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## Cognitive change in cognitive-behavioural therapy

Leanne Quigley

David J A Dozois  
ddoizois@uwo.ca

R Michael Bagby

Daniela S S Lobo

Lakshmi Ravindran

*See next page for additional authors*

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**Authors**

Leanne Quigley, David J A Dozois, R Michael Bagby, Daniela S S Lobo, Lakshmi Ravindran, and Lena C Quilty

Cognitive Change in Cognitive Behavioural Therapy versus Pharmacotherapy for Adult  
Depression: A Longitudinal Mediation Analysis

Leanne Quigley<sup>1</sup>, David J. A. Dozois<sup>3</sup>, R. Michael Bagby<sup>2,4</sup>, Daniela S. S. Lobo<sup>2,4</sup>, Lakshmi  
Ravindran<sup>2,4</sup>, and Lena C. Quilty<sup>2,4</sup>

<sup>1</sup>Yeshiva University, New York, United States

<sup>2</sup>Centre for Addiction and Mental Health, Toronto, Canada

<sup>3</sup>Department of Psychology, Western University, London, Canada

<sup>4</sup>Department of Psychiatry, University of Toronto, Toronto, Canada

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Address correspondence to:

Lena C. Quilty, Ph.D.  
Centre for Addiction and Mental Health  
Department of Psychiatry, University of Toronto  
33 Russell Street, Suite 1026  
Toronto, ON M5S 2S1  
lena.quilty@camh.ca

## Abstract

**Background.** Although cognitive behavioural therapy (CBT) is a well-established treatment for adult depression, its efficacy and efficiency may be enhanced by better understanding its mechanism(s) of action. According to the theoretical model of CBT, symptom improvement occurs via reductions in maladaptive cognition. However, previous research has not established clear evidence for this cognitive mediation model.

**Methods.** The present study investigated the cognitive mediation model of CBT in the context of a randomized controlled trial of CBT versus antidepressant medication (ADM) for adult depression. Participants with major depressive disorder were randomized to receive 16 weeks of CBT ( $n = 54$ ) or ADM ( $n = 50$ ). Depression symptoms and three candidate cognitive mediators (dysfunctional attitudes, cognitive distortions, and negative automatic thoughts) were assessed at Week 0 (pre-treatment), Week 4, Week 8, and Week 16 (post-treatment). Longitudinal associations between cognition and depression symptoms, and mediation of treatment outcome, were evaluated in structural equation models.

**Results.** Both CBT and ADM produced significant reductions in maladaptive cognition and depression symptoms. Cognitive content and depression symptoms were moderately correlated within measurement waves, but cross-lagged associations between the variables and indirect (i.e., mediated) treatment effects were non-significant.

**Conclusions.** The results provide support for concurrent relationships between cognitive and symptom change, but not the longitudinal relationships hypothesized by the cognitive mediation model. Results may be indicative of an incongruence between the timing of measurement and the dynamics of cognitive and symptom change.

*Keywords:* Depression; cognitive behavioural therapy; pharmacotherapy; antidepressant medication; dysfunctional attitudes; cognitive distortions; automatic thoughts; mediation; treatment mechanism; treatment outcome.

## **Cognitive Change in Cognitive Behavioural Therapy versus Pharmacotherapy for Adult Depression: A Longitudinal Mediation Analysis**

Cognitive-behavioural therapy (CBT) for depression is among the most widely used and studied treatments for depression. Despite its demonstrated efficacy overall (Cuijpers *et al.* 2013), clinical trials demonstrate that over one-third of depressed patients do not respond to CBT (DeRubeis *et al.* 2005b; Dimidjian *et al.* 2006; Leichsenring, 2001). According to the cognitive model of depression, negatively biased cognition contributes to the onset and maintenance of depression (Beck *et al.* 1979; Clark *et al.* 1999). CBT is thought to improve depression symptoms by producing adaptive change in cognition. The hypothesized model of change, wherein CBT interventions produce changes in cognition, which in turn ameliorate depression symptoms, is termed the cognitive mediation model of CBT.

### **Evidence for the Cognitive Mediation Model of CBT**

Mediation models seek to explain how an effective treatment leads to symptom improvement (Kraemer *et al.* 2002; MacKinnon *et al.* 2007). A variable that mediates treatment outcome is intermediate in the causal path from the treatment to the outcome (MacKinnon, 2008). A mediator of treatment suggests a possible mechanism of action, which may then be targeted in the development of more potent and/or efficient treatments (Kraemer *et al.* 2002). Demonstration of statistical mediation of treatment outcome requires a significant indirect effect of treatment condition on the outcome, where the indirect effect is the product of: (a) the effect of treatment condition on the mediator ('a' path) and; (b) the effect of the mediator on the outcome, controlling for the effect of treatment condition on the outcome ('b' path; Baron and Kenny 1986; MacKinnon *et al.* 2007).

Mediation specifies a temporal order, such that change in the mediator follows the initiation of treatment and precedes change in the outcome. The full temporal ordering of variables cannot be specified in cross-sectional designs and prospective designs with only two measurement points, and must instead be assumed (Cole & Maxwell, 2003). Maxwell and Cole (2007) demonstrated that temporal assumptions are often erroneous and cross-sectional tests of longitudinal mediation processes produce substantially biased parameter estimates. Longitudinal mediation analysis with three or more measurement points allow tests of the effects of treatment condition on change in the mediator at a later time point ('a' path) and of change in the mediator on change in the outcome at a later time point ('b' path; Cole & Maxwell, 2003; MacKinnon, 2008). The indirect, or mediated, effect in longitudinal analysis is similarly given by the product 'ab'; however, given that the mediator and outcome are measured at repeated time points, there is more than one 'a' path and 'b' path, and thus more than one indirect effect ('ab') evaluated for significance.

Empirical support exists for individual components of the cognitive mediation model of CBT. CBT leads to increased use of cognitive restructuring and other CBT skills, as well as decreased negative automatic thoughts and dysfunctional attitudes (see Garratt *et al.* 2007; Lorenzo-Luaces *et al.* 2015; and Oei & Free, 1995, for reviews). CBT thus has a demonstrated effect on the mediator (i.e., cognition), which is one component of the model. Some researchers have argued that a fundamental assumption of the cognitive mediation model is that cognitive change is specific to CBT, and CBT should, therefore, have a greater effect on cognition than other treatments that presumably work via alternative mechanisms (Garratt *et al.* 2007; Whisman, 1993). In general, this specificity hypothesis has not been supported. The magnitude of cognitive change is similar across CBT and other psychotherapies for depression (Garratt *et*

*al.* 2007; Lorenzo-Luaces *et al.* 2015; Oei & Free, 1995). Garratt *et al.* (2007) argued that cognition is likely directly or indirectly targeted by other psychotherapies, and the specificity hypothesis may be best evaluated by contrasting CBT and pharmacotherapy, as cognitive change may occur in pharmacotherapy but is not thought to be the mechanism of symptom improvement. Comparisons of CBT and pharmacotherapy have yielded mixed evidence, with some studies reporting greater cognitive change in CBT (e.g., Dozois *et al.* 2009; Fresco *et al.* 2007; Ma & Teasdale, 2004) and others reporting no differences between treatments (DeRubeis *et al.* 1990; Fournier *et al.* 2013; Quilty *et al.* 2014; Quilty *et al.* 2008).

There is also evidence for the second component of the model, namely the association between the mediator (i.e., cognition) and outcome, although mostly in the form of concurrent associations. Several studies have found that cognitive change and symptom change co-vary over the course of CBT for depression (Garratt *et al.* 2007; Lorenzo-Luaces *et al.* 2015; Oei & Free, 1995). However, it is necessary to establish the temporal precedence of cognitive change to rule out the possibilities that change in depression symptoms precedes change in cognition or that changes occur simultaneously. A few studies have distinguished concurrent and temporal relationships between cognitive and symptom change, and have found strong evidence for concurrent but not temporal relationships (Lemmens *et al.* 2017; Vittengl *et al.* 2014; Warmerdam *et al.* 2010; but see DeRubeis *et al.* 1990).

Psychotherapy research has only recently begun to incorporate advances in statistical mediation research, including longitudinal designs and analyses (Lemmens *et al.* 2016). The few studies that have evaluated temporal order have found null or weak evidence for the cognitive mediation model of CBT for depression (Lemmens *et al.* 2017; Vittengl *et al.* 2014). Using latent difference score models, Lemmens *et al.* (2017) did not observe indirect effects of cognitive



versus interpersonal therapy on change in depression symptoms via changes in any of the examined mediators (dysfunctional attitudes, interpersonal problems, rumination, self-esteem, and therapeutic alliance). Vittengl *et al.* (2014) evaluated temporal relationships between change in cognitive variables (dysfunctional attitudes, attributions for negative events, hopelessness, and positive coping) and change in depression symptoms during cognitive therapy in a large sample of outpatients with recurrent major depressive disorder (MDD). Structural equation models (SEMs) provided weak evidence for cross-lagged relations in which cognitive change precedes symptom change and vice versa.

### **The Current Study**

The current study incorporated contemporary recommendations for research on mediation models of psychotherapy (Lemmens *et al.* 2016; Lorenzo-Luaces *et al.* 2015) to evaluate the cognitive mediation model of CBT for depression. Pharmacotherapy was used as a comparison treatment to test the specificity of cognitive change and mediation to CBT. Longitudinal SEM was used to evaluate reciprocal relationships between multiple candidate cognitive mediators and depression symptoms (MacKinnon, 2008). Dysfunctional attitudes, cognitive distortions, and negative automatic thoughts were selected as the candidate mediators based on their relevance to cognitive theory and the CBT protocol for depression (Beck *et al.* 1979) and use in previous cognitive mediation research (e.g., DeRubeis *et al.* 1990; Lemmens *et al.* 2017; Quilty *et al.* 2008; Vittengl *et al.* 2014). The following hypotheses were made based on the cognitive mediation model: (1) CBT would lead to greater change in the cognitive variables than pharmacotherapy; (2) the cognitive variables would predict depression symptoms at subsequent time points; and (3) there would be a significant indirect (i.e., mediated) effect of treatment condition on depression symptoms via change in the cognitive variables (i.e., a

significant mediated effect). The data for this study are from a randomized controlled trial (RCT) of CBT versus pharmacotherapy for adult depression (Quilty *et al.* 2014)<sup>1</sup>.

## Methods

### Participants

The sample consisted of 104 participants with a primary diagnosis of MDD (53% female; mean age = 33.61 years,  $SD = 9.97$ ). Eligibility was based on the diagnostic criteria from the *Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition* (DSM-IV; APA, 1994) and determined with the *Structured Clinical Interview for DSM-IV* (SCID-IV; First *et al.* 1995). Participants were required to be between 18 and 65 years inclusive, fluent in English, and capable of giving informed consent. Exclusion criteria included a diagnosis of bipolar disorder, psychotic disorder, substance dependence, or organic brain syndrome; current treatment with antidepressant medications; or electroconvulsive therapy in the past 6 months.

Participants were randomized to a CBT ( $n = 54$ ) or antidepressant (ADM) condition ( $n = 50$ ). Forty-nine participants in CBT and 43 participants in ADM completed at least 8 weeks of treatment. Participants self-identified according to the following Statistics Canada ethno-racial groupings: Caucasian (69.2%); South Asian (15.4%), Black (5.5%); Visible Minority (3.3%); Chinese (2.2%); Latin American (2.2%); Arab/West Indian (1.1%); and Aboriginal (1.1%).

### Measures

**Depression symptoms.** The primary outcome was depression symptoms as measured by the *Hamilton Depression Rating Scale* (HAM-D; Hamilton, 1960). The HAM-D is a 17-item semi-structured interview that assesses depression symptom severity over the past week. The HAM-D was selected as the primary outcome because it is interviewer-administered and consists

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<sup>1</sup> Quilty *et al.* (2014) reported on cognitive structure and processing in CBT versus pharmacotherapy; the current investigation focused on cognitive content as a potential mediator of outcome across the two therapies.

of less cognitive content than commonly used self-report measures including the *Beck Depression Inventory – Second Edition* (BDI-II; Beck *et al.* 1996). These properties are preferable in assessing relationships between depression symptoms and cognitive content (see immediately below) because shared variance due to assessment method and overlapping item content is minimized. Cronbach's alpha values for the HAM-D in the present sample were .69 at Week 0, .77 at Week 4, .83 at Week 8, and .86 at Week 16.

**Cognitive content.** The *Dysfunctional Attitudes Scale* (DAS; Weissman & Beck, 1978) consists of 40 items that measure depressotypic attitudinal statements. Respondents rate their agreement with each statement. The DAS showed high internal consistency in the present sample at each assessment point (Cronbach's  $\alpha = .92$  to  $.94$ ).

The *Cognitive Distortions Scale* (CDS; Covin *et al.* 2011) consists of 20 items that measure 10 cognitive errors that were initially described by Burns (1980) and are commonly discussed in CBT protocols. Respondents indicate how frequently they make each type of error in interpersonal and achievement situations. The CDS showed high internal consistency in the present sample at each assessment point (Cronbach's  $\alpha = .91$  to  $.96$ ).

The *Automatic Thoughts Questionnaire–Negative* (ATQ-N; Hollon & Kendall, 1980) consists of 30 items that measure negative automatic thoughts. Respondents indicate the frequency of negative automatic thoughts during the past week. The ATQ-N showed high internal consistency in the present sample at each assessment point (Cronbach's  $\alpha = .96$  to  $.98$ ).

## **Procedure**

Participants were randomly assigned to 16 weekly sessions of CBT administered according to the protocol outlined by Beck and his colleagues (Beck *et al.* 1979) or 16 weeks of ADM according to Canadian Network for Mood and Anxiety Treatment (CANMAT) guidelines

(Lam *et al.* 2009). CBT was provided by nine study clinicians, including three licensed clinical psychologists and six doctoral-level trainees. ADM was provided by four psychiatrists.

Depression symptoms and cognitive content were measured at Week 0 (pre-treatment), Week 4, Week 8, and Week 16 (post-treatment). Additional details about the original RCT are reported in Quilty *et al.* 2014.

### **Statistical Analyses**

All models were tested using maximum likelihood estimation in Mplus Version 8.1 (Muthén & Muthén, 1998 - 2017). Bias-corrected bootstrapping with 5000 samples was used to compute standard errors. Model fit was evaluated using the model chi-square test, with non-significant chi-square values indicating good model fit, the Comparative Fit Index (CFI), with values  $\geq .95$  indicating close model fit, the Root Mean Square Error of Approximation (RMSEA), with values  $\geq .10$  indicating poor model fit, and the Standardized Root Mean Square Residual (SRMR), with values  $\leq .08$  indicating acceptable fit. The Akaike Information Criterion (AIC) was used to compare alternative models, with lower values indicating better fit.

Four-wave (Week 0, Week 4, Week 8, Week 16) cross-lagged SEMs were estimated to evaluate the longitudinal relationships between treatment condition (dummy-coded 1 for the CBT condition and 0 for the ADM condition), the cognitive variables (DAS, CDS, and ATQ-N) and depression symptoms as measured by the HAM-D (Cole & Maxwell, 2003; MacKinnon, 2008). An advantage of cross-lagged panel models is that all of the effects relevant to mediation (i.e., 'a' paths, 'b' paths, and 'ab' product term) are modeled and tested simultaneously. For each cognitive variable, a model including all cross-lagged paths between the cognitive variable and depression symptoms was specified (Figure 1; MacKinnon, 2008<sup>2</sup>). Although testing the

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<sup>2</sup> The reader is referred to MacKinnon, 2008 for further information on longitudinal SEMs that may be applied in longitudinal mediation analysis.

cognitive mediation hypothesis (i.e., mediation of treatment condition on depression symptoms via change in the cognitive variables) was of primary interest, a model that included all cross-lagged paths between the cognitive variable and depression symptoms was more conceptually plausible than assuming paths from depression symptoms to the cognitive variable are zero, given effects of depressed mood on cognition (e.g., Fresco *et al.* 2006; Miranda & Persons, 1998). Autoregressive relations between the same variable at adjacent waves were included, as well as covariances or residual covariances among the variables within each measurement wave. Measurement error was corrected for in the models by using latent variables with single indicators for each variable, and fixing the variance of the indicator variables to  $a$ , where  $a = (1 - \text{reliability}) \times \text{variance}$  for each variable (see Figure 1; Muthén & Muthén, 1998 - 2017). Reliability was estimated using each variable's Cronbach's  $\alpha$  value.

The assumption of equivalence of cross-lagged relationships between each cognitive variable and depression symptoms across the ADM and CBT groups was tested in two-group models. To provide an additional test of the significance of the cross-lagged paths between the cognitive variables and depression symptoms, the fit indices of cross-lagged models were compared to those of models that included only autoregressive relations between the same variables at adjacent measurement waves and covariances or residual covariances between variables within the same measurement wave.

Indirect (i.e., mediated) effects and their standard errors and 95% CIs were computed for all longitudinal indirect effects between the treatment condition, the cognitive variable, and depression symptoms. Thus, eight indirect effects were tested for each model. Four reflected the cognitive mediation model, with the cognitive variable (M) mediating the effect of treatment condition (X) on depression symptoms (Y): 1)  $X \rightarrow \text{Week 4 M} \rightarrow \text{Week 8 Y}$ ; 2)  $X \rightarrow \text{Week 8 M}$

→ Week 16 Y; 3) X → Week 4 M → Week 8 M → Week 16 Y; and 4) X → Week 4 M → Week 8 Y → Week 16 Y. The other four indirect effects were the same as above but reflected the reverse mediation model, with depression symptoms (M) mediating the effect of treatment condition (X) on the cognitive variable (M). Note that each of the indirect effects represents an ‘ab’ product term, wherein the ‘a’ path is the effect of X on M and the ‘b’ path is the effect of M on Y, controlling for the effect of X on Y.

## Results

### Descriptive Statistics

Table 1 presents the mean scores on the DAS, CDS, ATQ-N, and HAM-D for the ADM and CBT conditions at each measurement wave. Participants in both conditions showed significant decreases on each of the cognitive variables and depression symptoms over the treatment period. Bivariate correlations between the raw study measures are reported in the Appendix.

### Longitudinal Models

The fit indices for the DAS, CDS, and ATQ-N cross-lagged models showed good fit to the data (Table 2). Standardized parameter estimates and standard errors from the three models are displayed in Table 3<sup>3</sup>. There was moderate to high stability of the cognitive variables ( $\beta$ s = 0.64 - 0.87) and depression symptoms ( $\beta$ s = 0.54 – 0.92), across measurement waves, as well as significant correlations between the cognitive variables and depression symptoms within each

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<sup>3</sup> STDXY estimates are reported for parameter estimates with continuous covariates and STDY estimates are reported for parameter estimates with binary covariates (Muthén & Muthén, 1998 – 2017). The standardized coefficient for STDXY standardization is interpreted as the change in y in y standard deviation units for a standard deviation change in x. The standardized coefficient for STDY standardization is interpreted as the change in y in y standard deviation units for the CBT relative to ADM condition.

measurement wave ( $r_s = 0.29 - 0.82$ )<sup>4</sup>. Wald tests within two-group models indicated no significant difference in the magnitude of the cross-lagged paths across the ADM and CBT conditions, for all three models, all  $p_s > .05$ . Thus, the assumption of equivalence of the cross-lagged paths across the CBT and ADM conditions was met, which justifies the use of the cross-lagged models that included participants in both treatment conditions and modeled treatment condition as a two-level predictor variable (as depicted in Figure 1).

**Hypothesis 1: CBT would lead to greater change in the cognitive variables than pharmacotherapy.** Treatment condition was a significant predictor of cognition at Week 4 for the DAS and ATQ-N, and a marginally significant predictor of the CDS at Week 4 (Table 3; a1 paths). However, the direction of this effect was opposite to hypothesis, as participants in the ADM condition reported lower maladaptive cognition (Table 3, a1 paths). At Week 16, the direction of the effect reversed, and participants in the CBT condition had lower levels of maladaptive cognition, although this effect was only marginally significant for the CDS model again. Similarly, participants in the ADM condition had significantly lower depression symptoms at Week 4, but higher symptoms at Week 16, relative to participants in the CBT condition.

**Hypothesis 2: the cognitive variables would predict depression symptoms at subsequent time points.** The cognitive variables did not significantly predict depression symptoms at subsequent time points, as the cross-lagged paths from the cognitive variable to depression symptoms were non-significant in the three models (Table 3; b1, b2, b3 paths). The reverse b paths in all three models (i.e., prediction of subsequent maladaptive cognition by

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<sup>4</sup> The cross-lagged models were also estimated with participant age and biological sex included as covariates. The inclusion of these covariates did not change the results substantively but resulted in reduced model fit relative to the original models. Thus, the results of the original models without the covariates are reported.

depression symptoms) were also non-significant (Table 3; b4, b5, b6 paths). In addition, autoregressive models that eliminated the cross-lagged paths did not result in a significant increase in model misfit for each model (see Table 2), providing additional evidence for the lack of longitudinal relationships between the cognitive variables and depression symptoms.

**Hypothesis 3: there would be a significant indirect effect of treatment condition on depression symptoms via change in the cognitive variables (i.e., a significant mediated effect).** All longitudinal indirect (i.e., mediated) effects of treatment condition on depression symptoms via cognition, and on cognition via depression symptoms, were non-significant for all three models (Table 4).

### Discussion

This study evaluated the cognitive mediation model of CBT for depression in the context of an RCT of CBT versus ADM. SEM was used to evaluate concurrent and longitudinal associations between depression symptoms and three forms of maladaptive cognition relevant to cognitive models of depression etiology and treatment (Beck *et al.* 1979), namely dysfunctional attitudes, cognitive distortions, and negative automatic thoughts. There were significant concurrent, but not longitudinal, relationships between cognition and depression symptoms. Longitudinal indirect (i.e., mediated) effects were non-significant, such that the cognitive variables did not mediate the effect of treatment on depression symptoms and depression symptoms did not mediate the effect of treatment on cognition.

### Effect of Treatment Condition on Cognition and Depression Symptoms

Participants in both the CBT and ADM conditions demonstrated a significant reduction in depression symptoms and maladaptive cognition over the 16 weeks of treatment. Mixed support was found for the hypothesis that CBT would lead to greater change in the cognitive



variables than pharmacotherapy. Change in cognition occurred earlier in the ADM condition than the CBT condition, as indicated by group differences at Week 4. By the end of treatment, the pattern shifted and levels of maladaptive cognition were lower in the CBT condition. However, these effects were small, and they were only marginally significant for the CDS model. This pattern of findings parallels those observed for depression symptoms.

ADM thus appears to produce changes in depression-relevant cognition, at a near-comparable level to CBT. Although this finding contradicts the specificity hypothesis, it is consistent with prior studies that have not found differences in cognitive change in CBT versus pharmacotherapy (DeRubeis *et al.* 1990; Fournier *et al.* 2013; Quilty *et al.* 2014; Quilty *et al.* 2008). It is possible that cognitive change occurred in the ADM condition subsequent to reductions in depression symptoms produced via a biochemical mechanism. In support of this notion, robust concurrent relationships between cognitive and symptom change were observed. A potential explanation for the lack of longitudinal relationship observed is that the majority of change in both depression symptoms and cognition occurred in the first 4 weeks of treatment in the ADM condition, and any temporal relations during this period would be unobserved.

Garratt *et al.* (2007) argued that although pharmacotherapy may lead to reductions in maladaptive cognition, these reductions may more superficial and unstable than the cognitive change produced by CBT. They referred to studies by Segal *et al.* (1999; 2006) that found that dysfunctional attitudes decreased similarly in depressed patients treated with CBT and pharmacotherapy, but patients treated with pharmacotherapy had greater negative cognition in response to induced negative mood than patients treated with CBT. This cognitive reactivity to depressed mood, in turn, was associated with a higher rate of relapse. It would be valuable to

replicate this finding in future studies that include a post-treatment mood induction and/or follow-up period.

### **Association between Change in Cognition and Change in Depression Symptoms**

Evidence for concurrent but not longitudinal associations between cognitive and symptom change is consistent with prior research (e.g., Lemmens *et al.* 2017; Vittengl *et al.* 2014; Warmerdam *et al.* 2010). Several explanations for the lack of longitudinal relationships are possible. As argued by others (Burns & Spangler, 2001; Vittengl *et al.* 2014), some unknown mechanism may have caused simultaneous change in both cognition and depression symptoms. Depression-relevant constructs such as low self-esteem, hopelessness, and cognitive networks or schemas have been proposed as candidates (Burns & Spangler, 2001), but extant evidence does not support their role as mediators or temporal predictors of symptom change (Lemmens *et al.* 2017; Quilty *et al.* 2014; Vittengl *et al.* 2014). One might also posit the therapeutic alliance, therapist empathy, or homework compliance (“common factors”, cf. Rosenzweig, 1936) as common causes of cognitive and symptom change. However, although common treatment factors have been shown to predict outcome (Castonguay *et al.* 1996), these variables have not been found to mediate outcome in CBT (Burns & Spangler, 2001; Lemmens *et al.* 2017), and the mechanisms by which they may relate to outcome are unclear (DeRubeis *et al.* 2005a).

It is possible that the timing of measurement precluded detection of cognitive mediation of symptom outcome. If the dynamics of cognitive and symptom change occur on a more rapid scale than the timing of measurement, then mediation will not be observed. Variables were assessed earlier in treatment and at shorter intervals in the present study than previously (e.g., Lemmens *et al.* 2017; Vittengl *et al.* 2014), but even more frequent measurement (e.g., weekly) may be required. Another compelling possibility is that the timing of change in cognition and

symptoms, and the temporal relationship between these variables, varies across individuals. For some individuals, treatment-related change in cognition and symptoms may occur quickly and/or be tightly coupled in time, whereas for others changes may occur slowly and/or be further related in time. Measurement approaches that allow for between-subject variability in the temporal dynamics of cognitive and symptom change and mediation of change (i.e., ecological momentary assessment) may therefore be preferable. In RCTs comparing psychotherapies, hypothesized cognitive mediators may also be assessed on a session-by-session basis via independent ratings of session audiotapes.

Antidepressant medication was selected as a comparison treatment in this study to provide a stringent test of the specificity of cognitive change and mediation to CBT. Given that one component of the test of mediation is the effect of treatment condition on the mediator, it will be more difficult to detect mediation in an RCT if both treatment conditions produce similar effects on the hypothesized mediator. Future studies of cognitive mediation in CBT may include both an appropriate comparison treatment to test specificity, as well as a control condition that is expected to have a weaker effect on cognition than CBT (e.g., supportive therapy) to provide a more powerful overall test of mediation. It should be noted that the similar effects of the treatment conditions on cognition do not account for the lack of longitudinal relationships between cognition and depression symptoms observed in this study, as discussed above.

### **Study Limitations and Conclusions**

A limitation of this study was the sample size, which, although relatively large for a psychotherapy trial, was modest for mediation analysis. A larger sample would enhance the precision and reliability of the findings, as well as the power of the study to detect small effects (such as the effect of treatment condition on the CDS, which was only marginally significant at

Week 4 and Week 16). Another notable limitation is the lack of a follow-up assessment, which precluded evaluation of the stability of cognitive and symptom change following ADM and CBT. It would be particularly interesting to evaluate whether cognitive change over treatment differentially predicts relapse to depression for participants treated with ADM versus CBT, and/or whether cognitive reactivity to depressed mood differs between the conditions at post-treatment and is predictive of relapse. The candidate cognitive mediators examined in this study were selected because they are central constructs in cognitive theory of depression and targeted in CBT protocols (Beck *et al.* 1979). The selected measures of these constructs have established psychometric properties and have been used in previous investigations of cognitive mediation, which allowed for comparison with extant findings (e.g., DeRubeis *et al.* 1990; Lemmens *et al.* 2017; Quilty *et al.* 2008; Vittengl *et al.* 2014). Future research may evaluate other cognitive constructs (e.g., rumination, self-esteem, attributions) and/or alternative measures that may have greater utility or specificity as mediators of CBT outcome. It is also possible that the relationship between CBT and change in cognition is itself mediated by treatment variables such as homework completion. Future studies that assess treatment variables, cognition, and depression symptoms at multiple time points would be able to test these complex relationships. Finally, the internal consistency of the HAM-D was lower at Week 0 compared to later assessment points; however, unreliability was corrected for in the SEMs which improves the accuracy of parameter estimates (e.g., Goldsmith *et al.*, 2018).

To conclude, the present study investigated the cognitive mediation model of CBT using a longitudinal mediation analysis. Both CBT and ADM produced significant reductions in maladaptive cognition and depression symptoms. There was robust evidence for concurrent but not the hypothesized longitudinal relationships between cognitive and symptom change. Future

research on mediators of psychotherapy outcome may benefit from using measurement approaches that allow for more frequent assessment and between-subject variability in the temporal dynamics of change.

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### **Conflict of Interest**

None.

### **Ethical Standards**

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

### References

- American Psychiatric Association.** (1994). *Diagnostic and Statistical Manual of Mental Disorders (4th ed.)*. American Psychiatric Association: Washington, DC.
- Beck AT, Rush AJ, Shaw BF, Emery G** (1979). *Cognitive Therapy of Depression*. Guilford: New York.
- Beck AT, Steer RA, Brown GK** (1996). *Manual for the Beck Depression Inventory – II*. Psychological Corporation: San Antonio, TX.
- Burns DD, Spangler DL** (2001). Do changes in dysfunctional attitudes mediate changes in depression and anxiety in cognitive behavioral therapy? *Behavior Therapy* **32**, 337-369.
- Castonguay LG, Goldfried MR, Wiser S, Raue PJ, Hayes AM** (1996). Predicting the effect of cognitive therapy for depression: a study of unique and common factors. *Journal of Consulting and Clinical Psychology* **64**, 497-504.
- Clark DA, Beck AT, Alford BA** (1999). *Scientific Foundations of Cognitive Theory and Therapy of Depression*. Wiley: New York.
- Cole DA, Maxwell SE** (2003). Testing mediational models with longitudinal data: questions and tips in the use of structural equation modeling. *Journal of Abnormal Psychology* **112**, 558-577.
- Covin R, Dozois DJ, Ogniewicz A, Seeds PM** (2011). Measuring cognitive errors: Initial development of the Cognitive Distortions Scale (CDS). *International Journal of Cognitive Therapy*, **4**, 297-322.
- Cuijpers P, Berking M, Andersson G, Quigley L, Kleiboer A, Dobson KS** (2013). A meta-analysis of cognitive-behavioural therapy for adult depression, alone and in comparison with other treatments. *The Canadian Journal of Psychiatry* **58**, 376-385.

- DeRubeis RJ, Evans MD, Hollon SD, Garvey MJ, Grove WM, Tuason VB (1990).** How does cognitive therapy work? Cognitive change and symptom change in cognitive therapy and pharmacotherapy for depression. *Journal of Consulting and Clinical Psychology* **58**, 862–869.
- DeRubeis RJ, Brotman MA, Gibbons CJ (2005a).** A conceptual and methodological analysis of the nonspecifics argument. *Clinical Psychology: Science and Practice* **12**, 174-183.
- DeRubeis RJ, Hollon SD, Amsterdam JD, Shelton RC, Young PR, Salomon RM, O’Reardon JP, Lovett ML, Gladis MM, Brown LL, Gallop R (2005b).** Cognitive therapy vs medications in the treatment of moderate to severe depression. *Archives of General Psychiatry* **62**, 409-416.
- Dimidjian S, Hollon SD, Dobson KS, Schmaling KB, Kohlenberg RJ, Addis ME, Gallop R, McGlinchey JB, Markley DK, Gollan JK, Atkins DC (2006).** Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the acute treatment of adults with major depression. *Journal of Consulting and Clinical Psychology* **74**, 658-670.
- Dozois DJ, Bieling PJ, Patelis-Siotis I, Hoar L, Chudzik S, McCabe K, Westra HA (2009).** Changes in self-schema structure in cognitive therapy for major depressive disorder: A randomized clinical trial. *Journal of Consulting and Clinical Psychology* **77**, 1078-1088.
- First MB, Spitzer RL, Gibbon M, Williams JBW (1995).** *Structured Clinical Interview for DSM-IV Axis I Disorders – Patient edition (SCID – IV), version 2*. Biometric Research Department, New York State Psychiatric Institute: New York.



**Fournier JC, DeRubeis RJ, Hollon SD, Gallop R, Shelton RC, Amsterdam JD (2013).**

Differential change in specific depressive symptoms during antidepressant medication or cognitive therapy. *Behaviour Research and Therapy* **51**, 392-398.

**Fresco DM, Heimberg RG, Abramowitz A, Bertram TL (2006).** The effect of a negative

mood priming challenge on dysfunctional attitudes, explanatory style, and explanatory flexibility. *British Journal of Clinical Psychology*, **45**, 167-183.

**Fresco DM, Segal ZV, Buis T, Kennedy S (2007).** Relationship of posttreatment decentering

and cognitive reactivity to relapse in major depression. *Journal of Consulting and Clinical Psychology* **75**, 447 - 455.

**Garratt G, Ingram RE, Rand KL, Sawalani G (2007).** Cognitive processes in cognitive

therapy: evaluation of the mechanisms of change in the treatment of depression. *Clinical Psychology: Science and Practice* **14**, 224–239.

**Goldsmith KA, Chalder T, White PD, Sharpe M, Pickles A (2018).** Measurement error, time

lag, unmeasured confounding: Considerations for longitudinal estimation of the effect of a mediator in randomised clinical trials. *Statistical Methods in Medical Research* **27**, 1615–1633

**Hamilton M (1960).** A rating scale for depression. *Journal of Neurology, Neurosurgery, and*

*Psychiatry* **23**, 56-62.

**Hollon SD, Kendall PC (1980).** Cognitive self-statements in depression: Development of an

automatic thoughts questionnaire. *Cognitive Therapy and Research*, **4**, 383-395.

**Kraemer HC, Wilson T, Fairburn CG, Agras WS (2002).** Mediators and moderators of

treatment effects in randomized clinical trials. *Archives of General Psychiatry* **59**, 877–883.

- Lam RW, Kennedy SH, Grigoriadis S, McIntyre RS, Milev R, Ramasubbu R, Parikh SV, Patten SB, Ravindran AV** (2009). Canadian Network for Mood and Anxiety Treatments (CANMAT) Clinical guidelines for the management of major depressive disorder in adults.: III. Pharmacotherapy. *Journal of Affective Disorders* **117**, S26-S43.
- Leichsenring F** (2001). Comparative effects of short-term psychodynamic psychotherapy and cognitive-behavioral therapy in depression: a meta-analytic approach. *Clinical Psychology Review* **21**, 401-419.
- Lemmens LH, Galindo-Garre F, Arntz A, Peeters F, Hollon SD, DeRubeis RJ, Huibers MJ** (2017). Exploring mechanisms of change in cognitive therapy and interpersonal psychotherapy for adult depression. *Behaviour Research and Therapy* **94**, 81-92.
- Lemmens LH, Müller VN, Arntz A, Huibers MJ** (2016). Mechanisms of change in psychotherapy for depression: An empirical update and evaluation of research aimed at identifying psychological mediators. *Clinical Psychology Review* **50**, 95-107.
- Lorenzo-Luaces L, German RE, DeRubeis RJ** (2015). It's complicated: The relation between cognitive change procedures, cognitive change, and symptom change in cognitive therapy for depression. *Clinical Psychology Review* **41**, 3-15.
- Ma SH, Teasdale JD** (2004). Mindfulness-based cognitive therapy for depression: replication and exploration of differential relapse prevention effects. *Journal of Consulting and Clinical Psychology* **72**, 31-40.
- MacKinnon D** (2012). *Introduction to Statistical Mediation Analysis*. Routledge.
- MacKinnon DP, Fairchild AJ, Fritz MS** (2007). Mediation analysis. *Annual Review of Psychology* **58**, 593-614.

- Maxwell SE, Cole DA** (2007). Bias in cross-sectional analyses of longitudinal mediation. *Psychological Methods* **12**, 23-44.
- Miranda J, Persons JB** (1988). Dysfunctional attitudes are mood-state dependent. *Journal of Abnormal Psychology*, **97**, 76-79.
- Muthén, LK, Muthén BO** (1998-2017). *Mplus User's Guide. Eighth Edition*. Muthén & Muthén: Los Angeles, CA.
- Oei TPS, Free ML** (1995). Do cognitive behaviour therapies validate cognitive models of mood disorders ? A review of the empirical evidence. *International Journal of Psychology* **30**, 145–180.
- Quilty LC, Dozois DJ, Lobo DS, Ravindran LN, Bagby RM** (2014). Cognitive structure and processing during cognitive behavioral therapy vs. pharmacotherapy for depression. *International Journal of Cognitive Therapy* **7**, 235-250.
- Quilty LC, McBride C, Bagby RM** (2008). Evidence for the cognitive mediational model of cognitive behavioural therapy for depression. *Psychological Medicine* **38**, 1531-1541.
- Rosenzweig S** (1936). Some implicit common factors in diverse methods of psychotherapy. *American journal of Orthopsychiatry* **6**, 412-415.
- Segal ZV, Gemar M, Williams S** (1999). Differential cognitive response to a mood challenge following successful cognitive therapy or pharmacotherapy for unipolar depression. *Journal of Abnormal Psychology* **108**, 3-10.
- Segal ZV, Kennedy S, Gemar M, Hood K, Pedersen R, Buis T** (2006). Cognitive reactivity to sad mood provocation and the prediction of depressive relapse. *Archives of General Psychiatry* **63**, 749-55.

- Tofighi D, MacKinnon DP** (2011). RMediation: An R package for mediation analysis confidence intervals. *Behavior Research Methods* **43**, 692-700.
- Vittengl JR, Clark LA, Thase ME, Jarrett RB** (2014). Are improvements in cognitive content and depressive symptoms correlates or mediators during acute-phase cognitive therapy for recurrent major depressive disorder? *International Journal of Cognitive Therapy* **7**, 251-271.
- Warmerdam L, van Straten A, Jongma J, Twisk J, Cuijpers P** (2010). Online cognitive behavioral therapy and problem-solving therapy for depressive symptoms: Exploring mechanisms of change. *Journal of Behavior Therapy and Experimental Psychiatry* **41**, 64-70.
- Weissman AN, Beck AT** (1978). Developmental validation of the Dysfunctional Attitude Scale. Paper presented at the Annual Meeting of the Association of Advancement of Behavioral Therapy, Chicago.
- Whisman MA** (1993). Mediators and moderators of change in cognitive therapy of depression. *Psychological Bulletin* **114**, 248–265.