

# The Three-Month Effect of Mobile Internet-Based Cognitive Therapy on the Course of Depressive Symptoms in Remitted Recurrently Depressed Patients: Results of a Randomized Controlled Trial

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## Key Words

Internet-based therapy · Recurrent depression · Monitoring · Treatment · Cognitive therapy

## Abstract

**Background:** Internet-based cognitive therapy with monitoring via text messages (mobile CT), in addition to treatment as usual (TAU), might offer a cost-effective way to treat recurrent depression. **Method:** Remitted patients with at least 2 previous episodes of depression were randomized to mobile CT in addition to TAU ( $n = 126$ ) or TAU only ( $n = 113$ ). A linear mixed model was used to examine the effect of the treatment condition on a 3-month course of depressive symptoms after remission. Both an intention-to-treat analysis ( $n = 239$ ) and a completer analysis ( $n = 193$ ) were used. Depressive symptoms were assessed using the Inventory of Depressive Symptomatology (IDS-SR<sub>30</sub>) at baseline and 1.5 and 3 months after randomization. **Results:** Residual depressive symptoms showed a small but statistically significant decrease in the intention-to-treat group over 3 months in the mobile CT group relative to the TAU group (difference:  $-1.60$  points on the IDS-SR<sub>30</sub> per month, 95% CI =  $-2.64$  to  $-0.56$ ,

$p = 0.003$ ). The effect of the treatment condition on the depressive symptomatology at the 3-month follow-up was small to moderate (Cohen's  $d = 0.44$ ). All analyses among completers ( $\geq 5$  modules) showed more pronounced treatment effects. Adjustment for unequally distributed variables did not markedly affect the results. **Conclusions:** Residual depressive symptoms after remission showed a more favorable course over 3 months in the mobile CT group compared to the TAU group. These results are a first indication that mobile CT in addition to TAU is effective in treating recurrently depressed patients in remission. However, demonstration of its long-term effectiveness and replication remains necessary.

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## Introduction

According to the Global Burden of Disease study (GBD, 2010), the highest proportion of the total burden of disease of all mental and substance use disorders is

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caused by major depressive disorder (MDD) [1]. MDD is a highly recurrent disease [2]. Effective treatment strategies for the prevention of relapse/recurrence are crucial to reducing the burden of depression [3]. The longer patients remain well, the lower the risk of relapse [4]. Depressive relapse/recurrence is difficult to prevent using antidepressants only [5]. Cognitive therapy (CT) after the acute phase of depression reduces the risk of relapse [6–12]. In addition, brief psychotherapy, i.e. preventive CT, well-being therapy, and mindfulness-based CT, lowers the relapse rates compared to treatment as usual (TAU) [13–22]. Importantly, mindfulness-based CT and preventive CT are more effective in patients with a higher number of previous episodes [6, 12, 14, 16–18]. To describe the course of depression and interpret treatment outcomes, the operational criteria of Frank et al. [23] are often cited. According to these criteria, remission refers to a depression-free period of at least 2 months, and relapse refers to an onset of depression during the remission period. Recovery is considered once remission exceeds 6 months without relapse, and recurrence refers to the onset of depression after recovery.<sup>1</sup> Clinical practice guidelines for MDD treatment recommend long-term monitoring and guidance for patients with recurrent episodes and/or residual depressive symptoms [24–26]. However, resources are generally scarce and there is a limited availability of therapists [27, 28]. Therefore, Internet-based CT including monitoring via text messages and therapist support by telephone (mobile CT) may be a feasible approach. Internet-based CT is easily accessible and therapist involvement may be reduced, as demonstrated in acute-phase Internet-based treatment [29]. In addition, monitoring via text messages allows relapse detection by patients and therapists as early as possible. A recent study demonstrated that offering Internet-based treatment positively influenced long-term outcomes (e.g. longer remission/recovery) in patients who met the criteria for a current mental disorder [30]. So far, only one study has examined the effect of an Internet-based cognitive behavior therapy, in comparison to a control group, on the depressive symptomatology and the subsequent course of depression. That study was carried out in a sample of patients who responded to treatment but were only partially remitted [31, 32]. The findings suggested that at the 6-month follow-up there was a significant further reduction of depressive symptoms in the treatment group, and that the relapse rates at 2 years were also sig-

nificantly lowered (Cohen's  $d$  pre- to posttreatment effect = 0.33 with the MADRS-S and  $d$  = 0.29 with the BDI-II). However, no study has been conducted using these technologies aimed at relapse prevention in patients remitted/recovered for at least 2 months but not longer than 2 years. In the current randomized controlled trial the effect of mobile CT added to TAU on a 3-month course of depressive symptomatology was compared to TAU in remitted recurrently depressed patients.

## Methods

In order to be included in the randomized controlled trial [33], participants had to: (1) be between 18 and 65 years old and (2) be in remission/recovery from recurrent MDD for at least 2 months but not longer than 2 years according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) as assessed using the Structured Clinical Interview (SCID-I) based on the DSM-IV-TR [34] and a maximum score of 10 on the 17-item Hamilton Rating Scale for Depression (HRSD<sub>17</sub>) [35]. Further, participants had to have Internet access. Exclusion criteria assessed using the SCID-I interview were: (1) a predominant anxiety disorder requiring treatment, (2) a current or past mania or hypomania, (3) current alcohol or drug abuse, and (4) past or present psychosis. Additional exclusion criteria were: insufficient mastery of the Dutch language, recent electroconvulsive therapy, and organic brain damage. This study was approved by the Medical Ethics Committee of the University Medical Center Groningen, and all participants provided written informed consent.

### Study Design

Participants were recruited via media, general practitioners, and mental health care institutions. When interested, participants provided the researchers with their contact information, after which the researchers contacted and screened them using a short form via telephone. If subjects were deemed eligible, an SCID-I interview and HRSD<sub>17</sub> were scheduled and performed via telephone by trained researchers and psychologists. All interviews were audiotaped and regular consensus meetings were held under the supervision of a licensed clinical psychologist. The interviewers were blinded to the treatment condition. After inclusion, participants received an e-mail with a link to a series of online self-report questionnaires. Randomization to the treatment condition took place after completion of the online self-report questionnaires ( $T_0$ ), at an individual level. Randomization was undertaken by an independent researcher using computer-generated random numbers. The random numbers were generated by an independent statistician using STATA version 11. Data on participants that were recruited from March 2010 until March 2013 were used for the current study.

### Treatment

Mobile CT was based on a previously evaluated face-to-face preventive CT [17, 18]. Preventive CT is based on CT for acute depression [36]. Like regular CT, preventive CT has a fixed struc-

<sup>1</sup> For readability, we will refer to the more conservative term relapse in the case of both relapse and recurrence [61].

ture, with agenda setting, a review of homework, an explanation of the rationale for each session, and the assignment of homework. Preventive CT targets, in particular, underlying cognitive vulnerability factors that are 'depressogenic assumptions' and that are associated with depressive relapse [37]. Compared to standard CT for acutely depressed patients [e.g. 36], preventive CT is less focused on teaching the individual to challenge a wide range of negative thoughts. Instead, it starts with the identification of some specific negative thoughts and dysfunctional attitudes, aided by the Dysfunctional Attitude Scale [38]. Preventive CT consists of 8 structured sessions including cognitive interventions specifically developed to prevent relapse in recurrent depression in remitted patients. A specific manual describing the structure of the treatment and interventions used is available [39].

Mobile CT was offered completely over the Internet with minimal therapist support, i.e. in a maximum of 4 telephone sessions. Participants were advised to do 1 module per week. Each module included assignments with automatically generated feedback and could be completed in approximately 20 min. In the first module, the main aim was to identify negative thoughts. In the second module, participants had to identify their dysfunctional beliefs (Dysfunctional Attitude Scale) [38]. Module 3 consisted of weighing the advantages and disadvantages of their dysfunctional beliefs. In modules 4–7, multiple CT-based challenging techniques were used that focused on dysfunctional beliefs, such as identifying positive/dream beliefs [18, 39]. In modules 4–6, participants were asked to keep a diary of their positive experiences and feelings. In modules 5–8, participants formulated specific relapse prevention strategies. All information gathered throughout the modules was used to make a personal prevention plan in module 8 [40]. Automated checks were conducted to ascertain that the participants had completed the modules and understood them correctly. Participants received friendly reminders via text message or e-mail to proceed with the intervention after an absence of 6 weeks. The researchers scheduled at least 2 voluntary telephone sessions with trained mental health psychologists. Therapist support was aimed at working through the modules and finishing the therapy [based on 41, 42]. Therefore, the focus was on the intervention, using CT-based challenging techniques. For example, a question on the agenda for therapist support session 1 was: Did the participant manage to formulate a dysfunctional belief? If yes, compliment! Check whether the belief is related to the participant. Use the downward arrow technique when needed. If not, help the participant to choose one. [40] Participants could ask for at most 2 additional telephone sessions and could initiate e-mails without any frequency restrictions.

**Mobile Mood Monitoring.** Twice a month, participants in the mobile CT group received a text message or e-mail to fill in a mood monitor, consisting of 2 questions about last week's mood and interests in order to check for the 2 core symptoms of depression [43], to be answered on a Likert type scale ranging from 1 to 10. If a decrease in mood or interests occurred twice in a row (score <3), participants automatically received a request to fill out the 16-item Quick Inventory of Depressive Symptomatology (QIDS) [44]. When the score exceeded 10 or indicated suicidal ideation, the researchers checked for relapse by administering the HRSD<sub>17</sub> and the depression section of the SCID-I. If the HRSD<sub>17</sub> score was 10 or higher and the SCID-I was indicative of a DSM-IV-TR relapse, participants were advised to contact their general

practitioner, psychiatrist, or psychologist [for a more detailed description of mobile CT, see 40].

TAU could consist of multiple types of treatment, such as antidepressant medication treatment, maintenance or continuation therapy by a psychologist or psychiatrist, or no treatment at all. There were no restrictions to the type of TAU. In the TAU condition, participants did not receive text message-based monitoring although, like in the experimental condition, regular assessments were done using the Inventory of Depressive Symptomatology (IDS-SR<sub>30</sub>) [44] (8 times after baseline) and SCID-I (3 times after baseline). In case of a depressive relapse, participants were advised to contact their general practitioner, psychiatrist, or psychologist (if available).

#### Outcome Measures

The outcome measure was the 3-month course of self-reported residual depressive symptoms in: (1) mobile CT added to TAU and (2) TAU alone. The depressive symptomatology was assessed at baseline, 1.5 months after randomization (T1), and 3 months after randomization (T2) using the Dutch translation of the IDS-SR<sub>30</sub> [44]. The inventory consists of 30 symptom items to be answered on a 4-point Likert scale ranging from 0 (no symptoms) to 3 (almost always troubled by a symptom). A score of 0–13 is categorized as no symptoms, a score of 14–25 represents mild symptoms, a score of 26–38 is indicative of moderate symptoms, a score of 39–48 is categorized as severe symptoms, and a score above 49 represents very severe symptoms. Its reliability, as assessed in the present study, was good, with a Cronbach  $\alpha$  of 0.87, which is in accordance with values reported by Rush et al. [44] ( $\alpha$  = 0.79–0.85).

The 17-item HRSD was used to assess baseline depressive symptom levels. The HRSD was administered via telephone by trained researchers and psychologists before treatment allocation. The HRSD is an often used semi-structured clinical interview. Scores can range from 0 to 52 [35]. The internal consistency appeared to be adequate in this study, with a Cronbach  $\alpha$  of 0.66.

#### Data Analyses

The primary analysis was performed in agreement with the intention-to-treat (ITT) principle, including all randomized patients, regardless of treatment adherence, dropouts, and completeness of outcome assessments. To check whether the randomization had been successful, the characteristics of the study population according to treatment group were compared.<sup>2</sup>

A linear mixed model (LMM) was used to examine differences in the linear rate of change between the randomized groups in depressive symptoms over the 3-month course, i.e. the treatment effect. LMM is the preferred method to analyze multivariate longitudinal data [45]. LMM makes optimal use of the available data because incomplete cases are included in the analyses under the assumption that missing data are missing at random. This assumption means that the probability of a value being missing, and the most likely value itself, can be predicted from the observed variables. An LMM was fitted with the IDS-SR<sub>30</sub> score as

<sup>2</sup> The baseline characteristics of the treatment groups were compared using  $\chi^2$  tests to evaluate differences in dichotomous variables, and independent-samples t tests were applied to normally distributed continuous variables; for nonnormally distributed variables the nonparametric Mann-Whitney U statistic was used.

the dependent variable and time (in months) as the independent variable. The apparent nonlinearity of the rate of change of the IDS-SR<sub>30</sub> score was accommodated by including a time<sup>2</sup> variable. While thus taking into account an overall quadratic time trend, we included a between-group-by-time interaction to represent the between-group difference in the linear rate of change. Graphical inspection of the course of the symptoms did not suggest an interaction of treatment with time<sup>2</sup>. Further, the addition of a mobile CT  $\times$  time<sup>2</sup> variable with the lower-order interaction term (mobile CT  $\times$  time) already in the model appeared statistically nonsignificant. Therefore, it was left out of the final model. The dependency of the repeated assessments of depression within the same participant was taken into account by adding a random intercept and a random slope for participants using an unstructured variance-covariance matrix. Removal of the random slope worsened the fit of the model in a statistically significant way and it was therefore retained. Similarly, a secondary LMM analysis was conducted based on the completer group. Completion was defined as finishing at least 5 of the 8 modules of mobile CT.<sup>3</sup> Both the ITT and the completer analyses were supplemented with analyses in which we included the type of aftercare (no aftercare, antidepressants, and aftercare by a mental health professional), the continuous number of episodes, the duration of remission, and possible imbalances in baseline prognostic factors between the randomized groups as covariates. The number of episodes has been previously shown to influence treatment effects in relapse prevention [for meta-analyses see 9, 13], and the type of aftercare could influence the treatment outcome as well. We conservatively defined the effect size of 3-month treatment as the crude difference between the randomized groups in the mean IDS-SR<sub>30</sub> scores at the final assessment and expressed it as Cohen's *d*. We included 239 patients, allowing us to demonstrate statistically significant effect sizes of 0.36 or more with 80% power ( $1 - \beta$ ) at a 2-sided significance level of 5%. SPSS version 20.0 was used when we considered a 2-sided  $p < 0.05$  to be statistically significant. A two-sided test was performed because, while we expected participants to profit from mobile CT added to TAU, the effects of mobile CT have not been studied previously and we wanted to be sure not to miss any potentially negative effect. A power analysis was performed for the primary outcome relapse as described in the trial design paper [31]. However, the current study reports on the secondary outcome, i.e. depressive symptoms. Consequently, the power of this secondary analysis had to be calculated post hoc.

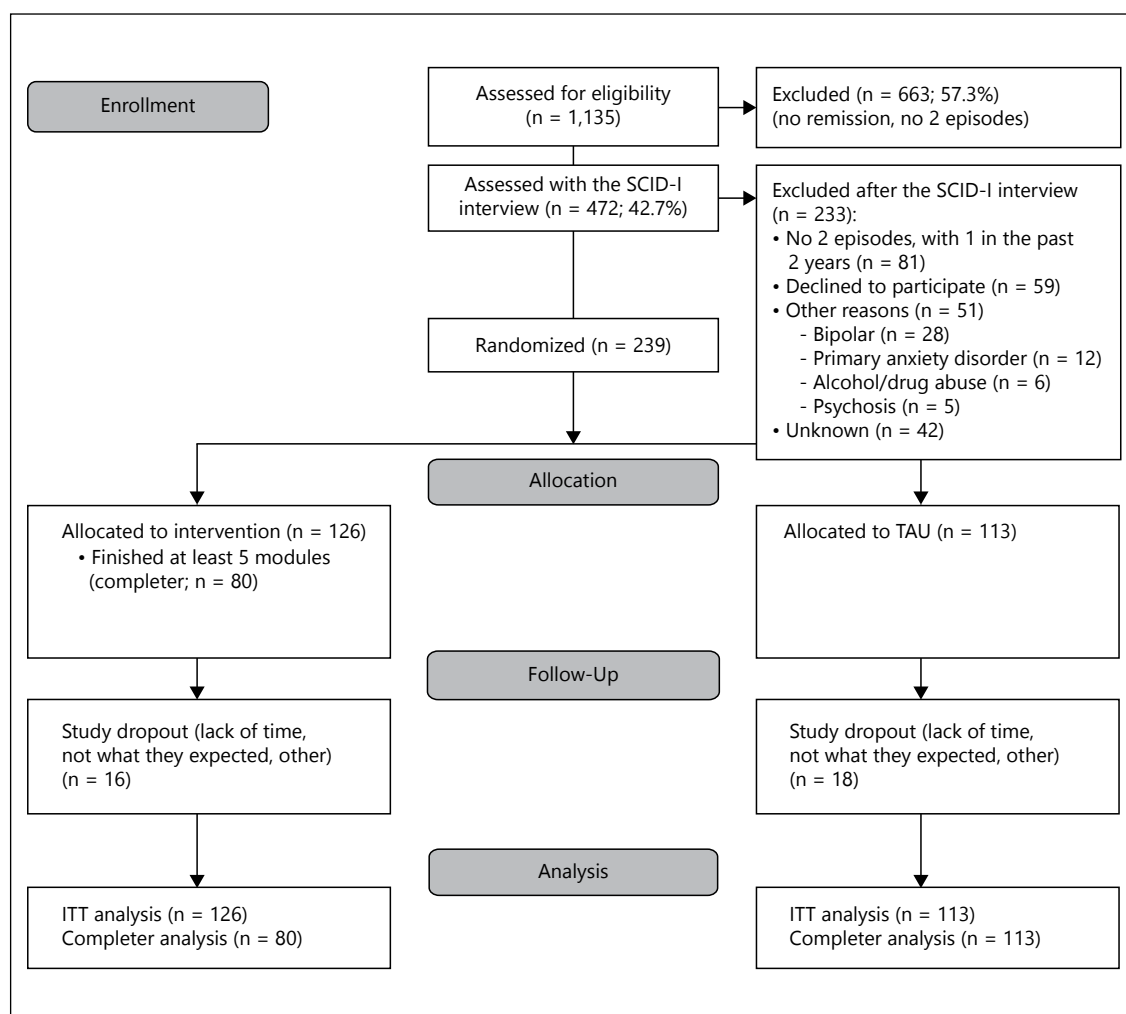
## Results

### *Baseline Characteristics and Study Flow*

Out of 1,157 patients screened for eligibility, 663 patients (57.3%) did not meet the inclusion criteria after the

first screening. This led to 494 patients (42.7%) who were interviewed using the SCID-I. Most patients were excluded because they did not have 2 previous episodes ( $n = 81$ ) or because they declined to participate before randomization ( $n = 59$ ), which was mostly due to a lack of time of the participants. Finally, 239 patients (20.7%) were randomized and used for the ITT analysis. Figure 1 provides an overview of the participant flow and participant numbers used for the ITT and completer analyses. The highest proportion of included patients was recruited via media (64.4%). After completion of the baseline questionnaires, patients were randomized to either TAU ( $n = 113$ ) or mobile CT added to TAU ( $n = 126$ ). In table 1, the baseline demographics of the ITT group are presented. The median number of previous depressive episodes was 4 in both the mobile CT group and the TAU group (IQR = 2.3–2.5 for both). In both groups, the mean time since the last episode was around 8 months (TAU: mean = 7.98, SD = 6.2; MCT: mean = 8.23, SD = 6.5). For 38.1% of the mobile CT group and 37.2% of the TAU group, TAU consisted of no treatment at all; 47.6% of the mobile CT and 51.3% of the TAU group received antidepressant medication treatment, and 21.4% of the mobile CT and 21.2% of the TAU group received care from a mental health professional (e.g. a psychologist or psychiatrist). Most baseline characteristics seemed equally distributed. However, the TAU group had an overall higher severity of the last episode, assessed using the SCID-I, compared to the mobile CT group (30.1% for TAU vs. 15.9% for mobile CT,  $p = 0.029$ ). Given this imbalance, additional ITT analyses were performed while controlling for this variable. During follow-up, a total of 34 (14.2%) participants dropped out of the trial ( $n = 13$  in both groups at 1.5 months,  $n = 3$  in the mobile CT group, and  $n = 5$  in the TAU group at 3 months). After using a test of difference in attrition between cells, we found no difference between dropout rates in the mobile CT and TAU groups ( $\chi^2 = 0.5096$ ,  $p = 0.48$ ). Of the 126 participants randomized to the group of mobile CT added to TAU, 80 participants (63.5%) finished at least 5 modules and were defined as being completers. Therefore, the completer analysis was performed with 193 participants (mobile CT,  $n = 80$ ; TAU,  $n = 113$ ). All variables at baseline were equally distributed in the mobile CT and TAU conditions in the completer group (all  $p > 0.05$ ). In addition, there were no substantial differences between the ITT and completer groups (all  $p < 0.05$ ). However, the ITT group had an earlier age at the first onset of depression than the completers ( $p = 0.029$ , mean = 26.23 and SD = 10.6, and mean = 30.07 and SD = 13.0, respectively).

<sup>3</sup> The baseline characteristics of the ITT and completer groups were compared using  $\chi^2$  tests to evaluate differences in dichotomous variables, and independent-samples *t* tests were applied to normally distributed continuous variables; for nonnormally distributed variables the nonparametric Mann-Whitney *U* statistic was used.



**Fig. 1.** CONSORT flow diagram of participant flow over the 3-month follow-up.

### Mobile CT Usage

Full adherence (all 8 modules finished) was achieved in 53.1% (60/113) of cases. Of the 80 participants who were defined as completers, 80% ( $n = 64/80$ ) finished at least 5 modules within 3 months. The mean amount of total time per therapist per participant during the complete mobile CT was 18 min ( $SD = 8.2$ ). While each participant was invited for a second telephone session with the therapists, only 56.5% of the 113 participants used this option. Only 1 participant used the optional telephone support sessions, which lasted 5 min. The percentage of participants who asked questions via e-mail was 40.5%.

**Mobile Mood Monitor.** Of the 113 participants who finished the first module, during follow-up 13 participants rated their mood and interests as lower than 3 twice

in a row. Their therapists received an automated message about this. Of these, 6 filled in the Q-IDS<sub>R16</sub> after receiving an automatic request.

### Three-Month Course of Depressive Symptoms in the Mobile CT and TAU Groups

The depressive symptoms measured with the IDS-SR<sub>30</sub> increased from baseline to 1.5 months of follow-up in both groups (table 2). However, after 3 months of follow-up a small decrease was observed in the mobile CT group and a considerable increase was noticeable in the TAU group. The results of the LMM analyses are presented in tables 3 and 4. There was a significant linear time trend ( $F = 9.818$ ,  $p < 0.001$ ) and a significant time<sup>2</sup> trend ( $F = 6.788$ ,  $p = 0.010$ ). The interaction between time and treatment indicating the difference in

**Table 1.** Baseline demographic and descriptive characteristics of the study population according to randomized groups

	Mobile CT (n = 126)	TAU (n = 113)	p <sup>a</sup>
Age, years	45.52±10.9	47.48±10.8	0.914
Female gender	100 (79.4)	79 (69.9)	0.092
Marital status			
Single	38 (30.2)	29 (25.7)	0.370
Married or cohabiting	76 (60.3)	71 (62.8)	
Divorced	8 (6.3)	11 (9.7)	
Widowed	2 (1.6)	0 (0.0)	
Missing	2 (1.6)	2 (1.8)	
Education			
Primary school	1 (0.8)	1 (0.9)	0.871
Secondary education	5 (4.0)	8 (7.1)	
Vocational education	40 (31.7)	31 (27.4)	
Preuniversity education	2 (1.6)	3 (2.7)	
Higher education	53 (42.1)	44 (38.9)	
University	25 (19.8)	21 (18.6)	
Missing	0 (0.0)	5 (4.4)	
ADM at recruitment	60 (47.6)	58 (51.3)	0.567
Treatment by a mental health professional	27 (21.4)	24 (21.2)	0.835
Age at the first MDD episode, years	28.67±12.3	30.11 (13.1)	0.293
Median previous MDD episodes (IQR)	4.0 (2.3)	4.0 (2.5)	0.631
Total HRSD <sub>17</sub> <sup>b</sup> , n	3.58±2.8	3.42 (2.9)	0.587
Depressive symptomatology (IDS-SR <sub>30</sub> <sup>b</sup> ), n	16.44±10.5	16.06±9.5	0.172
Severity of the last episode <sup>c</sup>			
Minor	33 (26.2)	23 (20.4)	0.029
Moderate	71 (56.3)	56 (49.5)	
Severe	20 (15.9)	34 (30.1)	
Missing	2 (1.6)	0 (0.0)	

Values are presented as numbers (%) or means ± SD unless otherwise stated. ADM = Antidepressant medication. <sup>a</sup> Based on the  $\chi^2$  statistic for categorical variables and analyses of variance for continuous variables and the Mann-Whitney U test for previous episodes of MDD. <sup>b</sup> Depressive symptoms. <sup>c</sup> Based on the number of SCID-I depression symptoms (5 symptoms corresponds to minor, 6–7 symptoms corresponds to moderate, and 8–9 symptoms corresponds to severe depression).

**Table 2.** Three-month course of depressive symptoms in the mobile CT and TAU groups

Depressive symptomatology	Mobile CT	TAU
Baseline	16.44±10.5	16.06±9.5
6 weeks	18.61±12.2	20.76±12.1
3 months	16.38±10.9	21.52±12.4

Values are presented as means ± SD.

**Table 3.** Three-month course of depressive symptoms in the mobile CT and TAU groups

#### a Unadjusted estimates in the ITT group

Variable	Estimate	95% CI	t	p
Intercept	9.444	4.69 to 14.19	3.909	0.000
Time	9.517	4.02 to 15.02	3.404	0.001
Time <sup>2</sup>	-1.827	-3.21 to -0.45	-2.605	0.010
Mobile CT × time	-1.600	-2.64 to -0.56	-3.022	0.003

#### b Unadjusted estimates in the completer group

Variable	Estimate	95% CI	t	p
Intercept	9.831	4.99 to 14.67	3.993	0.000
Time	9.058	3.54 to 14.58	3.229	0.001
Time <sup>2</sup>	-1.701	-3.08 to -0.32	-2.422	0.016
Mobile CT × time	-2.102	-3.20 to -1.01	-3.776	0.000



**Table 4.** Three-month course of depressive symptoms in the mobile CT and TAU groups

**a** Adjusted estimates in the ITT group

Variable	Estimate	95% CI	t	p
Intercept	5.000	-1.70 to 11.66	1.464	0.144
Time	9.394	3.89 to 14.90	3.358	0.001
Time <sup>2</sup>	-1.817	-3.20 to -0.44	-2.589	0.010
Mobile CT × time	-1.498	-2.54 to -0.46	-2.828	0.005
Severity of the last episode	1.412	-0.40 to 3.22	1.538	0.125
Duration of remission	-0.058	-0.26 to 0.14	-0.575	0.566
Number of episodes	2.075	-0.43 to 4.58	1.630	0.104
Type of aftercare	2.205	-0.39 to 4.80	1.673	0.096

**b** Adjusted estimates in the completer group

Variable	Estimate	95% CI	t	p
Intercept	5.746	1.29 to 12.78	1.606	0.109
Time	9.009	3.48 to 14.53	3.208	0.001
Time <sup>2</sup>	-1.700	-3.08 to -0.31	-2.414	0.016
Mobile CT × time	-2.050	-3.15 to -0.95	-3.665	0.000
Severity of the last episode	1.076	-0.90 to 3.05	1.077	0.283
Duration of remission	-0.080	-0.30 to 0.14	-0.710	0.479
Number of episodes	2.142	-0.56 to 4.84	1.566	0.119
Type of aftercare	1.918	-0.95 to 4.79	1.319	0.189

the linear rate of change between groups, i.e. the treatment effect, was statistically significant ( $F = 9.130$ ,  $p = 0.003$ ). Compared to the TAU group, the rate of change in the IDS-SR<sub>30</sub> score in the mobile CT group was -1.60 points per month ( $t = -3.022$ ,  $p = 0.003$ , 95% CI = -2.64 to -0.56) (table 3a). Repetition of the analysis in the completer group ( $\geq 5$  modules of mobile CT) showed a larger treatment effect, with a between-group difference of -2.10 points per month ( $t = 3.776$ ,  $p = 0.000$ , 95% CI = -3.20 to -1.01) (table 3b). Adjusting for the severity of the last episode, the duration of remission, the type of TAU, and the number of previous episodes did not affect the results of the ITT analysis (table 4a) or the results of the completer group (table 4b). Cohen's  $d$  for the effect of treatment on the depressive symptoms over 3 months was 0.44 (ITT group) and 0.54 (completer group), which indicates a small to moderate effect. In addition, the depressive symptom levels measured with the HRSD<sub>17</sub> interview were higher at the 3-month follow-up in the TAU group compared to the mobile CT group as well (TAU: mean = 5.44, SD = 6.1 vs. mobile CT: mean = 4.25, SD = 4.3;  $p = 0.042$ ).

## Discussion

To the best of our knowledge, this is the first study to examine the effect of mobile Internet-based CT with minimal therapist support as a relapse prevention strategy in remitted/recovered recurrently depressed patients. Given that the depressive symptom levels were very low at baseline (HRSD<sub>17</sub>, mean = 3.52, SD = 2.9), the symptoms were likely to increase over time [4]. This expectation notwithstanding, a small but significant decrease in depressive symptoms over the course of follow-up was observed in the mobile CT condition but not in the TAU condition, in which a pronounced increase was found. The difference between groups was considerably larger when participants finished at least 5 modules of mobile CT. The mean 18 min of total therapist support time per participant (via telephone and e-mail) was far less than mostly found in other studies, where the total time ranges from 180 to 352 min [46, 47]. The rate of full adherence to mobile CT (all modules finished) was 53.1%, which is comparable to the adherence rates for Internet-based depression psychotherapies assessed in ample randomized controlled trials (50–85%) [e.g. 48]. Telephone support is said to increase adherence [49], and our results indicate that, even with limited telephone support from therapists, an Internet-based intervention may generate appreciable adherence rates. However, this only held true for remitted/recovered patients and not for the depressed phase. More information on the topic of support and adherence is needed. Presence and fluctuations of residual depressive symptoms are well known predictors of relapse [19, 24, 50–52]. Residual symptoms may progress and become prodromal symptoms of relapse, and targeting residual symptoms might yield long-term benefits [13, 53]. Judd et al. [54] suggested that prevention of relapse is related to the reduction of residual symptoms with treatment. While there is an indication that the outcome of the prevention of relapse treatment is dependent on residual symptom levels [55], this relation has not always been observed [7, 8, 56]. A longer follow-up is needed to examine whether the effect of mobile CT on relapse is mediated by a decrease in residual symptoms. Alternatively, other potentially modifiable vulnerability factors, such as dealing with (daily) stress, might mediate the effect on relapse. Daily stress was found to predict depressive relapse [20, 56–58]; however, after preventive CT daily stress did not predict relapse anymore [56].

Although these first results on low-intensity preventive treatment using mobile CT in addition to TAU are promising, they have to be interpreted in light of some

study limitations. First, participants were remitted/recovered at the start of the study, and with a follow-up of only 3 months this might have reduced the likelihood of observing treatment effects. However, an effect was observed, and though the effect might seem small during remission/recovery even small increases in depressive symptoms are predictive of relapse/recovery [50]. Therefore, we think it is of value to report these 3-month results. We will continue with a follow-up of 24 months to examine whether this effect is maintained. Nevertheless, replication will be required before firm conclusions can be drawn about the longer-term preventive effects of mobile CT as an add-on to TAU. Second, the information on depressive symptoms was restricted to the follow-up assessments; therefore, variations in between could have been missed. Third, although the SCID-I interview is known as the gold standard for assessing current and lifetime depression, we conducted the SCID-I interview via telephone. This could have influenced the validity; however, in previous studies diagnostic interviews via telephone have proven to be valid [59]. Fourth, the number of previous episodes of depression was retrospectively assessed with the SCID-I and recall could have been affected by memory bias. Fifth, although we did not find any differences in the use of mental health care and antidepressant medication treatment (yes vs. no), we cannot fully rule out that there was no difference between the conditions on the frequency of mental health care visits and antidepressant doses. Sixth, LMM provided valid estimates under the assumption that data were missing at random. Although we consider this assumption likely, since we included multiple variables with observed values into our models, it can-

not be proven. Nevertheless, only 16 participants in the mobile CT group and 18 participants in the TAU group were lost to follow-up, which limits the potential for bias. Finally, we did not control for the effects of all nonspecific factors. For example, motivation and expectations can affect the treatment outcome [5, 60]. Overall, for recurrently depressed patients, ongoing monitoring and preventive treatment are internationally recommended by clinical guidelines [24, 26]. Promising effects of mobile CT on the 3-month course of residual depressive symptoms were demonstrated in remitted/recovered recurrently depressed patients compared to TAU, irrespective of the type of TAU, including antidepressant medication treatment. Replication is necessary and future studies should examine the preventive effects of mobile CT compared to face-to-face preventive strategies.

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