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DIABETIC Medicine

SYSTEMATIC REVIEW

The effectiveness of cognitive behavioural therapy and third-wave cognitive behavioural interventions on diabetes-related distress: A systematic review and meta-analysis

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Abstract

Aim: Diabetes-related distress is common in diabetes and has implications for well-being. Cognitive behavioural therapy (CBT) and third-wave CBT hold promise as treatments for diabetes-related distress, although previous findings are inconclusive. We aimed to conduct a systematic review with meta-analysis to understand the efficacy of these interventions in treating diabetes-related distress, while also assessing the associative benefits of these interventions on depression, anxiety and glycaemic control. We also aimed to conduct a narrative synthesis, and subgroup analyses to identify intervention components most useful in treating diabetes-related distress.

Method: We searched seven electronic databases from inception to April 2021. Data extraction was independently performed by two reviewers. Methodological quality was assessed. The protocol was registered with the Prospective Register Of Systematic Reviews (PROSPERO): CRD42021240628.

Results: We included 22 randomised controlled trials investigating the efficacy of CBT and third-wave CBT interventions on diabetes-related distress. CBT for diabetes-related distress significantly reduced distress (SMD = −0.278, $p = 0.010$) and depression (SMD = −0.604, $p = 0.016$). Third-wave CBT for diabetes-related distress significantly reduced anxiety (SMD = −0.451, $p = 0.034$). No significant effect of either intervention on glycated haemoglobin was observed. CBT interventions that included a digital component, were delivered by a psychological practitioner, and included behavioural activation bolstered the effects on diabetes-related distress.

Conclusions: CBT aiming to target diabetes-related distress is beneficial for distress and depression. Third-wave CBT for diabetes-related distress is beneficial for anxiety. More work is needed to optimise interventions to improve both mental and physical health outcomes in people with diabetes.

KEYWORDS
acceptance and commitment therapy, cognitive behavioural therapy, diabetes mellitus, type 1, diabetes mellitus, type 2, mindfulness, psychological distress

1 | INTRODUCTION

Psychological distress is common in diabetes. People with diabetes are two times more likely to experience depression compared to those without diabetes,[1,2] and have a 25% higher prevalence of anxiety.[3] Furthermore, diabetes-related distress is estimated to occur among 40% of people with diabetes.[4,5] Diabetes-related distress is an illness-specific psychological distress that reflects a person's emotional response to the demands and challenges of living with diabetes.[6] It considers psychosocial adjustment and challenges faced by individuals with diabetes.[5] Although related,[6] diabetes-related distress is distinct from depression and anxiety,[6,7] as these disorders are assessed using thresholds of somatic and affective symptomology[8] irrespective of context or cause.[9] Unlike depression or anxiety, diabetes-related distress is said to be closely attached to the day-to-day experience of living with diabetes whereas depression and/or anxiety is generally unrelated to a specific condition.

A lot of research to date has focused on depression and anxiety in diabetes. This may be explained by evidence associating depression with poorer glycaemic control,[10] increased risk of diabetes complications[11] and reduced quality of life.[12,13] However, researchers have been investigating diabetes-related distress as a key psychological outcome in diabetes for over 25 years.[5,14,15] Psychological distress seen within diabetes is often conceptually different to that in those living with general depression and anxiety (e.g., emotional burden of diabetes management, the burden of potential future complications and the social impact of diabetes[16,17]). Indeed, evidence now suggests that diabetes-related distress may be more closely linked to glycaemic control than depression.[18–20] Furthermore, it has shown associative relationships with quality of life[21] and self-management behaviours[18,22] that may have implications for metabolic outcomes. Therefore, understanding treatment for diabetes-related distress, may potentially be imperative to improve emotional well-being and physical outcomes in diabetes. Psychological therapies offer one treatment strategy in this regard.

In the United Kingdom, cognitive behavioural therapy (CBT) is the recommended psychological treatment for managing anxiety and/or depression in the context of long-term conditions such as diabetes.[23,24] CBT posits that cognitions are central to behavioural, emotional and physical responses[25–27] with each of these elements constantly interacting and influencing each other.[28] Most previous review studies have explored the effectiveness of CBT for depression, anxiety and glycaemic control, with diabetes-related distress as an additive component. A 2017 meta-analysis[29] investigated the effect of CBT interventions on glycated haemoglobin (HbA_{1c}) as a primary outcome, along with depression, anxiety and diabetes-related distress as secondary outcomes. CBT significantly reduced depression and anxiety in the short and medium term with moderate effect. CBT also significantly reduced depression in the long term with small effect. For HbA_{1c}, CBT had a small statistically significant effect in the short and medium term but not the long term. Too few studies were identified to meta-analyse diabetes-related distress outcomes.

A second 2017 review[30] investigated the effects of CBT for people with diabetes and a co-morbid depression. The review found that CBT produced a significant moderate reduction in depression. CBT did not have a significant effect on anxiety or HbA_{1c}. Furthermore, only two studies in this review looked at diabetes-related distress and meta-analysis showed that CBT did not have a statistically significant effect on this outcome. A third review in 2020,[31] explored

Novelty statement

What is already known?

- CBT is effective at treating depression in diabetes but findings for diabetes-related distress are inconclusive.

What has this study found?

- CBT interventions significantly reduced distress and depression.
- Third-wave CBT significantly reduced anxiety.
- There were no significant effects for either therapy on glycated haemoglobin.
- Interventions delivered by a psychological practitioner including a digital component and behavioural activation appeared to bolster the effects of CBT on distress.

Implications of the study

- This review compared CBT and third-wave CBT for diabetes-related distress and provides clinical utility by identifying intervention components that may be most useful for treating diabetes-related distress.

the effects of CBT on studies reporting either depression or anxiety, or HbA_{1c} as primary outcomes. Across all follow-up time points CBT had a large significant effect on depression. However, no statistically significant effect on anxiety was observed. For HbA_{1c}, CBT showed a significant moderate effect. Diabetes-related distress was not included in the review.

Overall, the meta-analytic evidence to date suggests that CBT may be effective at reducing depression. However, findings regarding anxiety and HbA_{1c} are mixed. Furthermore, given the high prevalence of diabetes-related distress and its implications on clinical outcomes, more research is needed on the effectiveness of CBT for diabetes-related distress. No previous reviews exploring CBT in diabetes have placed diabetes-related distress as the primary outcome, meaning that relevant studies are missed. Considering such studies will help to disentangle the effectiveness of CBT interventions on diabetes-related distress specifically. Measuring depression, anxiety and HbA_{1c} as secondary outcomes, may enable a greater understanding of the added benefits for these outcomes when targeting diabetes-related distress.

Alongside consideration of traditional CBT, the potential of third-wave CBT[32] approaches such as acceptance and commitment therapy (ACT; an approach encouraging acceptance of unwanted thoughts and feelings)[33] and mindfulness-based therapy (aiming to increase present moment awareness)[34] may help define what psychological interventions are most effective in treating diabetes-related distress. Third-wave interventions differ from traditional CBT interventions in their content. Third-wave techniques are primarily focused on how individuals respond to their emotions, behaviours and cognitions. Whereas traditional CBT commonly focuses on the appraisal or modification of antecedent emotions, behaviours and cognitions.[32] A review on the use of third-wave interventions to reduce diabetes-related distress in type 2 diabetes alone,[35] failed to find that mindfulness and acceptance-based interventions significantly reduced diabetes-related distress up to 1-month post-intervention. However, the included interventions in this review showed benefits for improving depression, anxiety and glycaemic control. Another review[36] investigated the use of mindfulness-based interventions alone in type 1 and type 2 diabetes. The authors concluded that the treatment–control comparison effect estimates were small and unreliable, so no meta-analysis was conducted. This suggests that further investigation is needed into the efficacy of third-wave interventions on diabetes-related distress for individuals with type 1 and type 2 diabetes.

Additionally, a more in-depth analysis of the type of interventions offered (i.e., their active ingredients) and their mode of delivery will further the development of diabetes-related distress interventions, as similar, earlier reviews[31] did not include diabetes-related distress as an outcome. Furthermore, the inclusion, and separate analysis of traditional CBT and third-wave interventions may limit treatment heterogeneity, informing conclusions about the efficacy of each intervention type as a tool for treating diabetes-related distress and may inform future intervention development. Therefore, this review has six objectives:

1. To examine the effectiveness of all traditional CBT interventions on diabetes-related distress alone.
2. To examine the effectiveness of CBT interventions that target diabetes-related distress primarily on diabetes-related distress, depression, anxiety and HbA_{1c}.
3. To examine the effectiveness of all third-wave CBT interventions on diabetes-related distress alone.
4. To examine the effectiveness of third-wave CBT interventions that target diabetes-related distress primarily on diabetes-related distress, depression, anxiety and HbA_{1c}.
5. To describe the content of CBT interventions and data permitting perform subgroup analyses to examine how the content and mode of delivery influences treatment effects on diabetes-related distress alone.
6. To describe the content of third-wave CBT interventions and data permitting perform subgroup analyses to examine how the content and mode of delivery influences treatment effects on diabetes-related distress alone.

2 | METHODS

The review protocol was pre-registered on PROSPERO (CRD42021240628). The research objectives were slightly refined to home in on diabetes-related distress as a primary intervention target. Our findings are reported in line with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidance.[37]

2.1 | Eligibility criteria

Two reviewers (EJ and IK) screened studies against the inclusion and exclusion criteria outlined in Table 1. Restrictions were placed on the language of publication (English only).

2.2 | Information sources

The following electronic databases were searched in April 2021: OVID MEDLINE, psycINFO, EMBASE, Cumulative Index to Nursing and Allied Health literature (CINAHL), Web of Science, PubMed and Cochrane Central Register of Controlled Trials (CENTRAL). No restrictions were placed on publication date. Reference lists of relevant

TABLE 1 PICOS inclusion/exclusion criteria.

Variable	Inclusion	Exclusion
Population	• Participants with type 1 diabetes and type 2 diabetes. This includes both doctor-diagnosed and self-reported diabetes. • Adults aged ≥18. • Female and male. • All nationalities.	• Participants without type 1 diabetes or type 2 diabetes. • Participants with pre-diabetes (e.g. impaired glucose tolerance) and gestational diabetes. • Family members/carers of those with type 1 and type 2 diabetes. • Age < 18.
Intervention	• CBT interventions including both a cognitive and behavioural element. • Third-wave CBT interventions (ACT/mindfulness-based interventions). • Delivered by psychologists, mental health workers, diabetes nurses, any professional trained to give the intervention or self-guided. • Delivered remotely or face to face in either an individual or group format.	• Non-CBT interventions. • Non-third-wave CBT interventions (ACT/mindfulness-based interventions). • Lifestyle interventions. • Interventions which were not targeting diabetes-related distress
Comparator	• Usual care. Education is recommended as part of routine care for diabetes management by the NICE guidelines, hence education may form part of usual care. • Waitlist control, defined as a control condition where individuals can access the active treatment after a waiting period. • Placebo control, defined as a control condition that is similar to the intervention in components and structure without the therapeutic content. • Active control, where individuals in the comparator group receive an alternative active treatment. Education was not defined as an active control in this review.	• No comparator.
Outcome	• All studies included in this review had to measure diabetes-related distress as either a primary or secondary outcome. • The primary outcome of this review: Diabetes-related distress as measured by validated scales such as the PAID or DDS. • Secondary outcomes of this review: i) psychological outcomes; Depression and anxiety measured through validated scales. ii) physical outcomes; Glycaemic control objectively assessed by glycated haemoglobin (HbA_{1c}) levels.	• Psychosocial stress other than measures of distress/depression, such as measures of work stress or perceived stress. • Depression measured through diagnostic clinical interview. • Anxiety measured through diagnostic clinical interview. • Glycaemic control objectively assessed through fasting plasma glucose.
Study design	• RCT's or quasi-RCT's; where 'random' is used to describe the method for assigning subjects to groups.	• nRCT's.

Abbreviations: ACT, acceptance and commitment therapy; CBT, cognitive behavioural therapy; DDS, diabetes distress scale; HbA_{1C}, glycated haemoglobin; nRCT, non-randomised controlled trial; PAID, problem areas in diabetes scale; RCT, randomised controlled trial.

articles were screened to identify articles not retrieved by the electronic search. Where protocols, or conference abstracts were identified, authors were contacted to retrieve the full text.

2.3 | Search strategy

The search strategy included MeSH terms with appropriate Boolean operators (see Table S1 in Appendix S2).

2.4 | Data extraction

Two reviewers (EJ and IK) independently extracted the data onto a purpose designed data extraction table. Data were extracted on: publication characteristics (e.g., place of origin), participant characteristics, baseline characteristics (e.g., baseline mood and HbA_{1c}) and outcomes of interest, specifically continuous measures of diabetes-related distress, depression, anxiety and HbA_{1c}. We extracted data on the timing of the post-intervention measurement.

The post-intervention time point was defined as the earliest post-intervention data collection time point. Where studies used more than one measure to assess an outcome of interest, we prioritised extraction of the author identified primary outcome. Where the author did not differentiate between the primary and secondary outcome, we extracted data on the outcome that was most common across the included studies to enable data pooling. Where data were missing or unclear, authors were contacted. Details of intervention content were extracted by one reviewer (EJ) based on the Template of Intervention Description and Replication (TIDieR) guidance.[38] These details were extracted from published articles, their supplementary materials, study protocols and where possible, manuals from authors.

3 | QUALITY AND RISK OF BIAS (RoB) ASSESSMENT

3.1 | Within-study bias

Methodological RoB was assessed independently (EJ and IK) following Cochrane Handbook[39] guidance. Each study was classified as having high, low or unclear RoB on the following domains: random sequence generation; allocation sequence concealment; blinding of participants, blinding of outcome assessment, completeness of outcome data and selective outcome reporting. RoB ratings are presented using RevMan5.[40]

3.2 | Between-study bias

Publication bias was a criterion selected to evaluate to if studies reporting statistically significant results were more likely to be published, potentially leading to an overestimation of the real effect size.[41] This was tested using funnel plots and Egger's test.[42]

3.3 | Data synthesis and analysis

Analyses were conducted using STATA v16.0. For each included study individual effect sizes were calculated based on extracted data. Treatment effect estimates were pooled using random-effects meta-analysis with 95% confidence intervals (CIs) using the *metan* command. Results were pooled based on intervention type (CBT vs. third-wave CBT) for each outcome (i) diabetes-related distress (ii) depression (iii) anxiety and (iv) HbA_{1c}. The treatment effect on each outcome was expressed as standardised mean difference (SMD) between the intervention and control group at the post-intervention time point. In the case of multiple intervention or control groups we followed Cochrane Handbook guidance.[39,43] For those trials where groups were similar, we combined data into a single intervention and control group so that the counting of participant data was not repeated. For those groups that were heterogeneous, we accounted for this by splitting the sample size of the shared group by the number of control or intervention groups to ensure that the study was not overpowered. Statistical heterogeneity was estimated using I^2, which describes variability in effect sizes due to treatment heterogeneity compared to variability due to chance.[43] Following Cochrane guidance, $I^2 > 50\%$ represents moderate heterogeneity.[43,44] Where cluster trials were included an intra-cluster coefficient (ICC) 0.002 was used.[43] Where data were available for different outcome follow-up time points, pooled effect size estimates were generated for each time point, if the number of studies was >10 and the distribution of studies across the subgroups was relatively even, in line with Cochrane guidance.[43]

Intervention content was descriptively reported in accordance with the TIDieR checklist.[38] Statistical subgroup analyses were then performed based on a priori defined intervention criteria to examine their impact on diabetes-related distress for CBT and third-wave CBT interventions (1) whether the intervention was diabetes specific, (2) whether the intervention included a digital component, (3) whether the intervention was delivered by a psychological practitioner, (4) the delivery format (5) whether between session homework was given, and whether the intervention included (6) goal setting, (7) cognitive restructuring, (8) psychoeducation, (9) behavioural activation, (10) the cultivation of acceptance (assessed among third-wave interventions only). As above, subgroup analyses were only conducted if there were > 10 studies and the distribution of studies across subgroups was approximately even.[43]

4 | RESULTS

4.1 | Study selection

The combined online and manual searches retrieved 1037 citations. After removing duplicates, 671 unique citations remained (Figure 1). Two independent reviewers (EJ and IK) reviewed citation titles and abstracts and identified 80 studies that were potentially relevant. Following full text screening, 22 studies were identified as meeting the inclusion criteria.

4.2 | Study characteristics

The 22 identified RCTs comprised of 4123 participants (Table S2 within Appendix S2). A total of 20 studies

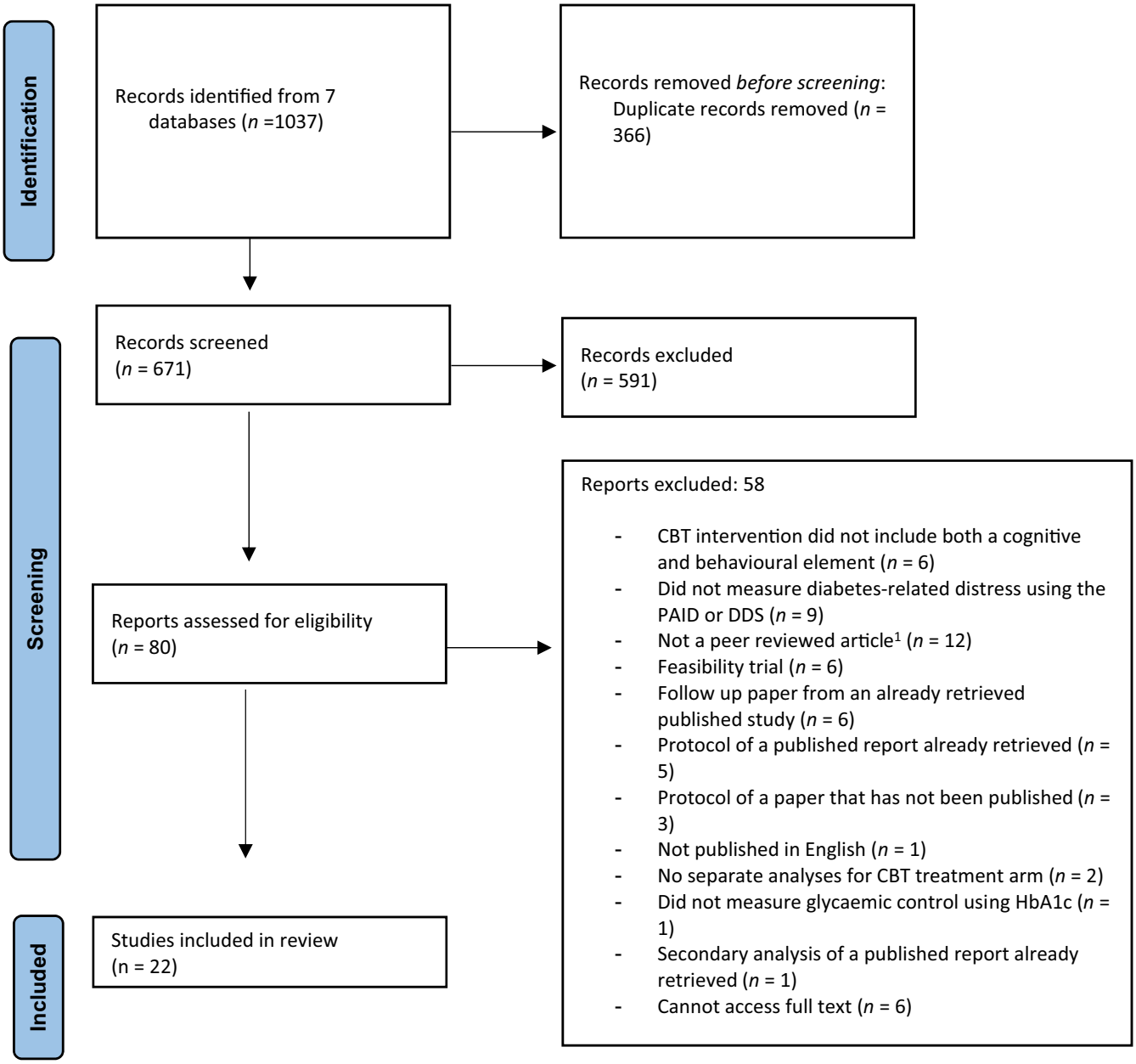


FIGURE 1 PRISMA flowchart diagram.[1] The citations received were individual study supplementary material ($n = 9$), poster presentations ($n = 2$) and conference abstracts ($n = 1$). CBT, cognitive behavioural therapy; DDS, diabetes distress scale; HbA_{1c}, glycated haemoglobin; PAID, problem areas in diabetes scale.

randomised participants at an individual level and two studies randomised by clusters of health clinics.[45,46] The trials were published from 2004[47] to 2021[48] and were conducted across 12 countries. The mean age of participants ranged from 37.8[49] to 70.7 years.[50] The sample was predominantly female (54.9%).

A total of 10 trials included participants with type 2 diabetes.[45, 46, s50-s57] The remainder included participants with type 1 diabetes [49, s58] or participants with both type 1 and 2 diabetes.[47, 48, s59-s66] Of the included trials, 14 screened for elevated diabetes-related distress or depression, using clinical interviews[50, s52, s61] or specified cut-offs within validated scales.[45, 48, s51, s53, s56, s57, s60, s62-s65] Similarly, eight trials had a screening cut-off for HbA_{1c}.[45, 46, 48, 49, s55, s57, s58, s66]

Diabetes-related distress was the primary outcome in just over half of the studies ($k = 12$; 54.5%). In 13 trials the Problem Areas In Diabetes (PAID) scale was used to measure diabetes-related distress[47-50, s55, s56, s58, s61-s66] and in eight trials the Diabetes Distress Scale (DDS) was used.[45, 46, s51-s54, s57, s59] One study included both measures.[s60] All studies measured diabetes-related distress post-intervention, but the timing of the measurement varied from less than 6 weeks[45, 47, 48, s50-s52, s54-s57, s59-s65] to more than 6 weeks post-intervention.[46, 49, s53, s58, s66] Traditional CBT interventions

accounted for 18 and third-wave CBT interventions accounted for five of the included studies respectively. One study[s63] had a CBT intervention arm and a third-wave CBT arm.

4.2.1 | Objective 1: Meta-analysis of all traditional CBT interventions on diabetes-related distress

Only 17 studies with 18 comparisons provided sufficient data for meta-analysis, as one study had multiple control arms.[s66] There was a small statistically significant effect of CBT on diabetes-related distress (SMD = −0.149, $p = 0.021$; 95% CI −0.276 to −0.023, $I^2 = 54.8\%$, $p = 0.003$; Figure 2). Another study that did not provide sufficient data to be pooled,[s52] reported that CBT alongside CBT and exercise led to a significant reduction in distress ($p = 0.003$ and $p = 0.008$ respectively). Subgroup analyses showed that the effectiveness of CBT on diabetes-related distress dissipated with a post-intervention outcome collection time point greater than 6 weeks (Appendix S1). There was no significant impact on efficacy estimate when diabetes-related distress questionnaires (PAID and DDS) were analysed separately (data not shown).

4.2.2 | Objective 2: Meta-analysis of traditional CBT interventions targeting diabetes-related distress primarily on outcomes

4.2.3 | Diabetes-related distress

Only eight studies cited diabetes-related distress as the primary outcome and provided sufficient data for meta-analysis. There was a small statistically significant effect of CBT on diabetes-related distress, when it was the primary intervention outcome (SMD = −0.278, $p = 0.010$; 95% CI −0.488 to −0.068, $I^2 = 62.8\%$, $p = 0.009$; Figure 3).

4.2.4 | Depression

Pooling data from three studies, there was a moderate significant effect of CBT for diabetes-related distress on depression (SMD = −0.604, $p = 0.016$; 95% CI = −0.198 to −0.111; I^2 82.3%, $p < 0.003$; Figure 4a).

4.2.5 | Anxiety

Pooled analyses could not be conducted as only one study[s61] measured anxiety. The individual study estimate evidenced a large statistically significant effect of CBT for diabetes-related distress on anxiety ($g = 0.72$, $p = 0.002$).

4.2.6 | HbA_{1c}

HbA_{1c} was measured in six trials. Pooled analyses revealed a small statistically non-significant effect of CBT for diabetes-related distress on HbA_{1c} levels (SMD = −0.045, $p = 0.812$; 95% CI = −0.417 to 0.326; $I^2 = 74.7\%$ $p = 0.001$; Figure 4b).

For all outcomes within this objective, there were too few studies to explore the impact of data collection time point on reported effect sizes.

4.2.7 | Objective 3: Meta-analysis of all third-wave CBT on diabetes-related distress

There was a small but non-significant effect of third-wave CBT interventions on diabetes-related distress across five studies (SMD = −0.135, $p = 0.504$; 95% CI = −0.532 to 0.262, $I^2 = 73.1\%$, $p = 0.005$; Figure 5).

There were too few studies to explore the impact of data collection time point on reported effect sizes.

There was no significant impact on efficacy estimate when diabetes-related distress questionnaires were analysed separately (data not shown).

4.2.8 | Objective 4: Meta-analysis of third-wave CBT interventions targeting diabetes-related distress primarily on outcomes

Diabetes-related distress

In four included studies diabetes-related distress was the primary outcome and these provided sufficient data for meta-analysis. There was a small but non-significant effect of third-wave CBT interventions on diabetes-related distress across four studies (SMD = −0.122, $p = 0.619$; 95% CI = −0.605 to 0.360, $I^2 = 79.8\%\%$, $p = 0.002$; Figure 6).

Depression

A small statistically non-significant effect of third-wave CBT for diabetes-related distress on depression was observed in pooled analyses of three studies (SMD = −0.205, $p = 0.509$; CI = −0.811 to 0.402; $I^2 = 82.7\%$, $p = 0.003$; Figure 7a).

Anxiety

Only two studies measured the effect of third-wave interventions for diabetes-related distress on anxiety. There was a moderate statistically significant effect detected in pooled analyses (SMD = −0.451, $p = 0.034$; 95% CI = −0.867 to −0.035; $I^2 = 52.2\%$. $p = 0.148$; Figure 7b).

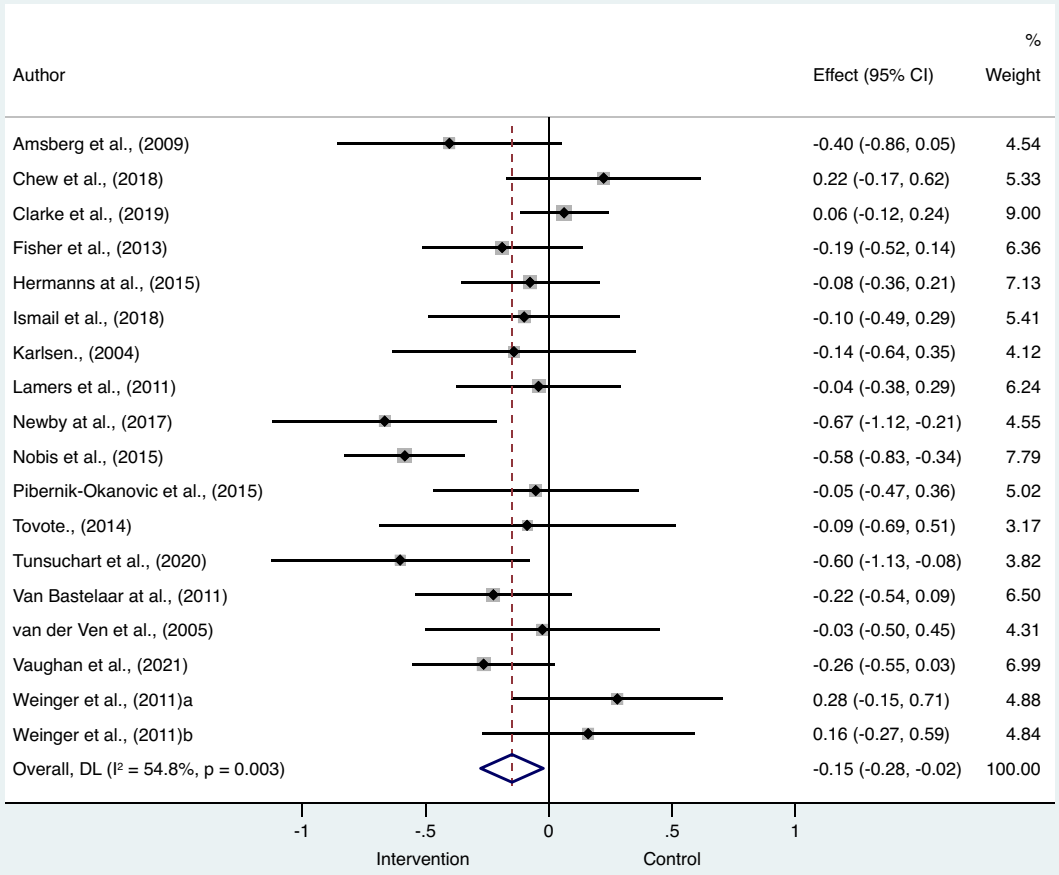


FIGURE 2 Forest plot of the effect cognitive behavioural therapy interventions on diabetes-related distress using first time point data. This diagram is a graphical representation of the meta-analytic findings, showing the earliest time point effect sizes and errors of each included study. There was a significant effect of cognitive behavioural therapy interventions on diabetes distress, in favour of the intervention. Note, when looking at data from Weinger et al., (2011), [a]represents study data using a placebo control condition, [b]represents study data using treatment as usual control condition.

HbA_{1c}

There was no statistically significant effect of third-wave CBT for diabetes-related distress on HBA_{1c} in pooled analyses of three RCTs (SMD = 0.016, p = 0.910; 95% CI = −0.265 to 0.297; I^2 = 22.6%, p = 0.275; Figure 7c).

For all outcomes within this objective, there were too few studies to explore the impact of data collection time point on reported effect sizes.

4.2.9 | Objectives 1–4: RoB analysis

Within-study RoB

There was a high prevalence of unclear or high RoB across the included studies (Figures 8 and 9). The categories of allocation concealment, blinding of outcome assessment and selective reporting were often not adequately reported. Due to the therapeutic nature of the interventions, it was often not possible to blind participants and personnel to treatment and downgrading evidence because of this alone may not be reasonable.[s67] Therefore, we considered other areas that could impact bias (e.g., treatment adherence, fidelity).

Between-study bias

There was no evidence of publication bias. Results from the Egger's test ranged from p = 0.17 to p = 0.72 (for funnel plot representation see Figures S7–S15 within Appendix S2).

4.2.10 | Objective 5: Content of CBT interventions

CBT interventions ranged from 5 days[s60] to 12 months[46] in length (see Table S3 and S4 within Appendix S2). Of the

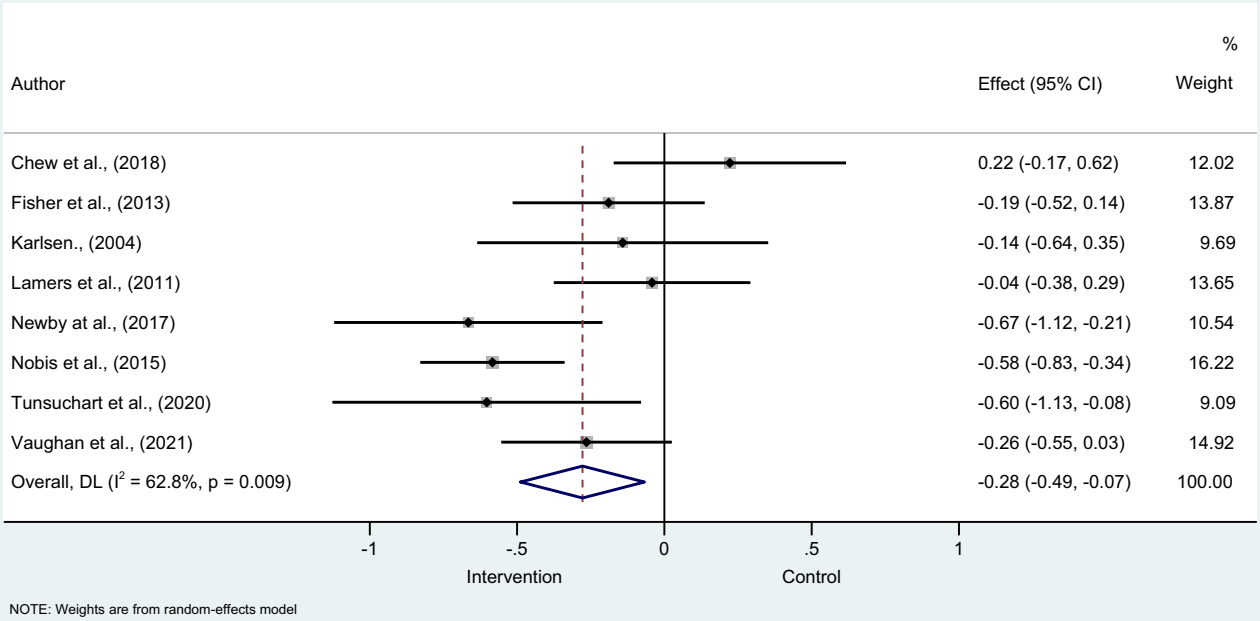
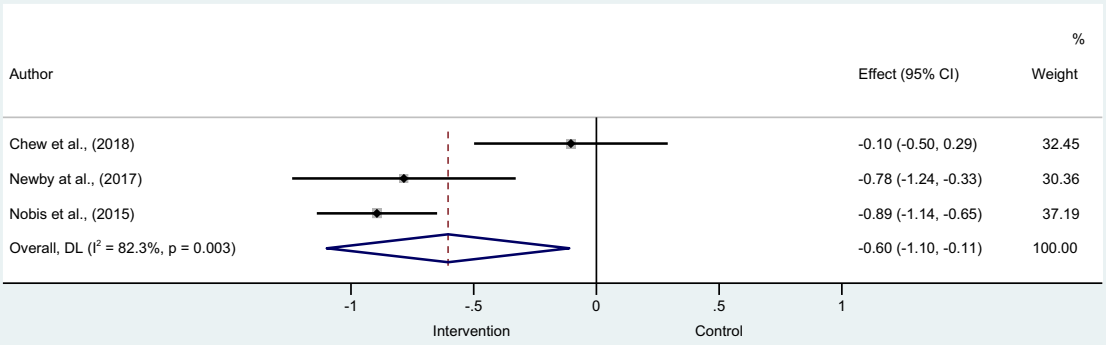


FIGURE 3 Forest plot of the effect of cognitive behavioural therapy interventions that aim to target diabetes-related distress primarily on diabetes-related distress using first time point data. This diagram is a graphical representation of the meta-analytic findings, showing the earliest time point effect sizes and errors of each included study. There was a significant effect of cognitive behavioural therapy interventions to treat diabetes-related distress on diabetes-related distress.

included interventions four (23%) were web-based self-guided interventions with minimal[s61, s62, s64] or no clinician support.[s51] Another study[s53] was predominantly web based with an additional face-to-face problem-solving therapy session delivered by university graduates. One intervention[48] was telephone based. The remaining interventions were delivered by a range of health care professionals in either a face-to-face group format, or on an individual basis. The face-to-face interventions were predominantly delivered within the community. Most CBT interventions ($k = 11$; 61%) were diabetes specific (defined as including diabetes-specific content or following diabetes-specific protocols). CBT interventions commonly included the identification and management of unhelpful thoughts relating to low mood, beliefs about diabetes and diabetes self management. A key therapeutic technique used was cognitive restructuring ($k = 11$; 61.1%). Over half of the CBT interventions ($k = 12$; 66%) used psychoeducation. Predominantly psychoeducation focused on the link between mood difficulties and diabetes[45, s52, s58, s60, s62, s64] or education regarding diabetes treatment and management.[47, 48, s66] When psychoeducation was not diabetes

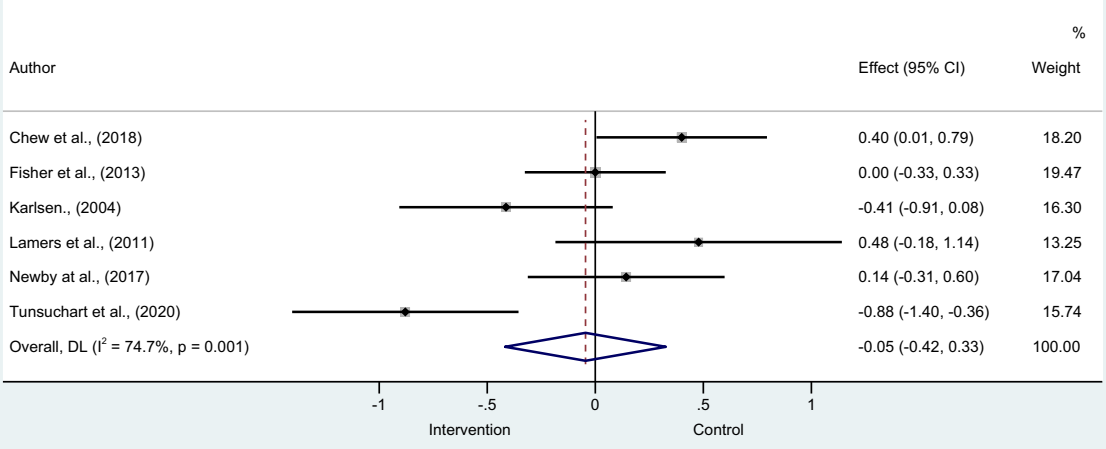
FIGURE 4 (a) Forest plot of the effect of cognitive behavioural therapy interventions that aim to target diabetes-related distress primarily on depression using first time point data. This diagram is a graphical representation of the meta-analytic findings, showing the earliest time point effect sizes and errors of each included study. There was a significant effect of cognitive behavioural therapy interventions for diabetes-related distress on depression. (b) Forest plot of the effect of cognitive behavioural therapy interventions that aim to target diabetes-related distress primarily on HbA_{1c} using first time point data. This diagram is a graphical representation of the meta-analytic findings, showing the earliest time point effect sizes and errors of each included study. There was a non-significant effect of cognitive behavioural therapy interventions for diabetes-related distress on HbA_{1c}, in favour of the intervention.

(a)



NOTE: Weights are from random-effects model

(b)



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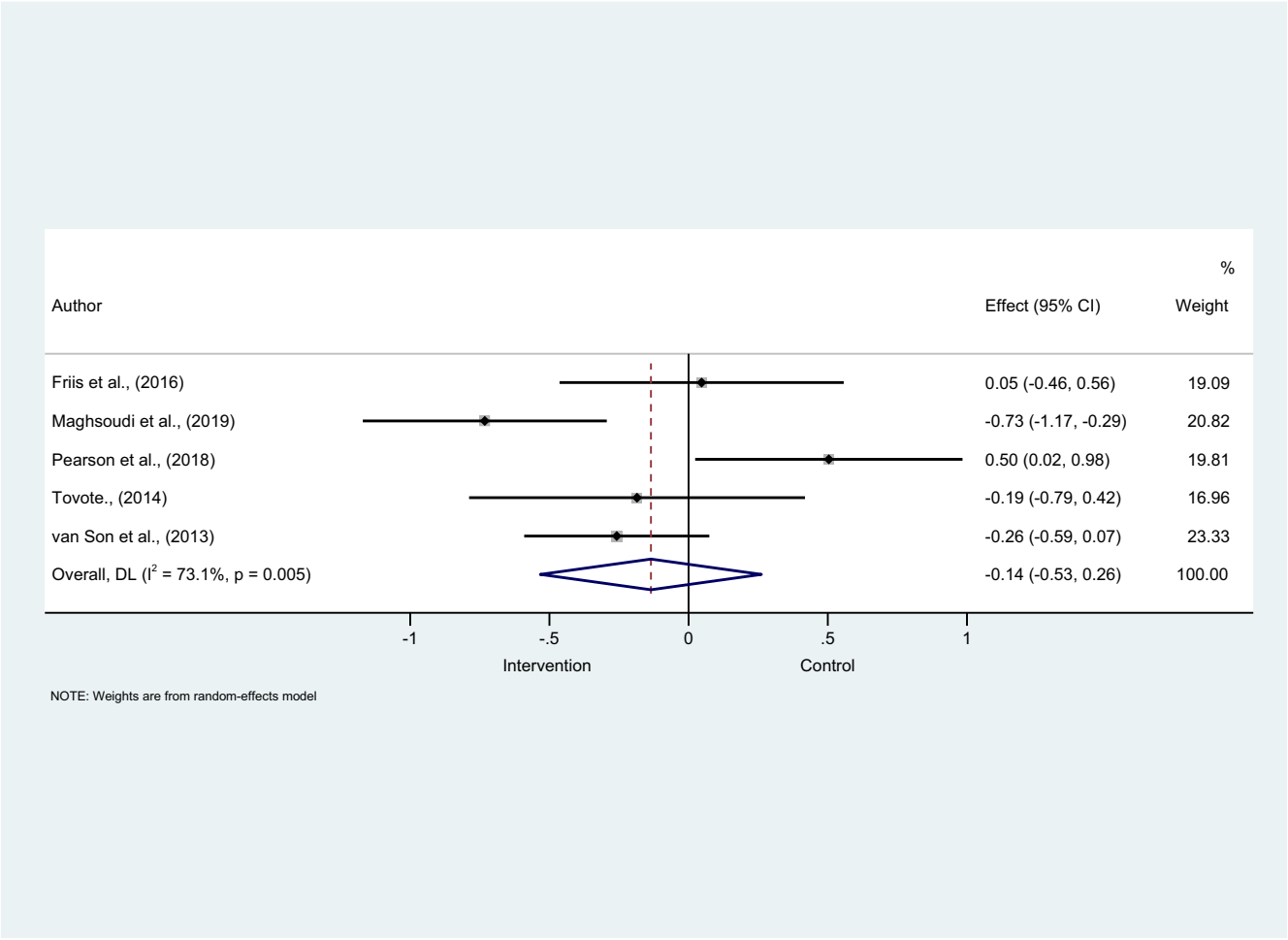


FIGURE 5 Forest plot of the effect third-wave cognitive behavioural therapy interventions on diabetes-related distress using first time point data. This diagram is a graphical representation of the meta-analytic findings, showing the earliest time point effect sizes and errors of each included study. There was a non-significant effect of third-wave cognitive behavioural therapy interventions on diabetes distress, in favour of the intervention.

specific, it focused on the link between mental and physical well-being.[s56, s61, s63] Behavioural activation was utilised in eight CBT interventions.[46, 48, s53, s56, s61-s64] This involved pleasant activity scheduling to increase mood, self-efficacy and physical activity.

Subgroup analyses

Of the eight a priori defined potential moderators of CBT treatment effects on diabetes-related distress the following variables bolstered the effects of CBT: having a digital component (SMD = −0.30, $p = 0.05$) versus not having a digital component (SMD = -0.08, $p = 0.19$); delivered via a psychological practitioner (SMD = −0.26, $p \leq 0.001$) versus not delivered by a psychological practitioner (SMD = −0.06, $p = 0.54$); individual (SMD = −0.23, $p = 0.01$) versus group delivery formats (SMD = −0.15, $p = 0.60$); and including a behavioural activation component (SMD = −0.29, $p = <0.001$) versus interventions without behavioural activation (SMD = −0.02, $p = 0.76$) (for full analyses see Table 2).

4.2.11 | Objective 6: Content of third-wave CBT interventions

Interventions used approaches such as psychological flexibility which underpins ACT[s54] and mindfulness (Tables S5 and S6 within Appendix S2). The mindfulness-based interventions included mindful self-compassion (MSC),[s59] mindfulness-based cognitive therapy (MBCT)[s63, s65] and self-guided mindfulness practice.[s55] These interventions were all 8 weeks in length. Session frequency ranged from daily[s55] to weekly.[s54, s59, s63, s65] Psychological practitioners provided four of the interventions.[s54, s59, s63, s65] These were delivered face to face in a group format within the community. The remaining intervention was self-guided to be completed at home.[s55] None of the third-wave CBT interventions were diabetes specific. Techniques within the interventions were heterogeneous due to differing therapeutic approaches, however, some commonalities

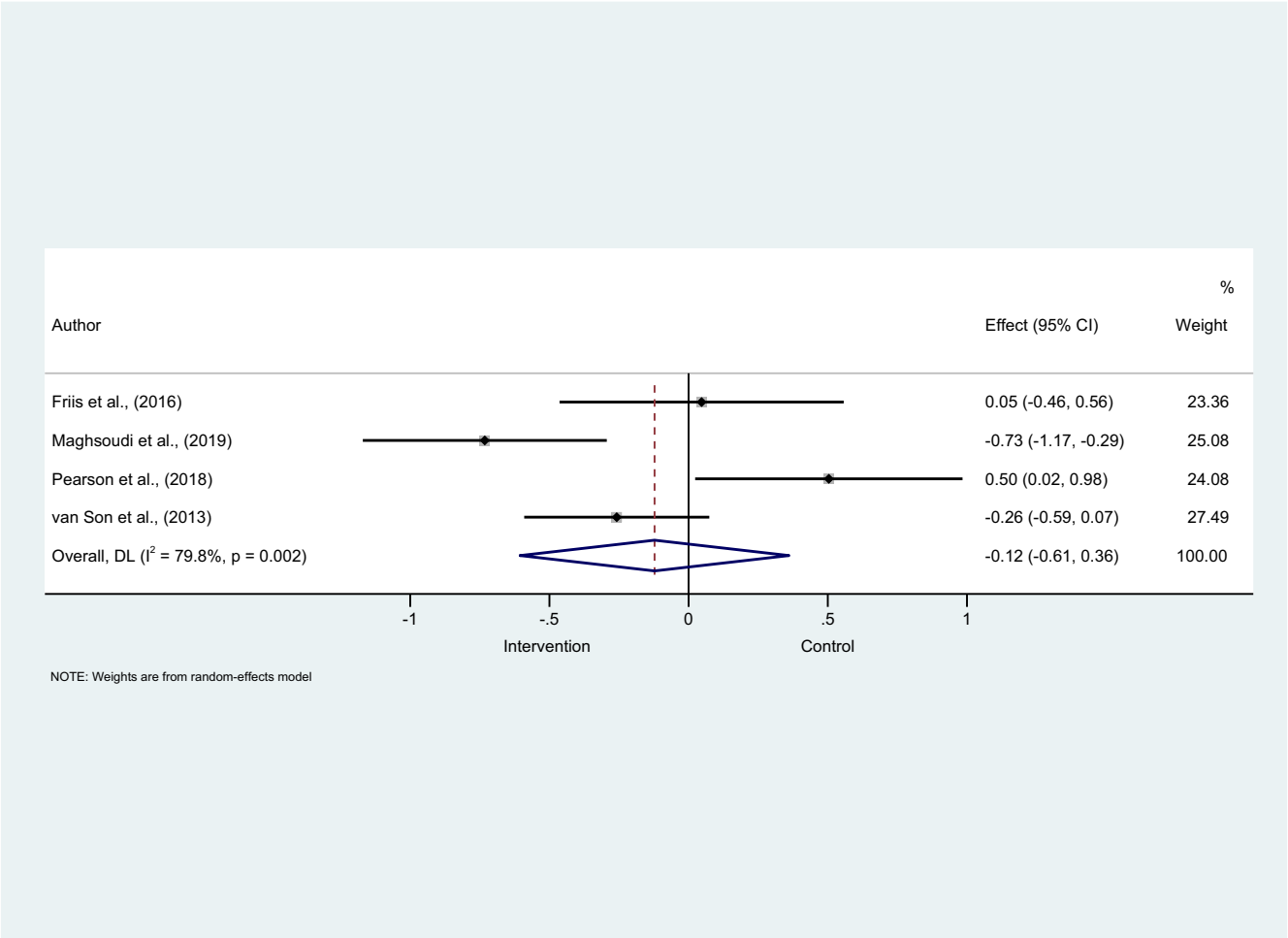


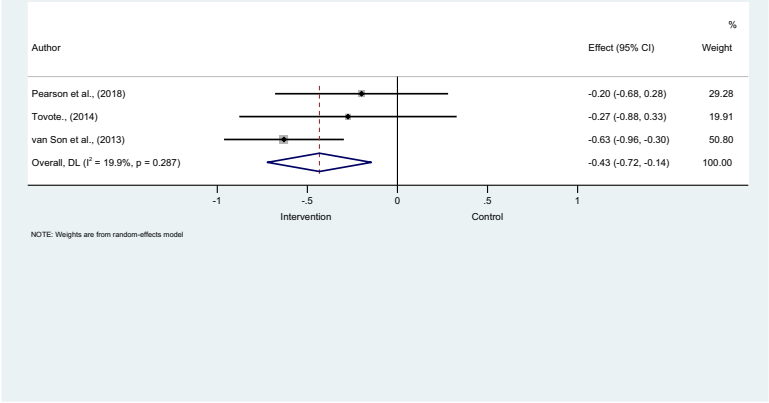
FIGURE 6 Forest plot of the effect of third-wave cognitive behavioural therapy interventions that aim to target diabetes-related distress primarily on diabetes-related distress using first time point data. This diagram is a graphical representation of the meta-analytic findings, showing the earliest time point effect sizes and errors of each included study. There was a non-significant effect of third-wave cognitive behavioural therapy interventions to treat diabetes-related distress on diabetes-related distress, in favour of the intervention. Forest plot of the effect third-wave cognitive behavioural therapy interventions on depression using first time point data. This diagram is a graphical representation of the meta-analytic findings, showing the earliest time point effect sizes and errors of each included study. There was a non-significant effect of third-wave cognitive behavioural therapy interventions on depression, in favour of the intervention.

existed. Over half of the interventions ($k = 3$; 60%) involved psychoeducation[s54, s59, s63] which focussed on providing an understanding around how the intervention may influence emotional well-being.

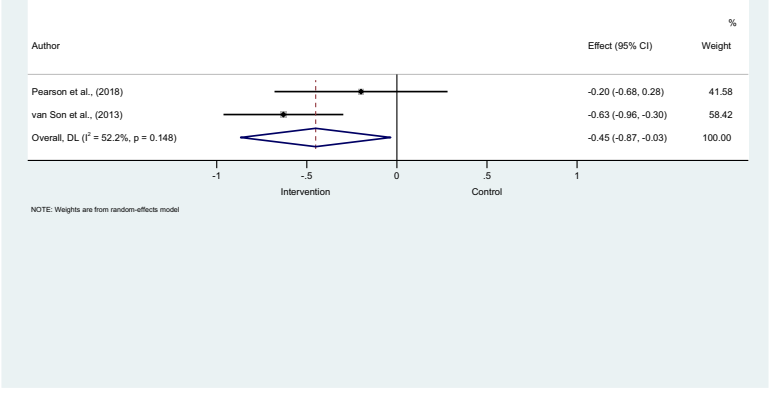
The mindfulness-based interventions encouraged the cultivation of mindfulness and encompassed guided meditation to increase present moment awareness. Some interventions ($k = 2$) included meditations focused

FIGURE 7 (a) Forest plot of the effect of third-wave cognitive behavioural therapy interventions that aim to target diabetes-related distress primarily on depression using first time point data. This diagram is a graphical representation of the meta-analytic findings, showing the earliest time point effect sizes and errors of each included study. There was a non-significant effect of third-wave cognitive behavioural therapy interventions for diabetes-related distress on depression, in favour of the intervention. (b) Forest plot of the effect of third-wave cognitive behavioural therapy interventions that aim to target diabetes-related distress primarily on anxiety using first time point data. This diagram is a graphical representation of the meta-analytic findings, showing the earliest time point effect sizes and errors of each included study. There was a significant effect of third-wave cognitive behavioural therapy interventions for diabetes-related distress on anxiety. (c) Forest plot of the effect of third-wave cognitive behavioural therapy interventions that aim to target diabetes-related distress primarily on HbA_{1c} using first time point data. This diagram is a graphical representation of the meta-analytic findings, showing the earliest time point effect sizes and errors of each included study. There was a non-significant effect of third-wave cognitive behavioural therapy interventions for diabetes-related distress on HbA_{1c}, in favour of the control condition.

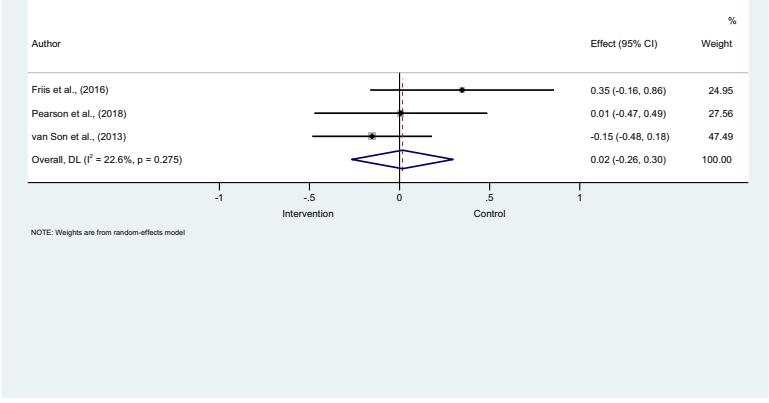
(a)


Author
Effect (95% CI)
%
Weight
Pearson et al., (2018)
-0.20 (-0.68, 0.28)
29.28
Tovote., (2014)
-0.27 (-0.88, 0.33)
19.91
van Son et al., (2013)
-0.63 (-0.96, -0.30)
50.80
Overall, DL (I² = 19.9%, p = 0.287)
-0.43 (-0.72, -0.14)
100.00
-1
-.5
0
.5
1
Intervention
Control
NOTE: Weights are from random-effects model

(b)


Author
Effect (95% CI)
%
Weight
Pearson et al., (2018)
-0.20 (-0.68, 0.28)
41.58
van Son et al., (2013)
-0.63 (-0.96, -0.30)
58.42
Overall, DL (I² = 52.2%, p = 0.148)
-0.45 (-0.87, -0.03)
100.00
-1
-.5
0
.5
1
Intervention
Control
NOTE: Weights are from random-effects model

(c)


Author
Effect (95% CI)
%
Weight
Friis et al., (2016)
0.35 (-0.16, 0.86)
24.95
Pearson et al., (2018)
0.01 (-0.47, 0.49)
27.56
van Son et al., (2013)
-0.15 (-0.48, 0.18)
47.49
Overall, DL (I² = 22.6%, p = 0.275)
0.02 (-0.26, 0.30)
100.00
-1
-.5
0
.5
1
Intervention
Control
NOTE: Weights are from random-effects model

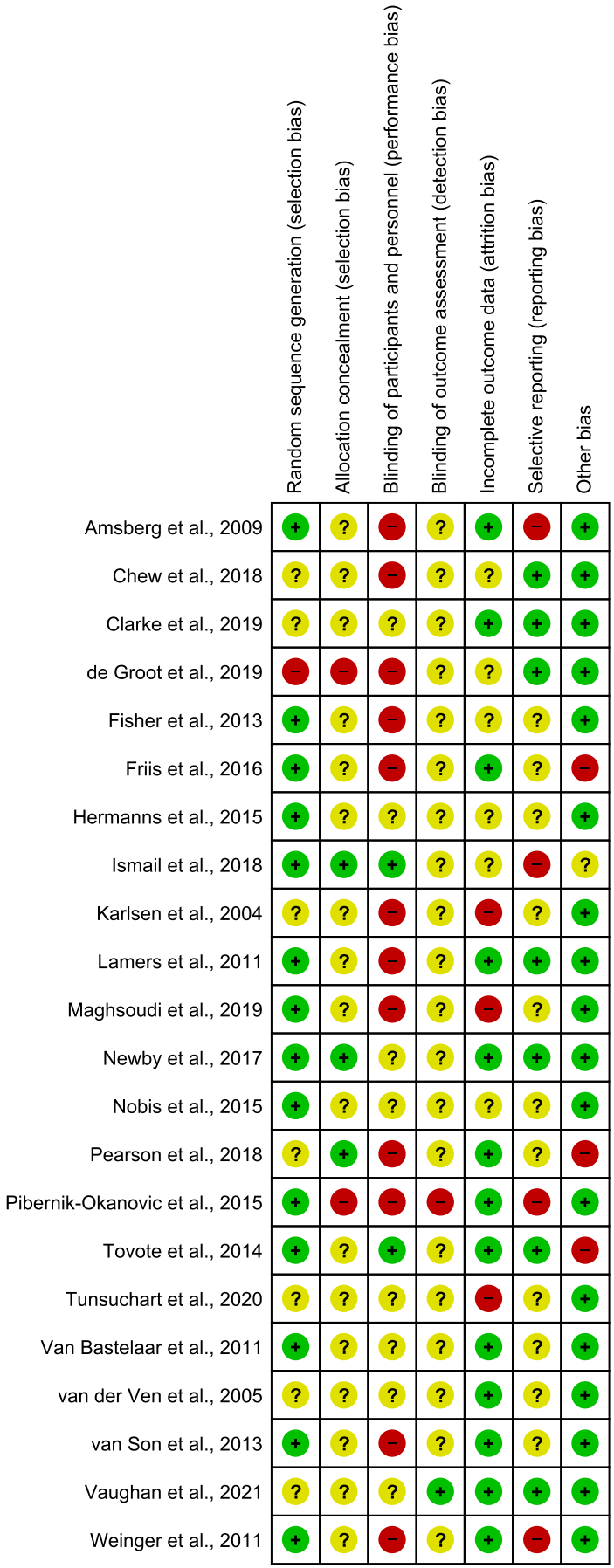


FIGURE 8 Risk of Bias summary: review authors' judgement about each risk of bias item for each included study.

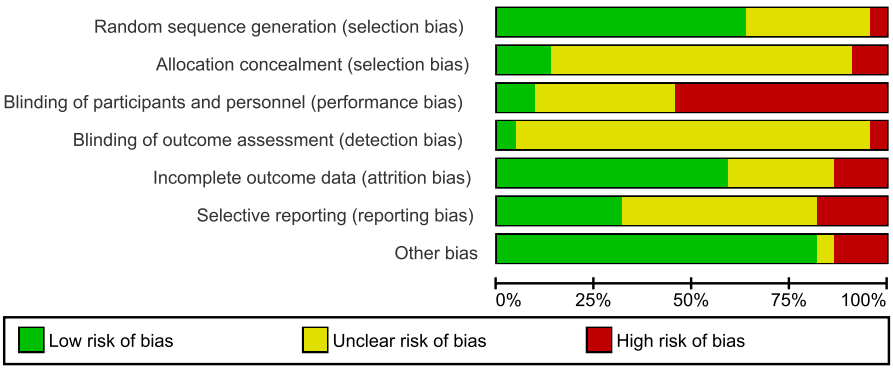


FIGURE 9 Risk of Bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

on enhancing self-compassion, with the aim of providing participants with tools to develop a compassionate inner voice.[s59, s65] Within the MBCT interventions[s63, s65] the management of distress centred around the identification of unhelpful cognitions and included behavioural activation. The ACT intervention[s54] involved techniques such as cognitive defusion in which individuals aim to step back from their distress to reduce its impact and influence. The identification of values and utilising committed action (taking actions to live in line with your values) were also techniques used to manage distress within this intervention.

A priori defined subgroup analyses

As only five third-wave CBT studies were identified these were not performed.

5 | DISCUSSION

This review of 22 RCT studies indicates that traditional CBT interventions successfully improve symptoms of diabetes-related distress. More specifically, where diabetes-related distress was the primary outcome of the CBT studies the overall effect on diabetes-related distress was significantly larger than when it was not. Findings were similar for third-wave CBT interventions, albeit non-significant. Furthermore, we found that CBT aiming to treat diabetes-related distress also significantly reduced depression. Moreover, third-wave CBT aimed at treating diabetes-related distress significantly reduced anxiety. Our narrative synthesis explored the effects of all CBT interventions and findings suggest that while CBT in diabetes is mainly delivered face to face, internet and telephone formats are also used. Furthermore, these CBT interventions tended to be tailored for diabetes. In contrast, all third-wave interventions were delivered face to face and were not adapted for diabetes. Based on data availability, we could only explore moderators of CBT treatment effects. Our results suggest that CBT interventions that are delivered one-to-one by a psychologically trained professional, include a digital delivery format, and a behavioural activation component are likely to improve the effectiveness of CBT on diabetes-related distress.

5.1 | Diabetes-related distress

This is the first review to meta-analyse diabetes-related distress outcomes for CBT interventions and show that CBT can improve it. This is in contrast with previous reviews that were unable to meta-analyse diabetes-related distress outcomes[29] or found no effect of CBT on diabetes-related distress based on two studies.[30] In these reviews, diabetes-related distress was not the primary outcome, and therefore they likely did not capture all relevant studies. This may account for the diverging findings.

In our review we conducted separate analyses for all studies including diabetes-related distress (as a primary or secondary outcome) and studies where diabetes-related distress was the primary outcome. We assume that where diabetes-related distress was the primary outcome, the intervention was aiming to target this specifically. We found that interventions targeting distress primarily were more effective. This has implications for treatment delivery and outcomes and enables a clearer understanding of the efficacy of targeted interventions. This also has implications for future study planning when selecting the primary endpoint and conducting power calculations.

Another novel aspect of this review is the identification of intervention components that are likely to enhance the effects of CBT interventions. We were unable to limit subgroup analyses to studies where diabetes-related distress was the primary outcome, due to the small number of studies where this was the case ($k = 8$). This increases uncertainty around how these components may bolster the effects on diabetes-related distress specifically. CBT including a digital component and delivered by a psychological practitioner produced a significantly larger effect on diabetes-related distress than interventions not including these components. Although, a previous review[s68]

TABLE 2 Results from subgroup analyses for cognitive behavioural therapy interventions.

Intervention type	Potential moderator	Subgroups	Number of studies	SMD	*p*-value	Lower 95% CI	Upper 95% CI	I[a]	*p*-value
CBT (total $n = 17$)									
	Diabetes-specific intervention	Yes	12[b]	−0.137	0.078	−0.290	0.015	53.4%	0.014
		No	6	−0.186	0.140	−0.434	0.061	60.4%	0.027
	Included a digital component	Yes	5	−0.299	0.047*	−0.594	−0.004	81.4%	<0.001
		No	13[b]	−0.080	0.185	−0.198	0.038	11.9%	0.325
	Delivered by a psychological practitioner	Yes	8	−0.262	≤0.001**	−0.409	−0.115	12.5%	0.333
		No	10[b]	−0.057	0.537	−0.236	0.123	64.4%	0.003
	Delivery format	Individual	9	−0.226	0.013*	−0.405	−0.047	65.2%	0.003
		Group	9[b]	−0.147	0.602	−0.274	−0.020	34.0%	0.146
	Between session homework	Yes	12[b]	−0.163	0.057	−0.330	0.005	64.3%	0.001
		No	1	−0.141	0.575	−0.635	0.352	NR	
		Not reported	5	−0.104	0.356	−0.326	0.117	43.5%	0.132
	Included: goal setting	Yes	13[b]	−0.145	0.065	−0.299	0.009	55.1%	0.008
		No	5	−0.162	0.201	−0.409	0.086	58.1	0.049
	Cognitive restructuring	Yes	11[b]	−0.124	0.103	−0.274	0.025	31.5%	0.147
		No	7	−0.176	0.126	−0.401	0.049	73.7%	0.001
	Behavioural activation	Yes	8	−0.294	<0.001**	−0.453	−0.136	37.1%	0.133
		No	10[b]	−0.022	0.758	−0.159	0.115	28.4%	0.183
	Psychoeducation	Yes	12[b]	−0.167	0.059	−0.340	0.006	60.2%	0.004
		No	6	−0.080	0.315	−0.235	0.076	23.5%	0.257

[a] 'Included a digital component' is defined as any study where the intervention that had a digital element/delivery format. This may have been in conjunction with face-to-face treatment or a standalone digital intervention (for more information on the intervention content of each study, see Tables S2 and S3).

[b] This estimate includes two data points from the same study with two separate control groups.

* Significant to 0.05.; ** Significant to 0.001.

found that interventions delivered by general clinicians reduced distress the most, this review was not specific to CBT interventions which may account for the contrasting findings. Our work suggests that CBT interventions in particular may be more beneficial when delivered by a trained psychological practitioner.[s69] Digital interventions provide advantages such as increased treatment accessibility, reduced costs and increased scalability when compared with traditional face-to-face delivery.[s70, s71] These are important factors to consider in diabetes, as the existing treatment burden can be high.[s72, s73]

Furthermore, CBT interventions that included behavioural activation (a technique in which people are encouraged to adopt experiences that they find rewarding) reduced distress at a significantly greater rate than interventions that did not. This finding is in keeping with earlier work linking this technique with reduced distress in cancer survivors.[s74] Living with diabetes is complex and can be challenging. Therefore, behavioural activation may enable individuals with diabetes to engage in things they enjoy thus reducing distress. For example, our narrative synthesis suggests this technique can increase self-efficacy and physical activity.[s62] As diabetes-related distress is associated with poor self-efficacy and poor self-management behaviour[9, s75] by targeting these factors using behavioural activation people with diabetes may feel an increased sense of mastery around diabetes management which may improve distress.

Studies that were tailored to diabetes appeared to hold promising treatment potential, although the effect estimate was non-significant. When comparing this to studies that were not tailored to diabetes the pooled effect size was smaller. One explanation for this may be that within the non-diabetes-specific subgroup, there were two large individual study estimates. These studies may have acted as outliers, skewing the overall magnitude of the findings. Caution is therefore, needed in interpreting this particular result. Taken as a whole, our findings offer the possibility that tailoring CBT interventions to diabetes may bolster the effects of CBT on reducing diabetes-related distress.

Third-wave CBT interventions produced a comparable (although non-significant) effect estimate to that of traditional CBT for diabetes-related distress. The results were also comparable in analyses where diabetes-related distress was the primary outcome. However, this result was also small and non-significant. Due to the low number of studies in the analyses ($k = 5$ and $k = 4$ respectively) we were likely underpowered to detect a significant effect.[s76] The small difference in these effect estimates may also be due to the small number of included studies. Therefore, more research is needed to understand the efficacy of third-wave interventions on diabetes-related distress.

Analyses exploring potential moderators of treatment effects were not possible for third-wave interventions due to the small number of studies available. However, our narrative synthesis suggests that mindfulness meditation, cognitive restructuring, behavioural activation, cultivation of acceptance, cognitive defusion and utilising committed action were key techniques utilised to try and reduce diabetes-related distress within these interventions.

5.2 | Secondary outcomes

CBT to treat diabetes-related distress was effective at significantly reducing depression. This is promising as it suggests that CBT to treat diabetes-related distress may have associative benefits for depression outcomes for people with diabetes. However, it is important to note that the pooled effect estimate was small, contrasting with the moderate[29,30] to large[31] effect estimates seen in previous reviews. In two of these previous reviews depression[30,31] was the primary outcome. Consistent with Medical Research Council guidance[s77] our analyses found that interventions targeting distress specifically, bolstered the effect of CBT on this outcome. This may also be the case for depression thus leading to larger effect estimates in previous reviews.

A pooled estimate investigating CBT to treat diabetes-related distress for anxiety could not be calculated as only one study included diabetes-related distress as the primary outcome and measured anxiety. This is surprising as one element of diabetes-related distress surrounds anxieties linked to the condition.[14] The one study[s61] in our review evidenced CBT for diabetes-related distress significantly reduced anxiety. Although, this conclusion cannot be generalised. In contrast with our review, previous reviews have included three[29,30] to eight[31] studies that measure anxiety. However, these studies did not consider diabetes-related distress primarily. These previous reviews considered anxiety alongside general depression as the primary outcome[30,31] which may account for these mixed findings. As highlighted above, it could be that where diabetes-related distress is the primary outcome (as measured by a diabetes-specific assessment tool) the target of these interventions may be focused on diabetes-specific anxieties (such as fear of hyper[78]/hypoglycaemia[79] and fear of future complications[s80, s81]) rather than general anxieties which appear conceptually different and may require different therapeutic techniques. Therefore, this may explain why many of our studies did not assess anxiety as an outcome. Hence, questions remain about the associative benefits of CBT for diabetes-related distress on anxiety. This suggests that more RCTs are needed to explore this.

CBT for diabetes-related distress was not associated with a significant reduction in HbA_{1c}. Our findings

diverge from evidence showing that CBT improves glycaemic control with moderate effect[31] and in the short and medium term.[29] Like depression, one explanation for this may be that HbA_{1c} was the primary outcome of interest in these two reviews not diabetes-related distress. A previous review[s82] of psychological interventions (not just CBT) found that HbA_{1c} was only significantly reduced in response to diabetes specific, not generic interventions. This is further supported elsewhere[s83] which suggests that diabetes-specific CBT interventions may hold potential to improve glycaemic control alongside diabetes-related distress.

There was a small non-significant reduction in depression following third-wave interventions that aimed to treat diabetes-related distress. However, only three studies assessed the effect of CBT for diabetes-related distress on depression, so we may have been underpowered to detect a statistically significant effect. However, our finding diverges from a recent review[35] which found mindfulness and acceptance-based interventions efficacious at significantly reducing depression with moderate effect in type 2 diabetes. The main outcome of interest within this review[35] was diabetes-related distress and glycaemic control. The inclusion criteria for this review were studies that included diabetes-related distress or glycaemic control as a study outcome. This is promising; however, it is unclear how many of the intervention studies had diabetes-related distress as the primary outcome. Therefore, this may account for the diverging findings.

We found third-wave CBT interventions significantly reduced anxiety, with a moderate effect. Our findings are in line with recent review evidence.[35] Although, it is important to consider that only two studies were included in the pooled estimate. Despite this, our findings suggest that third-wave CBT treatment aimed at reducing diabetes-related distress can also significantly reduce anxiety for individuals with diabetes. This is promising as it implies that third-wave interventions for diabetes-related distress can benefit anxiety in parallel. It is also needs to be considered that although the two studies had a diabetes-specific primary outcome, none of the third-wave interventions were tailored to the condition of diabetes. This poses the potential that unlike CBT interventions, third-wave CBT interventions may not need to include diabetes-specific content to improve anxiety outcomes. However, more work is needed to investigate this.

Our findings highlighted a small, non-significant effect of third-wave CBT for diabetes-related distress on HbA_{1c} favouring the control rather than the intervention condition. Similar to depression, this diverges from earlier review evidence.[35] However, only three of the included third-wave CBT interventions measured HbA_{1c}. This is surprising as glycaemic control is an integral part of diabetes management. Therefore, more RCT's examining third-wave CBT interventions that consider emotional, and physical health outcomes are needed. Moreover, as highlighted above none of the third-wave interventions in our review were diabetes-specific. Previous trial evidence[s84] found that a diabetes-specific ACT intervention significantly improved HbA_{1c} compared to diabetes education alone. Therefore, tailoring third-wave interventions to include diabetes-specific components may result in parallel improvements in emotional and physical outcomes in diabetes. It is also important to note that assessing improvement in glycaemic control is not unidirectional. Unlike emotional health outcomes, some individuals may benefit from a lowering HbA_{1c}, whereas others may benefit from increasing HbA_{1c}, depending on specific self-management behaviours, physical health status and the underpinnings of their diabetes-related distress. Therefore, caution should be taken when interpreting our mixed results for glycaemic control.

Our review provides a novel contribution to the literature as it enables the comparison between CBT and third-wave CBT interventions on diabetes-related distress. Moreover, the review enables a greater understanding of the associative benefits of CBT and third-wave CBT for diabetes-related distress on other emotional and physical health outcomes. Furthermore, the narrative synthesis and exploratory subgroup analyses highlights intervention techniques that may have the greatest influence when treating distress. However, this review is not without limitations. Despite the focus of the review being on the benefit of interventions to treat diabetes-related distress specifically, our subgroup analyses did not reflect this. We included studies where diabetes-related distress was the primary and secondary outcome measure to increase statistical power and to keep in line with recommendations.[43] We only included studies published in English which may have influenced the generalisability of our findings. There was moderate statistical heterogeneity present within the analyses. There was also evidence of high or unclear RoB on numerous domains. Furthermore, due to the small number of included studies, particularly for the third-wave intervention type, we may have been underpowered to detect a statistically significant effect for some outcomes. Therefore, our meta-analytic findings should be interpreted with caution.

6 | CONCLUSIONS

This review suggests CBT is effective at reducing diabetes-related distress overall and this effect is increased when diabetes-related distress is the primary outcome. CBT targeted to treat diabetes-related distress also significantly

reduced depression but not anxiety and HbA_{1c}. Third-wave CBT interventions for diabetes-related distress were effective at reducing anxiety. Given methodological limitations, our findings should be interpreted with caution. Moving forward, more robust interventional studies aimed at treating diabetes-related distress primarily, are required. There is also a need to consider both mental and physical health outcomes in future CBT and third-wave CBT interventions in diabetes, as evidence in this area is currently lacking.

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CONFLICT OF INTEREST

None to declare.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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