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No Sustainable Effects of an Internet-Based Relapse Prevention Program over 24 Months in Recurrent Depression: Primary Outcomes of a Randomized Controlled Trial

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As major depressive disorder (MDD) is highly recurrent, international practice guidelines recommend maintenance antidepressant medication and/or psychological treatment after acute MDD to prevent relapse/recurrence [1]. Preventive cognitive therapy (PCT) is specifically developed for relapse prevention in depression and is effective in reducing relapse/recurrence over 2–10 years [2, 3]. Since resources in clinical practice are scarce, internet-based relapse prevention programs might be a promising alternative. Small to moderate effects of internet-based interventions were found without therapist support and higher effects with therapist support [4]. The short-term (secondary) results of the current randomized controlled trial showed a more favorable course of depressive symptoms over 3 months in participants receiving an internet-based version of PCT (mobile cognitive therapy, M-CT) added to treatment as usual (TAU) compared to TAU alone [5]. Thus far, little is known about the long-term effectiveness of internet-based relapse prevention programs. Only one study in partially remitted participants has examined the effect of a 10-week guided internet-based relapse prevention program for recurrent depression over 24 months, showing promising results [6]. The aim of this single-blind 2-arm parallel randomized controlled trial (trial registration NTR2503; approved by METIGG, an independent medical ethics committee) was to examine whether adding M-CT to TAU is clinically superior to TAU alone over 24 months (primary outcome) in remitted recurrently depressed individuals. Details about the study design can be found elsewhere [7].

Individuals were recruited via media, general practitioners, and mental health care institutions, and screened for eligibility with a telephone version of the Structured Clinical Interview for DSM-IV axis I disorders (SCID-I) and the Hamilton Rating Scale for Depression (HRSD). Individuals aged between 18 and 65 years were included if they had experienced at least 2 (unipolar) depressive episodes, had been in remission for at least 8 weeks but no longer than 24 months according to the DSM-IV assessed with the SCID-I, and had a current score of ≤10 on the HRSD. Participants provided informed consent prior to randomization and were included between mid-September 2010 and August 2013. Simple randomization was undertaken (1:1 ratio) by an independent researcher using computer-generated random numbers with STATA. M-CT consisted of 8 online modules based on PCT, a face-to-face treatment targeting cognitive vulnerability factors. In M-CT, participants were recommended to work on 1 module per week, taking approximately 20 min plus 10-min homework assignments. Minimal therapist support was administered, yielding a minimum of 2 telephone sessions with a maximum duration of 30 min with a licensed clinical psychologist. TAU consisted of no treatment, (after) care by a general practitioner, or (after) care in a specialized mental health care center.

To detect an absolute difference of 20% in the cumulative incidence of depressive relapse/recurrence over 24 months, with 80% power, a 2-sided 5% alpha level, and assuming relapses/recurrences in 50% of the participants and a 20% attrition rate, we aimed to include 268 participants. The intention-to-treat (ITT) principle was used, analyzing all participants regardless of adherence to the randomized condition. The primary outcome was time-related proportion of relapse/recurrence according to the DSM-IV assessed with the SCID-I by blinded interviewers after 3, 12, and 24 months. Treatment response conditional on number of previous depressive episodes assessed with the SCID-I, chronic somatic illness assessed with the Nemesis Somatic illnesses list, and type of TAU were examined explicitly. Secondary outcomes were number of relapses/recurrences based on DSM-IV criteria assessed with the SCID-I and the level of depressive symptoms assessed with the Inventory of Depressive Symptomatology Self-Report (IDS-SR) at 10 intervals.

In total, 288 individuals were eligible, of whom 264 were randomized to M-CT added to TAU ($n = 132$) or TAU alone ($n = 132$). Most participants were highly educated (61%) and female (75%), with a mean age of 46 years (±10.8) and median number of previous depressive episodes of 4. Overall, 29 participants dropped out immediately after randomization and 24 were lost to follow-up.

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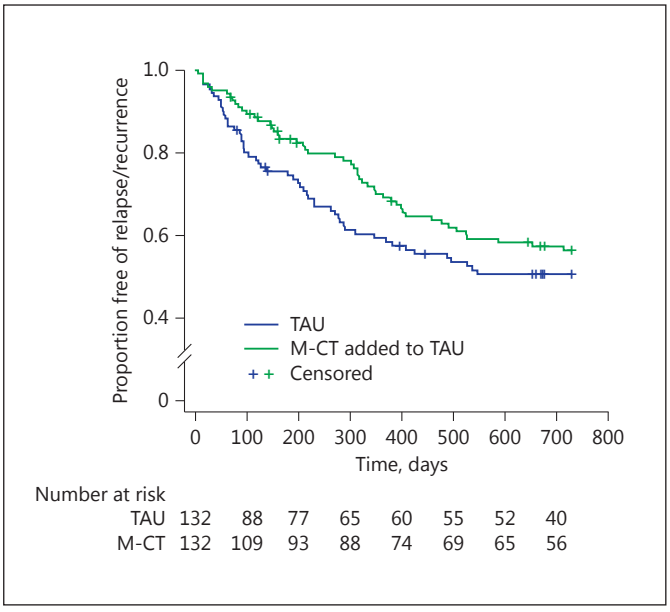

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Fig. 1. Survival curves over 24 months in mobile cognitive therapy (M-CT) added to treatment as usual (TAU) (n = 132) and TAU alone (n = 132).

Baseline characteristics in the ITT sample and of participants with follow-up data were comparable and balanced over treatment conditions, except for a slight imbalance in gender and severity of the last depressive episode. Mean total therapist support in M-CT was 17.3 min per participant (range: 0–70), and 68% (n = 90) finished at least 5 modules.

After 24 months, the cumulative relapse/recurrence rate according to Kaplan-Meier estimates was 0.44 in M-CT and 0.49 in TAU. Figure 1 shows that over time, the proportion free of relapse/recurrence was higher in M-CT compared to TAU, but this effect was not statistically significant (log-rank $X^2[1] = 1.73$, $p = 0.189$). The Cox regression showed no statistically significant difference between conditions (hazard ratio, HR = 0.77, 95% CI = 0.53–1.14, $p = 0.190$). Treatment condition did not interact with number of previous depressive episodes (HR = 0.74, 95% CI = 0.34–1.61, $p = 0.447$), chronic somatic illness (HR = 0.60, 95% CI = 0.26–1.35, $p = 0.216$), and type of TAU (HR = 0.87, 95% CI = 0.57–1.35, $p = 0.543$). Sensitivity analyses controlling for imbalanced baseline variables, including only participants that completed at least 5 modules, and using multiple imputation to address missing data, yielded comparable results. No statistically significant results were found on secondary outcomes (Poisson regression on number of relapses: incidence rate ratio = 0.87, 95% CI = 0.64–1.19, $p = 0.393$; linear mixed models on depressive symptoms: B = 0.31, 95% CI = –0.09–0.70, $p = 0.131$). Additional information about the methods and results can be found at https://www.claudibockting.com/research/supplementary-material.

We did not find statistically significant effects on our primary and secondary outcomes over 24 months, which indicates that M-CT has no long-term protective effect. This finding is in line with a recent meta-analysis demonstrating that guided and unguided internet-based treatments were effective in the short term but not beyond 6 months posttreatment [8]. However, our sobering long-term findings contrast with our initial finding where M-CT resulted in a favorable course of depressive symptoms over 3 months [5] and with the promising findings of Holländare et al. [6] in partially remitted individuals using an internet-based relapse prevention program. Long-term effects of face-to-face PCT and other face-to-face relapse prevention strategies such as mindfulness-based cognitive therapy and well-being therapy have been demonstrated [9]. As internet-based interventions have better effects with therapy support [4], we hypothesize that actively prescribing more support might have maintained our short-term results. In the guided internet-based relapse prevention program of Holländare et al. [6], the mean therapist time was 150 min whereas in our study this was 17.3 min. Moreover, in a randomized controlled trial examining a similar population, PCT administered as bibliotherapy with 110.2 min of therapy support did significantly reduce the risk of relapse/recurrence after 12 months [10]. Future studies should examine whether increased therapist support is associated with better effects in relapse prevention studies.

Since most participants in M-CT used minimal therapist support, we were not able to examine whether high therapist support is associated with better outcomes. Several other limitations need to be acknowledged, including the generalizability (relatively high number of highly educated females) and the fact that we could not examine the effects of mood monitoring in M-CT on depressive relapse/recurrence.

In contrast to our expectations, a psychological internet-based relapse prevention program added to TAU did not result in a substantially better protection against relapse/recurrence compared to TAU alone. Future studies should examine the long-term effectiveness of internet-based interventions and the optimal dosage of therapist support.

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Disclosure Statement

Claudi L.H. Bockting and Evelien van Valen developed M-CT, which was integrated in the platform of the Trimbos Institute in collaboration with Filip Smit. No other disclosures are reported.

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