Long-Term Effects of Preventive Cognitive Therapy in Recurrent Depression: A 5.5-Year Follow-Up Study

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Objective: Major depressive disorder (MDD) was projected to rank second on a list of 15 major diseases in terms of burden in 2030. A crucial part of the treatment of depression is the prevention of relapse/recurrence in high-risk groups, ie, recurrently depressed patients. The long-term preventive effects of group cognitive therapy (CT) in preventing relapse/recurrence in recurrent depression are not known. This article reports on the long-term (5.5-year) outcome of a randomized controlled trial to prevent relapse/recurrence in patients with recurrent depression. We specifically evaluated the long-term effects of CT in relation to the number of previous episodes experienced.

Method: From February through September 2000, patients with recurrent depression (*DSM-IV*–diagnosed) who were in remission (N = 172) were recruited from primary and specialty care facilities. They were randomly assigned to treatment as usual (TAU) versus TAU augmented with brief group CT. The primary outcome measure was time to relapse/recurrence, which was assessed over 5.5 years.

Results: Over 5.5 years, augmenting TAU with CT resulted in a significant protective effect ($P = .003$), which intensified with the number of previous depressive episodes experienced. For patients with 4 or more previous episodes (52% of the sample), CT significantly reduced cumulative relapse/recurrence from 95% to 75% (medium effect size).

Conclusions: Our findings indicate that brief CT, started after remission from a depressive episode on diverse types of treatment in patients with multiple prior episodes, has long-term preventive effects for at least 5.5 years. Implementation of brief relapse prevention CT should be considered in the continued care of patients with recurrent depression.

Trial Registration: ccmo-online.nl Identifier: NTR454

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Recently, major depressive disorder (MDD) was projected to rank second on a list of 15 major diseases in terms of burden in 2030.[1] This major contribution of MDD to disability is largely due to its highly recurrent nature.[2] Accordingly, a crucial part of the treatment and management of depression is the prevention of these recurrences in high-risk groups, ie, recurrently depressed patients. There is accumulating evidence that cognitive (behavior) therapy (CT) applied during the acute depressed phase has enduring preventive effects on relapse and recurrence,[3–7] as recently summarized in a meta-analysis.[6] Additionally, sequential treatment in which CT is offered in other higher-risk groups for recurrence (ie, partially remitted depressed patients) also seems an effective strategy to prevent recurrence.[8,9] A sequential approach in which CT is offered to recovered recurrently depressed patients, remitted on diverse treatments (CT, antidepressant treatment, psychological treatment), is effective in preventing relapse and recurrence in recurrently depressed patients.[6,10]

However, so far, the long-term effects of this sequential approach are unknown in recurrent depression. Only 1 preliminary study suggests long-term effects of CT over 6 years as applied in remitted recurrently depressed patients.[11] In this relatively small trial (N = 40), successfully treated recurrently depressed patients who were currently taking antidepressants were randomly assigned to CT or clinical management (CM). In both groups, antidepressant treatment was withdrawn. Cognitive therapy resulted, over 6-year follow-up, in a significantly lower relapse rate than CM (40% vs 90% relapse). However, these results have to be considered as preliminary because the sample size was far too small for the evaluation of long-term effects and because CT was delivered by 1 therapist only who was also the researcher. In addition, 13% (CT, 60%; CM, 40%) of the sample was not able to withdraw from antidepressant treatment and was excluded from analysis.

We therefore set up a study with a considerable sample size that evaluates long-term effects (5.5 years) of CT applied

For Clinical Use

- Preventing relapse in depression is a must in patients who have remitted from multiple episodes.
- Antidepressant continuation and maintenance treatment does not seem to prevent relapse and recurrence for a large proportion of patients.
- Implementing brief relapse prevention cognitive therapy for recurrent depression could be a type of continued care that at least disrupts the rhythm of depression.

in remitted recurrently depressed patients and delivered by several therapists. Brief group CT was offered after remission on various types of treatment typically provided in the acute treatment of depression, ie, medication and/or psychological therapy or no treatment at all.[10] Remitted patients (N = 172) were randomly assigned to treatment as usual (TAU), including continuation of pharmacotherapy, or to TAU augmented with brief CT (TAU + CT). At the 2-year follow-up, augmenting TAU with CT resulted in a significant protective effect that intensified with an increasing number of previous episodes experienced,[10] ie, the most well-known predictor of relapse/recurrence.[12,13] We found that for patients with 5 or more previous episodes (41% of the sample), CT reduced relapse/recurrence significantly from 72% to 46%.[10] In our study, we therefore specifically evaluated the effects of CT in relation to the number of previous episodes. The present article reports on the duration of the effects of CT in preventing relapse/recurrence in recurrently depressed patients at 5.5-year follow-up.

METHOD

Patients

To be eligible, patients had to meet the following criteria: experienced at least 2 major depressive episodes (MDEs) in the previous 5 years, as defined according to the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*)[14] and assessed with the Structured Clinical Interview for *DSM-IV* (SCID)[15] administered by trained interviewers; currently in remission, according to *DSM-IV* criteria, for longer than 10 weeks but no longer than 2 years (ie, a high-risk group for relapse/recurrence); and obtained a current score of < 10 on the Hamilton Depression Rating Scale.[16]

Exclusion criteria were current mania or hypomania or a history of bipolar illness; any psychotic disorder (current and previous); organic brain damage; alcohol or drug misuse; predominant anxiety disorder; recent electroconvulsive therapy; recent cognitive treatment or receiving CT at the start of the study; and current psychotherapy with a frequency of more than 2 times a month (for patient flow, see Figure 1). Patients were recruited from February 2000 through September 2000 in The Netherlands at psychiatric centers (31% of the patients) and through media announcements (69% of the patients) and followed up through 2006. After a complete description of the study to the subjects, written informed consent was obtained prior to random assignment of the patients. The protocol was approved by the relevant institutional ethics review committees.

Patients were screened on inclusion and exclusion criteria with the telephone version of the SCID. The kappa statistic (κ) for interrater agreement between the interviewers (psychologist/research assistants) regarding inclusion or exclusion criteria, as based on audiotaped interviews, was 0.77 (good/excellent agreement). Patients meeting the inclusion criteria were randomly allocated to TAU or TAU + CT.

Randomization was organized and administered by an independent research associate using random permutated blocks and was stratified by study location and type of aftercare (family physician, psychiatric center, or no aftercare). Consecutively numbered sealed envelopes contained computer-generated cards with concealed assignment codes.

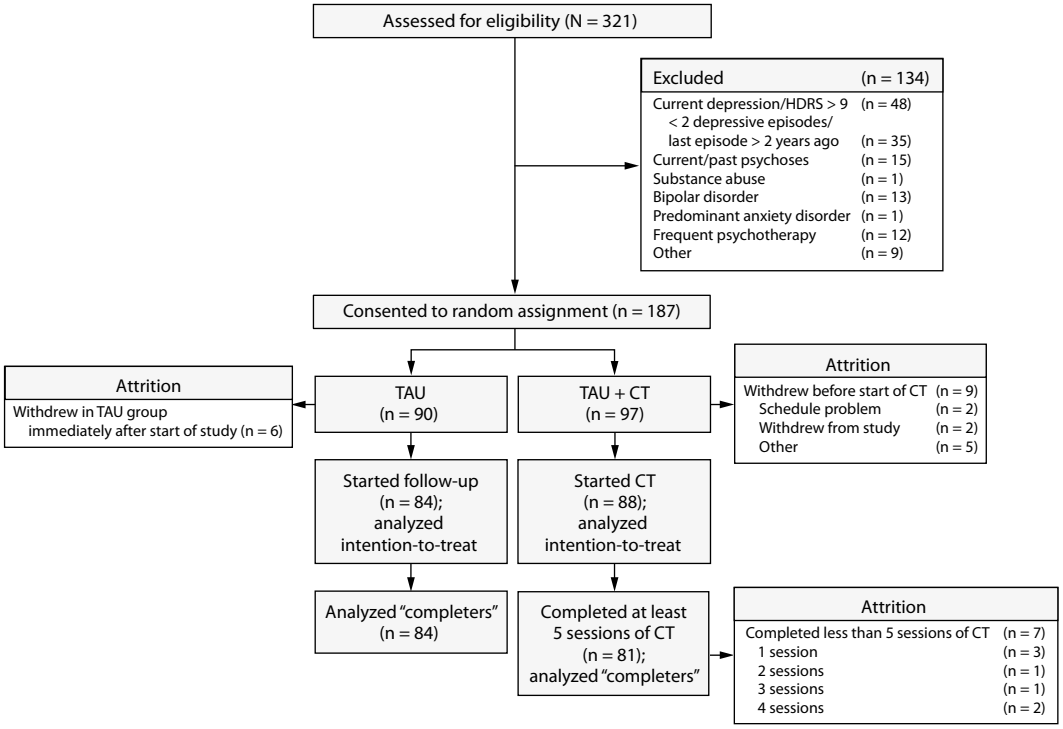
Treatment

Cognitive therapy. Cognitive therapy in the experimental condition involved 8 weekly 2-hour group sessions (7–12 members). We used a closed format with each CT session following a fixed structure, with agenda setting, review of homework, explanation of rationale of each session, and assignment of homework. Nine specifically trained (16 hours of training) psychologists (1 was the principal investigator) delivered the manualized prevention module; all were fully trained cognitive therapists. All intervention group sessions were audiotaped to enable treatment integrity to be evaluated using a checklist of all particular interventions. Any adherence or competence issues were resolved with the therapist prior to the subsequent session.

The preventive CT was focused mainly on identifying and changing dysfunctional attitudes, enhancing specific memories of positive experiences by keeping a diary of positive experiences, and formulating specific relapse/recurrence prevention strategies[10] (treatment manual available from first author on request).

Treatment as usual. Treatment as usual involved "naturalistic" care (ie, standard treatment [including no treatment]) as typically provided by the referring agencies. There was

Figure 1. Flow Diagram of Patients Through Follow-Up, Including Attrition



Abbreviations: CT = cognitive therapy, HDRS = Hamilton Depression Rating Scale, TAU = treatment as usual.

no restriction on the use of pharmacotherapy, including use of antidepressants, during the period from entry through follow-up. Patients agreed to report the use of medication, counseling, and visits to general practitioners over the follow-up period.[10]

Outcome

Primary outcome: relapse/recurrence. Relapse/recurrence was assessed using the SCID-I. At 5 follow-up points (3, 12, 24, 36, and 66 months), current and past MDEs were checked. To maintain the assessors' unawareness of treatment condition, we instructed participants not to reveal this information to the interviewers. The κ for interrater agreement on relapse/recurrence between the interviewers and the psychiatrist ranged over the follow-up period from 0.94 to 0.96, indicating high agreement. The severity of a relapse during the follow-up period was assessed by the SCID (low, < 6 symptoms; moderate, 6–7 symptoms; severe, 8–9 symptoms).

Medication and other psychological treatment. Every 3 months for the first 2 years, information on antidepressant medication (type and dosage) and other psychological treatment (number of counseling or psychotherapy sessions) over the previous months was monitored with the Trimbos/iMTA Self-Report Questionnaire for Costs Associated with Psychiatric Illness.[17] In addition, information on continuous versus intermitted use of antidepressants was collected using a structured medication interview (for a full description see Mathers and Loncar[1] and Bockting et al[18]).

Statistical Method

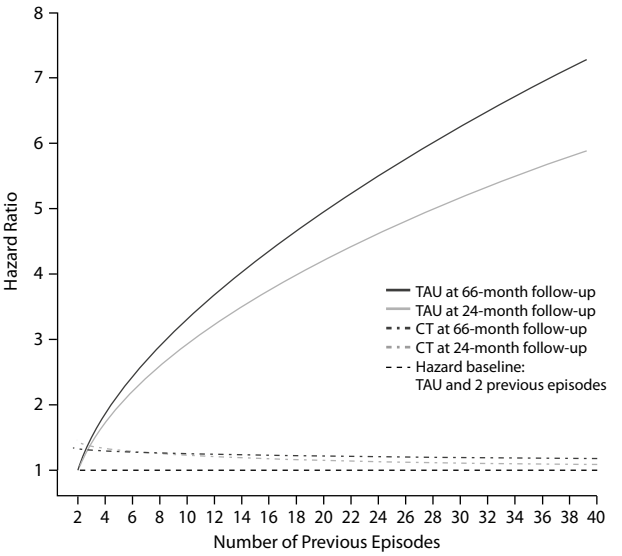
To detect time to first relapse/recurrence over 5.5 years, survival analyses were conducted in 2 steps. First, a proportional hazards approach to survival analysis (Cox regression) was used, with relapse/recurrence as the dependent variable and treatment condition as the independent variable. The analysis was performed using an intention-to-treat (ITT) approach. In the second step, we fitted a proportional hazards model with relapse/recurrence as the dependent variable and treatment condition, number of previous episodes, and the interaction of treatment condition with the number of previous episodes as independent variables. This model was used to estimate survival in the TAU + CT group, stratified on the basis of the number of previous episodes. The estimated hazard ratios were defined relative to the TAU group with 2 previous MDEs. The end point for all survival analyses was relapse/recurrence. Patients who dropped out or had experienced no relapse/recurrence during the study period were considered censored. We used Cox regression analyses, including the stratification variables (ie, site, type of treatment), to assess the individual confounding or modifying effects of each of these stratification variables on the treatment effect parameter. As no effects of site or type of treatment on the

Table 1. Demographic and Clinical Characteristics at Start of the Study

Characteristic	TAU + CT (n = 88)	TAU (n = 84)
Sex, female, %	73	74
Race, white, %	98	99
Age, y, mean ± SD	45.9 ± 9.1	43.4 ± 9.8
Years of education, mean ± SD	14.1 ± 2.5	14.4 ± 2.6
Marital status, %		
Single	19	29
Married/cohabiting	59	57
Divorced/widowed	22	12
Type of current treatment, %		
Family doctor	32	25
Psychiatric help	29	33
No treatment	39	42
Antidepressant medication at entry, %	52	50
HDRS-17 score, mean ± SD	3.8 ± 2.8	3.7 ± 2.9
Previous episodes		
> 2 previous episodes, %	88	75
Median of previous episodes ± IQR	4 ± 3–7	3 ± 2–6
Age at first onset, y, mean ± SD	28.7 ± 12.6	28.1 ± 12.5

Abbreviations: CT = cognitive therapy, HDRS = Hamilton Depression Rating Scale, IQR = interquartile range, MDE = major depressive episode, TAU = treatment as usual.

Figure 2. Hazard Ratios of TAU + CT and TAU With the Number of Previous Episodes (ITT, N = 172) for 2-Year and 5.5-Year Follow-Up



Abbreviations: CT = cognitive therapy, ITT = intention-to-treat, MDEs = major depressive episodes, TAU = treatment as usual.

effect of treatment condition on relapse/recurrence were observed, further analyses were performed without these stratifying variables.

In secondary analyses, we explored the effects of treatment on percentage of time free of depression, severity of the MDE, and number of times patients experienced a relapse/recurrence during the 5.5 years of follow-up. We applied the general linear model univariate analysis of variance (ANOVA) approach with depression severity as the dependent variable and treatment condition, number of previous episodes (< 4 vs ≥ 4), and the interaction of treatment condition by number of previous episodes as the independent variables.

To compare the severity of relapse/recurrence, we computed the mean severity over all relapses (1. light relapse, 2. moderate relapse, 3. severe relapse). To compare the number of times a patient relapsed, differences in follow-up time were converted to the number of relapses per 5.5 years at risk.

RESULTS

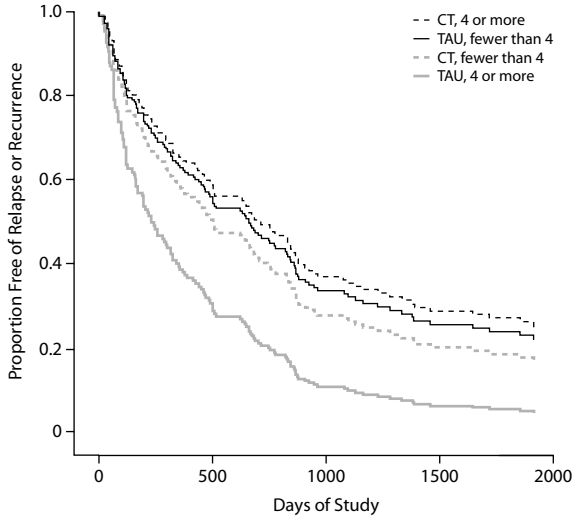
Overall, 135 patients (79%; N = 172) had experienced relapse/recurrence at least once at the 5.5-year follow-up point.

Demographic and clinical characteristics of the ITT group are summarized in Table 1. Both groups were comparable on each of the variables (all *P* values > .10) except for number of previous episodes, $\chi^2_{1,172} = 4.43$, $P = .04$ (77 of 88 from the TAU + CT group had more than 2 previous episodes vs 63 of 84 from the TAU group); the subjective experience of daily hassles, $t_{170} = 2.27$, $P = .03$ (TAU + CT group, mean = 3.5, SD = 1.0; TAU group, mean = 3.8, SD = 0.8; higher in TAU group); and the experience of negative life events before the 16th year, $\chi^2_{1,172} = 6.74$, $P = .01$ (84 of 88 in the TAU + CT group experienced negative life events vs 70 of 84 in the TAU group). In both the ITT analyses and completers analyses for each individual potential confounder, we detected no confounding effect of treatment.[10] However, a modifying effect did appear to be present for the number of previous depressive episodes. Consequently, the number of previous episodes and the interaction of previous episodes with treatment condition were included as covariates in all of the analyses.

Effectiveness of Cognitive Therapy

As in 2-year follow-up, difference in outcome was dependent on the number of previous MDEs (ITT). However, analyses for treatment condition effect alone revealed a nonsignificant difference at the level of a trend ($Wald_{1,172} = 2.86$, $P = .09$, hazard ratio = .747, 95% CI, 0.533–1.047). Cox regression analyses, with previous episodes as covariate, revealed a significant interaction effect between previous episodes and treatment condition, $Wald_{1,172} = 8.80$, $P = .003$, hazard ratio = .561, 95% CI, 0.383–0.822); for treatment condition in model with interaction, $Wald_{1,172} = .959$, $P = .33$, hazard ratio = 1.334, 95% CI, 0.749–2.375; and for number of previous episodes effect in this model, $Wald_{1,172} = 16.655$, $P = .000$, hazard ratio = 1.719, 95% CI, 1.325–2.231. Results are closely similar for the completers group (attended ≥ 4 CT sessions, n = 165; for interaction with previous episodes effect, $Wald_1 = 8.363$, $P = .004$, hazard ratio = .358, 95% CI, 0.179–0.718).

Figure 3. Proportion of Relapse/Recurrence in Patients With 4 Previous Episodes and Patients With 4 or More Previous Episodes in the TAU Group Versus the TAU + CT Group Over 5.5-Year Follow-Up



	Semester										
Group	1	2	3	4	5	6	7	8	9	10	11
TAU + CT, 4 or more (n = 49)	40 (9, 0)	33 (16, 0)	29 (20, 0)	24 (25, 0)	17 (31, 1)	14 (33, 2)	13 (34, 2)	11 (36, 2)	11 (36, 2)	11 (36, 2)	1 (36, 12)
TAU, fewer than 4 (n = 43)	33 (10, 0)	28 (15, 0)	20 (22, 1)	18 (23, 2)	15 (26, 2)	11 (28, 4)	10 (29, 4)	9 (30, 4)	9 (30, 4)	9 (30, 4)	0 (32, 11)
TAU + CT, fewer than 4 (n = 39)	28 (11, 0)	22 (17, 0)	18 (21, 0)	13 (25, 1)	9 (28, 2)	9 (28, 2)	9 (28, 2)	8 (29, 2)	8 (29, 2)	6 (31, 2)	2 (31, 6)
TAU, 4 or more (n = 41)	20 (19, 2)	14 (25, 2)	12 (27, 2)	10 (29, 2)	6 (33, 2)	4 (34, 3)	2 (35, 4)	1 (36, 4)	1 (36, 4)	1 (36, 4)	0 (36, 5)

Abbreviations: CT = cognitive therapy, TAU = treatment as usual.

To compare survival in the 2 groups for the number of previous episodes, the fitted proportional hazards model was used to estimate survival in both groups stratified on number of previous episodes. The hazard ratios were defined relative to TAU patients with 2 previous episodes in the TAU group. An increasing hazard ratio for TAU indicates that the risk of a relapse/recurrence increases with the number of previous episodes. Figure 2 shows that for patients in the TAU group, their hazard increased (their survival prospect decreased) with the number of previous episodes (ITT) for 2-year and 5.5-year follow-up. Also after 5.5-year follow-up, for patients in the TAU + CT group, the effect of the number of previous episodes is neutralized. For both follow-up periods, for an increasing number of previous episodes, CT tended to have an increasing protective effect. The protective effect over 5.5 years is comparable to the effect over 2 years, and the lines diverge even more over 5.5 years, ie, difference in survival prospect between TAU and TAU + CT patients increases over 5.5 years.

According to this model, the beneficial effect of CT became statistically significant at 4 or more previous episodes. Dichotomization of the number of previous episodes in fewer than 4 versus 4 or more previous episodes revealed a significant interaction effect between treatment condition and previous episodes, $\text{Wald}_{1,172} = 7.76$, $P = .02$, hazard ratio = .379, 95% CI, 0.192–0.750; for treatment condition effect, $\text{Wald}_{1,172} = .43$, $P = .51$, hazard ratio = 1.179, 95% CI, 0.719–1.934; and for dichotomized number of previous episodes effect, $\text{Wald}_{1,172} = 8.48$, $P = .004$, hazard ratio = 2.044, 95% CI, 1.263–3.306). The mean survival time for the group of patients with fewer than 4 episodes in the TAU + CT group was 774.3 weeks, 95% CI, 541.9–1006.6 (median 502.0), and for TAU group, mean survival time was 868.5 weeks, 95% CI, 641.8–1095.3 (median 502.0). For patients with 4 or more episodes in the TAU + CT group, mean survival time was 916.4 weeks, 95% CI, 707.3–1125.6 (median 713), and for the TAU group, mean survival time was 440.1 weeks, 95% CI, 277.4–602.8 (median 205.0).

Figure 3 shows the survival curves comparing cumulative relapse/recurrence in the TAU + CT group and the TAU group for patients with fewer than 4 previous episodes (82% vs 79%; TAU + CT, n = 39 vs TAU, n = 43, respectively) versus those with 4 or more previous episodes (75% vs 95%; TAU + CT, n = 49 vs TAU, n = 41, respectively). Figure 3 shows only small differences (log-rank test and Bonferroni adjustment, 2 comparisons, $P < .025$) between TAU + CT and TAU for the group of patients with fewer than 4 episodes, $\chi^2_{1,82} = 0.40$, $P = .528$. For patients with 4 or more previous episodes, CT did significantly reduce relapse/recurrence compared to TAU, $\chi^2_{1,90} = 11.53$, $P < .001$.

Over the total study period of 66 months, the Kaplan-Meier cumulative rate for relapse/recurrence for the 90 patients with 4 or more previous episodes was 95% for TAU patients (95% CI, 83%–100%; n = 41) and 75% for TAU + CT patients (95% CI, 61%–86%; n = 49), a 20% difference in favor of the TAU + CT group. In the 82 patients with fewer

than 4 previous episodes, the figures for TAU patients were 79% (95% CI, 64%–90%; n = 43) compared with 82% (95% CI, 67%–93%; n = 39) for TAU + CT patients.

Secondary Outcomes

We also explored the effect of treatment on 3 secondary outcomes: severity of relapse, percentage of depression-free time, and number of times patients experienced relapse/recurrence during the 5.5-year follow-up (total number of relapses = 351). Overall, there was no difference on these 3 outcomes between the 2 treatment groups (all *P* values > .10). Three general linear model univariate ANOVAs with treatment condition and number of previous episodes (< 4 vs ≥ 4) as the dependent variables and the interaction of treatment condition by number of previous episodes as the independent variables also revealed no significant interaction between treatment condition and previous episodes on these 3 outcomes: severity of relapses, $F_{1,131} = .071$, mean square = 10.236, $P = .790$; multiple relapses, $F_{1,131} = .002$, mean square = .006, $P = .964$; and the percentage of time free of depression during follow-up in patients that relapsed, $F_{1,131} = .019$, mean square = 4.703, $P = .891$.

DISCUSSION

In patients with MDD at high risk for recurrence (ie, patients with multiple previous episodes), an 8-session preventive group cognitive therapy started after remission had a substantial and enduring effect on relapse/recurrence over a 5.5-year follow-up period. Augmenting TAU with CT resulted in a significant protective effect over this follow-up period, which intensified with the number of previous MDEs experienced by the patient. More specifically, the present findings show that preventive cognitive treatment significantly reduced relapse/recurrence for high-risk patients who experienced approximately 4 or more previous episodes (52% of the sample) and were in remission following various treatments. Of the patients with 4 or more previous episodes, the cumulative relapse/recurrence rate was 95% versus 75%, respectively, in the TAU versus the CT group (h = 0.62; medium effect size). As reported previously, the beneficial effect observed in the TAU + CT group could not be attributed over the first 2 years of follow-up to other psychological treatments or use of antidepressant medication.[10]

These findings are in line with prophylactic effects of acute CT,[3,6,7] long-term prophylactic effects of CT in partially remitted patients over up to 3.5 years,[8,9] and with the preliminary results of the effects of sequential CT in remitted recurrently depressed patients as well as in patients with residual depressive symptoms as reported by Fava and colleagues,[11,19] (both studies over a comparable follow-up period of 6 years).

The apparent indication of the number of episodes experienced for CT to be beneficial should be interpreted with caution because of the modest sample size. Cognitive therapy seemed to have no significant protective effect on patients with 2 previous episodes, in line with some other relapse prevention studies.[20,21] Several explanations have been offered for this differential effect. The subtype hypothesis[10,20] states that some categories of depression may be closely associated with reaction to life events, possibly reflecting the group of patients with fewer previous episodes in our study. The other type of depression may be brought about by rumination, reflecting the group of patients with a higher number of episodes. Another hypothesis presumes that relapse/recurrence in patients with more previous episodes is thought to be attributable to autonomous relapse/recurrence processes involving reactivation of depressogenic thinking patterns by dysphoria. With repeated experiences of episodes of major depression, less environmental stress is required to provoke relapse/recurrence.[22] The prophylactic effect of CT (including mindfulness interventions) may arise from disruption of those processes at times of potential relapse/recurrence by reducing the extent to which patterns of depressive thinking reactivated by sad moods could feed factors responsible for relapse/recurrence.[20,23] It may be that the group of patients characterized by a lower age at onset, as previously reported,[10,21] and more previous episodes suffers from a more biologic subtype of depression with a weaker link between stress and relapse/recurrence.

Alternatively, the differential effect of relapse prevention CT could be simply explained by a time effect (in general, a longer time to relapse in patients with 2 previous episodes), since other relapse prevention studies have a maximum 2-year follow-up. We found some support for this time effect in our 5.5-year follow-up results; the apparent indication of the number of episodes experienced for CT to be beneficial seemed decreased compared to our 2-year follow-up. (CT is effective in patients with 3 previous episodes at the level of a trend, and in patients with 4 or more previous episodes significantly, compared to 5 of more previous episodes with a 2-year follow-up.) Long-term studies including at least 10 years of follow-up are needed to rule out whether patients with fewer episodes can benefit from preventive psychological strategies.

We are not aware of any other follow-up study including 172 patients that evaluated the true long-term effects of a brief psychological intervention on preventing relapse/recurrence in recurrent depression. Our patient group included patients remitted on antidepressants, other psychotherapies, psychiatric help, counseling, or no treatment at all, as typically provided in clinical practice. Moreover, there were no restrictions in using medication at entry to the study. Therefore, this study was designed to maximize external validity, which suggests good generalizability of the findings.

There were several limitations that need to be acknowledged. Although this long-term follow-up trial is the first study with a considerable sample size, the sizes decreased over time; therefore, these findings require replication. A

limitation of the present design is that there was no control for nonspecific factors, such as extra attention and group participation. In addition, it is unclear whether the beneficial effect was attributable to specific skills in CT or to the total package of TAU in combination with CT. Future research is necessary to control for these nonspecific factors. Finally, although the beneficial effect observed in the CT group could not be attributed to other psychological treatments or use of antidepressant medication over the first 2 years, we could not completely rule out if these treatments influenced the effect over the last 3.5 years.

In summary, our findings extend the evidence that sequential, brief CT after remission has long-term effects in preventing relapse/recurrence in high-risk groups for recurrence in primary care and specialty care. Adding this brief group CT, at relatively low costs, to regular care (or to no care at all) may provide us with an important tool to protect a high-risk group from relapse/recurrence. Despite promising evidence on the prolonged effects of relapse prevention therapy for a couple of years, further research into the endurance of acute CT and relapse prevention CT is necessary.

Besides a clinically significant reduction of relapse/recurrence using CT, we should be aware that the actual relapse rates in recurrent depression are still dramatically high, as they are also high in the group of patients in this study that received relapse prevention CT. Unfortunately, use of antidepressants does not seem to be the answer to preventing relapse/recurrence for a large proportion of patients. Cognitive therapy during the acute phase of depression is not available to a large proportion of patients and does not reduce recurrence rates sufficiently.[24] Therefore, we should join efforts from different perspectives and disciplines to bring relapse rates down and evaluate disease management programs (including long-term monitoring of this high-risk group). Alternative combinations of treatment strategies should be evaluated in randomized controlled trials, such as offering relapse prevention CT while stopping antidepressant treatment compared to continuation of antidepressant treatment and a placebo continuation arm. Given the recent positive results on acute behavioral activation, this intervention should be further evaluated as an alternative preventive strategy, and easily implemented strategies should be developed and evaluated, like E-mental health computer-based programs.[7,25,26] Further research on essential ingredients of psychological interventions and what works for whom gives us the opportunity to develop more effective psychological interventions for treating and preventing recurrence.

For now, implementing brief relapse prevention CT for recurrent depression could be a type of continued care that at least disrupts the rhythm of depression. Future research will give us an indication of how many years the rhythm can be disrupted and how we can bring relapse rates further down, ie, prevent immense human misery in patients and their families.

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration–approved labeling has been presented in this article.
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