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Could Treatment Matching Patients' Beliefs about Depression Improve Outcomes?

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Abstract

Patients' beliefs about depression and expectations for treatment can influence outcomes of major depressive disorder (MDD) treatments. We hypothesized that patients with weaker biological beliefs (less endorsement of (a) biochemical causes and (b) need for medication), and more optimistic treatment expectations (greater improvement and shorter time to improvement), have better outcomes in cognitive therapy (CT). Outpatients with recurrent MDD who received acute-phase CT ($N = 152$), and a subset of partial or unstable responders ($N = 51$) randomized to 8 months of continuation CT or fluoxetine with clinical management, completed repeated measures of beliefs, expectations, and depression. As hypothesized, patients with weaker biological beliefs about depression, and patients who expected a shorter time to improvement, experienced greater change in depressive symptoms and more frequent response to acute-phase CT. Moreover, responders who received continuation treatment better matched to their biological beliefs (i.e., responders with weaker biological beliefs about depression who received continuation CT, or responders with stronger biological beliefs about depression who received continuation fluoxetine)

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had fewer depressive symptoms and less relapse/recurrence by 32 months after acute-phase CT than did responders who received mismatched continuation treatment. Specific screening and/or intervention targeting patients' biological beliefs about depression could increase CT efficacy.

Keywords

depression; cognitive therapy; beliefs; expectations; relapse; recurrence

Persons with major depressive disorder (MDD) often reflect on potential causes and solutions for their mood disturbance and functional impairment (e.g., social, occupational, or cognitive dysfunction). Although some of this process may be related to the "rumination" correlated with depressive disorders (Addis & Carpenter, 1999), patients' views may also inform their treatment seeking, expectations, engagement, and outcomes (e.g., Constantino et al., 2018; Elkin et al., 1999; Kemp, Lickel, & Deacon, 2014). The current study aimed to clarify the type and extent to which patients' beliefs about depression and their expectations regarding treatment predicted: (a) changes in their depressive symptoms (and vice versa) during acute-phase cognitive therapy (A-CT) for recurrent MDD, and (b) residual symptoms and relapse/recurrence during and after continuation treatment with cognitive therapy (C-CT) or fluoxetine (FLX) plus clinical management.

In cognitive therapy, patients learn about cognitive models of depression (e.g., thoughts influence mood, and thoughts and associated behaviors can be changed) as a rationale and framework for collaboratively assessing, testing, and modifying unrealistically negative beliefs and assumptions. Both A-CT and C-CT are more efficacious than inactive control conditions (e.g., pill placebo) and at least as efficacious as antidepressant medication (Biesheuvel-Leliefeld et al., 2015; Cuijpers et al., 2013). Even so, biological models of depression have been ascendant in recent decades, in part through direct marketing of medications (Lacasse & Leo, 2015). Cognitive therapists are advised to elicit and explore patients' biological beliefs about depression (e.g., "I need medication because I have a chemical imbalance"; "Because my mother was depressed my depression is genetic") emerging during CT, as these beliefs have the potential to undermine progress in CT (Beck et al., 1979). How often cognitive therapists actively elicit and address patients' biological views about depression is likely variable and not often measured in existing datasets.

Biological beliefs correlate broadly with lower stigma but higher pessimism about mental illness (Haslam & Kvaale, 2015). For example, experimentally induced beliefs attributing depression to a "chemical imbalance" decreased self-blame for depression, increased perceived need for medication, and increased expected benefits of antidepressant medication but decreased expected benefits of psychosocial treatment (Deacon & Baird, 2009; Kemp et al., 2014). In contrast, education about biopsychosocial models of depression and epigenetics (e.g., that genes can be "turned on or off" by the environment) reduced pessimism and increased perceived potential efficacy of psychosocial treatments (Deacon & Baird, 2009; Lebowitz, Ahn, & Nolen-Hoeksema, 2013).

Patient expectations (i.e., beliefs about the likely results of treatment) have indirectly or directly predicted treatment outcomes in a number of studies in past decades (Greenberg,

Constantino, & Bruce, 2006; Constantino et al., 2018). More recently, among persons with MDD receiving acute-phase treatment (supportive-expressive psychotherapy, or clinical management plus either pill placebo or active medication), those with favorable outcome expectations developed a stronger therapeutic alliance, which in turn predicted better outcomes (Barber et al., 2014). Moreover, among patients receiving CT for depression in a partial hospitalization program (Beard et al., 2016), and in a sample of outpatients receiving CT for seasonal affective disorder (Meyerhoff & Rohan, 2016), favorable treatment expectations predicted better response.

Thus, there are important links between patients' beliefs about the etiology of depression and what they expect from and believe about treatment. Patients' beliefs and expectations, however, may operate differently across distinct treatments. In the Treatment of Depression Collaborative Research Program, patients randomized to a treatment that better fit their personal conceptualizations of depression (a "psychotherapy" or "medication" profile of beliefs) were more engaged with treatment and less likely to drop out (but did not have a greater reduction in depression scores) after 4 weeks of psychotherapy (CT or interpersonal psychotherapy) or medication (imipramine; Elkin et al. 1999). The psychotherapy profile included predominant cognitive and/or interpersonal beliefs about the origins of patients' depression, whereas the medication profile reflected the predominant belief that pharmacotherapy was needed. Nonetheless, patients' global outcome expectations (i.e., amount of overall improvement anticipated during treatment) predicted response roughly equally across all treatment conditions (Sotsky et al., 1991). In an effort to replicate and extend past research, we used the Patient Attitudes and Expectations (PAE) questionnaire from the Treatment of Depression Collaborative Research Program in the current analyses to assess each patient's beliefs and expectations.

Data analyzed here were drawn from a two-site, multi-phase clinical trial (Jarrett & Thase, 2010). Outpatients with recurrent MDD received A-CT, and responders with higher risk for relapse (judged a priori based on residual symptoms) were randomized to 8 months of continuation phase cognitive therapy (C-CT) or clinical management plus either fluoxetine (FLX) or matched pill placebo, and assessed up to 24 additional months. The C-CT and FLX conditions produced less relapse and fewer residual symptoms than the pill placebo control condition during the 8-month continuation phase, but C-CT and FLX did not differ significantly during the continuation phase, and the three conditions did not differ after active treatment was discontinued during the 24-month follow-up (Jarrett et al., 2013; Vittengl et al., 2014). The pill placebo arm was not analyzed here because pill placebo is rarely used in routine clinical practice and produced significantly poorer outcomes than C-CT or FLX. We tested the hypotheses that (1) patients with weaker biological beliefs about depression have better outcomes in acute-phase CT; (2) biological beliefs moderate continuation treatment outcomes, with better outcomes for patients who are "matched" (i.e., responders with weaker biological beliefs about depression randomized to C-CT, or responders with stronger biological beliefs about depression randomized to FLX) versus "mismatched" to continuation treatment; and (3) patients with more optimistic treatment expectations (including anticipation of shorter time to improvement and better outcomes) will have better outcomes in both acute and continuation treatments. We also conducted related exploratory analyses where past research and theory did not clearly support

directional hypotheses. In particular, we explored (1) whether cognitive and interpersonal beliefs about depression predicted treatment outcomes; and (2) whether changes in depressive symptoms predicted changes in patients' beliefs and expectations.

Methods

Data were drawn from a clinical trial described in detail by Jarrett and Thase (2010) with primary outcomes found in Jarrett et al. (2013). Institutional review boards at the University of Texas Southwestern Medical Center and University of Pittsburgh Medical Center approved the study protocol and procedures annually. Here we summarize methods relevant to the current analyses.

Participants

From 2000-2008, participants were recruited by clinical referrals, public service announcements, and advertisements. Participants were outpatients who (a) provided written informed consent; (b) met *DSM-IV* criteria for recurrent MDD (American Psychiatric Association, 2000); (c) had remitted between previous depressive episodes, had at least one prior episode with complete inter-episode recovery, or had antecedent dysthymic disorder; and (d) scored ≥ 14 on the 17-item HRSD. Patients were excluded if they (a) had poorly controlled or severe medical disorders that could cause depression; (b) had organic or psychotic mental disorders, active substance dependence, bipolar disorder, or primary eating or obsessive-compulsive disorders; (c) could not complete questionnaires in English; (d) presented active suicide risk; (e) were not 18-70 years old; (f) had failed to respond to at least 8 weeks of CT or 6 weeks of fluoxetine previously; or (g) were pregnant or planned to become pregnant within 11 months. After telephone triage, potential participants presented at research clinics for mood disorders within the Departments of Psychiatry at The University of Texas Southwestern Medical Center and the University of Pittsburgh. Diagnoses were made using the Structured Clinical Interview for *DSM-IV* (First, Spitzer, Gibbon, & Williams, 1996). Participants were informed about, and consented to, the full clinical trial protocol at the screening and again at evaluation for the study, which included acute phase CT followed by randomization of responders to continuation CT, fluoxetine, or pill placebo with clinical management. The current analyses focused on a subset of patients ($N = 152$ of 523 total consenting patients) who entered the study after the PAE measure was added to the assessment battery in order to increase the range of secondary hypothesis tests. These 152 patients were $M = 45$ ($SD = 13$) years old and had completed $M = 15$ ($SD = 3$) years of education; 67% were women; 82% were white, 10% black, and 9% other races/ethnicities. Patients' mean age of MDD onset was 22 ($SD = 11$) years, and they had experienced a median of 4 (minimum 2) depressive episodes. Figure 1 shows patient flow through the multi-phase study.

Acute phase

Before entering the A-CT protocol, consenting patients were either not taking or were withdrawn from psychotropic medications. Medication was not prescribed during the acute-phase protocol. Goals of A-CT include increasing patients' behavioral activation by re/engaging sources of reinforcement and improving functioning; assessing and restructuring

patients' negative automatic thoughts; and identifying and changing patients' broader negative assumptions (schema) about the world, self, and future. The 16 cognitive therapists (12 doctoral-and 4 masters-level; 12 women, 4 men) completed at least 1 year of supervised CT training and maintained mean Cognitive Therapy Scale (Young & Beck, 1980) scores 40 to demonstrate competence. Cognitive therapists received feedback on strengths and weaknesses by submitting session videotapes for review in weekly group supervision. The A-CT protocol lasted 12 weeks with 2 additional weeks allowed for rescheduling. The protocol included 2 CT sessions per week for 4 weeks. Then patients with $\geq 40\%$ reduction in HRSD scores received 8 additional weekly sessions (16 total sessions), whereas patients with less early improvement received 8 twice-weekly, followed by 4 weekly sessions (20 total sessions). Patients with less early symptom reduction received more CT sessions to increase the likelihood of response (by independent evaluation, no MDE and HRSD ≥ 12 at the end of A-CT). Responders were stratified into a-priori-defined lower (the last 7 acute-phase HRSD scores all ≤ 6) and higher (one or more of the last 7 acute-phase HRSD scores ≥ 7) risk groups (Jarrett & Thase, 2010). In the current subsample, 16 (10.5%) were lower-risk responders, 88 (58.0%) were higher-risk responders, and 48 (31.6%) were non-responders, similar to the full sample (Jarrett et al., 2013).

Continuation phase

Only higher-risk A-CT responders were offered continuation treatment. Non-responders were referred for non-protocol treatment. Current analyses of the 8-month continuation and 24-month follow-up phases focused on higher-risk responders who completed the PAE after A-CT and were randomized to C-CT ($n = 27$) or FLX ($n = 24$). Independent evaluators assessed *DSM-IV* MDD with the SCID (First et al., 1996) and the Psychiatric Status Ratings from the Longitudinal Interval Follow-up Evaluation (Keller et al., 1987) at the end of months 4 and 8 (and interim, if relapse was suspected). Patients who met MDD criteria were referred out for additional treatment.

The C-CT protocol included 4 biweekly and then 6 monthly (10 total) sessions of about 60 minutes each (Jarrett, 1989; Jarrett, Vittengl & Clark, 2008). Building on A-CT, C-CT patients learned to apply compensatory skills to residual and emergent depressive symptoms and to restructure depressive assumptions. Continuation phase CT focused on generalizing therapeutic skills (e.g., across problems, time, and situations) and on coping preemptively with cognitive and behavioral risks for depression. Patients worked with the same A-CT and C-CT therapists, with a few exceptions (e.g., due to a therapist's maternity leave).

Experienced pharmacotherapists provided the double-blinded fluoxetine and pill placebo clinical-management protocol (Fawcett et al., 1987), with 10 sessions on the same schedule as C-CT. The initial session lasted up to 45 and subsequent sessions up to 30 minutes. Clinical management facilitated high-quality pharmacotherapy by providing supportive contact involving discussion of the signs and symptoms of depression, beneficial and unwanted medication effects, and information about depression. Pharmacotherapists were prohibited from using CT methods or other depression-specific psychotherapies. Research pharmacies at each site dispensed active fluoxetine or visually identical placebo capsules. Patients received 10 mg/day for the first 2 weeks, then 20 mg/day for 2 additional weeks,

and finally 40 mg/day, but pharmacotherapists could decrease doses to lessen side effects (Jarrett et al., 2013).

Follow-up phase

Patients who completed the continuation phase discontinued protocol treatment and entered a 24-month follow-up (CCT $n = 24$ and FLX $n = 18$, in the current analyses). Evaluators blinded to cell assignment assessed patients every 4 months using the same procedures as in the continuation phase. Patients were encouraged to contact study staff for interim evaluation if they experienced depressive symptoms. Patients who met criteria for MDD were referred out for treatment within the community

Measures

Patient attitudes and expectations.—Before and after A-CT, patients completed the PAE questionnaire developed for the Treatment of Depression Collaborative Research Program (Elkin et al., 1985). The PAE consists of 46 objective and free-response items assessing a wide range of beliefs about “the problems that brought you to the clinic,” treatment, and treatment outcomes. Because patients presented to depression clinics, were diagnosed with MDD, consented to treatment of depression, and completed the PAE in this context, we refer to patients’ responses about their presenting problems as about their depression (e.g., we use the phrase “beliefs about depression”). In particular, we scored three scales reflecting biological, cognitive, and interpersonal beliefs derived by Elkin et al. (1999) by averaging the relevant items, each rated from 1-7. Higher scores marked more intense beliefs.

The biological-beliefs items reflected patients’ attributions of depression to “poor physical health” and “physical or biochemical problems” plus the assertion that “medication” would be helpful treatment. The interpersonal-beliefs items marked attributions of depression to “never having really learned how to get along with people,” “being alone or lonely too much of the time,” and “many arguments and conflicts with my family,” plus the assertions that “learning how to resolve my family conflicts,” “learning how to reach out to other people,” and “learning how to get along better with other people” would be therapeutic. The cognitive-beliefs items reflected attributions of depression to “having bad feelings about myself,” “pessimistic attitudes about many things,” “being too much of a perfectionist, and being very self-critical,” plus assertions that “learning more realistic attitudes about myself and the world,” and “learning to be more hopeful and optimistic” would be therapeutic. In the larger pre-A-CT sample, alpha internal consistency reliabilities for the 6-item interpersonal (.77) and 5-item cognitive (.82) beliefs scales were moderate. Internal consistency for the biological beliefs scale (.59) fell below the common benchmark of .70, in part because the scale was short (3 items). Nonetheless, the mean (.32) and all pairwise (range .19-.42) correlations among the biological beliefs items fell in the target range of .15-.50 (Clark & Watson, 1995).

We also analyzed two items assessing treatment outcome and time-to-improvement expectations. Treatment outcome expectations were rated on a 1-5 scale from “don’t expect to feel any different” to “completely better” as a result of treatment. In addition, patients

provided a numerical estimate from 1-52 weeks indicating “how soon do you expect you will begin to feel better as a result of the treatment you will receive here?”

Depressive symptoms.—Clinicians completed the 17-item HRSD (Hamilton, 1960) at intake, approximately weekly during A-CT, at the end of A-CT / randomization to continuation treatment, and every 4 months for the following 32 months. We focused on the clinician-reported HRSD in the current analyses to reduce potential bias in correlations of patient beliefs and expectations with self-reported depressive symptoms due to shared method variance or “self-fulfilling prophecies.” The HRSD had high estimated inter-rater reliability (.91) in the current study.

Relapse and recurrence.—The Longitudinal Interval Follow-Up Evaluation (Keller et al., 1987) is a semi-structured retrospective interview and was completed by independent evaluators every 4 months after A-CT, at study exit, and when patients, therapists, or follow-up evaluators suspected major depressive relapse or recurrence. Weekly psychiatric status ratings of *DSM-IV* MDD of 1 (no symptoms) or 2 (one or two mild symptoms) for 35 continuous weeks defined recovery. Relapse and recurrence were 2 weeks with psychiatric status ratings of 5 (meets MDD criteria) or 6 (meets MDD criteria with severe impairment and/or psychosis) before and after recovery, respectively (Jarrett & Thase, 2010). Weekly psychiatric status ratings of MDD showed high estimated inter-rater reliability (.93) in the current study.

Statistical analyses

Among the 152 patients analyzed here, 137 and 101 completed the PAE before and after A-CT, respectively. Completion of the PAE did not correlate significantly with concurrent depression severity before or after A-CT ($p > .24$). Repeated-measures multilevel models with maximum likelihood estimation and autoregressive error structures were used to test changes in levels of depressive symptoms, beliefs, and expectations, as well as prediction of depressive symptoms after acute-phase CT. From multilevel models, effect sizes were estimated using the outcome variable's *SD* before acute-phase CT. Path analyses with full-information maximum likelihood estimation, which allowed inclusion of cases with some missing data, were used to test possible reciprocal influences in changes in depressive symptoms and changes in beliefs and expectations. Finally, Cox regression was used to predict time to relapse/recurrence from beliefs. An alpha level of $p < .05$, two-tailed, was used for hypothesis tests and additional exploratory analyses.

Results

What do patients believe about depression and expect from treatment?

As shown in Table 1, patients had progressively stronger biological, interpersonal, and cognitive beliefs about depression (e.g., before A-CT, means of roughly 3, 4, and 5, respectively, on the scale of 1-7). Patients were moderately optimistic about treatment (e.g., mean outcome expectation of about 4 on the 1-5 scale, and mean time-to-improvement estimate of 10 weeks). Biological, cognitive, and interpersonal beliefs about depression decreased during A-CT, whereas treatment expectations did not change significantly, in a

series of repeated-measures multilevel models. After controlling depressive symptoms, changes in biological ($M = 0.05$, $SE = 0.21$, $p = .82$) and cognitive ($M = 0.25$, $SE = 0.19$, $p = .20$) beliefs from before to after A-CT were non-significant, whereas the decrease in interpersonal beliefs was reduced but remained significant ($M = 0.46$, $SE = 0.20$, $p = .02$).

Table 2 shows correlations among the beliefs, expectations, and depressive symptom severity (HRSD score) variables before CT. Biological, cognitive, and interpersonal beliefs about depression were positively inter-correlated, suggesting that patients did not see these beliefs about depression as mutually exclusive. Instead, patients may have endorsed stronger beliefs when they had more severe depression to attribute to various sources, as reflected in positive correlations of the beliefs variables with HRSD scores. Patients with stronger biological (but not cognitive or interpersonal) beliefs expected a longer period of time in treatment before feeling better, whereas patients with stronger cognitive and interpersonal (but not biological) beliefs were more optimistic about their global level of improvement during treatment.

Do patients' pre-treatment beliefs and expectations predict improvement during A-CT?

Yes, some pre-treatment beliefs and expectations predicted improvement during A-CT, as follows. We clarified relations of patient beliefs and expectations with depressive symptom severity during A-CT in a series of cross-lagged path analyses. As depicted in Figure 2, we were interested in the extent to which patient beliefs and expectations predicted subsequent changes in depressive symptom and vice versa. Table 3 shows the resulting standardized path coefficients. In support of our hypothesis, patients with weaker biological beliefs about depression before A-CT had more improvement in depressive symptoms during A-CT. The reverse was not evident: Depressive symptom severity did not predict changes in beliefs about depression or treatment expectations during A-CT significantly. In addition, patients with shorter time-to-improvement expectations had more improvement in depressive symptoms during A-CT.

To illustrate the potential clinical relevance of these findings, we predicted response to A-CT from pre-treatment biological beliefs and treatment expectations. Response was defined a priori (Jarrett et al., 2013) as three ordered categories, stable/lower-risk response (no MDD and the last 7 acute-phase assessments all with HRSD ≤ 6), unstable/higher-risk response (no MDD and final HRSD ≤ 12 but at least one HRSD score ≥ 7 during the last 7 acute-phase assessments), or non-response (MDD and/or final HRSD ≥ 13). In ordinal regression models, the odds of a better treatment response (i.e., moving up the hierarchy from non-response to unstable response, or from unstable to stable response) were better for patients with lower biological beliefs, odds ratio (OR) = 1.44, $p = .04$, and shorter expected duration of treatment until feeling better, OR = 1.85, $p = .002$ (ORs scaled to reflect 1 *SD* differences in predictor variables).

Do A-CT responders' beliefs and expectations predict depressive symptom levels during continuation treatment and during follow-up?

Yes, some beliefs and expectations among responders predicted depressive symptom levels during continuation treatment and during follow-up, as detailed below.¹ We tested patients'

beliefs and expectations assessed after A-CT as predictors of, and moderators of continuation treatments' effects on, depressive symptoms using a series of repeated-measures multilevel models. As shown in Table 4, biological beliefs about depression interacted with continuation treatment (C-CT or FLX) to predict level of depressive symptoms. In support of our hypotheses, patients with higher biological beliefs had lower symptoms with FLX, whereas patients with lower biological beliefs had lower symptoms with C-CT, $d = 0.87$. A 1 SD increase in the biological beliefs scale predicted a 2.37 ($SE = 0.50$, $p < .001$) increase in mean HRSD scores among C-CT patients but a 1.31 ($SE = 0.62$, $p = .04$) decrease in mean HRSD scores among FLX patients. Interactions with time were not significant, suggesting that this pattern was relatively stable across the observation period. Using a median split of patients' biological beliefs scores, Figure 3 illustrates the interaction of continuation treatment with biological beliefs predicting depressive symptoms.

The cross-over interaction for biological beliefs indicated that patients had better outcomes in terms of continuous HRSD scores when randomization "matched" patients to C-CT versus FLX. We tested whether matching was associated with delayed MDD relapse or recurrence, as well. Using a median split on the biological belief variable, patients with higher biological beliefs randomized to FLX, and patients with lower biological beliefs randomized to C-CT, were categorized as "matched" to the treatment fitting their beliefs, whereas other patients were "mismatched." As shown in Figure 4, patients who were matched to a continuation treatment (18.0%) had less frequent estimated relapse/recurrence within 32 months compared to mismatched patients (49.0%) in a Kaplan-Meier survival analysis, log-rank $\chi^2 = 4.93$, $p = .03$, risk difference = 31.0%.

In addition, stronger interpersonal beliefs about depression predicted higher depressive symptoms as a main effect ($d = 0.23$) but not as an interaction with continuation treatment (see Table 4). A 1 SD increase on the interpersonal beliefs scale predicted a 0.98 ($SE = 0.42$, $p = .02$) point increase in mean HRSD scores. However, the cognitive beliefs and expectations variables did not predict HRSD scores as main effects or interactions with continuation treatment.

Discussion

Many persons seeking treatment for recurrent MDD undoubtedly have spent considerable time reflecting on the nature of their mood disturbance and associated problems, asking why their depression started and what (including which treatments) will help it end. Patients tend to state that if they can understand the source of their problems, they will better understand how to ameliorate the problems. We tested the hypotheses that patients with weaker biological beliefs about depression, and more optimistic treatment expectations, have better outcomes in CT. In support of these hypotheses, patients with shorter time-to-improvement expectations had better outcomes in A-CT. Further, patients' biological beliefs predicted outcomes in both A-CT and C-CT. In particular, adults with weaker biological beliefs

¹Receipt of extra-protocol treatment was uncommon. Although patients were referred for non-protocol treatment at depressive relapse or recurrence, only 17.0% of the current sample reported receiving any during the 32 months of assessment after the acute phase. Moreover, biological beliefs assessed at the end the acute phase did not correlate significantly with receipt of extra-protocol treatment, either in the pooled group or in the C-CT or FLX arms separately, $ps > .70$.

measured pre-treatment had lower depressive symptoms at the end of A-CT and were more likely respond to A-CT. Moreover, higher-risk A-CT responders had fewer residual symptoms and were less likely to relapse/recur within 32 months if they were randomized to a continuation treatment matching their post-A-CT biological beliefs about depression. That is, responders with weaker biological beliefs had better outcomes with C-CT, whereas responders with stronger biological beliefs had better outcomes with FLX.

Our finding that biological beliefs predicted actual treatment outcomes extends prior research showing that biological beliefs about depression correlated with expected treatment outcomes (Deacon & Baird, 2009; Kemp et al., 2014) and initial engagement in treatment for depression (Elkin et al., 1999). If replicated, our finding that patients with weaker biological beliefs have better outcomes in A-CT, and in C-CT relative to FLX, may inform clinical research and decision making. Possible applications include (a) matching patients to continuation treatments, and (b) interventions to address biological beliefs about depression and promote engagement in CT. Patient-treatment matching might use existing beliefs measures and treatment protocols, and thus be an expedient means to improve depression care.

Addressing patients' beliefs may hold additional potential to improve depression care, if mechanisms connecting beliefs to treatment outcomes are known and effectively targeted. Cognitive therapists have long been advised to address patients' beliefs in biological causes for their depression in an effort to improve treatment process and outcomes (Beck et al., 1979). More recent experiments showed that education about biopsychosocial (as opposed to bio-dominated) models of depression increased optimism about psychosocial treatment (Lebowitz, Ahn, & Nolen-Hoeksema, 2013). In this context, an important next step would be to test whether actively eliciting or screening for patients' beliefs about depression and subsequently targeting logical analyses within CT and/or education about biopsychosocial models of depression and its associated problems improves CT outcomes. Similarly, pre-treatment role induction (e.g., education via videotapes and/or interviews to clarify patient and therapist activities during psychotherapy) has often (but not always) been shown to improve treatment engagement and outcomes (e.g., Delgadillo & Groom, 2017; Monks, 1996; Strassel et al., 2015; Swift et al., 2012). More broadly, future research on the mechanisms of possible effects of biological beliefs, including beliefs' interactions with treatment modality (e.g., CT homework or medication compliance), will be important in identifying targets for improving depression care.

Our exploratory analyses of cognitive and interpersonal beliefs about depression suggested that these beliefs are less relevant to treatment outcomes, or alternatively, are already adequately addressed in CT. Unlike pre-treatment biological beliefs, cognitive and interpersonal beliefs measured before A-CT did not predict changes in depression during A-CT and did not predict residual symptoms immediately after A-CT. In addition, interpersonal beliefs measured after response to A-CT predicted more residual symptoms after A-CT, regardless of which continuation treatment responders received. This finding underscores the fact that depression occurs in an interpersonal context and highlights the importance of targeting interpersonal functioning during CT, which improves less and more slowly than do depressive symptoms (Vittengl, Clark, & Jarrett, 2004) and may benefit from

dyadic treatment (Beach & Whisman, 2012). However, cognitive beliefs measured after response to A-CT did not predict symptoms after acute-phase CT or moderate continuation treatment effects. Thus, cognitive and interpersonal beliefs, while important to assess for change, did not appear helpful for matching A-CT responders to C-CT versus FLX. Of course, our exploratory findings regarding cognitive and interpersonal beliefs must be considered tentative. For example, future research using different or better measures of beliefs might uncover important relations with treatment outcomes that we were unable to detect.

Our finding that mean scores on the biological, interpersonal, and cognitive beliefs scales decreased from before to after acute-phase CT suggests hypotheses for future research. The observed mean decreases were moderate (d s 0.41-0.53) and largely accounted for by simultaneous (and substantially larger) decreases in depressive symptoms. One possible explanation is that many patients had more depression to attribute to various causes before versus after CT, leading to decreases in mean ratings on the beliefs scales. Future research might explore patients' rationales for their beliefs and attributions about depression longitudinally as their mood changes.

Patients' treatment outcome expectations did not predict observed outcomes in either A-CT or continuation treatment, unlike past research using the same measure that showed forward prediction of symptom levels at the end of acute-phase treatment (A-CT, interpersonal psychotherapy, or clinical management with imipramine or pill placebo; Sotsky et al., 1991). On the other hand, patients' time-to-improvement expectations did predict depressive symptom changes in A-CT significantly. In this sense, patients were partly correct in forecasting their acute-phase outcomes. It is important to note that treatment outcomes were assessed with clinician reports (HRSD and DSM MDD symptom severity, also used to compute response, relapse, and recurrence statuses) in the current analyses. Using clinician reports may reduce concerns about measurement artifacts or "self-fulfilling prophecies" that might have inflated relations between patient expectations and self-reported depressive symptoms.

Limitations

Characteristics our sample, measures, and design limit the current conclusions. First, conclusions from the current sample of patients with carefully diagnosed recurrent MDD treated by expert therapists in a supervised research protocol may not generalize to other patient groups and treatment settings. Our study enrolled depressed people who consented to discontinue antidepressant medications and to receive an initial course of 12 weeks of A-CT, followed by randomization of responders to continuation CT, medication, or pill placebo. Patients who predicted they would not accept randomization to any of the three arms were excluded. These inclusion/exclusion criteria could have skewed sampling with respect to attitudes and beliefs about various treatments for depression. Similarly, because all patients received CT in the acute phase, our conclusions about continuation CT versus FLX do not inform choices between acute treatments but do propel hypotheses regarding selecting continuation phase treatments. Second, reflecting the broad applicability of the PAE, patients reported beliefs about their presenting problems and not about "depression" specifically.

Although patients completed this measure after presenting to depression clinics and consenting to treatment of diagnosed depression, individuals' specific response-frames are unknown. Future research might focus on development of a more specific and refined measure, especially of biological beliefs. Third, the treatment expectations measures were single self-report items. More reliable and nuanced measurement of expectations may yield stronger prediction of treatment outcomes. Fourth, observed effect sizes were moderate. Clearly, other variables in addition to patient beliefs and expectations are also important prognostically and prescriptively in identifying which patients are likely to succeed in A-CT and C-CT versus FLX, respectively. Fifth, our analyses did not reveal mediators and/or mechanisms by which patient beliefs and expectations may influence treatment outcomes, and this topic is worthy of future research. Sixth, we did not measure patients' preferences for type or modality of continuation-phase treatment, and thus we cannot comment directly on how these findings may relate to patient preferences for antidepressant treatment. Finally, although our findings about biological beliefs fit the research literature well and are consistent with best practices in CT, replication is needed before routinely assessing biological beliefs to gauge patients' suitability for C-CT versus FLX, particularly because the post-acute-CT sample analyzed here was relatively small ($N = 51$).

Conclusions

The current analyses suggest that patients' biological beliefs about depression provide clinically useful information when considering treatment with CT in a shared decision-making framework. In particular, patients with weaker biological beliefs may improve more in A-CT and be better candidates for C-CT versus FLX. Consistently matching to C-CT or FLX based on patients' beliefs may provide an absolute risk reduction of about 31% for relapse/recurrence within 32 months. This level of risk reduction meets or exceeds the average benefit of continuation treatments versus inactive control conditions for MDD found in meta-analyses (19-29%; Biesheuvel-Leliefeld et al., 2015; Hansen et al., 2008; Vittengl et al., 2007). Building on the current findings, future prospective studies might profitably test whether matching patients to treatments based on biological beliefs about depression, actively eliciting and addressing biological beliefs, and/or educating patients on the biopsychosocial model during CT, are cost-effective means to improve treatment outcomes.

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Highlights

- Patients hold varying beliefs about their problems and treatment expectations.
- We studied outpatients with recurrent major depressive disorder (MDD).
- Biological beliefs predicted poorer outcomes in acute-phase cognitive therapy (CT).
- Responders with fewer biological beliefs relapsed less with continuation CT.
- Responders with more biological beliefs relapsed less with continuation fluoxetine.

Figure 1.
CONSORT diagram showing patient flow through the multi-phase clinical trial.

Figure 2.

Cross-lagged path model estimating relations among depressive symptoms and patient beliefs and expectations about treatment. A-CT = acute-phase cognitive therapy. Depressive symptoms measured with the 17-item Hamilton Rating Scale for Depression. e1-e4 are error terms. See Table 2 for estimated values of path coefficients.

Figure 3.

After unstable response to acute-phase cognitive therapy, patients' beliefs moderated continuation treatments' effects on depressive symptoms. Low and high biological beliefs based on a median split of patients. HRSD = 17-item Hamilton Rating Scale for Depression.

Figure 4.

Major depression relapse/recurrence was less frequent among patients matched ($n = 25$) versus mismatched ($n = 26$) to continuation cognitive therapy (CT) or fluoxetine based their beliefs about the biological origin of depression after unstable response to acute-phase CT.

Patient Beliefs, Expectations, and Symptom Severity Before and After Acute-phase Cognitive Therapy (A-CT)

Table 1

Measure	Before A-CT			After A-CT			Change	
	N	M	SD	N	M	SD	M	SE d
Patient beliefs about depression								
Biological	137	2.76	1.23	101	2.08	0.91	0.65**	0.12 0.53
Interpersonal	137	3.68	1.28	101	3.08	1.17	0.57**	0.11 0.51
Cognitive	137	4.79	1.33	101	4.21	1.17	0.54**	0.10 0.43
Patient expectations								
Outcome	137	3.77	0.70	101	3.74	0.73	0.03	0.09 0.04
Time to improvement	134	10.42	11.45	92	10.21	10.44	-0.94	1.06 -0.08
Hamilton Rating Scale for Depression	152	21.53	4.23	118	8.64	5.57	12.85**	0.58 3.04

Note. Mean change estimated in multilevel models. Effect size *d* = mean change divided by pre-treatment *SD*.

* $p < .05$,
** $p < .01$, two-tailed.

Table 2

Correlations among Patient Beliefs, Expectations, and Symptom Severity Before Cognitive Therapy

Variable	1	2	3	4	5
1. Biological beliefs	---				
2. Interpersonal beliefs	.24	---			
3. Cognitive beliefs	.21	.56	---		
4. Outcome expectation	.09	.21	.19	---	
5. Time-to-improvement expectation	.18	.05	.00	-.16	---
6. Depression symptom severity	.20	.22	.20	.12	.03

Note. $N = 134$ -137. Correlations of .18 and stronger,

$p < .05$, two-tailed.

Relations among Depressive Symptom Severity (HRSD) and Patient Beliefs and Expectations (B/E) during Acute-phase Cognitive Therapy

Table 3

Model: B/E Variable	Cross-lagged Paths		Concurrent Correlations		Retest Stability	
	HRSD -> B/E (b1)	B/E -> HRSD (b2)	Pre-A-CT (r1)	Post-A-CT (r2)	HRSD (rr1)	B/E (rr2)
1. Biological beliefs	.10	.31**	.20*	.26**	.02	.38**
2. Cognitive beliefs	-.05	.04	.19*	.02	.06	.70**
3. Interpersonal beliefs	.05	.09	.22**	-.09	.05	.63**
4. Outcome expectation	.02	-.11	.11	-.17	.09	.16
5. Time-to-improvement expectation	.01	.35**	.03	.08	.09	.60**

Note. $N = 152$. A-CT = acute-phase cognitive therapy. Tabled standardized coefficients derived from path models estimated via full information maximum likelihood. Path coefficient abbreviations in parentheses are depicted in Figure 2. HRSD = 17-item Hamilton Rating Scale for Depression.

* $p < .05$,

** $p < .01$, two-tailed.

Table 4

Prediction of Depressive Symptom Severity after Acute-phase Cognitive Therapy from Continuation Treatment and Patient Beliefs and Expectations

	Patient Beliefs about Depression			Patient Treatment Expectations	
	Biological	Cognitive	Interpersonal	Overall outcome	Time to improvement
Time					
$F(8,199-230)$	0.50	0.99	1.01	2.30	1.00
Treatment					
$F(1,72-84)$	12.90**	0.68	0.28	0.04	3.25
Time $\times$ Treatment					
$F(8,199-230)$	0.81	1.50	0.27	0.88	0.58
B/E variable					
$F(1,75-83)$	1.76	0.16	5.53*	2.50	1.62
B/E $\times$ Time					
$F(8,206-231)$	0.51	1.04	1.33	0.58	0.63
B/E $\times$ Treatment					
$F(1,75-83)$	21.30**	1.80	1.93	0.25	0.01
B/E $\times$ Time $\times$ Treatment					
$F(8,206-231)$	0.92	1.67	1.18	0.88	0.23

Note. $N = 51$ acute-phase cognitive therapy responders randomized to 8 months of continuation treatment (cognitive therapy or fluoxetine plus clinical management) plus 24 months of followup. B/E = belief or expectation variable. Time reflects assessment of depressive symptom severity (17-item Hamilton Rating Scale for Depression) every 4 months. F -test denominator df based on Satterthwaite adjustment in repeated-measures multilevel models.

* $p < .05$,

** $p < .01$.