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Outcomes of Mindfulness-based Stress Reduction and Mindfulness-based Cognitive Therapy in Adults with diabetes: A Systematic Review

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Abstract

Objectives: Diabetes Mellitus (DM) is a global and progressive chronic medical condition with increasing prevalence and associated costs throughout the world. Psychological problems are common in people with DM and when they co-occur are associated with negative patient and societal outcomes. Mindfulness-Based Stress Reduction (MBSR) and Mindfulness-Based Cognitive Therapy (MBCT) were to be effective in treating a variety of psychological problems in various health conditions. Thus, using MBSR and MBCT in DM patients may help alleviate psychological problems of anxiety and depression and improve glycaemic control as a result. In this systematic review, we investigated the effectiveness of MBSR and MBCT in improving glycaemic control, anxiety and depression in adults with DM.

Interventions: Randomised-Controlled Trials (RCTs) and Pilot Studies (RCPS) evaluated the effectiveness of MBSR or MBCT. Electronic searches were carried out of the following databases CINAHL, CENTRAL, EMBASE, MEDLINE, PsycINFO, PubMed, and ongoing clinical trials websites.

Main outcomes: This research examined the effectiveness of MBSR and MBCT on depression, anxiety and glycaemic control in adults with T1DM or T2DM.

Results: Research evidence has shown that patients with mental illnesses such as schizophrenia and anxiety disorders have a higher risk of developing DM than the general population. Explicitly, evidence indicates that the prevalence of psychological problems is much higher than in the general population and globally, with a two-fold increase in the prevalence of depression and anxiety in DM patients. 3 RCTs and 1 RCPS found a total of 365 participants. Narrative and data synthesis indicated significant reduction in levels of anxiety and depression at short-term and long-term time points. However, no significant effect on glycaemic control was established. MBSR and MBCT are feasible and efficacious methods for depression and anxiety treatment in adults with T1DM or T2DM.

Introduction

Psychological disorders found in diabetes vary from disease-specific concerns to eating and anxiety disorders [1]. The presence of these co-morbidities impairs quality of life, cost of care, treatment adherence, glycaemic control and self-management [2]. Evidence indicates patients with these co-morbidities have increased disease burden, work disability, medical device(s) dependence and symptom severity compared to patients with only diabetes [3-5].

Historically, non-pharmacological interventions for the treatment of diabetes have tended to focus on lifestyle advice and patient education [6,7]. Over the last decade, there has been an adoption of holistic care models with emphasis on psychological care for DM patients [8]. Research has shown psychotherapeutic interventions have the ability to improve glycaemic control, reduce emotional distress and improve levels of anxiety and depression in DM patients [9].

Mindfulness-Based Stress-Reduction (MBSR) and Mindfulness-Based Cognitive Therapy (MBCT) are two emerging therapies that could benefit DM patients. MBSR and MBCT are structured group programmes that use mindfulness meditative techniques drawn from Buddhist practices and attempt to cultivate mindfulness skills and attitudes in order to alleviate suffering [10]. Participants were asked to use a non-judgemental, committed and accepting attitude in order to develop skills and attitudes of focusing, sustaining and switching attention, and accepting their present moment experience [11].

This research systematically examines the effectiveness of MBSR and MBCT on depression, anxiety and glycaemic control outcomes in adults with T1DM or T2DM.

Methods

Search Strategy

The search strategy involved examination of the databases MEDLINE (1946-2017), CINAHL, Web of Science, PsycINFO (1806-2017), EMBASE (1974-2017), CENTRAL and PubMed using keywords such as, "Mindfulness", "Meditation", "Diabetes", "Mindfulness-based Stress-reduction", "Mindfulness-based Cognitive Therapy", "Glycaemic control", depression" and "Anxiety". The title, index terms, abstract and keywords found in the results of this preliminary search were analysed. Differences in the use of terminologies and regional variations in spelling (British and American) as well as common abbreviations such as "MBSR", "MBCT", "DM", "T1DM" and "T2DM" were accounted for. Truncations, wildcards, proximity terms, Boolean phrases and MeSH terms were used as appropriate. Comprehensive search filters were developed for each database including researched search strategies for finding RCTs and RCPS on the searched databases.

Selection of Studies

This review considered only RCTs and RCPS. Both male and female participants; Aged 18 - 80 years; Diabetes (type 1 or type 2); Elevated levels of depressive symptoms and/or diabetes-related distress; Low levels of emotional well-being. Studies on participants with acute psychosis or intention to commit suicide were excluded; severe physical co-morbidity (i.e., severe forms of cancer or heart failure); patients not experiencing psychological symptoms; unstable treatment with an antidepressant. The assessment of glycosylated haemoglobin (HbA1c) was carried out in all studies.

Methodological Quality

The Cochrane Collaboration's tool for assessing risk of bias was used to assess the methodological quality of included studies. To reduce the risk of bias a minimum of two independent reviewers (JM/GGA) were used to perform selection of studies, data extraction and methodological assessment.

Data Extraction

Data extraction was performed by reviewers (JM/GA) using the 'Cochrane collaboration data collection form for intervention reviews: RCTs only'. The data extracted in this form was categorised into methods, participants, intervention groups, outcomes, data and analysis, and other information.

Excluded Studies

23 studies were excluded after detailed evaluation of the full text. The reasons for exclusion were: Non-RCT or RCPS (n=4), Non-MBSR or MBCT intervention (n=14), Non-MBSR or MBCT for DM (n=1), On-going trials (n=2), study did not include any relevant outcomes (n=1) and study written in non-English language and unable to translate (n=1).

Results

Risk of Bias in Included Studies

Methodologically sound studies were categorised as those with ≥ 5 low risk scores on the risk of bias summary, achieved by the Tovote and DIAMIND studies.

Allocation concealment was considered low risk in only the Tovote study, which used measures to conceal allocation to both participants and investigators. The HEIDIS and DIAMIND studies did not give sufficient information on how allocation took place to make a judgement. The Schroevers study was deemed to be high risk as allocation concealment was not ensured.

Only Tovote's study ensured blinding of participants but was unclear if there was any blinding of personnel. The other three studies were carried out as open-label trials.

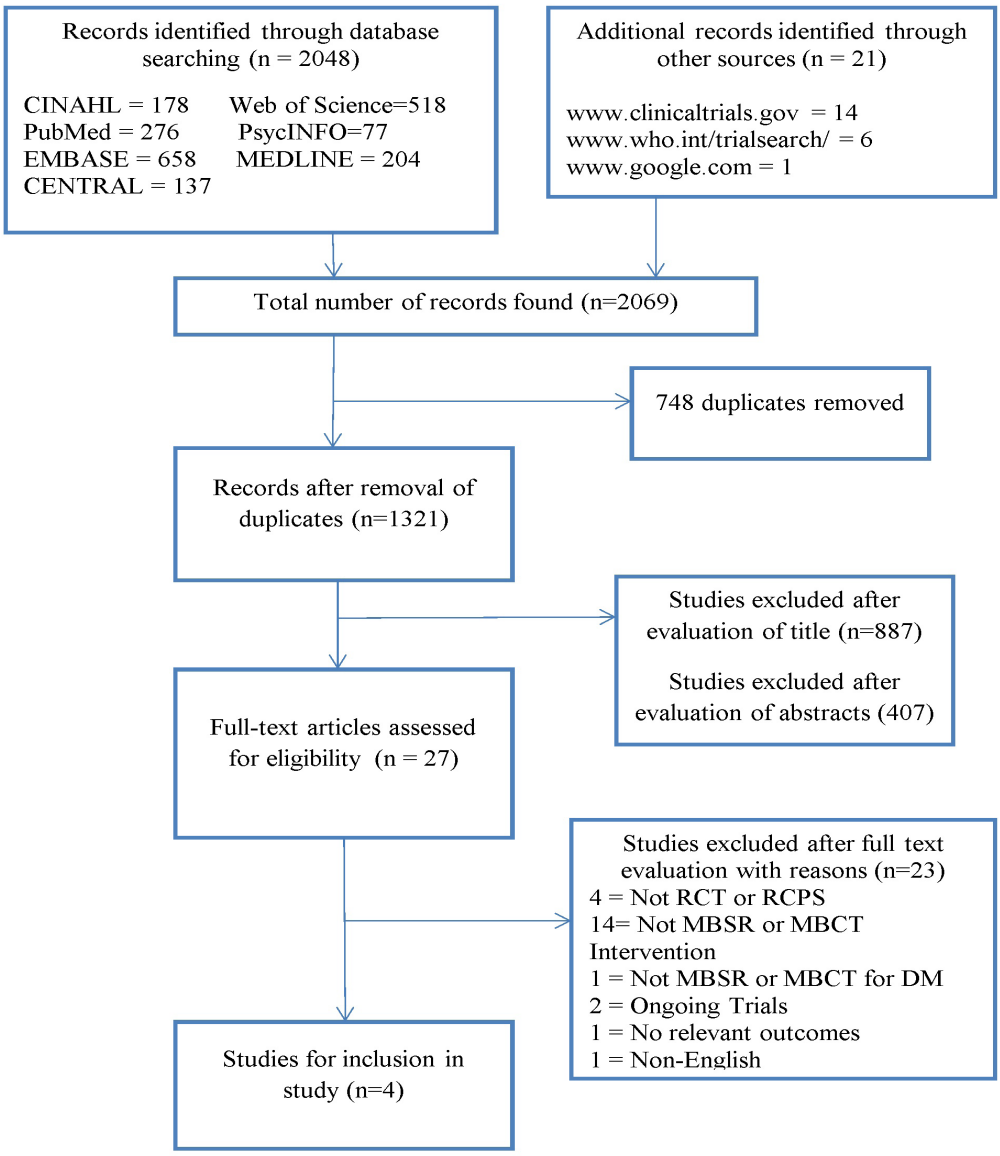

Figure 1: Flow diagram representing studies for inclusion.

The three studies that used glycaemic control as an outcome were judged to be at low risk of bias as all used HbA1c as an objective measure. The outcomes that measured depression and anxiety using self-reporting mechanisms were judged at low risk only in Tovote's study as this was the only study that blinded participants, the outcome assessors. In the three other studies, participants were not blinded and thus risk of bias was high. Only Tovote's study used a non-self-reported depression and anxiety outcome, rated as high risk of bias as there was no blinding at of the assessor at post-intervention assessment.

Intention-to-treat analysis was conducted in all four studies with missing values estimated by means of multiple imputations using the linear regression method in three studies and Schroevers study using the last-observed response carried forward method for imputation of the missing values. Risk of bias for incomplete outcome data was judged to be low risk for all four studies as these were considered appropriate methods for imputing missing data and reasons for attrition were documented in all studies.

Selective outcome reporting is a legitimate concern with RCTs, with a particular concern that non-significant results be withheld from publication (Hutton and Williamson, 2000). The DIAMIND and Tovote studies were classified as low risk of bias for outcome reporting as both have protocols available and reported all the pre-specified outcomes as detailed in their protocols. Both the HEIDIS and Schroevers studies do not have a protocol available and were, therefore, judged to have a high risk of bias.

A total of 2048 studies were identified from the database search and 21 studies were identified from additional sources such as trial registry websites, references of relevant articles and searches of generic internet search engines. All studies were imported into EndNote X7, after which 748 duplicates were removed. After examining the titles and abstract, a further 1321 studies were excluded, because the subject matter was not relevant to the review. The remaining 27 studies were then retrieved and full text evaluation against the inclusion and exclusion criteria took place, leading to the exclusion of 23 studies. Three RCTs and 1 RCPS met the inclusion criteria and were included in the data synthesis. Figure 1 illustrates the study identification process.

Characteristics of Included Studies

Characteristics of included studies and participants have been summarised in Tables 1a, b, c. The RCPS (Schroever's) was a pilot for the Tovote study, which is also included. This decision was made to include both separately as the RCPS met all the inclusion criteria and was sufficiently different from the Tovote study to merit inclusion. There was no risk of cross-contamination in participants, as the exclusion criteria for Tovote's study would rule out all participants of Schroever's study. Waiting-list control groups were used for comparison in three studies, of which the Tovote study also compared with a CBT group. The HEIDIS study used a treatment-as-usual control group for comparison. The waiting-list control group is a common feature of trials on psychotherapeutic interventions due to being more ethically sound as it allows for the provision of care, although delayed, to all participants needing help whilst still permitting a non-intervention evaluation.

Sample sizes ranged from 24 to 139 with a median of 92 participants. All studies used a face-to-face format for the interventions. Three studies used an adapted form of MBCT. Two of these were in groups while the Tovote study used an individual format. The HEIDIS study used an adapted form of MBSR in a group format.

All four studies examined depression as an outcome while three examined glycaemic control and two examined anxiety. The HEIDIS and Schroevers studies both used specified individual healthcare settings whereas the DIAMIND and Tovote studies both used multi-centre approaches in unspecified healthcare settings across the Netherlands.

No.	Study	Design	Types of Comparison	Country	Intervention	Format of Intervention	Sample Size (Total no. randomized)	Outcomes of interest	Setting	Duration (Start of Intervention to last follow-up)
1	DIAMIND (van Son, et al., 2011/2013/2014)	RCT	waiting-list control group	Netherlands	MBCT (Adapted)	Face-to-face Group	139	Glycaemic Control, Anxiety Depression	Diabetes Outpatient Clinics across the Netherlands (not specified)	8 months

2	HEIDIS (Hartmann et al., 2012; Kopf, et al., 2014)	RCT	treatment-as-usual control group	Germany	MBSR (Adapted)	Face-to-face Group	110	Depression, Glycaemic Control	Diabetes Outpatient Clinic at the University of Heidelberg	3 years
3	Schroevers, et al. (2013)	RCPS	waiting-list control group	Netherlands	MBCT (Adapted)	Face-to-face Individual	24	Depression	University of Groningen Medical Center	3 months
4	Tovote et al., (2013/2014/2015)	RCT	CBT and waiting-list control group	Netherlands	MBCT (Adapted)	Face-to-face Individual	94	Depression, Anxiety, Glycaemic Control	Various hospitals across the Netherlands (not specified)	11 months

Table 1a: Characteristics of Included Studies.

Characteristics of Participants

The total number of participants in the four included studies was 367. The respective dropout rates of each study were: 33 of 139 or 23.7% (DIAMIND), 21 of 110 or 19.1% (HEIDIS), 2 of 23 or 8.3%) (Schroevers) and 24 of 94 or 25.5% (Tovote).

The mean age of participants ranged from 49.8±13.3 years and 59.3±7.8 years. All studies included both genders with the range of male participants varying from 47% to 80.7%. The mean duration of DM was 11.0±7.5 years to 20.5±13.7; the DIAMIND study did not report this data (Table 1b).

The Percentage of T2DM participants varied from 42% to 74% in the three studies that included both T1DM and T2DM participants. The criteria that featured in all four studies, were the inclusion criteria of adults aged between 30 and 70 with T2DM and the exclusion criteria of serious psychopathology.

The Schroevers and Tovote studies used a depression score above a specified cut-off point for validated scales as an inclusion criterion. Otherwise no cut-off was specified for a depression score and no studies featured cut-off scores for anxiety or HbA1c (Table 1c).

#	Study	Sample Size					Mean Age (years)			Gender (male, n, %)			Type 2 diabetess (n, %)			Mean Duration of diabetes (years)		
		# Randomised	IG	CG	Dropout/Excluded	Completers	IG	CG	Overall	IG	CG	Overall	IG	CG	Overall	IG	CG	Overall
1	**DIAMIND** (van Son, et al., 2011/2013/ 2014)	139	70	69	33/0	106	56± 13	57±13	56.49 ±13	33 (47)	37 (54)	70 (50.3)	52 (74)	45 (65)	97 (69.8)	Not Stated		
2	**HEIDIS** (Hartmann et al., 2012; Kopf, et al., 2014)	110	53	57	21/0	89	58.7± 7.4	59.3± 7.8	59.01 ± 7.62	40 (70.2)	46 (80.7)	86(-78.1)	53(100)	57(100)	110(100)	11.0± 7.5	12.2± 7.6	11.62 ± 7.56
	1 year Follow-up		52	51														
	3 year Follow-up		47	42														
3	**Schroevers**, et al. (2013)	24	12	12	2/0	22	54.9± 10.3	55.9± 8.2	55.4± 9.30	7(58)	7(58)	14(58.3)	8(67)	5(42)	13(54.1)	16.6± 14.4	20.5± 13.7	18.55 ± 14.05
4	**Tovote** et al., (2013/2014 /2015)	94	MBCT: 31 CBT: 32	31	24/0	70	MBCT: 49.8± 13.3 CBT: 54.6± 11.3	54.7± 10.5	53.1± 11.8	MBCT: 17 (55)	15 (48)	48 (51)	MBCT:16 (52) CBT: 21 (66)	20 (65)	57 (61)	MBCT: 17.8 (13.0) CBT: 15.0 (11.4)	17.0 (11.4)	16.6± 11.9
	9 month follow-up	28 (from CD)	MBCT: 45 CBT: 46	0						CBT: 16 (50)								

Table 1b: Characteristics of Participants

No.	Study	Mean baseline for glycosylated haemoglobin (%)			Mean baseline score for depression (Study cut off)			Mean baseline score for Anxiety (Study cut off)		
		IG	CG	Study cut off	IG	CG	Study cut off	IG	CG	Study Cut off
1	**DIAMIND** (van Son, et al., 2011/2013/2014) [12]	7.5± 1	7.6± 1	Not Stated	HAD: 7.9±3.8	HAD: 8.9±3.9	Not stated	HAD: 8.4±3.3	HAD: 9.2±3.6	Not stated
					POMS: 25.3±5.8	POMS: 26.6±6.3		POMS: 20.3±4.5	POMS: 20.1±4.4	
2	**HEIDIS** (Hartmann et al., 2012 [13]	7.26± 1.08	7.27± 1.06	Not Stated	PHQ-9 depression: 6.4± 4.9	PHQ-9 depression: 5.7± 4.3	Not stated	Not Stated		
3	**Schroevers**, et al. (2013) [14]	8.2±1.2	8.1±1.5	Not Stated	CES-D: 22.9±8.0	CES-D: 20.2±8.7	≥16	Not Stated		
4	**Tovote** et al., (2013/2014/2015) [15]	MBCT: 8.0±0.9 CBT: 8.3±1.4	None Stated	Not Stated	**BDI-II MBCT: 23.6±7.7 CBT: 25.6±8.7**	**BDI-II 24.3±8.0**	BDI-II score≥14 HAM: Not stated	GAD-7 MBCT: 12.6±5.3 CBT: 11.9±4.9	GAD-7 9.8±5.0	Not Stated
					HAM-D7 MBCT: 8.9±3.5 CBT: 9.4±3.8	HAM-D7 7.5±2.8				

Table 1c: Characteristics of Participants.

Description of Interventions

The interventions varied in terms of format, difference to traditional MBSR or MBCT and duration of sessions. There were also commonalities in terms of the professional background of therapists, frequency of sessions and adherence of course structure to traditional MBSR or MBCT. The characteristics of the interventions in the four studies are detailed in Table 2.

In all four studies psychologists were used as therapists. This was either alone (DIAMIND and Schroevers), alongside a resident of internal medicine (HEIDIS) or with a diabetes nurse (Tovote). In all studies therapists had previous experience and training in MBSR or MBCT, with specialist training in the adapted intervention given prior to the intervention starting in three of the studies.

Checklists were used in all three studies by participants and therapists to determine attendance and adherence to the intervention protocol and homework. The Tovote study used two independent observers who watched videotapes of each session and rated therapist adherence to the protocol. The HEIDIS study did not provide information on any measures to ensure treatment adherence. Post-intervention adherence to mindfulness practice was not recorded in any of the studies.

#	Study	MBSR or MBCT	Regimen and Nature of MBSR/MBCT in Intervention Group	Therapist (training)	Differences to traditional MBSR or MBCT	Regimen in control group	Measures to maintain control group

1	**DIAMIND** (van Son, et al., 2011/2013 /2014)	MBCT	8 weekly 2 hour long face-to-face group sessions of 4 to 10 participants. Homework of 30 minutes length for 5 days a week 2 hour booster session three months after end of intervention Total Time (Excluding homework):18 hours Total Time (including homework): 38 hours	Psychologist (4 years experience of Mindfulness practice and one certified mindfulness instructors training of 8 days)	No Preclass participant interview. No Silent Day Session 1 - a discussion about the relationship between diabetes, diabetes management, diabetes outcomes and emotional distress Homework 5 days a week instead of 6	Wait-list control group. Treatment as usual.	Not specified
2	**HEIDIS** (Hartmann et al., 2012; Kopf, et al., 2014)	MBSR	8 weekly face-to-face group sessions of 6-10 participants (length of sessions not stated but traditional MBSR is 2.5 -3.5 hours) Homework not stated (if follows traditional MBSR would be 50-60 minutes 6 days a week) Booster session after 6 months (duration not stated) Unable to determine total time	Psychologist (formal training in MBSR) and a resident in internal medicine	Included practices for difficult thoughts and feelings related to diabetes (no other information given) Silent retreat day not mentioned	Treatment-as-usual	All patients seen by a resident in internal medicine in the outpatient clinic before intervention, after 10 weeks and then yearly. Additionally, both groups were routinely seen by their diabetologist every 3-4 month on top of the study visit. All treatment recommendations were based on national diabetes-guidelines.

3	**Schroevers**, et al. (2013)	MBCT	8 weekly 60 minute long face-to-face individual sessions. Homework of 30 minutes length for 6 days a week Total Time (Excluding homework):8 hours Total Time (including homework): 32 hours	Psychologist (degree in clinical psychology, experience in delivering psychological treatment e MBCT group program . Received 3-days training in I-MBCT by an exper ienced qualified mindfulness therapist)	No Preclass participant interview. No Silent Day Individual rather than Group format 60 minute sessions rather than 120-150 minute sessions Duration of exercises shortened in sessions Session 2 - Cognitive exercise removed Sessions 4 and 5 - psycho-educational component was focused on a broader range of stress- and depression-related symptoms, rather than specific depression symptoms Session 7 - relapse prevention removed Instead of watching the video "Healing from within," we introduced the reaction-response model from MBSR	Wait-list	Not stated

4	Tovote et al., (2013/2014/2015)	MBCT	MBCT and CBT: 8 weekly 45-60 minute long face-to-face individual sessions Homework of 30 minutes length for 6 days a week Total Time (Excluding homework):8 hours Total Time (including homework): 32 hours **CBT:** Treatment protocol based on CBT for depression developed by Beck et al. (1979). The first part of treatment is devoted to behavioural components of CBT. Second part of the treatment focuses on dysfunctional thinking patterns, allowing patients to recognize, challenge, and adjust their negative automatic thoughts.	MBCT and CBT: Trained Therapists, one a diabetes nurse who is a qualified mindfulness therapist, all other therapists have a master's degree in clinical psychology and most of them have experience with diabetes patients. All therapists have experience in the delivery of the specific treatment (therapists receive an additional three day training by an experienced, qualified MBCT or CBT therapist who also provides supervision every three weeks throughout the intervention and study period.)	No Preclass participant interview. No Silent Day. Individual rather than Group format. 60 minute sessions rather than 120-150 minute sessions. Duration of exercises shortened in sessions. Session 2 -Cognitive exercise removed. Sessions 4 and 5 - psycho-educational component was focused on a broader range of stress- and depression-related symptoms, rather than specific depression symptoms. Session 7 - relapse prevention removed Instead of watching the video "Healing from within," we introduced the reaction-response model from MBSR	Wait-list control	Not stated

Table 2: Characteristics of Interventions.

Outcome Measures of Included Studies

With the exception of HbA1c, which was a requirement for inclusion in the review, no other measures were the same across the studies.

Time points measured for the outcomes varied but all studies measured results at baseline and post-intervention in all reported outcomes.

Therefore, the values shown (Table 3) represent a much larger time period either side of the intervention in comparison to the HEIDIS study which arranged for blood samples to be taken on a specified measuring. In the DIAMIND study, post-intervention HbA1c results can be from before the intervention has even finished.

The reliability of the psychometric tests used were good (Cronbach α=0.75-0.88) across the self-reported measures. The lowest Cronbach α (0.65) was for the HAM-D7, the only non-participant assessed psychometric measure.

#	Study	Outcomes Measures	Scale	Reliability	Time points measured	Method of measuring/ reporting
1	**DIAMIND** (van Son, et al., 2011/2013/2014)	Glycaemic Control: HbA1c	Percentage (%)		Pre-intervention - between 24 weeks before and 1 week after the start of the intervention Post-intervention - between 6 and 24 weeks after the intervention) 6-month Follow-up	Retrieved from hospitals' computerised patient records. Not stated who did this.
		Depression: Hospital Anxiety and Depression Scale (HADS) Profile of Mood States (POMS)	HADS: 0-21 0-7 = Normal 8-10 = Borderline abnormal 11-21 = Abnormal POMS=0-60	HADS: Cronbach α = 0.81. POMS: Cronbach α = 0.77-0.93	T1 - Baseline T2 - 4 weeks T3 - 8 weeks 6-months Follow-up	Self-report by participants
		Anxiety: Hospital Anxiety and Depression Scale (HADS)	HADS:0-21 0-7 = Normal 8-10 = Borderline abnormal 11-21 = Abnormal POMS=0-36	HADS: Cronbach α = 0.75 POMS: Cronbach α = 0.77-0.93	T1 - Baseline T2 - 4 weeks T3 - 8 weeks 6-months Follow-up	Self-report by participants

2	**HEIDIS** (Hartmann et al., 2012; Kopf, et al., 2014)	Glycaemic Control: HbA1c	Percentage (%)		Baseline Post-intervention - 10 weeks 1 year follow-up 2 years follow-up 3 years follow-up	Blood samples were taken on the day of the respective visit in fasting state. Not stated who did this.
		Depression: Patient Health Questionnaire - 9 (PHQ-9)	0-27	Not Stated	Baseline Post-intervention - 10 weeks 1 year follow -up	Self-report by participants
		Anxiety: Not stated				
3	**Schroevers**, et al. (2013)	Glycaemic Control: Not stated				
		Depression: Center for Epidemiology Studies Depression Scale (CES-D)	0-60 (20 questions, scored 0-3) ≥16 is used to define patients at risk for a clinical depression.	Cronbach α=0.85	T1 - 2-3 weeks before start of intervention T2 - Within 2 weeks of finishing intervention (8-10 weeks from start) T3 - 3 months after finishing intervention	Self-report by participants
		Anxiety: Not stated				

4	**Tovote** et al., (2013/2014/2015)	Glycaemic Control: HbA1c	Percentage (%)		Pre-treatment - average of all assembled values of 0-6 months prior to the intervention. Post-treatment - average of all values between 1 and 6 months after the Intervention. 9- month Follow-up - average of all values between 6 and 12 months after the intervention.	From Patients' Records Not stated who did this.
		Depression: Beck Depression Inventory-II (BDI-II) Toronto Hamilton Depression Rating Scale (HAM-D7)	BDI-II: 0-63 (21-item questionnaire each scored 0-3) 14-19 indicates mild depression 20-28 moderate depression, ≥29 indicates severe depression HAM-D7: 0-26 (7-item semi structured clinical interview) ≥4 mild depression, 12-20 moderate depression >20 severe depression	BDI-II: Cronbach α = 0.84 HAM-D7: Cronbach α = 0.65	Premeasurement After Treatment (8 weeks) 3-month Follow-up 9-month Follow-up (BDI-II only)	BDI-II: Self-reported by participants HAM-D7: trained psychologists Blinded at pre-measurement Not blinded at post-measurement
		Anxiety: Generalized Anxiety Disorder 7 (GAD-7)	0-21 (7-item self-report instrument, each scored 0 to 3) A total sum score of ≥5 indicates mild anxiety, a score of 11-15 moderate anxiety, and a score of >15 indicates severe anxiety	Cronbach α = 0.88	Premeasurement After Treatment (8 weeks) 3-month Follow-up 9-month Follow-up	Self-reported by participants

Table 3: Outcome Measures of Included Studies.

Study Results and Data Synthesis

For this synthesis an effect size (Cohen's d) of >0.8 was considered large, <0.8 and >0.5 was medium and <0.5 was small. The P value significance level was 0.05.

Glycosylated Haemoglobin

Glycosylated haemoglobin was reported as an outcome in 3 of the 4 included studies, all of which were RCTs. The results are shown in Table 4a. The results were organised into short-term (post-intervention, up to 6 months) and long-term (between 6 months and 1 year) in order to allow for comparison. The results in all three studies show a statistically and clinically insignificant effect on glycosylated haemoglobin at both short-term and long-term time points. In all measures reported (mean HbA1c, P, d) the results indicate no significant effect of MBSR or MBCT on HbA1c.

The average change in mean HbA1c across all of the MBSR and MBCT groups was -0.04% at both long-term and short-term time points, a clinically insignificant change. Effect sizes and in all studies and at all time points remained small as, with the exception of the HEIDIS study, all effect sizes remained ≤0.15. *P* values also reflected this with no statistically significant values reported (P value=<0.05). The HEIDIS study also reported HbA1C time points at 2 and 3 years. While effect sizes did increase from the 1-year follow-up onwards and mean HbA1c levels improved in the intervention group in comparison to the control group, the size of this effect remained small (d<0.5).

Study		Mean HbA1c Baseline (SD)	Mean HbA1c Short-term (SD)	Absolute Difference (to baseline)	P value	Mean HbA1c Long-term (SD)	Absolute Difference (to baseline)	P value	Effect Size (Cohen d) Baseline to Short-term vs. CG (95% CI)	Effect Size (Cohen d) Baseline to Long-term vs. CG (95% CI)
DIAMIND (van Son, et al., 2011/2013/2014)	IG	7.5 (1.2)	7.5 (1.1)	0	0.37	7.6 (1.1)	0.1	0.816	0.14 (0.06-0.23)	0.06 (not stated)
	CG	7.6 (1.2)	7.8 (1.5)	0.2		7.7 (1.5)	0.1			
HEIDIS (Hartmann et al., 2012; Kopf, et al., 2014)	IG	7.26 (1.08)	7.2 (0.73)	-0.06	0.7015	7.2 (1.02)	-0.06	0.151	0.09 (not stated)	0.37 (not stated)
	CG	7.27 (1.06)	7.1 (0.83)	-0.17		7.5 (1.21)	0.23			
Tovote et al., (2013/2014/2015)	MBCT	8.0 (0.9)	7.9 (1.0)	-0.1	0.92	7.7 (0.9)	-0.3	0.53	0.03	0.10 (-0.31 to 0.51) (not vs. CG)
	CBT	8.3 (1.4)	8.2 (1.2)	-0.1	0.72	7.9 (1.0)	-0.4	0.38	0.08	0.15 (-0.27 to 0.56) (not vs. CG)
◊◊◊ = Large Positive Effect (d and CI >0.80) ◊◊ = Medium Positive Effect (d>0.80 and if stated CI ≤0.80) ◊= Small Positive Effect (d and if stated CI = >0.50 and ≤0.80										

Table 4a: Glycosylated Haemoglobin Outcomes of Included Studies.

Depression

Depression was reported as an outcome in all four included studies. Scores were organised into baseline, short-term (post-intervention up-to 3 months) and long-term (6 months to 1-year post-intervention) as these reflected the common results reported in the studies. The results of the findings in the studies are displayed in Table 4b. All reductions in scores indicated an improvement in levels of depression. All studies found reductions in levels of depression at both short-term and long-term time points in comparison to the baseline.

The short-term results showed a significant positive effect on levels of depression compared with the control groups in the DIAMIND study (P=<0.01 and <0.001), the Schroevers study (P=0.002) and the Tovote study (P=<0.001). The effect sizes (Figure 1) for these results were medium in both the DIAMIND study outcome measures (d= 0.59, 0.71). Otherwise the effect sizes were large with the Tovote and Schroevers studies finding effect sizes over 1 for the CES-D and HAM-D7 outcome measures. The HEIDIS study, which was the only study to use MBSR, was the only study in the short-term to find an insignificant positive effect on levels of depression compared with a control group (P= 0.9090, d=0.03).

The results for long-term effects of MBSR or MBCT on levels of depression were varied and only reported in 3 studies. All results remained statistically significant (P value <0.05) but effect sizes (Figure 1) reduced in all studies except HEIDIS. Effect sizes were small in the POMS DIAMIND outcome (d=0.48) and medium in all other outcome measures (d=0.51 - 0.77). The HEIDIS study saw a dramatic improvement in the effect size (d=0.03 to 0.71) and P value (P=0.9090 to 0.007). However, the reduction in the depression score (PHQ-9) was relatively small while the control group scores increased, indicating the intervention was effective in preventing progression in the long-term rather than a true reduction in depression.

Long-term follow-up results also increased in comparison with the short-term results in two studies.

Study		Baseline (SD)	Short-term	Absolute Difference (to baseline)	P value	Long-term	Absolute Difference (to baseline)	P value	Effect size (d) Baseline - Short-term vs. CG (95% CI)	Effect size (d) Baseline - Long-term vs. CG (95% CI)
DIAMIND (van Son, et al., 2011/2013/2014)	HADS: IG	7.9 (3.8)	5.3 (4.1)	-2.6	<0.01	5.2 (3.6)	-2.7	0.004	0.59 (0.56-0.61)◊	0.51 (not stated)◊
	HADS: CG	8.9 (3.9)	8.5 (4.7)	-0.4		8.2 (4.5)	-0.7			
	POMS: IG	25.3 (5.8)	21.6 (4.5)	-3.7	<0.001	21.8 (4.7)	-3.5	0.016	0.71 (0.68-0.75)◊	0.48 (not stated)
	POMS: CG	26.6 (6.3)	26.2 (7.0)	-0.4		25.7 (7.3)	-0.9			
HEIDIS (Hartmann et al., 2012;	PHQ-9: IG	6.4 (4.9)	5.7(3.9)	-0.7	0.909	5.3 (3.5)	-1.1	0.007	0.03 (not stated)	0.71◊
	PHQ-9: CG	5.7 (4.3)	5.8 (4.4)	0.1		7.3 (4.2)	0.1			

Schroevers, et al. -2013	CES-D: IG	22.9 (8.0)	14.4 (7.5)	-8.5	0.002	No data	No data	No data	1.23 (not stated)◊◊	No data
	CES-D: CG	20.2 (8.7)	23.6 (7.4)	3.4		No data	No data	No data		No data
Tovote et al., (2013/2014/2015)	BDI-II: MBCT	24.2 (8.3)	15.9 (11.9)	-8.3	<0.001	16.8 (10.8)	-7.4	<0.001	0.80 (0.27-1.31)◊	0.77 (0.34 - 1.19) (not vs. CG)◊
	BDI-II: CBT	25.6 (8.7)	17.4 (11.9)	-8.2	<0.001	18.7 (10.8)	-6.9	<0.001	1.00 (0.47-1.51)◊◊	0.62 (0.19 - 1.04) (not vs. CG)◊
	BDI-II: CG	24.3 (8.0)	23.5 (10.3)	-0.8	0.52	No data	No data	No data		No data
	HAM-D7: MBCT	8.9 (3.5)	4.7 (4.3)	-4.2	<0.001	No data	No data	No data	1.17 (0.61-1.69)◊◊	No data
	HAM-D7: CBT	9.4 (3.8)	4.6 (3.4)	-4.8	<0.001	No data	No data	No data	1.09 (0.55-1.60)◊◊	No data
	HAM-D7: CG	7.5 (2.8)	7.1 (3.7)	-0.4	0.49	No data	No data	No data		No data
◊◊◊ = Large Positive Effect (d and CI >0.80) ◊◊ = Medium Positive Effect (d>0.80 and if stated CI ≤0.80) ◊= Small Positive Effect (d and if stated CI = >0.50 and ≤0.80										

Table 4b: Depression Outcomes of Included Studies.

Anxiety

Two of the four studies examined the effect of MBSR or MBCT on anxiety, both of which were RCTs. Table 4c represents the data for anxiety outcomes in these studies. All reductions in scores indicated an improvement in levels of anxiety.

Changes in the mean scores of the three anxiety outcome measures illustrate that in all MBCT or MBSR intervention groups, scores for anxiety reduced compared to baseline by at least 3 times more than the control groups at both short-term and long-term time points. Reduced anxiety scores remained consistent at the long-term follow-up time point measured.

P values corroborated the reductions in anxiety scores as all were statistically significant.

Figure 2 illustrates the effect sizes reported in the studies. Effect sizes for MBSR or MBCT intervention groups compared to control groups were large (data not shown), with a small effect (d=0.44). At the 6-month follow-up in the DIAMIND study both the HADS and POMS outcome measures had a large effect size as both anxiety scores continued to reduce in the intervention groups. Tovote reported the same medium effect size (d = 0.78) for both MBCT and CBT in comparison to the baseline scores.

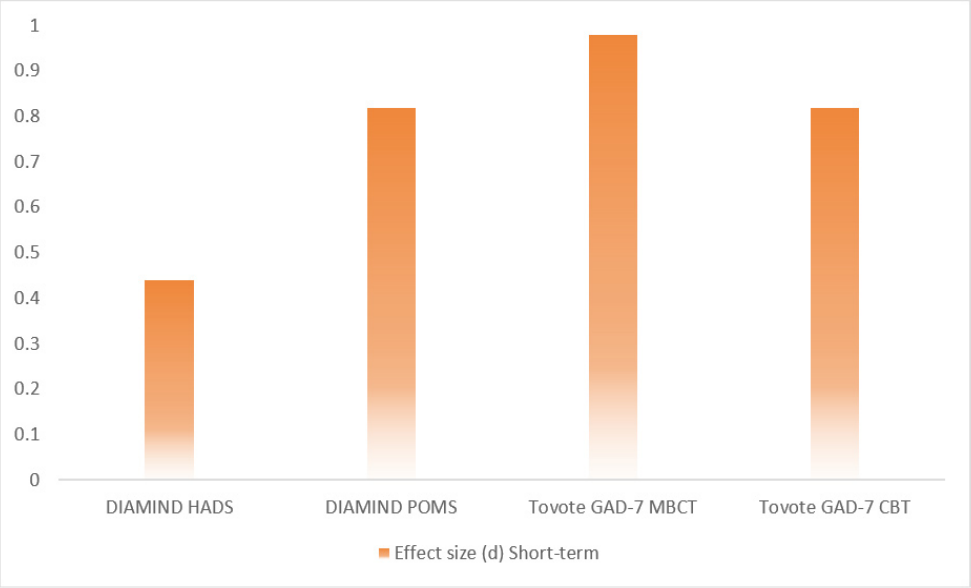

Figure 2: Effect studies reported in studies

Study		Baseline (SD)	4 weeks	8 weeks	Absolute Difference (8 weeks to baseline)	P value	6-month FU	Absolute Difference (6-month FU to baseline)	P value	Effect Size (Cohen d) Baseline 8 weeks vs. CG (95% CI)	Effect Size (Cohen d) Baseline to 6-month FU vs. CG (95% CI)
DIAMIND (van Son, et al., 2011/2013/2014)	HADS: IG	8.4 (3.3)	7.5 (4.1)	6.3 (3.5)	-2.1	0.02	5.4 (3.1)	-3	<0.001	0.44 (0.42-0.46)	0.83 (not stated)◊◊
	HADS: CG	9.2 (3.6)	9.0 (3.7)	8.7 (4.1)	-0.5		8.8 (3.9)	-0.4			
	POMS: IG	20.3 (4.5)	19.0 (5.2)	17.3 (4.1)	-3	<0.001	16.4 (3.4)	-3.9	<0.001	0.82 (0.80—0.85)◊◊	0.92 (not stated)◊◊
	POMS: CG	20.1 (4.4)	20.0 (4.6)	19.7 (5.1)	-0.4		19.4 (5.0)	-0.7			
Study		**Baseline (SD)**	**After Treatment**	**3-month FU**	**Absolute Difference (3-month FU to baseline)**	**P value**	**9-month FU**	**Absolute Difference (9-month FU to baseline)**	**P value**	**Effect Size (Cohen d) Baseline 8 weeks vs. CG (95% CI)**	**Effect Size (Cohen d) Baseline to 0-month FU (95% CI)**
Tovote et al., (2013/2014/2015)	GAD-7: MBCT	11.4 (5.5)	7.0 (4.5)	6.5 (4.9)	-4.9	<0.001	7.2 (5.1)	-4.2	<0.001	0.98 (0.44-1.49)◊◊	0.78 (0.36 - 1.21)◊
	GAD-7: CBT	10.7 (5.0)	6.1 (4.6)	7.0 (4.4)	-3.7	<0.001	7.2 (3.9)	-3.5	<0.001	0.82 (0.29-1.32)◊◊	0.78 (0.35 - 1.2)◊
	GAD-7: CG	9.8 (5.0)	No data	8.2 (4.6)	-1.6		No data				
◊◊◊ = Large Positive Effect (d and CI >0.80) ◊◊ = Medium Positive Effect (d>0.80 and if stated CI ≤0.80) ◊= Small Positive Effect (d and if stated CI = >0.50 and ≤0.80											

Table 4c: Anxiety Outcomes of Included Studies and absolute differences.

Discussion

This research examined the effectiveness of MBSR and MBCT on depression, anxiety and glycaemic control in adults with T1DM or T2DM.

Depression

Three of the four included studies reported a significant reduction in levels of depression in comparison to control groups at short-term, with these levels either decreasing further or remaining stable at long-term measurements in all studies. In the one study that also compared to a CBT group, the reductions were of a similar value. The results of the four studies gave a promising indication that depression levels in DM patients were positively affected by MBSR and MBCT [16]. These preliminary findings on the research are, therefore, congruent with the results reported for the effectiveness of MBSR and MBCT in treating depression in other disorders [17]. However, definitive conclusions cannot be drawn based on the data in this review as there is insufficient evidence from the four studies and no meta-analysis (M-A) has been performed to combine the findings. Results were not uniformly of a large effect size and therefore must be treated with caution until more RCTs are performed and subsequent M-A can be done on enough studies to be meaningful.

The reduction in levels of depression could be attributed to the cultivation of increased awareness of one's thoughts in order to be able to reappraise negative thoughts and experiences that are a feature of depression [18-19].

Anxiety

MBCT and MBSR reduced anxiety levels significantly more than control groups and slightly more than a CBT group at both short-term and long-term measurements. However, only two studies reported results for anxiety outcomes so, although the results were promising, they must be taken as inconclusive. While a M-A could theoretically be performed on these studies, the validity of results would be called into question so more research is needed from large-scale RCTs before any conclusive judgements can be made. Despite this, results were still in line with previous research that has indicated MBSR and MBCT are effective in reducing anxiety levels in the general population [20].

The reduction in anxiety levels of the participants in the two included studies could be attributed to the cultivation of skills to focus the mind and detach from one's thoughts. In this way when anxiety arises participants are able to step-back and see anxiety as clearly an emotional state that may pass in time.

Glycaemic Control

MBSR and MBCT were found to have had no statistically or clinically significant effect on HbA1c levels in the short-term or long-term. There was no indication of a positive difference between MBSR and MBCT and control groups or CBT, with mean HbA1c levels remaining relatively consistent in all groups from baseline to up to 3 years. The results, while not conclusive, are important as they are in contrast to findings from smaller-scale non-randomised studies by [18-19]. Methodological flaws of measuring HbA1c in 2 of the 3 RCTs in this review may partially explain the variance. Rather than arrange for blood tests at set time points during the studies, patient's records were used resulting in non-specific HbA1c results. Glycaemic control was also not the primary focus of any of the included studies in this review, partially explaining the methodological flaws as studies sought to not overload participants with measurements. This contrasts with studies [21-22] that specifically focussed on glycaemic control, measuring HbA1c at specific time points and using HbA1c parameters in the inclusion criteria in order to select poorly controlled diabetes patients. Despite this, these studies were small-scale and non-randomised so the validity of their findings is still questionable.

Consequently, more research from large-scale RCTs that focus on glycaemic control as a primary outcome, target poorly controlled DM patients and use methodologically sound measurements of blood glucose levels are needed in order to make definitive conclusions.

Conclusion

The aim of this review was to evaluate the effectiveness of MBSR and MBCT on glycaemic control, anxiety and depression in adult Diabetes Mellitus (DM) patients. Three RCTs and one RCPS met the inclusion criteria and were included in the data synthesis. Findings of the included studies showed no significant effect of MBSR and MBCT on glycaemic control, but a significant reduction in depression and anxiety levels was established with effects consistent for up-to a year.

Based on these findings, it is strongly recommended that more large-scale methodologically sound RCTs are carried out on MBSR and MBCT in DM patients so that these positive trends for can be investigated further. Also, MBSR and MBCT can very tentatively be considered as a means for improving anxiety and depression in DM patients. However, these findings should be interpreted with caution as due to the limitations of the review, the high risk of bias, the paucity of relevant evidence found and the lack of any statistical analysis, this review does not have the power to make any significant conclusions. The findings however, are promising and certainly warrant further investigation.

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