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Moderators of Continuation Phase Cognitive Therapy's Effects on Relapse, Recurrence, Remission, and Recovery from Depression

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Abstract

About half of patients who respond to acute-phase cognitive therapy (CT) for major depressive disorder (MDD) will relapse/recur within 2 years; continuation-phase CT lowers this risk. We analyzed demographic, clinical, cognitive, social-interpersonal, and personality variables to clarify which patients continuation-phase CT helps to avoid relapse and recurrence and achieve remission and recovery. Participants had recurrent MDD, responded to acute-phase CT, were randomized to 8 months of continuation-phase CT (n = 41) or assessment control (n = 43), and were assessed 16 additional months (Jarrett, Kraft, Doyle et al., 2001). Consistent with an underlying risk-reduction model, continuation-phase CT was helpful for responders to acute-phase CT with greater risk and/or dysfunction as follows: Younger patients with earlier MDD onset who displayed greater dysfunctional attitudes and lower self-efficacy; personality traits suggesting low positive activation (e.g., reduced energy, enthusiasm, gregariousness); and transiently elevated depressive symptoms late in acute-phase CT and residual symptoms after acute-phase CT response. We emphasize the need for replication of these results before clinical application.

Keywords

depression; continuation-phase cognitive therapy; moderators; recurrence; recovery

Acute-phase cognitive therapy (CT) for major depressive disorder (MDD) reduces depressive symptoms more than non-active comparison conditions (e.g., placebo, no treatment) and as much as pharmacotherapy, interpersonal psychotherapy, and behavior therapy (Craighead et al., 2007; Nemeroff & Schatzberg, 2007). For example, roughly two-thirds of patients who complete acute-phase CT no longer meet criteria for a major depressive episode (Craighead et al., 2007). If acute-phase CT is discontinued after response, however, about half of patients

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will have a major depressive episode within 2 years (Dobson et al., 2008; Vittengl et al., 2007), a rate comparable to continued pharmacotherapy (Dobson et al., 2008; Hollon et al., 2006). The goal of post-acute-phase CT applied after response to an acute-phase treatment (see Vittengl et al., 2007 for types) is to decrease relapse and recurrence (defined as having a major depressive episode before and after recovery, respectively; Frank et al., 1991), and to increase remission and recovery (defined as 6 and 35 weeks, respectively, of few or no depressive symptoms; Jarrett et al., 2001). The purpose of the current analyses is to identify demographic, cognitive, social-interpersonal, and personality variables that moderate the effects of one form of post-acute-phase CT, continuation-phase CT (described below), in a randomized clinical trial (Jarrett et al., 2001). In particular, we aim to clarify which responders most need continuation-phase CT to achieve remission and recovery, and to avoid relapse and recurrence, after response to acute-phase CT, and which responders have positive outcomes without further immediate treatment. Identification of such moderators of intervention is critical to developing personalized preventive care (National Institute of Mental Health, 2008).

Prior research shows that post-acute-phase CT helps some but not all patients. Compared to inactive controls, post-acute-phase CT reduces but does not eliminate relapse (e.g., average 12% vs. 38% of patients relapsed during 9 months of treatment; Vittengl et al., 2007) and increases but does not assure recovery (84% vs. 62% of patients recovered within 2 years after ending acute-phase CT; Vittengl et al., 2009). These data also reveal that some responders to an acute-phase treatment stay well without post-acute-phase CT (e.g., 62% of patients did not relapse/recur within 9 months, and 62% recovered within 24 months, of ending acute-phase treatment; Vittengl et al., 2007, 2009). Understanding which patients benefit most from post-acute-phase CT would clarify the treatment's theory and application, and if replicated inform public health policy.

We analyzed patient-level variables based on Jarrett's risk-reduction model of continuation-phase CT (Jarrett, 1989; Jarrett et al., 2008b). In this biopsychosocial model, three overlapping domains of risk increase the likelihood of relapse and recurrence, and decrease patients' chances of remission and recovery: Dysfunction in (a) genetic, biological, family, and developmental conditions; (b) personality, interpersonal, and social functioning; and (c) cognitive processing or content. After responding to acute-phase CT, recurrence or absence of recovery may result from dysfunction in these domains, especially when residual depressive symptoms, and such challenges as stressful life events, activate depressive cognition and ineffective behavior to overwhelm poorly learned or disused CT skills, and/or as the time away from active treatment increases. Continuation-phase CT aims to promote recovery and prevent recurrence by improving functioning in changeable domains (e.g., social-interpersonal, cognitive), reducing the consequences of less changeable domains (e.g., temperament dimensions), lowering residual symptoms, decreasing the probability of negative life events, and managing challenges better by understanding sources of risk and knowing when to activate new compensatory and coping skills. In the current analyses, we take initial steps in testing the intra-patient risks within the model, leaving the tests of their interactions with external life events for future studies.

Distinctions between acute-phase CT (Beck et al., 1979) and Jarrett's continuation-phase CT (Jarrett, 1989; Jarrett et al., 2008b) are reflected in the phases' primary goals and emphases. Although acute-phase CT, undoubtedly, includes relapse prevention given its aim to help the patient acquire CT skills, its *primary* goal is to reduce depressive symptoms, which is marked by a treatment response. Too often in clinical practice, it can take all of the 16-20 acute phase sessions to help patients acquire basic CT skills (e.g., facility with a thought record) and obtain a treatment response. The practical result is that there is insufficient time left to focus on relapse prevention, stress inoculation, and otherwise promoting a full recovery. In contrast, during continuation-phase CT responders focus on preventing relapse and recurrence, and on

promoting remission and recovery. These aims are achieved as patients consistently maintain and generalize the skills that helped them previously to reduce symptoms. When patients' CT skills were poorly learned in acute-phase CT or fall into disuse, and/or when stressful life events challenge their available repertoire of skills, and thus depressive symptoms occur, continuation-phase CT sessions may resemble acute-phase CT. In other words, skill acquisition and symptom reduction again become the focus. However, when patients evidence few symptoms and high mastery of skills, continuation-phase CT involves enhancing patients' strengths and practicing, reinforcing, and extending CT skills to address individual patients' risks in cognitive and interpersonal spheres. Both phases of CT rely heavily on a cognitive conceptualization (Beck, 1995).

Other researchers' models of post-acute-phase CT share features with Jarrett's model of continuation-phase CT and with one another. For example, Paykel et al.'s (1999) post-acute-phase CT model emphasizes reduction of residual symptoms, resolution of individual problems, and modification of underlying beliefs and schema through behavioral and cognitive techniques. Similarly, in Fava et al.'s (1998) conceptualization, post-acute-phase CT reduces residual symptoms through cognitive change and lifestyle modification to lower stress, and adds well-being therapy to reinforce behaviors promoting wellness and personal growth. Bockting et al. (2005) emphasize evaluating dysfunctional attitudes and fostering realistic attitudes, as well as interventions to enhance patients' memory of specific positive experiences. Finally, Segal et al.'s (2002) mindfulness therapy teaches patients to disengage from (rather than change) dysfunctional cognitions activated by dysphoria, and instead to view negative thoughts and feelings as transient mental events. Treatments derived from these five models of post-acute-phase CT have been shown to decrease relapse or recurrence of major depression (Bockting et al., 2005; Fava et al., 2004; Jarrett et al., 2001; Ma & Teasdale, 2004; Teasdale et al., 2000; Paykel et al., 1999).

These theoretical models, including Jarrett's continuation-phase CT, suggest that post-acute-phase CT may be more helpful for patients who are at greatest risk for relapse or recurrence and for failure to remit and recover. Conversely, other acute-phase treatment responders simply may not need immediate additional treatment and may experience positive outcomes for varying durations. Although a relatively large body of research identifies risk factors for relapse and recurrence of depression, very little research has identified the moderators of post-acute-phase CT 's effects.

It is important to distinguish between risk factors and moderators of treatment effects—not all risk factors are moderators or vice versa. Risk factors are pretreatment or baseline variables that predict poor outcomes overall (i.e., main effects in statistical models), whereas moderators are pretreatment or baseline variables that predict outcomes differently in one treatment condition compared to another condition (i.e., interactions in statistical models; Kraemer, Wilson, Fairburn, & Agras, 2002). For example, high scores on test *A* may predict relapse equally well in both continuation-phase CT and control conditions (*A* is a risk factor), and high scores on test *B* may predict relapse in controls but not in continuation-phase CT patients (*B* is a moderator).

The current analyses contribute to the literature by identifying potential moderators of continuation-phase CT's effects on relapse, recurrence, remission, and recovery. Further, our *a priori* definitions of remission and recovery (6 and 35 weeks of few or no depressive symptoms, respectively; Jarrett et al., 2001; Vittengl et al., 2009) intentionally are more rigorous than in most previous research (e.g., low symptoms at the end of acute-phase CT, DeRubeis et al., 2005; Dimidjian et al., 2006; absence of a major depressive episode during follow-up, Dobson et al., 2008; Hollon et al., 2005). Specifically, our definitions of remission and recovery capture outcomes that arguably are more important to patients and their families

because they require a longer duration (Rush et al., 2006), and because few to no symptoms preclude significantly fluctuating and residual symptoms of depression that produce substantial psychosocial impairment (e.g., at work, in social relationships; Judd et al., 2000). Raising standards for defining positive outcomes will make research more clinically significant and have greater potential to improve public health in ways that matter significantly to patients and their families (Rush et al., 2006; Vittengl et al., 2009; Jarrett & Vittengl, in press).

Demographic, clinical, cognitive, social-interpersonal, and personality variables all have been identified as risks for relapse/recurrence in past research. For example, Burcusa and Iacono (2007) reviewed the literature to conclude that earlier age of onset of MDD, a history of more major depressive episodes, comorbid dysthmia, family history of depression, negative cognitive content, personality (e.g., high neuroticism), and poorer social support are frequently documented risks for recurrence. Fava et al. (2002) concluded that residual symptoms of depression also are strong predictors of relapse and recurrence of a major depressive episode after response to acute-phase treatment. Fava (2007) further conceptualized negative cognitive content and psychosocial dysfunction as broad markers of residual symptoms that predict failure to recover. Also related to residual symptoms, unstable remission involves elevated depressive symptoms late in acute-phase treatment and predicts relapse (Thase et al., 1992; Jarrett et al., 2001).

Among published clinical trials of post-acute-phase CT, presently the only partially replicated moderator of post-acute-phase CT ’s effects of which we are aware is the number of major depressive episodes. In particular, some forms of post-acute-phase CT may prevent relapse/recurrence for patients with at least 3 (Ma & Teasdale, 2004; Teasdale et al., 2000) or 5 (Bockting et al., 2005) prior major depressive episodes, but not for those with fewer episodes. Both research groups noted that patients with more major depressive episodes tended to have an earlier age of MDD onset, as would be expected (Ma & Teasdale, 2004; Teasdale et al., 2000; Bockting et al., 2005). In their general review of depression recurrence, Burcusa and Iacono (2007) discussed that earlier age of onset and more major depressive episodes are significantly correlated (but not synonymous), although it is unclear which variable is more fundamental or what underlying process (e.g., genetics and/or familial environment) may link them and account for recurrence. In the current dataset, Jarrett et al. (2001) reported that continuation-phase CT prevented relapse/recurrence during the 24 months after acute-phase CT for patients whose MDD began before age 18. Jarrett et al. (2001) also found that continuation-phase CT reduced relapse/recurrence for patients with unstable remission in acute-phase CT. Additional research suggests that post-acute-phase CT applied after partial remission of MDD with pharmacotherapy may prevent relapse partly via tempering dichotomous attributions for life events (e.g., attributing the cause of negative events entirely to oneself or entirely to other people; Teasdale et al., 2001).

The current analyses included patients with recurrent MDD who responded to 20 sessions of acute-phase CT, were randomized to 8 months of continuation-phase CT or assessment control, and were followed 16 additional months (Jarrett et al., 2001). Here we extend analyses of this dataset, and of continuation-phase CT in general, to test demographic (e.g., age, gender, ethnicity), clinical (e.g., residual symptoms, age of MDD onset, number of depressive episodes), social-interpersonal (e.g., social adjustment, interpersonal problems), cognitive (e.g., dysfunctional attitudes, self-efficacy), and personality (trait dimensions derived from basic research and *DSM* Axis II diagnoses) variables as potential moderators of continuation-phase CT’s effects. These variables are relevant to Jarrett’s continuation-phase CT model, fit established patterns of risk after remission of major depressive episodes, and were measured with well-established instruments. We tested the general hypothesis that patients with greater dysfunction before and after response to acute-phase CT would benefit more from continuation-phase CT than their counterparts with less dysfunction. We analyzed a wide range

of variables to maximize generation of hypotheses about specific variables for validation in future studies before clinical application (Kraemer et al., 2002).

The current analyses add to the published literature in distinct ways. Although past research has addressed predictors of depressive relapse and recurrence (e.g., Burcusa & Iacono, 2007; Fava, 2007) and potential moderators of acute-phase CT's effects (e.g., depression severity, presence of personality pathology, level of maladaptive cognition; Hollon et al., 2005), we examine a wide range of potential moderators of continuation-phase CT's effects. Especially because depressed patients enter acute-phase CT, but treatment responders enter Jarrett's continuation-phase CT, findings from the acute-phase may not generalize to continuation-phase CT. Additionally, we moved beyond a traditional focus on relapse, recurrence, and short-term cross-sectional estimates of positive outcomes to examine rigorously, longitudinally defined remission and recovery (few or no symptoms consistently for extended periods) as clinically significant outcomes (Rush et al., 2006; Vittengl et al., 2009; Jarrett & Vittengl, in press). From these analyses, we offer empirical guidance for future research that will test specific hypotheses about which patients most need continuation-phase CT, and perhaps other post acute phase CT treatments, to prevent negative and attain positive outcomes.

Method

Participants

Adult outpatients presenting with *DSM-IV* nonpsychotic, recurrent MDD with clear inter-episode recovery (≥2 months of at least nearly normal functioning; American Psychiatric Association, 1994) who scored ≥16 on the 17-item Hamilton Rating Scale for Depression (Hamilton, 1960) participated. Doctoral-level clinicians made diagnoses using the Structured Clinical Interview for *DSM-III-R* (outpatient version; Spitzer, Williams, Gibbon, & First, 1989), with additional questions to assess *DSM-IV* disorders and subtypes. Patients in the experiment (continuation-phase CT vs. control; $N = 84$) were $M = 42.7$ ($SD = 10.4$) years old with $M = 15.4$ ($SD = 2.7$) years of education; 72.6% were women; and 3.6% were African American, 3.6% Hispanic, 2.4% Native American, and 90.5% Caucasian. In addition to MDD, participants' concurrent Axis I diagnoses at intake were social phobia (17.9%), specific phobias (10.7%), panic disorder without (9.5%) and with (1.2%) agoraphobia, posttraumatic stress disorder (8.3%), dysthymic disorder (4.8%), obsessive-compulsive disorder (1.2%), agoraphobia without a history of panic disorder (1.2%), and hypochondriasis (1.2%).

Procedure

Patients ($N = 156$) consented to a 12-14 week acute-phase CT protocol (Beck et al., 1979) including 20 individual sessions (50-60 minutes each). Acute phase CT aims to reduce depressive symptoms by eliciting thoughts associated with dysphoria, teaching patients to test the thoughts' validity logically and empirically, and generating more realistic thoughts when negative thoughts are not supported. Responders to acute-phase CT (i.e., completed the protocol; no MDD and Hamilton Rating Scale for Depression ≤ 9 by an independent evaluator) who consented were randomized to continuation-phase CT (Jarrett, 1989; Jarrett et al., 2008b; $n = 41$) or assessment control ($n = 43$); 3 responders did not consent. The 8-month continuation-phase CT protocol included 10 individual sessions (60 minutes each, but 90 minutes allowed if necessary) provided by each patient's acute-phase CT therapist. The 8-month control protocol included 10 evaluation visits scheduled as in continuation-phase CT. Evaluators of control patients had not provided acute-phase CT and did not use psychosocial interventions. Patients who relapsed were asked to complete all sessions and, if not receiving continuation-phase CT, were referred for treatment outside of the study. The follow-up protocol included 10 assessments scheduled over 16 months (ending 24 months post-acute-phase CT). Pharmacotherapy was not provided in this study.

Therapists

Five therapists with a PhD in clinical psychology or MD (i.e., trained as a psychiatrist), completed ≥ 1 year of CT training and demonstrated competence (scores ≥ 40 on the Cognitive Therapy Scale; Young & Beck, 1980) before treating study patients. Therapists received weekly group supervision (and additional supervision when requested) during both acute and continuation-phase CT from a PhD clinical psychologist with extensive experience supervising CT. To facilitate treatment competence and adherence, an offsite consultant (a PhD clinical psychologist with extensive experience evaluating CT) reviewed videotapes of the 4th and a randomly selected session of both acute and continuation-phase CT, scored therapists on the Cognitive Therapy Scale, and provided them written feedback. All therapists achieved mean Cognitive Therapy Scale scores > 40 during acute (grand $M = 47.1$, $SE = 0.35$) and continuation (grand $M = 46.3$, $SE = 1.17$) phase CT (Jarrett et al., 2001). Scores of 40 and above mark competence within both CT protocols.

Measures

Attributional Style Questionnaire—On the Attributional Style Questionnaire (Peterson et al., 1982), patients generate causes for hypothetical negative and positive situations and rate internal, global, and stable contributions to each cause. Negative and positive situations' ratings are averaged (18 items each) to form failure and success composites (Peterson & Seligman, 1984); higher scores indicate stronger internal, global, and stable (i.e., hypothesized depressogenic) attributions. Correlations with self-report measures of depressive symptoms and self-concept support the measure's validity (Tennen et al., 1987). Median alpha internal consistency was .88 for the failure composite and .84 for the success composite used in the current analyses (Jarrett et al., 2007).

Dysfunctional Attitudes Scale—The Dysfunctional Attitudes Scale (Form A; Weissman, 1979) includes 40 self-report items to measure attitudes hypothesized to relate to depression. Higher scores reflect stronger dysfunctional attitudes. The Dysfunctional Attitudes Scale's validity has been demonstrated by correlations with depressive symptoms and negative cognitive content (e.g., Dobson & Breiter, 1983; Haeffel et al., 2005; Ilardi & Craighead, 1999). Median alpha internal consistency was .95 for the Dysfunctional Attitudes Scale total score used in the current analyses (Jarrett et al., 2007).

Self-Efficacy Scale—The Self-Efficacy Scale (Sherer et al., 1982) includes 23 self-report items measuring expected persistence and success in several domains. Higher scores mark greater self-efficacy. Correlations with interpersonal competency (Sherer et al., 1982) and self-esteem (Lansford et al., 2005) support the scale's validity. Median alpha internal consistency was .92 for the Self-Efficacy Scale total score used in the current analyses (Jarrett et al., 2007).

Social Adjustment Scale—Self Report—The Social Adjustment Scale—Self Report (Weissman & Bothwell, 1976) includes 56 self-report items measuring functioning in important social domains (e.g., work, family, recreation). Patients complete sections reflecting their social roles (e.g., some omit marital and parenting). Higher scores reflect poorer adjustment. In support of its validity, the Social Adjustment Scale—Self Report correlates with clinical ratings of adjustment and is sensitive to change in psychopathology (Weissman & Bothwell, 1976; Weissmann et al., 1978). Median alpha internal consistency was .85 for the Social Adjustment Scale—Self Report total score used in the current analyses (Vittengl et al., 2004).

Inventory of Interpersonal Problems—The Inventory of Interpersonal Problems (Horowitz et al., 1988) measures the extent to which particular behaviors, thoughts, and

feelings cause problems in personal relationships. The measure includes 127 self-report items, and higher values indicate greater problems. The scale correlates appropriately with measures of psychiatric symptoms, and decreases with psychotherapy (Horowitz et al.,1988). Median alpha internal consistency was .98 for the Inventory of Interpersonal Problems total score used in the current analyses (Vittengl et al., 2004).

Dyadic Adjustment Scale—The Dyadic Adjustment Scale (Spanier, 1976) measures satisfaction and positive adjustment in committed romantic dyads (e.g., marital). The scale includes 32 self-report items, and higher scores represent better relationship quality. Spanier (1976) provide data supporting both content and criterion-related validity. Median alpha internal consistency was .96 for the Dyadic Adjustment Scale total score used in the current analyses (Vittengl et al., 2004).

Working Alliance Inventory—The Working Alliance Inventory (Horvath & Greenberg, 1989) is a 36-item questionnaire completed by the therapist and the patient/client to rate the quality of the therapeutic relationship. Higher composite scores indicate a stronger alliance. Alpha internal consistency was .97 for the therapist form, and .96 or the patient form, at acute-phase CT session 18 in the current sample.

Schedule for Nonadaptive and Adaptive Personality—Personality was assessed with the Schedule for Nonadaptive and Adaptive Personality (Clark et al., in press), a 390-item, self-report instrument relevant to both normal and disordered personality. The inventory assesses the core of three higher order temperament dimensions (positive temperament, negative temperament, disinhibition) that reflect the instruments' factor structure and 12 lower order trait dimensions (e.g., mistrust, impulsivity, detachment) derived from *DSM* Axis II disorders and other conceptualizations of nonadaptive personality. The scales have shown good internal consistency (*Mdn* alphas .80-.85 in student, adult, and patient samples), test-retest reliability (e.g., in normal adults, 1 week to 4 months mean $r = .87$), and discriminant validity (mean interscale $r = \sim |.20|$; Clark et al., in press). Studies support the scales' validity in relation to interview measures of personality disorder (Clark et al., in press), informant reports of personality (e.g., Ready & Clark, 2002), and external variables such as psychosocial functioning (e.g., Morey et al., 2007). The median alpha internal consistency was .82 for the 17 scales used in the current analyses (Clark et al., 2003).

Depressive symptoms—Two clinician-rated measures, the 17-item Hamilton Rating Scale for Depression and the Inventory for Depressive Symptomatology clinician version (Rush et al., 1986, 1996), and two self-report measures, the Beck Depression Inventory (Beck et al., 1961) and the Inventory for Depressive Symptomatology self-report version (Rush et al., 1986, 1996), demonstrated high convergence within and across time in the current sample, indicating that they measure the same symptom construct (Vittengl et al., 2005). Higher scores on each reflect more depressive symptoms. Median alpha internal consistency for the four measures' standardized composite was .95 in this dataset (Vittengl et al., 2004) and indexed residual symptoms at randomization. Unstable response to acute-phase CT was defined as any Hamilton Rating Scale for Depression score ≥ 7 at the last 6 acute-phase CT sessions or at randomization (Jarrett et al., 2001).

Longitudinal Interval Follow-Up Evaluation—The Longitudinal Interval Follow-Up Evaluation (Keller et al., 1987), a semi-structured interview, measures *DSM-IV* Axis I psychopathology retrospectively. Independent evaluators completed the interview every 4 months post-acute-phase CT, at study exit, and when patients, therapists, or follow-up evaluators suspected major depressive relapse or recurrence. Independent evaluators were uninformed to group assignment at months 4, 8, 12, and 24, but not at months 16 and 20 because

the primary aim of the parent study was to evaluate outcomes through 1 year from randomization and uninformed evaluations were costly. Independent evaluators did not provide acute or continuation-phase CT in this study and were highly experienced clinicians trained in the application of *DSM-IV* criteria, depressive symptom measures, and the Longitudinal Interval Follow-Up Evaluation. Weekly psychiatric status ratings of *DSM-IV* MDD (on a 1-6 scale) defined remission and recovery, respectively, as ≥ 6 and ≥ 35 continuous weeks of psychiatric status rating of 1 (no symptoms) or 2 (one or two mild symptoms); and relapse and recurrence as ≥ 2 weeks of psychiatric status rating of 5 (meets MDD criteria) or 6 (meets MDD criteria with severe impairment and/or psychosis) before and after, respectively, meeting criteria for recovery (Jarrett et al., 2001). Patients who relapsed before remission or recovery were coded as not achieving remission or recovery, respectively. Psychiatric status rating inter-rater reliability was .80 in the current dataset (Vittengl et al., 2009).

Analytic Strategy

To identify moderators, Kraemer et al. (2002) recommend that researchers compute statistical models including the main effect of treatment group, the main effect of the potential moderator, and the variables' interaction. Moderators reflect baseline characteristics of participants, predict outcomes as interactions with treatment, and may operate with or without a main effect of treatment. We tested demographic, clinical, cognitive, social-interpersonal, and personality variables as predictors (main effects) and moderators (interactions with treatment group) of four outcome variables in Cox regression time-to-event analyses: Relapse over the 8-month experiment, relapse/recurrence over the 8-month experiment plus 16-month follow-up (24 months), remission over 24 months, and recovery over 24 months. These four outcome variables reflect the 8-month experimental design (relapse) plus extended follow-up (relapse/recurrence) as well as an emerging emphasis on patients attaining long-lasting positive outcomes (remission and recovery; e.g., Rush et al., 2006), which are only moderately correlated with avoidance of relapse and recurrence (Vittengl et al., 2009). We centered variables before regression analyses, and followed-up on interactions by computing simple slopes for each treatment group (Cohen, Cohen, West, & Aiken, 2003).

Because the goal of our analyses is to generate hypotheses about personalizing preventive care rather than to test hypotheses about specific variables, we emphasize findings that are clinically meaningful ($r \geq .20$) and likely to replicate ($p_{rep} \geq .90$). Effect size $r = .20$ is roughly the average effect of continuation-phase CT versus non-active control on relapse/recurrence at the end of treatment (Vittengl et al., 2007). Kraemer et al. (2002) recommend that hypothesis-generating studies identify "strong" moderators, so in the context of continuation-phase CT, we highlight moderators as strong as the treatment itself. Effect size $r = .20$ also marks roughly 20% differences in event (e.g., relapse, recovery) probabilities between groups for dichotomous variables (e.g., employed vs. unemployed) and between +/- 1 *SD* contrasts for continuous variables (e.g., low vs. high social adjustment), and thus is likely important in most clinical situations. The statistic $p_{rep} \geq .90$ indicates that there is at least a 90% chance of replicating the effect (r of the same sign) in a new sample from the same population (Killeen, 2005). Focusing on p_{rep} instead of p (e.g., $p < .05$ in null hypothesis significance testing) matches our goal to identify potential moderators that can be tested profitably in future clinical trials aimed at providing guidelines for matching patients to treatments (Kraemer et al., 2002). In this report, we label and interpret findings meeting both criteria, $r \geq .20$ and $p_{rep} \geq .90$, as "substantive."

Relevant Results from Previous Analyses of the Current Dataset

It is important to consider the current findings in the context of previously reported results in this sample. Jarrett et al. (2001) reported that continuation-phase CT reduced relapse compared to assessment control (10% vs. 31%) over the 8-month experiment, and continuation-phase CT reduced cumulative relapse/recurrence compared to control over the full 2 years of follow-

up after acute-phase CT among patients with early-onset MDD (16% vs. 67%) or unstable acute-phase remission (37% vs. 62%). Jarrett et al. (2008a) reported that continuation-phase CT reduced relapse (over 8 months) and relapse/recurrence (over 2 years) for acute-phase CT responders with higher-than-average residual symptoms (measured as a standardized composite of four measures at randomization: Hamilton Rating Scale for Depression, $M = 3.6$, $SD = 2.8$; Beck Depression Inventory, $M = 3.8$, $SD = 4.3$; Inventory for Depressive Symptomatology clinician report, $M = 6.3$, $SD = 5.0$; and Inventory for Depressive Symptomatology self-report, $M = 7.6$, $SD = 6.4$). Finally, Vittengl et al. (2009) found that relative to controls, a few more patients in continuation-phase CT remitted (88% vs. 97%) and significantly more recovered (62% vs. 84%) during 2 years after acute-phase CT.

Results

Table 1 lists variables tested as potential moderators of continuation-phase CT's effects. Variables measured at intake to acute-phase CT included age, age of MDD onset, gender, years of education, length of depressive episode, number of depressive episodes, family history of depression, and number of comorbid axis I diagnoses. Variables assessed "late" were measured at the 18th acute-phase CT session (therapeutic alliance), during the last 6 acute-phase CT sessions and at randomization (un/stable symptom level), or after response to acute-phase CT at randomization to continuation-phase CT or assessment control (employment status, cognitive, social-interpersonal, personality, and residual symptom variables). Patients with higher residual symptoms have poorer outcomes in many studies (e.g., Fava et al., 2002), and relapsed and recurred less with continuation-phase CT (vs. control) in the current dataset (Jarrett et al., 2008a). Moreover, residual depressive symptoms and our outcome variables (depressive relapse, recurrence, remission, recovery) overlap conceptually. Consequently, we controlled residual symptoms (main effect and interaction with treatment group) in analyses of other "late" variables to find incremental predictors and moderators of continuation-phase CT's effects.

Predictors and Moderators of Continuation Phase CT's Effects on Four Outcomes

Relapse—We defined relapse as meeting criteria for MDD before recovery during the 8-month experiment after acute-phase CT. As shown in Table 1, higher failure attributions, lower self-efficacy, greater interpersonal problems, poorer social adjustment, higher mistrust, and lower exhibitionism (marking social inhibition) predicted relapse as main effects. In addition, patients' age, manipulativeness, and exhibitionism interacted with treatment group. Younger age and lower exhibitionism predicted relapse in assessment control but not in continuation-phase CT (see Table 2). Simple slope analyses of manipulativeness did not yield substantive results.

Relapse/Recurrence—We defined recurrence as meeting criteria for MDD after recovery, and we analyzed relapse and recurrence cumulatively during the 24 months of follow-up after acute-phase CT. Younger age, higher aggression, and lower exhibitionism (marking social inhibition) predicted relapse/recurrence as main effects. Further, patients' age, dyadic adjustment (for participants in long-term romantic relationships), entitlement, and detachment interacted with treatment group (see Table 1). Younger age, higher dyadic adjustment, lower entitlement (reflecting a negative self-view), and higher detachment (reflecting social and emotional distance) predicted relapse/recurrence in control but not in continuation-phase CT (see Table 2). Number of major depressive episodes did not predict relapse or recurrence.

Remission—We defined remission as at least 6 continuous weeks of few or no depressive symptoms during the 24 months of follow-up after acute-phase CT. No variables predicted remission as main effects, but residual symptoms and exhibitionism interacted with treatment

group (see Table 1). Higher residual symptoms predicted less remission in control but not in continuation-phase CT. Simple slope analyses of exhibitionism did not yield substantive results (see Table 2).

Recovery—We defined recovery as at least 35 continuous weeks of few or no depressive symptoms during the 24 months of follow-up after acute-phase CT. Older age, later age of onset of depression, lower residual symptoms, lower failure attributions, lower dysfunctional attitudes, and greater self-efficacy predicted recovery as main effects. In addition, age, residual symptoms, stability of response to acute-phase CT, dysfunctional attitudes, self-efficacy, manipulativeness, positive temperament, exhibitionism, and entitlement interacted with treatment group (see Table 1). Older age, lower residual symptoms, stable response to acute-phase CT, lower dysfunctional attitudes, higher self-efficacy, higher manipulativeness (marking less selflessness and less hyperresponsibility), greater positive temperament, and greater exhibitionism (marking less social inhibition) predicted recovery in control but not in continuation-phase CT (see Table 2). Simple slope analyses of entitlement did not yield substantive results.

Overlap among Substantive Predictors and Moderators

Eighteen tested variables were substantive predictors and moderators of C-CT's effects. Although these variables are often considered independently in clinical contexts, understanding their empirical overlap may inform theory of risk for relapse and recurrence, and failure to remit and recover. Table 3 shows correlations among these 18 variables. Correlations typically were small (median $r = |.17|$), although several were strong ($r \geq |.50|$). Perhaps unsurprisingly, younger patients tended to have an earlier age of onset of MDD. Residual symptoms correlated strongly with greater dysfunctional attitudes and poorer social adjustment. Further, dysfunctional attitudes correlated strongly with greater interpersonal problems and poorer social adjustment; and poorer social adjustment additionally related to more interpersonal problems and poorer dyadic adjustment. Finally, lower self-efficacy correlated strongly with more interpersonal problems and mistrust, and mistrust additionally correlated with more interpersonal problems and detachment. Judged by the number of strong correlations (4 each), social adjustment and interpersonal problems were most central to this group of variables.

Discussion

Our analyses identified potential moderators of continuation-phase CT's effects on relapse, recurrence, remission, and recovery among patients with recurrent MDD who responded to acute-phase CT. We note that the predictors and moderators of these four outcomes are distinct, supporting the idea that the constructs are also distinct. Consistent with Jarrett's theoretical model (Jarrett, 1989; Jarrett et al., 2008b) and supporting our general hypothesis, we found variables that predicted relapse/recurrence or failure to remit/recover in the assessment control group but did not predict these outcomes for patients receiving continuation-phase CT. Our interpretation of this pattern is that continuation-phase CT "neutralized" some risks for poor outcomes after response to acute-phase CT. With replication of these moderators, our results may inform theory and application of continuation-phase CT by identifying acute-phase CT patients who likely require further treatment, such as continuation-phase CT, to avoid relapse or recurrence and to achieve recovery. Conversely, other acute-phase CT responders are less likely to need immediate continued care. Our research group is undertaking this replication and clinical translational research in a larger, ongoing two-site randomized controlled trial of continuation-phase CT compared to clinical management plus fluoxetine or matched pill placebo (Jarrett & Thase, in preparation). With the current hypothesis-generating goal in mind, below we summarize our findings as descriptions of patients more likely to avoid relapse/recurrence and to achieve remission and recovery if they receive continuation-phase CT.

Among patients who responded to acute-phase CT, patients more likely to need continuation-phase CT may stand out as having had a long course of illness beginning by late adolescence. Continuation phase CT appeared to neutralize the risk for relapse/recurrence attributable to younger age and age of onset. We also found that continuation-phase CT appeared to neutralize risk from residual symptoms for non-remission and non-recovery. The current findings for remission and recovery add to previous findings in this dataset that continuation-phase CT reduces residual symptoms' prediction of relapse/recurrence (Jarrett et al., 2008a). We therefore controlled residual symptoms in evaluating other moderators of continuation-phase CT assessed late in acute-phase CT.

Beyond residual symptoms assessed at randomization, continuation-phase CT may be helpful for patients who display transiently elevated depressive symptoms late in acute-phase CT (i.e., show incomplete or partial acute-phase remission), report greater depressive cognitive content, and have low positive activation (e.g., low energy, enthusiasm, initiation and enjoyment of social contact; Clark et al., 1994). Other researchers have concluded that personality traits reflecting behavioral passivity present risk for poor outcomes after acute-phase CT (Gollan, Gortner, & Dobson, 2006), and our research suggests that continuation-phase CT reduces this risk. More research is needed to determine the extent to which these variables represent distinct constructs or are largely overlapping.

Among moderators assessed late in acute-phase CT, continuation-phase CT neutralized risk for relapse attributable to low exhibitionism (marking social inhibition); risk for relapse/recurrence attributable to low entitlement (marking low self-esteem) and high social and emotional detachment; and risk for non-recovery attributable to unstable remission to acute-phase CT, dysfunctional attitudes, low self-efficacy, low manipulativeness (marking selflessness and hyperresponsibility) low positive temperament, and low exhibitionism (marking social inhibition). Unexpectedly, higher dyadic adjustment predicted more relapse/recurrence in assessment control (but not in continuation-phase CT). Why relatively better dyadic adjustment was a risk among our control patients is unclear, but we note that mean dyadic adjustment for the full sample (102) and for control patients who relapsed/recurred (107) was below average for married couples (M = 115, SD = 18; Spanier, 1976). The unclear risk for relapse/recurrence in this range of dyadic adjustment was "neutralized" by continuation-phase CT.

Several limitations of our analyses may be important for future research that builds on our findings. The current results with Jarrett's continuation-phase CT (Jarrett, 1989; Jarrett et al., 2008b) applied to acute-phase CT responders and thus may not generalize to other acute- and continuation-phase treatments or to acute-phase treatment non-responders. For example, we did not replicate findings that other models of post-acute-phase CT prevent relapse/recurrence for patients with at least 3 (Ma & Teasdale, 2004) or 5 (Bockting et al., 2005) prior major depressive episodes (but not for those with fewer prior episodes). We did find that the related variable of earlier age of onset of MDD predicted less recovery overall, and more relapse/recurrence in only the control group. Pending replication, these findings raise the hypothesis that unlike other forms of post-acute-phase CT, continuation-phase CT may prevent relapse and recurrence in patients with 2 or more episodes and the risk factors mentioned above. To improve understanding of risk factors and moderators, future research might test this hypothesis against alternative hypotheses about differences in patient samples among studies.

We analyzed many potential moderator variables (i.e., 12 demographic/clinical, 4 cognitive, 3 social-interpersonal, and 17 personality variables) of four outcomes (relapse, relapse/recurrence, remission, and recovery) to maximize identification of potential moderators for confirmation in future research (Kraemer et al., 2002). Because we used a hypothesis-generating analytic strategy (i.e., computed and focused on r and p_{rep} instead of p), the issue

of Type I error does not apply in the conventional sense. Nonetheless, replication is essential to rule out sampling error in novel findings before clinical application. Because the observed effects were modest in size (effect size *r* was in the .2-.4 range), future research aimed at replication of these putative moderators with traditional hypothesis testing may require large samples for adequate statistical power (e.g., roughly 200 patients to achieve power = .80, given rho = .20 and alpha = .05, two-tailed; Cohen, 1988). Furthermore, additional unmeasured variables (e.g., therapists' characteristics, patients' genetic markers or developmental histories) may also moderate continuation-phase CT's effects. Finally, observed predictors and moderators typically were not highly interrelated but exceptions (e.g., the negative relation between self-efficacy and mistrust) are consistent with hypothesized overlap among vulnerabilities to depression (e.g., between depressive cognition and personality pathology; Ilardi & Craighead, 1999; Otto et al., 2007).

Our patients had carefully diagnosed recurrent MDD with clear inter-episode recovery and received acute-phase CT and continuation-phase CT from closely supervised expert therapists. Moreover, our definitions of remission and recovery intentionally mark and attempt to motivate a higher standard of patient success than definitions in most of the depression treatment literature (Vittengl et al., 2009). We cannot rule out the possibility of bias at months 16 and 20 when evaluators were not blind to patients' treatment with continuation-phase CT or assessment-only control. In sum, moderators of continuation-phase CT's effects may vary by the subpopulation of MDD patients studied, therapist qualifications and supervision, and definitions and measurement of patients' outcomes during follow-up.

The current analyses are the most comprehensive examination of moderators of continuation-phase CT's effects of which we are aware. Our results both replicate previous findings of risks for poor outcomes after response to acute-phase treatment (e.g., early age of MDD onset, poor social-interpersonal and cognitive functioning, residual symptoms, personality pathology; Burcusa & Iacono, 2006; Fava et al., 2007) and also add to the literature by identifying demographic, clinical, cognitive, and personality variables that may moderate continuation-phase CT's effects on relapse, recurrence, remission, and recovery. Our moderator results with the SNAP, a trait dimensional assessment derived largely from *DSM* personality disorder criteria, extend previous findings regarding personality disorder as a risk for poorer post-acute-phase treatment outcomes (e.g., Ilardi, Craighead, & Evans, 1997; Mulder et al., 2006). Continuation phase CT, and other preventive and related models, arose in recognition that, despite acute-phase treatments' reduction of depressive symptoms, MDD often is a chronic or recurrent illness and effective treatment can require extended intervention. Our reports have summarized continuation-phase CT's benefits–but also identified limitations–in reducing relapse/recurrence and producing recovery. We offer these findings to stimulate efforts to test hypotheses about when to treat patients with continuation-phase CT to maximize benefits, and to personalize preventive care and reduce the burden of illness for patients with MDD.

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Table 1

Predictors and Moderators of Continuation Phase CT's Effect on Relapse, Recurrence, Remission, and Recovery: Effect size *r*

				Relapse		Relapse/Recurrence		Remission		Recovery	
Test Variable	***n***	***M* / %**	***SD***	**Predict**	**Moderate**	**Predict**	**Moderate**	**Predict**	**Moderate**	**Predict**	**Moderate**
Patient Characteristics											
Age	84	42.7	10.4	-.05	**.21***	**-.24***	**.28***	.08	.00	**.24***	**-.21***
Age of Onset	84	20.5	9.2	Addressed by Jarrett et al. (2001)				.11	-.08	**.22***	-.16
Quality of Acute Phase CT Response											
Residual Symptoms	84	11.7	6.9	Addressed by Jarrett et al. (2008a)				-.17	**.24***	**-.22***	**.24***
Stable Symptom Level	84	38%		Addressed by Jarrett et al. (2001)				.00	.00	.13	**-.20***
Cognitive Content											
ASQ-Failure Comp.	84	3.7	0.9	**.23***	.18	.01	-.13	-.11	.08	**-.25***	.01
Dysfunc. Attitudes	84	97.4	30.6	.16	-.12	.15	-.16	.03	.15	**-.20***	**.24***
Self-Efficacy Scale	84	85.5	14.2	**-.27***	.08	-.14	.13	.00	-.13	**.22***	**-.23***
Social-Interpersonal Functioning											
Interpersonal Probs.	83	0.8	0.5	**.20***	-.03	.04	-.13	.14	.12	-.06	.08
(Low) Soc. Adjustment	84	1.6	0.3	**.23***	.14	.13	.03	.12	.08	-.16	.05
Dyadic Adjustment	47	102.0	23.0	.02	.02	.01	**-.37***	-.18	---	-.07	.12
Schedule for Nonadaptive and Adaptive Personality											
Mistrust	77	4.4	4.0	**.23***	-.06	.11	-.12	.04	.11	-.18	.15
Manipulativeness	77	3.1	2.5	.00	**.26***	-.03	.03	.18	-.14	.11	**-.25***
Aggression	77	3.3	2.8	.07	.13	**.23***	.13	.17	.06	-.09	.01
Eccentric Perceptions	77	2.0	2.1	-.04	.14	.13	.19	.13	**-.20**	-.09	-.14
Positive Temperament	77	17.4	6.0	-.11	.19	**-.20**	.15	-.13	-.13	.16	**-.23***
Exhibitionism	77	6.2	3.4	**-.25***	**.21***	**-.27***	.17	.12	**-.21***	.19	**-.26***
Entitlement	77	8.0	3.2	-.19	.18	-.13	**.23***	.07	-.19	.00	**-.22***
Detachment	77	5.8	3.5	.13	-.16	.04	**-.21***	-.04	.13	-.16	.06

Note. Table contains effect size *r* estimated from Cox regression analyses. *r*s ≥ |.20| in bold type. CT = cognitive therapy. Nonspecific predictors are main effects of test variables; moderators are interactions of the test variables with treatment group (continuation-phase CT vs. assessment-only control). Analyses of cognitive content, social-interpersonal functioning, personality, and working alliance controlled residual depressive symptoms assessed at randomization and their interaction with treatment group. ASQ = Attributional Style Questionnaire. --- = variable excluded to allow the model to converge. Variables with all effect sizes < |.20| are not shown: gender; years of education; employment status; length of depressive episode; number of depressive episodes; family history of depression; total number of comorbid axis I diagnoses, Working Alliance--Therapist and Patient Reports; ASQ-Success Composite; and personality scales Negative Temperament, Self-harm, Dependency, Disinhibition, Impulsivity, Propriety, Workaholism, Low Self-esteem and Suicide Proneness (Self-harm subscales). Gender, family history, employment, and stable symptom level are dichotomous; all other test variables are continuous.

* $p_{rep} \geq .90$

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Table 2

Simple Slope Analyses for Moderators of Continuation Phase CT's Effects: Effect size *r*

	Group	
Test Variable	**Assessment Control**	**Continuation Phase CT**
Moderators of Relapse		
Patient Age	**-.25***	.09
SNAP Manipulativeness	-.18	.18
SNAP Exhibitionism	**-.30***	-.03
Moderators of Relapse/Recurrence		
Patient Age	**-.38***	.02
Dyadic Adjustment Scale	**.29***	**-.25**
SNAP Entitlement	**-.27***	.07
SNAP Detachment	**.21***	-.10
Moderators of Remission		
Residual Symptoms	**-.25***	.07
SNAP Exhibitionism	.18	-.12
Moderators of Recovery		
Patient Age	**.28***	.03
Residual Symptoms	**-.30***	.02
Stable Symptom Level	**.22***	-.05
Dysfunctional Attitudes Scale	**-.24***	.05
Self-Efficacy Scale	**.26***	.00
SNAP Manipulativeness	**.20***	-.15
SNAP Positive Temperament	**.24***	-.05
SNAP Exhibitionism	**.26***	-.07
SNAP Entitlement	.17	-.15

Note. Table contains effect size *r* estimated from Cox regression analyses. *r*s ≥ |.20| in bold type. CT = cognitive therapy. SNAP = Schedule for Nonadaptive and Adaptive Personality.

* *prep* ≥ .90

Table 3

Correlations among Substantive Predictors and Moderators

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. Age	---																
2. Age of Onset	**.50**	---															
3. Residual Symptoms	.10	.15	---														
4. Stable Symptom Level	-.15	-.07	-.46	---													
5. Failure Attributions	.04	.15	.42	-.18	---												
6. Dysfunctional Attitudes	.12	.04	**.55**	-.32	.44	---											
7. Self-Efficacy	.08	-.10	-.36	.12	-.24	-.47	---										
8. Interpersonal Problems	-.02	.30	.43	-.22	.45	**.60**	**-.71**	---									
9. (Low) Social Adjustment	.07	.17	**.61**	-.22	.29	**.55**	-.49	**.54**	---								
10. Dyadic Adjustment	-.12	-.20	-.31	.43	-.17	-.19	.13	-.24	**-.61**	---							
11. Mistrust	-.16	-.01	.23	.03	.39	.36	**-.50**	**.63**	.41	-.11	---						
12. Manipulativeness	.04	.11	.13	.12	.03	.13	-.30	.28	.28	.13	.30	---					
13. Aggression	-.07	.05	.06	.19	.15	.15	-.27	.37	.29	-.01	.46	.24	---				
14. Eccentric Perceptions	.02	.07	.29	-.19	.14	.07	-.14	.09	.13	-.13	.22	.14	.11	---			
15. Positive Temperament	.09	.12	-.27	.03	-.08	-.29	.49	-.32	-.40	.24	-.30	-.11	-.13	.11	---		
16. Exhibitionism	.11	-.02	-.14	.10	-.09	-.23	.25	-.23	-.18	.05	-.23	.10	-.11	.12	.35	---	
17. Entitlement	.20	.00	.07	-.20	.02	-.12	.34	-.29	.01	-.06	-.11	.11	-.02	.16	.17	.27	---
18. Detachment	-.13	-.04	.14	-.17	.17	.17	-.40	.44	.31	-.11	**.52**	.26	.34	.11	-.32	-.29	-.12

Note. $rs \geq |.50|$ in bold type.