Anxiety in older adults: prevalence and low-threshold psychological interventions

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PREDICTORS OF TREATMENT RESPONSE TO ACCEPTANCE AND COMMITMENT THERAPY AND COGNITIVE BEHAVIORAL THERAPY IN OLDER ADULTS WITH ANXIETY SYMPTOMS

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Abstract

Background: A recent trial in older adults with anxiety symptoms found no differences between an ACT intervention and a CBT intervention regarding their effect on anxiety symptom severity.

Objective: To follow up these earlier findings, the current study aimed to identify moderator variables, that predict differential treatment response to these two interventions. Secondary, the study aimed to identify non-specific predictors, that predict treatment response in both conditions.

Methods: The sample consisted of 314 older adults with anxiety symptoms, randomized to ACT or CBT. The following baseline characteristics were examined: 1) demographics (sex, age, education, work hours, relationship status, negative life events); 2) (psycho) pathology (anxiety severity, depression severity, presence anxiety disorder, medication use, somatic comorbidity); 3) social support (problem solving support, affective support); 4) psychological processes (self-esteem, mastery, experiential avoidance, mindfulness, emotion regulation). Anxiety symptom severity (measured with the GAD-7) was the outcome variable.

Results: No moderator variables were identified. Two non-specific predictors were identified: more severe depression symptoms predicted worse short-term (b=0.20, p=.02) and long-term (b=0.25, p=.002) response to ACT and CBT, and higher levels of mastery predicted better short-term treatment response (b=-0.17, p=.03) in both conditions.

Conclusions: Since no moderator variables were identified, both the ACT and CBT intervention can for now be offered to all older adults with anxiety symptomatology. The prognostic effects of depression symptom severity and mastery may hold implications regarding treatment enhancement strategies.

Introduction

Anxiety disorders and symptoms are one of the most prevalent mental health issues in older adults and are associated with considerable distress and impairment [11,20,229]. Although anxiety in later life has received an increasing amount of scientific attention over the last decades, the literature on psychological treatment for older adults with anxiety symptoms is still limited and mainly focused on the evaluation of face-to-face cognitive behavioral therapy (CBT) [35]. To broaden the scope of this field of research and advance treatment of anxiety symptoms in later life, we conducted a randomized controlled trial (RCT) to evaluate the short- and long term effectiveness of a blended Acceptance and Commitment Therapy (ACT) intervention in a sample of older adults with anxiety symptoms. ACT is a behavior therapy that promotes an acceptance-based attitude towards (negative) feelings and thoughts, and stimulates people to (re)connect with their core values and act in accordance with these [52]. In the RCT, the blended ACT intervention was compared to face-to-face CBT, which could be considered optimized treatment-as-usual in the study setting. We found no differences in effectiveness of ACT and CBT on anxiety symptom severity at posttreatment and one-year follow-up. Looking at the within-group effect sizes, both groups showed a large and significant decline in anxiety symptom severity from baseline to posttreatment. This decrease was sustained one year after baseline in both conditions [250].

Findings like those from our RCT, namely that two (or more) active treatments appear equally effective for a certain patient population, are common in the field of clinical psychology [261]. Notwithstanding the importance of such findings, they do present a challenge for evidence-based clinical practice, as they do not provide information about how individual patients are likely to respond to (a) particular treatment(s) [261]. Therefore, the goal of the current study is to examine predictors of short- and long term anxiety symptom improvement in ACT and CBT for anxiety symptoms in later life. There are two types of predictors of treatment response: non-specific predictors and moderators. Non-specific predictors are variables that are predictive of treatment response, irrespective of treatment type. Such variables provide *prognostic* information by clarifying which subgroups of patients are likely to benefit more or less from treatment in general. Moderators, on the other hand, are baseline characteristics that differentially predict response to two or more interventions in a patient population [7]. Moderators thus provide *prescriptive* information about treatment selection, as they indicate subgroups of patients who respond differentially to different types of treatment. Compared to non-specific predictors, the clinical implications of

findings on treatment moderators are therefore more profound: ultimately, information about moderators could be used to transform mental health care into *'precision mental health care'*, where patients are provided with the intervention that is likely to be most effective for them based on their pretreatment characteristics, thereby improving treatment outcomes.

To our knowledge, two studies so far have examined moderators and non-specific predictors of treatment response to ACT and CBT for anxiety, both using data from a trial that compared face-to-face ACT and CBT in a sample of 121 adults (maximum age of 60 years, mean age of 37.93 years (*SD*=11.79)) with mixed principal anxiety disorder diagnoses [262,263]). The first study [262] examined multiple demographic and psychological variables and found ACT to be the optimal treatment (in terms of anxiety symptom improvement) for patients with a comorbid mood disorder at baseline, while CBT outperformed ACT among patients without a comorbid mood disorder. Furthermore, it was found that among the participants with moderate baseline levels of anxiety sensitivity, CBT outperformed ACT. Neuroticism was identified as a non-specific predictor, with higher baseline levels being associated with poorer outcomes in both ACT and CBT. In the other study, Davies et al. [263] focused on physiological and behavioral indices of emotion dysregulation as potential moderators and found that patients with higher behavioral avoidance (operationalized as the unwillingness to endure physical sensations caused by a hyperventilation task) benefitted more from ACT than CBT. Heartrate variability emerged as a non-specific predictor, with higher variability being predictive of overall poorer treatment outcome.

Both Wolitzky-Taylor et al. [262] and Davies et al. [263] used a statistical approach that is common in studies concerned with the identification of treatment moderators: in a series of regression analyses they tested for statistical interaction between baseline person characteristics and treatment type, examining each person characteristic in isolation. In other words, the effect of each putative moderator variable was investigated with a separate regression model. Results from such analyses offer little guidance to clinicians, as it is unclear how the information about the moderators should be combined when deciding upon the optimal treatment for a specific patient [264], especially when findings on different individual moderators lead to conflicting treatment recommendations. For example, the results from the study by Wolitzky-Taylor et al. [262] pose a problem for a therapist who has to select the optimal treatment for a patient with an anxiety disorder, moderate anxiety severity (related to superior outcomes for CBT) and a comorbid mood disorder (related to superior outcomes for ACT).

Clearly, for findings on moderator variables to inform clinical practice in a meaningful way, they should be integrated and translated into treatment recommendations for individual patients. This was also recognized by DeRubeis et al. [265], who developed a statistical procedure in which data from clinical trials are used to create a model that predicts treatment outcomes for the different interventions for each trial participant, based on their pattern of pretreatment characteristics. The method builds upon classical moderated regression analysis, but goes beyond the approach of examining each putative moderator in isolation by combining the information from the univariate analyses into one prediction model. Such a model can be used for individualized treatment selection, by providing patients with the treatment they are predicted to respond to optimally based on their pretreatment characteristics. Previous studies have shown that this method indeed holds promise as a tool for individualized treatment assignment [266-268].

In sum, in the current study we will examine moderators of short term and long term treatment response to blended ACT and face-to-face CBT for older adults with anxiety symptoms. Secondary, we are also interested in non-specific predictors of treatment response to the two interventions. Since there is no solid body of scientific literature to inform hypotheses about putative moderators and non-specific predictors of treatment response to ACT and CBT for anxiety symptoms in later life, we will use an exploratory approach and include a selection of demographic and clinical baseline variables. Furthermore, if the analyses will identify multiple moderator variables, we will follow the statistical procedure from DeRubeis et al. [265] to create an algorithm that uses the identified moderator(s) to predict (optimal) treatment outcomes for individual trial participants.

Methods

This study used data from a cluster-randomized single blind controlled trial that was conducted in the Netherlands. The trial evaluated the effectiveness of a brief blended ACT intervention compared to brief face-to-face CBT over a period of 12 months. Randomization took place at the level of the therapists that participated in the study (n=40), who consequently either only provided blended ACT (n=20) or only CBT (n=20) to study participants. Details about the study design and methods have been published elsewhere [236]. The trial was registered in the Netherlands Trial Register and approved by the medical ethics committee.

Participants and procedure

Between November 2017 and March 2019, participants were recruited in 38 general practices in the Netherlands. Patients (aged 55-75) from the participating general practices were sent a letter that contained information about the study and an invitation to participate. Those interested in participation could register on a study website, after which they entered a screening procedure. Inclusion criteria were: age between 55 and 75 years, presence of mild to moderate anxiety symptoms (Generalized Anxiety Disorder-7 [131] score between 5 and 15), mastery of the Dutch language, internet access and the possibility to spend up to 30 min per day on the intervention. Exclusion criteria were: unstable severe medical condition(s); severe cognitive impairment; very high or low anxiety symptom severity (GAD-7 score < 5 / > 15); severe depressive symptoms (PHQ-9 [170] score ≥ 20); psychological or psychopharmacological treatment (stable benzodiazepine or SSRI use excepted) within the last 3 months; severe role impairment in at least 2 life areas (score of ≥ 8 on two or three items of the Sheehan Disability Scale (SDS) [171]); high suicide risk (M.I.N.I.-Plus [139]); substance use disorder (M.I.N.I.-Plus); lifetime diagnosis of bipolar disorder or schizophrenia (medical record and M.I.N.I.-Plus).

Eligible participants signed an online informed consent form and completed the baseline assessment, after which they were informed about their treatment allocation. Participants completed 4 main assessments: at baseline (T0), posttreatment (T1; 3 months after baseline), 6 months after baseline (T2) and 12 months after baseline (T3). In the current study, we will use data from T0, T1 and T3. The assessments consisted of online self-report questionnaires and a telephone interview conducted by trained and supervised research assistants that were blind to randomization.

Interventions

Therapists

Treatment was provided by mental health counselors working in general practices in the Netherlands. Around 2008, general practices in the Netherlands started employing mental health counselors in response to the increasing demand for treatment of psychological problems and the high costs and limited capacity of mental health care institutions [234]. The counselors provide short term psychological treatment to patients with mild to moderately severe psychological complaints. The occupation is fulfilled by mental health professionals with different educational backgrounds. Most counselors participating in the study were master graduates in psychology (n=13), social psychiatric nurses (n=14) or social workers (n=5). Their years of experience

with providing individual psychological treatment ranged from 3 to 42, with a median of 16 years.

Blended Acceptance and Commitment therapy

Participants in the Blended ACT condition completed the online ACT-module 'Living to the Full' [179,180] and attended 4 face-to-face sessions with the mental health counselor at their general practice. The module consists of 9 lessons that revolve around the 6 core processes of ACT: acceptance, cognitive defusion, contact with the present moment, self as context, personal values and committed action. Participants completed the module in 9 to 12 weeks. The 4 face-to-face sessions with the mental health counselor followed a protocol developed by the authors of Living to the Full and served to increase motivation, repeat key exercises and discuss problems that arose while working with the module.

Cognitive Behavioral Therapy

Participants in the CBT condition attended 4 face-to-face sessions and completed homework exercises. The sessions took place in a timespan between 9 to 12 weeks. A treatment protocol was developed that focused on identifying and challenging negative cognitions and reducing anxiety-related avoidance behavior. Furthermore, it contained information and exercises related to specific types of anxiety (panic, worrying, social anxiety) and common side effects of anxiety (sleeping problems, physical tension). After the intake session, the counselor and client collaboratively set treatment goals. In the second and third session, homework was evaluated, key exercises/information repeated and the counselor and participant agreed on a planning regarding homework exercises for the succeeding weeks. The last session was dedicated to an evaluation of the progress of the client and the formulation of a relapse prevention plan.

Measurements: outcome variable

Anxiety symptom severity

Anxiety symptom severity at T1 and T3 was assessed with the GAD-7, a widely-used seven-item anxiety screener with good psychometric properties [171]. Total scores range from 0 to 21, with higher scores reflecting more severe anxiety symptoms in the last two weeks. Values for Cronbach's alpha for the GAD-7 in the current study sample at T1 and T3 were α= 0.86 and α=0.87, respectively.

Measurements: predictor variables

All predictor variables were assessed during the baseline measurement.

Demographic variables

Age, gender, romantic relationship status, education level and weekly work hours (both paid and voluntary work) were assessed with a self-developed questionnaire.

Recent negative life events

Recent negative life-events were assessed with a self-developed yes/no question: "In the past 6 months, did you experience one or more major negative events?". Participants that responded yes, could describe the event in a textbox.

Somatic problems

Physical problems in the previous year were assessed with a self-developed checklist, listing the 25 most common (chronic) medical conditions, according to Statistic Netherlands. Participants could also report somatic problems they experienced that were not included in the checklist.

Psychiatric medication use

Participants completed a yes/no question to indicate if they had used benzodiazepines and/or SSRIs during the preceding 3 months.

Presence of anxiety disorder

Trained research assistants conducted The Mini-International Neuropsychiatric Interview [139] by phone to assess the presence of generalized anxiety disorder, panic disorder, agoraphobia, specific phobia, social phobia, obsessive-compulsive disorder, posttraumatic stress disorder and illness anxiety disorder.

Depression symptom severity

Depression symptom severity was measured with the PHQ-9 [170], a nine item self-report questionnaire with good psychometric properties. Total scores range from 0 to 27 with higher scores indicating higher symptom severity in the previous two weeks. Cronbach's alpha for the PHQ-9 in the current sample was $\alpha = 0.73$.

Self-esteem, mastery and social support

Bovier, Chamot and Perneger [206] developed a 14-item questionnaire to measure social support and psychological resources. The questionnaire consists of 4 scales, measuring self-esteem (defined as one's overall sense of worthiness as a person; 4 items), mastery (people's belief that their life's course is under their own control in contrast to being fatalistically ruled; 4 items), affective social support (the availability of people who express emotional involvement with and care for the participant during challenging situations; 2 items) and problem solving social support (the availability of people one can confide in and receive advice from when challenging situations occur; 4 items). Items are answered on a scale ranging from 0 to 4 and higher scores on each subscale represent higher levels of the measured construct. All four scales have proper psychometric properties [206]. In the current study sample, Cronbach's alpha values were: α= 0.76 for self-esteem, α= 0.78 for mastery, α= 0.87 for affective social support and α= 0.83 for problem solving social support.

Experiential Avoidance

The Acceptance and Action Questionnaire-II (AAQ-II) is a validated unidimensional measure [191] that assesses experiential avoidance. Experiential avoidance is a key concept in ACT and refers to the unwillingness to remain in contact with aversive private experience and the behaviors aimed at altering these experiences or the events that elicit them [191]. AAQ items are scored on a 7-point scale and total scores range from 7 to 49 with higher scores reflecting higher levels of experiential avoidance. Cronbach's alpha for the AAQ-II at T0 in the current study sample was α= 0.87.

Mindfulness

The Five Facet Mindfulness Questionnaire-Short Form (FFMQ-SF) was used to assess mindfulness, defined as the ability to bring one's attention to experiences in the present moment in a nonjudgmental manner [195]. The questionnaire is comprised of 24 6-point items (ranging from 0 to 5) that measure five facets of mindfulness: observing (4 items), describing (5 items), acting with awareness (5 items), non-judging (5 items) and non-reactivity (5 items). The sum score of all items reflects the level of mindfulness, with higher scores indicative of higher levels. The questionnaire has good psychometric properties [195]. Cronbach's alpha for the FFMQ-SF at T0 in the current study sample was α= 0.69.

Cognitive Emotion Regulation Strategies

Participant completed the subscales self-blame, rumination, positive reappraisal and catastrophizing. of the Cognitive Emotion Regulation Questionnaire (CERQ) [188]. The subscales consist of four 5-point items each, with total scores for each scale ranging between 0 and 16. Higher scores on a subscale indicate that this cognitive coping strategy is more often used to regulate emotions. The CERQ has good psychometric qualities [188]. Cronbach's alpha values for the four scales in the current study sample were: α=0.79 for self-blame, α= 0.77 for rumination, α= 0.86 for positive reappraisal and α= 0.82 for catastrophizing.

Anxiety symptom severity at baseline

Anxiety symptom severity at T0 was measured with the GAD-7 [131]. Cronbach's alpha for the GAD-7 at T0 in the current study sample was α= 0.78.

Statistical analysis

All analyses were performed using the R statistical software environment [96]. Analyses followed the intention-to-treat principle, which required missing data imputation. We used Multiple Imputation by Chained Equations (MICE), with the predictive mean matching procedure, in which the missing outcome of a participant is imputed with the observed outcome from another participant with a comparable predicted mean outcome. This procedure ensures that the imputed data have plausible values [237]. A total of 100 imputed datasets were analyzed and their results pooled to arrive at the presented estimates.

Analyses were conducted separately for short term (T0-T1) and long term (T0-T3) treatment response. To identify moderators and non-specific predictors, we used a domain approach similar to the one outlined by Fournier et al. [269] and more recently by Huibers et al. [265]. Continuous variables were standardized and categorical variables were effect coded. First, we grouped the predictors in 4 domains (Table 1). To prevent excessive multiple testing, we conducted omnibus tests to compare the fits of three nested models within each domain: a simple model (regressing GAD-7 end-score on baseline GAD-7 score and treatment condition), an additive model (adding main effects of all the predictors in the domain) and a full prediction model (also adding interaction terms between treatment condition and each predictor in the domain). Using the Wald test, we tested whether the full prediction model fit the data significantly

(α=0.05) better than both the simple model and the additive model. If the omnibus tests indicated that the full domain model had a superior fit, we used a stepwise procedure to identify the prescriptive and prognostic variables within that domain. In step 1, the full prediction model was inspected and variables that were significant at a threshold of α=0.2 were selected and combined into a new model. If an interaction between a predictor variable and the treatment variable fell below the significance threshold, the main effect of the predictor was carried through to the next step, irrespective of it being significant itself (maintaining the principle of marginality). The main effects of baseline anxiety symptom severity and treatment condition were always carried through to the next step, irrespective of their statistical significance. In step 2, the second model was examined and a same process was applied using a stricter threshold value of α=0.1. In Step 3, the same process was repeated, but with a threshold of α=0.05.

In domains where the full prediction model did not provide the superior fit, but the additive fit the data better than the simple model, we used the same procedure, but only aimed at identifying non-specific predictors.

We build a final prediction model combining the variables from all the domains that were significant at the 0.05 level in the third step of the domain specific analyses. The variables that remained significant at the 0.05 level in this final model, were considered moderators and/or non-specific predictors

If multiple moderators were identified, we followed the guidelines from DeRubeis et al. [265] to predict the optimal treatment for each individual participant with a model that regressed GAD-7 end-scores on the identified moderators and non-specific predictors. Outcome estimates for each participant were calculated with a leave-one-out cross-validation procedure, where the estimates for an individual participant are derived from a prediction model based on the data from all other participants. For each participant, a 'factual' prediction (predicted outcome for the intervention the participant was assigned to in the RCT) was calculated by entering their observed values on the independent variables in the model. The counterfactual prediction (predicted outcome for the intervention the participant was not assigned to in the RCT) was then calculated by changing the value of the treatment variable to reflect the intervention they had not received during the RCT. The factual and counterfactual predictions were compared to see which intervention was expected to be optimal for each participant (e.g., predicted to lead to the lowest GAD-7 score at T1/T3).

Table 1. Domains of baseline variables

Domain 1: Demographics
Sex (male=0, female=1)
Age
Education level (0=low, 1=middle, 2=high)
Weekly workhours
Relationship status (0=married or in a relationship, 1=not married or in a relationship)
Recent negative life events (0=no recent event, 1=recent event)
Domain 2: (Psycho)pathology
Anxiety symptom severity (GAD-7)[1]
Depression symptom severity (PHQ-9)
Presence of anxiety disorder(s) (MINI-Plus)
Psychiatric medication use (0=no medication use, 1=medication use)
Somatic comorbidity (continuous variable, reflecting the number of somatic problems during the previous year)
Domain 3: Social Support
Problem solving social support (Questionnaire developed by Bovier, Chamot & Perneger)
Affective social support (Questionnaire developed by Bovier, Chamot & Perneger)
Domain 4: Psychological processes
Self-esteem (Brief scale developed by Bovier, Chamot & Perneger)
Mastery (Brief scale developed by Bovier, Chamot & Perneger)
Experiential avoidance (AAQ-II)
Mindfulness (FFMQ-SF)
Self-blame (CERQ)
Rumination (CERQ)
Positive reappraisal (CERQ)
Catastrophizing (CERQ)

[1] baseline anxiety severity was only examined as potential moderator of treatment effect and not as a potential non-specific predictor, as the main effect of baseline anxiety severity was included as a control variable in all analyses.

Results

A total of 35,820 older adults (all living independently) received an information/invitation letter, of which 683 were screened after they registered for study participation. 314 people were included; 150 in the blended ACT group, 164 in the CBT-group. Table 2 presents the baseline characteristics of the sample. The T1 measurement was completed by 222 participants: 101 participants (67%) in the blended ACT-group and 121 participants (74%) in the CBT-group. The T3 measurement was completed by 178 participants: 82 (55%) in the blended ACT-group and 96 (59%) in the CBT-group.

Table 2. Baseline characteristics of the study sample

Characteristics	Blended ACT (*n*=150)	CBT (*n*=164)	Total sample (*n*=314)
Age (years), M (SD), [range]	62.75 (5.69) [55-75]	63.33 (5.71) [55-75]	63.06 (5.70) [55-75]
Sex, n (%)			
Female	100 (66.67)	92 (56.08)	192 (61.15)
Male	50 (33.33)	72 (43.92)	122 (38.85)
Nationality, n (%)			
Dutch	149 (99.33)	159 (96.96)	308 (98.01)
Dutch and other	0 (0.00)	5 (3.04)	5 (1.59)
Other	1 (0.77)	0 (0.00)	1 (0.40)
Education, n (%)			
Low	22 (14.67)	15 (9.15)	37 (11.78)
Middle	70 (44.67)	74 (45.12)	144 (45.86)
High	56 (37.33)	74 (45.12)	130 (41.40)
Unknown	2 (0.63)	1 (0.61)	3 (0.96)
Relational status, n (%)			
Married/in a romantic relationship	120 (80.00)	129 (78.66)	249 (79.30)
Not married/in a romantic relationship	30 (20.00)	35 (21.34)	65 (20.70)
Work status, n (%)			
Paid employment	77 (51.33)	76 (46.34)	153 (48.73)
Voluntary work	49 (32.67)	56 (34.15)	105 (33.44)
No work	53 (35.33)	59 (35.98)	112 (35.67)
Living situation, n (%)			
Alone	36 (24.00)	39 (23.78)	75 (23.89)
With partner	97 (64.67)	103 (62.80)	200 (63.69)
With children	11 (7.33)	13 (7.93)	24 (7.64)
With partner and children	6 (4.00)	8 (4.88)	14 (4.46)
Other	0 (0.00)	1 (0.61)	1 (0.32)
Somatic comorbidity, n (%)			
No somatic problems	29 (19.33)	32 (19.51)	61 (19.43)
One or more somatic problems	121 (80.67)	132 (80.49)	253 (80.57)
Psychiatric medication use, n (%)			
SSRI	10 (6.67)	12 (7.32)	22 (7.01)
Benzodiazepine	19 (12.67)	15 (9.15)	34 (10.83)
No psychotropic medication	121 (80.67)	137 (83.54)	258 (82.17
Anxiety disorder, n (%)			
Any anxiety disorder	42 (28.00)	39 (23.78)	81 (25.80)
No anxiety disorder	108 (72.00)	125 (76.22)	233 (74.20)

Moderators

None of the full prediction models provided a superior fit to the data (see Table 3). Thus, no moderators were identified for short term or long term treatment response to blended ACT and CBT.

Table 3. Results of the omnibus tests comparing domain specific simple, additive and full prediction models

	Short term					Long term				
Model comparison	***DF1***	***DF2***	***ΔR²***	***f***	***p***	***DF1***	***DF2***	***ΔR²***	***f***	***p***
Demographic domain										
Additive vs. simple	7	208.03	0.04	1.52	0.16	7	282.28	0.03	1.25	0.28
Full vs. additive	7	287.20	0.04	0.70	0.67	7	165.04	0.04	0.47	0.85
Psychopathology domain										
Additive vs. simple	4	285.48	0.06	4.18	.003*	4	269.24	0.06	2.73	0.03*
Full vs. additive	5	287.78	0.01	0.38	0.86	5	278.49	0.01	0.34	0.89
Support domain										
Additive vs. simple	2	278.09	0.02	2.93	0.06	2	235.46	0.02	1.53	0.22
Full vs. additive	2	276.88	0.00	0.52	0.60	2	257.24	0.00	0.25	0.78
Psychological processes domain										
Additive vs. simple	8	290.64	0.08	2.61	.009*	8	281.85	0.06	1.14	0.34
Full vs. additive	8	285.87	0.03	0.74	0.66	8	280.08	0.02	0.32	0.96

Note. All statistics are derived from pooling the results of 100 imputed datasets. R^2 of the simple model predicting short term treatment response was 0.12, the R^2 of the long term simple model 0.13.
*p<.05

Non-specific predictors

Short term treatment response

Of the additive models predicting short term treatment response, the psychopathology domain model (F(4, 285.48)=4.18, p=.003) and psychological processes domain model (F(8, 290.64)=2.61, p=.009) fit the data significantly better than the simple model (see Table 3). See Table 4 and 5 for the results of the stepwise inspection of the predictors in these domains. In the psychopathology domain, depression symptom severity (b=0.26, p < .001) was a significant predictor of treatment outcome: more severe symptoms of depression at baseline were associated with worse treatment outcomes, regardless of treatment condition. In the psychological processes domain, mastery (b=-0.19, p=.006) significantly predicted short term treatment response: higher baseline levels were related to better treatment outcome, irrespective of the treatment being blended ACT or CBT.

In the final prediction model (see Table 6), both depression symptom severity (*b*=0.20, *p*=.02) and mastery (*b*=-0.17, *p*=.03) were significantly associated with anxiety symptom severity at T1. Therefore, depression symptom severity and mastery were considered non-specific predictors of short term treatment response to the blended ACT and CBT intervention. The R^2 of the final model (that contained condition and baseline anxiety symptom severity as control variables, and baseline depressive symptom severity and mastery as predictors) was 0.19 [95% CI: 0.10 to 0.28].

Table 4. Stepwise inspection of non-specific predictors of short term treatment response: (psycho) pathology domain

Predictors	*b*	Std. error	*t*	*p*
Model 1				
Condition	-0.03	0.12	-0.21	.84
Anxiety symptom severity	0.16	0.07	2.16	.03***
Depression symptom severity	0.24	0.08	3.08	.00***
Anxiety disorder	0.22	0.14	1.55	.12*
Psychiatric medication	0.17	0.17	1.01	.32
Somatic comorbidity	0.07	0.06	1.04	.30
Model 2 (retained effects at p < .20)				
Condition	-0.03	0.13	-0.22	.83
Anxiety symptom severity	0.15	0.07	2.06	.04***
Depression symptom severity	0.27	0.08	3.53	<.001***
Anxiety disorder	0.23	0.14	1.59	.12
Model 3 (retained effects at p < .10)				
Condition	-0.02	0.13	-0.13	.90
Anxiety symptom severity	0.18	0.07	2.50	.01***
Depression symptom severity	0.26	0.08	3.42	<.001***

Note. All statistics are derived from pooling the results of 100 imputed datasets. The regression coefficients for anxiety symptom severity and depression symptom are standardized coefficients, because the variables were standardized before entering the model. *= p<.20; *** p<.05

Table 5. Stepwise inspection of non-specific predictors of short term treatment response: psychological processes domain

Predictors	*b*	Std. error	*t*	*p*
Model 1				
Condition	-0.05	0.12	-0.40	.69
Anxiety symptom severity	0.20	0.08	2.64	.00***
Self-esteem	-0.04	0.06	-0.59	.56
Mastery	-0.19	0.08	-2.53	.01***
Mindfulness	-0.15	0.08	-1.91	.06**
Experiential avoidance	0.12	0.09	1.36	.17*
Self-blame	-0.11	0.08	-1.49	.14*
Rumination	0.02	0.08	0.25	.81

Table 4. Continued

Predictors	*b*	Std. error	*t*	*p*
Positive reappraisal	0.06	0.07	0.89	.38
Catastrophizing	-0.09	0.07	-1.30	.20*[1]
Model 2 (retained effects at p < .20)				
Condition	-0.05	0.12	-0.38	.71
Anxiety symptom severity	0.21	0.07	2.88	.01***
Mastery	-0.18	0.07	-2.49	.01***
Mindfulness	-0.13	0.08	-1.69	.09**
Experiential Avoidance	0.12	0.09	1.35	.18
Self-blame	-0.09	0.07	-1.33	.19
Catastrophizing	-0.08	0.07	-1.26	.21
Model 3 (retained effects at p <.10)				
Condition	-0.06	0.12	-0.50	.62
Anxiety symptom severity	0.21	0.07	3.00	.00***
Mastery	-0.19	0.07	-2.76	.01***
Mindfulness	-0.14	0.07	-1.92	.06

Note. All statistics are derived from pooling the results of 100 imputed datasets. All regression coefficients are standardized coefficients, because continuous variables were standardized before entering the model All regression. [1] =rounded up to 0.20, original value was 0.196. *= p<.20; ** p<.10; *** p<.05

Table 6. Final prediction model short term treatment response

Predictors	*b*	Std. error	*t*	*p*
Condition	-0.04	0.12	-0.29	.77
Anxiety symptom severity	0.16	0.07	2.28	.02***
Depression symptom severity	0.20	0.08	2.32	.02***
Mastery	-0.17	0.07	-2.26	.03***

Note. All statistics are derived from pooling the results of 100 imputed datasets. All regression coefficients are standardized coefficients, because continuous variables were standardized before entering the model All regression *** p<.05

Long term treatment response

Of the additive models predicting long term treatment response, only the psychopathology domain model fit the data significantly better than the simple model (F(4, 269.24)=2.73, p=.03) (see Table 3). Stepwise inspection of the variables in the domain indicated that -similar to the short term analysis- baseline depression symptom severity (b=0.25, p=.002) was a non-specific predictor of long term treatment outcome (see Table 7): participants with higher depression symptom severity at baseline had more severe anxiety symptoms at the twelve month follow-up, irrespective of treatment condition. The R^2 of the final model (that contained condition and baseline anxiety

symptom severity as control variables, and baseline depressive symptom severity as predictor) was 0.18 [95% CI: 0.08 to 0.28].

Table 7. Stepwise inspection of non-specific predictors of long term treatment response: (psycho) pathology domain

Predictors	***b***	**Std. error**	***t***	***p***
Model 1				
Condition	-0.07	0.13	-0.54	.59
Anxiety symptom severity	0.21	0.08	2.55	.01***
Depression symptom severity	0.23	0.08	2.81	.01***
Anxiety disorder	0.04	0.16	0.27	.79
Psychiatric medication	0.09	0.18	0.52	.60
Somatic comorbidity	0.07	0.07	1.06	.29
Model 2 (retained effects at p < .20)				
Condition	-0.07	0.13	-0.57	.57
Anxiety symptom severity	0.20	0.08	2.57	.01***
Depression symptom severity	0.25	0.08	3.15	.00***

Note. All statistics are derived from pooling the results of 100 imputed datasets. The regression coefficients for anxiety symptom severity and depression symptom are standardized coefficients, because continuous variables were standardized before entering the model. *= p<.20; ** p<.10; *** p<.05

Optimal treatment prediction

Since we did not identify any moderators of treatment response, we could not conduct the planned second step of the analyses in which a prediction model would be built to predict optimal treatment (outcome) for individual participants.

Discussion

This study examined predictors of short term and long term treatment response to a blended ACT intervention vs. a face-to-face CBT intervention in older adults with anxiety symptoms. These two brief interventions were previously found to be equally effective for this patient population [5]. We were primarily interested in identifying moderator variables, as insight into how ACT and CBT differentially affect certain subgroups of patients could inform evidence-based personalized treatment assignment. With this study, we wanted to go beyond the common approach of only examining putative moderators in isolation and aimed to integrate the results from the moderator analyses into a model for assigning treatment to individual patients based on their pattern of pretreatment characteristics. We did not identify any moderators of treatment response

to the blended ACT intervention and CBT intervention. This precluded the development of a treatment assignment model following the procedure from DeRubeis et al [265].

The secondary aim of this study was to identify non-specific predictors of treatment response. These predictors provide prognostic information about which subgroups of anxious older adults are likely to respond more or less favorably to treatment, irrespective of the treatment being the ACT or the CBT intervention. Two non-specific predictors were identified. First, more severe depression symptoms at baseline were found to be predictive of poorer short term and long term treatment response to both the ACT and CBT intervention. Second, baseline mastery levels were predictive of short term treatment response, with higher levels being associated with more favorable responses in both treatment conditions.

Regarding baseline depression symptom severity, earlier studies into the prescriptive and prognostic effects of comorbid depression on treatment response in anxious patients present mixed findings. Some studies found comorbid baseline depression to be associated with worse anxiety outcomes across different treatments [270-273], while others found that it did not predict posttreatment anxiety severity [274-277]. In the study from Wolitzky-Taylor and colleagues [8], depressive comorbidity was found to be a moderator of treatment response. Patients with a comorbid depressive disorder responded better to ACT than CBT, which the authors ascribed to ACT being a more transdiagnostic treatment that targets psychological constructs related to both anxiety and depression. Considering the mixed findings so far, more research into how comorbid depressive symptoms are associated with treatment response in anxious patients is indicated. Ultimately, these studies could inform clinical practice on whether and how the subgroup of anxious patients with comorbid depression (symptoms) could benefit from additional/adapted treatments.

Mastery, the other prognostic variable identified in this study, is part of a set of closely connected psychological constructs (a.o., locus of control, self-efficacy) that are all related to one's perceived control over situations or events [278]. Perceived control variables have been examined in the context of psychological treatment and higher baseline values of different measures have repeatedly been demonstrated to be related to more favorable treatment outcomes across a wide spectrum of psychological conditions (including anxiety) and treatments [279-282]. People with higher levels of perceived control show increased task motivation and stronger intentions to complete planned behaviors and also demonstrate more effort and persistence when faced with obstacles or adversity [283,284]. In a psychotherapy setting, this might translate

into an increased ability and motivation to actively engage with the treatment, thereby improving treatment outcomes. The current finding implies that patients with lower levels of mastery at the outset of treatment might benefit from additional therapeutic strategies to enhance their mastery. Further research is needed to establish if and how mastery can be directly targeted, and whether such treatment enhancement strategies indeed lead to more favorable treatment outcomes.

Some limitations of the current study have to be discussed. First, like most studies into treatment moderators, the current study was a post-hoc analysis of RCT-data, which was not primarily designed to test for treatment moderators, and might therefore be underpowered to detect multiple modest interaction effects [285]. To truly advance evidence-based personalized treatment assignment in mental health care, moderator analyses should be conducted in larger study samples. This could also be achieved by combining participant level data from multiple studies using individual patient data (IPD) meta-analyses. Furthermore, studies specifically designed to confirm variables' moderating effects are essential for the development of decision tools for personalized treatment assignment, but these are lacking at the moment [286]. A second limitation is the absence of a non-active control condition. Because of this, we cannot ascertain whether the identified prognostic effects truly reflect a difference in *treatment response* between participants, or if individuals scoring higher on mastery and lower on depression severity would have also shown relatively larger symptom improvement without (active) treatment. Third, a substantial number of participants did not complete the posttreatment and/or follow-up measurements, which resulted in a considerable amount of missing data. However, we aimed to handle this problem optimally by imputing data using predictive mean matching, which is a well-established imputation method [237]. Fourth, generalizability of the results is limited by the fact that several exclusion criteria were used during participant recruitment for the RCT. Most importantly, people over 75 years and those with more severe psychological and/or physical conditions were excluded from participation. This reduces the heterogeneity and representability of the study sample. Last, we did not examine interactions between predictor variables, as we already conducted a large number of statistical tests. Therefore, we do not know if the prognostic effects we observed vary as a function of other predictor variables. Examining these more complicated relations between predictor variables is an important task for future studies.

Despite these limitations, the current study adds to the scientific literature, as it was the first to examine moderators and non-specific predictors of treatment response

to an ACT and CBT intervention in older adults with anxiety symptoms. We did not identify any moderators of short term or long term treatment response. These results indicate that, for now, the choice between blended ACT and face-to-face CBT for anxiety symptoms in later life can be guided by client- and therapist preferences and practical considerations. Regarding non-specific predictors, we found that higher levels of baseline depression symptom severity predicted poorer treatment response across the interventions on both the short and long term. Furthermore, higher baseline levels of mastery were predictive of more favorable short term treatment response in both the ACT and CBT intervention. Before these preliminary findings can be translated into clinical recommendations, they should be replicated and elaborated upon in future research, preferably in studies primarily designed to investigate prescriptive and non-specific predictors of treatment outcomes in anxious patients.