthesize and analyse the data, with primary analysis to determine the overall prevalence of DSD in people with Type 2 DM, and secondary meta-analyses and meta-regression to explore the prevalence across different variables.

Results

Fifty-six studies (n=37137), of 159 eligible for the review, were included in the meta-analysis and demonstrated an overall prevalence of 36% for DSD in people with Type 2 DM. **Prevalence of DSD was significantly higher in samples with a higher prevalence of comorbid depressive symptoms and with a female sample-majority.**

Conclusions

DSD is a prominent issue in people with Type 2 DM that is associated with a female gender and comorbid depressive symptoms. It is important to consider the

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relationship between DSD and depression and the significant overlap between conditions. Further work is needed to explore psychological comorbidity in Type 2 DM to better understand how best to identify and appropriately treat individuals.

Introduction

Psychological comorbidity is high in people with Type 2 diabetes (Type 2 DM) with extensive research demonstrating that approximately 30% of patients experience depressive affect [1-3]. More recently linked to Type 2 DM is diabetes-specific emotional distress (DSD), which encapsulates a much wider affective experience compared to depression, constituting distinctive emotional concerns within the 'spectrum of patient experience' for those living with a progressive and chronic condition [4-7]. DSD refers to psychological distress specific to living with diabetes and can encompass a wide range of emotions, such as feeling overwhelmed by the demands of self-management required through adherence to diet, exercise and medication prescriptions. People with Type 2 DM may worry and ruminate about existing or future complications, hold concerns about existing comorbidities, be fearful of hypoglycaemia and harbour feelings of guilt or shame, notably in relation to obesity or lifestyle [8,9].

Both depression and DSD have been shown to impact negatively in Type 2 DM through poor adherence and reduced self-care [10-12]. Whilst depression and DSD are correlated conditions, research has drawn a distinction between the two conditions suggesting that DSD is more widespread than depression [13]. In addition, the literature suggests that DSD has a greater impact upon, and is more closely associated with, diabetes self-management and diabetes-related behavioural and biomedical outcomes than depression. Most notably, there appears to be an effect of DSD on HbA1c whereas the impact of depression appears to be equivocal [9,14-18]. A study by Fisher et al [19] looking specifically at the relationships between depression, DSD and HbA1c demonstrated that only DSD, and not major depressive disorder or depressive symptoms, held cross-sectional and time-varying

longitudinal relationships to HbA1c, highlighting the importance to explore the concept of DSD in this patient population.

A large proportion of research combines Type 1 DM and Type 2 DM populations together when exploring DSD, however this can be problematic since the way in which DSD manifests in the two populations can be contextually different; such as fear of hypoglycaemia being a more prominent fear in patients with Type 1 DM, or feelings of guilt/shame being more prominent in patients with Type 2 DM. The two validated scales used to assess DSD are the Problem Areas in Diabetes (PAID) scale [20] and the Diabetes Distress Scale (DDS) [21]. The PAID can be used for both Type 1 DM and Type 2 DM, whereas the DDS offers a more comprehensive assessment, to overcome psychometric limitations of the PAID, and is specifically for people with Type 2 diabetes. It has been previously emphasised that the information collected from patients with Type 1 DM using the PAID scale would likely differ from that found in people with Type 2 DM or a mixed Type 1 DM/Type 2 DM population [22], with leading authors recently developing a separate DDS scale for people with Type 1 DM, the T1-DDS [23].

To date, there has been no systematic review and meta-analysis looking specifically at the prevalence of DSD in people with Type 2 DM only. The current review sought to address this gap in the literature and provide novel data on the prevalence of DSD in people with Type 2 DM, acknowledging the need to assess this separately from individuals with Type 1 DM to be able to give greater clarity of understanding and extrapolation of findings to further research and clinical practice.

Methods

Search strategy and selection

Bibliographic databases were searched using a combination of free-text and medical subject heading (MeSh)/Thesaurus terms, including EMBASE (1974 to 2016 week 44), MEDLINE (1946 to week 44 2016), PSYCINFO (1954-2016), CINAHL (1993-2016), The Cochrane Library, the Applied Social Sciences Index and Abstracts (ASSIA) (All dates) and SCOPUS (All years to present). The search strategy was circulated to members of the project team (KK, FS, NR, MD) to advise on any further potential terms and these were added to the search. The finalised search [Supplementary Fig. S1] for this review was conducted on the 5th November 2016.

The inclusion and exclusion criteria for this review were developed alongside the review question using the PICOS (participants, interventions, comparisons, outcomes, and study design) approach [24]. The criteria were deliberately broad, focusing only on 'participants' and 'outcome', to capture as many studies as possible within the DSD literature since this is a relatively new field of study and data was limited. Studies were selected, regardless of methods, if they reported a baseline outcome measure of DSD within an adult population (≥ 18 years) of people with Type 2 DM. In studies where both Type 1 DM and Type 2 DM populations were present, studies with a majority of Type 2 DM ($\geq 70\%$) were included. To ensure external validity, experimental studies were appraised to ensure a representative sample. Studies were excluded if their sample had the potential to skew the findings, such as inclusion criteria necessitating existing psychological concerns. Studies were excluded if they were not reported in the English language.

Two reviewers (NP, SB) independently assessed abstracts and titles for eligibility and retrieved potentially relevant articles using a shared paper-selection form developed specifically for purpose to facilitate mutual understanding [Supplementary Fig. S2]. The reviewers then met to discuss any differences in opinion, which were resolved through discussion; there were few instances where this occurred (<5%) and no requirement for a third reviewer.

Data extraction

The main outcome measure to be extracted was a measure of DSD, taken as the number and percentage of the overall population scoring over the threshold for significant distress, dependent on the measure used. For studies reporting the PAID scale as their outcome measure, the cut-off point was set at 40 as this is deemed high and has discriminative validity [25,26]. For studies reporting the PAID-5, a short-form version of the PAID, the cut off was ≥ 8 [27]. For studies using the DDS, where the total is taken as an average, rather than cumulatively, with moderate distress considered as 2.0-2.9, the cut of was ≥ 2 for the purposes of this review [28]. Further data extracted included: study design; outcome measure used; study location and year; sample size; distribution; population demographics; biomedical outcomes such as HbA1c and body mass index (BMI); and comorbid depression scores. Data was extracted by one reviewer (NP) using a standardised form in Microsoft Excel (v.14.2.3) [Supplementary Fig. S3]. Where the primary outcome (DSD) data were missing, incomplete or unclear, study authors were contacted for additional data and/or clarification. If authors were unreachable due to out of date contact information or did not respond then studies were excluded from the final analyses.

Meta-analyses

The primary outcome was the total number of participants and number of participants demonstrating significant levels of DSD, which we analysed using 'metaprop', a statistical program implemented to perform meta-analyses of proportions [29] in STATA (v.14.1). Metaprop delivers both fixed and random effects pooled estimates and we used the Freeman-Tukey double arcsine transformation to stabilise the variances [30]. Heterogeneity was assessed using an I^2 statistic to establish whether variations between studies included in this meta-analyses were due to chance. The value is expressed as a percentage of the total variation across studies that is attributed to heterogeneity rather than chance, which was quantified as low (25%), moderate (50%) and high (75%) using tentative cut-off points suggested by previous authors [31]. Publication bias was assessed using Egger's test [32] and a funnel plot.

Secondary random-effects meta-analyses were conducted to determine and compare the prevalence of DSD and to identify potential sources of heterogeneity using meta-regression analyses across the following variables: DSD scale used (DDS; PAID; PAID-5); study location (region); population culture (eastern; western); mean age of participants (30-39; 40-49; 50-59; 60-69; 70-79 years); gender majority ($\geq 50\%$ female; $\geq 50\%$ male); ethnicity majority ($\geq 50\%$ white; $\geq 50\%$ non-white); mean BMI (≤ 30 ; ≥ 30); mean HbA1c (7.0-7.9%; 8.0-8.9%; 9.0-9.9%; 12-12.9%); mean years since diagnosed with Type 2 DM (2.0-3.9; 4.0-5.9; 6.0-7.9; 8.0-9.9; 10.0-11.9; 12.0-13.9; 14.0-15.9); percentage of diabetes-related complications and/or comorbidities (10-19%; 20-29%; 30-39%; 40-49%; 50-59%; 60-69%; 70-79%; 80-89%; 90-99%); and comorbid depressive symptoms (0-9%; 10-19%; 20-29%; 30-39%; 40-49%; 50-59%; 60-69%). All available data was extracted and meta-

regression variables were determined a posteriori once sufficient available data was determined.

Due to varied reporting of complications and/or comorbidities across studies, careful consideration was given to data inclusion within the analysis. Twenty-nine studies reported data for complications and/or comorbidities, with terms used interchangeably across studies. The current reporting of 'comorbidities and/or complications' is defined as physical conditions only. Studies that did not state whether their data pertained to physical or psychological conditions were excluded from the analysis. Where possible, meta-regression analyses were performed for individual comorbid conditions, with sufficient data available for: hypertension, dyslipidaemia, retinopathy, heart disease, neuropathy, nephropathy and foot ulcers. Study location regions were grouped into the six regions articulated by the World Health Organisation [33]; Americas, Eastern Mediterranean, Western Pacific, South East Asia, European, Africa. Regarding culture, populations were split into either Eastern or Western cultures; Western cultures were defined as those developing from Europe and their historic expansion into the Americas and Australasia.

Results

Fig. 1 demonstrates the study selection process. Searches generated 6048 citations, of which 3105 titles and abstracts were screened for eligibility once duplicates were removed. Of these, 283 potentially relevant studies were selected for full text retrieval, of which 159 were eligible for the review, and fifty-five were eligible and provided sufficient data to be included within the meta-analyses [e1-e54]. One paper [e8] reported data for two separate studies and these were separated for the analyses.

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Studies included in the meta-analyses are summarised in Table 1. DSD was measured using either the PAID (n=25), the PAID-5 short-form version (n=9), or the DDS (n=21).

Studies were conducted within the last sixteen years, with data collected from the USA (n=20), Canada (n=7), the Netherlands (n=5), Australia (n=6), China (n=3), Singapore (n=2), France (n=1), Germany (n=1), Italy (n=1), India (n=1), Iran (n=1), Japan (n=1), Malaysia (n=1), Norway (n=1) Serbia (n=1), Slovenia (n=1), South Africa (n=1) and one multi-national study.

The majority of studies in this review adopted an observational design (cross-sectional/longitudinal n=43) with twelve experimental studies (RCT n=9, uncontrolled pre/post-test n=3). Samples sizes within the studies ranged from 21 through to 8596. The average age of participants in the studies was 57.4 years (range: 32.3 to 70.0), with an even split of gender (51% men). The minority of people (38%) were of white ethnicity. Participants had been diagnosed with Type 2 DM for an average of 9.7 years (range: 2.9 - 15.6 years) and an average HbA1c of 8.3% (range: 7.0 to 12.0%; 53.0 to 107.7 mmol/mol). The average BMI in participants was 31.7 (range 26.5 to 36.8 kg/m²).

Fifty-five studies, with a total of 36,998 participants, reported the number/percentage of participants demonstrating significant DSD and were included in fixed- and random-effects meta-analyses to determine the overall prevalence of DSD in people with Type 2 DM [Fig. 2].

The overall prevalence of DSD was 36%; random-pooled effect size (ES) 0.360 (95% CI = 0.308, 0.413), fixed-pooled ES 0.356 (95% CI = 0.351, 0.361).

Heterogeneity was shown to be very high with $I^2 = 99.03$, with meta-regression

analyses identifying potential confounders in gender distribution ($p=0.011$) and comorbid depressive symptoms ($p=0.009$); finding prevalence to be increased in studies with a female sample majority and in samples with comorbid depressive symptoms [Table 2]. Eggers test ($p=0.119$) suggested that publication bias was absent. The funnel plot, however, demonstrated asymmetry, with a greater representation of studies where higher DSD proportions were seen, indicating potential for bias [Supplementary Fig. S4].

Discussion

Key findings

This comprehensive meta-analysis of fifty-five studies showed that the overall prevalence of DSD using established cut-off scores in people with Type 2 DM was 36%, with secondary analyses identifying gender ($p=0.010$) and comorbid depressive symptoms ($p=0.008$) as significant factors affecting prevalence.

Strengths and limitations

This is the first known systematic review and meta-analyses of the existing literature to determine the prevalence of DSD in a solely Type 2 DM population. As such, it provides novel information for a gap in the literature. The methods used to carry out this review were robust, adopting strategies to gain all relevant outcome data available, even when not reported.

While it is a potential strength that this review is the first of its kind, it meant that the data available was limited, since the field of DSD is a relatively new one. This was further hindered by the vast majority of papers not reporting the data required for the analyses, and despite extensive efforts to contact authors for any missing data or to

clarify any discrepancies, this often proved unsuccessful, either due to contact details no longer being valid and/or receiving no reply.

There was high heterogeneity between studies with particular concern lying in the reporting of DSD and the scales used. A number of studies that reported DDS scores conveyed the score as a cumulative rather than an average, meaning that their results were dramatically higher than the majority of studies. As such, if authors did not respond to requests for an average score, these studies needed to be excluded so as not to bias the results. Similarly the reporting of comorbid **depressive symptoms**/depression was highly varied with ten different scales reported, two studies reporting diagnoses by clinical diagnostic interview and one study merely stating the percentage that has “regular MD” (major depression). While further heterogeneity between studies was evident in terms of study location and population demographics, this was useful in terms of understanding the prevalence of DSD across variables.

Analyses to determine if publication bias was evident offered inconsistent results. While the funnel plot shows asymmetry, Egger’s test deemed that publication bias was not present. It is possible that the distribution within the funnel plot, namely an excess of studies to the right of the plot, could suggest a bias in that studies with higher results of DSD are more likely to be published.

Surrounding evidence and implications

Elevated levels of DSD appear to be widespread with estimates given by leading authors varying from between 18% to 35% [7,28] in combined Type 1 DM and Type 2 DM populations, with a recent systematic review and meta-analysis looking into the prevalence of DSD in research populations demonstrating a prevalence of 22% [34].

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A study by Fisher *et al* in 2008 explored the longitudinal rates of affective disorders, including DSD, demonstrating an approximate point prevalence of 46% in people with Type 2 DM [16]. The current findings demonstrated a 36% prevalence of DSD in people with Type 2 DM, which is higher than the research combining Type 1 DM and Type 2 DM populations and could be indicative of a difference between how DSD manifests and presents in these populations. Although research has shown that rates are similar when appropriate type-specific scales are used, with a 42.1% point prevalence and 54.4% incidence of DSD in people with Type 1 DM, and 46.2% and 54.3% in people with Type 2 DM respectively [23]. The current review is the first systematic review and meta-analysis of DSD in Type 2 DM and highlights the importance of understanding how DSD manifests in this population specifically.

The results demonstrated that DSD was significantly higher in samples with a majority of women compared with samples with a majority of men. Previous studies have recognised a link between female gender and DSD, as well as depression and anxiety, with greater risk in women compared to men [13,16]. This increased presence of expressed emotional difficulties in women with Type 2 DM may be attributable to differing social conventions regarding gender: men appear less likely to seek help and/or admit distress due to a need to appear capable or for fear of being emasculated by showing weakness [35]. A further argument could be that men may try to fulfill 'masculine' gender identities, such as problem solving, which could encourage them to privilege treatment advice to overcome their condition [36]. While such stereotypes may be less prevalent in younger cohorts, amongst older generations, who are over represented in the studies reviewed, these gender identities may pertain and partially explain why emotional difficulties appear less common in men. This reiterates a need to take into account an individual's personal

presentation and circumstance when approaching assessment of wellbeing both psychologically and in terms of physiological diabetes-related issues, to ensure the best identification of issues to treat and offer appropriate management of these.

Our findings also demonstrated a significant difference in DSD rates when accounting for the prevalence of comorbid depression in the samples, with significantly lower prevalence of DSD in samples with low to no prevalence of comorbid depression. This supports existing research highlighting that DSD and depression are highly correlated constructs [37-42]. Research has emphasised concerns with poor recognition in both depression [43-47] and DSD [42,48,49], with a substantial overlap between symptoms and presentation of both conditions. It is important to consider when assessing psychological status in people with Type 2 DM that these are different constructs that can either coexist, occur in isolation, or present distinct from one another.

Prevalence of DSD appeared higher in studies reporting the DDS compared to the PAID and the PAID-5 scales, although this difference was non-significant. A recent study comparing the DDS and PAID scales acknowledged that while both scales are excellent psychometric self-report measures, they bear fundamental differences in terms of the domains they address [50]. For example, the authors noted that the PAID scale encapsulates a broader range of emotional concerns compared to the DDS, the latter encompassing factors more closely linked to diabetes self-management. This could explain the differences in prevalence between the measures found in the present findings, since the scales themselves explore fundamentally different aspects of DSD. This also elucidates concerns about the disparity in defining and assessing DSD; since there is no one-single definition or diagnostic criterion for DSD, this leaves open further obstacles in properly

identifying, and thus treating, people with Type 2 DM who present with comorbid psychological difficulties. This issue is further clouded when considering the grouping of Type 1 DM and Type 2 DM together when exploring the notion of DSD. Whilst there is evidence to suggest that there are no fundamental differences in reported diabetes-related stressors between the two condition types using the PAID scale [26], using specific scales developed for Type 1 and Type 2 diabetes, such as the T1-DDS and T2-DDS, may foster better understanding of the experience and care needs of these individuals.

Conclusion

The findings of this review demonstrate that DSD is a prominent issue in people with Type 2 DM, and that **it is greater in groups with a female gender majority and with higher prevalence of comorbid depressive symptoms.** Depression and DSD are highly related and both appear to be under-recognised and inadequately treated in Type 2 DM. The findings of this review highlight the importance of identification and subsequent management of DSD and/or depression in people with Type 2 DM, with particular priority given to the use of appropriate scales and the interpretation of findings to allow for patient-centred and suitably tailored care. Further work is required to explore psychological comorbidity in people with Type 2 DM and gain better understanding of how best to support them.

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Conflicts of interest

None declared

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