Effectiveness of cognitive behavioural therapy on glycaemic control and psychological outcomes in adults with diabetes mellitus: a systematic review and meta-analysis of randomised controlled trials.

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ABSTRACT

Background: Diabetes is a chronic progressive condition presenting physical, social and psychological challenges that increase risk of co-morbid mental health problems. Cognitive behavioural therapy (CBT) has been effective in treating a variety of psychological disorders; and as such may have benefits for CBT in diabetes may potentially improve glycaemic control and psychological outcomes in diabetes.

Aim: This systematic review and meta-analysis aims to establish the effectiveness of CBT on glycaemic control and co-morbid diabetes-related distress, depression, anxiety and quality of life in the short, medium and longer-term among adults with diabetes.

Method: Electronic search was conducted in PubMed, Embase, MEDLINE, PsycINFO, CINAHL, Web of Knowledge, Cochrane Central Register of Controlled Trials and references in reviews. 12 randomised controlled trials (RCTs) were identified which evaluated the effectiveness of CBT on at least one of: glycaemic control, diabetes-related distress, anxiety, depression or quality of life in adults with Type 1 or Type 2 diabetes. Cochrane risk of bias tool and review manager version 5.3 were used for risk of bias assessment and meta-analysis respectively.

Results: CBT is effective in reducing short-term and medium-term glycaemic control although no significant effect was found for long-term glycaemic control. CBT improved short and medium-term anxiety and depression, and long-term depression. Mixed results were found for diabetes-related distress and quality of life.

Conclusion: CBT is beneficial for adults with diabetes in improving depression. It may have benefits for improving glycaemic control and other aspects of psychological health although findings are inconclusive.

Introduction

Diabetes is a chronic medical condition that requires people with diabetes to engage in a lifelong therapeutic self-management regimen in order to maintain glycaemic control(1, 2). The diagnosis of diabetes and efforts towards self-management especially lifestyle modification, demands of daily treatment regimen and thoughts about risk of developing diabetes complications are behaviourally and psychologically challenging (3). It is estimated that 50% of patients demonstrated decreased psychological states at the time of diabetes diagnosis (4). Therefore, among people with diabetes commonly observed co-morbid mental health conditions include diabetes-related distress, anxiety and depression resulting in poor glycaemic control and reduced quality of life (5-7). Diabetes-related distress affected 13.8%-44.6% of people with diabetes (8). Diabetes doubles the odds of co-morbid depression and 12-27% of people with diabetes experience depression at a rate two to three times that of the general population (9-11). Anxiety also occurs in about 14% of people with diabetes while 40% elevated levels of subsyndromal anxiety (12).The relationship between diabetes and co-occurring psychiatric disorders are complex and bidirectional because they both influence each other and are affected by biological pathways, social and psychological factors (13). This review addresses psychological disorders whose pathogenesis results as a complication of living with diabetes. Given that the barriers to coping with diabetes management are mostly cognitive and behavioural, rather than related to insufficient knowledge or skill, an intervention comprising of cognitive and behavioural components may result in improvement. Therefore this review focuses on cognitive behavioural therapy (CBT) as it is recommended as the primary psychological therapy for effectively challenging dysfunctional thoughts, beliefs and negative behaviours in people with long term conditions and replacing these with cognitions that are more self-helping and realistic (14-16). This reduces the feeling of being overwhelmed and aids effective coping with the demands imposed on them by daily stressors and the treatment regimen.

Although CBT has proved to be effective in managing psychiatric co-morbidities in a wide range of somatic illnesses (17-20), research on the use of CBT in diabetes is limited. The use of CBT for the management of glycaemic control and co-morbid psychological disorders and symptoms in adults with diabetes are documented (21-32) with varying results.

Given the mixed results on the effect of CBT on adults with diabetes, this review seeks to determine its pooled effectiveness among people with diabetes in the short, medium and longer term.

Previous systematic reviews have examined various psychological interventions in same review and found that CBT did not improve glycaemic control in adults (5, 33-35) and have not considered the duration of effects of CBT (36). Nevertheless, these studies found that CBT improved depression and other psychological outcomes. It is noteworthy that the combination of various psychological interventions in one review could mask the overall effectiveness of each single included intervention. Therefore this review focuses specifically on studies that performed CBT on adults with type 1 diabetes, type 2 diabetes or combination of both types. The justification for this choice is that although they may be physiologically different, the psychological challenges they face are similar especially as insulin is increasingly being used in the treatment of type 2 diabetes nowadays. They are all predisposed to diabetes-related distress, anxiety, depression, sub-optimal glycaemic control and reduced quality of life. The duration of effectiveness of CBT is warranted because it will aid in planning for psychological care in diabetes management. This is the first systematic review and meta-analysis of RCTs which examines the effectiveness of CBT on glycaemic control and co-morbid psychological outcomes in the short, medium and longer-term in adults with diabetes.

Aim of the review

To critically appraise, synthesise and systematically review the available published evidence on the effectiveness of CBT on glycaemic control and co-morbid diabetes-related distress, depression, anxiety and quality of life in the short, medium and longer-term among adults with diabetes.

Research question

In adults with diabetes, what is the effectiveness of CBT on glycaemic control and co-morbid diabetes-related distress, depression, anxiety and quality of life in the short, medium and longer-term?

Methods

Study eligibility

Studies eligible for inclusion in the present review included only those with study populations of adults ≥18 years clinically diagnosed with either type 1 or type 2 diabetes of ≥6months duration. Participants had at least one of: glycated haemoglobin (HbA1c), diabetes-related distress, anxiety, depression, or quality of life score above normal limit for the standardised scale used.

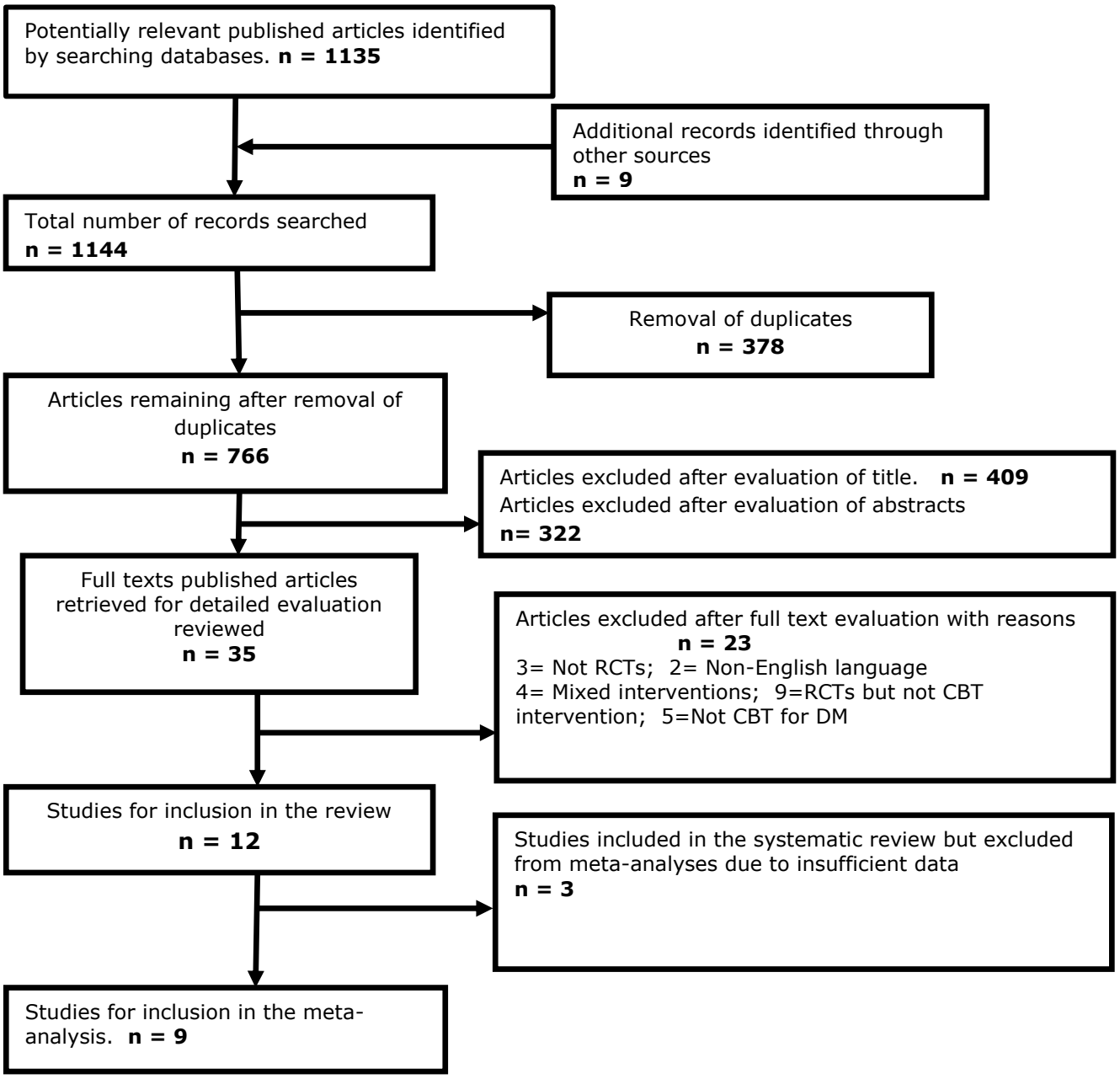
The study intervention was psychotherapy involving the combination of cognitive and behavioural strategies (CBT) which had to be more than a one-off session. This includes CBT delivered face to face, via the telephone or the internet, to individuals or groups and by psychologists or trained therapists. Comparison included those who received non-CBT interventions, usual care or waiting list control groups. The primary outcome of interest was glycaemic control. Secondary outcomes were diabetes-related distress, anxiety, depression and quality of life. Study designs were only randomised controlled trials. All outcomes were measured with validated scales.

Search methods

The search strategy was aimed at locating published and unpublished studies. There was no limitation on geographical area, language or year of publication. Comprehensive search filters were developed for database search using the identified keywords and index terms across all included databases. Included databases were MEDLINE (1946-2014), CINAHL, Web of Knowledge, PsycINFO (1806 - 2014), EMBASE (1974 – 2014), Cochrane Central Register of Controlled Trials and PubMed. Websites such as www.controlled-trials.com, www.clinicaltrials.gov and www.who.int/trialsearch were also searched for on-going trials. The reference lists of all review articles were searched extensively by hand for additional studies. Two reviewers (CU and HB) independently assessed the abstracts of relevant articles identified from the search. Studies whose abstract did not conform to the inclusion criteria were excluded. Full articles of abstracts that suggested potential eligibility were retrieved. Consensus was reached through discussion. Studies were included based on agreement by the authors and reasons for exclusion were recorded. Disagreements were presented to a third reviewer for final decision on inclusion or exclusion of the article.

Total of 1144 studies were identified from the search. 35 full text articles were evaluated against the inclusion criteria. 12 RCTs met the inclusion criteria for the review (fig. 1). However, only nine studies were included in the meta-analysis because two studies had insufficient data for inclusion in the meta-analysis (28, 29) and one was a three-arm trial (32) therefore their results were reported narratively.

Figure 1: Flow chart for the identification of included studies.



Data extraction and study quality

CU and HB independently extracted data for the study using the Cochrane collaboration data collection form for randomised controlled trials and variations in the data extracted were resolved through discussion. Data extracted included general study information and demographic data as well as characteristics of participants, interventions and outcomes. Missing data were obtained from trial authors where possible.

The methodological quality of articles was assessed independently by the reviewers, based on the quality criteria specified by the Cochrane collaboration risk of bias tool (37). Where consensus could not be reached, a third reviewer was consulted to make the final decision. For the purpose of this review, alterations were made to the tool

such that blinding of participants and personnel and incomplete outcome data were separated and two more parameters (similarity of baseline characteristics between groups and timing of outcome measurement) were added.

Included studies consisted of both methodologically sound and less methodologically sound studies. Methodologically sound studies were categorised as studies with seven or more positives on the risk of bias summary (22-25, 32). Given the small number of studies found, no study was excluded on the basis of methodological quality.

Randomisation of participants was performed in nine studies (21-28, 32). Davazdahemamy et al., (29) and Amsberg et al., (30) used the word "randomly allocated" but the randomisation process was unclear because there was insufficient information to aid judgement. Henry et al. (31) had high risk of bias because they generated allocation based on judgement of the primary care physician. Allocation concealment prior to assignment of study participants to either intervention or control groups was performed in six trials (23-27, 32). Three trials had insufficient information to aid judgement on this criterion (22, 29, 30). Three other trials (21, 28, 31) were judged high risk for selection bias because allocation concealment was not ensured. Safren et al., (24) blinded both participants and personnel whilst four studies (22, 28, 30, 32) blinded study personnel but were either unclear or high risk regarding participant blinding. Three studies blinded outcome assessors (22, 24, 32) whist others were unclear regarding this criterion. All studies except Davazdahemamy et al.,(29) reported on loss to follow up with reasons for drop-out. Intention-to-treat (ITT) analysis was conducted in seven of the studies indicating low risk of attrition bias (21-25, 28, 30). van Bastelaar et al.,(28) reported high dropout rate especially in the CBT group. Three studies (26, 27, 32) had high risk for attrition bias because they did not perform ITT analysis so measures were reported for completers only. Two of the studies were unclear about this criterion (29, 31). In eight studies, outcomes were measured in both completers and non-completers (21, 22, 24-28, 30). All included studies had intervention and control groups with similar demographic factors, diabetes related psychological symptoms and baseline scores for study outcomes. They also reported outcome measures periodically. Wherever other biases could not be ascertained, there was limited information to aid judgement.

Measures of treatment effect

In this review, control group was defined as participants with either type 1 diabetes or type 2 diabetes who did not participate in the intervention and against which comparison with the intervention group will be made. RCT referred to studies which include both intervention and control groups with diabetes, whose participants were randomized to either group at the beginning of the study. Calculation of effect size was based on the difference in change of a measurement before and after the intervention between the CBT groups and control (non-CBT) groups. Effect sizes were expressed as relative risk for dichotomous data and standardised mean difference for continuous data. Effect sizes were categorised along a continuum of small (ES<0.20), moderate (0.33≤ES<0.55) and large (ES>0.56)(38). Standardised mean difference was also used as a summary estimate for the overall effect size with 95% confidence interval.

Data synthesis

Data from included RCTs were pooled in statistical meta-analysis and synthesised using the review manager software (RevMan version 5.3 Cochrane Collaboration, Oxford, UK). All data were subject to double entry to minimise error. The fixed effects analysis was performed when heterogeneity was below 50% while the random effect analysis was done when heterogeneity was between 50% - 85% (39). Where statistical pooling was not possible due insufficient data, the findings were synthesised narratively. Heterogeneity between studies was assessed using chi-square test and Higgin's I^2 test.

Characteristics of included studies

Sample sizes ranged from 19 to 339 participants with a median of 124 participants. All studies were published between 1997 and 2014, of which five were carried out in U.S.A (21-24, 32), four in Netherlands (25-28), one in Australia(31), one in Sweden(30) and one in Iran (29). Three trials were conducted with participants who had type 1 diabetes only (26, 27, 30), seven trials focused on participants with type 2 diabetes (21-25, 29, 31) and two RCTs included participants with both types 1 and 2 diabetes (28, 32). In terms of outcomes, eleven studies examined glycaemic control (21-24, 26-32), five studies (26-28, 30, 32) examined diabetes-related distress, eleven studies (21-31) examined depression, four studies (21, 29-31) examined anxiety, and five studies (21, 23, 25, 29, 32) examined quality of life.

Characteristics of interventions

Although all included studies conducted CBT for intervention groups, they varied in terms of format, duration, total number of sessions and professional background of therapists. CBT was conducted on a weekly basis by psychologists, nurses and/or dieticians who were pre-trained in performing CBT. The nurses worked with psychologists in three studies (26, 27, 30). Interventions for CBT groups consisted of cognitive and behavioural components whereas interventions for the control groups differed slightly across the studies but was most commonly usual care. Total number of CBT sessions ranged between six to 21 sessions while duration of sessions ranged between 30 minutes per session to two hours per session spanning over a period of six weeks to four months. Three studies (21, 23, 24) administered booster CBT sessions to participants in the intervention groups. Booster sessions refer to sessions that were aimed at reinforcing lessons learnt from previous CBT sessions. With the exception of van Bastelaar et al., (28) which performed web-based CBT, all studies were carried out in health care settings. The format of CBT across studies included face to face individual sessions (24, 25), face to face group sessions (21, 22, 26, 27, 30-32), individual telephone sessions (23), web-based sessions (28) and one study did not specify the format used (29).

Characteristics of participants

The total number of participants in the included studies was 1445 and a total of 354 participants dropped out of the studies. Highest dropout were recorded in van Bastelaar et al.,(28) and lowest dropout in Henry et al.,(31). The mean age of participants was between 37.4±11.1 years to 61±10.8 years. The mean duration of diabetes was between 6.4±8.7 years to 21.6±10.8 years. Two trials did not provide data on participant's mean duration of diabetes though participants ought to have had diabetes for ≥6months to be eligible for recruitment into the study (23, 29).

Inclusion criteria were similar across all studies: age ≥18 years; ability to read and write; diabetes duration of ≥ 6 months; HbA1c levels, diabetes-related distress, anxiety, depression or quality of life score above specified cut-off points for validated scales used. The most commonly cited exclusion criteria reported in included studies were pregnancy, severe medical comorbidity, and presence of current alcohol/substance abuse disorder, bipolar depression or any other psychotic disorder. All study outcomes were measured with validated scales. Diabetes-related distress was commonly measured with the Problem Areas in Diabetes (PAID) scale. Depression was measured using different tools, including the Beck Depression Inventory (≥14), the Centre for Epidemiological Studies Depression Scale (CES-D(≥16)) and the Hospital Anxiety and Depression Scale (HADS (1-7)). Anxiety was commonly measured using the State Trait Anxiety Scale (≥35), although the Hospital Anxiety and Depression Scale (HADS (1-7)) and Depression Anxiety Stress Scale (DASS-42) were also used in other studies.

Characteristics of study outcomes

All studies measured outcomes at baseline and follow up periods with some trials providing follow-up data at specific intervals up to 12 months post-intervention.

Results

Glycated haemoglobin

Glycated haemoglobin was measured in 11 out of 12 included RCTs (21-24, 26-32). Eight of these studies provided sufficient data for meta-analysis and provided results for outcome measures at specific durations of follow up. These time points will be synthesised in the meta-analysis as short term (up to four months), medium term (up to eight months) and long term (up to 12 months).

Short term effects of CBT on HbA1c.

Eight trials measured short term HbA1c (21, 22, 24, 26, 28, 29, 31, 32), five of which were appropriate for meta-analysis. A fixed effect model meta-analysis (5 studies, 272 participants) produced a standardised mean difference of -26mmol/mol (95% CI -29 to -24) [-0.2% (95% CI -0.5 to 0.02%)] that was significantly different from 0 (Z=1.78; P= 0.07). Effect sizes in four of the five studies were <0 with no significant heterogeneity between studies (chi^2 =2.23; P=0.69; I^2=0%) (fig. 2). Sensitivity analysis excluding the study rated as having high risk of bias (31) produced no difference in the overall effect.

Of the studies that could not be pooled in the meta-analysis, one trial reported that CBT had significant effect in decreasing HbA1c score (P=0.005) (29). Conversely, another found no significant short term treatment effect of CBT (P>0.05) on HbA1c even when only participant with elevated baseline A1C levels were examined (28). One study performed three arm trial of CBT, attention control and individual control groups but found that although all three groups showed improved HbA1c levels after three months, the CBT groups showed more improvement than other control groups (mean HbA1c change at three months: CBT group -32mmol/mol (−0.8%) vs -28mmol/mol (−0.4%) for attention group controls and -28mmol/mol (−0.4%) for individual controls) (32).

Medium term effect of CBT on HbA1c.

Seven trials measured medium term HbA1c (21, 22, 24, 25, 27, 30, 32). A fixed effect model meta-analysis (six studies, 459 participants) produced a standardised mean difference of -28mmol/mol (95% CI -30 to -26) [-0.4% (95% CI -0.6 to -0.2)] that was significantly different from 0 (Z=3.81; P=0.0001). Effect sizes in five of the six studies included in the meta-analysis were <0. There was no significant heterogeneity between studies (chi^2= 8.93, P=0.11, I^2=44%) (fig. 2). Result from the three arm study that could not be pooled in the meta-analysis reported that glycated haemoglobin slightly deteriorated (P=0.45) at six months across all three groups (32).

Long term effect of CBT on HbA1c

Long term effect of CBT on HbA1c was measured in six trials (23-25, 27, 30, 32). A fixed effect model meta-analysis (five studies, 644 participants) was used to synthesise the findings (fig. 2). The meta-analysis found a non-significant effect of CBT on HbA1c in the long term with a standardised mean difference of -25mmol/mol (-27 to –22; P=0.18) [-0.1% (95% CI -0.3 to 0.1)]. On exclusion of studies that did not offer booster sessions (25, 27, 30), a non-significant effect was also found (-25 mmol/mol; 95%CI -27 to -21) [-0.1%, (95% CI -0.3 to 0.2, P=0.56). The

three-arm trial by Weinger et al., (32) reported that HbA1c was maintained at 12 months for the CBT and attention control groups but not in the individual control group.

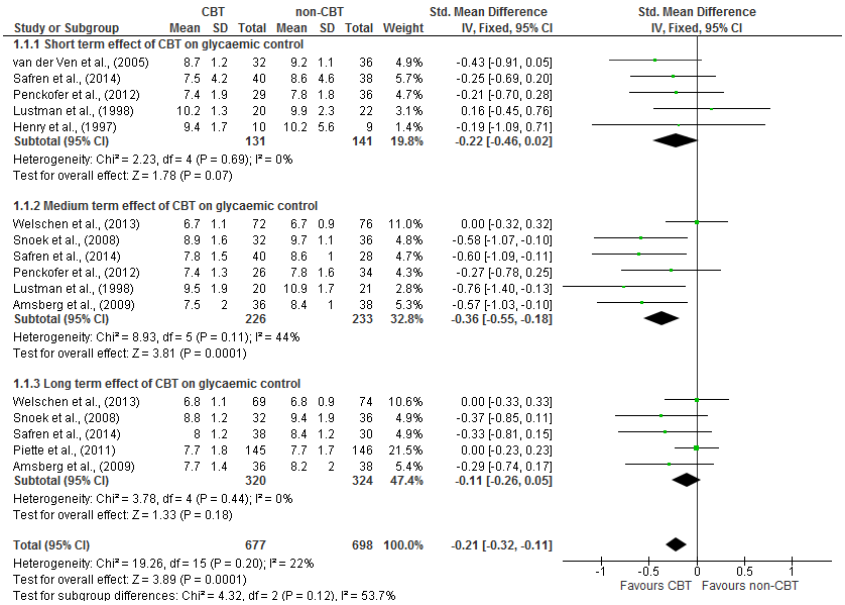


FIGURE 2: Forest plot for short-, medium- and long-term effects of CBT on HbA1c.

Diabetes-related distress

Five studies examined diabetes-related distress (26-28, 30, 32). Due to varying effect measures reported across these studies, their results were not pooled in a meta-analysis. van der Ven et al.,(26) and Van Bastelaar et al., (28) reported a short term decrease in diabetes-related distress (one month; P=0.01 and three months; P<0.001 respectively) while in Weinger et al., (32), CBT did not improve diabetes-related distress at short, medium and long term measurements. In Amsberg et al.,(30), significant effect was observed between CBT and control groups regarding diabetes-related distress in medium term (-6.88 (95% CI (-11.50 to -2.25); P = 0.019), which improved at 48 week follow up period (P = 0.004). In Snoek et al., (27), there was no significant difference in diabetes-related distress score between CBT group and control group. Even at six months and one year follow up, participants still reported high levels of diabetes-related distress (p=0.99 and p=0.68 respectively).

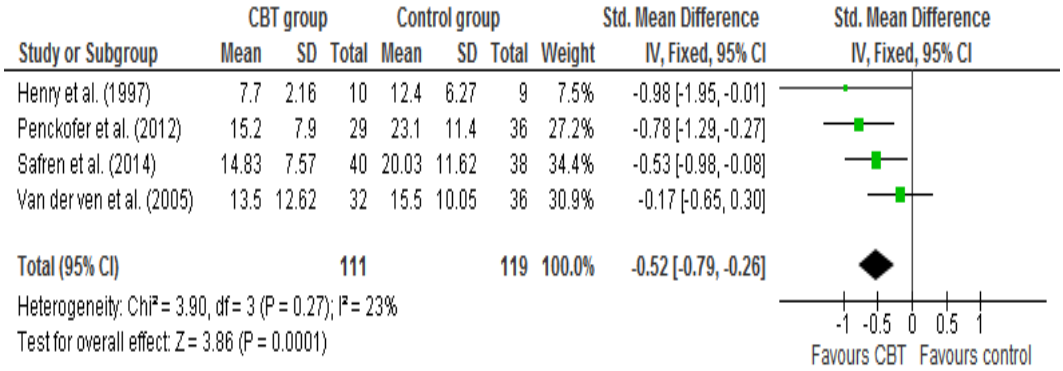
Depression

Eleven out of 12 included RCTs measured depression at baseline (21-31), eight of which had sufficient data to be included in the meta-analysis. The forest plots present short term (up to four months), medium term (up to eight months) and long term (up to 12 months) results for depression. Given that different psychometric scales were also used for assessing depression, the standardised mean difference (SMD) was used as a summary statistic in order to standardise the results of the studies to a uniform scale.

Four studies were analysed for short term effect of CBT on depression (21, 24, 26, 31). With a heterogeneity level of 23%, the fixed effect method analysis found a large effect size and a significant difference in depression scores in favour of CBT (-0.52, 95% CI -0.79 to -0.26, P=0.0001). This indicates a significant short term improvement in

depression in favour of CBT (fig. 3a). The findings from trials by Davazdahemamy et al., (29) that were not included in the meta-analysis also revealed that CBT had positive short term effect on depression with P-values of P=0.012 and P <0.001 respectively. Five studies (21, 24, 25, 27, 30) provided information for medium term effect of CBT on depression. With a substantial heterogeneity level of 73%, the random effect method was used for data synthesis. The resulting finding was a moderate effect size (-0.43, 95% CI -0.79 to -0.06, P=0.02). This result indicates that CBT had a significant medium term effect on depression (fig. 3b). Interestingly, on exclusion of the studies that did not provide booster sessions, a non-significant result was found with a large overall effect estimate of -0.54 (95% CI –1.28 to 0.21, P=0.16). The five trials (23-25, 27, 30) that measured long term effect of CBT on depression were included in a meta-analysis (fig. 3c). Due to a moderate heterogeneity level of 44%, the fixed effect method was used to synthesise the data. The result of the analysis demonstrates a significant difference in depression scores with a further reduced and fairly small effect size at 12 months follow up in favour of CBT (-0.26, 95% CI -0.41 to -0.10, P=0.001). On exclusion of studies that did not offer booster sessions to participants, I^2 decreased to 0% hence the fixed effect model analysis found a significant effect (P=0.003). Also, an increased but moderate effect size was found for long term effect of CBT on depression (-0.38, 95% CI -0.59 to -0.17) from studies that offered booster sessions. In Davazdahemamy et al.,(29), there was significant decrease in depression (P<0.001) whilst in van Bastelaar et al., (28), CBT yielded significant effect on depressive symptoms (P<0.001) even at follow up (d=0.29 [95%CI 0.17-0.40])

The study by Lustman et al.,(22) provided dichotomous data on depression outcome with regards to remission of depression and clinically significant improvement in depressive symptoms. For each result, data was provided at three months (post intervention) and six month follow-up respectively and produced a trend towards significance, as CBT participants were 2.31 times more likely to achieve remission of depression than controls (RR 2.31,95% CI 1.45 to 3.67, P=0.0004). From the results, it is also evident that CBT participants were 1.88 times more likely to achieve clinically significant improvement in depressive symptoms compared to controls (RR 1.88, 95% CI 1.25 to 2.84, P=0.003). The test for overall effect also suggested a significance difference (P<0.00001) between CBT participants and controls. However, these findings are the result of a single RCT and should therefore be interpreted with caution.



3a. Short term effect of CBT on depression in adults with diabetes

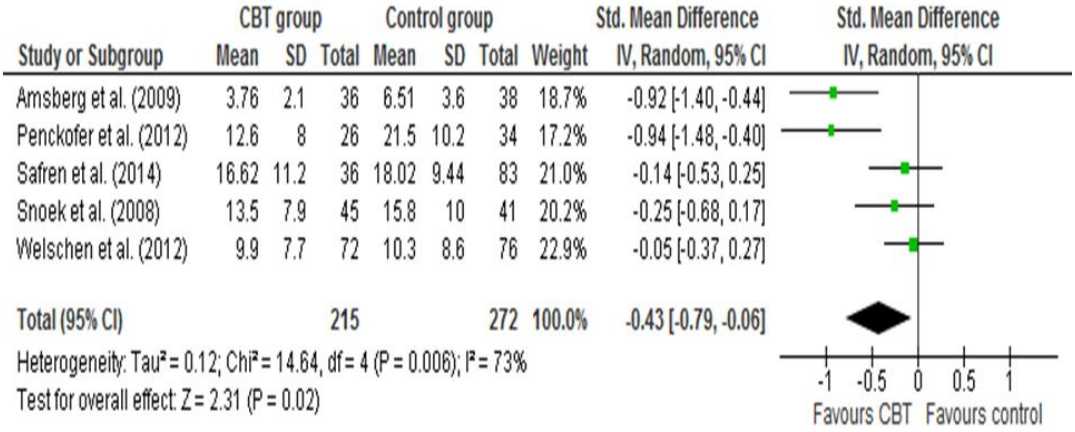


Figure 3b: Medium term effect of CBT on depression

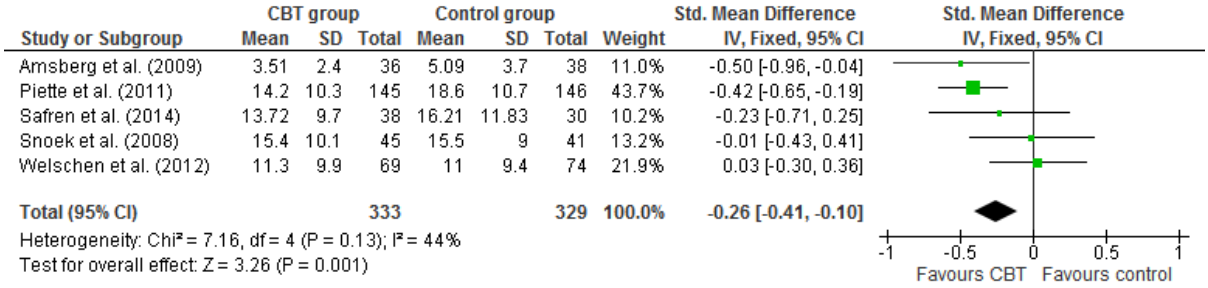


Figure 3c: Long-term effect of CBT on depression in adults with diabetes

Anxiety

Four trials (21, 29-31) examined of the effect of CBT on anxiety, of which three were included in the meta-analysis due to lack of sufficient data in one of the trials (29). This analysis was completed according to periods of anxiety outcome measurement (three months, six months and 12 months). Penckofer et al., (21) reported both state anxiety and trait anxiety and these were included in the meta-analysis as two separate anxiety results. The fixed effect method was used in pooling the data since the level of heterogeneity was 32% (fig. 4). The results yielded a large effect size and indicated that there was a significant reduction in mean anxiety between groups in favour of CBT compared to the control groups at three months (-0.55, 95% CI -0.88 to -0.21, P=0.001). However, one of these trials (31) produced a greater reduction in anxiety than observed in the other studies but this may be related to the smaller sample size (n=19). Nevertheless, on exclusion of this study, there remained a significant improvement in anxiety with a moderate effect size (-0.41, 95% CI -0.76 to -0.06, P=0.02) in the CBT groups compared to the control groups and heterogeneity reduced to 0%. At six months, although the overall effect estimate did not

significantly increase there was still a significant difference in anxiety scores in favour of the CBT groups (-0.56, 95% CI -0.85 to -0.27, P=0.0002). At 12 months, only one trial (30) measured anxiety and found no significant difference in anxiety level between CBT and control groups (-0.33, 95% CI -0.79 to 0.13, P=0.16). However, the test for overall effect yielded a large effect size and a significant improvement in anxiety levels (-0.51, 95% CI -0.71 to -0.31, P<0.00001). This finding from just one study should be interpreted with caution.

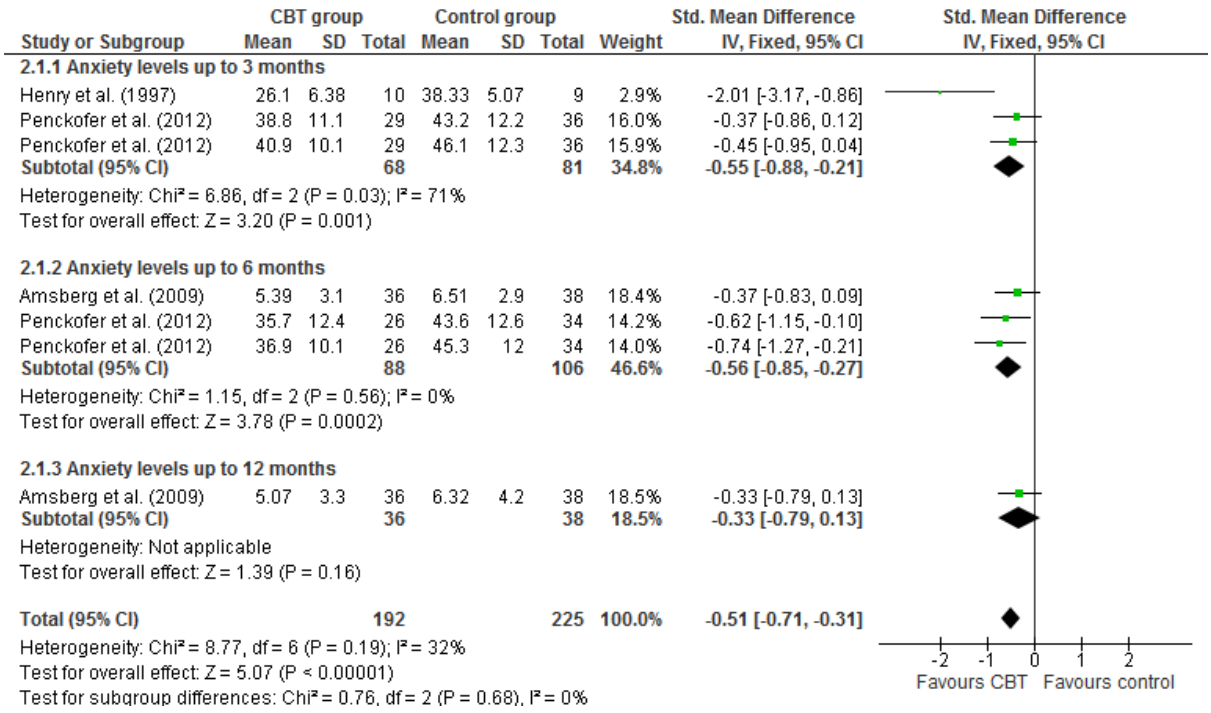


Figure 4: Forest plot for short, medium and long term effects of CBT on anxiety.

Quality of Life

Four trials examined the effect of CBT on Quality of Life (21, 25, 32, 40). Given the varying scales used, their results were presented in dissimilar patterns and unsuitable for synthesis in a meta-analysis. Penckofer et al.,(21) reported improvement quality of life (P<0.001) especially on the mental and psychological components compared to the control group in the short and medium term. In Davazdahemamy et al., (29), CBT also effectively improved short term quality of life (P=0.011). However, little improvement was seen in Welschen et al., (25) between CBT and control group. The CBT group showed statistically significant improvement in quality of life between baseline and six months whereas participants in the control group showed deterioration in their quality of life. Also, Weinger et al., (32) found significant improvement in quality of life for short term follow up though this was not sustained in the medium and long terms respectively as no significant improvement was observed at six and 12 months follow up.

DISCUSSION

Glycaemic control

Concerning meta-analysis of studies that measured short term and medium term glycaemic control, there was a significant short term reduction in mean HbA1c in favour of CBT when compared to control groups and a

significantly greater reduction was evident in the medium term. This indicates that CBT interventions may hold possible benefits for these time points. The findings support the view of Turner et al., (41) that CBT holds potential clinically relevant benefits for people with sub-optimal pre-treatment levels of HbA1c. The improvement in glycaemic control could be attributed to the effect of CBT in changing negative thoughts, attitudes and beliefs regarding diabetes, which is likely to lead to a change in diabetes self-care behaviours and subsequent glycaemic control (42). However, the effect of CBT on glycaemic control was not maintained on the longer-term, even when booster CBT sessions were provided which have been shown previously to sustain CBT outcomes (24, 43). This might be due to the generally acknowledged difficulty in achieving behaviour change thus people have the tendency to return to their usual habits due to an inablility to incoporate new bahaviours into their daily lives (25). It is possible that the CBT interventions were too short to generate lasting effects, or were not tailored to the specific needs of the people with diabetes. However, there was insufficient evidence to draw conclusions about long term effects due to the small number of studies that included long term outcomes of CBT. Diabetes is a lifelong condition requiring continuous psychological assessment and management in order to stabilise peoples' behaviours, which in turn translates into significant improvement in glycaemic control. Further well-designed RCTs are required to demonstrate whether CBT (with or without booster sessions) can sustain glycaemic control in the long term. These findings are important because they represent the overall treatment effect from studies recruiting people with sub-optimal HbA1c.

Effect of CBT on psychological outcomes

CBT significantly improved depression in adults with diabetes in the short, medium and long term although the effect sizes reduced over time. The positive effect of CBT on depression in this review is congruent with results reported for the effectiveness of CBT in treating depression in those with conditions such as chronic pain, stroke, social phobia, post-traumatic stress disorder and HIV/AIDS; it has even been reported to be somewhat superior and more tolerated in comparison to antidepressants in treating adult depression (44, 45). Since depression is characterised by repetitive and uncontrolled negative thoughts which generate feelings such as guilt, low mood and low self-esteem (46), these positive effects could be attributed to the influence of CBT in challenging and replacing dysfunctional thoughts with positive and life-enhancing thoughts. The high drop-out rate in some studies that measured depressive symptoms might be due low self-esteem, lack of motivation and pessimism (47). This review did not compare between trials with depressed and non-depressed people with diabetes therefore results reflect that of people with diabetes and co-morbid depression.

Although CBT seemed to be effective in the short term management of diabetes-related distress, results at medium and long term periods were mixed. It should be noted that the included studies measuring diabetes-related distress also measured depression. Where depression improved and improvements in depression (although reducing in magnitude) were sustained over time, there was non-improvement in diabetes-related distress over time. This may potentially be due to a lack of tailoring of the CBT interventions to the problem areas specific to diabetes self-care. Recent research emphasises the importance of distinguishing between diabetes-related distress and depression. Fisher et al., (48) suggests that among people with diabetes, depression and diabetes-related distress may present with similar symptoms but are not necessarily the same. The latter develops from living with diabetes therefore interventions need to be tailored to the specific needs of the different groups The mixed findings for diabetes-related distress warrant further research with specifically designed CBT interventions to highlight distinguishing factors for diabetes participants.

Overall, CBT significantly reduced anxiety levels in the short and medium term, and potentially in the longer term. This suggests that CBT may be an effective treatment for anxiety amongst adults with diabetes. Due to the limited number of studies examining anxiety levels as an outcome, the findings should be interpreted with caution.

Notwithstanding, this finding is not surprising as CBT has been noted to be effective in the short, medium and longer term anxiety management as well as superior to pharmacotherapy for anxiety disorders (45). The finding of this review is congruent with previous reviews demonstrating the effectiveness of CBT on anxiety in adults within the general population (49, 50). The significant reduction in anxiety levels of participants could be attributed to the acquisition of problem solving skills which enabled participants to modify negative thoughts and engage in behaviours and/or activities necessary to cope adequately with diabetes. Also, participants in these studies were provided with information about diabetes as part of the CBT intervention, which may have further helped to allay condition-related anxieties and aid coping.

Poor diabetes management and psychological health negatively impacts quality of life. Although there is growing interest in both quality of life outcomes and features in the therapeutic goals of diabetes care, they are rarely the focus of most interventions. This perhaps explains the paucity of studies measuring the effect of CBT on quality of life. Based on limited evidence, this review showed mixed results for quality of life of people with diabetes with CBT improving quality of life in some studies whilst having non-significant effect in others especially in the medium and long term periods. Nevertheless, the positive findings concurs with those of Welschen, et al. (51) who reported that in diabetes, the relationship between CBT and quality of life is indirect such that improvements in psychological status and glycaemic control can result in concomitant improvements in quality of life.

Strengths and limitations of the review

This study included only RCTs which are the gold standard of research on effectiveness of interventions and which yields the highest quality of evidence (52). Bias was minimised by the use of Cochrane risk of bias tool, and critical appraisal of potentially eligible studies by at least two reviewers. Meta-analysis was used for generating the most findings of the review. With regards risk of publication bias across included studies, Duval's trim and fill method which aims both to identify and correct for funnel plot asymmetry arising from publication bias (53) showed negligible effect size shifts with included imputed studies. Furthermore, using the Begg's funnel plot, no difference between observed and imputed studies was shown. This indicated that there is little evidence of publication bias and that the reported effect is valid.

It should be noted that this review was not a-priori registered and did not have a-priori review protocol. Although the review methodology was rigorous, there is a possibility that we failed to include some published or unpublished studies. Due to limited resources, studies published in foreign languages could not be translated or included. The overall quality of the included RCTs was not optimal and none were conducted in the United Kingdom (UK), Africa or Asia. Most studies neither provided follow-up data nor performed ITT analysis despite high attrition rates. Furthermore, this review does not provide information on cost-effectiveness, gender-specific effects and the length of CBT sessions or format that is most beneficial and preferred by people or whether people differing in type of diabetes may benefit more or less from CBT interventions due to of the lack of relevant trials. Sub-group analysis between type 1 diabetes and type 2 diabetes was not undertaken as this was beyond the scope of this review. Nevertheless, statistically significant improvements of the magnitude reported in this review demonstrate the potential positive effects of CBT on glycaemic control and psychological outcomes. However, regarding generalisability of our findings, some caution is required as we were unable draw a robust conclusion due to the small number of trials that met the inclusion criteria of which the majority had small sample sizes. There is a need for further research that examines whether the positive effects of CBT are sustained over several years, to confirm the clinical importance of this intervention in the management of diabetes as a life-long condition.

Agreement and disagreement with previous reviews

As previously reported, few reviews have examined the effects of non-pharmacological psychological interventions on glycaemic control. However, only one review specifically examined CBT for glycaemic control in diabetes (36) but found no overall statistically significant impact from meta-analysis of CBT on glycaemic control. Nevertheless, only four trials were included in the meta-analysis and durations of the expected effectiveness of CBT were not highlighted. In recognition of limited human and financial resources to health services in various countries, it is necessary to ascertain the supposed duration of effectiveness of any intervention for planning purposes.

Recommendations for further research

Well-designed RCTs are required with larger sample sizes, to assess the effectiveness of CBT in improving glycaemic control over the longer term. More studies are needed that assess the impact of CBT over time on condition-specific psychological outcomes, such as diabetes-related distress. There is scope to increase knowledge about the best mechanisms for delivery of CBT in this group. Whilst group CBT format has clear advantages in terms of efficiency for delivery, it is not yet clear which format of CBT (group, individual, face to face, web-based) is preferred by people with diabetes, and we need to better understand the stage of diabetes in which delivery of CBT is most effective. Future research might examine potential gender-specific effects of CBT intervention, the effectiveness of CBT in preventing poor glycaemic control amongst people with normal glycaemic control, and the barriers to long term effectiveness of CBT in those who do not improve. Qualitative research should be undertaken on participant's experiences and satisfaction with CBT intervention. With advances in information technology and the rapid increase in web-based interventions for self-management of chronic illness, trials of web-based CBT treatments in other conditions have reported patient outcomes that are comparable to those found with face-to-face interventions (54-56). There is certainly scope to further investigate the impact of web-based CBT intervention specifically for adults with diabetes. In the included studies, the trained personnel delivering the CBT were most commonly diabetes nurses and this may have been due to the cost implications of CBT delivered by psychologists or trained health professionals from services outside of the clinical team. However, the included studies did not provide sufficient information to examine the cost implications of delivering CBT to people with diabetes, which needs to be assessed. Finally, this review revealed a lack of research evidence on CBT and diabetes conducted in the UK, Africa and Asia. There is a need for well-designed RCTs in these settings to enhance the generalisability of findings.

Conclusions and Implications for practice

In people with type 1 and type 2 diabetes, CBT is effective in improving short and medium term glycaemic control. No significant effect was found for long term glycaemic control, although there are limited studies measuring longer term clinical outcomes. CBT improves depression in people with diabetes in the short, medium and longer term. It improves anxiety in the short and medium term, and has potential for longer term benefits although there are too few studies assessing long term outcomes to draw firm conclusions. The evidence for the effects of CBT on diabetes-related distress and quality of life is mixed, and based on a small number of studies with heterogeneity in interventions and reporting of outcomes.

We conclude that CBT based approaches may be beneficial in diabetes care, although it is recommended that programs to ensure maintenance and sustainability of its positive effects are incorporated into diabetes management. Psychologists should work together with diabetes care teams to promote psychological care for

people with diabetes, and there is a need for diabetes care teams to be specially trained in current approaches for CBT to enhance its utilisation as part of clinical practice. This review recommends the provision of CBT for adults with diabetes to improve psychological health and instil coping strategies for better self-management, which will invariably enhance clinical outcomes for diabetes management and impact on quality of life.

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