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Perfectionism as Possible Predictor for Treatment Success in Mindfulness-Based Cognitive Therapy and Metacognitive Training as Third-Wave Treatments for Obsessive-Compulsive Disorder

Nathalie Claus¹ · Franziska Miegel² · Lena Jelinek² · Sarah Landmann² · Steffen Moritz² · Anne Katrin Külz³ · Julian Rubel⁴ · Barbara Cludius^{1,2}

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Abstract

Background Identifying predictors of treatment outcome can guide treatment selection and optimize use of resources. In patients affected by obsessive-compulsive disorder (OCD), perfectionism has emerged as one possible predictor, with some data suggesting that cognitive-behavioral therapy outcomes are poorer for more perfectionistic patients. Findings so far are inconsistent, however, and research has yet to be extended to newer treatment approaches.

Methods We administered measures of concern over mistakes, clinical perfectionism, as well as OCD and depression symptom severity to a sample of OCD patients in out-patient group treatments (N=61), namely, metacognitive training (MCT-OCD) or mindfulness-based cognitive therapy (MBCT) for OCD. Hierarchical data over time was submitted to multi-level analysis.

Results Neither concern over mistakes nor clinical perfectionism at baseline predicted OCD symptoms across time points. However, concern over mistakes at baseline did significantly predict comorbid depressive symptoms. Furthermore, exploratory analysis revealed change in clinical perfectionism during treatment as a predictor of OCD symptoms at follow-up. **Conclusion** These results suggest that initial concern over mistakes may not prevent patients with OCD from benefitting from third-wave treatments. Change in clinical perfectionism may present a putative process of therapeutic change. Limitations and avenues for future research are discussed.

Keywords Obsessive-compulsive disorder \cdot Perfectionism \cdot Treatment outcome \cdot Mindfulness \cdot Metacognitive therapy \cdot Multi-level model

Nathalie Claus nathalie.claus@psy.lmu.de

- ¹ Division of Clinical Psychology and Psychological Treatment, Department of Psychology, Ludwig-Maximilians-University Munich, Leopoldstr. 13, 80802 Munich, Germany
- ² Department of Psychiatry and Psychotherapy, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
- ³ Department of Psychiatry and Psychotherapy, University Medical Center Freiburg, Freiburg, Germany
- ⁴ Department of Clinical Psychology and Psychotherapy, Justus-Liebig-University Gießen, Gießen, Germany

Introduction

Identifying predictors of treatment outcome is crucial in trying to improve treatment success (Olatunji et al., 2013). Taking into consideration that not all patients benefit from the same treatment in the same way (Blatt et al., 2010), determining prognostic indicators may guide treatment selection, particularly for patients at risk of poorer outcome, and thus optimize use of limited healthcare resources (Knopp et al., 2013). This seems especially relevant for a disorder such as obsessive-compulsive disorder (OCD). Even though evidence-based treatments such as Cognitive-Behavioral Therapy (CBT, with or without exposure) exist for OCD, drop-out rates are high (Hezel & Simpson, 2019; Ong et al., 2016) and maintenance of treatment effects is limited (Cabedo et al., 2018). Hence, finding ways to improve treatments and treatment selection for these patients is essential. Aside from commonly used outcome predictors such as demographic variables, symptom characteristics, and comorbidity (see Knopp et al. (2013) for a review), an increasing number of studies have been investigating the impact of cognitions relevant to OCD. Of particular interest are key beliefs such as intolerance of uncertainty or inflated responsibility, which have been identified as core cognitive domains of OCD (Obsessive Compulsive Cognitions Working Group, 1997).

One such core cognitive domain of OCD is perfectionism, illustrating its assumed key role in the etiology and maintenance of the disorder. In general, perfectionism can be understood as "the tendency to set high standards and employ overly critical self-evaluations" (Frost & Marten, 1990, p. 559). Research suggests perfectionism to be a multidimensional construct, with factor analyses consistently generating two factors: perfectionistic strivings and perfectionistic concerns (Stöber & Otto, 2006). Perfectionistic strivings encapsulate setting high standards in order to strive for perfection, whereas perfectionistic concerns refer to a concern over mistakes, doubts about one's actions and abilities, and self-criticism (Frost et al., 1990). Both dimensions of perfectionism have been linked to psychopathology, yet perfectionistic strivings have been found to be especially relevant for eating disorders, whereas perfectionistic concerns yield larger and more consistent effects for OCD, depression, and anxiety disorders (Limburg et al., 2017). In an attempt to better capture the clinically relevant aspect of perfectionism, the term "clinical perfectionism" was introduced. Conceptualized as an "overdependence of self-evaluation on the determined pursuit of personally demanding, self-imposed standards in at least one highly salient domain, despite adverse consequences" (Shafran et al., 2002, p. 778), it differs from the multidimensional construct mentioned above in that it puts central emphasis on the self-worth relying on achieving high standards. This includes biased performance evaluation, self-criticism if standards are not met, and reappraising standards as insufficiently demanding if they are met. In this article, we will be homing in on perfectionistic concerns and clinical perfectionism when discussing the impact of perfectionism on treatment success. Patients with OCD report significantly higher levels of perfectionism compared to nonclinical controls (Antony et al., 1998a, 1998b; Miegel et al., 2020b), both globally and on the dimension "concern over mistakes" in particular (Boisseau et al., 2013; Sassaroli et al., 2008). In a meta-analysis, perfectionistic concerns are significantly correlated with both a diagnosis of OCD and symptoms of OCD (Limburg et al., 2017).

Perfectionism has been shown to limit success of CBT treatments—in both individual and group settings—across mood (Blatt et al., 1995, 1998; Hawley et al., 2022), anxiety (Ashbaugh et al., 2007; Mitchell et al., 2013), and eating disorders (Bizeul et al., 2001; Sutandar-Pinnock et al., 2003).

Several hypotheses exist on how perfectionism reduces treatment success. It could be that patients with higher levels of perfectionism may struggle building a stable alliance with their therapist (Blatt & Zuroff, 2002; Zuroff et al., 2000), feel ambivalent about change and thus respond with more rigidity (Egan et al., 2011), or pay particularly selective attention to slow treatment gains (Shafran et al., 2002). These challenges may arise in OCD specifically, when cognitions typical of OCD, such as intolerance of uncertainty and inflated responsibility, interact disadvantageously with perfectionism. For instance, a patient with OCD may not only believe that executing an exercise in a perfect manner is possible (perfectionistic belief), but indeed necessary, because even minor mistakes could cause serious harm (inflated sense of responsibility) (Obsessive Compulsive Cognitions Working Group, 1997). This could lead to patients either trying too hard to be "the perfect patient" or avoiding engaging with exercises altogether (Pinto et al., 2011).

Indeed, the impeding effect of perfectionism on CBT treatment effects extends to OCD as well (Kyrios et al., 2015; Manos et al., 2010; Pinto et al., 2011). This has been demonstrated in both individual and group settings (Chik et al., 2008). However, results on the predictive qualities of perfectionism in the treatment of OCD have been inconsistent. Kyrios et al. (2015) investigated several predictors of outcome in individual CBT treatment for OCD over 16 weeks. They found that both baseline perfectionism and baseline to post-treatment change in perfectionism were significant predictors of clinician-rated OCD symptom severity at post-treatment, while controlling for baseline symptom severity. The perfectionism change score especially has repeatedly been shown to be a significant predictor of treatment outcome (Manos et al., 2010), preceding behavioral symptom reduction (Wilhelm et al., 2015). A recent study by Wheaton et al. (2020), for instance, examined the impact of perfectionism in an inpatient setting. While their analyses yielded no significant effect of baseline perfectionism on OCD outcome, changes in perfectionism did significantly account for clinician-rated OCD severity at post-treatment. Additionally, they could show that more perfectionistic patients stayed in treatment for a longer period. Other studies, however, showed no such effects. When investigating the effect of OCD-typical cognitions on outcome in 12-session individual CBT treatment, Woody et al. (2011) found that perfectionism consistently failed to predict clinicianrated obsessions at post-treatment. In an outpatient OCD treatment focused specifically on exposure (Su et al., 2016), perfectionism decreased significantly, but neither baseline perfectionism nor change in perfectionism were associated with clinician-rated OCD severity at post-treatment. Another study by Grøtte et al. (2015) sampled inpatients with OCD and found no significant change in perfectionism during intensive CBT treatment.

These inconsistencies may be partly due to different perfectionism measures being used. Most studies to date have measured perfectionism using the Obsessive Beliefs Questionnaire (OBQ; Obsessive Compulsive Cognitions Working Group, 2003, 2005), a measure developed to assess the above-mentioned core cognitions in OCD. The OBQ subscale "perfectionism/intolerance of uncertainty" compounds not only both perfectionistic strivings and perfectionistic concerns, but also the arguably separate facet of uncertainty tolerance. So far, only one study investigating the effect of perfectionism on OCD treatment outcome has used a specific perfectionism measure, namely the Frost Multidimensional Perfectionism Scale (FMPS; Frost et al., 1990). However, they found that only baseline scores on the subscale "doubts about actions" predicted clinician-rated OCD severity at post-treatment. This subscale was derived from a measure of OCD symptoms and has thus been argued to primarily reflect those symptoms, rather than perfectionism specifically (Shafran & Mansell, 2001). No study to date has investigated the role of clinical perfectionism in OCD treatment. In sum, perfectionism is assumed to be an important factor in OCD, yet its impact on treatment success requires further investigation. This is the case for both "classic" CBT treatment as well as younger treatment approaches which have been introduced in recent years.

These upcoming treatments include Mindfulness-Based Cognitive Therapy for OCD (MBCT; Külz et al., 2013, 2019) and Metacognitive Training for OCD (MCT-OCD; Jelinek et al., 2018; Miegel et al., 2020a, 2021). Both MBCT and MCT-OCD are treatments devised for the group setting and count among the so-called third-wave approaches, as in, they utilize CBT elements but specifically address experiential avoidance and foster distance from and acceptance of distress (Abramowitz et al., 2009). In MBCT the goal is for patients with OCD to accept rather than escape from their intrusive thoughts and difficult feelings, which may then reduce the need for compulsions (Fairfax, 2008; Hanstede et al., 2008). Small studies show significant reduction in OCD symptoms after MBCT treatment, compared to a waitlist-control (Key et al., 2017; Selchen et al., 2018). A recent randomized-controlled trial presents MBCT for OCD as superior to psychoeducation and equivalent to psychopharmacological treatment (Zhang et al., 2021). MCT-OCD, on the other hand, aims at helping patients to develop more cognitive flexibility (Rees & Anderson, 2013), in order to reduce the stress caused by disorder-specific cognitions (key beliefs, e.g., intolerance of uncertainty and perfectionism) and metacognitions (beliefs about one's thoughts, e.g., action fusion) (Moritz & Lysaker, 2018). This is achieved through CBT techniques (e.g., cognitive and behavioural experiments) as well as third-wave strategies (e.g., acceptance and observing internal experiences from a distance) (Moritz et al., 2016). In an uncontrolled pilot study with an inpatient sample, a face-to-face version of MCT-OCD

obtained a significant decline in OCD symptoms at posttreatment and a stable effect at 6-month follow-up (Miegel et al., 2020a). In a subsequent RCT, patients that participated at MCT-OCD decreased more compared to a care-as-usual control group in an outpatient sample with a medium effect size ($\eta_p^2 = 0.078$) (Miegel et al., 2021). Taken together, preliminary evidence shows both MBCT and MCT-OCD could be beneficial for patients with OCD.

The aim of the current study was to investigate perfectionism as a predictor of symptom outcome in third-wave group treatments (namely MBCT and MCT-OCD) for OCD. We were interested in examining the effect of both baseline perfectionism and the change in perfectionism on treatment outcome. To this end, we combined existing datasets from two randomized-controlled trials (Külz et al., 2019; Miegel et al., 2021), using baseline, post-treatment, and follow-up data. These data were submitted to multi-level analyses, since multi-level models allow for a flexible analysis of changes over time and let individuals vary in their baseline scores (random intercepts) and how they change (random slopes) (Curran et al., 2010). In addition to OCD symptoms, we assessed depressive symptoms as a secondary outcome. since OCD and depression are highly comorbid (Brakoulias et al., 2017; Rickelt et al., 2016) and perfectionistic concerns are closely related to depression (Smith et al., 2021). In extension of previous studies, we used pertinent questionnaire measures, namely the Frost Multidimensional Perfectionism Scale (FMPS; Frost et al., 1990) and the Clinical Perfectionism Questionnaire (Fairburn et al., 2003), to assess concern over mistakes and clinical perfectionism specifically. To the best of our knowledge, this makes the current study the first to examine clinical perfectionism as a predictor of OCD treatment outcome.

We hypothesized that greater perfectionism at baseline would predict greater OCD symptom severity at post treatment and follow-up (H1), controlling for symptom severity at baseline. We further expected that a greater decrease in perfectionism from baseline to post-treatment would predict lower OCD symptom severity at follow-up (H2), controlling for symptom severity at post-treatment. Both hypotheses were tested for one primary outcome, namely clinician-rated OCD symptom severity (H1 and H2), and two secondary outcomes, namely self-rated OCD and depressive symptom severity (H3 and H4). The study was preregistered before data analysis (https://osf.io/hjfst/).

Method

Study Design

Two independent sets of data were combined which have been analyzed and published previously. The group treatments which were originally investigated with these two data sets were reasonably similar in duration and setting. Both studies included perfectionism measures but did not analyze or report them. Further details regarding the original RCTs can be found elsewhere (Cludius et al., 2020; Külz et al., 2019; Miegel et al., 2021).

This current study employed a 2×5 mixed factorial design, with participants from two different treatment groups (MBCT or MCT-OCD) and assessments at five different measurement points (baseline, post-treatment, follow-ups at 3, 6, and 12 months). Analyses for the baseline and post-treatment assessments combined data from both groups (8 weeks apart). Follow-ups, however, were analyzed separately for the two treatment groups, since MCT-OCD participants were only tested at 3 months after treatment completion, whereas MBCT participants were only tested at 6 and 12 months.

Participants

A total of 61 patients with a primary diagnosis of OCD were included for main analyses. This sample combined those participants for whom perfectionism data was available, i.e., 22 participants from an MBCT group and 39 participants from an MCT-OCD group. All participants were assessed at baseline using the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) and the Yale-Brown Obsessive Compulsive Scale (Y-BOCS; Goodman et al., 1989a, 1989b) to confirm diagnosis. Inclusion criteria for both studies were a primary diagnosis of OCD (DSM-5); age ranging from 18 to 70 years; sufficient German language skills. Additionally, the RCT conducted by Külz et al. (2019) required patients to have completed at least 20 sessions of CBT within the last three years, since this study aimed to investigate group treatment for non-responders. Both studies excluded patients with a history of psychosis or mania, a severe neurological disorder, or current substance use disorder. Additionally, the RCT conducted by Külz et al. (2019) excluded patients with borderline personality disorder, Asperger syndrome, current severe depressive episode, acute suicidal tendencies, an IQ below 70, and patients who had started/modified psychotherapeutic or pharmacological treatment in the last 12 weeks. Enrollment and randomization took place at the university clinics in Freiburg and Hamburg, between September 2014 and December 2019. No additional compensation besides access to the respective group treatments was provided.

Demographic as well as clinical characteristics are shown in Table 1. Participants at baseline assessment showed moderate OCD symptoms (Y-BOCS) and moderate depressive symptoms (BDI-II). Compared to community samples (Egan et al., 2016), scores on both perfectionism measures were elevated.

Interventions

All participants received OCD-specific group treatment. Both treatments consisted of eight weekly group sessions in an outpatient setting.

MCT-OCD was based on the MCT for psychosis (Moritz & Woodward, 2007) and adapted specifically for OCD patients (Jelinek et al., 2018; Miegel et al., 2020a). Modules targeted dysfunctional cognitions and metacognitions considered relevant to OCD (Obsessive Compulsive Cognitions Working Group, 2003, 2005; Wells et al., 2017). The group was conducted in an open-group format, so that patients could join any time. Sessions lasted approximately 90 min each. Details can be found in Miegel et al. (2021).

MBCT was based on MBCT for recurrent depression (Segal et al., 2004) and adapted specifically for OCD patients (Külz et al., 2013). Modules conveyed the core principles of mindfulness (e.g., attention for the present moment, non-judgmental attitude) as well as elements of cognitive therapy, applied to OCD symptoms. Sessions lasted approximately 120 min each. Details can be found in Külz et al. (2019).

Measures

Frost Multidimensional Perfectionism Scale (FMPS)

The FMPS (Frost et al., 1990; German version: Stöber, 1995) served as the predictor of interest. It consists of 35 items, all of which are rated on a 5-point scale (strong disagreement to strong agreement), with its six subscales (concern over mistakes, doubts about actions, parental criticism, parental expectation, personal standards, order and organization) aiming to represent perfectionism as a multidimensional construct. The questionnaire is well established as a valid and reliable measure for perfectionism (Frost et al., 1990). Internal consistency in the current sample is excellent (Cronbach's $\alpha = 0.92$).

For analyses, the sum score of the 9-item subscale "concern over mistakes" was used in order to specifically assess this aspect of perfectionistic concerns, with subscale scores ranging between 9 and 45. Items measure excessive mistake avoidance and an all-or-nothing attitude towards success/failure. Among the six subscales, "concern over mistakes" has been shown to have one of the highest reliabilities and overall good psychometric properties (Frost et al., 1990).

For participants in the MBCT group, FMPS data is available only at baseline. For participants in the MCT-OCD group, FMPS data was collected at all assessments. Table 1Demographic andclinical characteristics ofsample at baseline

	Total sample $(N=61)$						
	$\overline{M(SD)}$ or %	MBCT $(n=22)$	MCT-OCD (<i>n</i> = 39) 38.1 (10.4)				
Age at enrollment in years ¹	38.3 (10.1)	38.8 (9.8)					
Range	19–63	23–59	19–63				
Gender (female) ¹	54.1	59.1	51.3				
Education in years ^{3,a}	16.5 (3.7)	14.7 (3.1)	17.6 (3.7)				
Current psychotherapy (yes) ¹	39.3	72.7	20.5				
Current psychopharmacological medication (yes) ⁶	65.6	68.2	64.1				
Change in medication during group treatment (yes) ⁵	16.4	23.8	14.7				
Mean duration of illness in years ⁴	17.6 (12.3)	10.0 (10.1)	21.2 (11.7)				
Number of comorbidities ¹							
None	16.4	22.7	12.8				
One	45.9	50.0	43.6				
Two or more	37.7	27.3	43.6				
Clinician-rated OCD symptoms (Y-BOCS) ¹	20.4 (5.9)	19.8 (6.0)	20.8 (5.8)				
Y-BOCS obsessions	9.9 (3.0)	9.7 (2.3)	9.9 (3.4)				
Y-BOCS compulsions	10.6 (3.8)	10.1 (4.0)	10.8 (3.7)				
Self-rated OCD symptoms (OCI-R) ³	27.1 (11.8)	25.8 (11.6)	27.8 (12.0)				
Depressive symptoms (BDI-II) ²	21.5 (12.6)	16.6 (10.1)	24.1 (13.1)				
Concern over mistakes (FMPS-CM) ¹	29.0 (8.9)	28.0 (9.1)	29.6 (8.9)				
Clinical perfectionism (CPQ) ⁷	29.0 (6.8)	NA	29.0 (6.8)				

Y-BOCS Yale-Brown Obsessive Compulsive Scale, *OCI-R*Obsessive-Compulsive Inventory, *BDI-II* Beck Depression Inventory-II, *FMPS-CM* Frost Multidimensional Perfectionism Scale, subscale "concern over mistakes", *CPQ* Clinical Perfectionism Questionnaire

^aTotal amount, including school, vocational training, university

n = 61 2n = 60 3n = 59 4n = 58 5n = 55 6n = 547n = 39

Clinical Perfectionism Questionnaire (CPQ)

In exploratory analyses, the CPQ (Fairburn et al., 2003; German version: Roth et al., 2021) was used as an alternative predictor. It was administered only to participants in the study by Miegel et al. (2021), i.e., the MCT-OCD group. The 12-item self-report measure was developed based on the model of clinical perfectionism (Shafran et al., 2002) and displays high internal reliability (Steele et al., 2011). Total scores range between 12 and 48, with two reverse scored items. Internal consistency in the current sample is good (Cronbach's α =0.82).

Yale-Brown Obsessive Compulsive Scale (Y-BOCS)

Primary outcome was OCD symptom severity as measured by the Y-BOCS (Goodman et al., 1989a, 1989b; German version: Büttner-Westphal & Hand, 1991). It is a half-structured interview which yields total scores ranging from 0 to 40, with separate sub-scores for obsessions and compulsions. Due to its good psychometric properties, including a high interrater reliability (r=.90; Jacobsen et al., 2003), it's considered the gold standard in assessing OCD severity (Goodman et al., 1989a, 1989b). Internal consistency in the current sample is adequate (Cronbach's α =0.74). Assessors were blinded to group allocation. For analyses, the total sum score was used.

Obsessive-Compulsive Inventory Revised (OCI-R)

As a secondary outcome, the OCI-R (Foa et al., 2002; German version: Gönner et al., 2008) was used. It is a widely used self-report measure of OCD symptom severity and shows good psychometric properties (Gönner et al., 2008). Its 18 items yield a score between 0 and 72. Internal consistency in the current sample is adequate (Cronbach's α =0.78).

Beck Depression Inventory-II (BDI-II)

The BDI-II (Beck et al., 1996; German version: Kühner et al., 2007) served as another secondary outcome. It is a well-established self-report measure of depressive symptom severity, with good psychometric properties (Kühner et al., 2007). Its 21 items yield a score between 0 and 63. Internal consistency in the current sample is excellent (Cronbach's $\alpha = 0.93$).

Statistical Analyses

All statistical analyses were performed using R (R Core Team, 2021), version 4.1.2.

Data Exclusion and Missing Data

All available data was used. Imputation of missing values was performed using the R packages *naniar* (Tierney et al., 2021) and *zoo* (Zeileis & Grothendieck, 2005), see Online Appendix (7.1) for details.

Multi-level Modelling

Due to the nested data structure, we used linear mixed models to test the predictive value of perfectionism for symptom severity. Each model had a two-level structure, with repeated assessments modelled as level 1 and participants as level 2. Models were estimated using maximum-likelihood estimation and included random subject-level intercepts to account for nested observations. Starting from a basic model including only the intercept, complexity was added progressively in terms of fixed and random effects. Additionally, random slopes were added for each predictor to allow them to vary across participants. The error covariance matrix was modelled as autoregressive to account for repeated measures. At each step, a Likelihood Ratio Test with a level of significance of $\alpha = 0.05$ was used to compare model-fit and aid decisions about including specific terms. Thus, for each hypothesis, the model with the best fit was used to extract model parameters.

First, to determine the level of non-independence in the data (repeated measures nested in patients), we estimated the basic model for each hypothesis and calculated the intraclass correlation coefficient (ICC) at patient level. In order to test the effect of perfectionism on changes in OCD after treatment (H1), we estimated a model with the OCD symptoms (Y-BOCS total score) as the dependent variable and the following predictors: concern over mistakes (FMPS-CM score, at baseline), OCD symptom severity (OCI-R total score, at baseline), time (weeks since baseline), and an interaction between concern over mistakes and time. We used the same model to estimate the changes on the

secondary outcomes, namely, self-reported OCD (OCI-R) and depressive symptoms (BDI-II) (H3). To investigate the effect of *change* in perfectionism on changes in OCD after treatment (H2), we estimated a model with the OCD symptoms (Y-BOCS total score) at follow-up as the dependent variable, and change in concern over mistakes (FMPS-CM score, from baseline to post-treatment) and OCD symptom severity (OCI-R total score, at post-treatment) as predictors. Again, we used the same model to estimate the changes on the secondary outcomes, self-reported OCD (OCI-R) and depressive symptoms (BDI-II) (H4). Change in concern over mistakes was computed using residuals of a linear regression: PerfectionismPost_i ~ b₀ + b₁ * PerfectionismBaseline_i. Assumed equations of multi-level models can be found in the Online Appendix (see 7.2).

When controlling for earlier symptom severity, different symptom scores than the outcome scores were used in order to circumvent merely calculating a measure's correlation with itself. Thus, when predicting symptom severity as measured by the Y-BOCS, the OCI-R score was used as the control score; when predicting symptom severity as measured by the OCI-R or BDI-II, the Y-BOCS score was used.

Models were built using the R package *nlme* (Pinheiro et al., 2022). Assumptions of multi-level modelling (linearity, homogeneity of variances, normal distribution of residuals) were checked by visual inspection.

Logistic Regression

To test the effect of concern over mistakes on clinically significant change after treatment, a logistic regression was calculated. It used concern over mistakes (FMPS-CM score) at baseline to predict recovery (recovered/unchanged as defined based on Y-BOCS scores) at post-treatment.¹ See Online Appendix for the corresponding model Eq. (7.2). Similar to the original RCTs, a binary measure for clinically significant change was computed based on a two-fold criterion: patients with a Y-BOCS total score at or below 14 and a decrease of at least 35% from baseline were classified as recovered; patients who did not fulfil this criterion were classified as unchanged.

¹ Preregistration included a second logistic regression which predicted recovery at follow-up, using perfectionism at post-treatment and time since post-treatment as predictors. This calculation was dropped because it was not possible with the available data. Posttreatment perfectionism data existed only for MCT-OCD participants, i.e., participants with follow-up at 3 months only. Thus, time since post-treatment held no meaning as a predictor.

Centering

The predictors concern over mistakes and symptom scores were grand-mean centered, using the respective mean at baseline. Time was transformed to measure weeks since the baseline assessment (i.e., baseline = 0, post-treatment = 8, follow-up at 3 months = 20, follow-up at 6 months = 32, follow-up at 12 months = 56).

Exploratory Analyses

Hypotheses 1 and 2, i.e., the effect of concern over mistakes and of change in concern over mistakes (FMPS-CM) on OCD after treatment, were tested using clinical perfectionism as the independent variable instead (as measured by the CPQ). Additionally, hypotheses 1 and 3, i.e., the effect of concern over mistakes (FMPS-CM) on OCD and depressive symptoms after treatment, were tested using group allocation as an additional predictor. These analyses followed the same analysis plan as described above.

Results

Multi-level Modelling

Results of all final models are presented in Table 2, with alpha adjusted to account for multiple comparisons (four separate models per time point; $\alpha = 0.05 / 4 = 0.0125$). Bivariate correlations between all variables are documented in the Online Appendix (see 7.3). The Online Appendix also holds statistical values used for data-driven model selection (see 7.4) and equations of the final models (see 7.5) after stepwise inclusion of predictors, interaction terms, and random slopes.

Effect of Baseline Perfectionism on OCD Symptom Severity (Hypothesis 1)

In the basic model, patients explained a large proportion of the variance in outcome, ICC = 0.62. After contrasting models, the model with the best fit included the predictors concern over mistakes (FMPS-CM) at baseline, symptoms (OCI-R) at baseline, and time, but did not include the interaction between concern over mistakes and time as a predictor. Further, the model with a random slope for time but not for baseline concern over mistakes and baseline symptoms fit the data best. By excluding the interaction term between concern over mistakes and time, we assume concern over mistakes did not have an effect on change of symptoms across time. By excluding the random slopes for The final model showed that baseline concern over mistakes had no significant influence on OCD symptoms (Y-BOCS total score) across time points. Only OCD symptoms (OCI-R score) at baseline had significant impact on OCD symptoms (Y-BOCS total score); that is, higher OCD symptoms (OCI-R score) at baseline were associated with higher OCD symptoms (Y-BOCS total score) across time points. While intercepts varied considerably between individuals, slopes varied only marginally, with a negative random slope-intercept correlation ($\sigma^2 = 12.97$, $\tau_{00} = 16.79$, $\tau_{11} = 0.02$, $\rho_{01} = -0.13$). Fixed effects explained 19% of variance, with the entire model (including random effects) explaining 70%. This model used data from 59 participants (2 participants had incomplete OCI-R data), with ICC = 0.63.

Effect of Change in Perfectionism on OCD Symptom Severity (Hypothesis 2)

In the basic model, patients explained a large proportion of the variance in outcome, ICC = 0.88. After contrasting models, the model with the best fit included the predictors change in concern over mistakes from pre- to post-treatment (FMPS-CM score) and OCD symptom severity at post-treatment (OCI-R score), with no random slopes. By excluding the random slopes for change in concern over mistakes and symptom severity at post-treatment, we assume the effects of those predictors are invariant across participants.

The final model showed that neither pre-post change in concern over mistakes (FMPS-CM) nor OCD symptom severity (OCI-R) at post-treatment had a significant influence on OCD symptoms (Y-BOCS total score) at follow-up. Fixed effects explained 68% of variance ($\sigma^2 = 2.34$, $\tau_{00} = 16.65$, ICC = 0.88). This model used data from 29 participants (complete FMPS data at baseline and post-treatment as well as Y-BOCS data at follow-up). Since visual inspection revealed violated assumptions of variance homogeneity and normal distribution of residuals, a multi-level model may not have been the ideal fit for the data.

Effect of Baseline Perfectionism on Secondary Outcomes (Hypothesis 3)

Using self-reported OCD symptoms (OCI-R) as outcome, patients explained a large proportion of the variance in outcome in the basic model, ICC = 0.69. After contrasting models, the model with the best fit included the predictors concern over mistakes (FMPS-CM) at baseline, OCD symptoms (Y-BOCS) at baseline, and time, but did not include the interaction between concern over mistakes and time as

Table 2 Results of the final multi-level models

	п	β^{a}	95% CI	SE	t	р
H1: Dependent variable: OCD symptom severity (Y-BOCS)	59					
Intercept		19.97	18.63 to 21.31	0.68	29.19	< 0.001
Concern over mistakes at baseline (FMPS-CM)		- 0.03	- 0.19 to 0.13	0.08	- 0.32	0.75
OCD symptoms at baseline (OCI-R)		0.23	0.11 to 0.35	0.06	3.86	< 0.001
Time		- 0.07	- 013 to - 0.01	0.03	- 2.23	0.03
H2: Dependent variable: OCD symptom severity (Y-BOCS) at follow-up	29					
Intercept		18.37	16.41 to 20.33	1.01	18.22	< 0.001
Change in concern over mistakes (FMPS-CM)		0.18	- 0.11 to 0.46	0.15	1.18	0.25
OCD symptoms at post-treatment (OCI-R)		0.14	- 0.02 to 0.30	0.08	1.67	0.11
H3: Dependent variable: OCD symptom severity (OCI-R)	61					
Intercept		- 19.32	- 27.81 to - 10.83	4.34	- 4.46	< 0.001
Concern over mistakes at baseline (FMPS-CM)		0.23	- 0.04 to 0.49	0.13	1.71	0.09
OCD symptoms at baseline (Y-BOCS)		0.89	0.49 to 1.29	0.20	4.38	< 0.001
Time		- 0.07	- 0.15 to 0.02	0.04	- 1.50	0.14
H3: Dependent variable: depressive symptom severity (BDI-II)	61					
Intercept		- 9.85	- 16.43 to - 3.28	3.36	- 2.94	< 0.01
Concern over mistakes at baseline (FMPS-CM)		0.56	0.36 to 0.76	0.10	5.50	< 0.001
OCD symptoms at baseline (Y-BOCS)		0.43	0.12 to 0.73	0.15	2.75	< 0.01
Time		- 0.18	-0.28 to -0.08	0.05	- 3.61	< 0.001
H4: Dependent variable: OCD symptom severity (OCI-R) at follow-up	29					
Intercept		- 20.85	- 31.21 to - 10.49	5.32	- 3.92	< 0.001
Change in concern over mistakes (FMPS-CM)		0.37	- 0.26 to 1.00	0.32	1.15	0.26
OCD symptoms at post-treatment (Y-BOCS)		0.91	0.32 to 1.49	0.30	3.03	< 0.01
H4: Dependent variable: depressive symptom severity (BDI-II) at follow-up	29					
Intercept		- 16.45	- 23.19 to - 9.71	3.46	- 4.75	< 0.001
Change in concern over mistakes (FMPS-CM)		0.17	- 0.23 to 0.58	0.21	0.83	0.41
OCD symptoms at post-treatment (Y-BOCS)		0.52	0.14 to 0.90	0.20	2.67	0.01
Exploratory: Dependent variable: OCD symptom severity (Y-BOCS)	39					
Intercept		19.80	18.12 to 21.48	0.86	23.05	< 0.001
Clinical perfectionism at baseline (CPQ)		0.03	- 0.24 to 0.29	0.13	0.20	0.84
OCD symptoms at baseline (OCI-R)		0.23	0.08 to 0.38	0.08	3.00	< 0.01
Time			- 0.16 to 0.00	0.04	- 1.86	
Exploratory: Dependent variable: OCD symptom severity (Y-BOCS) at follow-up	29					
Intercept		17.62	15.96 to 19.28	0.84	21.03	< 0.001
Change in clinical perfectionism (CPQ)			0.13 to 0.88	0.19		0.01

Bold *p* values denote significance below $\alpha = 0.0125$ (Bonferroni-corrected for multiple comparisons)

Y-BOCS Yale-Brown Obsessive Compulsive Scale, *FMPS_CM* Frost Multidimensional Perfectionism Scale, "concern over mistakes" subscale, *OCI-R* Obsessive-Compulsive Inventory Revised, *BDI-II* Beck Depression Inventory II, *CPQ* Clinical Perfectionism Questionnaire

 $^{a}\beta$ (=fixed effect) denotes magnitude of change in the outcome variable as the predictor increases by one point relative to grand-mean at baseline

a predictor. Further, adding random slopes for any of the predictors did not improve model fit. By excluding the interaction term, we assume concern over mistakes did not have an effect on change of symptoms across time. By excluding the random slopes for all predictors, we assume the effects of those predictors are invariant across participants.

The final OCI-R model showed that baseline concern over mistakes (FMPS-CM) had no significant influence on OCD symptoms (OCI-R), nor did time. Only OCD symptoms (Y-BOCS total score) at baseline had significant impact on OCD symptoms (OCI-R); that is, more severe OCD symptoms (Y-BOCS total score) at baseline were associated with stronger OCD symptoms (OCI-R) across time points. Fixed effects explained 26% of variance ($\sigma^2 = 94.36$, $\tau_{00} = 9.72$). Scores of individual participants were not strongly correlated (ICC=0.09). This model used data from all 61 participants.

Using self-reported depressive symptoms (BDI-II) as outcome, patients explained a large proportion of the variance in outcome in the basic model, ICC = 0.59. After contrasting models, the model with the best fit included the predictors concern over mistakes (FMPS-CM) at baseline, OCD symptoms (Y-BOCS) at baseline, and time, but did not include the interaction between concern over mistakes and time as a predictor. Further, the model with a random slope for time but not for baseline concern over mistakes and baseline OCD symptoms fit the data best. By excluding the interaction term between concern over mistakes and time, we assume concern over mistakes did not have an effect on change of symptoms across time. By excluding the random slopes for baseline concern over mistakes and baseline OCD symptoms, we assume the effects of those predictors are invariant across participants.

The final BDI-II model showed that baseline concern over mistakes had a significant influence on depressive symptoms (BDI-II); i.e., stronger concern over mistakes (FMPS-CM) at baseline were associated with stronger comorbid depressive symptoms (BDI-II) across time points. OCD symptoms (Y-BOCS total score) at baseline and time since baseline also had a significant impact on depressive symptoms (BDI-II); that is, more severe OCD symptoms (Y-BOCS total score) at baseline were associated with more severe depressive symptoms (BDI-II) across time points, and every additional week since baseline reduced depressive symptoms (BDI-II). While intercepts varied considerably between individuals, slopes varied only marginally, with a strong negative random slope-intercept correlation ($\sigma^2 = 53.76$, $\tau_{00} = 35.32, \tau_{11} = 0.04, \rho_{01} = -0.87$). Fixed effects explained 37% of variance, with the entire model (including random effects) explaining 43%. This model used data from all 61 participants, with a low ICC = 0.09.

Effect of Change in Perfectionism on Secondary Outcomes (Hypothesis 4)

Using self-rated OCD symptoms (OCI-R) as outcome, patients explained a large proportion of variance in outcome in the basic model, ICC=0.88. After contrasting models, the model with the best fit included the predictors change in concern over mistakes from pre- to post-treatment (FMPS-CM) and OCD symptom severity at post-treatment (Y-BOCS), with no random slopes. By excluding the random slopes, we assume the effects of both predictors are invariant across participants.

The final OCI-R model showed pre-post change in concern over mistakes had no significant influence on OCD symptom severity (OCI-R) at follow-up. Only clinician-rated OCD symptoms (Y-BOCS total score) at post-treatment had significant impact on OCD symptoms (OCI-R) at follow-up; that is, more severe OCD symptoms (Y-BOCS total score) at post-treatment were associated with more severe OCD symptoms (OCI-R) at follow-up. Fixed effects explained 80% of variance ($\sigma^2 = 12.12$, $\tau_{00} = 86.21$, ICC = 0.88). This model used data from 29 participants (complete FMPS data at baseline and post-treatment as well as Y-BOCS data at follow-up). Since visual inspection revealed violated assumptions of variance homogeneity and normal distribution of residuals, a multi-level model may not have been the ideal fit for the data.

Using self-rated depressive symptoms (BDI-II) as outcome, patients explained a large proportion of variance in outcome in the basic model, ICC = 0.88. After contrasting models, the model with the best fit included the predictors change in concern over mistakes from pre- to post treatment (FMPS-CM) and OCD symptom severity at post-treatment (Y-BOCS), with no random slopes. By excluding the random slopes, we assume the effects of both predictors are invariant across participants.

The final BDI-II model showed pre-post change in concern over mistakes (FMPS-CM) had no significant influence on comorbid depressive symptom severity (BDI-II) at follow-up. Only OCD symptoms (Y-BOCS total score) at post-treatment had significant impact on depressive symptoms (BDI-II) at follow-up; that is, more severe OCD symptoms (Y-BOCS total score) at post-treatment were associated with more severe comorbid depressive symptoms (BDI-II) at follow-up. Fixed effects explained 75% of variance (σ^2 = 5.14, τ_{00} = 36.52, ICC = 0.88). This model used data from 29 participants (complete FMPS data at baseline and post-treatment as well as BDI-II data at follow-up). Since visual inspection revealed violated assumptions of variance homogeneity and normal distribution of residuals, a multilevel model may not have been the ideal fit for the data.

Logistic Regression

To investigate the effect of baseline concern over mistakes on pre- to post-treatment change in OCD symptom severity (H1) in regard to clinically significant change, we used logistic regression analysis. Baseline concern over mistakes had no significant effect on recovery at post-treatment (OR0.94, 95% CI [0.85, 1.03], p = .23). With Tjur's R² = 0.025, the model had low discriminating power. This model used data from 54 participants (7 participants had incomplete Y-BOCS data).

Exploratory Analyses

We investigated the effect of baseline perfectionism (H1) as well as change in perfectionism (H2) on OCD symptom severity (Y-BOCS total score) using the CPQ as a measure for clinical perfectionism (see Table 2). CPQ data (n=39) was available only for participants of the study by Miegel

et al. (2021). The same multi-level model analyses as described above, with clinical perfectionism (CPQ) as the dependent variable, showed no significant impact of baseline clinical perfectionism on OCD symptom severity (Y-BOCS). However, change in clinical perfectionism (CPQ) did show a significant impact on OCD symptom severity (Y-BOCS) at follow-up; that is, with every point decrease in clinical perfectionism (CPQ) from baseline to post-treatment, OCD symptoms (Y-BOCS total score) at follow-up decreased. After data-driven model fitting, this model contained only change in clinical perfectionism (CPQ) as a fixed effect, with random intercept and no random slope, and used data from 29 participants (complete CPQ data at baseline and post-treatment as well as Y-BOCS data at follow-up). Fixed effects explained 68% of variance ($\sigma^2 = 2.32$, $\tau_{00} = 16.52$, ICC = 0.88). Crucially, visual inspection revealed assumptions of variance homogeneity and normal distribution of residuals to be violated.

Further, we added group allocation as an additional predictor to the final models determined by main analyses, in order to explore possible differences between treatment groups in the effect of baseline perfectionism on OCD and depressive symptoms (H1 and H3). Group allocation did not significantly predict any of the symptom outcomes (group as predictor for Y-BOCS: p = .70, for OCI-R: p = .71, for BDI-II: p = .19).

Discussion

The present study investigated the impact of perfectionism, particularly concern over mistakes and clinical perfectionism, on treatment outcome in MBCT for OCD and MCT-OCD. To our knowledge, this is the first study to examine whether perfectionism predicts treatment outcome in thirdwave treatments for OCD. Additionally, this is the first study to explore clinical perfectionism as an impending factor for OCD treatment success.

Neither concern over mistakes (FMPS-CM) nor clinical perfectionism (CPQ) at baseline were significantly related to OCD treatment outcome (Y-BOCS or OCI-R). This is in contrast to some prior reports showing an association between greater baseline perfectionism and poorer OCD outcome (Chik et al., 2008; Kyrios et al., 2015; Manos et al., 2010; Pinto et al., 2011). However, there have been previous studies which also failed to find such a predictive effect in OCD treatment (Su et al., 2016; Wheaton et al., 2020; Woody et al., 2011). Part of the reason behind this could simply be that the predictive effect of concern over mistakes is relatively small and not detectable within a small sample such as ours. Indeed, in previous studies perfectionism accounted for only a small proportion of change in OCD symptoms. Another reason for these inconsistencies,

as outlined above, could be the use of the OBQ as a perfectionism measure (Kyrios et al., 2015; Manos et al., 2010), which combines the perfectionism subscale with a subscale on "intolerance of uncertainty". Interestingly, the one study which also used the FMPS (Chik et al., 2008) found an effect only for the subscale "doubts about actions", the use of which we have criticized above, but no effect for "concern over mistakes" (FMPS-CM). Our replication of this null effect seems to suggest that concern over mistakes may play less of a role in OCD treatment than previously assumed. Future research may need to assess concern over mistakes and intolerance of uncertainty with separate distinct measures (e.g., using FMPS-CM and the Intolerance of Uncertainty Scale (Buhr & Dugas, 2002)), ideally in larger patient samples, in order to parse effects observed using the OBQ. Another reason for our null results could be related to the type of treatment provided. Considering the scarcity of extant literature on perfectionism in group treatments for OCD, it may be that perfectionism has less of an impact in the current group setting than it does in previous studies which examined individual treatment. There is, however, sufficient evidence for an impeding effect of perfectionism in group treatments for mood and anxiety disorders (Ashbaugh et al., 2007; Hawley et al., 2022; Mitchell et al., 2013), and one study showing this effect for OCD (Chik et al., 2008). Thus, rather than the manner of treatment presentation, the content of third-wave approaches may account for our null results. Previous studies investigated exclusively "classic" CBT treatments for OCD. Whereas both MCT-OCD and MBCT draw on CBT techniques, they additionally promote a non-judgmental and accepting attitude, which may in fact attenuate the disadvantageous effect of perfectionism. Through being encouraged to view mistakes as an opportunity to learn rather than a reason to criticize themselves (Leeuwerik et al., 2020), patients may have been able to be more open towards exercises and their outcomes. This explanation would be in line with at least one of the two perfectionism measures (CPQ) changing significantly through treatment in our sample. Replication by future studies on third-wave treatments for OCD, such as Acceptance Commitment Therapy (Twohig et al., 2014), will need to ascertain this finding. Additionally, further research is needed on potential differences between individual and group settings, both for CBT and third-wave treatments.

Contrary to our expectations, only reductions in clinical perfectionism (CPQ) predicted recovery from OCD symptoms (Y-BOCS), but not reduction in concern over mistakes (FMPS-CM). Change in clinical perfectionism preceded symptom change. Several previous studies have found an effect of change in perfectionism on OCD treatment outcome (Kyrios et al., 2015; Manos et al., 2010; Wheaton et al., 2020; Wilhelm et al., 2015). However, the one study which also used the FMPS to measure concern over mistakes found only an effect of baseline perfectionism, but not of change in perfectionism on OCD treatment outcome (Chik et al., 2008). Since the CPQ, in contrast to the FMPS, was created specifically with the purpose of measuring change within treatment (Fairburn et al., 2003), it is perhaps not surprising that it would turn out to be the more change-sensitive measure. Moreover, the CPQ measures both concern over mistakes and adherence to unrealistic expectations that interfere with one's functioning (Shafran & Mansell, 2001). This may contribute to the CPQ measuring the aspects of perfectionism most relevant to a clinical sample and experiences throughout treatment. There are in fact CBT treatments that target clinical perfectionism which result in reductions not only of clinical perfectionism, but also psychopathology such as anxiety, depression, and eating disorders (see Galloway et al., 2022 for a meta-analysis), presenting change in clinical perfectionism as a promising process of therapeutic change. In this current study, CPQ data was available only for the MCT-OCD group of the sample, a treatment that dedicates a whole module to acceptance in the face of "imperfections". Our findings indicate that MCT-OCD is effective in reducing clinical perfectionism. While we could not investigate this effect for the MBCT group of the sample, a recent study with OCD patients suggests MBCT to be effective in reducing perfectionism as well (Mathur et al., 2021). It is important to note, however, that our analyses using the CPQ were merely exploratory. The model which showed the best fit included change in clinical perfectionism as the only predictor, with OCD symptoms at post-treatment having been eliminated through data-driven model fitting. This means that the effect of change in clinical perfectionism (CPQ) was not controlled for post-treatment symptom severity, whereas the model investigating change in concern over mistakes (FMPS-CM) was. This may offer another explanation as to why only change in clinical perfectionism yielded a predictive effect. Since the current study was the first to look at clinical perfectionism as a predictor of OCD outcome, this finding will need to be replicated.

Whereas concern over mistakes (FMPS-CM) did not predict OCD symptoms in our sample, it did indeed predict depressive symptoms (BDI-II) across time points. This fits in with extant literature for both healthy and patient samples (see Smith et al., 2021 for a recent meta-analysis). Overall, meta-analytic effect sizes regarding the relationship between concern over mistakes and symptom severity are larger for depression than OCD (Limburg et al., 2017), which may render effects more easily detectible in depression compared to OCD. Aside from effect sizes, another explanation may lie in treatment specificity. It seems the eight-week treatment programs investigated in this current study sufficed to treat an adverse association between perfectionism and the core OCD symptoms targeted by group modules. They may not have been enough, however, to curb the impeding effect of perfectionism in the recovery from comorbid symptoms on top of that, be it because treatments were too specific to OCD or not intense enough for more severely ill patients (i.e., those suffering from comorbid disorders). Interestingly, even though MCT is assumed to target beliefs relevant across disorders, previous MCT studies have found no significant reduction of comorbid depression symptoms in patients with OCD (Miegel et al., 2021; Rees & van Koesveld, 2008). It is possible that this is due to a more obstructive effect of perfectionism in regard to comorbid symptoms. Finally, a purely methodological explanation for the discrepancy between our findings for OCD and depressive outcomes lies in our control measures. Since no second depression measure was available, we controlled for baseline OCD symptom severity when predicting both the OCD measures and the depression measure. Compared to an OCD outcome controlled for OCD symptoms, a depression outcome controlled for OCD symptoms should leave more variance in the data.

Strengths and Limitations

Results of the current study contribute new insights into perfectionism in OCD treatment, extending the literature to third-wave treatment approaches. Data was collected from a clinical sample with confirmed OCD diagnosis in a standardized RCT setting. We used two different and specific perfectionism measures, to pinpoint concern over mistakes and clinical perfectionism respectively. To our knowledge, it is the first study to investigate clinical perfectionism as a predictor of outcome in the treatment of OCD.

However, some limitations should be considered when interpreting these results. Firstly, generalizability is limited due to a highly educated (47.5% with a university degree) and relatively small sample. This precludes assumptions that the observed effects should be universal. Since we combined pre-existing data of two separate studies to increase power, no a priori power analysis was conducted. We decided against a post-hoc analysis since "observed power" calculations are known to yield misleading results (Hoenig & Heisey, 2001; Zhang et al., 2019), meaning we cannot judge the statistical power of the presented analyses. Power issues might have impacted results for the effect of change in perfectionism on follow-up outcomes in particular, since the required data was available only for a small subsample (n=29). Similarly, all analyses regarding clinical perfectionism were restricted to the MCT-OCD subsample, are only exploratory, and should thus be interpreted with caution. Finally, we combined two treatments which, despite their similarities, differ in certain ways (e.g., open vs. closed groups; 90- vs. 120-min sessions; including specific interventions like mindfulness exercises vs. association splitting). Our analyses could not differentiate between effects in MBCT and MCT-OCD groups, and thus further studies are required to test these effects separately.

Clinical Implications

We would encourage clinicians to assess perfectionism before treatment of OCD. Given that we found no evidence for an impeding effect of baseline perfectionism in thirdwave treatments for OCD, it would make sense to offer these treatments to those patients with high perfectionism scores. The accepting and non-judgmental approach inherent to treatments such as MBCT and MCT-OCD may increase the chances for particularly perfectionistic patients to benefit from therapy. The importance of considering a patient's perfectionism holds especially true for patients with comorbid depression, who constitute a large portion of approximately 60% of OCD patients (Brakoulias et al., 2017; Rickelt et al., 2016). Lastly, we suggest clinical perfectionism in particular be addressed, since it appears a promising target for symptom change in MCT-OCD. To monitor progress over time, the CPO should be the preferred perfectionism measure, as it appears more change-sensitive and clinically relevant.

Conclusion

Taken together, our results highlight the need for further research in order to isolate the role of perfectionism in OCD treatment. Pre-treatment levels of perfectionism may not have such a strong obstructive effect on outcome in third-wave treatments (e.g., MBCT and MCT-OCD) as they do in classic CBT. In this context, effects on comorbid disorders such as depression, as well as change in clinical perfectionism as a possible mechanism of symptom change, will require particular attention.

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Data Availability Data and analysis code have been uploaded to OSF (https://osf.io/hjfst/).

Declarations

Conflict of Interest Nathalie Claus, Franziska Miegel, Lena Jelinek, Sarah Landmann, Steffen Moritz, Anne Katrin Külz, Julian Rubel, Barbara Cludius declare that they have no conflict of interest.

Ethical Approval All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the 1964 Helsinki Declaration and its later amendments.

Animal Rights No animal studies were carried out by the authors for this article.

Informed Consent Informed consent was obtained from all participants.

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