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Relapse and recurrence prevention in depression: Current research and future prospects

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ABSTRACT

There is a growing body of literature which indicates that acute phases of psychotherapy are often ineffective in preventing relapse and recurrence in major depression. As a result, there is a need to develop and evaluate therapeutic approaches which aim to reduce the risk of relapse. This article provides a review of the empirical studies which have tested the prophylactic effects of therapy (cognitive-behavioral, mindfulness-based, and interpersonal psychotherapy) targeting relapse and recurrence in major depression. For definitional clarity, relapse is defined here as a return to full depressive symptomatology before an individual has reached a full recovery, whereas recurrence in defined as the onset of a new depressive episode after a full recovery has been achieved. Psychotherapeutic efforts to prevent relapse and recurrence in depression have been effective to varying degrees, and a number of variables appear to moderate the success of these approaches. A consistent finding has been that preventive cognitive-behavioral and mindfulness-based therapies are most effective for patients with three or more previous depressive episodes, and alternative explanations for this finding are discussed. It is noted, however, that a number of methodological limitations exist within this field of research, and so a set of hypotheses that may guide future studies in this area is provided.

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1. Introduction

Recent data have led to the suggestion that cognitive-behavioral therapy might reduce the risk of relapse or recurrence relative to pharmacotherapy (Dobson et al., 2008; Hollon, Stewart, & Strunk, 2006). Several studies that employ naturalistic follow-up procedures after the cessation of acute phase cognitive therapy indicate that anywhere from 6.9% (Shapiro et al., 1995) to 83% (Jarrett et al., 2000) of individuals who have recovered from a depressive episode will go on to experience a subsequent new episode of depression. According to a recent meta-analysis (Vittengl, Clark, Dunn, & Jarrett, 2007), the mean proportion of patients who experience relapse or recurrence after receiving acute phase cognitive therapy was 29% in the first year and 54% in the second year. Although acute cognitive therapy

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did significantly better than its pharmacotherapeutic counterpart in reducing relapse and recurrence rates, these figures are still a concern when the burden of depression and the toll it takes on the lives of its sufferers are considered.

As Vittengl et al. (2007) point out, relapse/recurrence rates vary considerably across studies, and it is likely that a number of moderators of these rates are involved. Recently, Bockting, Spinhoven, Koeter, Wouters, and Schene (2006) reported that risk factors for relapse/recurrence included a high number of previous episodes, more residual depressive symptomatology and psychopathology, and finally, more daily hassles. In a 5.5 year follow up of this study, Bockting et al. (2009) also reported that in addition to a high number of previous episodes and residual depressive symptoms, two potentially modifiable predictors of recurrence in remitted recurrently depressed patients included a more avoidant way to deal with problems and a lower capacity to 'refocus on positive matters'.

Burcusa and Iacono (2007) discuss a number of theories which have been offered as explanation for recurrence, which are reviewed below. One of the hypotheses the authors forward is that "individuals at high risk for multiple episodes possess the necessary characteristics to make them prone to recurrent depression, and such characteristics exist even before their first episode" (p. 974). As such, these authors suggest that vulnerability to depression in general is a non-specific premorbid marker of depression. If this argument is valid, recurrence can therefore be thought of as an almost inevitable sequel of the disorder. Alternatively, the increasing vulnerability for relapse with episodes might be caused by 'scarring' as a result of previous episodes. One aspect of the scar hypothesis is related to the idea of "kindling", which is the proposition that less stress is required to provoke each subsequent episode (Monroe & Harkness, 2005; Post & Weiss, 1995). There is indeed some evidence for the kindling hypothesis (Bockting, Spinhoven, Koeter, Wouters, Visser, et al., 2006; Kendler, Thornton, & Gardner, 2000; Lewinsohn, Rohde, Seeley, Klein, & Gotlib, 2000; ten Doesschate, Bockting, Koeter, Schene, & the DELTA Study Group, 2010). Another explanation for the increasing vulnerability with increasing episodes is the stress generation hypothesis (Hammen, 1991), which presumes that there is an increase in the generation of stressful events with more episodes, and that these events in turn increase the risk of recurrence. This hypothesis might hold especially for interpersonal stress (Hammen, 1991). However, instead of scarring as a result of previous episodes, premorbid characteristics might also be responsible for the generation of stress in recurrent depression. Indeed, Holahan, Moos, Holahan, Brennan, and Schutte (2005) found that avoidant coping might play a role in the generation of stress, and thus might be linked to future depressive symptoms. An avoidant problem-solving style resulted in a higher number of daily hassles and life events which are linked to depressive symptoms.

Another rendition of the scar hypothesis, namely the *differential activation hypothesis*, was forwarded by Teasdale in his revised cognitive model of depression (Teasdale, 1988). According to this hypothesis, depressive thinking results from repeated associations between the depressed state and negative thinking patterns. The strengthening of these associations with repeated episodes is assumed to contribute to an increased risk of recurrence following each subsequent episode. There is some empirical evidence for this presumed heightened cognitive reactivity as a potential causal risk factor for recurrence (Lau, Segal, & Williams, 2004).

The chronic nature of depression and the relative failure of acute psychotherapy to prevent its relapse dictate that efforts with the primary aim of relapse prevention should be liberally employed to stave off this disorder (Bieling & Antony, 2003). A number of published studies have focused exclusively on stand-alone treatments which have the goal of relapse prevention. Given the methodological and operational variability that exists in this literature, the meta-analytical approach (cf. Guidi, Fava, Fava, & Papakostas, 2010; Vittengl et al., 2007) might paint a somewhat misleading picture of the data. Limitations of meta-analyses include, but are not limited to, publication bias (otherwise known as file drawer effect), magnification of study bias, and subjective selection (Eysenck, 1994; Moncrieff, 1998). Given such criticisms, this paper provides a qualitative review of relapse prevention programs in depression that takes this variability into account, and provides a set of possible mechanisms for their success or failure. It is also our aim to present a set of guiding hypotheses that may direct future research regarding relapse prevention. Before such a task can be appropriately accomplished, however, the definitions for commonly used terms throughout are provided.

2. Definitions of relapse and recurrence

While the goal of relapse prevention programs is to reduce the reoccurrence of depressive disorders, different conceptions of this idea exist. Indeed, different researchers use the term "relapse" as a general concept to capture all reoccurrences of depression, when more precise definitions may be required. The current review uses the Frank et al. (1991) definitions of remission, recovery, relapse and recurrence. These researchers define *partial remission* to mean a brief period in which the individual is no longer fully symptomatic (i.e., below the clinical threshold to diagnose Major Depression) but still displays more than minimal symptoms. A *full remission* is defined as a brief (less than 8 weeks) asymptomatic period, whereas *recovery* was defined as an absence of depressive symptoms for at least 8 weeks. Within this framework, *relapse* was defined by Frank et al. (1991) to indicate a return to full depressive symptomatology (beyond clinical threshold for a diagnosis) but before the individual has reached a full recovery. *Recurrence*, on the other hand, occurs when an individual experiences a new depressive episode after a full recovery had been achieved.

Although the distinction between relapse and recurrence makes conceptual sense, and although clear operational criteria have been proposed by Frank et al. (1991), the majority of researchers do not formalize this distinction in the research that they conduct. For example, much of the research involving the prediction of relapse or recurrence fails to distinguish among participants who remit by the end of acute treatment, versus those who fully recover. This distinction is important, however, as evidence suggests that recurrence rates following recovery are lower than relapse rates following remission. Long-term follow up studies are needed to detect several recurrences, the rates of which may otherwise be underestimated in the field. Further, even for individuals who are not clinically depressed at the end of the acute phase of treatment, researchers most often fail to stipulate the length of time for a new episode of depression in the follow-up period, but treat all new episodes of depression as conceptually equal. Most often, the research also fails to distinguish among cases of relapse versus recurrence. As such, in the following discussion the language adopted is "prevention of relapse", even though it should be understood that some of the relapse cases included in these studies likely met criteria the Frank et al. (1991) criteria for recurrence.

3. Search strategy and study selection

A comprehensive literature review was conducted in order identify all studies that examine relapse prevention and recurrence in depression. The databases PsychINFO and PubMed were searched using keywords such as "relapse", "recurrence", "prevention", "depression", "cognition", "mindfulness", "interpersonal", and "therapy". Studies adhering to the following criteria were included in this review: a) the use of adult participants (i.e., 18 and over), b) studies employing a form of psychotherapy, c) the psychotherapy is used as a stand-alone procedure directly targeting relapse and recurrence prevention (i.e., the therapy is not only employed in the acute phase of the disorder but is also administered after remission and/or recovery), and d) studies which employed either a treatment

or a non-treatment control group. Using such criteria, 24 studies were identified.

4. Psychosocial interventions for the prevention of depression relapse

What follows is a review of those studies which employed a form of psychotherapy as an explicit intervention to maintain the gains made during the acute phase of therapy, and to prevent or forestall a depression relapse. As mentioned above, these studies represent stand-alone procedures which directly target relapse and recurrence. The major intervention models used to date in this fashion include cognitive therapy, mindfulness-based cognitive therapy, and interpersonal therapy, each is described in turn (see Table 1).

5. Prevention efforts in cognitive therapy

Cognitive therapy (CT) was first developed as a treatment for patients who currently met diagnostic criteria for Major Depression (Beck, Rush, Shaw, & Emery, 1979), and most of the trials of CT focus on outcomes during the acute phase of treatment. It has also been recognized, however, that acute phase CT has enduring effects (Vittengl et al., 2007), which in some instances have been shown to be as potent as even a continued course of antidepressant medication. In this section, however, the use of CT as a preventive effort is highlighted. These efforts include the provision of CT after the end of acute phase treatment. In some cases, these trials included continued CT during a follow-up phase of treatment, maintenance phase CT provided after successful psychotherapy or antidepressant medication, or a stand-alone CT prevention program.

Blackburn, Eunson, and Bishop (1986) conducted the first controlled attempt to document the prophylactic value of maintenance cognitive therapy. In their study, patients ($N=64$) were randomly assigned to receive one of acute CT, antidepressant medication (ADM), or combined CT plus ADM. Patients who responded to any acute treatment [defined as a Beck Depression Inventory (BDI) score<9 and/or a Hamilton Rating Scale for Depression (HRSD) score<8] were provided a booster session every 6 weeks for the 6 months that followed the acute phase. The maintenance treatment corresponded to the acute treatment to which the individuals responded (i.e., those who responded to pharmacotherapy were maintained on the same drug for 6 months). When the groups were compared at 6 months (at the end of the maintenance phase), it was found that significantly more patients (30%) in the pharmacotherapy only group had "relapsed" (defined as a BDI>9 or HRSD>8) compared to the CT only group (6%) and the combination group (0%). Assessment at the end of a 2-year follow-up period revealed that only 21% of the individuals in the combined CT-pharmacotherapy group had relapsed, compared to 23% in the CT only group, and 78% in the ADM only group. Overall, the authors concluded that both CT only and in combination with medications did significantly better to reduce relapse rates than did the drug only condition.

In an extension of Blackburn et al. (1986), Blackburn and Moore (1997) tested the efficacy of a maintenance phase CT in reducing relapse in depression. Seventy-five depressed outpatients were randomized into one of 3 treatment groups: 1) acute phase ADM followed by a 2-year maintenance dose of ADM, 2) acute phase ADM followed by the same period of CT maintenance sessions (3 sessions in the first and second months, and monthly for the remaining 22 months), or 3) acute CT followed by maintenance CT. They found that all three treatment groups were comparably effective in reducing depressive symptoms during the acute phase, which was a 16 week period. At the end of the 2-year maintenance phase, no statistical differences in relapse rates among groups were found. The relapse rate (HRSD>14) in the group treated and maintained with CT was 24%, compared to 31% for the group treated and maintained with ADM, and 36% for the group that switched from ADM in the acute phase to CT as maintenance. There was a trend which favored the acute and maintenance CT group compared to the other two groups over time. Unfortunately, this study did not employ a group which only received treatment during the acute phase, to serve as a control group. As such, there is no *direct* comparison of the superiority of maintenance CT in reducing relapse rates for depression over and above the prophylactic effects of acute treatment for this disorder.

It has been recognized that patients who complete acute phase treatment, even if they have remitted, may have varying levels of what are termed "residual symptoms". Fava, Grandi, Zielezny, Canestrari, and Morphy (1994, 1996); Fava, Grandi, Zielezny, Rafanelli, and Canestrari (1996); Fava, Rafanelli, Grandi, Canestrari, and Morphy (1998); Fava, Rafanelli, Grandi, Conti, and Belluardo (1998) tested the efficacy of CT for residual symptoms as a means to curb relapse rates in depression. In the first study (Fava et al., 1994), 40 depressed outpatient participants were successfully treated in the acute phase with ADM. These participants were then randomly assigned into either a CT group for residual symptoms (20 participants each), which involved cognitive restructuring, or a standard clinical management group, which focused on the provision of medical status review and support. Both groups were given 10 40-minute sessions every other week after the initial treatment. Individuals in the CT condition experienced significantly fewer residual symptoms than individuals in the clinical management condition. Further, although only 15% (3/20) of the participants in the CT condition experienced relapse, in comparison to 35% (7/20) in the clinical management condition, relapse rates did not significantly differ between groups at the 2-year follow-up. In the 4-year extension (Fava et al., 1996), the trend favoring CT reached significance; after 4 years, only 35% of the participants in the CT group (7/20) relapsed compared to 70% (14/20) of individuals in the clinical management group. In the 6-year follow-up assessment (Fava, Rafanelli, Grandi, Canestrari, & Morphy, 1998), the two groups leveled off once more (50% relapse in the CT group, compared to 75% in the clinical management group), and the difference between interventions was nonsignificant.

Kühner et al. (1996) tested the efficacy of the Coping with Depression (CWD) program in the prevention of depression and its ability to maintain treatment gains made with CT. CWD is a group form of CT, with an emphasis on relapse prevention. A total of 259 inpatient participants were recruited into this study one to seven months after discharge from a psychiatric setting, and 190 were followed after discharge from the acute phase treatment within. The remaining 69 participants received the CDW course four weeks after discharge. A number of exclusionary criteria were applied and data from only 42 patients ($n=21$) in both groups were included in the final analyses. The groups were matched on socioeconomic and disorder characteristics (e.g., age, gender, depressive symptomatology, etc.). Based on relapse criteria that incorporated the an expansion of the Present State Examination to yield a DSM-III-R diagnosis for Major Depressive Episode, it was found that individuals who received the CDW course were significantly less likely to relapse (14.3%) than were matched controls who received no maintenance therapy (42.9%).

Jarrett et al. (1998) compared the relapse rate among 37 depressed patients who received standard acute CT alone, with that of 17 patients receiving a continuation phase of CT. The latter treatment focused on the prevention of relapse and recurrence and generalization of the skills gained in acute therapy, and was offered over 8 months following response to acute CT. To qualify for inclusion, participants met criteria for a major depressive episode as determined by DSM-III-R (Structured Clinical Interview/RDC), in addition to a score of 17 or higher on the HRSD. Relapse and recurrence were both defined as meeting Research Diagnostic Criteria (DSM-III-R) for a major depressive episode. At a 2-year follow-up period, individuals who received the continuation phase of CT had significantly lower relapse and recurrence rates (36%), in comparison to

Table 1
The Efficacy and design characteristics of current empirical studies examining relapse and recurrence prevention in depression.

Treatment type	Study	Sample characteristics and design	Measures and criteria	Follow-up period	Results	Risk ratio (95% C.I.)
*CT, ADM	Blackburn et al. (1986)	$N=64$; CT only vs. ADM vs. CT + ADM. Booster sessions every 6 weeks for 6 months following acute therapy.	Remission defined as BDI<9 and/or HRSD<8; relapse defined as BDI>9/HRSD>8	2 years	- Relapse in combined (21%) and CT (23%) significantly less than ADM alone (78%).	Combined vs. ADM: 0.28 (0.10–0.80) CT vs. ADM: 0.30 (0.10–0.85)
CT, ADM	Blackburn and Moore (1997)	$N=75$; outpatient groups: 1) acute-ADM + Maintenance ADM group ($n=26$), 2) acute CT + maintenance CT group($n=27$), and 3) acute ADM + maintenance CT ($n=22$).	RDC; (HRSD>16 to qualify for acute phase; HRSD<14 for recovery).	2 years. Assessment every 4 weeks of acute therapy (16 weeks), and every 4 month in maintenance	- Follow-up: NS difference in relapse; trend favoring group 2.	Maintenance CT groups vs. Maintenance ADM group: 0.94 (0.35–2.52)
CT	Fava et al. (1994; 1996; 1998)	$N=40$; outpatient Groups: 1) CT for residual symptoms, 2) Clinical management	RDC; relapse = occurrence of an RDC episode	6-year follow up; Assessment every 2 years.	- NS difference between CT (15%) and clinical management (35%; 1994). - CT (35%) had significantly lower relapse rates than clinical management (70%) at 4 year follow up (1996). - NS difference between groups at 6-year follow-up (50% vs. 75%; 1998).	0.43 (0.13–1.43) 0.50 (0.26–0.97) 0.67 (0.11–1.06)
CT	Kühner et al. (1996)	$N=259$; 190 naturalistic follow-up vs. 69 receiving CT course. Only 42 patients in both groups ($n=21$) qualified. Participants in both groups matched on socioeconomic and disorder characteristics.	Extension of Present State Examination. Relapse = DSM-III-R criteria for MDE	7 months	- Individuals in CT group significantly less likely to relapse than matched controls (14.3% vs. 42.9%).	0.33 (0.11–1.06)
CT	Jarrett et al. (1998)	$N=54$; 37 receiving standard acute CT alone vs. 17 receiving continuation CT over 8 months after acute phase.		2-year	- Continuation CT group had significantly lower relapse rates than individuals in acute CT alone after 2-year follow-up (36% vs. 74%).	0.49 (0.29–0.85
CT, ADM	Paykel et al. (1999)	$N=158$ (only 127 qualified); Continuation CT (16 sessions, $n=61$) vs. Clinical management only. Participants in both groups remained on ADM.	Relapse = DSM-III-R criteria for Major depressive episode for minimum of 1 month AND HRSD>17	68 weeks.	- Individuals in continuation CT group had significantly lower relapse rates in comparison to individuals in the clinical management condition (29% vs. 47%). - Relapse rates were not significantly different at 6 year follow-up (Paykel et al., 2004).	0.62 (0.41–0.94) 0.92 (0.72–1.17)
CT	Jarrett et al. (2001)	$N=156$ (only 84 qualified); Continuation CT (10 sessions, $n=41$) vs. evaluation only control.	Remission = No MDD status and HRSD<9; Used Frank et al. (1991) definition of relapse.	8 months and 24 months.	- At 8 months, continuation CT condition had significantly lower relapse rates than control (10% vs. 31%). - At 24 month, relapse in continuation CT remained significantly lower than control condition (16% vs. 67%).	0.32 (0.12–0.91) 0.25 (0.13–0.51)
CT, ADM	Perlis et al. (2002)	$N=132$ (85 qualified); maintenance dose of ADM (Fluoxetine) + 19 sessions of Continuation CT vs. ADM + medication management.	Remission = HRSD of 7 or lower for 3 consecutive weeks); Relapse =	~ 7 month (28 weeks)	- NS difference in relapse rates of ADM + CT group (6%) and ADM + medication management group (8%).	0.80 (0.23–2.85)
CT	Klein et al. (2004)	$N=82$; Maintenance CT (52 weeks of eclectic form of CT) vs. Assessment only	Relapse = DSM-IV diagnosis of MDD and a score of 16 and higher on HRSD.	12-month follow up	- Depending on criteria, relapse rates were 2.6–10.7% in CT group and 20.9–32.0 in assessment only group.	0.36 (0.14–0.91)
CT	Bockting et al. (2005)	$N=187$; TAU vs. TAU + continuation CT (8 sessions)	Relapse/recurrence = meeting criteria for MDD according to SCID (DSM-IV).	24-month follow-up (with assessments at 3, 12 and 24 months).	- For participants with 5 or more previous MDEs, relapse significantly less in the CT condition (46%) than in TAU condition (72%). - For participants with 4 or less previous MDEs relapse was 63% in CT condition and 59% in TAU condition (not significant).	0.65 (0.43–0.97) 1.07 (0.78–1.45)
CT	Bockting et al. (2009)	$N=172$; TAU vs. TAU + continuation CT (8 sessions)	Relapse/recurrence = meeting criteria for MDD according to SCID-I (DSM-IV-TR).	5.5-year follow-up.	- For participants with four or more previous episodes, relapse significantly less in the CT condition (75%) than in TAU condition (95%).	0.79 (0.67–0.95)

Table 1 (*continued*)

Treatment type	Study	Sample characteristics and design	Measures and criteria	Follow-up period	Results	Risk ratio (95% C.I.)
					- For participants with 4 or less previous episodes, no significant difference in relapse between CT (82%) and TAU condition (79%).	1.04 (0.84–1.28)
CT	Vittengl et al. (2009)	$N=84$; continuation CT ($n=41$; 10 sessions) vs. assessment control ($n=43$).	Remission = minimal or no symptoms for 6 weeks (according to LIFE, a semistructured interview and HRSD 9 and less) Recovery = minimal or no symptoms for 8 months (according to LIFE, a semistructured interview and HRSD 9 and less).	24 months follow-up. Assessment at 4, 8, 12, 16, 20 and 24 months).	- NS differences in remission rates between continuation CT condition (97%) and control (88%).	1.10[a] (0.98–1.24)
					- Significantly more recovery in the continuation CT condition (84%) in comparison to control (62%),	1.32[a] (1.01–1.73)
CT, AMD	Petersen et al. (2010)	$N=52$; Combined continuation CT + ADM (Fluoxetine) vs. ADM alone vs. CT + placebo vs. Placebo alone.	Recurrence = Score above 7 on the 17-item HRSD.	~ 7 months (28 weeks)	- No significant differences between 4 groups	CBT + ADM: 0.91 (0.40–2.05) ADM: 0.57 (0.22–1.50) CBT + placebo: 0.91 (0.40–2.05)
MBCT	Teasdale et al. (2000)	$N=145$; TAU vs. TAU + MBCT (8 sessions)	Relapse/recurrence = Meeting criteria for MDD according to SCID (DSM-III-R)	~ 15 months (60 weeks)	- For individuals with 3 or more previous MDEs, relapse for the MBCT group was significantly less than the TAU group (40% vs. 66%).	0.61 (0.41–0.89)
					- No significant difference in relapse in the two groups for individuals with 1 or 2 previous MDEs (56% in MBCT and 31% in TAU group).	1.80 (0.77–4.19)
MBCT	Ma and Teasdale (2004)	$N=75$; TAU vs. TAU + MBCT (8 sessions)	Relapse/recurrence = Meeting criteria for MDD according to SCID (DSM-IV)	12 months	- For individuals with 3 or more previous MDEs, relapse for the MBCT group was significantly less than the TAU group (37% vs. 78%).	0.46 (0.27–0.79)
					- No significant difference in relapse in the two groups for individuals with 1 or 2 previous MDEs (50% in MBCT and 20% in TAU group).	2.50 (0.60–10.34)
MBCT, ADM	Kuyken et al. (2008)	$N=123$ (individuals with 3 or more MDEs only); MBCT 8 sessions) + Tapered ADM vs. Maintenance ADM only.	Relapse/recurrence = meeting criteria for MDD according to SCID (DSM-IV-R).	15 months	- NS difference in relapse rates between and MBCT (47%) and maintenance ADM (60%) conditions.	0.80 (0.52–1.11)
MBCT, CT	Dobson and Mohammadkhani (2007)	$N=354$; 8 weeks of maintenance CT vs. 8 weeks of maintenance MBCT vs. TAU	Remission = not meeting MDD criteria (diagnostic interview).	One-year follow up	- Significantly less relapse in MBCT (11.7%) and CT (13.4%) groups in comparison to TAU (41.1%) groups.	MBCT: 0.29 (0.17–0.49) CT: 0.33 (0.20–0.56)
MBCT	Godfrin and van Heeringen (2010)	$N=106$ (individuals with 3 or more MDEs only): MBCT (8 sessions) + TAU (Wait-list) vs. TAU only.	Remission = not meeting MDD criteria (SCID-I) and HRSD score of <14. Relapse = meeting DSM-IV-TR criteria (SCID-I).	56 week follow up. Assessment at 2, 8 and 14 months period.	- Significantly less relapse in MBCT + TAU (30%) group in comparison to TAU alone (68.1%).	0.44 (0.26–0.74)
MBCT	Bondolfi et al. (2010)	$N=60$ (individuals with 3 or more MDEs only): MBCT ($n=31$; 8 sessions) + TAU (availability of mental health providers). Vs. TAU only ($n=29$).	Relapse = meeting DSM-IV criteria for MDD (SCID).	14 months follow-up.	- NS differences in relapse between MBCT + TAU (29%) and TAU only (34%).	0.84 (0.40–1.77)
IPT, ADM	Frank et al. (1990)	$N=128$; Medication clinic + ADM (imipramine) vs. IPT + ADM vs. medication clinic and pill placebo, vs. IPT alone vs. IPT and pill placebo.		3 year follow-up	- Groups featuring either IPT or ADM had a significantly longer mean time to relapse/recurrence.	Medication clinic + ADM: 0.27 (0.13–0.58) IPT + ADM: 0.31 (0.15–0.64) IPT: 0.79 (0.54–1.14) IPT + placebo: 0.84 (0.59–1.19)

(*continued on next page*)

Table 1 (*continued*)

Treatment type	Study	Sample characteristics and design	Measures and criteria	Follow-up period	Results	Risk ratio (95% C.I.)
IPT, ADM	Reynolds et al. (1999)	$N=107$; pill placebo only vs. AMD only vs. placebo + IPT vs. AMD + IPT	Remission = HRSD<10; Recurrence = Meeting RDC for MDD (according to a structured interview).	3-year follow-up	- Significantly less relapse in IPT only (64%), ADM only (43%), and ADM + IPT (20%) groups in comparison to placebo only group (90% relapse).	IPT: 0.71 (0.52–0.98) ADM: 0.48 (0.31–0.75) ADM + IPT: 0.22 (0.10–0.49)
IPT, ADM	Reynolds et al. (2006)	$N=116$; partially or fully recovered elderly patients (>70 years) randomly assigned to one of 4 maintenance conditions: ADM + Clinical management, ADM + IPT, placebo + IPT, placebo + clinical management.	Recurrence = Meeting criteria for MDD (according to SCID) + HRSD>15.	2-year follow-up.	- Significantly lower recurrence in groups receiving ADM (27%) than those not receiving ADM (56%). - Maintenance IPT without ADM not found to significantly reduce recurrence (68% with placebo compared to 35% with ADM).	ADM + Clinical management: 0.67 (0.37–1.22) ADM + IPT: 0.64 (0.34–1.23) Placebo + IPT: 1.23 (0.77–1.98)
IPT, ADM	Frank et al. (2008)	$N=131$; remitted participants through IPT alone vs. IPT + ADM assigned to weekly vs. biweekly vs. monthly maintenance IPT.	Remission = 3 consecutive weeks of HRDS<7. Recurrence = meeting DSM-IV criteria for MDD (according to structured interview).	2-year follow-up	- Significantly less relapse in the group remitted by IPT alone (26%) than the group remitted by IPT + ADM (50%). No significant differences in relapse between "doses" of IPT.	0.51 (0.30–0.89)

Note. ADM = Anti-depressant medication; CT = cognitive therapy; BDI = Beck Depression Inventory; HRSD = Hamilton Rating Scale for Depression; MBCT = Mindfulness Based Cognitive Therapy; NS = Nonsignificant; IPT = Interpersonal Psychotherapy; MDD = Major Depressive Disorder; SCID = Structured Clinical Interview for the DSM = IV; TAU = Treatment as Usual.

[a] Risk ratio represents probability of remission/recovery for members of the experimental group relative to the probability of remission/recovery in the control group.

individuals who only received the acute phase CT (74%). It is important to note, however, that the two groups in this study came from disparate populations.

Paykel et al. (1999) randomized 158 participants, who were partially remitted from depression (HRSD<8, and BDI<9) following a course of ADM, into either a 16-session continuation CT condition (with 2 booster sessions offered at weeks 26 and 32), or a clinical management only condition, which offered regular sessions every 4 weeks for a 20-week period. Individuals in the latter group were offered support and prescription information, but no psychotherapy. Participants in both conditions remained on ADM during the follow-up period. Relapse was defined by these researchers using DSM-III-R criteria for Major Depression for a minimum of 1 month, in addition to a score of 17 or more on the HRSD. Only data from 127 participants (66 in clinical management group, and 61 in CT group) were included in the final analysis. Over the 68-week follow-up period, individuals in the continuation CT condition had significantly lower relapse rates compared to individuals in the clinical management condition (29% and 47%, respectively). Paykel et al. (2004) conducted a 6-year follow-up to the original study (Paykel et al., 1999) in order to assess the long-term prophylactic effects of continuation CT. The authors found that the differences in recurrence rates between the CT and clinical management only conditions were attenuated approximately four years after the commencement of the continuation phase. The groups were not statistically different by the sixth year, although a trend favoring CT remained.

Jarrett et al. (2001) have also evaluated a continuation phase CT that was specifically targeted to reduce relapse and prevention. These researchers treated 156 depressed patients with acute phase CT, and then randomized the responders (defined as no MDD status and HRSD<9) to 10 sessions of continuation phase CT or an evaluation only control condition. This study defined relapse and recurrence in accordance with the criteria provided in Frank et al. (1991). Only data from 84 participants (C-CT $n=41$) were included in the final analysis. The researchers found that over an 8-month follow-up period, 10% of individuals in the continuation phase CT experienced relapse in comparison to 31% of those in the control condition. The differences became pronounced at a 24-month evaluation, as only 16% of patients who received continuation CT had relapsed, as opposed to 67% of those in the control condition. This superiority of continuation CT held even for patients who had unstable remission during the end of the acute phase (37% vs. 62% in control).

Perlis et al. (2002) examined the efficacy of continuation CT in reducing relapse when combined with ADM (20 mg of Fluoxetine). A total of 132 participants met criteria for remission (defined as an HRSD of 7 or lower for 3 consecutive weeks) following 8 weeks of treatment with ADM. Only 85 patients of the 132 completed the continuation phase of treatment, however. Consenting remitted participants ($n=85$) were then randomized to receive either a maintenance dose of Fluoxetine (40 mg) combined with 19 sessions of CT (which targeted residual symptoms and coping skills), or increased dosages of Fluoxetine combined with standard medication management. The researchers found that the ADM combined with CT group "failed to [significantly] reduce relapse over the 28-week study period" when compared to the ADM and standard medication management group (6% vs. 8%, respectively). The ADM-CT condition also failed to significantly reduce residual symptoms over and above the ADM-medication management condition. According to the authors, relapse rates were low in both study groups due to the use of ongoing medication, and these low rates of relapse precluded finding significant group differences.

In an effort to prevent recurrence in major depression, Klein et al. (2004) tested an eclectic form of psychotherapy (Cognitive-Behavioral Analysis System of Psychotherapy; CBASP), which combines cognitive, behavioral, interpersonal and psychodynamic elements. Participants who responded to an acute intervention ($N=82$) were randomized to either 52 weeks of maintenance CBASP (sessions conducted every 4 weeks), or an assessment only condition. Over the 12-month follow-up period, it was found that individuals who were in the CBASP condition had a significantly lower recurrence rate (defined as a DSM-IV diagnosis of MDD and a score of 16 and higher on HRSD) than those in the assessment only condition. Depending on the specific criteria used, the rates for recurrence were 2.6–10.7% in the CBASP condition and 20.9–32.0% in the assessment only condition.

Bockting et al. (2005) evaluated the protective effects of continuation CT, which targeted the cognitive content of negative thinking, and was delivered in a group format. The researchers randomly assigned 187 remitted individuals to either treatment as usual (TAU) group, or TAU combined with the CT prevention group. Relapse and recurrence were defined using DSM-IV criteria for MDD, in accordance to a diagnostic interview (SCID). The results indicated that the CT group was associated with reduced risk of relapse at 24 months, but only for those patients with 5 or more episodes of depression. For individuals with fewer than 5 previous episodes, the relapse rates were 59% in the TAU condition and 63% in the CT condition. In contrast, the relapse rates for individuals with 5 or more previous episodes in the TAU condition were 72% in comparison to 46% for individuals with the same level of chronicity in the CT condition. This 26% difference in relapse was observed in the initial three months and was maintained throughout the follow-up period. This interaction between number of previous episodes and treatment type was also significant for recurrence severity, whereby individuals with 5 or more previous episodes in the CT condition experienced a recurrent episode, it was typically less intense than individuals with 5 or more previous episodes in the TAU group. Bockting et al. (2005) also compared individuals with 5 or more previous episodes to those who experienced 4 or less on a number of disorder characteristics. It was found that, on average, individuals with a history of 5 or more episodes experienced their first episode at a younger age, fewer of them stayed in remission for longer than 6 months, and more often had family members with other psychiatric disorders in comparison to those with a history of 4 or less episodes.

Given the results of the initial study, a follow-up study (Bockting, Spinhoven, Koeter, Wouters and Schene, 2006) was conducted to examine the predictors of response to preventative CT. The researchers recruited remitted individuals with a history of at least two previous episodes of depression ($N = 172$) and randomized them into either a TAU condition, or TAU in combination with preventative CT (8 weekly 2-hour group sessions) condition. A number of demographic and illness-related variables were found to interact with the treatment type to predict relapse and recurrence. For example, being a female in the CT condition predicted a shorter time to recurrence than being a male. Further, as the number of previous episodes increased, so did relapse and recurrence in the TAU condition, whereas there was no effect of the number of previous episodes in the CT condition. Third, an avoidant coping style significantly predicted relapse/recurrence in both the CT and TAU condition. When the number of previous episodes was added to treatment type and avoidance style as a third interactive variable, it was found that the relationship between relapse and avoidance in TAU condition was attenuated with an increase in the number of previous episodes. On the contrary, the relationship between relapse and avoidance was accentuated in the CT condition with an increasing number of previous episodes. It was also found that higher levels of daily hassles predicted earlier recurrence only in the TAU condition, while experiences of major negative life events between 16 and the start of the study predicted recurrence only in the CT condition. As an explanation of the latter result, the authors suggested that CT may thwart the activation of depressive schemas, which in turn are activated by daily hassles.

Recently, an extension of the Bockting et al. (2005) trial examined the enduring effect of preventive CT intervention over 5.5 years (Bockting et al., 2009; ten Doesschate et al., 2010). Similar to previous methodology, relapse and recurrence in this extension was defined as meeting DSM-IV-TR criteria for a major depressive episode (as confirmed by the SCID-I). The researchers found that over 5.5 years, 135 of 172 patients (79%) experience relapse/recurrence at least once. In line with the results obtained after the 2-year follow up, there were no significant differences in relapse/recurrence rates between the CT (82%) and treatment as usual (79%) conditions for individuals with fewer than four previous depressive episodes. However, the protective effects of CT intensified for individuals with four or more episodes. For such participants, relapse/recurrence was significantly lower in the CT condition (75%) in comparison to the treatment as usual condition (95%).

In an expansion of the evidence base, Vittengl, Clark, and Jarrett (2009) examined the effects of continuation phase CT on the length of time remitted and recovered patients stayed in remission and recovery (defined as 6 weeks and 8 months, respectively, demonstrating minimal to absent depressive symptoms). Such researchers randomized 84 patients who responded to acute CT to either a continuation CT ($n = 41$) or assessment control ($n = 43$) condition. Response to acute CT was defined as not meeting criteria for MDD and a HRSD score of 9 or less. Recovery and remission were defined according to the same diagnostic tools and criteria. Continuation CT included 10 sessions of individual therapy over an 8-month period, and focused on maintenance and generalization of skills learned in acute CT, and a reduction in residuals depressive symptoms. Participants were assessed every four months for the 24-months study period. The results indicated that 92% of responders to acute therapy remitted (6 weeks of minimal or absent symptoms) between weeks 6 and 16, while 73% recovered (8 months of minimal or absent symptoms) between weeks 35 and 70. There were no significant differences between the number of participants who remitted in the continuation CT condition (97%) and assessment control (88%). In other words, only 3% of participants in the CT condition experienced relapse in comparison to 12% in the control condition. However, recovery was significantly higher in the CT condition (84%) than the control condition (62%). That is, only 16% of individuals in the CT condition experienced recurrence compared to 38% of individuals in the control condition.

Petersen et al. (2010) have compared the effects of maintenance CT and ADM (Fluoxetine) on relapse and recurrence rates in depression. Participants ($N = 52$) were randomized into one of four groups: CT plus ADM (40 mg of Fluoxetine), ADM only, CT plus placebo, and placebo only, and the effects at 28-weeks were observed. The maintenance phase CT therapy consisted of a slightly altered form of CT, which included a focus on residual symptoms and the enhancement of coping skills. CT was administered weekly for the first 12 weeks, and biweekly thereafter for the remaining weeks. Recurrence was defined as a score above 7 on the 17-item HRSD. The results showed that the four groups did not significantly differ in prevention of recurrence, which the researchers attributed to a small sample size and thus lack of power to detect differences.

In sum, with the exception of a few investigations, continuation and/or maintenance CT seems to reduce relapse and recurrence rates for major depression. It is noteworthy, however, that although some studies have adopted the Frank et al. (1991) criteria, the definitions of relapse and recurrence vary considerably among the various studies, and some studies even equate the two constructs . It also appears that some researchers employ arbitrary cutoff points on measurement scales to define relapse and recurrence. Further, the actual CT interventions used vary among the various studies. Some of these studies employ fairly standard cognitive restructuring methods, while others use a combination of standard interventions plus interventions to encourage medication adherence, and yet others employ fairly specific CT variants, such as the Coping with Depression course, or CBASP. Thus, although CT has demonstrated some prophylactic benefits, it is certainly premature to make definitive statements regarding its ability to disrupt the chronicity of the depressive course.

6. Prevention efforts with mindfulness-based cognitive therapy

Mindfulness-Based Cognitive Therapy (MBCT; Segal, Williams, & Teasdale, 2002) was developed as an explicit intervention to reduce relapse and recurrence in depression. The model which underpins

MBCT posits that a key aspect of the vulnerability to relapse into depression is not the content of negative thinking, but rather the process. This approach builds on the pioneering work of Kabat-Zinn (1990; 1994) which helped patients with chronic health problems to develop awareness skills and meditation to adopt a new attitude towards experience, which was not to minimize or control health problems, but to experience and accept these as part of life. In like manner, MBCT teaches people who have experienced prior depression that negative feelings and thoughts will inevitably occur as part of one's future life, and that rather than worry or ruminate about these experiences, and potentially cycle downwards into a recurrence of depression, it is possible to become aware of, and disengage from cognitive patterns that might otherwise initiate the depressive episode. Indeed, the core skills taught in MBCT are mindful awareness, and acceptance of the range of bodily and emotional experience. MBCT attempts to move patients from a "doing mode", in which they take action to cope with problems or stressors, to a "being mode", in which the patient can sit with and simply "be", regardless of their emotional state.

In the first attempt to apply Mindfulness-Based Cognitive Therapy (MBCT) as a preventative measure for recurrent depression, Teasdale et al. (2000) randomized 145 recovered patients into one of two groups: treatment as usual, or treatment as usual combined with MBCT training. The program was delivered in eight weekly 2-hour group sessions. Follow-up assessment was conducted bimonthly throughout the 60-week duration of the study. Relapse and recurrence were defined based on DSM-III-R criteria for a major depression, as assessed by the SCID. Although the authors did not differentiate between relapse and recurrence, it was found that, at the end of the 60-week study period, relapse/recurrence rate for individuals in the MBCT condition with three or more previous depressive episodes was 40%. This rate was significantly lower than the 66% of individuals with 3 or more episodes in the treatment as usual group who experienced relapse/recurrence over the course of the investigation. When individuals with a history of only one or two depressive episodes were compared, there was no significant difference in relapse/recurrence rates between treatment groups (56% and 31% in the MBCT and treatment as usual condition, respectively).

In a replication of the Teasdale et al. (2000) study, Ma and Teasdale (2004) randomized 75 recovered patients to continue with treatment as usual, or treatment as usual combined with MBCT training. In addition to the assessment procedures employed in the first study, this study also investigated negative life events and how they may affect rates of relapse/recurrence. At the end of the one-year follow-up period, the MBCT group had a significantly lower relapse/recurrence rate than the treatment as usual group for patients with three or more previous episodes. Only 36% of individuals in the MBCT condition, as compared to 78% of individuals in the treatment as usual group, experienced relapsed/recurrence. No significant difference emerged in the relapse/recurrence rate for participants with only one or two previous depressive episodes. The authors also found that MBCT worked effectively to prevent relapse when there were no reported negative life events. The prophylactic effects of MBCT were significantly diminished, however, when participants reported that their experienced relapse was provoked by a significant life event.

In a more recent trial, Kuyken et al. (2008) compared MBCT to maintenance ADM in the prevention of relapse in depression. These researchers randomized 123 remitted participants with a history of three or more episodes into two groups: traditional maintenance ADM, or an 8-week MBCT group class that included support to taper their maintenance medication dosage. Relapse and recurrence were defined according to DSM criteria, and were assessed by the SCID. Over the 15-month study period, and despite a trend in favor of MBCT, there were no significant differences in the relapse rates between the two treatment conditions, which were 47% and 60% for the MBCT and maintenance ADM conditions, respectively. The authors noted that participants in the MBCT group reported significantly fewer residual symptoms, however, as well as significantly better quality of life, and significantly fewer comorbid conditions. Lastly, the researchers conducted a cost analysis which revealed that per-person costs did not significantly differ between treatment groups.

In an unpublished study, Dobson and Mohammadkhani (2007) reported on a randomized clinical trial on the prevention of relapse and recurrence in depression. Patients who were in remissions from an index episode of depression, as confirmed by a diagnostic interview, were randomly assigned to 8 weeks of group MBCT, 8 weeks of group CT, or treatment as usual. The group CT used typical elements of CBT (e.g. behavioral activation, cognitive restructuring), but in a preventive manner, given that patients were not acutely depressed. As the study was conducted in Tehran, all materials were translated into Farsi, and the therapists were trained in the various treatment modalities there, with some minor cultural adaptations (e.g. MBCT was conducted in chairs). A total of 354 patients were followed for one year after treatment, with minimal loss to follow-up (approximately 10% in treatment as usual; 4% in the other two conditions). Survival analysis reveal a significant effect of treatment group, with both the MBCT and CBT prevention groups having significantly fewer lapses than in treatment as usual. The final relapse rates, at one-year follow-up, were 41.1% in treatment as usual, versus 11.7% in MBCT and 13.4% in CT. In a subsequent analysis, chronicity of depression (defined as one or two episodes, versus three or more) did not moderate the treatment effect in MBCT or CT. However, this was a relatively less chronic group of participants overall, with an average of only just over 2 episodes of depression, to the limited range of chronicity may have limited the ability to find significant results on this variable. Overall, the results of this study reveal that MBCT can be transported to another culture successfully, but its preventive power may be no greater than a brief prevention oriented course of CBT. The effect of the CBT intervention used in this study requires replication in another sample.

Furthermore, Godfrin and van Heeringen (2010) compared MBCT plus treatment as usual (TAU; wait-list control condition) to TAU alone in the reduction of relapse and recurrence in a group of recovered depressed patients. A total of 106 recovered patients with a history of three or more depressive episode were randomized to either a MBCT or TAU condition. Participants in the MBCT condition received manualized, group sessions (165 minutes per week for 8 weeks), focused on the ability to attend to and non-judgmentally monitor bodily sensations and thought patterns. Relapse was defined according to DSM-IV-TR criteria, as confirmed through a diagnostic interview (SCID-I). The results revealed that participants in the MBCT plus TAU group exhibited significantly less relapse (30%) in comparison to the TAU condition (68.1%). Participants in the MBCT plus TAU condition had a significantly longer mean time to first relapse (53.7 weeks) than their TAU only counterparts (39.5 weeks).

In the first independent, published cross-cultural replication of this work, Bondolfi et al. (2010) examined the efficacy of MBCT to decrease depressive relapse over a 14 months period. These researchers randomized 60 remitted, Swiss participants with a history or 3 or more episodes to either a MBCT plus treatment as usual or treatment as usual alone condition. Relapse was defined according to DSM-IV criteria for MDD (as confirmed through the SCID). As with previous studies, the MBCT condition in this investigation consisted of eight weekly 2-hour group sessions, while the treatment as usual condition consisted of informing participants to seek help from their family physicians or other sources as they normally would. The results revealed that no significant differences in relapse rates emerged between the MBCT plus treatment as usual (29%) and treatment as usual alone (34%) conditions. As the relapse rates in the treatment as usual condition were unusually low, the authors suggested that this may be accounted for by the differences in the Swiss and North

American mental health care systems, wherein health care services and providers are more accessible in the former than the latter.

In summary, most of the reviewed studies indicate that MBCT had a significant preventive effect in recurrent depression, relative to treatment as usual. Notably, however, this effect was only found for patients with a more chronic course of depression, defined as having had three or more episodes of depression. This result implies that the history of depression may affect the outcomes of preventative efforts, wherein individuals with more episodes may be more suited for MBCT. One possibility is that patients with less chronic depression still resist the experience and wish to rid of it, and thus do not respond as well to an intervention that encourages giving up that attitude. In contrast, it may make sense to patients with more chronic depression to accept this experience, and try to incorporate it into their usual life without having secondary appraisals or ruminative reactions to negative experiences.

In addition to the earlier studies, the more recent trial implies that MBCT is as effective as ongoing medication in the prevention of relapse, although MBCT does have a number of ancillary effects not observed with medication. Similar to CT studies reviewed above, it appears that the prophylactic effect of MBCT is reduced and possibly eliminated by negative life events. The amount of evidence with respect to MBCT is to date still somewhat limited, as such, more trials are recommended.

7. Prevention efforts in interpersonal therapy

A few studies have applied Interpersonal Therapy (IPT; Klerman, Weissman, Rounsaville, & Chevron, 1984) as a preventative measure in depression. In an early trial, Frank et al. (1990) examined the efficacy of various treatments in preventing recurrence in depression. The researchers randomly allocated 128 patients with recurrent unipolar depression to one of five groups: medication clinic and active ADM (imipramine), combined psychotherapy (a version of IPT) and ADM, medication clinic and pill placebo, psychotherapy alone, and psychotherapy and pill placebo. This study found all treatment groups that included either medication or psychotherapy as components had a significantly longer mean time to first recurrence of depression in comparison to groups not featuring an active therapy/medication, with the group that combined maintenance IPT and ADM showing the longest mean survival time to recurrence (131 weeks). Groups which included any form of ADM showed a trend of longer mean survival times than groups not featuring this component, although direct comparisons between active therapy/medication groups were not made, perhaps due to relatively low cell sizes and limited statistical power.

In a second study, Reynolds et al. (1999) compared maintenance ADM (nortriptyline) and IPT for recurrent depression. These researchers randomly allocated 107 recovered (HRSD<10), elderly participants into one of four maintenance treatment conditions: pill placebo only, AMD only, placebo and IPT, and combined AMD and IPT. Maintenance IPT was more formally conceptualized in this study as opposed to acute treatment IPT, in that maintenance IPT focuses on supplementing the skills gained in IPT, and helping individuals to assume responsibility to prevent future episodes. Patients who received maintenance IPT were seen for one 50-minute monthly session over the course of the trial, and recurrence was defined according to research diagnostic criteria as assessed by a structured interview. The results revealed that, over a three-year period, recurrence was significantly less in all active treatment groups when compared to the pill placebo condition. Specifically, the recurrence rate in pill placebo was 90%, whereas the recurrence rates were 43% in ADM only, 64% in IPT only, and 20% for the combination of ADM and IPT condition. Patients who were 70 and older benefited less than those 60–69.

Reynolds et al. (2006) compared the prophylactic effects of maintenance antidepressants (paroxetine) and IPT in a group of remitted elderly individuals (>70 years of age). One-hundred and ninety five patients meeting criteria for a depressive episode were assigned to short-term therapy (10–40 mg of paroxetine combined with IPT). Those who achieved full or partial recovery ($N=116$) were randomly assigned to one of 4 maintenance conditions: paroxetine plus monthly clinical management sessions (consisting of 30-min sessions with a focus on symptoms), placebo plus monthly clinical management sessions, paroxetine plus monthly psychotherapy (45 minutes of manualized IPT), and placebo plus monthly psychotherapy. Patients were seen monthly by the same clinician (nurse, psychologist, social worker) who was involved in the acute phase of their treatment. Recurrence was defined as meeting DSM-IV-TR criteria for MDD (according to the SCID), and a score of 15 or higher on the HRSD. The results revealed that the two groups which received maintenance antidepressants had significantly lower recurrence rates (27%) than the two groups that did not receive antidepressants (56%), regardless of the presence or absence of maintenance IPT. The recurrence rates for paroxetine plus monthly clinical management sessions, placebo plus monthly clinical management sessions, paroxetine plus monthly psychotherapy, and placebo plus monthly psychotherapy conditions were 37%, 58%, 35%, and 68%, respectively. The authors concluded that, although maintenance antidepressants demonstrated efficacy in curbing recurrence rates in depression, maintenance IPT did not.

Frank et al. (2008) tested the efficacy of various "doses" of maintenance IPT to decrease relapse in depression. Women who had been treated and who remitted with acute IPT or with combined IPT and ADM ($N=131$) were assigned to weekly, biweekly, or monthly maintenance IPT. Remission was defined in this study as 3 consecutive weeks of HAM-D scores of equal to or less than 7. Similar to the design of the Reynolds et al. (1999) study, maintenance IPT in this study also emphasized augmentation of treatment gains during the acute phase. Recurrence in this study was defined according to DSM-IV criteria for MDD. Over the two-year study period, statistically significant results were obtained whereby 26% of the individuals who were remitted with IPT alone experienced a relapse or recurrence, as compared to 50% of participants who were provided the combined IPT and ADM treatment. No significant differences in recurrence were found across "doses" of IPT. The authors concluded that maintenance therapy administered as infrequently as once a month may protect against recurrent depression. Notably, however, this study failed to have a no treatment, or treatment as usual comparison, so definitive conclusions are difficult to make.

In sum, although research related to the preventive effects of IPT is in its infancy, the available evidence suggests that IPT has a prophylactic effect against recurrent depression. As mentioned earlier, forms of cognitive-behavioral therapy which target relapse and recurrence may be less effective when the depressive cycle is a result of negative life events. As such, IPT may prove even more effective as it is teaches the sufferer to exercise some control over his/her social environment.

8. Possible mechanisms of change in relapse prevention

Given the relative scarcity of relapse prevention research in depression, attempts to understand the mechanisms of change must be considered tentative at best. In this section, we highlight some of the emergent patterns from the extant research, and hypothesize about potential mechanisms of change.

A consistent finding has been that the prevention effectiveness of CT and MBCT is moderated by the number of episodes experienced prior to therapy (Bockting, Spinhoven, Koeter, Wouters and Schene, 2006; Bockting et al., 2005; Monroe, Slavich, Torres, & Gotlib, 2007; Teasdale et al., 2000), as it appears that the prophylactic effects of these treatments are accentuated for patients with three or more

previous depressive episodes. Preventative CT and MBCT appear to do no better than TAU in reducing relapse rates for patients with a history of two or fewer episodes. There are a number of explanations which can be provided to account for this finding. First, some (Fava, Fabbri, & Sonino, 2002; Thase et al., 1992) have suggested that preventative CT works by thwarting residual symptoms of depression after the acute phase of therapy. This explanation is at best incomplete and at worst discordant with the previous finding; if CT functions to minimize residual symptoms, then its prevention effects could not depend on the number of previous episodes, unless the residual symptoms of a fourth or fifth depressive episode are more amenable to change than residual symptoms after a first or second episode. The role of residual symptoms in the etiology of depressive relapse has been inconclusive. While a number of studies (e.g., Bockting, Spinhoven, Koeter, Wouters and Schene, 2006; Conradi, de Jonge, & Ormel, 2008; Judd et al., 2002; Taylor, Walters, Vittengl, Krebaum, & Jarrett, 2010; ten Doesschate et al., 2010) suggest that residual symptoms are partially predictive of relapse, other emergent evidence suggests that self-reported residual symptoms are not significantly associated with increased risk for recurrence (Bertschy et al., 2010).

Secondly, Teasdale et al. (2000) have postulated that with each episode of depression, the association between depressive states and negative thinking patterns is strengthened. If this hypothesis is correct, it is possible that dysphoric states reactivate depressive thinking patterns and therefore initiate the depressive spiral. As such, environmental stressors may become less important for the initiation of recurrent depression, as this state may be easily invoked by rumination or other internal provocation (Monroe et al., 2007). Further, psychotherapy might then exert its preventive effect by disrupting this maladaptive set of thought patterns. The results of Bockting, Spinhoven, Koeter, Wouters, and Schene (2006) suggest that this latter explanation is the more plausible of the two provided thus far.

The above mentioned hypothesis also partially explains the preventative effects of IPT, as this treatment modality helps sufferers identify, anticipate and prevent environmental and social circumstances that make depressive reactions more likely. In other words, while CT and MBCT work to thwart internally propelled depressive patterns, which more often than not become ingrained by the third episode, IPT helps individuals stave off externally provoked depressive reactions which may occur well before the third episode. If this hypothesis is supported in future research, individual history of depressive episodes becomes one of the chief criteria upon which a psychotherapeutic modality is chosen, whereby individuals with less than 3 episodes would likely benefit from IPT and those with a history of 3 or more episodes would benefit from CT or MBCT. Also, and as revealed by the results obtained by Frank et al. (2008), the treatment modality chosen in the acute phase of therapy may affect maintenance/preventative phases of therapy. To date, research which examines the prophylactic effects of IPT is lacking, and thus future research is needed to validate the hypotheses forwarded here.

Third, the differential effect of relapse prevention CT based on the number of previous episodes could simply be explained by a time effect, since many relapse prevention studies have a maximum of 2 year follow-up. It may be for example, that although relapse or recurrence rates do not differ among treatments, there is a delay in relapse in CT, which gives the appearance of lower relapse, as most studies have a follow up time that does not exceed two years. Some support for this time effect has been reported over the 5.5 follow-up study on preventative CT (Bockting et al., 2009) since the apparent indication of the number of episodes experienced for preventative CT to be beneficial decreased with an increase of follow up time.

Finally, and as eluded to earlier, the degree of acceptance of one's condition may provide an explanation of the results wherein individuals with a history of three or more episodes fare better in treatment. That is, acceptance of depression as a chronic and reoccurring problem may be positively and linearly related to the number of previously experienced episodes, and this accepting stance my play a moderating role to therapeutic efforts.

It may be important to distinguish between cognitive structure and content, to provide a coherent narrative of mechanisms of relapse prevention. It has been argued that the long-term effectiveness of CBT may be a function of how well it induces profound, schematic change in its patients (Beck et al., 1979; Hollon, 2003; Hollon et al., 2006). Despite the conceptual clarity of this proposition, schema-focused CBT efforts do not appear to specifically prevent against depression beyond other aspects of CBT (Gortner, Gollan, Dobson, & Jacobson, 1998). A large body of literature also indicates that, although CBT changes surface-level negative thinking in depression, deep-seated cognitive vulnerability is often left unaffected as a result of therapy (see Ingram, Miranda, & Segal, 1998 for a comprehensive review). There is evidence (e.g., Clark, Chamberlain, & Sahakian, 2009) suggesting that such cognitive vulnerability corresponds to deficits in neural circuitry and abnormalities in certain brain regions implicated in emotional processing. As such, it may be possible to link risk etiology in depression to neurocognitive mechanisms. Also, if such a hypothesis is supported by future work, therapeutic work that aims to reorganize these seemingly dysfunctional neural networks may be necessary in curbing relapse in depression.

While the pragmatism of content-focused CBT may be an advantage for this type of therapy, any abandonment of schema-focused CBT may be somewhat premature. Maladaptive schemas may remain dormant, if they are not dealt with in acute phase treatment, until activated by environmental stressors (Dozois & Dobson, 2001). If this model is valid, two specific hypotheses may be engendered to guide future research in relapse prevention in depression. Firstly, CBT's effectiveness in relapse prevention may be mediated by its capacity to loosen the tightly knit negative self-schemas of depressed individuals. In other words, the effectiveness of CT as a prophylaxis for depression may depend on its ability to disorganize deep-seated depressive structures. Second, it may be that successful relapse prevention in depression depends on therapy's ability to better organize and interconnect loose positive self-schemas. As argued by Clark, Beck, and Alford (1999), all individuals possess both negative, potentially depressive schemas and adaptive, constructive schemas. Activation of negative schemas may be the default response to environmental stressors in individuals with a cognitive vulnerability to depression. Positive self-schemas, on the other hand, may be more readily activated in response to stress for healthy, nonvulnerable individuals. Thus, therapy that targets and bolsters these constructive schemas, and makes them the default mode of activation to negative life events, may function to significantly reduce relapse even for patients with a history of two or less depressive episodes.

It may be worthwhile to target cognitive structures and content associated with the processing of more insidious, ongoing stress as part of the therapeutic efforts to thwart relapse in depression. In corroboration with the results obtained in the Bockting, Spinhoven, Koeter, Wouters, and Schene, (2006) trial, Backs-Dermott, Dobson, and Jones (2010), found that chronic interpersonal stress (as opposed to cognitive or personality factors) was the only variable of etiological significance for depressive relapse. Future validation of this hypothesis, namely that daily hassles/ongoing stress is the strongest predictor of depressive relapse, is in order.

It is also possible that access to negative thinking, as opposed to structure in and of itself, may be one of the major culprits for recurrent depression. As argued by Teasdale et al. (2000), MBCT may function to reduce the association between dysphoric mood and depressive thinking. It is also possible that access to the more constructive, adaptive schemas becomes obstructed with recurrent depressive episodes, and that effective therapy works by making positive schemas more accessible (Hollon et al., 2006). Again, this is a provisional hypothesis which needs to be subjected to examination.

There has been little work to support previously postulated theories of mechanisms (such as that of Teasdale et al., 2000), nor are the authors aware of any work testing the validity of hypotheses provided in this paper. Thus, while the general literature on risk factors for recurrence in depression has grown (Burcusa & Iacono, 2007; Dozois & Dobson, 2004), the connection between this literature and the prevention of relapse remains limited.

Although the focus here as been exclusively on number of previous episodes as a moderator for relapse/recurrence prevention, Burcusa and Iacono (2007) have recently reviewed the risk factors for recurrence in depression. These researchers found some equivocal evidence in regards to a several factors (e.g., age at onset of first episode), they, however, identified several factors (e.g., severity of first episode, comorbid disorders for adults, family history of depression and anxiety, attribution style, dysfunctional beliefs, neuroticism, divorce, and paucity of social support) to be associated with recurrence in depression. Thus, it appears that there are a number of variables which increase the likelihood of relapse/recurrence in depression, and a number of such variables may act as moderators to prevention treatment success. The body of research at this stage is still miniscule, and thus more firm conclusions regarding risk factors and moderators are difficult to establish.

9. Conclusions and future directions

Even when it is effective, acute phase therapy does not protect many individuals with depression from experiencing future episodes of the disorder. Although there is evidence that many forms of psychotherapy can reduce the chronicity of depression, most of the studies to date have examined the prophylactic benefits of preventative cognitive therapy. There are a number of more recent studies which indicate that mindfulness-based cognitive therapy (MBCT) and interpersonal therapy (IPT) offer some promise in the prevention of relapse and recurrence of depression. Given the high social, emotional and economic costs associated with depression, and the strong logic associated with the prevention of relapse and recurrence of depression, further efforts in this direction are clearly warranted.

There are a number of theoretical and methodological issues which are apparent in the literature. First, there is a lack of definitional clarity as to what comprises relapse or recurrence in depression. As mentioned earlier, many researchers in the field have indeed conflated these terms despite the available operational definitions (Frank et al., 1991). Future research would benefit from a clearer distinction between relapse and recurrence, as the risk factors and effective interventions may well vary between these two conditions. Second, inconsistent methodologies make it difficult to generalize the results of one study to another. For example, some studies have used rating scales to define remission and relapse, while others have employed diagnostic interviews. Also, most of the studies reviewed have ignored the potential cumulative effects of psychotherapy. For example, some investigations have looked at the protective power of maintenance CBT in participants remitted with ADM, while others have looked at the same outcome variable but with individuals who achieved remission with acute phase CBT. Given the variability in the designs, it is unclear whether the administration of maintenance CBT after acute CBT more effectively curbs future episodes than just effective acute phase CBT. Third, most of the reviewed studies do not control or assess for known risk factors for recurrence (Burcusa & Iacono, 2007). This lack of assessment is problematic given that some studies (e.g., Bockting, Spinhoven, Koeter, Wouters and Schene, 2006; Teasdale et al., 2000) have shown certain factors may interact with the treatment condition to predict relapse and recurrence.

A number of investigations have demonstrated that the history of previous episodes is an important variable which may attenuate or accentuate the prophylactic effects of psychotherapy. In particular, it appears that preventive CT and MBCT works best for individuals with a history of three or more depressive episodes. This effect may be because maintenance treatment functions to disrupt the internal depressive associations which the sufferer tends to make during the course of his/her condition. As such, therapy was shown to be less effective in the reduction of recurrent episodes which are provoked by negative life events. Thus, therapeutic modalities that emphasize skill training and adaptive navigation of the interpersonal arena may work better for individuals with a shorter history of depression, as they allow the individual to practice some control over his/her external environment. Alternatively, it is a result of restricted follow up periods in current studies. True long-term studies are needed with a follow up of 5–10 year to rule out whether the differential effect depending on the number of episodes is simply a results of a time effect. Again, this research is in its infancy and such a hypothesis needs to be empirically validated before its injudicious clinical application.

The mechanisms of depression relapse and recurrence remain elusive (Dozois & Dobson, 2004). It is unclear whether effective prophylactic approaches help the sufferer to modify depressive schemas which become reinforced throughout the course of the disorder, or whether effective therapy helps individuals to better access more constructive and adaptive schemas. It may also be that a critical aspect of relapse prevention is related to the ability to better handle or cope with recurrent stressors and daily hassles. Yet another possible preventative mechanism includes the ability to notice, but not over-react to negative bodily sensations and experiences, which might happen from time to time. Empirical evidence in support of these hypotheses is needed before conclusions may be reached. As this evidence accumulates, however, it may be possible to design more effective and efficient models of relapse prevention, to reduce the burden that this disorder places on those who are affected.

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