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Cognitive therapy to prevent depressive relapse in adults

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The high prevalence, frequent relapse, and recurrence of major depressive disorder (MDD) increase its personal and societal costs. Cognitive therapy (CT) aims to decrease depressive symptoms and prevent relapse/recurrence. We review prevention evidence for acute, continuation, and maintenance CTs for patients whose depression is active, remitted, and recovered, respectively. Evidence suggests that patients relapse less often after discontinuing acute phase CT versus discontinuing pharmacotherapy. Continuation CT further decreases relapse relative to inactive controls and similarly to active pharmacotherapy. Maintenance CT may decrease recurrence but needs rigorous evaluation. Post-acute CT's preventive effects appear greater for higher-risk patients (e.g., with residual depressive symptoms, unstable acute-phase treatment response, childhood trauma, more prior depressive episodes), although risks may vary by specific CTs.

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Introduction

Major depressive disorder (MDD) is a common illness with a large public health cost (e.g., [58]). A curative treatment for MDD would eliminate underlying pathology, relieve all patients' depressive symptoms rapidly, restore psychosocial functioning fully, and prevent depressive relapses and recurrences entirely. Current treatments are far from these ideals. However, cognitive and cognitive-behavioral therapy (CT) for MDD reduces depressive symptoms, improves psychosocial functioning, and lowers the probability future depression in many patients. Here we review some of the most important and most recent research on CT for adults with MDD to inform prevention of relapse and recurrence.

What is major depressive disorder?

The experience of at least one major depressive episode (MDE) defines MDD [1]. MDEs reflect disturbances in mood (e.g., subjectively depressed and/or loss of pleasure in life's activates) with attendant changes in behavior (e.g., increased or decreased sleep, eating, activity level) and cognition (e.g., reduced concentration, increased guilt, suicidality), last at least two weeks, and produce significant life interference (e.g., as a student, worker, parent, friend, romantic partner; [2]). Reduced physical capacity [3] and increased mortality [4,5] often accompany MDD.

Both the prevalence and recurrence of MDD are high. For example, about 5–7% of the US population has experienced MDD over the past year and 13–17% will experience MDD over the lifetime [6–8]. Although 15–25% of persons with MDD display chronic depression [9,10], most eventually return to normal (or near-normal) mood, with or without treatment. Although a subset of persons experience only a single episode [11], among those who recover, perhaps 85% of patients experience a new MDE within 15 years [12]. CT aims to reduce the probability of both relapse (resurgence of an MDE that abated temporarily) and recurrence (a new MDE).

What is cognitive behavioral therapy?

Cognitive behavioral therapies for depression share efforts to change patients' distress-related cognition as a means to improve mood and functioning. Beck *et al.*'s [13] individual, in-person CT is prototypical. During a limited period (e.g., 16–20 one-hour sessions over 3–4 months), Beck's CT aims to increase patients' engagement with sources of reinforcement and adaptive functioning ('behavioral activation') and then to assess and restructure depressive cognition, including negative automatic thoughts (e.g., 'I am a loser') and schema (broader negative views about the self, world, and future; for example, 'Being loved by all is essential for happiness'). Many delivery methods and theoretical variants of CT exist, including treatments administered to groups (e.g., [14]), via books (e.g., [15]), and by computer (e.g., [16]); as well as treatments using behavioral activation without cognitive restructuring [17]; emphasizing cognitive restructuring over behavioral activation [18]; monitoring and distancing reactions to negative cognition rather than changing negative cognition itself (e.g., [19–21]); and emphasizing social-cognitive development and interpersonal functioning [22].

In addition, CT can be staged by depression's course [23]. Patients experiencing an MDE receive *acute phase* treatment with the goal of producing an initial treatment *response* (e.g., responders experience substantive reductions in depressive symptom severity and no longer meet criteria for an MDE). Ideally, acute phase treatment would fully prevent *relapse* (resurgence of the index MDE) and *recurrence* (experience of a new MDE). However, additional treatment is often beneficial for acute phase treatment responders with risk factors such as *residual symptoms* (subdiagnostic but impairing depressive symptoms) and *unstable response* (transiently elevated depressive symptoms late in acute phase treatment). In particular, acute phase treatment responders may receive *continuation phase* treatment to prevent relapse and promote *remission* and *recovery* (e.g., periods of several weeks and months, respectively, with minimal or absent depressive symptoms). Patients who have recovered from their index MDE may then receive *maintenance phase* treatment to sustain recovery and prevent recurrence. Following we review evidence about CTs' effects on relapse, recurrence, remission, and recovery. We organize our review by acute, continuation, and maintenance CT, although researchers have not always followed these theoretical and terminological distinctions (e.g., some studies of 'maintenance' fit our definition of 'continuation' treatment).

To what extent does cognitive behavioral therapy reduce relapse, recurrence, and residual symptoms of major depressive disorder?

Acute phase CT

Roughly 60–70% of patients no longer meet criteria for MDD after completing acute phase CT ([24,58]), and average symptom levels are comparable after acute phase CT versus pharmacotherapy [25]. Although CT and pharmacotherapy produce similar short-term outcomes, CT's preventive effects exceed pharmacotherapy after either acute phase treatment ends.

In an earlier meta-analysis of studies reporting follow-up data after response then discontinuation of acute phase treatment, relapse/recurrence frequency over an average of 68 weeks was 39% for CT compared to 61% for pharmacotherapy [26]. The 22% lower frequency of relapse/recurrence after CT versus after pharmacotherapy was similar to the 23% lower frequency of relapse/recurrence after acute phase CT plus pharmacotherapy versus after pharmacotherapy alone. However, based on a small number of studies, CT did not show lower relapse/recurrence compared to other psychotherapies (interpersonal, psychodynamic, behavioral activation; [26]).

An updated meta-analysis [27•] replicated these advantages for acute phase CT. In particular, in follow-ups of 6–18 months, the odds of relapse after discontinuing pharmacotherapy were about 2.6 times higher than after discontinuing acute phase CT. Stated another way, for every 5 patients treated with CT instead of with pharmacotherapy, 1 patient's relapse will be prevented. In addition, the odds of dropping out of acute phase CT were only about 0.6 versus dropping out of acute phase pharmacotherapy. Thus, patients are more likely to stay in CT, and so respond to CT, and then less likely to relapse after CT compared to after pharmacotherapy.

Acute phase CT responders vary in their risk for relapse/recurrence, and thus perhaps also in their need for continuation treatment to prevent relapse/recurrence. Arguably the strongest and best-replicated predictors of relapse are the extent and quality of remission during acute phase treatment. These predictors include unstable response (e.g., [28–30]) and residual symptoms (e.g., [31,32]). Additional predictors of relapse have included indicators of more severe illness, including MDD onset at younger ages, more prior depressive episodes, 'double depression' (dysthymic disorder comorbid with MDD), family history of depression, more depressive cognitive content, high neuroticism, and poor social support (e.g., [33,59]).

Continuation phase CT

Although patients relapse less after acute phase CT than after discontinuing pharmacotherapy [27•], many responders do eventually relapse or recur. For example, among MDD patients who respond and then discontinue acute phase CT, roughly one-quarter relapse/recur within a year and one-half within two years [26]. Continuation phase CT aims to prevent relapse among responders to acute phase treatments, and a growing literature supports continuation CT's efficacy (e.g., [34,58]). Meta-analyses suggest that continuation CT reduces relapse and recurrence by roughly 25–35% compared to inactive control conditions over 10–18 months, on average [26,35], comparable to (if not somewhat larger than) the average benefit of continuation pharmacotherapy versus placebo (e.g., [36]). However, the benefits of continuation CT may be larger for patients with greater illness liabilities (e.g., more prior MDEs, unstable response or remission of the index episode, greater residual symptoms; [33,35]) and when it is preceded by acute phase treatment [37].

Recent studies of continuation CT bolster these conclusions. For example, among patients with recurrent MDD who showed unstable remission to acute phase CT, 8 months of continuation CT or fluoxetine reduced relapse (from 33% to 18%) and residual symptoms (by about 0.2 SD) compared to pill placebo [38••,39•]. Similarly, among remitted MDD patients with a greater history of childhood trauma, 8 weeks of treatment as usual plus continuation CT reduced relapse over one