DIABETICMedicine

DOI: 10.1111/dme.13173

Research: Care Delivery

The 6-month effectiveness of Internet-based guided self-help for depression in adults with Type 1 and 2 diabetes mellitus

D. D. Ebert[1,2,3], S. Nobis[2], D. Lehr[2], H. Baumeister[4], H. Riper[2,5], R. P. Auerbach[6], F. Snoek[7,8], P. Cuijpers[2,5] and M. Berking[1,2]

[1]Department of Clinical Psychology and Psychotherapy, Friedrich-Alexander-University Erlangen-Nuremberg, Erlangen, Germany, [2]Division of Online Health Trainings, Innovation Incubator, Leuphana University, Lüneburg, [3]Department for Health Care Policy, Harvard University, Boston, MA, USA, [4]Department of Clinical Psychology and Psychotherapy, Institute of Psychology and Education, University of Ulm, Ulm, Germany, [5]Department of Clinical Psychology, VU University, Amsterdam, The Netherlands, [6]Department of Psychiatry, Harvard Medical School, McLean Hospital, Belmont, MA, USA, [7]Department of Medical Psychology, VU University Medical Centre and Academic Medical Center and [8]Institute for Health and Care Research (EMGO), VU University Medical Centre, Amsterdam, The Netherlands

Accepted 21 June 2016

Abstract

Aim The aim of this research is to examine the 6-month effects of an Internet-based guided self-help intervention for comorbid depressive symptoms in people with diabetes.

Methods Participants ($n = 260$) with Type 1 or 2 diabetes and elevated depressive symptoms [Center for Epidemiological Studies Depression Scale (CES-D) ≥ 23] were randomly assigned to a guided Internet-based self-help intervention or a control condition (treatment as usual + online psychoeducation about depression). The primary outcome was a change in depressive symptom severity (CES-D) from baseline to 6-month follow-up. The secondary outcomes included numbers of people achieving treatment response (reliable change of depressive symptoms) and remission (CES-D ≤ 16), as well as the effects on glycaemic control, diabetes-related emotional distress and diabetes acceptance. Repeated measures analysis of variance examined between-group differences using intent-to-treat principles.

Results Both conditions showed improvements in depression severity: intervention condition, $d = 1.48$ [95% confidence interval (95% CI): 1.21 to 1.76]; control condition $d = 0.55$ (95% CI: 0.30 to 0.80). Changes were significantly greater in the intervention condition with a large between-group effect size ($d = 0.83$, 95% CI: 0.57 to 1.08). Accordingly, effects on response [relative risk (RR) = 2.60 (95% CI: 2.01 to 3.36), $P < 0.001$] and remission [RR = 3.36 (95% CI: 2.98 to 5.44), $P < 0.001$] were in favour of the intervention group, as were differences in change in diabetes emotional distress ($d = 0.50$, 95% CI: 0.04 to 0.54), and physical and mental functioning [Short Form Health Survey (SF-12) Physical $d = 0.27$ (95% CI: 0.01 to 0.51) and SF-12 Mental $d = 0.68$ (95% CI: 0.11 to 0.40)]. The intervention group was not superior with regard to glycaemic control, diabetes self-management and diabetes acceptance.

Conclusions The trial indicates that Internet-based guided self-help treatments for depression in people with diabetes can have sustained effects on depressive symptoms, well-being and emotional distress associated with diabetes.

Diabet. Med. 34, 99–107 (2017)

Introduction

Depression is highly prevalent and one of the leading causes of disability worldwide. Individuals diagnosed with diabetes have a greater risk of developing depression [1], double the prevalence rate compared with people without diabetes [2]. Compared with non-depressed people with diabetes, people with diabetes and comorbid depression are also more likely to report diabetes treatment non-adherence [3], higher economic costs [4] and a higher mortality risk [5].

Depression in diabetes can be treated effectively with antidepressant medication [6], although there is no evidence for the sustainability of the treatment effects in this population [6]. However, many people do not adhere to

Correspondence to: David Daniel Ebert. E-mail: David.Ebert@fau.de
(Clinical Trial Registry No: DRKS00004748)

What's new?

- Data on the long-term effectiveness of treatments for comorbid depression and diabetes are scarce.
- Depressive symptoms in people with diabetes are undertreated.
- Results provide support for sustained benefits of Internet-based guided self-help for comorbid depressive symptoms and diabetes.
- Internet-based guided self-help could be one among other strategies to reduce the gap between the need for evidence-based treatments and their availability for people with comorbid depression and diabetes.

prescription guidelines or refuse medication, and thus, psychotherapy may be the preferred treatment option at least in these people. A recent Cochrane review on the basis of eight randomized trials provided evidence that psychological interventions can be an effective approach with regard to short-term reduction of depressive symptoms [standardized mean difference (SMD) = 1.47–0.14]; however, across these studies, there was significant heterogeneity in treatment response. Moreover, research on the long-term effects of psychological interventions is scarce. To the best of our knowledge, only three randomized controlled trials (RCTs) have been published that included follow-up assessments of at least 6 months [7–9]. Results provided by these studies are mixed and range from non-significant [8] and small effects (3 points difference in BDI; SMD = 0.31) [7,8] to significant and large effects (SMD = 1.1) [10]. Effects on diabetes-related outcomes, such as glycaemic control and diabetes management, also are mixed [11]. Thus, more research is needed to clarify the longer term effects of interventions targeting depression and diabetes-related outcomes in people with depression and diabetes.

A core disadvantage of psychological interventions for depression in diabetes is that they require well-trained mental health professionals, which reduces the availability of such interventions and increases their costs. Additionally, the available treatment options might be underutilized because: (1) there is often a stigma associated with pursing treatment for mental illness, and (2) many individuals report insufficient time to pursue needed services. These are among the many reasons why only a small percentage of people with depression and diabetes receive proper treatment. For example, in a recent survey in the USA, only 31% of people with depression and diabetes reported receiving antidepressive treatment, and only 6.7% reported receiving at least four sessions of psychotherapeutic treatment [12].

A recent development that may help reduce this problem is the use of Internet-guided self-help interventions. These interventions offer a number of advantages. First, they may attract people who do not want to make use of traditional mental health services, and perhaps given the stigma attached with traditional mental health services may not seek critical care otherwise. Second, Internet interventions are easily scalable; overcoming the challenge of finding mental health professionals with proficient knowledge of both diabetes and depression. Last, Internet-guided self-help interventions provides immediate accessibility [13,14].

The efficacy of Internet-guided self-help interventions for the treatment of comorbid depression and diabetes has been evaluated in only two RCTs [14–16]. Both trials found that Internet-based interventions were effective in reducing depressive symptoms in the short-term, with effects of $d = 0.29$ [16] and $d = 0.89$ [17]. However, the longer term effectiveness of these interventions on depression has not yet been investigated. Thus, it is unclear whether post-treatment effects are stable once the interventions are discontinued. Moreover, the effects of these interventions on glycaemic control are unclear. In the study by Bastelaar and colleagues, the intervention failed to improve glycaemic control, and these effects were not been reported in the study by Nobis *et al.* [17].

The aim of this study is to test the 6-month effectiveness of the GET.ON Mood Enhancer Diabetes intervention for comorbid depression and diabetes and examine the effects of these interventions on diabetes-specific outcomes.

Method

Design

A two-armed RCT was conducted to compare an Internet-guided self-help intervention for depression intervention condition and an active control condition (online psychoeducation on depression) [15]. Assessments took place at baseline (T1), post treatment (8 weeks, T2) and at 6-months follow-up (6-MFU) (T3; see Fig. 1). Details of the trial design [15] and short-term effects (pre–post changes) have been reported previously [17]. All procedures were approved by an independent ethics committee (DRKS00004748).

Participants and procedures

Participants were recruited from the general population via a large German health insurance company, via mailings to insured members of a diabetes disease management programme and through newspaper articles, on-air media and related websites. We included adults (≥ 18 years), with at least moderate symptoms of depression [Center for Epidemiological Studies Depression Scale (CES-D) ≥ 23] [18], with Internet access and sufficient German language skills in reading and writing. We excluded those with: (1) elevated suicide risk [> 1 Beck Depression Inventory (BDI) item 9, 'I feel I would be better off dead']; (2) that were in an

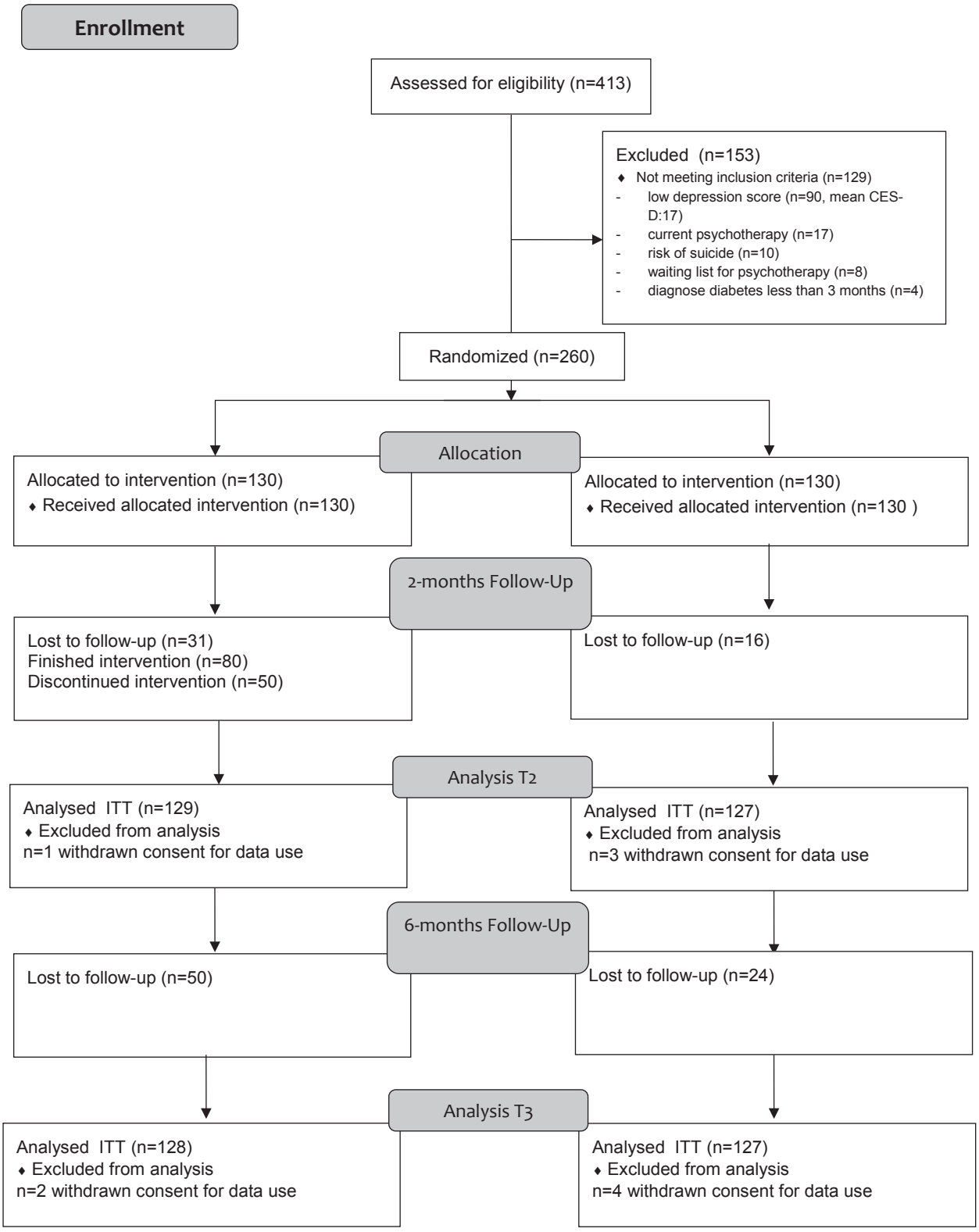

FIGURE 1 CONSORT flow chart

ongoing psychotherapeutic treatment; or (3) on a waiting list for such a psychotherapeutic treatment. In addition, we included a telephone-administered Structured Clinical Interview (SCID) to measure actual and past presence and of depressive episodes. Participants eligible for inclusion who provided their informed consent were randomly allocated to

study conditions at an individual level. The allocation was performed by an independent researcher, not otherwise involved in the study, using an automated computer-based random integer generator (randlist) with a block size of 2.

Interventions

Intervention condition

Participants of the intervention group received GET.ON Mood Enhancer Diabetes (for a detailed description see Ref. [15]). In brief, it is an online training with six sessions based on two core evidence-based treatment components (behavioural activation and problem solving). Two optional sessions address weight and sleeping problems. A seventh booster session (4 weeks after completion of the last session) aims at supporting participants to transfer skills into daily life routine. Each session addresses the reciprocal relationship between diabetes and depression. Weekly sessions can be completed in ~ 45–60 min. Within 48 h after session completion, participants received personalized written feedback from trained psychologists.

Control condition

Individuals in the control condition had full access to treatment as usual and were additionally offered self-help Internet-based psychoeducation on the same platform. Psychoeducation was based on the patient version of the German S3-Guideline/National Disease Management Guideline Unipolar Depression. It informed participants about the nature and evidence-based treatments of depression. We did not monitor the actual uptake of the intervention. Passive psychoeducational interventions have been shown to be effective in reducing depressive symptoms in non-medical patients with a pooled standardized-effect size of $d = 0.26$ [19].

Outcome measures

Primary outcome

The primary outcome was the depressive symptom severity, as measured by CES-D [18]. This widely used scale consists of 20 items. Subjects rate the frequency of symptoms (e.g. 'During the past week I felt sad.') during the past week on a 4-point Likert-scale (from 0 'rarely – less than one day' to 3 'most of the time – five to seven days'). The total score varies between 0 and 60. Evidence for the reliability, validity and sensitivity to change of the scale comes from several studies). Cronbach's alpha for this study was 0.91.

Secondary outcomes

In secondary analysis, the effects on the below-mentioned outcomes are reported. Higher scores indicate greater impairment, unless otherwise specified. Secondary outcomes include:

- glycaemic control (HbA_{1c} values);
- depressive symptoms (Hospital Anxiety and Depression Scales, HADS, which is especially suited for the use in somatic patients, HADS-D; 7 items; range 0–21; $\alpha = 0.86$) [20];
- physical and mental functioning (Short Form Health Survey, SF-12, 12 items; range 0–100) [21];
- emotional distress related to living with diabetes (Problem Areas in Diabetes scale, PAID, 5 items, range 0–20; $\alpha = 0.88$) [22];
- coping with diabetes (Acceptance and Action Diabetes Questionnaire, AADQ, 7 items, range 11–77; $\alpha = 0.77$, higher values indicate higher acceptance) [23]; and
- diabetes self-care (Diabetes Self-Management Questionnaire, DSMQ, 16 items, range 0–10, $\alpha = 0.77$) [24].

Statistical analysis

Analyses are reported according to the Consolidated Standards of Reporting Trials statement. Based on a pre-trial power calculation, we included 260 participants to detect a between trial arm effect size for depressive severity of $d = 0.35$, with a power $(1 - \beta)$ of 0.8 in a two-tailed test and an alpha of 0.05. Data were analysed according to intent-to-treat principles (ITT). We used Markov Chain Monte Carlo multivariate imputation algorithm (missing data module in SPSS 20) with 10 estimations per missing value to deal with the missing data. Additionally, completer's only analyses are reported, including only participants with available data. Analyses were performed with IBM SPSS version 22. A significance level of 0.05 (two-tailed) was used for all analyses.

Differences in change in depressive symptoms and other continuous secondary outcomes between intervention group and control group were assessed using analyses of covariance (ANCOVAs) with the respective baseline scores as covariates. Model assumptions for conducting ANCOVAs were met. Within and between group Cohen's d values and 95% confidence intervals (95% CI) were calculated. According to Cohen's d: 0.2 equals a small effect, 0.5 equals a medium effect and 0.8 equals a large effect. We included concurrent use of antidepressants, age, duration of diabetes and family status and use of other psychological treatments during the trial period as covariates in the primary outcome analysis. Because none of these variables was a predictor of the outcome, we excluded them from the final model. To determine the numbers of participants achieving a reliable positive outcome we coded participants as responders according to the widely used Reliable Change Index (RCI) [25]. Participants with a reliable positive change in depression (RCI > 1.96; ≥ 8.99 CES-D points) were classified as 'responders'. We examined the maintenance of gains from post treatment to the 6-MFU to investigate whether maintenance treatments following treatment discontinuation are

indicated. Post-treatment responders were classified as 'deteriorated' if their symptoms increased from post treatment to 6-MFU by 8.99 CES-D points. Participants were classified as 'relapsed' if remitters at post treatment reported a symptom deterioration above a score of 23 on the CES-D at the 6-MFU. In addition, we considered whether participants attained a near-to-symptom-free state. In the absence of reliable cut-off scores for remission on the CES-D, we applied Jacobsen's method to define a near-to-symptom-free state [25]. Accordingly, participants were classified as remitters, if they moved two standard deviations below the mean of the clinical group. This procedure resulted in a cut-off score of ≤ 16. The cut-off for clinical relevant symptoms in the German version of the CES-D is 23. Moreover, we considered whether participants were classified as being in the target range of HbA_{1c} values < 53 mmol (7%), as recommended by the American Diabetes Association. We also calculated RR and the numbers needed to be treated (NNT) in order to achieve one additional positive outcome compared with the control group and its 95% CI.

Results

Sample

The flow of participants is summarized in Fig. 1. Detailed demographic and clinical characteristics can be found in Table 1, and information pertaining to primary and secondary outcome measures are included in Table 2. Participants had high levels of diabetes-specific emotional distress at baseline as indicated by a mean > 10.4 (SD = 4.4) on the PAID, but were overall well controlled for HbA_{1c} at baseline (mean values of 58 mmol/mol, 7.5%). After 6 months, study attrition for the full sample was 29% (n = 74). Participants who did not provide data at one of the follow-up assessments did not differ from participants without missing data on baseline depression severity scores or any other baseline characteristics (all P-values > 0.10). The vast majority (n = 80; 74%) finished all six sessions. In addition, treatment completers did not significantly differ from non-completers on any of the assessed baseline variables.

Changes in primary and secondary outcomes from baseline to 6-MFU

Table 3 displays the results of ANCOVAs with the respective baseline value as covariate for all of the outcome measures. With regard to the primary outcome depression severity, there was a significant group effect (P < 0.001) indicating significant greater improvements in depression severity from baseline over time in the intervention condition compared with the control condition ($CES\text{-}D_{pre\text{-}6\text{-}MFU}$ = 12.4, d_{within} = 1.48, 95% CI: 1.2 to 1.8; control condition: $CES\text{-}D_{pre\text{-}6\text{-}MFU}$ = 4.7; P < 0.001; d_{within} = 0.55, 95% CI: 0.3 to

Table 1 Characteristics of the study sample at baseline

Characteristics	All participants (N = 256)	Intervention condition (n = 129)	Control condition (n = 127)
Sociodemographic characteristics			
Age (mean, SD)	50.8 (11.8)	50.3 (11.7)	51.4 (11.9)
Female, n (%)	114 (44.5)	82 (63.6)	80 (63.2)
Employed. n (%)	142 (55.5)	70 (54.4)	72 (56.7)
College degree, n (%)	114 (44.5)	51 (39.5)	63 (49.6)
Ethnicity Caucasian, n (%)	190 (74.2)	96 (74.4)	94 (74.0)
Married or in a relationship, n (%)	160 (62.6)	85 (65.9)	75 (59.1)
Diabetes-related characteristics			
Diabetes Type 2, n (%)	142 (55.)	64 (49.6)	78 (61.4)
Insulin-treated Type 2, n (%)	54 (21.1)	28 (21.7)	26 (20.5)
Duration of diabetes, 3–12 months, n (%)	18 (7.0)	10 (7.8)	8 (6.2)
Duration of diabetes, 1–10 years, n (%)	119 (46.5)	57 (44.2)	62 (48.1)
Duration of diabetes, > 10 years, n (%)	119 (46.5)	62 (48.1)	57 (44.9)
Diabetes complications, n (%)	63 (24.6)	33 (25.6)	30 (23.6)
PAID score (mean, SD)	10.41 (4.4)	10.25 (4.3)	10.6 (4.5)
HbA_{1c}, mmol/mol (%)	58 (7.5)	60 (7.6)	57 (7.4)
Depression			
CES-D score (mean, SD)	31.9 (7.2)	32.17 (7.0)	31.5 (7.5)
Major depressive disorder, n (%)	61 (23.8)	35 (27.1)	26 (20.6)
Recurrent major depression, n (%)	78 (30.5)	38 (29.5)	40 (31.5)
Major Depressive Disorder, currently partial remission, n (%)	87 (34.0)	42 (32.6)	45 (35.4)
Antidepressant use, n (%)	12 (4.7)	4 (3.1)	8 (6.3)
Experience with psychotherapy, n (%)	102 (40)	49 (38)	53 (42)
Use of psychological treatments after start of trial, n (%)	11 (9)	15 (12)	26 (9.85)

CES-D, Center for Epidemiological Studies Depression Scale; PAID, Problem Areas in Diabetes scale.
PAID: A total score of ≥ 8 indicates diabetes-related emotional distress.

Table 2 Means (M) and standard deviations (SD) of outcome variables at baseline, post treatment and 6-months follow-up (intention-to-treat sample)

	Baseline				Post-treatment				6-months follow-up			
	IG		CG		IG		CG		IG		CG	
Outcome	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
CES-D	32.2	7.0	31.5	7.5	21.1	8.8	28.9	8.7	19.8	9.6	26.8	9.4
HADS	12.0	3.2	11.7	3.1	8.1	3.9	11.3	3.7	7.4	4.1	10.3	4.0
PAID	10.3	4.3	10.6	4.5	8.4	3.9	10.9	4.7	8.1	4.2	9.9	4.5
HbA_{1c} nmol/mol (%)	60 (7.6)	1.6	57 (7.4)	1.3	–	–	–	–	60 (7.6)	1.6	57 (7.4)	1.4
DSMQ	4.8	0.7	4.7	0.7	4.8	0.6	4.7	0.6	4.6	0.5	4.7	0.6
AADQ	36.9	9.0	36.6	10.3	34.1	8.5	36.1	9.9	33.8	7.7	37.3	9.5
SF-12: Physical	40.1	11.0	42.0	10.6	42.0	10.8	42.1	11.4	41.9	10.9	41.3	10.0
SF-12: Mental	31.2	7.5	32.0	8.6	40.1	9.2	33.3	9.1	42.5	9.1	37.3	9.9

IG, Intervention group; CG, Control group; CES-D, Center for Epidemiological Studies Depression Scale; HADS, Hospital Anxiety and Depression Scale; PAID, Problem Areas in Diabetes scale; DSMQ, Diabetes Self-Management Questionnaire; AADQ, Acceptance and Action Diabetes Questionnaire; SF-12: Physical, Short Form Health Survey (Physical Health Summary Scale); SF-12: Mental, Short-Form Health Survey (Mental Health Summary Scale).

Table 3 Within- and between-group effect sizes for baseline to follow-up changes and ANCOVAs for differences in change in primary and secondary outcomes (intention-to-treat sample)

	ANCOVA[a]		Within-group changes baseline to 6 month follow-up		Between-group changes effect T3[b]
Outcome	F^c	P	$d_{IC,within}$	$d_{CC,within}$	$d_{between}$
CES-D	55.39	< 0.001	1.48 (1.2 to 1.8)	0.55 (0.3 to 0.8)	0.83 (0.6 to 1.1)
HADS-D	57.37	< 0.001	1.25 (1.0 to 1.5)	0.39 (0.1 to 0.6)	0.86 (0.0 to 0.5)
PAID	17.78	< 0.001	0.52 (0.3 to 0.8)	0.14 (−0.1 to 0.4)	0.50 (0.0 to 0.5)
HbA_{1c}	0.0	0.99	0.01 (−0.2 to 0.3)	−0.02 (−0.3 to 0.2)	0.15 (0.0 to 0.5)
DSMQ	2.28	0.13	0.26 (0.0 to 0.5)	−0.02 (−0.3 to 0.2)	−0.18 (−0.2 to 0.3)
AADQ	6.08	< 0.001	−0.38 (−0.6 to 0.1)	0.08 (−0.2 to 0.3)	−0.42 (−0.1 to −0.5)
SF-12: Physical	2.23	0.13	0.17 (−0.1 to 0.4)	−0.07 (−0.3 to 0.2)	0.27 (0.0 to 0.5)
SF-12: Mental	29.96	< 0.001	1.37 (1.1–1.6)	0.53 (0.3 to 0.8)	0.68 (−0.1 to 0.4)

CES-D, Center for Epidemiological Studies Depression Scale; HADS-D, Depression subscale from the Hospital Anxiety and Depression Scale; PAID, Problem Areas in Diabetes scale; DSMQ, Diabetes Self-Management Questionnaire; AADQ, Acceptance and Action Diabetes Questionnaire; SF-12: Physical, Short-Form Health Survey (Physical Health Summary Scale); SF-12: Mental, Short-Form Health Survey (Mental Health Summary Scale).
[a]Controlling for pre-treatment scores (T1). [b]Missing data imputed by multiple imputation. [c]Degrees of freedom not provided due to multiple imputation.

0.8). Differences in changes were large ($d_{between}$ = 0.83, 95% CI: 0.6 to 1.1). See Fig. 2 for a graphical representation of the course of depressive symptoms over time.

With regard to the secondary outcomes, there were significant effects in favour of the intervention condition for all outcomes except for HbA_{1c}, diabetes self-management and diabetes acceptance. Diabetes acceptance results in a significant negative effect of the treatment (d = −0.42, 95% CI: −0.1 to −0.5). There was no significant effect of the intervention on diabetes self-management (d = −0.18, 95% CI: −0.2 to 0.3) and numbers of people within the target range for glycaemic control (d = 0.15, 95% CI: 0.0 to −0.5).

Response, remission and deterioration

Depression response, remission and deterioration rates are included in Table 4. Significantly more participants in the intervention condition were classified as responders at 6-MFU compared with the control condition, with a RR of 2.6 (95% CI: 2.0 to 3.4) and a NNT in order to achieve one additional treatment response of 2.6 (95% CI: 2.4 to 3.7). Remission rates also were significantly and in favour of the intervention condition, with a RR of 3.4 (95% CI: 3.90 to 5.4) and a NNT of 3.1 (95% CI: 1.4 to 4.7).

Completers only

Completers only analysis including only those participants who completed all assessments for the primary outcome at 6-MFU (n = 182, 71%) confirmed the robustness of the findings. Similar to the ITT analysis, an effect size of d = 0.76 (CI: 0.5 to 1.1) was observed for changes in the primary outcome measure from baseline to 6-MFU. Effect sizes for secondary outcomes showed similar patterns as

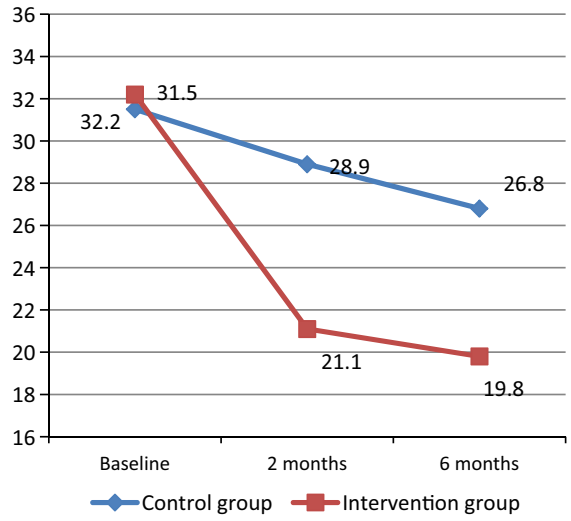

FIGURE 2 Course of depressive symptoms over time

those found in the ITT analysis. The significant positive effect sizes were $d = 0.81$ for the HADS (95% CI: 0.1 to 0.6), $d = 0.51$ for the PAID (95% CI: 0.1 to −0.7), $d = 0.56$ for the SF-12 MCS (95% CI: 0.2 to 0.4), and $d = 0.31$ for the SF-12 PCS (95% CI: 0.1 to 0.5). No significant effect sizes were found for HbA_{1c} ($d = 0.09$, 95% CI: 0.0 to 0.6) and diabetes self-management ($d = 0.17$, 95% CI: −0.1 to 0.5). Changes in diabetes acceptance were in favour of the control condition ($d = -0.36$, 95% CI: 0.1 to 0.5).

Maintenance of treatment effects from post treatment to 6-MFU

Of the 81 responders at post treatment in the intervention group, 10 (12.3%) experienced symptom deterioration from post treatment to 6-MFU, whereas this was the case for 5 (20.8%) of the 24 responders in the control group ($P > 0.10$). Depression relapse was experienced by 2 of 40 post-treatment remitters (5%) in the intervention condition, and 1 of 10 remitters in the control condition (10%, $P > 0.10$).

Discussion

The findings for the 6-month effect on depression severity compare favourably with the few trials of face-to-face psychological interventions in comorbid depression and diabetes that examined long-term effects (6 months +) [8–10]. Specifically, face-to-face cognitive–behavioural psychotherapy had large effects on depression severity at follow-up compared with diabetes education only [10]. However, another study found only small effects [7] and a recently published study [8] did not find psychotherapy to be superior over usual care in the long term, although this might be related to low power resulting from a small sample size ($N = 87$).

The clinical significance of the results is further supported by the effects on response (64.2% vs. condition: 28.6%, RR = 2.6) and remission (45.3% vs. 13.5%, RR = 3.4), which are comparable with post-treatment event rates found in a recent meta-analysis for face-to-face psychotherapy for depression compared with control conditions in non-medical populations (Response: 48% vs. 19%; Remission: 43% vs. 27%) [25]. Moreover, differences in response and remission rates are higher than those found in a recent meta-analysis for short-term effects of collaborative care management programmes for depression and diabetes compared with treatment as usual (Response: RR = 1.3, 95% CI = 1.1 to 1.7; Remission: RR = 1.5, 95% CI = 1.1 to 2.1) [26].

Although emotional distress regarding living with diabetes decreased, in contrast to our hypothesis, diabetes self-care, diabetes acceptance and glycaemic control did not improve. This finding is consistent with a number of previous studies that found psychological interventions to be not superior to usual care with regard to these outcomes [27,28]. Notwithstanding our non-significant findings, there are at least two randomized trials that found significant effects of psychotherapy on glycaemic control [8,26]. One explanation for these differences is that these psychotherapeutic interventions incorporated specific modules for improved diabetes management [11]. It is noteworthy, that in the Lustman study, the comparator condition was self-care for diabetes and the effects of psychotherapy in addition to diabetes self-care were nevertheless greater compared with self-care alone on glycaemic control. This may indicate that the combination of interventions for depression and diabetes self-care may interact to potentiate the effect on glycaemic control. This is in line with the assumption that depression treatment might be necessary to improve glycaemic control, but not sufficient [8]. To test this

Table 4 Even rates and effects on response and remission at 6-month follow-up

	ER_{IC}		ER_{CC}						
	%	*n*	%	*n*	RR	95% CI	*P*	NNT	95% CI
Response	64.2	86	28.6		2.6*	2.0 to 3.4	< 0.001	2.6	2.4 to 3.7
Remission	45.3	58	13.5	17	3.4*	3.0 to 5.4	< 0.001	3.1	1.4 to 4.7
Deterioration	0.8	1	3.2	4	0.2	0.0 to 2.2	0.19		

ER, event rate: numbers of participants displaying response and remission, respectively. IC, intervention condition; CC, control condition; RR, relative risk for a response, remission, deterioration, respectively. NNT, number needing to be treated.

hypothesis, future trials should compare psychotherapy in addition to diabetes self-care with diabetes self-care alone and with psychotherapy alone. It should also be noted that mean diabetes self-care (4.75 across groups) was not problematic at baseline (> 6), and also the mean HbA_{1c} value 58 (7.5%) across groups was already close to target at baseline.

Limitations of the study include the following. First, there was a drop-out rate of 28% at the 6-MFU. Although such attrition rates are common in follow-up studies of RCTs, we applied state-of-the-art methods to handle missing data. Nevertheless, we cannot rule out a potential bias due to missing data. Second, we did not conduct clinical interviews at the follow-up assessments, thus do not know whether diagnostic status has changed as a result of the intervention. Third, the block size in the randomization was 2 which is a potential source of bias. However, none of the research staff ever met the participants, participants were randomized in order of incoming informed consent, the researcher responsible for randomization was independent, not otherwise involved in the study, and did not have any information such as baseline characteristics of the participants. Finally, sleep and exercise were targeted within optional modules of the intervention, but we did not assess insomnia severity or weight as outcome, which should be considered in future studies.

Despite these limitations, our data suggest that Internet-based guided self-help for comorbid depression and diabetes is an effective approach that can result in sustained 6-month benefits. Internet-guided self-help interventions may be successfully integrated in existing diabetes care management or collaborative care programmes [26]. Thus, Internet interventions could be one among other strategies to reduce the gap between the need for evidence-based treatments and their availability for people with comorbid depression and diabetes. However, the acceptance of an intervention by the target population is always a necessary prerequisite for utilizing it and not all people might be willing to use Internet-guided self-help interventions [30]. Hence, we argue that these interventions should be offered as only one treatment option along with already established interventions for depression in people with diabetes.

Funding sources

The BARMER GEK and the European Union funded this study (EU EFRE: ZW6-80119999, CCI 2007DE161PR001).

Competing interests

David Daniel Ebert, Stephanie Nobis, Matthias Berking and Dirk Lehr are stakeholders of the 'Institute for Online Health Trainings', that aims to transfer scientific knowledge related to the present research into routine health care.

Acknowledgments

The BARMER GEK and the European Union funded this study (EU EFRE: ZW6-80119999, CCI 2007DE161PR001). We would further like to thank all participants who participated in this study. David Ebert, Matthias Berking, and Dirk Lehr are stakeholders of the "Institute for Online Health Trainings", that aims to transfer scientific knowledge related to the present research into routine health care.

Author contributions

DDE, SN, DL, HB, HMR, PC, FS and MB contributed to the design of the study. SN, DDE, DL, MB, FS and HMR developed the intervention content. HB contributed to the intervention content. DDE and SN performed the outcome analyses. DDE wrote the first draft of the manuscript and integrated co-author comments and edits. All authors contributed to the further writing of the manuscript and approved the final manuscript. David Ebert is the guarantor for the work.

References

1 Nouwen A, Winkley K, Twisk J, Lloyd CE, Peyrot M, Ismail K *et al*. Type 2 diabetes mellitus as a risk factor for the onset of depression: a systematic review and meta-analysis. *Diabetologia* 2010; **53**: 2480–2486.
2 Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 2001; **24**: 1069–1078.
3 Gonzalez JS, Peyrot M, McCarl LA, Collins EM, Serpa L, Mimiaga MJ *et al*. Depression and diabetes treatment nonadherence: a meta-analysis. *Diabetes Care* 2008; **31**: 2398–2403.
4 Hutter N, Schnurr A, Baumeister H. Healthcare costs in patients with diabetes mellitus and comorbid mental disorders – a systematic review. *Diabetologia* 2010; **53**: 2470–2479.
5 Katon WJ, Rutter C, Simon G, Lin EHB, Ludman E, Ciechanowski P *et al*. The association of comorbid depression with mortality in patients with type 2 diabetes. *Diabetes Care* 2005; **28**: 2668–2672.
6 Baumeister H, Hutter N, Bengel J. Psychological and pharmacological interventions for depression in patients with diabetes mellitus and depression. *Cochrane Database Syst Rev* 2012 Jan; **12**: CD008381.
7 Lamers F, Jonkers CCM, Bosma H, Kempen GIJM, Meijer J a MJ, Penninx BWJH *et al*. A minimal psychological intervention in chronically ill elderly patients with depression: a randomized trial. *Psychother Psychosom* 2010; **79**: 217–226.
8 Safren SA, Gonzalez JS, Wexler DJ, Psaros C, Delahanty LM, Blashill AJ *et al*. A randomized controlled trial of cognitive behavioral therapy for adherence and depression (CBT-AD) in patients with uncontrolled type 2 diabetes. *Diabetes Care* 2014; **37**: 625–633.
9 Lustman PJ. Cognitive behavior therapy for depression in Type 2 diabetes mellitus. *Ann Intern Med* 1998; **129**: 613.
10 Lustman PJ, Freedland KE, Griffith LS, Clouse RE. Predicting response to cognitive behavior therapy of depression in type 2 diabetes. *Gen Hosp Psychiat* 1998; **20**: 302–306.
11 Petrak F, Baumeister H, Skinner TC, Brown A, Holt RIG. Depression and diabetes: treatment and health-care delivery. *Lancet Diabetes Endocrinol* 2015; **3**: 472–485.

12 Katon WJ, Simon G, Russo J, Von Korff M, Lin EHB, Ludman E *et al*. Quality of depression care in a population-based sample of patients with diabetes and major depression. *Med Care* 2004; **42**: 1222–1229.
13 Ebert DD, Zarski A-C, Christensen H, Stikkelbroek Y, Cuijpers P, Berking M *et al*. Internet and computer-based cognitive behavioral therapy for anxiety and depression in youth: a meta-analysis of randomized controlled outcome trials. *PLoS One* 2015; **10**: e0119895.
14 Ebert DD, Berking M, Heber E, Riper H, Laferton J, Cuijpers P, Lehr D. Restoring depleted resources: Efficacy and mechanisms of change of an Internet-based unguided recovery training for better sleep and psychological detachment from work. *Health Psychology* 2015; 34 (Suppl): 1240–1251.
15 Nobis S, Lehr D, Ebert DD, Berking M, Heber E, Baumeister H *et al*. Efficacy and cost-effectiveness of a web-based intervention with mobile phone support to treat depressive symptoms in adults with diabetes mellitus type 1 and type 2: design of a randomised controlled trial. *BMC Psychiatry* 2013; **13**: 306.
16 van Bastelaar KMP, Pouwer F, Cuijpers P, Riper H, Snoek FJ. Web-based depression treatment for type 1 and type 2 diabetic patients: a randomized, controlled trial. *Diabetes Care* 2011; **34**: 320–325.
17 Nobis S, Lehr D, Ebert DD, Baumeister H, Snoek F, Riper H *et al*. Efficacy of a web-based intervention with mobile phone support in treating depressive symptoms in adults with Type 1 and Type 2 diabetes: a randomized controlled trial. *Diabetes Care*. 2015; **38**: 776–783.
18 Hautzinger M, Bailer M. *Allgemeine Depressions Skala. Manual*. Göttingen: Beltz Test GmbH, 1993.
19 Donker T, Griffiths KM, Cuijpers P, Christensen H. Psychoeducation for depression, anxiety and psychological distress: a meta-analysis. *BMC Med* 2009; **7**: 79.
20 Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002; **52**: 69–77.
21 Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE *et al*. Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. International Quality of Life Assessment. *J Clin Epidemiol* 1998; **51**: 1171–1178.
22 Lee E-H, Lee YW, Lee K-W, Kim YS, Nam M-S. Measurement of diabetes-related emotional distress using the Problem Areas in Diabetes scale: psychometric evaluations show that the short form is better than the full form. *Health Qual Life Outcomes* 2014; **12**: 142.
23 Schmitt A, Gahr A, Hermanns N, Kulzer B, Haak T. [Evaluation of the AADQ (German Version) in Measuring Diabetes Acceptance]. *Diabetes, Stoffwechsel und Herz* 2013; **22**: 9–15.
24 Schmitt A, Gahr A, Hermanns N, Kulzer B, Huber J, Haak T. The Diabetes Self-Management Questionnaire (DSMQ): development and evaluation of an instrument to assess diabetes self-care activities associated with glycaemic control. *Health Qual Life Outcomes* 2013; **11**: 138.
25 Jacobson NS, Truax P. Clinical significance: a statistical approach to denning meaningful change in psychotherapy research. *Psychology* 1991; **59**: 12–19.
26 Lustman PJ, Griffith LS, Freedland KE, Kissel SS, Clouse RE. Cognitive behavior therapy for depression in type 2 diabetes mellitus. A randomized, controlled trial. *Ann Intern Med* 1998; **129**: 613–621.
27 Cuijpers P, Karyotaki E, Weitz E, Andersson G, Hollon SD, van Straten A. The effects of psychotherapies for major depression in adults on remission, recovery and improvement: a meta-analysis. *J Affect Disord* 2014; **159**: 118–126.
28 Huang Y, Wei X, Wu T, Chen R, Guo A. Collaborative care for patients with depression and diabetes mellitus: a systematic review and meta-analysis. *BMC Psychiatry* 2013; **13**: 260.
29 Sharif F, Masoudi M, Ghanizadeh A, Dabbaghmanesh MH, Ghaem H, Masoumi S. The effect of cognitive–behavioral group therapy on depressive symptoms in people with type 2 diabetes: a randomized controlled clinical trial. *Iran J Nurs Midwifery Res* 2014; **19**: 529–536.
30 Markowitz SM, Gonzalez JS, Wilkinson JL, Safren SA. A review of treating depression in diabetes: emerging findings. *Psychosomatics* 2011; **52**: 1–18.
31 Baumeister H, Nowoczin L, Lin J, Seifferth H, Seufert J, Laubner K *et al*. Impact of an acceptance facilitating intervention on diabetes patients' acceptance of Internet-based interventions for depression: a randomized controlled trial. *Diabetes Res Clin Pract* 2014; **105**: 30–39.

