Patient Expectations in the Treatment of Depression: The Role of Outcome Expectancy in Therapeutic Change across Psychotherapy versus Pharmacotherapy

by

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Abstract

The present study extended previous research on outcome expectancy by exploring its temporal dynamics, as well its relation to depression improvement in two different treatment modalities. A sample of 104 patients with depression were randomized to receive either cognitive behavioural therapy (CBT) or pharmacotherapy for 16 weeks. Outcome expectancy was measured throughout treatment using the Depression Change Expectancy Scale (DCES), a measure comprising two subscales assessing pessimistic versus optimistic expectancies. Results corroborated the role of pre-treatment expectancy on treatment response in CBT. Moreover, associations between mid-treatment expectancy and treatment response were seen in pharmacotherapy. Notably, the associative patterns between expectancy and depression in CBT differed as a function of expectancy valence (i.e., pessimistic versus optimistic). Results support a possible mediational role of expectancy across different treatments for MDD. Future studies incorporating larger sample sizes and more frequent assessments of during-treatment expectancy will be needed to validate these results.
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Chapter 1: Introduction

1.1 Introduction

Depression is among the most common mental illnesses, with nearly 298 million cases of major depressive disorder (MDD) reported worldwide in 2010 (Ferrari, Charlson, Norman, Flaxman, et al., 2013). In Canada in 2012, the point and lifetime prevalence of MDD was 3.9% and 9.9%, respectively (Patten et al., 2015). The disorder further contributes to considerable global burden: in 2010, it represented the second leading cause of disability as measured in years lived with disability (Ferrari, Charlson, Norman, & et al., 2013). Moreover, impairment in both social and occupational functioning associated with MDD, which poses significant economic burden, is well documented (Rizvi et al., 2015).

The Canadian Network for Mood and Anxiety Treatments (CANMAT) guideline outlines pharmacological intervention with antidepressant medications and psychological interventions – particularly cognitive-behavioural therapy (CBT), interpersonal therapy (IPT) and behavioural activation (BA) - as current front-line approaches to the treatment of MDD (Kennedy, Lam, Parikh, Patten, & Ravindran, 2009; Parikh et al., 2016). Of the psychological treatments, CBT has received the most empirical investigation to date (Cuijpers, 2015). However, despite substantial empirical support for the efficacy of medications and the various psychotherapies for MDD, it is well recognized that a sizable proportion of patients do not respond to these treatments. Indeed, reported response rates for CBT for unipolar depression range from 51% – 87% (Hofmann, Asnaani, Vonk, Sawyer, & Fang, 2012). Similar response rates for antidepressant medications (~50%) have been evidenced in large randomized controlled trials (Trivedi et al., 2006).
Such findings highlight the need for a greater understanding of both factors which predict response to treatment in MDD as well as mechanisms by which treatment results in therapeutic change. One potentially important factor is underlying patient expectancies, cognitions regarding a probable future event (Schulte, 2008), which have long been considered to be a powerful determinant of perception and behaviour (Kirsch, 1985).

1.2 Outcome Expectancy

Expectancies are cognitive constructs which contribute to the course of various forms of psychopathology (Rief et al., 2015). Specifically, patient expectancies related to treatment are proposed to be important therapeutic factors which influence both treatment process and outcome (Constantino, Arnkoff, Glass, Ametrano, & Smith, 2011; Glass, Arnkoff, & Shapiro, 2001; Greenberg, Constantino, & Bruce, 2006; Rutherford, Wager, & Roose, 2010). For example, patients may have expectations related to what may transpire during treatment, including the duration and process of treatment, as well as expectations regarding the end outcome of treatment (Constantino, Ametrano, & Greenberg, 2012).

Previous work in the field summarize several theoretical models of psychotherapy, and to some extent, pharmacotherapy, which capture the importance of expectations in treatment to therapeutic outcome (Constantino et al., 2012; Dozois & Westra, 2005; Rutherford & Roose, 2013). Jerome Frank’s model of psychotherapy identifies changes in expectancies as the crucial common mechanism by which all psychotherapies exert their effects (Constantino et al., 2012; Frank, 1961; Swift & Derthick, 2013). According to this model, less optimistic expectancy for change prior to treatment reflects a state of demoralization. Participation in psychotherapy is proposed to lead to “remoralization”, which in turn facilitates greater patient engagement in the therapeutic process (Constantino et al., 2012; Wampold, 2015). The mobilization of positive
expectancies early in treatment are proposed to predict greater degree of therapeutic change (DeFife & Hilsenroth, 2011; Dozois & Westra, 2005). Snyder et al.’s (2000) theory of hope which expanded upon earlier models of “positive expectancies for goal attainment” include the interrelated involvement of expectancies i) regarding one’s ability to generate paths toward goal attainment, and ii) one’s ability to move along these goal paths (Snyder et al., 2000). Moreover, increases in the process of hope is thought to be a catalyst by which cognitive-behavioural interventions are effective (Snyder et al., 2000; Westra, Dozois, & Marcus, 2007).

Patient expectancies are also theorized to underlie the robust placebo response seen in pharmacological interventions, particularly for disorders considered amenable to psychological factors (DeFife & Hilsenroth, 2011; Wampold, Minami, Tierney, Baskin, & Bhati, 2005). Indeed, expectancy theory posits that expectancy is the foundational element to the placebo mechanism, with conscious expectancies of improvement mediating this response (Rutherford & Roose, 2013; Stewart-Williams & Podd, 2004). Importantly, as overall treatment efficacy has been conceptualized as the sum of placebo effects and the effects specific to the active pharmacotherapy, more optimistic expectancy may contribute to stronger treatment effects in active pharmacotherapy (Wampold et al., 2005).

Through conceptualizing treatment outcome as an overarching goal which subsumes several sub-goals, theories of goal attainment also provide further understanding of how expectancies may be important for treatment outcome. In the self-efficacy theory proposed by Bandura (1977), expectancy regarding personal efficacy to produce a future desired change is postulated to be a critical component to goal attainment and to be strengthened through various psychological interventions (Bandura, 1977; Constantino et al., 2012). Similarly, in Carver and Scheier’s (1998) theory of self-regulation of behaviour, both negative and positive expectations
of success have direct implications for whether one remains engaged with the goal at hand (Carver & Scheier, 1998).

Taken together, prominent theoretical models highlight the importance of patient expectancies in therapeutic improvement. Outcome expectancy - the prognostic belief that treatment will in fact lead to an improvement in health status – is a specific form of expectancy which has received the most empirical attention (Greenberg et al., 2006). Expectancy for change, the belief that a desired change in symptoms is indeed possible (Dozois & Westra, 2005), may be considered a variant form outcome expectancy.

Importantly, distinctions have been drawn within the expectancy literature between outcome expectancy and preferences for treatment as well as perceptions of treatment credibility (Constantino et al., 2012, 2011; Greenberg et al., 2006). While clearly related, it is recognized that either preference for a treatment or belief in the plausibility of the treatment upon hearing its rationale (i.e. treatment credibility) can exist independent of a belief in the possibility of change (i.e. expectancy for change) (Constantino, 2012). Previous work supports the relation between expectancy of treatment credibility and treatment outcome in psychotherapy, independent of outcome expectations (Mooney, Gibbons, Gallop, Mack, & Crits-Christoph, 2014). Similarly, while expectancy for change may mobilize motivation and intention to complete the treatment, these constructs are not equivalent. More positive expectancy may affect therapeutic outcomes via the related, but distinct intervening variables of motivation and intention (Constantino et al., 2012). Indeed, findings from previous treatment research in OCD samples have supported that motivation to change and expectancy for change are dissociable in predicting outcome (Steketee et al., 2011).
1.3 Empirical Support for the Role of Outcome Expectancy in Therapeutic Change

In the literature, outcome expectancy has largely been considered a pre-treatment patient characteristic, developed before the patient initiates treatment (Schulte, 2008). Across different diagnoses, a number of diverse factors have been shown to be associated with expectancy prior to treatment, including the severity of presenting symptomatology, positive beliefs about therapy, and other psychological factors such as hopefulness, levels of well-being and psychological-mindedness (Cohen, Beard, & Björgvinsson, 2015; Constantino et al., 2011; Constantino, Coyne, Mcvicar, & Ametrano, 2016; Constantino, Penek, Bernecker, & Overtree, 2013; Safren, Heimberg, & Juster, 1997; Swift, Whipple, & Sandberg, 2012; Tsai, Ogrodniczuk, Sochting, & Mirmiran, 2014; Vîslă, Flückiger, Constantino, Krieger, & Grosse Holtforth, 2018). A negative association between baseline severity of depression and outcome expectancies is consistently evidenced within this research (Cohen, Beard, & Bjorgvinsson, 2015; Constantino et al., 2016; Tsai et al., 2014), even in anxious samples (Lewin, Peris, Lindsey Bergman, McCracken, & Piacentini, 2011; Safren et al., 1997). Importantly, in a large study exploring predictors of patient expectations in a heterogeneous outpatient sample, depression severity was the only unique predictor among other symptom severity (i.e., generalized anxiety severity) and diagnostic variables (Cohen, Beard, & Bjorgvinsson, 2015). Results in fact suggest that patients with MDD report among the lowest expectancy compared to patients with other diagnoses (Cohen et al., 2015; Schulte, 2008). Notably, beyond depression severity at pre-treatment, recent results also support the relation between depression history and initial expectancy (Vîslă et al., 2018).

To date, there have been a number of psychotherapy trials exploring the association between pre-treatment or early treatment outcome expectancy and therapeutic outcome in heterogeneous patient samples as well as specific diagnostic groups (Greenberg et al., 2006). In a
comprehensive meta-analysis of 46 independent studies published before 2009, outcome expectancy at the beginning of psychotherapy was found to have a small, significant positive association with therapeutic outcomes, such as post-treatment symptom severity (Cohen’s $d = 0.24$) (Constantino et al., 2011). These results are in line with previous systematic review findings showing a modest but significant association between outcome expectancies and improvement in psychotherapy (Delsignore & Schnyder, 2007). More recently published investigations have corroborated this relation (Constantino et al., 2016) and have served to provide a more nuanced understanding of this link.

First, emerging evidence supports the variability in the strength of the association between expectancy and therapeutic outcome as a function of diagnosis (Schulte, 2008). Indeed, and in line with the evidence base reviewed above, there is evidence to suggest that the strongest association between expectancy and outcome may be in depressed samples. Schulte (2008) observed stronger correlations of expectancies and treatment outcome in those suffering from depression alone, compared to those with anxiety, with mixed anxiety and depression, or with other diagnoses. Similarly, Webb et al. (2013) reported that pre-treatment expectancy predicted symptom improvement only in their participants with MDD, and not in those with bipolar disorder or psychotic disorder (Webb, Kertz, Bigda-Peyton, & Bjorgvinsson, 2013). These authors proposed that treatment outcome expectancies may be responsible for a larger proportion of symptom improvement in depression in particular due to the usually time-limited nature of a depressive episode as well as potentially greater responsiveness of depressive symptoms to “remoralization” and hopefulness (Webb et al., 2013).

Second, recent research suggests that outcome expectancy is not a static construct; rather, the belief in the likelihood of improvement has been shown to dynamically change throughout
the course of treatment. In individuals with generalized anxiety disorder (GAD), Newman and Fisher (2010) demonstrated increases in a composite measure of outcome expectancy and treatment credibility during a critical period in CBT (Week 4 to Week 7) (Newman & Fisher, 2010). A similar pattern of increase in outcome expectancy was seen in the first 8 sessions of treatment within a large, mixed anxiety disorder sample who were receiving CBT, medication management, or a combination of both (Brown et al., 2014). Earlier increases in outcome expectancy (pre-treatment to session 4) have also been evidenced in an OCD sample receiving group CBT treatment (Vorstenbosch & Laposa, 2015). Change in this construct has also been demonstrated for treatment of mood disorders. In individuals with recurrent major depression with a seasonal pattern, outcome expectancy increased steeply over a 6-week course of group CBT for seasonal affective disorder (SAD) and modestly over a 6-week course of light therapy (Meyerhoff & Rohan, 2016). Finally, overall growth in outcome expectancy was recently demonstrated in depressed patients receiving a 14-week course of individual CBT (Vîslă et al., 2018).

Emerging empirical support for dynamic changes in this construct highlights the importance of evaluating outcome expectancy not only at pre-treatment, but also during treatment course. The demonstration of an association between expectancy during treatment and subsequent symptom improvement may serve to support a mediational role of expectancy. Indeed, change in expectancy during treatment has predicted symptom severity and functioning level at post-treatment in several studies (Brown et al., 2014; Newman & Fisher, 2010; Vorstenbosch & Laposa, 2015), whereas point estimates of outcome expectancy during treatment were linked to clinical outcomes in others (Meyerhoff & Rohan, 2016; Visła, Constantino, Newkirk, Ogrodniczuk, & Sochting, 2016). In Newman and Fisher (2010), change in expectancy
during treatment mediated the relation between pre- and posttreatment symptom severity. Meyerhoff and Rohan (2016) further observed treatment specific effects: treatment expectations at mid-treatment drove depressive symptom change only in the CBT arm, and not for light therapy (Meyerhoff & Rohan, 2016). Taken together, these findings underscore that in addition to the role of pre-treatment outcome expectancy as a prognostic indicator of clinical import, outcome expectancy during treatment may act as a mechanism of therapeutic improvement.

Third, the majority of investigations of the influence of patient outcome expectancies have been circumscribed to psychotherapy, where this cognitive construct has been theoretically regarded as a crucial common factor (DeFife & Hilsenroth, 2011; Greenberg et al., 2006; Wampold, 2015). Yet, expectation of change also appears highly relevant to therapeutic response in other treatment modalities (Rutherford et al., 2010), specifically pharmacotherapy. Indeed, the National Institute of Mental Health Treatment of Depression Collaborative Research Program demonstrated that participants who had lower expectations of change compared to those with higher expectations responded more poorly to both imipramine and placebo medication (Meyer et al., 2002; Sotsky et al., 1991). Most recently, Rutherford et al. (2017) demonstrated the importance of outcome expectancy to antidepressant response by experimentally manipulating participants’ expectancy: participants were randomly assigned to either an open citalopram arm or a placebo-controlled citalopram arm, with the former group demonstrating higher self-reported outcome expectancy post-randomization (Rutherford et al., 2017). Importantly, the study found that participants in the open citalopram arm experienced a significantly greater improvement in their depression at the end of treatment relative to those in the placebo-controlled arm, with post-randomization patient expectancy mediating this difference.
1.4 Outcome Expectancy as a Unique versus Common Mechanism

While pre-treatment patient expectancy appears to predict symptom improvement in both psychotherapy and pharmacotherapy, the causal significance of this construct across these different treatment modalities is presently unclear (Meyerhoff & Rohan, 2016). Notably, extant evidence suggestive of outcome expectancy as a mediator of therapeutic change comes largely from studies incorporating a CBT treatment arm (Brown et al., 2014; Meyerhoff & Rohan, 2016; Newman & Fisher, 2010; Visla et al., 2016; Vorstenbosch & Laposa, 2015). The significance of outcome expectancy to the therapeutic mechanism of CBT is theoretically tenable. As reviewed above, existing theories of therapeutic change in psychotherapy posit that mobilization of optimistic expectancies are central to improvement (DeFife & Hilsenroth, 2011; Frank, 1961; Snyder et al., 2000) and may work by motivating patients to actively engage in the psychotherapeutic process, perhaps by providing tangible pathways towards achieving their goal of improvement (Snyder et al., 2000). In support of this model, positive expectancies in CBT have been linked to homework compliance (Westra et al., 2007) and stronger therapeutic alliance (Westra, Constantino, & Aviram, 2011). Moreover, the CBT treatment protocol contains several opportunities by which outcome expectancy may be specifically bolstered such as therapist provision of treatment rationale (Newman & Fisher, 2010) - a process which has been empirically demonstrated to increase patient expectancy of symptom change (Ahmed & Westra, 2009; Ametrano, Constantino, & Nalven, 2017; Newman & Fisher, 2010).

In contrast to CBT, however, the question of whether or how expectancy changes during the course of antidepressant pharmacotherapy - a treatment for which there is some evidence for pretreatment predictive power of expectancy (Rutherford et al., 2017, 2010) - has not yet been fully explored. Importantly, theoretical models of antidepressant medication and CBT highlight
largely non-overlapping causal targets (Garratt, Ingram, Rand, & Sawalani, 2007). Moreover, the strategies employed for depression reduction clearly differ across these two treatment modalities; relative to CBT, pharmacotherapy may be considered to be less directive, involving fewer opportunities to alter expectancy through client-therapist engagement such as cognitive restructuring or behavioural experiments. Importantly, comparing the impact of outcome expectancy across different classes of treatment can provide greater insight into whether expectancy of change is a common mechanism of treatment.

1.5 Measurement of Outcome Expectancy

The measurement instruments used to assess patient outcome expectancy are consistently recognized limitations in the expectancy literature to date. As reviewed by Rutherford et al. (2010), the majority of self-report scales developed for the assessment of outcome expectancy were purpose-built for a specific investigation and have received limited psychometric validation beyond those investigations (Rutherford et al., 2010). However, a notable exception is the Credibility/Expectancy Questionnaire (CEQ) (Borkovec & Nau, 1972; Devilly & Borkovec, 2000). The CEQ assesses both treatment credibility and outcome expectancy using three questions for each factor (Rutherford et al., 2010). Notably, a major recognized limitation with this scale is that the composite score is often used in the literature, which renders interpretability of the specific relation between outcome expectancy and treatment change difficult (Greenberg et al., 2006). To circumvent this issue, a number of investigations have relied on only the few items thought best to estimate the construct of outcome expectancy (Constantino et al., 2016; Price, Anderson, Henrich, & Rothbaum, 2008; Snippe et al., 2015; Visla et al., 2016). Still others have utilized a single-item scale developed solely for their study (Brown et al., 2014; Delsignore & Schnyder, 2007; Meyer et al., 2002). The psychometric properties of these latter approaches
are unclear, but appear likely to be somewhat limited due to the very brief length of the instruments alone.

Moreover, an important consideration is that expectancies can be directed to the likelihood of positive outcomes (i.e. optimistic expectancy) as well as negative outcomes (i.e. pessimistic expectancy) (Schulte, 2008). The existence of optimistic and pessimistic expectancies is highly relevant to MDD; both these cognitions are seen in this disorder in the form of certainty in the absence of positive future events (i.e., low optimistic expectancy) and certainty in the presence of negative future events (i.e., high pessimistic expectancy) (Miranda, Fontes, & Marroquín, 2008), each proposed to stem from distinct underlying affective-motivational systems (MacLeod, 1996). Pessimistic beliefs regarding symptom control have been shown to be associated with higher dropout in CBT for depression, along with overall poorer treatment response (Westra, Dozois, & Boardman, 2002). In the context of depression, there is thus a particular need to ascertain outcome expectancy framed in both optimistic and pessimistic terms – beliefs in a lack of symptom improvement or whether symptoms will still be present at the end of treatment (Dozois & Westra, 2005; Eddington, Dozois, & Backs-Dermott, 2014; Schulte, 2008).

1.6 Overview of Current Proposal

Taken together, the growing literature supports an important role of pre-treatment patient outcome expectancy as a predictor of treatment response, with strong evidence for MDD. Moreover, recent studies have also implicated outcome expectancy during-treatment in therapeutic improvement, supporting a possible mediator role for this construct. However, as outlined above, there are notable limitations inherent in the literature as well as important questions remaining to be addressed. This present proposal will add to the growing expectancy
literature by first exploring the temporal dynamics of outcome expectancy during the course of treatment for MDD which has received more limited empirical attention to date. This study will also extend previous findings by exploring whether outcome expectancy during treatment serves as a predictor of therapeutic response and thereby a potential mediator of change across CBT and pharmacotherapy – the two most commonly used empirically supported treatments for depression. Importantly, as CBT and pharmacotherapy are distinct treatment modalities, we will also explore whether this construct represents a specific or non-specific mediator. Finally, this study will improve upon the current literature by measuring outcome expectancy using a more refined scale (the Depression Change Expectancy Scale (DCES) (Eddington et al., 2014)) designed to evaluate both pessimistic and optimistic expectancies specific to depression.

1.7 Research Aims and Hypotheses

1) To examine how outcome expectancy changes over the course of treatment during a 16-week course of pharmacotherapy versus CBT for MDD.

Growing evidence using more limited measures of expectancy have shown growth in this construct during psychotherapy (Brown et al., 2014; Meyerhoff & Rohan, 2016; Newman & Fisher, 2010; Vîslă et al., 2018; Vorstenbosch & Laposa, 2015), and some evidence exists for improvement during a distinct treatment modality (i.e. light therapy; (Meyerhoff & Rohan, 2016)). Insofar as outcome expectancy represents an important cognitive construct to the maintenance of depression, I predict that patient outcome expectancy will improve from pre-treatment to post treatment in CBT and pharmacotherapy as both treatment conditions have been shown to alter maladaptive cognitions in this disorder (Garratt et al., 2007). However, I predict that the greatest change in expectancy will be evident in CBT given the more
directive approach of CBT whereby many opportunities exist to alter expectancy through patient-therapist interaction (Newman & Fisher, 2010).

2) To examine the predictive utility of outcome expectancy during treatment on treatment outcomes in pharmacotherapy versus CBT for MDD.

In light of the extant literature implicating a predictive role of outcome expectancy at the beginning of treatment in depression symptom improvement in both CBT (Renaud, Russell, & Myhr, 2013; Schulte, 2008; Tsai et al., 2014; Webb, Beard, Auerbach, Menninger, & Bjorgvinsson, 2014; Webb et al., 2013) and treatment with antidepressants (Krell, Leuchter, Morgan, Cook, & Abrams, 2004; Meyer et al., 2002; Rutherford et al., 2010; Sotsky et al., 1991), I hypothesize that higher optimistic outcome expectancy and lower pessimistic expectancy at pre-treatment will predict subsequent depression severity in both treatments. However, given the proposed centrality of positive expectancies to therapeutic improvement in the theoretical mechanisms of change for psychotherapy (Constantino et al., 2012; DeFife & Hilsenroth, 2011; Frank, 1961), I hypothesize that the predictive association of outcome expectancy measured during treatment and depression outcome will be stronger in the CBT arm.

3) To examine differences in the role of pessimistic outcome expectancy versus optimistic outcome expectancy throughout treatment.

In light of limited empirical work on this topic, no specific hypotheses were made for this research aim.
Chapter 2: Methods

2.1 Participants

The current study used archival data previously collected at the Centre for Addiction and Mental Health in Toronto, Canada, with the primary aim of investigating the causal role of cognition in the treatment of MDD (Quilty, Dozois, Lobo, Ravindran, & Bagby, 2014). Participants met the following inclusion criteria: i) having a primary diagnosis of MDD as determined using the Structured Clinical Interview for DSM-IV Patient Version (SCID-I/P; (First, Spitzer, Gibbon, & Williams, 1995)); ii) being between 18 to 65 years of age; iii) demonstrating fluency in English; and iv) demonstrating capacity for consent. Moreover, participants: i) did not have a diagnosis of bipolar disorder, psychotic disorder, substance dependence or organic brain syndrome; ii) was not receiving current treatment with antidepressant medications, and iii) did not receive electroconvulsive therapy (ECT) in the 6-month period prior to study onset.

2.2 Procedures

Participants were recruited using a range of advertisement approaches, including online and print advertisements in local newspapers and classifieds; posters in the local transit system; posters and presentations within CAMH and mail-outs to nearby health care clinics. A total of 1415 individuals either responded to the advertisements or were referred by their physicians. Of this number, 333 completed telephone screening interview of eligibility criteria. A total of 175 individuals then completed an in-person screening interview. Of the 140 participants deemed eligible to participate, 104 were enrolled in the study following oral and written consent.

The 104 participants were randomized to receive either 16 sessions of CBT (n=54), or 16-weeks of antidepressant medication (n=50). Stratified randomization was used to match
participants on gender and depression recurrence across both treatments. There were 5 drop-outs in the CBT group and 7 dropouts in the medication group, resulting in 49 CBT treatment completers and 43 medication treatment completers (final \(N=92\)). Treatment completers had completed at least 8 sessions. A total of thirteen therapists and physicians were involved in providing the study treatment. Treatment with pharmacotherapy was guided by the Canadian Network for Mood and Anxiety Treatment (CANMAT) guidelines (Kennedy et al., 2009). Treatment with CBT was guided by the protocol outlined by Beck (Beck, Rush, Shaw, & Emery, 1979).

2.3 Measures

During treatment, assessments were conducted at four time points: at pre-treatment (week 0), week 4, week 8 and post-treatment (week 16; Quilty et al., 2014). Outcome expectancy and depression were measured using the following scales.

*Depression Change Expectancy Scale (DCES).* The Depression Change Expectancy Scale is a recently developed self-report questionnaire developed for the measurement of outcome/change expectancy in depression (DCES; Eddington et al., 2014), modified from an expectancy scale developed specifically for anxiety disorders (Dozois & Westra, 2005). The DCES assesses both broad as well as treatment focused expectations for change in depression symptoms, each measured using a Likert-type scale ranging from 1 (strongly disagree) to 5 (strongly agree). The DCES comprises the DCES-P and the DCES-O subscales, which include 11 pessimistically worded items and 9 optimistically worded items, respectively. The DCES-P items were reverse scored. In a psychometric evaluation using a clinical sample, the DCES demonstrated good internal consistency (coefficient \(\alpha = 0.75\) and 0.82), expected convergent,
divergent, and predictive validity with respect to short-term improvement in depression symptoms (Eddington et al., 2014).

**Beck Depression Inventory II (BDI-II).** The Beck Depression Inventory-II (BDI-II) is a commonly used self-administered inventory, comprising 21 items which assess severity of depressive symptoms (Beck, Steer, & Brown, 1996). Responses to items are given on a Likert-type scale ranging from 0 to 3. Previous psychometric analyses report notably high internal consistency (average coefficient $\alpha = 0.92$; Dozois & Covin, 2004). In the present sample, the coefficient $\alpha$ ranged from 0.84 to 0.94 across Weeks 0 through 16 (Quilty et al., 2014).

**Hamilton Depression Rating Scale (HAMD).** The Hamilton Depression Rating Scale (HAMD) is the most widely used clinician administered assessment of depression severity (Hamilton, 1960). This semi-structured interview demonstrates adequate internal, interrater and retest reliability estimates and adequate convergent, discriminant and predictive validity (Bagby, Ryder, Schuller, & Marshall, 2004). In the present sample, the coefficient $\alpha$ ranged from 0.69 to 0.86.

### 2.4 Statistical Analyses

Assumptions were tested using IBM SPSS Statistics Version 24.0. Analyses for the main study aims (see below) were conducted using Mplus Version 8.0. For item-level missing data, mean replacement of the missing item was used. Scale-level missing data in the measures of interest ranged from 0% (all measures at week 0) to 19.2% (HAMD at week 16) and was handled using full information maximum likelihood estimation in Mplus (Muthén & Muthén, 2017). Model fit was ascertained using the following fit indices: chi-square goodness of fit, standardized root mean square residual (SRMR), root mean-square error of approximation (RMSEA), and Bentler’s Comparative Fit Index (CFI). Based on the recommendations of Hu and Bentler
(1999), good model fit was defined as an RMSEA value of <0.05, SRMR value of <0.08 and a CFI value of > 0.95. RMSEA values of <0.08 were considered indications of adequate model fit and RMSEA values of >0.10 were considered poor fit (Hu & Bentler, 1999; Kline, 2011). In comparing models, information from all fit indices were considered. Moreover, in the case of nested models, difference testing using the Satorra-Bentler Scaled $\chi^2$ was used (Satorra & Bentler, 2001). To explore possible differences in depression and outcome expectancy at week 0 between treatment groups, the Wald Test of Parameter Constraints in Mplus (Muthén & Muthén, 2017) was used to measure whether the difference between variables across the two treatment groups was significantly different from 0, based on a $\chi^2$ with 1-degree of freedom.

Change in outcome expectancy was modeled using latent growth curve modeling (LGM) – a growth model approach to estimate between-participant differences in the latent trajectory of a variable (Curran, Obeidat, & Losardo, 2010) - using a structural equation modeling framework in Mplus. LGMs are flexible in modeling both linear and nonlinear trajectories (Newsom, 2015), and using data which are partially missing (Curran et al., 2010). Moreover, as suggested by Curran et al. (2010), such models have previously been successfully estimated using small samples ($n=22$; (Curran et al., 2010)). Two latent factors representing the intercept and slope were estimated, along with the covariance between the two factors. The mean of the intercept and slope represent fixed effects, indicating the average baseline value and average change over time, respectively. Variability in these factors between participants – i.e. random effects - are represented with the factor variances (Newsom, 2015).

To ascertain the relation between outcome expectancy and depression throughout treatment, cross-lagged panel models were employed. Cross-lagged modeling allows for the exploration of the causal relation between variables longitudinally. Specifically, by modelling
cross-lagged (bi-directional) paths between expectancy and depression, the directionality of this causal relation may be explored (Newsom, 2015). Moreover, through the inclusion of autoregressive paths for each variable, the estimated cross-lagged effects are controlled for the effect of previous time points within each variable (i.e., stability; (Newsom, 2015). To ensure equal time intervals were modelled, only week 0, week 8 and week 16 were included. A multi-group approach was taken in Mplus to model the panels separately in the medication and CBT group, allowing for an exploration of whether the cross-lagged associations differed as a function of treatment group. To limit the number of tests performed, the Wald Test of Parameter Constraints (Muthén & Muthén, 2017) was used to test the equality of the regression parameters in only the cross-lagged paths from expectancy to depression in the medication versus CBT treatment groups.

For all models, modification indices were examined upon indication of possible misspecification. Only theoretically tenable modifications were considered (Kline, 2011).
Chapter 3: Results

Examination of univariate skewness and kurtosis revealed estimates within recommended cutoffs for skewness (<2) and kurtoses (<7) (Curran, West, & Finch, 1996) for most variables of interest. However, the optimism subscale of the DCES demonstrated negative skew and kurtosis at week 16 for the CBT group (-2.09 and 8.29, respectively). As such, study analyses were conducted using a robust maximum likelihood estimation technique robust to non-normality in data (Muthén & Muthén, 2017). The estimated means and standard deviations of the DCES scores and depression scores are displayed in Table 1. As noted, DCES-P items were reverse scored.

3.1 Change in Outcome Expectancy

Visual inspection of the pattern of change for the optimism and pessimism subscales of the DCES in the two treatment groups suggested non-linear growth only in the medication group. As such, both linear (slope loadings = 0, 1, 2, 4) and freely estimated (slope loadings = 0, *, *, 4) unconditional models were compared for each subscale in the two treatment groups separately. The latter approach aims to optimally fit the slope to the data at hand, such as non-linear trends (Curran et al., 2010; Kline, 2011). Time was centered at week 0. As demonstrated by Preacher et al. (2008), model fitting began with a random intercept model. A fixed slope parameter was then introduced, and then subsequently freed, allowing growth parameters to co-vary; model fit indices were explored at each step of model building (Preacher, 2008). Consistent with the observed trends, the freely estimated slope demonstrated more favourable fit over the linear slope on all indices for the medication group. For the CBT group, the fit of the two conditional models (linear slope vs. freely estimated slope) was comparable. Importantly, the freely
estimated slopes approximated linear change in the CBT group (i.e. estimated slope loadings = 0, 1.2, 2.4, 4), supporting the observed pattern of change.

As we could not assume measurement invariance across our groups owing to the differing trajectories (and therefore, non-invariant factor loadings) (Kim & Willson, 2014; Newsom, 2015; Preacher, 2008), the latent growth curve model (LGCM) analyses were estimated in the CBT and medication groups separately. Model fits of all final models are reported in Table 2a. Unstandardized parameter estimates from all LGCMs are reported in Table 3.

### 3.1.1 Medication Group Results

In the medication group, the LGCM for pessimistic outcome expectancy including a random intercept and fixed slope resulted in very poor model fit ($\chi^2(5, n=50) = 35.21, p<0.001$, CFI = 0.74, RMSEA = 0.35, SRMR = 0.48). Introduction of a random slope resulted in an inadmissible model solution, indicating potential structural misspecification requiring modification. This model was deemed uninterpretable.

The LGCM for optimistic outcome expectancy including a random intercept and fixed slope revealed poor fit ($\chi^2(5, n=50) = 12.09, p=0.04$, CFI = 0.93, RMSEA = 0.17, SRMR = 0.31). The model with a random slope fit notably better (Table 2a) and was used as the final model. The estimated factor loadings – 0.00, 2.92, 4.18 and 4.00 – confirmed non-linear growth. The average pre-treatment score on the DCES-O was 29.06, and demonstrated significant variability across participants ($B = 20.96, p=0.03$). The mean slope indicated significant positive growth ($B=1.05, p<0.001$). There was a non-significant negative correlation between growth factors ($r= -0.10, p=0.77$), suggesting a lack of relation between initial expectancy and change throughout treatment.
3.1.2 CBT Group Results

While the LGCM for pessimistic outcome expectancy with a fixed slope did not fit poorly ($\chi^2(7, n=54) = 9.39, p=0.226$, CFI = 0.96, RMSEA = 0.08, SRMR = 0.15), better fit was demonstrated with a random slope (Table 2a). Therefore, the final LGM for pessimistic outcome expectancy included a random intercept, random slope and factor covariance. The average pre-treatment score on the DCES-P was 34.54, with significant variability across participants (B=48.47, $p<0.001$). The slope indicated significant positive linear growth on average ($B = 2.75, p<0.001$). The correlation between the two latent factors was negative and significant ($r = -0.48, p=0.001$), indicating that higher expectancy scores (measured using the DCES-P subscale) at pre-treatment tended to be associated with less increase in expectancy over time.

For optimistic outcome expectancy, introduction of a random slope factor resulted in an inadmissible model solution (correlation > 1.0 between latent factors). As such, the final model included a fixed linear slope, which demonstrated acceptable model fit (Table 2a). As the variance of the slope was fixed at 0, the covariance of the slope with the intercept was not estimated. The mean intercept was 30.78, and demonstrated significant variability across participants (B = 9.13, $p=0.001$). The slope indicated significant positive linear growth on average ($B = 1.47, p<0.001$).

Taken together, results of the LGCMs supported non-linear growth only in optimistic outcome expectancy within the medication group. Specifically, the growth curve demonstrated increases in expectancy from week 0 to week 8, followed by a decrease in expectancy from week 8 to week 16. Results of the LGCMs also indicated linear growth in optimistic outcome expectancy in the CBT group. Pessimistic outcome expectancy, reverse scored, also revealed linear growth in the CBT group. It is important to note that for most of the LGCMs, support for
model fit was mixed, with the SRMR values outside the recommended cutoff (<0.08; see Table 2a). As such, the presence of some model misfit is possible.

### 3.2 Links between Outcome Expectancy and Depression

The following cross-lagged panel models were developed to assess the causal relation between outcome expectancy and depression over time: pessimistic outcome expectancy modeled with the BDI-II (Model 1), pessimistic outcome expectancy modeled with the HAMD (Model 2), optimistic outcome expectancy modeled with the BDI-II (Model 3), and optimism expectancy modeled with the HAMD (Model 4).

Model-building began with an initial structure applied to all four models (1a-4a), which included all autoregressive and cross-lagged panel effects with only a time lag of 1 (i.e. depression at time t had an effect on depression at time t+1 and expectancy at t+1). Model fit indices of these initial models are displayed in Table 2b. With this structure, both the DCES-P models demonstrated good fit as per all indices. However, the DCES-O models were either adequate or poor fitting based on RMSEA values >0.06 and >0.10, respectively.

Based on both extant literature substantiating the relation between pre-treatment expectancy and post-treatment outcome, and previous work with similar study aims (Meyerhoff & Rohan, 2016), cross-lagged paths between week 0 and week 16 for the four models were added (models 1b-4b). This addition resulted in notably better fit for the DCES-O models (Table 2b) across all indices; the chi-square difference test for the addition of these paths was significant for the BDI-II model (adjusted Satorra– Bentler $\chi^2 (n=104, 4) = 12.06, p<0.05$), but was not significant for the HAMD model (adjusted Satorra– Bentler $\chi^2 (n=104, 4) = 7.07, p>0.05$). Addition of the week 0 to week 16 paths did not affect model fit for any of the indices in the DCES-P model with BDI-II as an outcome (Table 2b). However, the RMSEA value for the
modified DCES-P model with HAMD as an outcome was outside of the recommended cutoff for good fit (>0.06), although the \( \chi^2 \) difference test was not significant (adjusted Satorra–Bentler \( \chi^2 (n=104, 4) = 1.29, p>0.05 \)). To maintain consistency across models, the additional paths from week 0 to 16 were included in all four models. The overall model structure is shown in Figure 1.

### 3.2.1 Models 1b and 2b: Pessimistic Outcome Expectancy and Depression

In models 1b and 2b, all autoregressive paths for both pessimistic outcome expectancy and depression were significant in both treatment groups (\( p < 0.05 \)), with prior scores (\( t \)) positively predicting subsequent scores at a time lag of 1 (\( t+1 \)).

Cross-lagged paths from these models are presented in Table 4. In model 1b, the DCES-P score at week 8 was a significant negative predictor of week 16 BDI-II in the CBT group (\( \beta = -0.31, p = 0.02 \)), but not in the medication group (\( \beta = -0.23, p = 0.31 \)). Despite the finding that this path significantly differed from 0 only in the CBT group, the Wald test was not significant (\( \chi^2 (1, n=104) = 0.04, p=0.852 \)). This suggests that the path from expectancy measured using the DCES-P at week 8 to depression measured using the BDI-II at week 16 was not significantly stronger in CBT compared to medication.

In model 2b, the DCES-P score at week 8 was a significant negative predictor of HAMD score at week 16 in the medication group (\( \beta = -0.43, p=0.004 \)) and in the CBT group (\( \beta = -0.32, p=0.03 \)). Similar to model 1b, the Wald test indicated that the estimated coefficients for this path did not significantly differ across the two groups (\( \chi^2 (1, n=104) = 0.03, p= 0.872 \)). In both models 1b and 2b, none of the paths from depression to pessimistic outcome expectancy were significant in either of the two treatment groups (\( p>0.05 \)).
In summary, a significant relation between pessimistic outcome expectancy at week 8 and end of treatment depression was found in both models. The strength of this path did not significantly differ as a function of treatment modality.

### 3.2.2 Models 3b and 4b: Optimistic Outcome Expectancy and Depression

In models 3b and 4b, all autoregressive paths for optimistic outcome expectancy and depression were significant in both treatment groups ($p<0.05$), with prior scores ($t$) positively predicting subsequent scores at a time lag of 1 ($t+1$). Cross-lagged paths from the two optimistic outcome expectancy models are presented in Table 5.

In model 3b using the BDI-II, the DCES-O score at week 0 was negatively predictive of depression at week 8 in the medication group ($\beta = -0.30, p=0.031$), but not the CBT group ($\beta = 0.03, p=0.817$). The results of the Wald test indicated that the difference in this path across the two groups was not significant ($\chi^2(1, n=104) = 3.13, p=0.077$). Similarly, week 8 DCES-O was a significant negative predictor of week 16 BDI-II in the medication group ($\beta = -0.30, p=0.043$), but not the CBT group ($\beta = -0.13, p=0.412$). Testing the difference in this path across treatment groups revealed no significant differences ($\chi^2(1, n=104) = 0.623, p=0.430$). Finally, the path from DCES-O at week 0 to end of treatment BDI-II score was significant only for the CBT group ($\beta = -0.35, p<0.001$), and not the medication group ($\beta = 0.01, p=0.885$). The Wald test of Parameter Constraints in this particular path indicated significant differences between medication and CBT ($\chi^2(1, n=104) = 6.07, p=0.014$). In the medication group, none of the depression to outcome expectancy paths emerged as significant ($p>0.05$). However, in the CBT group, the path from BDI-II at week 8 to DCES-O at week 16 was significantly different from 0 ($\beta = 0.29, p=0.034$).
In contrast to model 3b, model 4b using the HAMD revealed a significant difference between medication and CBT ($\chi^2(1, n=104) = 5.61, p= 0.018$) in the path from week 8 DCES-O to week 16 HAMD, with a larger negative effect seen in the medication group ($\beta = -0.45$, $p<0.001$) compared to the CBT group ($\beta = 0.030$, $p=0.820$). No group differences were seen in the paths between week 0 DCES-O and week 8 HAMD ($\chi^2(1, n=104) = 0.98, p= 0.323$), and week 0 DCES-O and week 16 HAMD ($\chi^2(1, n=104) = 1.46, p= 0.227$). Similar to model 3b, there were no significant paths from depression to outcome expectancy in the medication group; however, HAMD at week 0 was negatively predictive of DCES-O at the end of treatment in the CBT group ($\beta = -0.28, p=0.047$).

In summary, similar patterns of the relation between optimistic outcome expectancy and depression were seen in the BDI-II (model 3b) and HAMD (4b) models. That is, for the medication group, DCES-O at week 8 negatively predicted depression at the end of treatment. In the HAMD model, the results of the Wald test supported that this aforementioned effect was specific to treatment with medication over treatment with CBT. Moreover, both models demonstrated a significant negative relation between pre-treatment optimistic expectancy and depression at the end of treatment. The results of the Wald test in the BDI-II model suggested the effect of pre-treatment expectancy on post-treatment depression was specific to CBT over medication. Notably, only the CBT group in both models (3b and 4b) revealed significant cross-lagged effects from depression to outcome expectancy (Table 5).
Chapter 4: Discussion

The present study, using data from a randomized trial, contributes to the growing literature on outcome expectancy in several ways. First, the time-varying, dynamic nature of outcome expectancy was explored within the context of empirically-supported treatments for MDD. Importantly, differences in the trajectory of outcome expectancy in pharmacotherapy versus CBT for depression were explored for the first time. Second, the RCT design also enabled the exploration of differences across treatments in the mediational role of outcome expectancy for depression reduction as treatment progresses. Finally, using a recently developed, depression-specific measure of outcome expectancy, the possible unique roles of both optimistic expectancy and pessimistic expectancy were explored.

4.1 Change in Expectancy Over Time

Results from latent growth model analyses supported significant positive, linear improvement in optimistic and pessimistic expectancy in CBT, reflecting consistent change throughout psychotherapy. In contrast to CBT, a clear significant quadratic trend in optimistic outcome expectancy was seen in our treatment group receiving solely pharmacotherapy for MDD, reflecting significant steep growth from week 0 to week 8, followed by a slight decrease by the end of the treatment. However, the posited model of change converged on an inadmissible solution for pessimistic expectancy in the pharmacotherapy group, rendering it uninterpretable. A number of causes underlying inadmissible solutions have been proposed (Kline, 2011). Monte-Carlo simulation studies of non-linear growth in latent growth models suggest small sample size, low model effect size, fewer time-points and low slope variability as factors associated with inadmissible solutions (Diallo, Morin, & Parker, 2014). As such, future related work with greater power for latent growth modelling is supported.
Increases in expectancy throughout the course of CBT has been established in previous investigations in patients with generalized anxiety disorder (Newman & Fisher, 2010), mixed anxiety disorders (Brown et al., 2014), seasonal affective disorder (Meyerhoff & Rohan, 2016) and MDD (Vișlă et al., 2018). The evidenced linear trend is consistent with the majority of the aforementioned studies (cf. (Brown et al., 2014)). Slowing of expectancy growth (i.e., quadratic trend) was seen in the study by Brown et al. (2014). This trend may be attributed to i) more frequent assessments in this study compared to others, ii) modeling of only the first 8 sessions of CBT (i.e., not the complete course) and iii) a possible confounding effect of medication treatment in this sample, obscuring the specificity of expectancy change to just CBT (Brown et al., 2014).

To the best of our knowledge, this is the first study to explore the trend of patient expectancy during antidepressant treatment. Previous investigations of this cognitive construct in pharmacotherapeutic studies have largely been limited to exploring the influence of pre-treatment expectancy on end of treatment outcome (Krell et al., 2004; Meyer et al., 2002; Rutherford & Roose, 2013; Sotsky et al., 1991). Evidence for dynamic changes in expectancy as treatment progresses substantiates the importance of this construct to therapeutic improvement with pharmacotherapy.

Importantly, in line with our hypothesis, growth was seen in both CBT and pharmacotherapy, with the trajectories differing across the two treatment modalities. The differing shapes of growth limited direct comparisons of the growth parameters (slope and intercept) between groups. However, the distinct shapes may be reflective of either treatment-specific processes influencing change in this construct, or similar processes acting at different time points throughout the course of the two treatments. Treatment specificity of putative
processes proposed to underlie outcome expectancy growth can be established with future studies where the mediational role of these processes is investigated in randomized comparisons of CBT and pharmacotherapy, much like in the present investigation.

The extant literature on how expectancy changes over treatment for MDD is notably small; yet evidence is sufficient to suggest a number of different processes that are largely common across treatments. In a recent antidepressant study in which patients with MDD were randomized into either an open-label citalopram group (100% chance of active drug) or a placebo-controlled citalopram group (50% chance of active drug), revealing group assignment post-randomization enhanced patient outcome expectancy only in the open-label group (Rutherford et al., 2017). Importantly, both groups were informed of the effectiveness of citalopram for depression and only differed in the level of certainty in receiving this medication, providing some support for the importance of treatment rationale for early expectancy change in pharmacotherapy treatment. Moreover, insofar as patient expectations of improvement underscore placebo effects seen in antidepressant trials (Rutherford & Roose, 2013), growing evidence for the influence of therapeutic alliance on treatment outcomes in the placebo arm (i.e., robustness of placebo effect) (Rutherford & Roose, 2013; Zilcha-Mano, Roose, Barber, & Rutherford, 2015) may also implicate alliance as a crucial process to expectancy change in pharmacotherapy.

Relatively, early suggestions that provision of a CBT treatment rationale is facilitative of hopefulness for change (Ilardi & Craighead, 1994) have been supported by more recent research with CBT (Ahmed & Westra, 2009; Ametrano et al., 2017). In both studies, providing a CBT treatment rationale alone (including information on social anxiety, a detailed description of the central elements of the CBT model as it relates to social anxiety, and framed CBT as an
empirically supported treatment) significantly increased expectancy in socially anxious analogue samples. Moreover, as suggested by Newman and Fisher (2010), although the fulsome rationale is typically presented at the beginning of treatment, there are opportunities throughout CBT to reiterate elements of the rationale, particularly as new strategies are being introduced (Newman & Fisher, 2010) or during the process of homework review. Second, in light of the cognitive nature of outcome expectancy, it has been suggested that active engagement with CBT strategies to challenge cognitions in the latter half of treatment (i.e. cognitive restructuring and behavioural experiments) may directly influence this construct (Newman & Fisher, 2010). Finally, there is some support for common elements of psychotherapy such as alliance on outcome expectations in CBT. Poor affiliation in the patient-therapist dyad has been shown to negatively influence the patient’s expectation for improvement in a GAD sample (Westra et al., 2011), whereas strong early alliance was evidenced to promote higher outcome expectancy measured at a subsequent time point in a depressed sample (Visla et al., 2016).

4.2 Mediational Role of Outcome Expectancy

Our hypothesis that outcome expectancy during treatment may mediate depression improvement in CBT, but not pharmacotherapy, was not supported by the results of the cross-lagged panel analyses. For the CBT group, the only significant cross-lagged effect evidenced was greater pre-treatment optimistic expectancy (week 0) predicting lower post-treatment depression (week 16). Although this same pattern of results emerged when modelling with HAMD, the effect size was stronger when depression was modeled using the BDI-II, with this latter model demonstrating a significant Wald test suggesting specificity of this effect to the CBT group only. In the pharmacotherapy group, higher optimistic expectancy at mid-treatment (week 8) was predictive of lower post-treatment depression. The Wald test of Parameter Constraints for
this parameter was significant for HAMD model, providing some support for the specificity of this effect to pharmacotherapy. Finally, unlike optimistic expectancy, the relation between pessimistic expectancy and depression did not differ across treatment groups. Indeed, in both CBT and pharmacotherapy, lower pessimistic expectancy (seen as higher scores on the pessimistic subscale of the DCES) at mid-treatment predicted lower depression at the end of treatment.

Comparing the present results to the existing literature where outcome expectancy has largely been explored using measures assessing optimistic expectations, our results are consistent with previous work establishing a small effect between pre-treatment expectancy and post-treatment symptom severity in psychotherapy (Constantino et al., 2011). This finding supports previous, long-standing suggestions that the beginning of therapy with CBT is a crucial point in which to shape treatment outcome by strengthening optimistic expectancies for improvement (Constantino et al., 2012; Ilardi & Craighead, 1994). Previous work on the possible mechanistic processes linking pre-treatment expectancy and post-treatment outcome implicate alliance formation (Abouguendia, Joyce, Piper, & Ogrodniczuk, 2004; Joyce, Ogrodniczuk, Piper, & McCallum, 2003; Meyer et al., 2002; Tsai et al., 2014; Visla et al., 2016; Webb et al., 2014), early homework compliance (Westra et al., 2007) and the use of CBT skills (Webb et al., 2013). Importantly, results from Visla et al. (2016) support the presence of chain associations throughout treatment by which baseline expectancy leads to early alliance formation, which in turn influences early-treatment expectancy, leading to more favourable post-treatment outcomes. A similar chain mechanism was speculated to take place between baseline outcome expectancy, homework compliance and anxiety reduction, although expectancy was not measured throughout the course of CBT in this study (Westra et al., 2007).
Our lack of association between during-treatment optimistic expectancy and depression outcomes in CBT is inconsistent with the results of the Meyerhoff et al. (2016) study in a seasonal affective disorder sample, where a significant effect of higher mid-treatment expectancy on lower end of treatment depression was evidenced (Meyerhoff & Rohan, 2016). However, the aforementioned study differs from the present investigation in that their measure of expectancy also assessed treatment credibility, and their sample had lower depression severity on average. Moreover, the possibility exists that during treatment optimistic expectations is impactful only in the early stages where the processes of alliance formation and homework compliance gain the most traction. Indeed, the group CBT format in the Meyerhoff et al. (2016) trial was only 6 weeks, with mid-treatment corresponding to week 3. Similarly, Visla et al. (2016) saw a robust negative association between session 3 expectancy and posttreatment depression at week 10 (Visla et al., 2016). While outcome expectancy was measured at 4 time points in the parent study (week 0, 4, 8, 16), we were limited in our ability to model all time points simultaneously due to sample size.

It is important to note that unlike optimistic expectancy, a negative association was seen in week 8 expectancy and posttreatment depression in CBT for the pessimistic expectancy. That is, poor treatment outcome was seen in those who maintained higher pessimistic expectancies (seen as lower scores on the pessimistic subscale on the DCES) at the midpoint of treatment. First, these differential effects of optimistic expectancies vs. pessimistic expectancies are intriguing as they suggest unique mechanisms of action on therapeutic improvement. Such findings align with extant theories of goal attainment which postulate persistent effort stemming from positive expectancies, and disengagement/abandonment stemming from negative expectancies (Carver & Scheier, 2000; Meyer et al., 2002). By the mid-point in the CBT protocol
for this study (week 8), participants would have received considerable exposure and practice with identifying and challenging negative automatic thoughts. In conceptualizing expectancy as a cognitive factor, pessimistic expectancies at treatment midpoint may be indicative of poorer assimilation of CBT skills, leading to subsequent disengagement or ‘giving up’. Future studies are needed to replicate the proposed differential roles of positive (optimistic) vs. negative (pessimistic) expectancies in CBT, particularly as they relate to the previously indicated mediators of alliance, engagement, compliance and development of CBT skills.

As noted by Rutherford & Roose (2013), expectancy effects have largely been conceived as an unwanted factor to be controlled for in antidepressant research (Rutherford & Roose, 2013). However, our results of robust negative associations between expectancy (both optimistic and pessimistic) at week 8 and posttreatment depression support a possible mechanistic role of this factor in pharmacotherapy treatment. Notably, previous studies on this topic are scant and therefore the possible mechanisms mediating this effect are poorly understood. However, existing work point to similar mechanisms as those evidenced in CBT. In the recent trial by Rutherford et al. (2017) where expectancy was experimentally manipulated by assigning participants to either open-administration or placebo-controlled administration of citalopram, the authors found increased improvement in depression severity in the open-label group compared to the placebo-controlled group, with the post-randomization expectancy score mediating this difference (Rutherford et al., 2017). Importantly, group differences in treatment response were not apparent until after the mid-point of the citalopram course (week 4 of 8-week course). The authors speculated that such a time-course reflected indirect mechanisms such as improved adherence to medication and therapeutic alliance in the effect of expectancy on depression. Relatedly, in the study by Meyer et al. (2002) where a subset of participants received imipramine
alongside clinical management, therapeutic alliance was shown to mediate the effect of patients’ pre-treatment expectancies on clinical improvement (Meyer et al., 2002). As suggested by Rutherford et al. (2017), future work is needed to better explicate the influence of expectancy in pharmacotherapy, potentially to inform revisions to existing clinical management protocols to incorporate optimization of expectancy effects (Rutherford et al., 2017).

4.3 Limitations

The results of this investigation meaningfully extend the literature on outcome expectancy; however, this study is not without limitations. First, in light of our smaller sample size, we were limited in the complexity of cross-lagged models we were able to estimate. The nature of the data (i.e., different trajectories across treatments) dictated the use of group-specific analyses, which further limited our statistical power. Second, while our measure of outcome expectancy improves upon previous assessment tools by i) disentangling credibility and treatment preference from expectancy and by 2) consisting of items that are not specific to any particular treatment, we did not collect independent information on these two former factors. Indeed, the influence of treatment preferences and credibility on one’s belief of the amenability of their symptoms to change is tenable and cannot be discounted. Third, our investigation of the mediational role of outcome expectancy was circumscribed to exploring the cross-lagged associations in point-estimates of expectancy and depression during treatment, and we did not explore the specific role of changes in this construct. Future studies with larger sample sizes will be necessary to substantiate outcome expectancy as a mechanism by measuring change throughout treatment. Moreover, as the parent randomized trial largely focused on the mediational role of cognition in therapeutic response, the variables of alliance, homework compliance and CBT skill acquisition – all possible mediators of the expectancy-outcome link – were not able to be included. As such,
we were unable to explore the putative associations of these previously proposed distal processes.

Nevertheless, our use of a randomized design in this study enabled exploration of treatment-specific roles of outcome expectancy in the two most widely used treatments for MDD. To further substantiate the mediational role of outcome expectancy, future studies should explore direct manipulation to enhance expectancy, and then examine the resulting effect of such intervention on treatment outcomes. As proposed by Kazdin (2007), in light of the potential for significant variability in the timing of change across participants, future studies should aim to include more frequent assessments throughout treatment (Kazdin, 2007), while balancing participant burden.

4.4 Conclusions

To the best of our knowledge, this is the first study to explore changes in outcome expectancy throughout the course of antidepressant treatment in MDD, as well as to compare the relation between expectancy and outcome across CBT and pharmacotherapy. The results of this study reiterate the critical role of pre-treatment expectancy for CBT response, and support a possible mechanistic role in antidepressant response. Indeed, the status of outcome expectation as a common factor in psychotherapy may be extended to represent a common mechanism in the treatment of depression overall. However, larger, future studies with more frequent assessments of during treatment expectancy will be needed to validate these results. Moreover, an important future direction includes greater attention to the valence of expectancy (optimistic vs. pessimistic) in studies aiming to further explicate this construct.
Table 1

*Estimated Descriptive Statistics for Study Variables*

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<th>Variables</th>
<th>Medication</th>
<th>CBT</th>
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<td>40.91</td>
</tr>
<tr>
<td></td>
<td>10.51</td>
<td>8.04</td>
</tr>
<tr>
<td></td>
<td>_</td>
<td></td>
</tr>
<tr>
<td>DCES-P week 16</td>
<td>42.15</td>
<td>45.67</td>
</tr>
<tr>
<td></td>
<td>10.93</td>
<td>7.00</td>
</tr>
<tr>
<td></td>
<td>_</td>
<td></td>
</tr>
</tbody>
</table>

*Note:* DCES-O: Optimistic outcome expectancy subscale of DCES; DCES-P: Pessimistic outcome expectancy subscale of DCES.
Table 2a

*Fit Indices for Final Latent Growth Curve Models*

<table>
<thead>
<tr>
<th>Medication</th>
<th>DCES-P</th>
<th>DCES-O</th>
<th>CFI</th>
<th>RMSEA</th>
<th>SRMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication</td>
<td>1.63 (3), p=0.652</td>
<td>1.00</td>
<td>0.00</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>CBT</td>
<td>3.97 (5), p=0.554</td>
<td>1.00</td>
<td>0.00</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>CBT</td>
<td>4.82 (7), p=0.683</td>
<td>1.00</td>
<td>0.00</td>
<td>0.16</td>
<td></td>
</tr>
</tbody>
</table>

*Note:* The model for DCES-P for the medication group is not presented due to notable misspecification; it was not interpreted.

Table 2b

*Fit Indices for Multi-Group Cross-Lagged Panel Models*

<table>
<thead>
<tr>
<th>Model</th>
<th>Expectancy</th>
<th>Outcome</th>
<th>$\chi^2$ (df), p-value</th>
<th>CFI</th>
<th>RMSEA</th>
<th>SRMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a.</td>
<td>DCES-P</td>
<td>BDI-II</td>
<td>2.46 (8), p=0.964</td>
<td>1.00</td>
<td>0.00</td>
<td>0.03</td>
</tr>
<tr>
<td>1b.</td>
<td>DCES-P</td>
<td>BDI-II</td>
<td>2.35 (4), p=0.671</td>
<td>1.00</td>
<td>0.00</td>
<td>0.03</td>
</tr>
<tr>
<td>2a.</td>
<td>DCES-P</td>
<td>HAMD</td>
<td>7.46 (8), p=0.488</td>
<td>1.00</td>
<td>0.00</td>
<td>0.03</td>
</tr>
<tr>
<td>2b.</td>
<td></td>
<td></td>
<td>6.18 (4), p=0.186</td>
<td>0.99</td>
<td>0.10</td>
<td>0.04</td>
</tr>
<tr>
<td>3a.</td>
<td>DCES-O</td>
<td>BDI-II</td>
<td>14.84 (8), p=0.062</td>
<td>0.96</td>
<td>0.13</td>
<td>0.06</td>
</tr>
<tr>
<td>3b.</td>
<td>DCES-O</td>
<td>BDI-II</td>
<td>2.36 (4), p=0.669</td>
<td>1.00</td>
<td>0.00</td>
<td>0.03</td>
</tr>
<tr>
<td>4a.</td>
<td>DCES-O</td>
<td>HAMD</td>
<td>10.18 (8), p=0.25</td>
<td>0.98</td>
<td>0.07</td>
<td>0.07</td>
</tr>
<tr>
<td>4b.</td>
<td>DCES-O</td>
<td>HAMD</td>
<td>3.00 (4), p=0.559</td>
<td>1.00</td>
<td>0.00</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*Note:* * Final models, which include paths from week 0 to week 16
Table 3

*Parameter Estimates for Final Latent Growth Curve Models*

<table>
<thead>
<tr>
<th>Model</th>
<th>Parameters</th>
<th>Medication</th>
<th>CBT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean (SE)</td>
<td>Variance (SE)</td>
</tr>
<tr>
<td>DCES-P</td>
<td>Intercept</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td></td>
<td>Slope</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>Growth factor</td>
<td>Correlation</td>
<td>_</td>
<td>- .48 [-0.75, -0.20]*</td>
</tr>
<tr>
<td>DCES-O</td>
<td>Intercept</td>
<td>29.06 (0.81)**</td>
<td>20.96 (9.63)*</td>
</tr>
<tr>
<td></td>
<td>Slope</td>
<td>1.05 (0.27)**</td>
<td>1.19 (0.62)</td>
</tr>
<tr>
<td>Growth factor</td>
<td>Correlation</td>
<td>-.10 [-0.79, 0.59]</td>
<td>_</td>
</tr>
</tbody>
</table>

*Note:* * p<0.05, ** p<0.001. Unstandardized mean and variance estimates are reported. Standardized covariance (correlations) between growth factors are reported. The model for DCES-P growth in the medication group is not presented due to notable misspecification.
Table 4

Pessimistic Outcome Expectancy and Depression Cross-Lagged Paths

<table>
<thead>
<tr>
<th></th>
<th>Medication</th>
<th>CBT</th>
<th>Wald $\chi^2$, $p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1b</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BDI-II w0 $\rightarrow$ DCES-P w8</td>
<td>-0.20 0.14 [-0.47, 0.08]</td>
<td>-0.04 0.09 [-0.22, 0.15]</td>
<td></td>
</tr>
<tr>
<td>BDI-II w0 $\rightarrow$ DCES-P w16</td>
<td>0.00 0.05 [-0.09, 0.09]</td>
<td>0.03 0.11 [-0.19, 0.24]</td>
<td></td>
</tr>
<tr>
<td>BDI-II w8 $\rightarrow$ DCES-P w16</td>
<td>0.12 0.14 [-0.15, 0.40]</td>
<td>0.05 0.16 [-0.27, 0.37]</td>
<td></td>
</tr>
<tr>
<td>DCES-P w0 $\rightarrow$ BDI-II w8</td>
<td>-0.20 0.15 [-0.48, 0.09]</td>
<td>-0.02 0.15 [-0.32, 0.28]</td>
<td>0.85, $p=0.358$</td>
</tr>
<tr>
<td>DCES-P w0 $\rightarrow$ BDI-II w16</td>
<td>0.02 0.10 [-0.18, 0.22]</td>
<td>-0.02 0.12 [-0.26, 0.22]</td>
<td>0.07, $p=0.795$</td>
</tr>
<tr>
<td>DCES-P w8 $\rightarrow$ BDI-II w16</td>
<td>-0.23 0.23 [-0.68, 0.22]</td>
<td>-0.31* 0.13 [-0.57, -0.05]</td>
<td>0.04, $p=0.852$</td>
</tr>
<tr>
<td><strong>Model 2b</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAMD w0 $\rightarrow$ DCES-P w8</td>
<td>-0.08 0.13 [-0.33, 0.16]</td>
<td>0.02 0.10 [-0.18, 0.22]</td>
<td></td>
</tr>
<tr>
<td>HAMD w0 $\rightarrow$ DCES-P w16</td>
<td>0.02 0.07 [-0.12, 0.15]</td>
<td>0.13 0.12 [-0.10, 0.36]</td>
<td></td>
</tr>
<tr>
<td>HAMD w8 $\rightarrow$ DCES-P w16</td>
<td>-0.04 0.08 [-0.20, 0.12]</td>
<td>-0.05 0.16 [-0.36, 0.27]</td>
<td></td>
</tr>
<tr>
<td>DCES-P w0 $\rightarrow$ HAMD w8</td>
<td>-0.02 0.15 [-0.31, 0.28]</td>
<td>0.02 0.12 [-0.22, 0.26]</td>
<td>0.03, $p=0.860$</td>
</tr>
<tr>
<td>DCES-P w0 $\rightarrow$ HAMD w16</td>
<td>-0.01 0.15 [-0.31, 0.29]</td>
<td>0.12 0.11 [-0.09, 0.33]</td>
<td>0.41, $p=0.523$</td>
</tr>
<tr>
<td>DCES-P w8 $\rightarrow$ HAMD w16</td>
<td>-0.43* 0.15 [-0.72, -0.14]</td>
<td>-0.32* 0.14 [-0.60, -0.03]</td>
<td>0.03, $p=0.872$</td>
</tr>
</tbody>
</table>

*Note:* * $p<0.05$, ** $p<0.001$. β= standardized parameter estimates; SE=standard error. Items in the DCES-P were reverse-scored.
Table 5

*Optimistic Outcome Expectancy and Depression Cross-Lagged Paths*

<table>
<thead>
<tr>
<th>Model 3b</th>
<th>Medication</th>
<th>CBT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>SE</td>
</tr>
<tr>
<td>BDI-II w0 → DCES-O w8</td>
<td>-0.19</td>
<td>0.16</td>
</tr>
<tr>
<td>BDI-II w0 → DCES-O w16</td>
<td>-0.08</td>
<td>0.12</td>
</tr>
<tr>
<td>BDI-II w8 → DCES-O w16</td>
<td>0.19</td>
<td>0.23</td>
</tr>
<tr>
<td>DCES-O w0 → BDI-II w8</td>
<td>-0.30*</td>
<td>0.14</td>
</tr>
<tr>
<td>DCES-O w0 → BDI-II w16</td>
<td>0.01</td>
<td>0.08</td>
</tr>
<tr>
<td>DCES-O w8 → BDI-II w16</td>
<td>-0.30*</td>
<td>0.15</td>
</tr>
<tr>
<td>Model 4b</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAMD w0 → DCES-O w8</td>
<td>-0.02</td>
<td>0.12</td>
</tr>
<tr>
<td>HAMD w0 → DCES-O w16</td>
<td>-0.10</td>
<td>0.13</td>
</tr>
<tr>
<td>HAMD w8 → DCES-O w16</td>
<td>0.04</td>
<td>0.18</td>
</tr>
<tr>
<td>DCES-O w0 → HAMD w8</td>
<td>-0.01</td>
<td>0.12</td>
</tr>
<tr>
<td>DCES-O w0 → HAMD w16</td>
<td>-0.02</td>
<td>0.12</td>
</tr>
<tr>
<td>DCES-O w8 → HAMD w16</td>
<td>-0.45**</td>
<td>0.12</td>
</tr>
</tbody>
</table>

*Note:* *p<0.05, **p<0.001. β= standardized parameter estimates; SE=standard error.
Figure 1

Cross-lagged panel structure for all models (1b-4b)
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