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Predictors of treatment response in obsessive-compulsive disorder

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Predictors of treatment response in obsessive-compulsive disorder

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Abstract

Obsessive-compulsive disorder (OCD) is a potentially impairing mental disorder. Even though there are effective treatment approaches, the identification of predictors of treatment response can help optimize therapy protocols and apply them correctly to each individual case.

This paper reviews studies on predictors of treatment response to psychological and pharmacological therapies for OCD. Studies were identified through a systematic review using the MEDLINE and SCOPUS databases, by searching bibliographies and contacting key authors. Search terms included “obsessive-compulsive disorder”, “treatment” and “predictors”.

Forty-one trials reporting association between baseline variables and OCD treatment outcome were included. The following factors showed were analyzed for potential association with treatment outcome: age at assessment, gender, marital status, quality of life, age at onset, OCD severity at onset, family history, length of illness, insight, OCD symptom dimensions, comorbid Axis I and II disorders, early response to therapy, previous treatment history, therapeutic alliance and treatment adherence. Results were inconsistent across most variables in the studied sample, so future implications for research and clinical applicability are still very limited.

Keywords

Obsessive-compulsive disorder; predictor; treatment; outcome; cognitive-behavioral therapy; selective serotonin reuptake inhibitors

Introduction

Obsessive-compulsive disorder (OCD) is a brain disorder, characterized by recurring obsessions and/or compulsions aimed at reducing the associated anxiety and fear, resulting in significant social and functional impairment. Obsessions are defined as recurrent and persistent thoughts, urges or images that are experienced as unwanted and intrusive, causing anxiety and distress, despite the attempts to ignore, neutralize or suppress such thoughts. Compulsions are repetitive behaviors or mental acts performed in response to an obsession, with the intent to reduce or neutralize a distressing event or situation, usually in an excessive or unrealistic manner (American Psychiatric Association, 2013).

OCD has a lifetime prevalence of approximately 1,6% across all age groups and of 0,1-4% in children (Heyman, 2001; Kessler et al., 2005). Onset is usually gradual and chronic, with stable symptoms over time, and it is more common in late adolescence and early adulthood, with a median age of onset of 19 years (Kessler et al., 2005; Mataix-Cols et al., 2002). Comorbid psychological illness is common, especially mood and anxiety disorders. Some studies suggest that up to 25% of patients with OCD have a current or past history of some form of tic disorder (Abramowitz, Taylor, & McKay, 2009; American Psychiatric Association, 2013; Torres et al., 2006).

Treatment of OCD is effective and can be divided in pharmacological and psychological approaches (Abramowitz, 1997). Cognitive-behavioral therapy (CBT), including exposure and response prevention (E/RP) is considered the first-line treatment for children and adults (Health & Excellence, 2005; March et al., 2004). Current evidence suggests that antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs) and clomipramine are also effective in the treatment of OCD in children and adults (Health & Excellence, 2005). Psychological and pharmacological therapies can also be used in combination, in case of severe OCD or treatment-resistant OCD.

Several treatment outcome studies suggest that certain factors may predict poorer or better treatment response and efficacy. The identification of such factors may allow the identification of patients at risk of a poorer prognosis, and an individualized treatment approach, resulting in better outcomes. Several potential predictors have already been identified, but there is limited consensus on which factors really predict a different outcome, limiting their appliance in clinical practice. Keeley et al. (2008) reviewed predictors of treatment response in open and controlled trials of cognitive-behavioral therapy for obsessive-compulsive disorder in adults and children, reporting several variables consistently associated with outcome, including: strength of the therapeutic relationship, patients' family environment, OCD severity, symptom subtypes, comorbid severe depression and comorbid personality disorder (Mary L Keeley, Storch, Merlo, & Geffken, 2008). Knopp et al. (2013) systematically reviewed the predictors of treatment response to psychological therapies for adults with OCD, finding associations between worse treatment outcome and hoarding pathology, increased anxiety, OCD severity, symptom subtypes, unemployment and being single/not married (Knopp, Knowles, Bee, Lovell, & Bower, 2013). Both reviews acknowledge the lack of consensus of their findings, as well as a significant variation in the measurement tools and methods across included trials. Given these limitations, the present review serves to strengthen currently existing evidence on predictors of treatment response to psychological and pharmacological therapies for OCD.

Methods

To identify predictors of OCD treatment response, we searched the literature of published open and controlled OCD treatment outcome trials of pharmacotherapy, CBT or combined therapy in adult or pediatric samples. Articles were identified by a systematic electronic literature search on the MEDLINE and SCOPUS databases using the keywords "obsessive-compulsive disorder", "treatment" and "predictors". Reference sections of the studies that emerged in the original search were scanned for additional

relevant articles and some authors were contacted for full versions of relevant articles unobtainable in the original search. Inclusion criteria permitted English language clinical trials, with a full-text published at the time of the search. Only studies that reported associations between baseline variables and treatment outcome on patients with a confirmed diagnosis of OCD were included. Follow-up studies that did not involve a standardized therapeutic intervention were excluded.

All potential predictors of treatment outcome reported in the included articles were noted. Potential predictors of outcome were organized in 4 categories: demographic characteristics, clinical aspects, comorbidities and treatment specific variables. Demographic characteristics include age at assessment, gender, marital status and quality of life. Clinical aspects include age at onset, OCD severity at onset, family history, length of illness, insight and OCD symptom dimensions. Evaluated comorbidities included Axis I and II disorders, as well as specific comorbid mood, anxiety or tic disorders and schizotypal and obsessive-compulsive personality disorders. Treatment-specific aspects include early response to therapy, previous treatment history, therapeutic alliance and treatment adherence. For each included predictor, its relationship with outcome was noted, in terms of statistical significance and direction (positive, negative or no relationship).

Results

The study selection process is detailed in a PRISMA diagram (Fig. 1). Forty-one studies were included in this review, with a total of 4670 participants (mean sample size = 114; SD = 106.8). Sixteen trials studied isolated pharmacological treatment, twenty-five studied psychological therapies and five studied the combined treatment approach. Overlap is due to the inclusion of studies with more than one studied sample, with different treatment approaches. Thirty-seven studies with adult samples and four with pediatric samples were included. Studies varied significantly in regard to the study design and the measurement tools used. Treatment interventions were also

variable in terms of content, duration and intensity. Characteristics of the included articles are specified in Table 1.

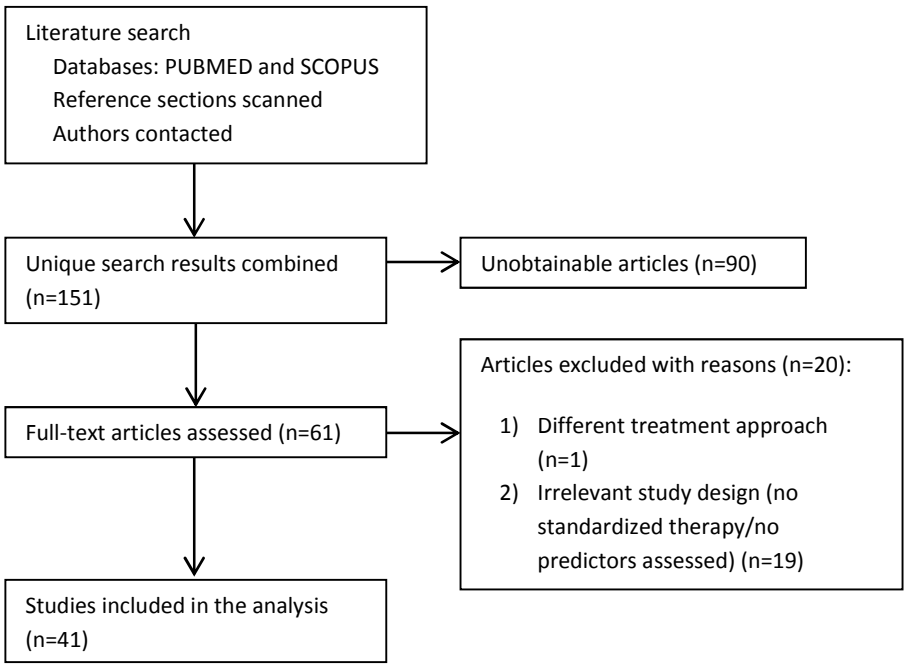

Figure 1. Diagram of study identification and selection

Table 1. Characteristics of included studies

Author	Year	Sample size	Sample age group	Intervention(s)	Studied predictors
Abramowitz	2000	87	Adult	CBT	Comorbid mood disorder
Abramowitz	2000	48	Adult	CBT	Comorbid mood disorder
Abramowitz	2002	28	Adult	CBT	Treatment adherence
Abramowitz	2003	132	Adult	CBT	OCD symptom subtypes
Bloch	2009	45	Pediatric	Combined therapy	Age at assessment; Gender; Age at onset; OCD severity at onset; Length of illness; OCD symptom subtypes; Comorbid mood disorder; Comorbid tic disorder
Bloch	2013	83	Adult	Pharmacological	Age at onset; Length of illness; OCD symptom subtypes; Comorbid mood disorder; Comorbid anxiety disorder; Comorbid tic disorder; Early response to therapy
Boschen	2010	114	Adult	CBT	Age at assessment; Gender; Marital status; Age at onset; Length of illness; Comorbid mood disorder; Comorbid anxiety disorder

Table 1. (continued)

Catapano	2006	79	Adult	Pharmacological	Age at assessment; Gender; Marital status; Age at onset; OCD severity at onset; Length of illness; Family history; Comorbid schizotypal PD; Comorbid obsessive-compulsive PD
Cavedini	1997	30	Adult	Pharmacological	Comorbid obsessive-compulsive PD
Cherian	2014	106	Adult	Pharmacological	Length of illness; Treatment history
da Conceição Costa	2013	128	Adult	Pharmacological	Early response to therapy
Dreessen	1997	52	Adult	CBT	Comorbid Axis II disorder
Erzegovesi	2001	159	Adult	Pharmacological	Age at assessment; Gender; Age at onset; OCD severity at onset; Length of illness; Family history; Insight; OCD symptom subtypes; Comorbid mood disorder; Comorbid tic disorder; Comorbid schizotypal PD; Comorbid obsessive-compulsive PD
Fricke	2006	55	Adult	CBT	Comorbid Axis II disorder
Garcia	2010	112	Adult	CBT; Pharmacological; Combined therapy	OCD severity at onset; Insight;
Haan	1997	99	Adult	CBT; Combined therapy	OCD severity at onset; Comorbid Axis II disorder
Hansen	2007	35	Adult	CBT	Comorbid anxiety disorder; Comorbid Axis II disorder
Jakubovski	2013	196	Adult	CBT; Pharmacotherapy	Age at onset; Length of illness; Family history; OCD symptom subtypes; Comorbid mood disorder; Comorbid anxiety disorder; Comorbid tic disorder; Early response to therapy
Keeley	2011	25	Pediatric	CBT	Therapeutic alliance
Kim	2011	249	Adult	Pharmacological	Age at assessment; Gender; Age at onset; OCD severity at onset; Length of illness; Family history; Insight; Comorbid mood disorder; Comorbid tic disorder; Comorbid Axis II disorder; Treatment history
Landeros-Weisenberger	2010	165	Adult	Pharmacological	OCD symptom subtypes
Langner	2009	154	Adult	CBT	Age at assessment; Gender; Marital status; Age at onset; Length of illness
Maher	2010	108	Adult	Combined therapy	Quality of life; OCD severity at onset; Insight; Hoarding symptom subtype; Comorbid Axis I disorders; Comorbid Axis II disorder;

Table 1. (continued)

Maher	2012	28	Adult	CBT	Hoarding symptom subtype; Therapeutic alliance; Treatment adherence
Mataix-Cols	1999	150	Adult	Pharmacological	OCD symptom subtypes
Moritz	2004	53	Adult	CBT	Age at assessment; Gender; Age at onset; Length of illness; Schyzotypal PD
Mundo	1999	50	Adult	Pharmacological	Age at assessment; Gender; Age at onset; Length of illness; Family history; Comorbid tic disorder
Piacentini	2002	42	Pediatric	CBT	Age at assessment; Gender; OCD severity at onset; Comorbid tic disorder
Pinto	2011	49	Adult	CBT	Obsessive-compulsive PD
Raffin	2009	181	Adult	CBT	Age at assessment; Gender; Marital status; Quality of life; Age at onset; OCD severity at onset; Length of illness; Family history; Insight; Comorbid anxiety disorder
Rufer	2006	104	Adult	CBT	OCD symptom subtypes
Shavitt	2006	41	Adult	Pharmacological	Gender; Age at onset; Length of illness; Family history; Comorbid tic disorder; Treatment history
Simpson	2011	30	Adult	CBT	Hoarding symptom subtype; Treatment adherence
Stein	2001	401	Adult	Pharmacological	Age at assessment; Gender; OCD severity at onset; Length of illness; Treatment history
Stein	2007	434	Adult	Pharmacological	OCD symptom subtypes
Steketee	2001	63	Adult	CBT	Comorbid mood disorder; Comorbid anxiety disorder, Comorbid Axis II disorder
Steketee	2011	39	Adult	CBT	OCD severity at onset; OCD symptom dimensions; Comorbid Axis I disorder
Stewart	2006	476	Adult	Combined therapy (IRT)	Gender; Comorbid tic disorder
Storch	2006	60	Adult	Pharmacological	Age at assessment; Gender; Age at onset; OCD severity at onset; Length of illness; Comorbid mood disorder; Comorbid tic disorder; Treatment history
Storch	2010	143	Adult	CBT	Comorbid mood disorder; Comorbid anxiety disorder
Vogel	2006	37	Adult	CBT	Therapeutic alliance

Note: CBT = cognitive behavior therapy; OCD = obsessive-compulsive disorder; PD = personality disorder

Demographic characteristics

Across ten studies, current age was not predictive of treatment response. These included eight adult and two pediatric samples and studied pharmacological, psychological and combined treatments (Bloch et al., 2009; Boschen, Drummond, Pillay, & Morton, 2010; Catapano et al., 2006; Erzegovesi et al., 2001; Kim et al., 2011; Moritz et al., 2004; Mundo, Bareggi, Pirola, & Bellodi, 1999; Piacentini, Bergman, Jacobs, McCracken, & Kretchman, 2002; Raffin, Guimaraes Fachel, Ferrao, Pasquoto de Souza, & Cordioli, 2009; D. Stein, Montgomery, Kasper, & Tanghoj, 2001). However, one trial (Langner et al., 2009) found that older age was associated with poor response to CBT, and one fluoxetine trial (Storch et al., 2006) found an association between older age and failure of treatment.

Fourteen studies investigated the effect of gender on treatment response. Three adult studies found an association between female gender and better treatment response. Raffin et al. (2009) reported this association for CBT, Mundo et al. (1999) for a Clomipramine trial and Stewart et al. (2006) for a combined approach for adults with severe OCD in intensive residential treatment. Eleven trials, including two pediatric studies, failed to find any association between gender and treatment response (Bloch et al., 2009; Boschen et al., 2010; Catapano et al., 2006; Erzegovesi et al., 2001; Kim et al., 2011; Langner et al., 2009; Moritz et al., 2004; Piacentini et al., 2002; Shavitt et al., 2006; D. Stein et al., 2001; Storch et al., 2006).

Of the four studies assessing the influence of marital status on treatment outcome, two found no significant association (Catapano et al., 2006; Raffin et al., 2009). However, Boschen and colleagues (2010) reported a better treatment response to CBT in married patients as compared to single, divorced or separated patients(Boschen et al., 2010). Langer et al. (2009) also found that being in a stable relationship (being married or living with a partner for ≥3 years) predicted better treatment outcome for patients with late-onset OCD.

A lower quality of life before treatment predicted a worse outcome in both a CBT trial and a combined treatment trial in adults (Maher et al., 2010; Raffin et al., 2009).

Clinical aspects

In ten adult and one pediatric trials, age of onset of OCD was not predictive of treatment response (Bloch et al., 2009; Bloch et al., 2013; Boschen et al., 2010; Catapano et al., 2006; Kim et al., 2011; Langner et al., 2009; Moritz et al., 2004; Mundo et al., 1999; Raffin et al., 2009; Shavitt et al., 2006; Storch et al., 2006). The exceptions to this trend in the adult literature were Erzegovesi et al. (2001) and Jakubovski et al. (2013), who reported early onset as a predictor of worse outcome.

OCD symptom severity at onset, measured using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), was consistently associated with a worse treatment response, across all treatment conditions, in adult and pediatric samples (Bloch et al., 2009; Catapano et al., 2006; Garcia et al., 2010; Haan et al., 1997; Kim et al., 2011; Maher et al., 2010; Piacentini et al., 2002; Raffin et al., 2009; D. Stein et al., 2001; Steketee et al., 2011; Storch et al., 2006). Only one trial failed to find a significant effect of severity at onset (Erzegovesi et al., 2001).

The length of illness was studied in fourteen adult and one pediatric trials. Longer duration of disease predicted worse outcome in three pharmacological treatment trials (Catapano et al., 2006; D. Stein et al., 2001; Storch et al., 2006) and in a combined approach trial (Jakubovski et al., 2013). Jakubovski et al. (2013) found that early onset of OCD is interconnected with length of illness, and suggested that their effects on treatment outcome may be related and require further investigation. In the rest of the studies, length of illness did not predict treatment response for different treatment approaches (Bloch et al., 2009; Bloch et al., 2013; Boschen et al., 2010; Cherian, Math, Kandavel, & Reddy, 2014; Erzegovesi et al., 2001; Kim et al., 2011;

Langner et al., 2009; Moritz et al., 2004; Mundo et al., 1999; Raffin et al., 2009; Shavitt et al., 2006).

Erzegovesi et al. (2001) reported a significant higher frequency of family history of OCD in first degree relatives among responders to a standardized pharmacological treatment. Jakubovski et al. (2013) found an association between worse treatment response in both CBT and pharmacological treatment samples and a family history of tics or anxiety disorders. This association wasn't significant for family history of OCD. In five other trials, family history of OCD was not a significant predictor of response to treatment (Catapano et al., 2006; Kim et al., 2011; Mundo et al., 1999; Raffin et al., 2009; Shavitt et al., 2006).

One study found a significant association between insight and response to CBT in adults (Raffin et al., 2009), while another trial found that patients with poor insight responded worse to pharmacological treatment (Erzegovesi et al., 2001). Garcia et al. (2010) reported a similar result in a pediatric sample, with patients with greater insight showing better improvement across all treatment categories. Two other studies with adult samples did not find any significant association between insight and treatment response (Kim et al., 2011; Maher et al., 2010).

The heterogeneity of OCD symptoms allows it to be split into different subtypes, which have been studied as possible predictors of treatment outcome. Three adult trials comparing hoarding, sexual/religious obsessions, contamination/cleaning, aggression/checking and symmetry/order subtypes found no evidence of a significant association between symptom dimensions and treatment response for pharmacological therapy and CBT (Bloch et al., 2013; Erzegovesi et al., 2001; Jakubovski et al., 2013). However, several other studies consistently show that the hoarding subtype is a predictor of poorer outcome, for both pharmacological and psychological treatment approaches (Abramowitz, Franklin, Schwartz, & Furr, 2003; Maher et al., 2012; Mataix-Cols, Rauch, Manzo, Jenike, & Baer, 1999; Rufer, Fricke, Moritz, Kloss, & Hand, 2006; Simpson et al., 2011; D. J. Stein, Andersen, & Overo, 2007). One study reported that

aggressive symptoms were associated with a better pharmacological treatment response. In this study, the hoarding subtype showed the highest percentage of non-responders, but the number of patients was insufficient to assess this dimension statistically (Landeros-Weisenberger et al., 2010). Steketee et al. (2011) reported that the presence of sexual OCD symptoms, but not religious, predicted a favorable treatment response to CBT. In one study using a pediatric sample, hoarding subtype was reported as a negative predictor of treatment outcome (Bloch et al., 2009).

Comorbidities

Three trials studied the influence of comorbid Axis I disorders on outcome in adult samples, with conflicting results. Steketee at al. (2011) found that Axis I comorbidities predicted greater improvement in a sample receiving CBT. On the other hand, Maher et al. (2013) and Jakubovski et al. (2013) reported a poorer outcome for patients ongoing combiner therapy for OCD with comorbid Axis I disorders.

Several other trials studied specific disorders and their effect on treatment response. Jakubovski et al. (2013), Steketee et al. (2000) and Abramowitz et al. (2001) found that comorbid Major Depressive Disorder (MDD) predicted poorer response to CBT. In another study, Abramowitz et al. (2000) also found that depression severity predicted worse CBT outcome, by dividing the sample in non-depressed and mildly, moderately and severely depressed groups and comparing post-treatment scores (Abramowitz, Franklin, Street, Kozak, & Foa, 2000). Five other adult studies and one pediatric study did not find depression and other mood disorders to be predictive of treatment response across all treatment conditions (Bloch et al., 2009; Bloch et al., 2013; Boschen et al., 2010; Erzegovesi et al., 2001; Kim et al., 2011; Storch et al., 2006).

Most studies assessing comorbid anxiety disorders found no significant association between these and treatment outcome for CBT (Boschen et al., 2010; Jakubovski et al., 2013; Raffin et al., 2009; Steketee, Chambless, & Tran, 2001; Storch

et al., 2010) or pharmacological treatment (Bloch et al., 2013; Jakubovski et al., 2013) in adults. One exception in the literature is Hansen et al. (2007) - that reported poorer treatment response for patients with comorbid generalized anxiety disorder (GAD) and/or panic disorder in an adult sample receiving CBT (Hansen, Vogel, Stiles, & Gotestam, 2007).

Despite the high rate of comorbid tic disorder in pediatric OCD, Piacentini et al. (2002) found that these do not predict response to CBT. In one other pediatric study, Bloch et al. (2009) reported that patients with comorbid chronic tic disorder (CTD) showed earlier OCD symptom remission after a combined treatment approach, and also had a higher rate of remission by adulthood. In adult samples, most studies did not find any significant effect of comorbid tic disorders on pharmacological treatment response (Bloch et al., 2013; Erzegovesi et al., 2001; Jakubovski et al., 2013; Kim et al., 2011; Mundo et al., 1999; Shavitt et al., 2006; Storch et al., 2006). However, Stewart et al. (2006) reported that patients who responded to intensive residential combined treatment had a significantly lower rate of comorbid tic disorders (Stewart, Yen, Stack, & Jenike, 2006).

The presence of comorbid Axis II disorders predicted a poorer treatment outcome in two CBT trials, across all clusters of personality disorders (Hansen et al., 2007; Steketee et al., 2001). Five other trials failed to find any association between Axis II comorbidities and treatment response (Dreessen, Hoekstra, & Arntz, 1997; Fricke et al., 2006; Haan et al., 1997; Kim et al., 2011; Maher et al., 2010). However, in one of these trials, Fricke et al. (2006) reported a trend towards significance for poorer treatment response in patients with a comorbid personality disorder, and found that these patients had a significantly longer duration of illness. Specific personality disorders have also been studied to some extent. Schizotypal symptoms predicted worse outcome in a CBT trial (Moritz et al., 2004), however Catapano et al. (2006) and Erzegovesi et al. (2001) found that schizotypal personality disorder did not predict response to pharmacological treatment. Two studies reported an association between

obsessive-compulsive personality disorder and poor response to pharmacological treatment (Catapano et al., 2006; Cavedini, Erzegovesi, Ronchi, & Bellodi, 1997). One trial found a similar association between obsessive-compulsive personality disorder and CBT response (Pinto, Liebowitz, Foa, & Simpson, 2011). Only Erzegovesi et al. (2001) found that obsessive-compulsive personality disorder did not predict treatment response for pharmacological treatment.

Treatment-specific variables

Three studies assessed the influence of early response to pharmacological treatment on long-term outcome in adults. All of them reported that an improved initial response predicts a better outcome (Bloch et al., 2013; da Conceição Costa et al., 2013; Jakubovski et al., 2013). Jakubovski et al. (2013) also reported that initial response correlated positively with long-term response in a sample ongoing fluoxetine treatment but not in a CBT sample. These results may have important implications for treatment strategies, allowing the earlier implementation of an alternative therapy in case of failure of the initial intervention.

Treatment history was studied in five trials of pharmacotherapy in adults. Three studies reported that patients who had been previously treated with a pharmacological intervention were less likely to respond to therapy as opposed to drug-naïve patients (Cherian et al., 2014; Kim et al., 2011; D. Stein et al., 2001). Storch et al. (2006) and Shavitt et al. (2006) also studied this relation but failed to find any significant results.

Therapeutic alliance positively predicted treatment outcome in two adult and one pediatric trials of CBT (M. L. Keeley, Geffken, Ricketts, McNamara, & Storch, 2011; Maher et al., 2012; Vogel, Hansen, Stiles, & Gotestam, 2006). In one of these studies, therapeutic alliance showed a significant correlation with treatment response in a post-treatment analysis, but not on a 12 month follow-up analysis, showing however, a trend towards significance (Vogel et al., 2006). Maher et al. (2012) reported that the effect of the therapeutic alliance on treatment outcome was mediated by its effect on

treatment adherence. Treatment adherence was significantly associated with a better treatment outcome in three adult CBT trials (Abramowitz, Franklin, Zoellner, & Dibernardo, 2002; Maher et al., 2012; Simpson et al., 2011).

Discussion

Overall, solid evidence regarding predictors of treatment response in obsessive-compulsive disorder is still lacking. Even though we found a significant number of trials reporting on the relationship between demographical variables and OCD treatment outcome, the results were mostly inconsistent. Younger age, female gender and marital status predicted a better outcome in a minority of the studies, however most evidence failed to support this association. Quality of life positively associated with treatment response, but it was evaluated in two studies only.

The studies we found on clinical variables also presented varying results, regarding the effect of age at onset, length of illness and family history of OCD on treatment outcome. More consistent findings were reported on the OCD severity at onset and insight variables, which were found to be predictors of a worse and better response, respectively, across most studies of our sample. The analysis of OCD symptom subtypes also shows a trend towards a worse treatment response for the hoarding subtype. Regarding comorbid disorders, gathered evidence varies greatly between non-significance and worse outcome across all conditions. In the studies we were able to gather, depression and personality disorders were more often associated with poorer treatment response than other comorbid disorders. The treatment-specific variables category provided the most consistent results, since in our sample early treatment response, being treatment-naïve, a good therapeutic alliance and treatment adherence all predicted a better outcome for OCD treatment.

Although evidence is still less than optimal, it has important implications for future research and clinical practice. In light of the differences in treatment response for OCD symptom subtypes, particularly for the hoarding subtype, further research should

focus on identifying and implementing specific and personalized treatments for this group of patients. Alternative treatments, such as monoamine oxidase inhibitors (MAOI) or deep brain stimulation (DBS) have been proposed but still require more extensive examination (Mataix-Cols et al., 1999; Sedrak et al., 2013; D. J. Stein et al., 2007). A tailored strategy for cognitive behavioral therapies directed at hoarding symptoms may also improve outcome. Techniques focused on improving patient's adherence, insight into the need to discard possessions, reducing excessive emotional attachment to items and increasing ability to categorize possessions, are examples of specific approaches to this subtype (Abramowitz et al., 2003; Mary L Keeley et al., 2008; Maher et al., 2012; Mataix-Cols et al., 1999).

The finding that depression is predictive of a worse outcome may also justify a different methodology. Authors propose that patients with comorbid depression may not benefit fully from treatment and/or have compromised treatment adherence (Abramowitz & Foa, 2000; Abramowitz et al., 2000; Jakubovski et al., 2013). Treating depressive symptoms before treatment for OCD or psychological treatment augmentation with antidepressant medication are examples of proposed strategies for this patient group. Similar implications can be found for comorbid personality disorders. Authors hypothesize that patients with OCD with a comorbid personality disorder may benefit form tailored therapies aimed at specific personality traits or symptoms. As an example, Fricke at al. (2006) propose low-dose atypical neuroleptics or specific psychotherapy modules aimed at positive schizotypal symptoms for patients with schizotypal personality traits.

The study of treatment-specific variables and their relation to treatment response yielded consistent results and some conclusions can be taken from their analysis. Since an early treatment response predicted a better outcome on a long-term follow-up, an alternative therapeutic approach should be considered in case of failure of the first method. Drug-naïve patients showed improved results compared to patients with a history of pharmacological treatment, therefore authors hypothesize that

ineffective anti-obsessive medication may decrease the effect of further pharmacological therapies and an alternative approach may be a better option (Kim et al., 2011). Strategies to enhance treatment compliance and specific therapist attributes and techniques than improve therapeutic alliance should be researched and developed, since these variables predict a positive response to treatment (M. L. Keeley et al., 2011; Maher et al., 2012).

Several limitations of this article should be noted. The article identification and selection process was far from optimal due to the unfunded nature of this review, since a great number of potential studies were excluded due to the need for a paid subscription to the respective publications, resulting in a very large number of "unobtainable" articles. Another important limitation is the heterogeneity of study design in the selected articles, which differed in regard to evaluated predictors, predictor and outcome measures, definitions of treatment response, inclusion and exclusion criteria and follow-up period. The studied interventions also varied greatly in terms of type, intensity, and content. As for the chosen analysis method, the classification based on statistical significance and effect direction does not consider a quantitative effect of the studied predictors, which would translate the magnitude of their effect on treatment outcome. Finally, the analysis of the results is greatly hindered by the inconsistent results found, making it difficult to make recommendations for future research and clinical practice.

Conclusions

While there is a growing number on studies focused on predictors of treatment response in OCD, representing a great interest on their possible application in clinical practice, findings are still very inconsistent. Future research should focus on expanding the known scope of possible predictors, as well as understanding possible moderators and mediators of their effect. Standardized and uniform study designs are necessary to assure high quality literature. In line with previous reviews, we conclude that based on

the results of current and further research, knowledge on predictors of OCD treatment outcome should ultimately be applied to clinical practice through the development of tailored and specific treatment approaches (Mary L Keeley et al., 2008; Knopp et al., 2013).

References

Abramowitz, J. S. (1997). Effectiveness of psychological and pharmacological treatments for obsessive-compulsive disorder: a quantitative review. *Journal of Consulting and Clinical Psychology, 65*(1), 44.

Abramowitz, J. S., & Foa, E. B. (2000). Does comorbid major depressive disorder influence outcome of exposure and response prevention for OCD? *Behavior Therapy, 31*(4), 795-800.

Abramowitz, J. S., Franklin, M. E., Schwartz, S. A., & Furr, J. M. (2003). Symptom presentation and outcome of cognitive-behavioral therapy for obsessive-compulsive disorder. *J Consult Clin Psychol, 71*(6), 1049-1057. doi: 10.1037/0022-006X.71.6.1049

Abramowitz, J. S., Franklin, M. E., Street, G. P., Kozak, M. J., & Foa, E. B. (2000). Effects of comorbid depression on response to treatment for obsessive-compulsive disorder. *Behavior Therapy, 31*(3), 517-528.

Abramowitz, J. S., Franklin, M. E., Zoellner, L. A., & Dibernardo, C. L. (2002). Treatment Compliance and Outcome in Obsessive-Compulsive Disorder. *Behavior Modification, 26*(4), 447-463. doi: 10.1177/0145445502026004001

Abramowitz, J. S., Taylor, S., & McKay, D. (2009). Obsessive-compulsive disorder. *The Lancet, 374*(9688), 491-499.

American Psychiatric Association, A. P. A. D. S. M. T. F. (2013). Diagnostic and statistical manual of mental disorders : DSM-5. from http://dsm.psychiatryonline.org/book.aspx?bookid=556

Bloch, M. H., Craiglow, B. G., Landeros-Weisenberger, A., Dombrowski, P. A., Panza, K. E., Peterson, B. S., & Leckman, J. F. (2009). Predictors of early adult outcomes in pediatric-onset obsessive-compulsive disorder. *Pediatrics, 124*(4), 1085-1093. doi: 10.1542/peds.2009-0015

Bloch, M. H., Green, C., Kichuk, S. A., Dombrowski, P. A., Wasylink, S., Billingslea, E., . . . Pittenger, C. (2013). Long-term outcome in adults with obsessive-compulsive disorder. *Depress Anxiety, 30*(8), 716-722.

Boschen, M. J., Drummond, L. M., Pillay, A., & Morton, K. (2010). Predicting outcome of treatment for severe, treatment resistant OCD in inpatient and community settings. *J Behav Ther Exp Psychiatry, 41*(2), 90-95. doi: 10.1016/j.jbtep.2009.10.006

Catapano, F., Perris, F., Masella, M., Rossano, F., Cigliano, M., Magliano, L., & Maj, M. (2006). Obsessive-compulsive disorder: a 3-year prospective follow-up study of patients treated with serotonin reuptake inhibitors OCD follow-up study. *J Psychiatr Res, 40*(6), 502-510. doi: 10.1016/j.jpsychires.2005.04.010

Cavedini, P., Erzegovesi, S., Ronchi, P., & Bellodi, L. (1997). Predictive value of obsessive–compulsive personality disorder in antiobsessional pharmacological treatment. *European Neuropsychopharmacology, 7*(1), 45-49.

Cherian, A. V., Math, S. B., Kandavel, T., & Reddy, Y. C. J. (2014). A 5-year prospective follow-up study of patients with obsessive–compulsive disorder treated with serotonin reuptake inhibitors. *J Affect Disord, 152–154*(0), 387-394. doi: http://dx.doi.org/10.1016/j.jad.2013.09.042

da Conceição Costa, D. L., Shavitt, R. G., Castro Cesar, R. C., Joaquim, M. A., Borcato, S., Valério, C., . . . Diniz, J. B. (2013). Can early improvement be an indicator of treatment response inobsessive-compulsive disorder? Implications for early-treatment decision-making. *J Psychiatr Res, 47*(11), 1700-1707.

Dreessen, L., Hoekstra, R., & Arntz, A. (1997). Personality disorders do not influence the results of cognitive and behavior therapy for obsessive compulsive disorder. *J Anxiety Disord, 11*(5), 503-521.

Erzegovesi, S., Cavallini, M. C., Cavedini, P., Diaferia, G., Locatelli, M., & Bellodi, L. (2001). Clinical predictors of drug response in obsessive-compulsive disorder. *J Clin Psychopharmacol, 21*(5), 488-492.

Fricke, S., Moritz, S., Andresen, B., Jacobsen, D., Kloss, M., Rufer, M., & Hand, I. (2006). Do personality disorders predict negative treatment outcome in obsessive-compulsive disorders? A prospective 6-month follow-up study. *Eur Psychiatry, 21*(5), 319-324. doi: 10.1016/j.eurpsy.2005.03.010

Garcia, A. M., Sapyta, J. J., Moore, P. S., Freeman, J. B., Franklin, M. E., March, J. S., & Foa, E. B. (2010). Predictors and moderators of treatment outcome in the Pediatric Obsessive Compulsive Treatment Study (POTS I). *Journal of the American Academy of Child & Adolescent Psychiatry, 49*(10), 1024-1033.

Haan, E. d., Oppen, P. v., Balkom, A., Spinhoven, P., Hoogduin, K., & Dyck, R. v. (1997). Prediction of outcome and early vs. late improvement in OCD patients treated with cognitive behaviour therapy and pharmacotherapy. *Acta Psychiatr Scand, 96*(5), 354-361.

Hansen, B., Vogel, P. A., Stiles, T. C., & Gotestam, K. G. (2007). Influence of co-morbid generalized anxiety disorder, panic disorder and personality disorders on the outcome of cognitive behavioural treatment of obsessive-compulsive disorder. *Cogn Behav Ther, 36*(3), 145-155. doi: 10.1080/16506070701259374

Health, N. I. f., & Excellence, C. (2005). *Obsessive-compulsive Disorder: Core Interventions in the Treatment of Obsessive-compulsive Disorder and Body Dysmorphic Disorder*: National Institute for Health and Clinical Excellence.

Heyman, I. (2001). Prevalence of obsessive--compulsive disorder in the British nationwide survey of child mental health. *The British Journal of Psychiatry, 179*(4), 324-329. doi: 10.1192/bjp.179.4.324

Jakubovski, E., Diniz, J. B., Valerio, C., Fossaluza, V., Belotto-Silva, C., Gorenstein, C., . . . Shavitt, R. G. (2013). Clinical predictors of long-term outcome in obsessive-compulsive disorder. *Depress Anxiety, 30*(8), 763-772.

Keeley, M. L., Geffken, G. R., Ricketts, E., McNamara, J. P., & Storch, E. A. (2011). The therapeutic alliance in the cognitive behavioral treatment of pediatric obsessive-compulsive disorder. *J Anxiety Disord, 25*(7), 855-863. doi: 10.1016/j.janxdis.2011.03.017

Keeley, M. L., Storch, E. A., Merlo, L. J., & Geffken, G. R. (2008). Clinical predictors of response to cognitive-behavioral therapy for obsessive–compulsive disorder. *Clinical Psychology Review, 28*(1), 118-130.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of general psychiatry, 62*(6), 593.

Kim, C.-H., Jeong, J.-W., Kim, E. J., Shin, Y. S., Suh, H. S., Lee, H. S., & Koo, M.-S. (2011). Clinical Predictors of Drug Response in Patients with Obsessive-Compulsive Disorder. *Clinical Psychopharmacology and Neuroscience, 9*(1), 23-28.

Knopp, J., Knowles, S., Bee, P., Lovell, K., & Bower, P. (2013). A systematic review of predictors and moderators of response to psychological therapies in OCD: do we have enough empirical evidence to target treatment? *Clin Psychol Rev, 33*(8), 1067-1081. doi: 10.1016/j.cpr.2013.08.008

Landeros-Weisenberger, A., Bloch, M. H., Kelmendi, B., Wegner, R., Nudel, J., Dombrowski, P., . . . Coric, V. (2010). Dimensional predictors of response to SRI pharmacotherapy in obsessive-compulsive disorder. *J Affect Disord, 121*(1-2), 175-179. doi: 10.1016/j.jad.2009.06.010

Langner, J., Laws, M., Roper, G., Zaudig, M., Hauke, W., & Piesbergen, C. (2009). Predicting therapy outcome in patients with early and late obsessive-compulsive disorder (EOCD and LOCD). *Behav Cogn Psychother, 37*(5), 485-496. doi: 10.1017/S1352465809990294

Maher, M. J., Huppert, J. D., Chen, H., Duan, N., Foa, E. B., Liebowitz, M. R., & Simpson, H. B. (2010). Moderators and predictors of response to cognitive-behavioral therapy augmentation of pharmacotherapy in obsessive-compulsive disorder. *Psychol Med, 40*(12), 2013-2023. doi: 10.1017/S0033291710000620

Maher, M. J., Wang, Y., Zuckoff, A., Wall, M. M., Franklin, M., Foa, E. B., & Simpson, H. B. (2012). Predictors of patient adherence to cognitive-behavioral therapy for obsessive-compulsive disorder. *Psychother Psychosom, 81*(2), 124-126. doi: 10.1159/000330214

March, J., Foa, E., Gammon, P., Chrisman, A., Curry, J., Fitzgerald, D., . . . Rynn, M. (2004). Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder-The Pediatric OCD Treatment Study (POTS) randomized controlled trial. *JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 292*(16), 1969-1976.

Mataix-Cols, D., Rauch, S. L., Baer, L., Eisen, J. L., Shera, D. M., Goodman, W. K., . . . Jenike, M. A. (2002). Symptom stability in adult obsessive-compulsive disorder: data from a naturalistic two-year follow-up study. *American Journal of Psychiatry, 159*(2), 263-268.

Mataix-Cols, D., Rauch, S. L., Manzo, P. A., Jenike, M. A., & Baer, L. (1999). Use of factor-analyzed symptom dimensions to predict outcome with serotonin reuptake inhibitors and placebo in the treatment of obsessive-compulsive disorder. *American Journal of Psychiatry, 156*(9), 1409-1416.

Moritz, S., Fricke, S., Jacobsen, D., Kloss, M., Wein, C., Rufer, M., . . . Hand, I. (2004). Positive schizotypal symptoms predict treatment outcome in obsessive–compulsive disorder. *Behaviour Research and Therapy, 42*(2), 217-227. doi: 10.1016/s0005-7967(03)00120-7

Mundo, E., Bareggi, S. R., Pirola, R., & Bellodi, L. (1999). Effect of acute intravenous clomipramine and antiobsessional response to proserotonergic drugs: is gender a predictive variable? *Biological psychiatry, 45*(3), 290-294.

Piacentini, J., Bergman, R. L., Jacobs, C., McCracken, J. T., & Kretchman, J. (2002). Open trial of cognitive behavior therapy for childhood obsessive–compulsive disorder. *J Anxiety Disord, 16*(2), 207-219.

Pinto, A., Liebowitz, M. R., Foa, E. B., & Simpson, H. B. (2011). Obsessive compulsive personality disorder as a predictor of exposure and ritual prevention outcome for obsessive compulsive disorder. *Behaviour Research and Therapy, 49*(8), 453-458.

Raffin, A. L., Guimaraes Fachel, J. M., Ferrao, Y. A., Pasquoto de Souza, F., & Cordioli, A. V. (2009). Predictors of response to group cognitive-behavioral therapy in the treatment of obsessive-compulsive disorder. *Eur Psychiatry, 24*(5), 297-306. doi: 10.1016/j.eurpsy.2008.12.001

Rufer, M., Fricke, S., Moritz, S., Kloss, M., & Hand, I. (2006). Symptom dimensions in obsessive-compulsive disorder: prediction of cognitive-behavior therapy outcome. *Acta Psychiatr Scand, 113*(5), 440-446. doi: 10.1111/j.1600-0447.2005.00682.x

Sedrak, M., Wong, W., Wilson, P., Bruce, D., Bernstein, I., Khandhar, S., . . . Sabelman, E. (2013). Deep brain stimulation for the treatment of severe, medically refractory obsessive-compulsive disorder. *Perm J, 17*(4), 47-51. doi: 10.7812/tpp/13-005

Shavitt, R. G., Belotto, C., Curi, M., Hounie, A. G., Rosario-Campos, M. C., Diniz, J. B., . . . Miguel, E. C. (2006). Clinical features associated with treatment response in obsessive-compulsive disorder. *Compr Psychiatry, 47*(4), 276-281. doi: 10.1016/j.comppsych.2005.09.001

Simpson, H. B., Maher, M. J., Wang, Y., Bao, Y., Foa, E. B., & Franklin, M. (2011). Patient adherence predicts outcome from cognitive behavioral therapy in obsessive-compulsive disorder. *J Consult Clin Psychol, 79*(2), 247-252. doi: 10.1037/a0022659

Stein, D., Montgomery, S., Kasper, S., & Tanghoj, P. (2001). Predictors of response to pharmacotherapy with citalopram in obsessive-compulsive disorder. *International clinical psychopharmacology, 16*(6), 357-361.

Stein, D. J., Andersen, E. W., & Overo, K. F. (2007). Response of symptom dimensions in obsessive-compulsive disorder to treatment with citalopram or placebo. *Revista Brasileira de Psiquiatria, 29*(4), 303-307.

Steketee, G., Chambless, D. L., & Tran, G. Q. (2001). Effects of axis I and II comorbidity on behavior therapy outcome for obsessive-compulsive disorder and agoraphobia. *Compr Psychiatry, 42*(1), 76-86. doi: 10.1053/comp.2001.19746

Steketee, G., Siev, J., Fama, J. M., Keshaviah, A., Chosak, A., & Wilhelm, S. (2011). Predictors of treatment outcome in modular cognitive therapy for obsessive-compulsive disorder. *Depress Anxiety, 28*(4), 333-341. doi: 10.1002/da.20785

Stewart, S. E., Yen, C. H., Stack, D. E., & Jenike, M. A. (2006). Outcome predictors for severe obsessive-compulsive patients in intensive residential treatment. *J Psychiatr Res, 40*(6), 511-519. doi: 10.1016/j.jpsychires.2005.08.007

Storch, E. A., Larson, M. J., Shapira, N. A., Ward, H. E., Murphy, T. K., Geffken, G. R., . . . Goodman, W. K. (2006). Clinical predictors of early fluoxetine treatment response in obsessive-compulsive disorder. *Depress Anxiety, 23*(7), 429-433. doi: 10.1002/da.20197

Storch, E. A., Lewin, A. B., Farrell, L., Aldea, M. A., Reid, J., Geffken, G. R., & Murphy, T. K. (2010). Does cognitive-behavioral therapy response among adults with obsessive-compulsive disorder differ as a function of certain comorbidities? *J Anxiety Disord, 24*(6), 547-552. doi: 10.1016/j.janxdis.2010.03.013

Torres, A., Prince, M., Bebbington, P., Bhugra, D., Brugha, T., Farrell, M., . . . Singleton, N. (2006). Obsessive-compulsive disorder: prevalence, comorbidity, impact, and help-seeking in the British National Psychiatric Morbidity Survey of 2000. *American Journal of Psychiatry, 163*(11), 1978-1985.

Vogel, P. A., Hansen, B., Stiles, T. C., & Gotestam, K. G. (2006). Treatment motivation, treatment expectancy, and helping alliance as predictors of outcome in cognitive behavioral treatment of OCD. *J Behav Ther Exp Psychiatry, 37*(3), 247-255. doi: 10.1016/j.jbtep.2005.12.001

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