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Improving outcome of anxiety and obsessive-compulsive disorders



Karin Remmerswaal

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Karin Remmerswaal

Colofon

The studies presented in this thesis were conducted at the Academic Department of GGZ inGeest and the Department of Psychiatry, Amsterdam UMC, VU University Medical Centre Amsterdam, within the Amsterdam Public Health research Institute.

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VRIJE UNIVERSITEIT

**IMPROVING OUTCOME OF ANXIETY AND
OBSESSIVE-COMPULSIVE DISORDERS**

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Contents

Introduction

Chapter 1	General introduction	9
-----------	----------------------	---

Predictors of course

Chapter 2	Risk factors of Chronic Course of Anxiety and Depressive Disorders: a 3-year Longitudinal Study in the General Population	25
-----------	--	----

Chapter 3	Quality of Life and Relationship Satisfaction of Patients with Obsessive-Compulsive Disorder	45
-----------	---	----

Chapter 4	Four-year Course of Quality of Life and Obsessive-Compulsive Disorder	73
-----------	--	----

Chapter 5	Predictors of Intensive Treatment in Patients with Obsessive- Compulsive Disorder	113
-----------	--	-----

Innovative treatments

Chapter 6	Feasibility and Outcome of a Brief CBT Family Intervention for Patients with Obsessive-Compulsive Disorder: a Pilot Study	137
-----------	--	-----

Chapter 7	Relieving the Burden of Family Members of Patients with Obsessive-Compulsive Disorder	145
-----------	--	-----

Chapter 8	Multifaceted, Brief Intensive Home-Based Exposure Treatment in Patients with Obsessive-Compulsive Disorder who are Non-Responsive to Regular CBT: an Uncontrolled Pilot Study	161
-----------	---	-----

Chapter 9	Effectiveness and Feasibility of Intensive versus Regular Cognitive Behaviour Therapy in Patients with Anxiety and Obsessive-Compulsive Disorders: a Meta-Analysis	193
-----------	--	-----

Chapter 10	Schema Therapy with Cognitive Behaviour Day-Treatment in Patients with Treatment-Resistant Anxiety Disorders and Obsessive-Compulsive Disorder: an Uncontrolled Pilot Study	233
------------	---	-----

Conclusions

Chapter 11 Summary and general discussion	259
---	-----

Appendix

Chapter 12 Appendix	283
Nederlandse samenvatting	284
Dankwoord	294
Publicaties	297
Curriculum Vitae	298
Dissertation series	299



CHAPTER 1

General Introduction

General introduction

This thesis focuses on the improvement of long-term course and treatment outcome in anxiety disorders and obsessive-compulsive disorder (OCD). Using data gathered in the context of the Nemesis-2 study in the Dutch general population, we explored predictors of long-term outcome in anxiety disorders to identify clues for influencing their course. With the cohort data of the Netherlands Obsessive-Compulsive Disorder Association (NOFDA) study, we investigated the relationship between severity of OCD and quality of life and how improving the severity of OCD influences quality of life of the participants in NOFDA. We conducted several uncontrolled pilot studies aiming to ameliorate treatment outcome in the disorders under study and systematically reviewed studies on intensifying CBT treatment. This introduction starts with a brief description of the clinical picture of the disorders mentioned. It continues with a global introduction into the epidemiology, comorbidity, course, quality of life, and evidence-based treatments for anxiety disorders and OCD. This chapter concludes with the aim of this thesis and a brief outline of its respective chapters.

Clinical picture

The classification of anxiety disorders and obsessive-compulsive and related disorders according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) is presented in Table 1. OCD was previously (DSM-IV and earlier versions) classified under the group ‘anxiety disorders’. However, since the introduction of the fifth edition of the DSM, OCD is classified in a separate category (American Psychiatric Association, 2013).

Table 1. Overview of anxiety disorders and obsessive-compulsive and related disorders in the DSM-5

Anxiety disorders	Obsessive-compulsive and related disorders
<ul style="list-style-type: none"> · Separation anxiety disorder · Selective mutism · Specific phobia · Social anxiety disorder · Panic disorder · Agoraphobia · Generalized anxiety disorder · Substance/medication-induced anxiety disorder · Anxiety disorder due to another medical condition · Other specified anxiety disorder · Unspecified anxiety disorder 	<ul style="list-style-type: none"> · Obsessive-compulsive disorder · Body dysmorphic disorder · Hoarding disorder · Trichotillomania · Excoriation disorder · Substance/medication-induced obsessive-compulsive and related disorder · Obsessive-compulsive disorder due to another medical condition · Other specified obsessive-compulsive and related disorder · Unspecified obsessive-compulsive and related disorder

Anxiety disorders are characterized by excessive anxiety and/or fear and accompanied by various somatic symptoms such as an accelerated heart rate, sweating, trembling, and dizziness. The excess of anxiety may take the form of panic attacks. Because of anxiety or panic, people may avoid anxiety-provoking situations, leading to several types of phobias. The anxiety disorders under study in this thesis include panic disorder, agoraphobia, social anxiety disorder, and generalized anxiety disorder. These syndromes are briefly described below.

Panic disorder is characterized by recurring unexpected panic attacks. A panic attack is a sudden and intense anxiety with physical and psychological symptoms such as palpitations, dizziness, sweating, chest pain, shortness of breath, and fear of dying, fainting, losing control over oneself, or going crazy. Typically, symptoms peak within ten minutes and can last from a few minutes to half an hour. Patients respond to these panic attacks by worrying about getting more panic attacks, worrying about the consequences of the panic attacks, or by a marked alteration in behaviour related to the attacks, such as avoidance of situations and places where panic attacks have occurred in the past.

Agoraphobia consists of fear and avoidance of public places such as being outside the home alone, using public transport, driving a car, going to the supermarket, waiting in a queue, going to a hairdresser, visiting restaurants or theatres, shopping at busy places, and being in crowds, closed-in spaces (e.g. an elevator), and wide-open spaces. Patients fear that escaping from these situations will be difficult or that help will not be available when they develop panic symptoms or other embarrassing symptoms. In DSM-5, agoraphobia is a 'standalone' classification. In previous editions of DSM, agoraphobia was usually diagnosed as a consequence of panic disorder: panic disorder with agoraphobia.

Social anxiety disorder, or social phobia, is characterized by excessive fear of social situations, such as meeting new people at a party, talking in meetings or groups, starting conversations, talking to authority figures, eating with company, going to a public toilet, speaking on the phone, working or engaging in sports activities with other people, going to school, expressing personal opinions, dating, and maintaining relationships. Patients fear negative evaluations from other people due to their behaviour or anxiety symptoms, such as blushing, trembling, and sweating. Patients with social anxiety disorder avoid social situations or endure them with intense fear. Also, anticipatory anxiety is commonly part of social anxiety disorder, including excessive worrying before a social event.

Generalized anxiety disorder consists of excessive anxiety and worries that are difficult to control concerning a wide range of situations and issues. Patients worry about disasters that may happen in the future, while there is no reason for these concerns. For example, they may worry about getting ill, experiencing financial problems, performing poorly at work, family members getting ill or having an accident, wars, and natural disasters. In addition, people may overthink plans and solutions to all possible worst-case scenarios. The worrying is accompanied by restlessness, tiredness, difficulty concentrating, irritability, muscle tension, and problems with sleeping. The symptoms are usually present most days and cause withdrawal from social contacts and work.

People with OCD experience obsessions and/or compulsions. Obsessions are defined as recurring, intrusive thoughts, urges, or images that cause tension or anxiety. Obsessions are ego-dystonic, which means that they are dissonant with the person's beliefs or self-image. Compulsions are repetitive and ritualized behaviours or mental acts aimed at reducing anxiety and distress. OCD is commonly accompanied by avoidance of situations that trigger obsessions or compulsions. People who meet the DSM-5 classification of OCD spend at least an hour a day with OCD symptoms. Based on the nature of the symptoms, OCD is divided into five main subtypes, described below.

- Contamination obsessions with cleaning compulsions: Fear of becoming contaminated or contaminating other people, combined with excessively cleaning and washing. For example, from fear for botulism, taking exceptionally long showers accompanied by washing rituals such as soaping three times in a specific way.
- Harm obsessions with checking compulsions: Fear of harming oneself or others, combined with excessively checking whether they, or others, are hurt. For example, from fear of having run someone over in a car unnoticed, going back all the way to check if someone was in fact injured.
- Symmetry obsessions with ordering compulsions: Feeling uncomfortable or distressed when items are not perfectly symmetrical or ordered in a specific way, combined with excessively aligning, arranging, and positioning items in a specific way. For example, ordering books according to size on a bookshelf, and arranging clothes according to colour in the closet.
- Obsessions without visible compulsions: Distressing and intrusive thoughts that are not accompanied by overt compulsions although mental compulsions are usually present. For example, having the intrusive thought that one does not actually love their partner, combined with mentally verifying one's feelings.

- **Hoarding:** Experiencing difficulty in discarding possessions regardless of their actual value, and persistent acquisition of objects. Possessions are collected in the home to such an extent that using the living space becomes difficult. For example, one cannot eat at the table anymore because the table and chairs are covered with objects. Since DSM-5, hoarding is a distinct classification.

It is a characteristic of anxiety disorders and OCD that people recognize that their fears are excessive or irrational. In addition, to meet the criteria for a formal DSM-5 classification, the symptoms of the disorder must lead to clinically significant distress or impairment in daily functioning. In the case of panic disorder, the symptoms must be present for at least one month, while generalized anxiety disorder is classified when the fear symptoms have existed for at least six months. In social anxiety disorder and agoraphobia, the DSM-5 mentions that the symptoms typically last six months or more. In OCD, DSM-5 mentions no duration criterion (American Psychiatric Association, 2013).

Epidemiology

The lifetime prevalence of anxiety disorders in the general population is 29%: about 1 in 3 to 4 people develop an anxiety disorder at some point in their lives (ten Have et al., 2023). More specifically, the lifetime prevalence of panic disorder is 5.6%, of agoraphobia 4.0%, of social anxiety disorder 13.1%, of generalized anxiety disorder 9.5%, and of OCD 0.9% (Bijl et al., 1998; ten Have et al., 2023). The 12-month prevalence of anxiety disorders in the general population is 15.2%, which is the percentage of people who had an anxiety disorder in the past year (ten Have et al., 2023). Breaking down this data for the specific anxiety disorders, the 12-month prevalence of panic disorder appears to be 2.2%, of agoraphobia 1.9%, social anxiety disorder 5.6%, generalized anxiety disorder 3.8%, and OCD 0.5% (Bijl et al., 1998; ten Have et al., 2023). These data suggest that anxiety disorders and OCD tend to run a chronic course (see further).

Comorbidity

Comorbid mental disorders, defined as other mental disorders simultaneously occurring with the primary mental disorder, are common in patients with anxiety disorders and OCD. Depending on the specific primary disorder, 65-97% of those in the general population with an anxiety disorder or OCD meet the criteria of at least one other mental disorder (Kessler, 2005). Most common comorbid mental disorders are other anxiety disorders and mood disorders (Ravelli et al., 1998).

Patterns of comorbidity of common mental disorders in the general population have been studied using factor analysis to determine the underlying latent structure. Anxiety disorders and depressive disorders share an underlying dimension that is labelled 'internalizing disorders' and characterized by primarily internal symptoms. In addition, a dimension underlying alcohol and drug dependency is established which is labelled 'externalizing disorders' and characterized by maladaptive behaviour directed toward the environment. Internalizing disorders are divided into a 'fear' factor, including panic disorder and the phobias, and an 'anxious-misery' factor, with generalized anxiety disorder, depressive disorder, and dysthymia, see Figure 1 (Vollebergh et al., 2001). In this study, OCD was not included.

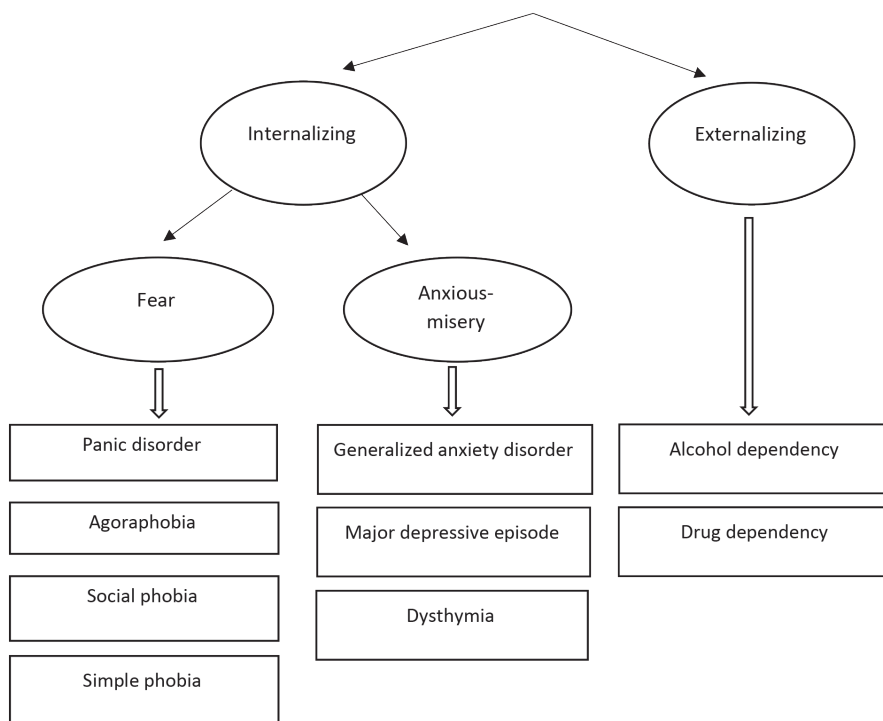


Figure 1. Underlying structure of common mental disorders. Adapted from Vollebergh et al. 2001.

Comorbidity patterns have also been studied in clinical populations, pertaining to people seeking help in specialised mental health care, including the most severe and chronic cases. 55% of the people with OCD in clinical populations have at least one comorbid mental disorder, most commonly anxiety disorders and depressive

disorder (Hofmeijer-Sevink et al., 2013). In a mixed sample of respondents from the general population and clinical population, 48%-68% of those with anxiety disorders had one or more additional anxiety disorders, while 63% also fulfilled the criteria of a depressive disorder (Lamers et al., 2011). In addition, comorbid personality disorders are frequently present. 41-52% of the patients with an anxiety disorder or OCD had a comorbid personality disorder according to a meta-analysis including 14,612 individuals from general and clinical populations (Friborg et al., 2013). So-called cluster C personality disorders are most common, characterized by anxiety, avoidance, inhibition, and control.

Course

Of those with anxiety disorders in the general population, 87% achieve remission within six years, 14% follow an intermittent course and 8% a chronic course (Schopman et al., 2021). Following remission, 15% experience recurrence of the anxiety disorder within six years (Scholten et al., 2021). Since symptoms may wax and wane, may develop anew and remit completely, a 'relapse' after remission may not always take place in the so-called 'index disorder'. Instead, the patient may fulfil the criteria of another disorder in a new episode. When this 'diagnostic instability' is also considered, the course of anxiety disorders worsens. The recovery rate of anxiety disorders then drops from 80% to 62% with a follow-up of 3-years (ten Have et al., 2022).

In naturalistic clinical studies, 37%-82% of patients recover from their anxiety disorder within twelve years, depending on the specific anxiety disorder, while 39%-58% experience recurrence (Bruce et al., 2005). The course of anxiety disorders worsens with comorbidity. Compared with 42% of the people with pure anxiety, 57% of those with comorbid depression had a chronic course in a mixed sample from general and clinical populations (Penninx et al., 2011). When diagnostic instability is also considered, the recovery rate of anxiety disorders drops significantly: 55% of the patients recovered from anxiety disorders, while 41% also recovered from depressive disorders and alcohol dependency after two years in a mixed sample from general and clinical populations (Bokma et al., 2022).

The course of OCD differs from that of anxiety disorders. OCD is chronic in 60% of the cases, while the recovery rate is estimated at 42% after fifteen years in naturalistic clinical studies (Marcks et al., 2011; Visser et al., 2014). Data suggest that the majority of patients recovered from OCD remain recovered: 25% of those with a remitted OCD relapse within fifteen years (Marcks et al., 2011).

Quality of life

Anxiety disorders and OCD interfere with daily functioning, such as self-care, family and social life, work, and leisure activity. Anxiety disorders, including OCD, are ranked as the sixth largest contributor to non-fatal health loss globally by the World Health Organization (World Health Organization, 2017). The impact of a mental disorder on a person's life can be expressed through the concept 'quality of life'. Quality of life is a container concept which commonly includes an evaluation of physical and mental health, and of social functioning, mapping the ability to function in several life domains. It also contains the subjective perspective of the patient of the ability to achieve personal goals in life. The World Health Organization defines quality of life as 'an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns' (<https://www.who.int/healthinfo/survey/whoqol-qualityoflife>; page 1). Patients consider quality of life highly important. They attach even more importance to quality of life than to absence of symptoms (Zimmerman et al., 2006).

Patients with anxiety disorders and OCD have an inferior quality of life, indicating that they experience much disability in functioning in several life domains (Koran et al., 1996; Olatunji et al., 2007). The more severe the anxiety and obsessive-compulsive symptoms are, the poorer the quality of life is. Moreover, comorbid mental disorders lower the quality of life even further. The relation between quality of life and the severity of symptoms is complex. Although the quality of life improves if symptoms reduce by treatment, it usually remains under the level of the general population, even when the anxiety disorder or OCD is in remission (Hofmann et al., 2014; Iancu et al., 2014). Hence, remission of symptoms is not sufficient for restoring quality of life. Besides severity of the index mental disorder and of comorbid disorders, little is known about the predictors of a poor quality of life in remitted patients, or, in other words, the factors that differentiate patients with a poor quality of life from those with a better one.

Family

Anxiety disorders and OCD affect the family life and intimate relationships of patients. Patients and their partners report marital distress and less relationship satisfaction than the general population (Abbey et al., 2007; Kasalova et al., 2018). The burden on relatives has mainly been investigated in OCD, and to a lesser extent in anxiety disorders. From these studies it appears that family members experience anxiety and depression symptoms, and a diminished quality of life as a consequence of the OCD of the patient (Albert et al., 2017). In addition, OCD disrupts the life of family members on home management, leisure activities, and social life (Laidlaw et al., 1999).

Patients commonly want help from their loved ones to ease the anxiety and discomfort from OCD. They may ask them, for instance, to stay around while they repeatedly check, causing their relatives to be late for an appointment; or patients may insist that their family members perform compulsive acts such as checking or cleaning. Most relatives comply with these requests, which is called 'accommodation'. The other side of accommodation is that relatives lose their patience, may criticize the patient, or physically restrain him/her from performing compulsions, termed 'antagonism'.

Accommodation and antagonism are accompanied by anxiety and depression symptoms, and a reduced quality of life in family members (Amir et al., 2000). In other words, the burden of family members from the OCD increases due to their response to OCD. Moreover, accommodation and antagonism also have negative consequences for the patient. The obsessive-compulsive symptoms of the patient are more severe if their family members accommodate or antagonize (Steketee, 1993).

Treatment

Evidence-based treatments for anxiety disorders and OCD consist of serotonergic antidepressants and cognitive behaviour therapy (CBT). This latter treatment focuses on changing cognition (thoughts, assumptions) and behaviour to reduce negative emotions. Cognitive therapy in anxiety disorders and OCD consists of learning to change a fearful interpretation of situations into a non-fear interpretation. Behaviour therapy comprises of exposure, in which patients learn to enter situations they would normally avoid out of fear. In OCD, exposure is extended with response prevention, which means that patients do not perform compulsions during exposure. CBT is effective in reducing anxiety and obsessive-compulsive symptoms. This has been soundly demonstrated with research. About 60%-80% of the patients with anxiety disorders benefit from CBT (Emmelkamp, 2004; Multidisciplinaire Richtlijn Angststoornissen, 2013). However, this also means that a significant group of patients does not benefit from CBT. In OCD, almost half of the patients still meet the diagnostic criteria after an adequately given evidence-based treatment (van Oppen et al., 2005).

When CBT and psychotropic medication are not effective and the symptoms severely interfere with the daily functioning of the patient, guidelines suggest intensifying treatment. An intensive treatment consists of day treatment or inpatient treatment. Commonly, it is a multimodal treatment, with CBT being the main therapy, offered in a group with other patients with anxiety disorders and OCD. Intensive treatment usually takes several days or parts of a day a week, up to 5 days a week for a few

months to a year. The effectiveness of intensive treatment has been demonstrated in patients with OCD (Veale et al., 2016).

Recent developments in clinical practice aim to increase the effectiveness of CBT. Three innovations will be highlighted here, as we have evaluated them in this thesis. The first innovation pertains to the involvement of family members in the treatment of OCD. Since it has been demonstrated that certain responses of family members have the effect of maintaining the OCD, treatments have been developed to teach family members not to accommodate or antagonize the obsessive-compulsive symptoms. In addition, patients learn not to request accommodation.

A second innovation is to change the planning of the sessions in such a way that sessions are concentrated. Commonly, CBT sessions are planned once a week over the course of several months. In a concentrated schedule, the same number of sessions are planned (almost) daily in a few weeks. A brief, intensive schedule might be superior to a regular schedule because patients have less opportunity to avoid feared situations in between sessions.

A third innovation is to target personality problems in treatment besides the anxiety disorder or OCD. It is believed that dysfunctional personality traits account for treatment resistance in patients with anxiety disorders and OCD. More specifically, persistent dysfunctional patterns formed early in life, also called early maladaptive schemas (EMSs), and the emotional states and coping responses arising when EMSs are activated (maladaptive schema modes), would result in the persistence of symptoms. Hence, treating EMSs and schema modes in conjunction with the anxiety disorder or OCD might improve the results of treatment. One treatment targeting EMSs and schema modes is schema therapy. Schema therapy postulates that EMSs and schema modes are developed when basic emotional needs are not met in childhood (Young et al., 2003). Schema therapy focuses on identifying and healing EMSs, connecting with core needs and feelings, and getting core needs met in everyday life.

Aim and outline of this thesis

This thesis aims to improve the course of OCD and anxiety disorders. The initial section focuses on identifying patients with a poor course, while the second part of this thesis, starting from chapter 6, examines a number of novel treatments.

Chapter 2 presents the prediction of a poor course of anxiety and depressive disorders in the general population. Data were used from Netherlands Mental Health Survey

and Incidence Study-2 (NEMESIS-2), which is a psychiatric epidemiological cohort study in the Dutch general population aged 18-64. We hypothesized that the course of anxiety and depressive disorders is less favourable when using a realistic, broad definition (presence of any mood, anxiety or substance use disorder during follow-up) compared to a commonly used, strict definition (presence of a mental disorder from the same diagnostic category as the index disorder).

In chapter 3 the relationship satisfaction and quality of life of patients with OCD is described, and characteristics of patients with a poor relationship satisfaction and quality of life are identified. Data were derived from the Netherlands Obsessive-Compulsive Association (NOCDA). The NOCDA study recruited a cohort of 419 adult patients referred to mental health care centres in the Netherlands with a lifetime diagnosis of OCD. We hypothesized that the mean quality of life is poor, the mean relationship satisfaction is moderate, and that patients with more severe obsessive-compulsive symptoms have a poorer quality of life and less relationship satisfaction.

Chapter 4 examines the four-year course of quality of life and its association with course of OCD. In addition, we identify which patients with a remitting OCD still have an inferior quality of life. As in chapter 3, data were derived from the NOCDA study. We hypothesized that: 1) quality of life improves over time but remains lower than in the general population; 2) quality of life and OCD are only weakly correlated; and 3) the course of quality of life is critically dependent on factors other than severity of OCD alone.

Chapter 5 identifies patients with OCD who will start intensive treatment in the following years. Data from the NOCDA cohort study were used. We hypothesized that patients with more severe symptoms, greater vulnerability, and a lower quality of life are more likely to end up in intensive treatment.

The feasibility and outcome of a brief family intervention is examined in chapter 6. In this uncontrolled pilot study, patients with OCD and a family member were treated for five sessions in addition to CBT of the patient. They learned how to deal best with the OCD in the context of their relationship without accommodating or antagonizing the obsessive-compulsive symptoms. We hypothesized that obsessive-compulsive symptoms, accommodation, and antagonism improve after completing the brief family intervention.

Chapter 7 investigates the family burden from the patient's OCD and whether family burden improves following the brief family intervention from the previous chapter.

The sample is identical to the sample described in chapter 6. We hypothesized that family members have a considerable burden and that the burden is eased after the brief family treatment.

Chapter 8 includes another uncontrolled pilot study into the feasibility and outcome of a brief, intensive exposure treatment at home in patients with OCD who did not respond to regular CBT. The treatment included psychoeducation and exercises on accommodation and antagonism, and was given to the patient and a family member most involved in caring for the patient. We hypothesized that obsessive-compulsive symptoms, comorbid anxiety and depression, functioning, accommodation, and antagonism all would improve. Furthermore, we hypothesized that dropout is comparable to regular CBT and satisfaction with the treatment is high.

In chapter 9 the effectiveness of short, intensive scheduling of CBT sessions in patients with anxiety disorders and OCD is meta-analysed. PubMed, PsycINFO and Embase were systematically searched for studies comparing short, intensive CBT with regular CBT. We hypothesized that: 1) the short, intensive schedules are superior to regular schedules in reducing anxiety, obsessive-compulsive and comorbid depressive symptoms; and 2) dropout is the same in both schedules.

Chapter 10 explores an innovative schema therapy (ST) with CBT day-treatment in patients with treatment-resistant anxiety disorders and OCD in an uncontrolled pilot study. The sample consisted of patients treated with the ST-CBT day-treatment. We hypothesized that general psychopathology improves with this treatment and that this improvement is correlated with improvement of EMSs and maladaptive schema modes.

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CHAPTER 2

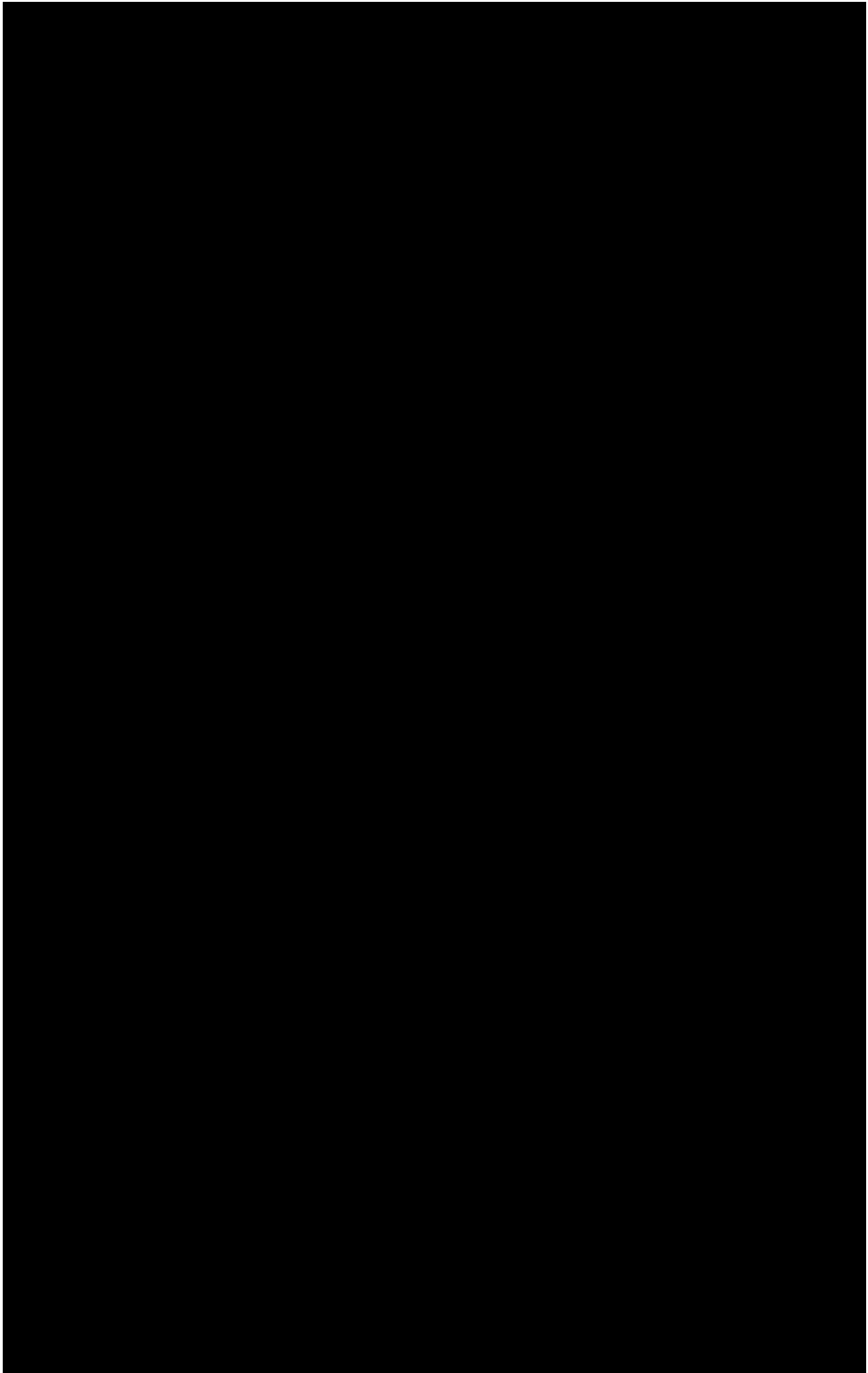
Risk Factors of Chronic Course of Anxiety and Depressive Disorders: a 3-Year Longitudinal Study in the General Population

Karin C.P. Remmerswaal, Margreet ten Have, Ron de Graaf, Anton J.L.M. van Balkom, Brenda W.J.H. Penninx¹, Neeltje M. Batelaan¹

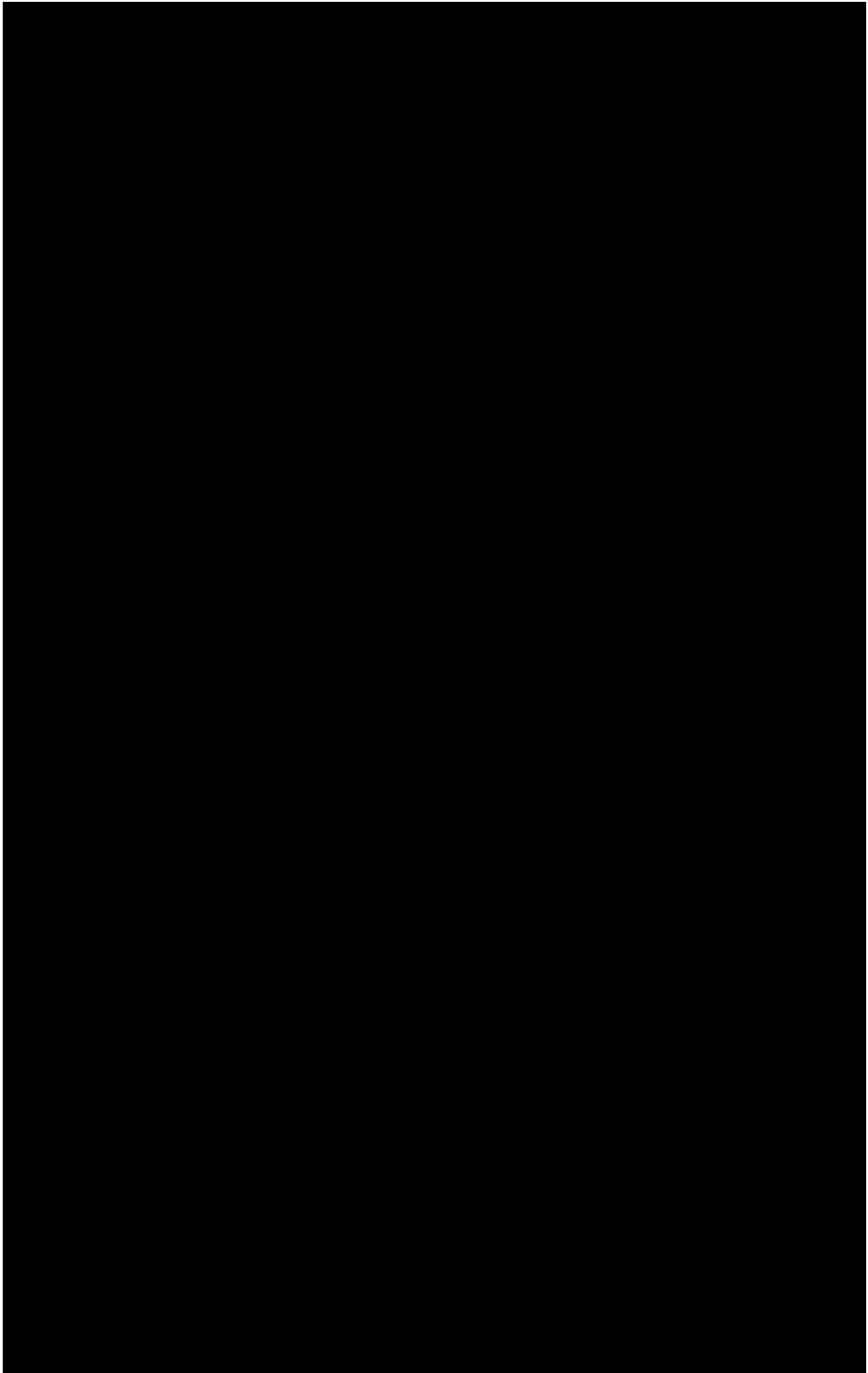
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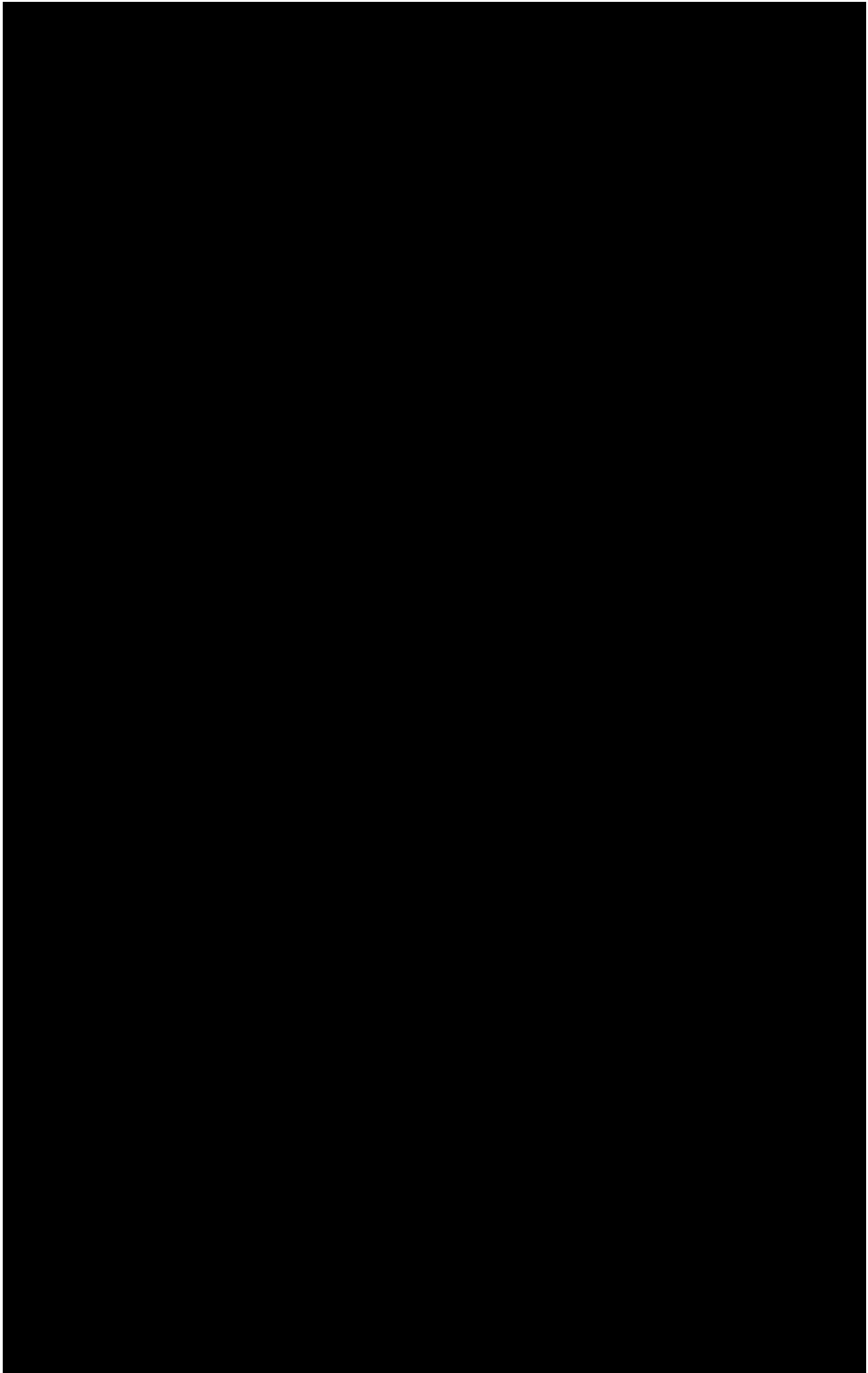


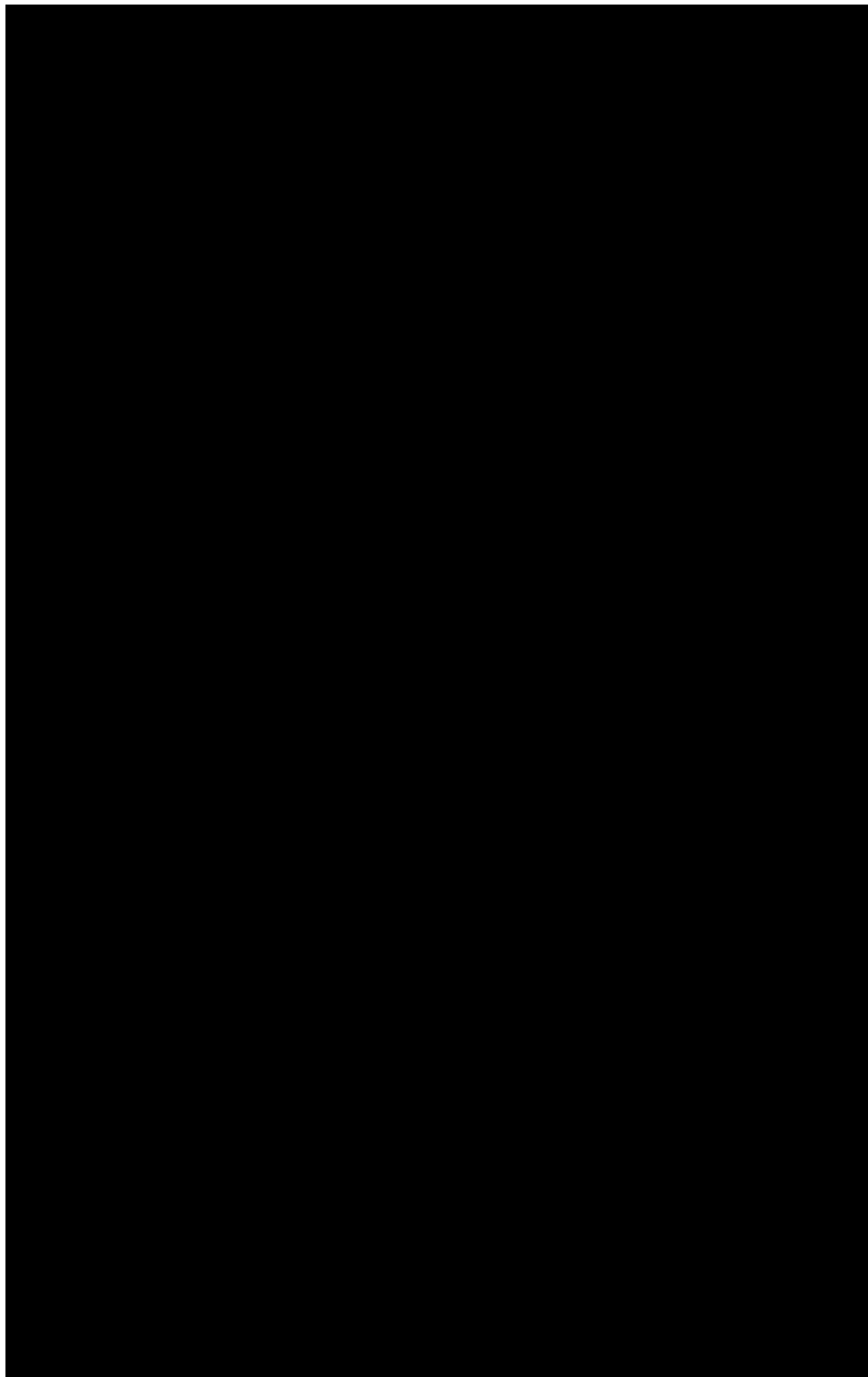


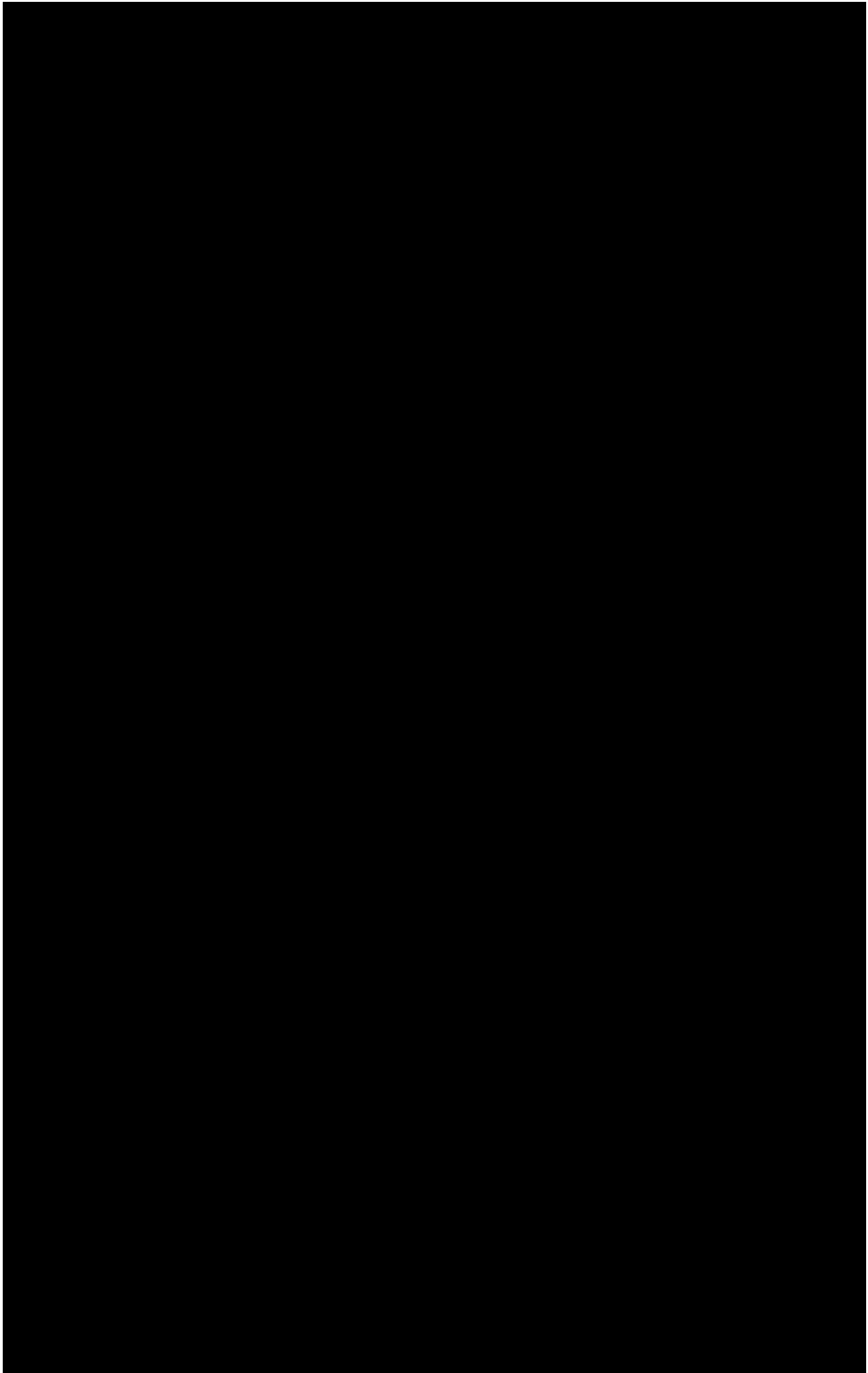




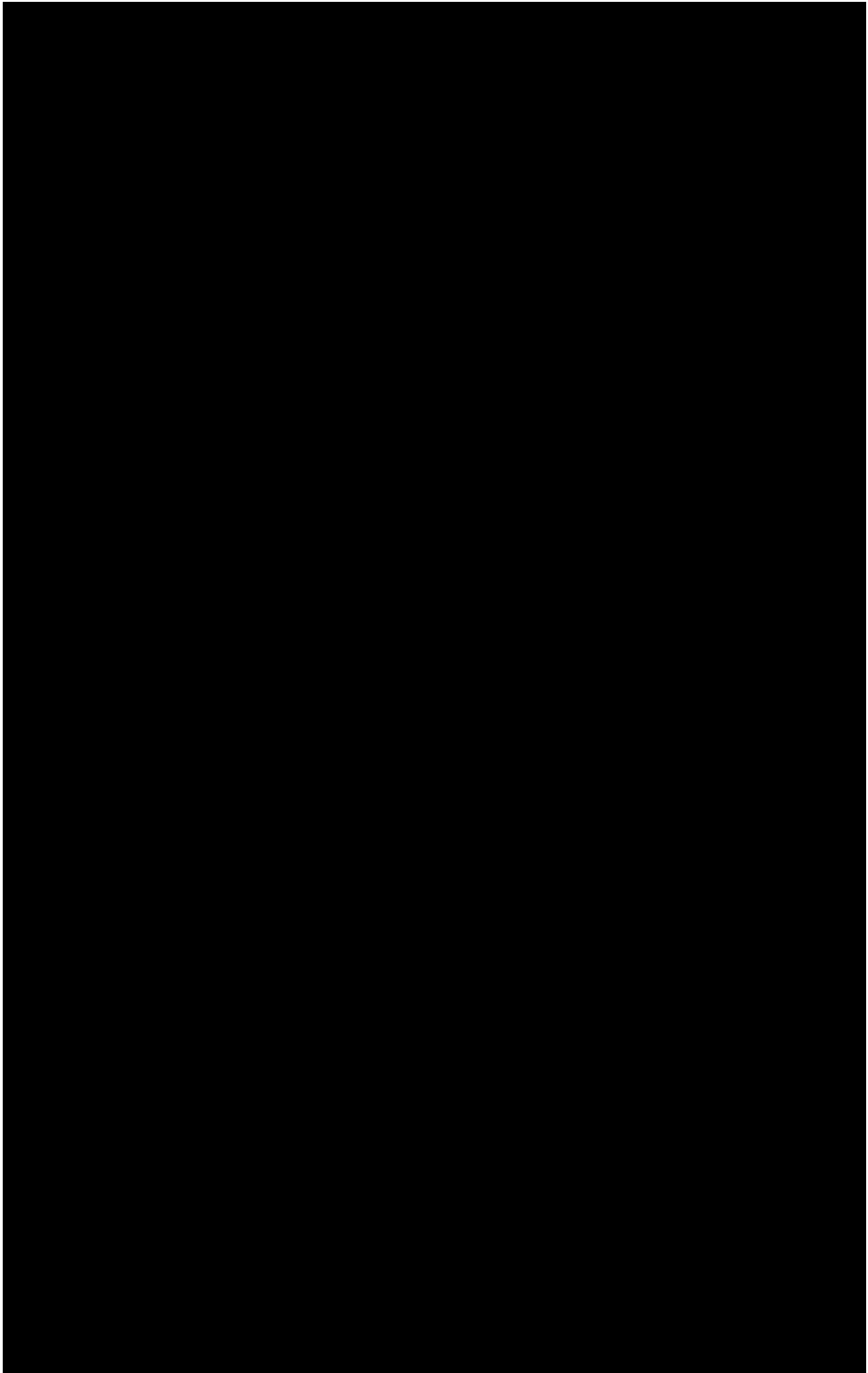


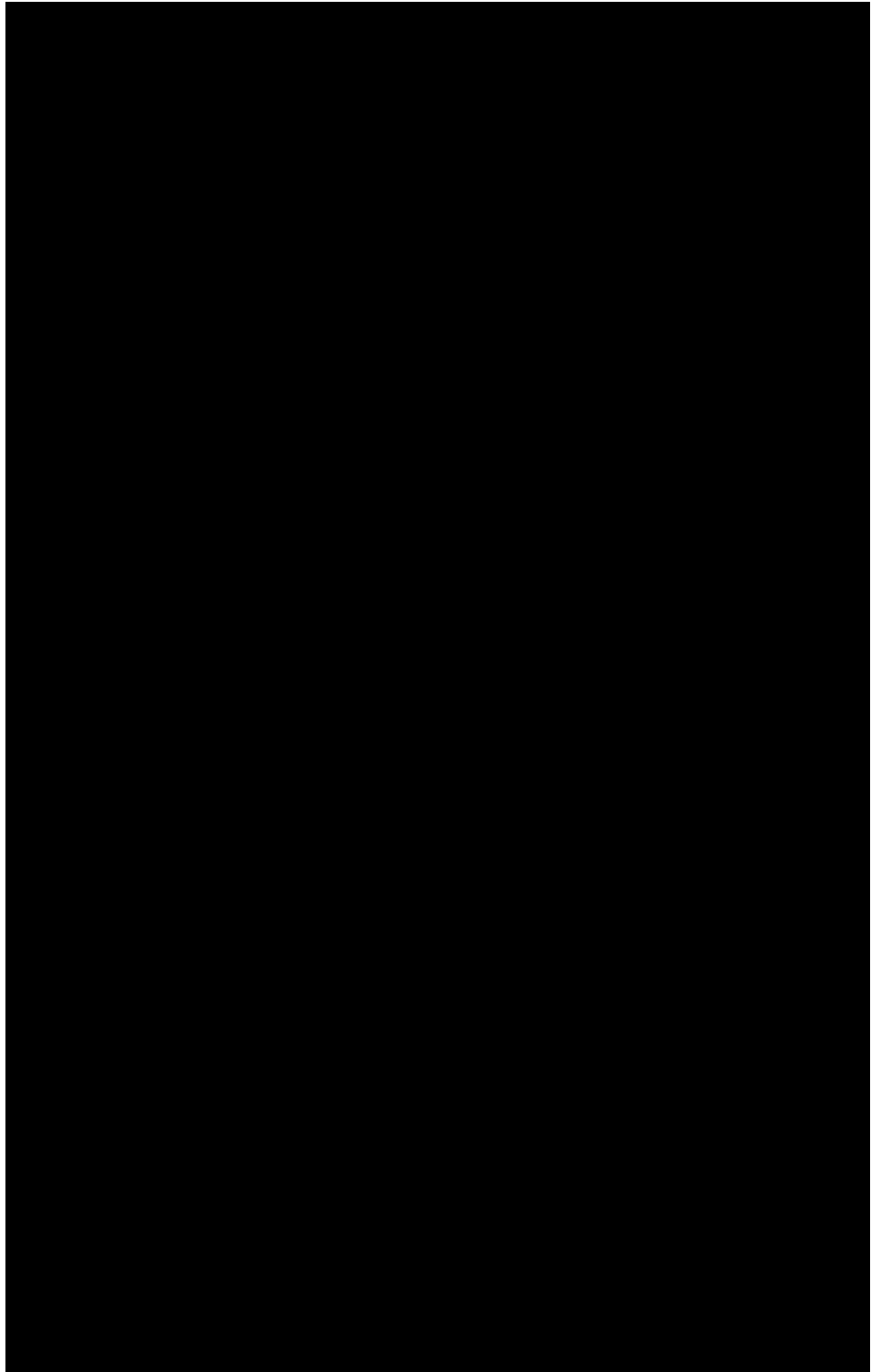


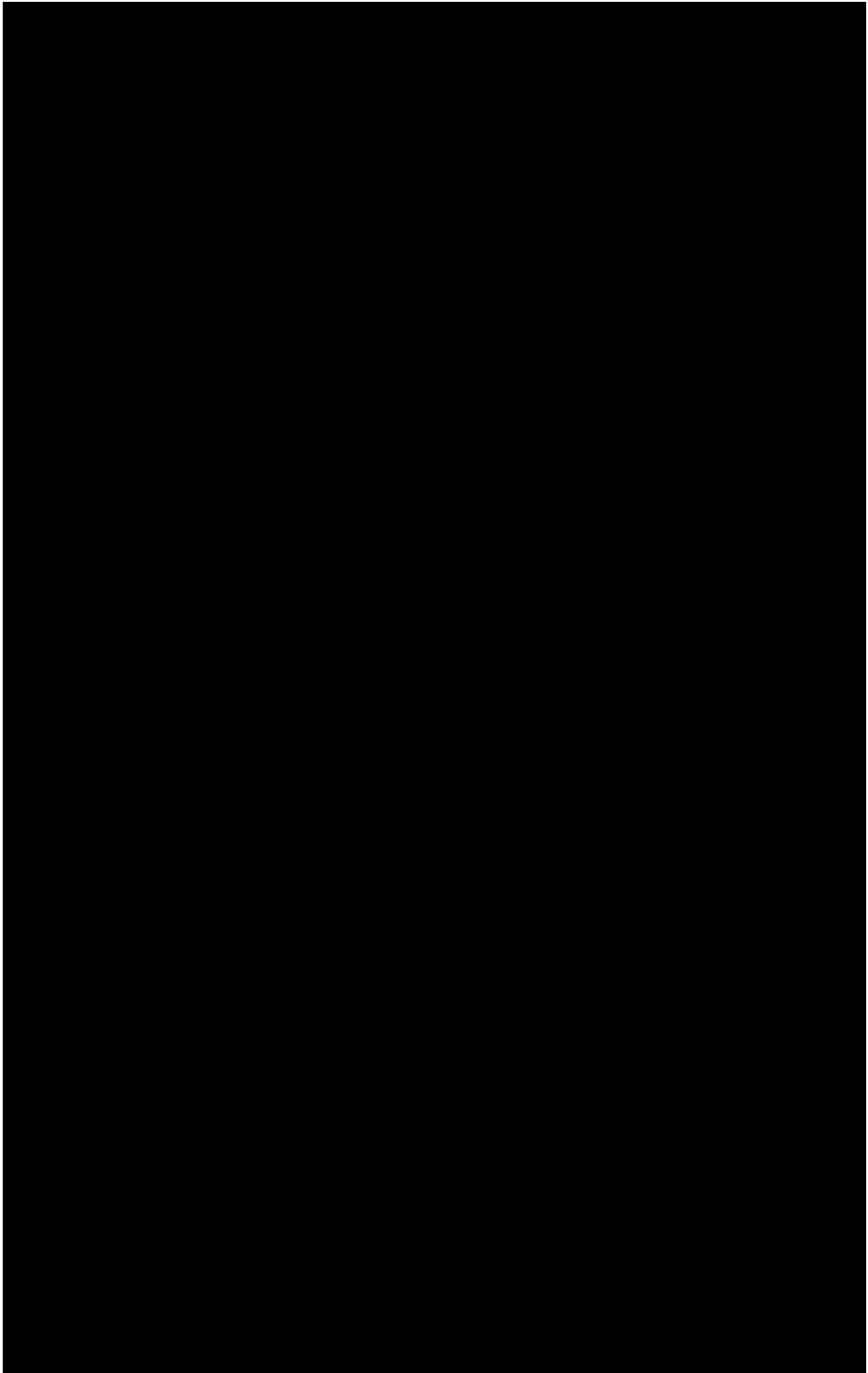


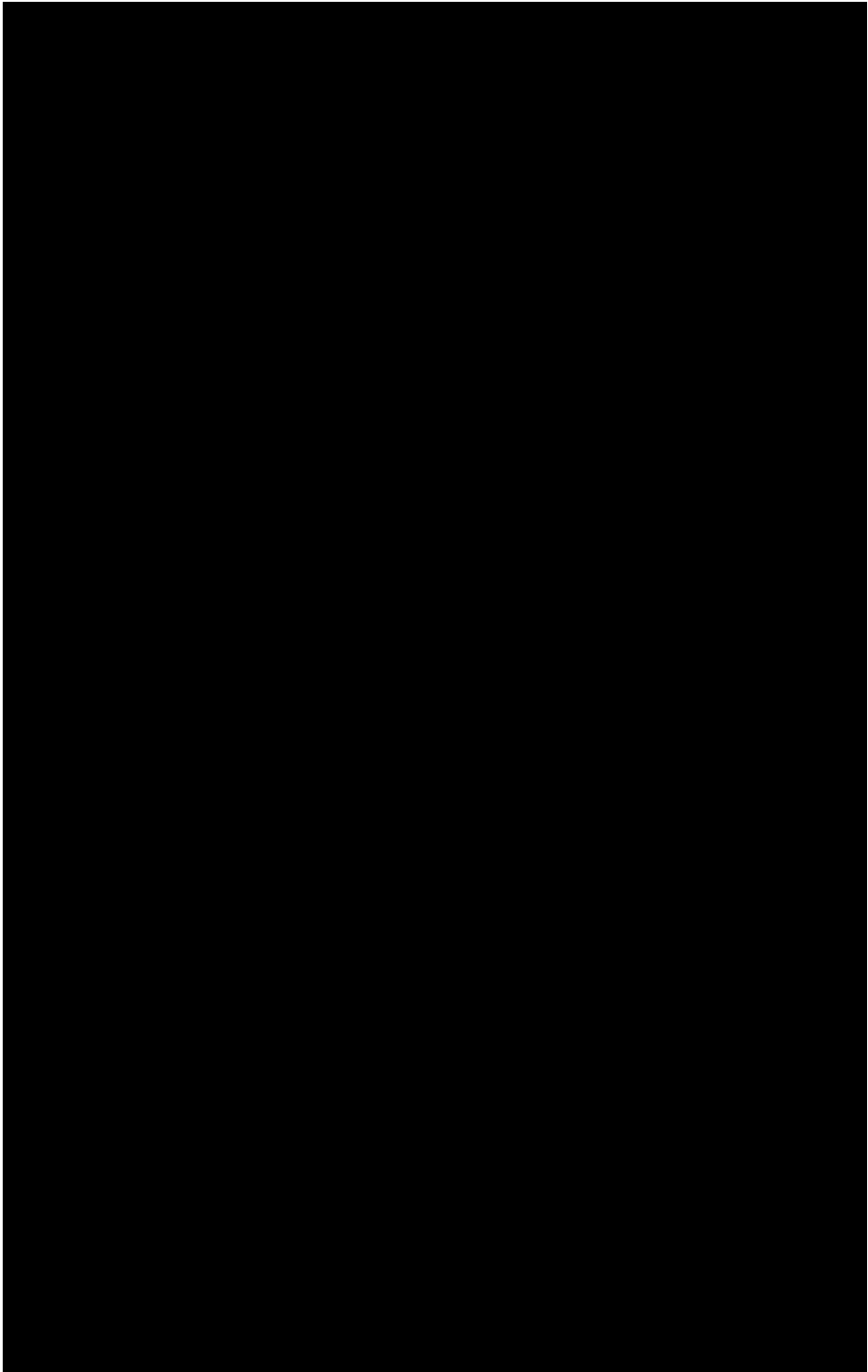


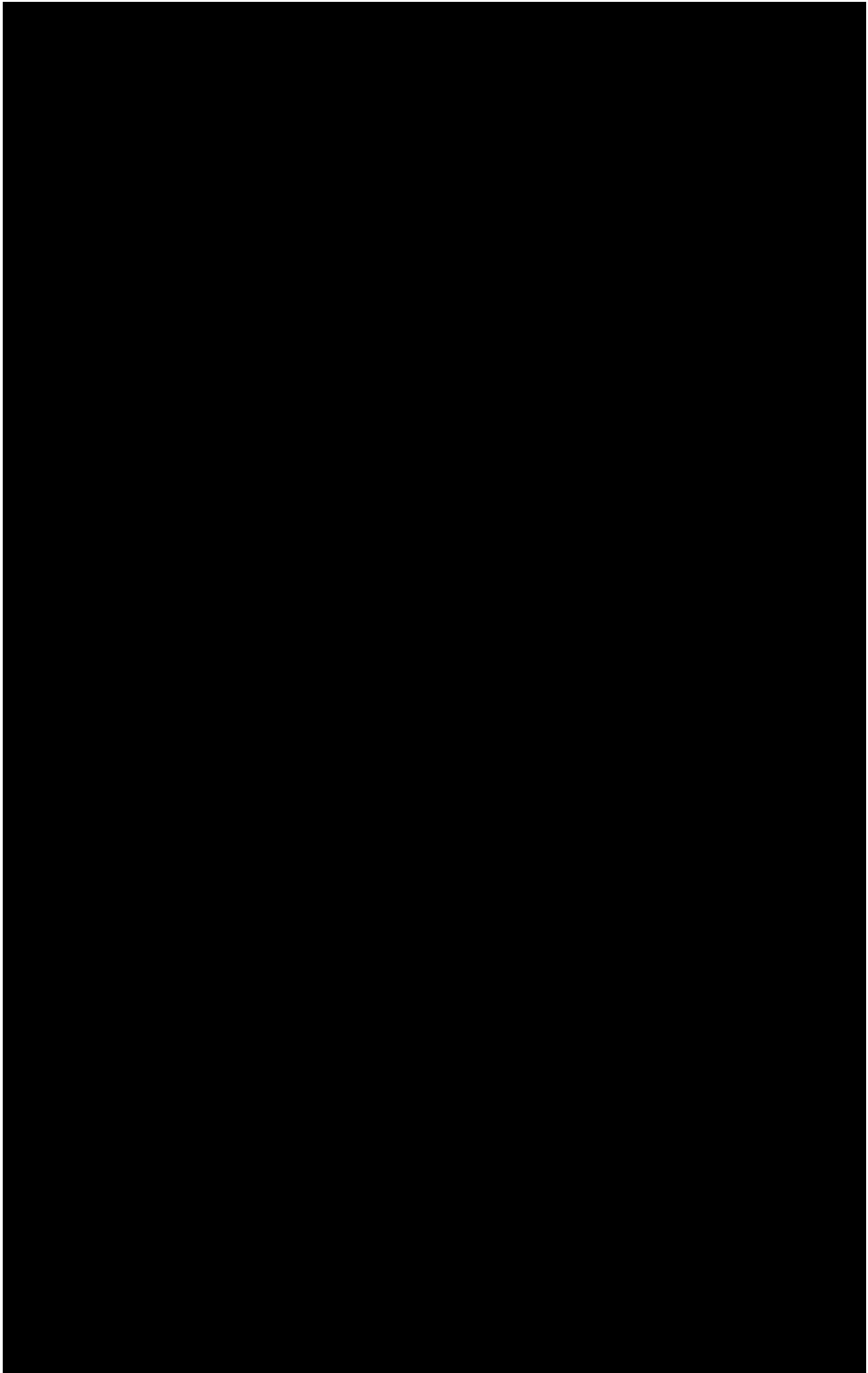


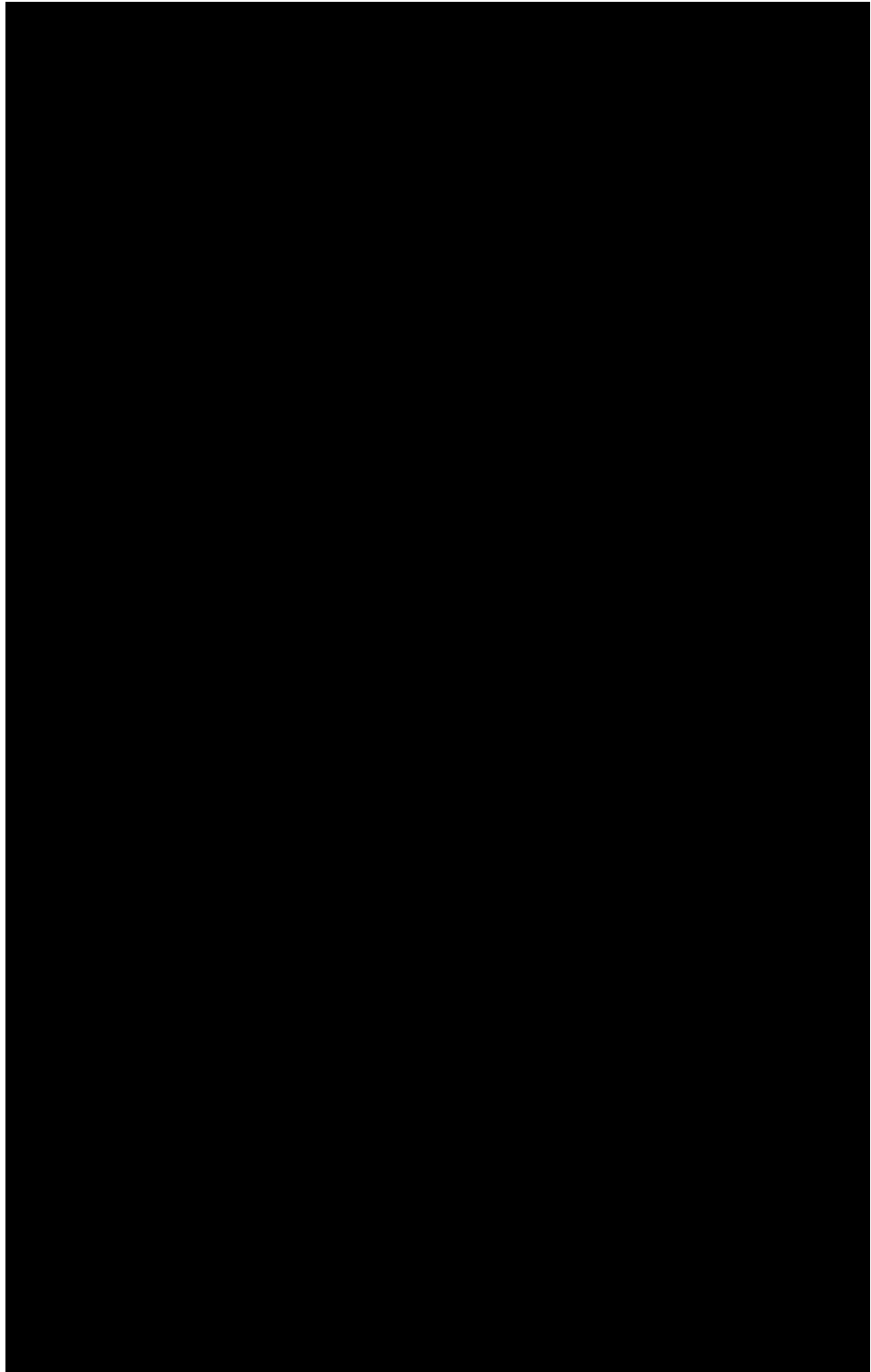


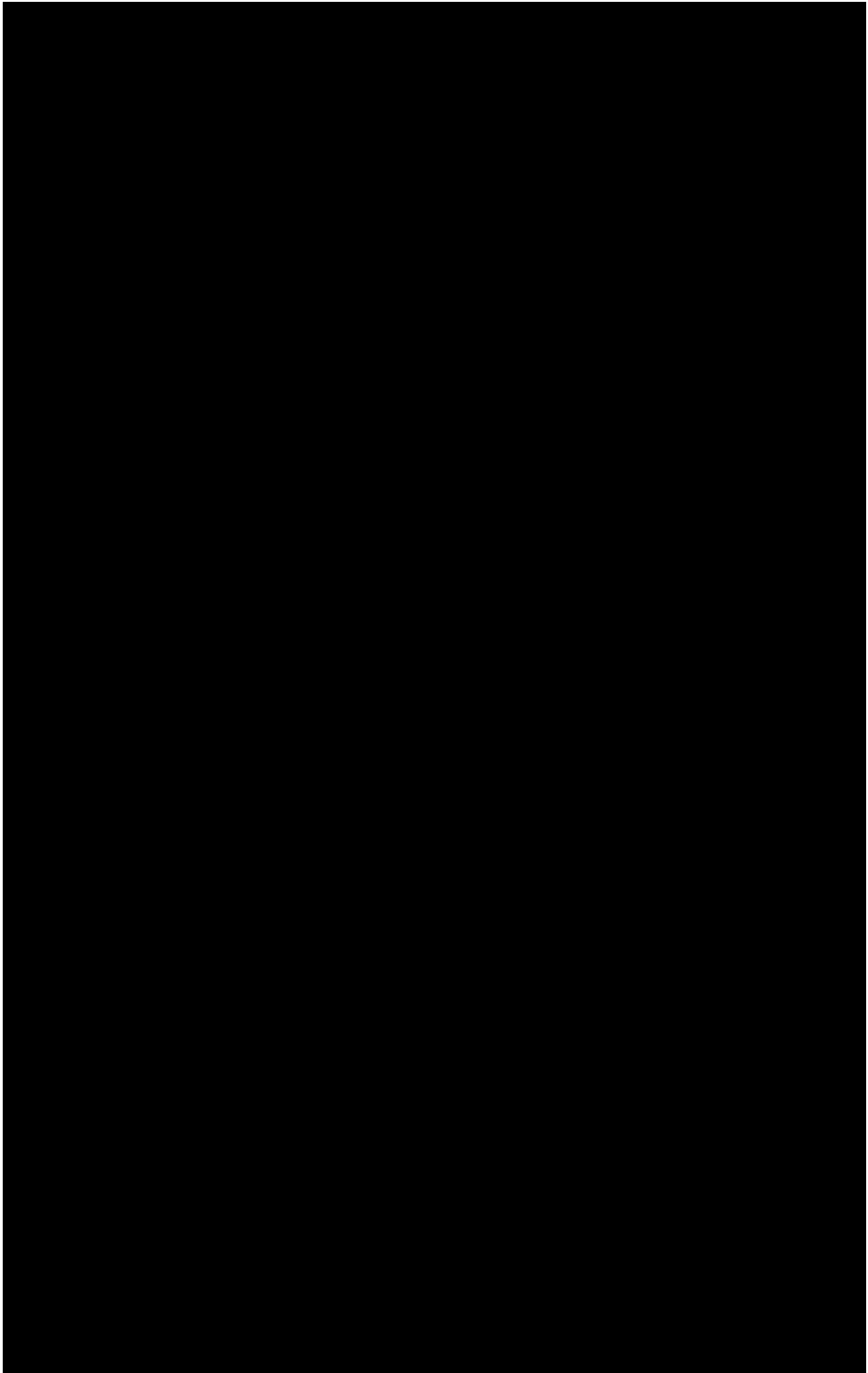


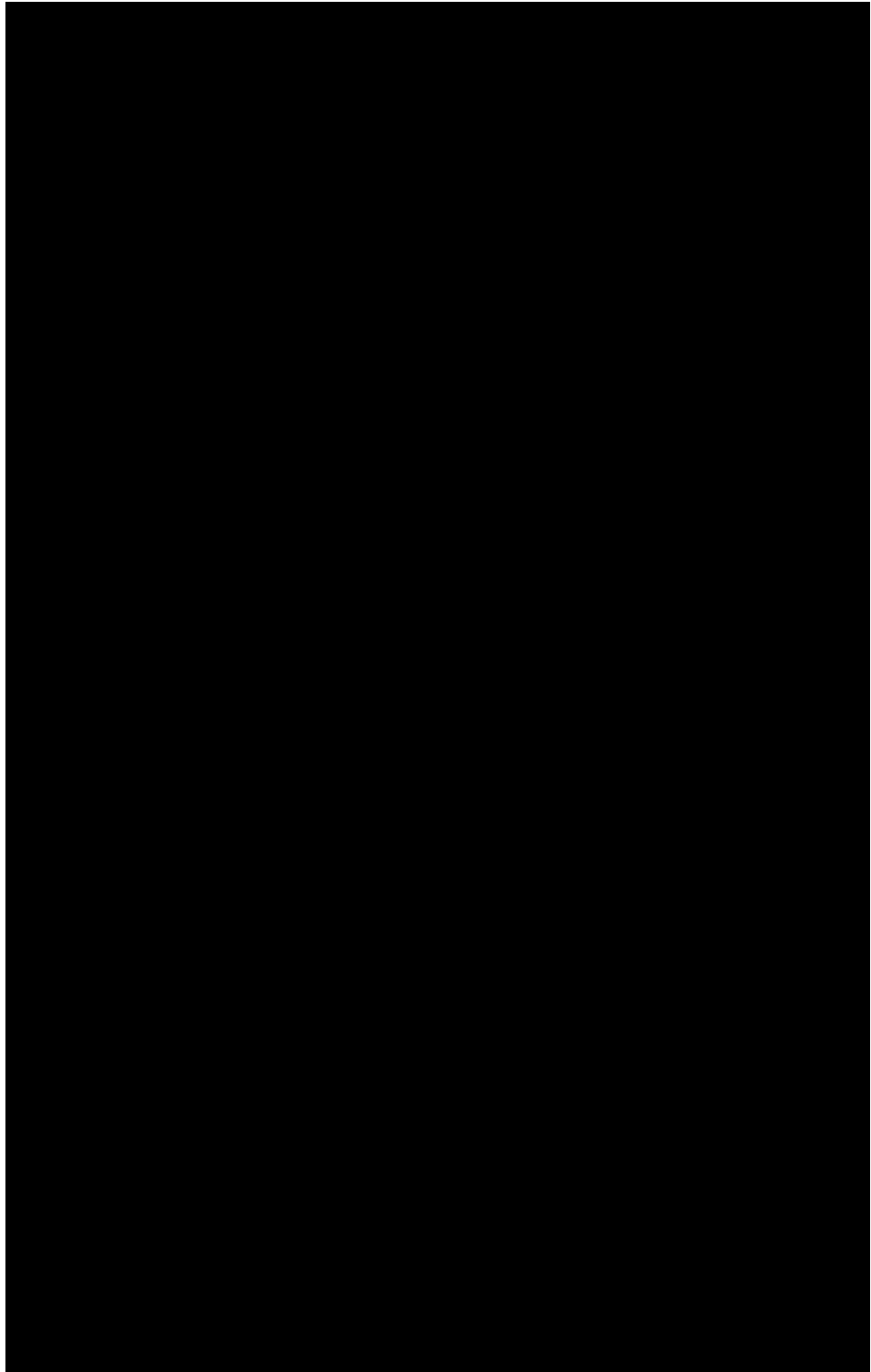


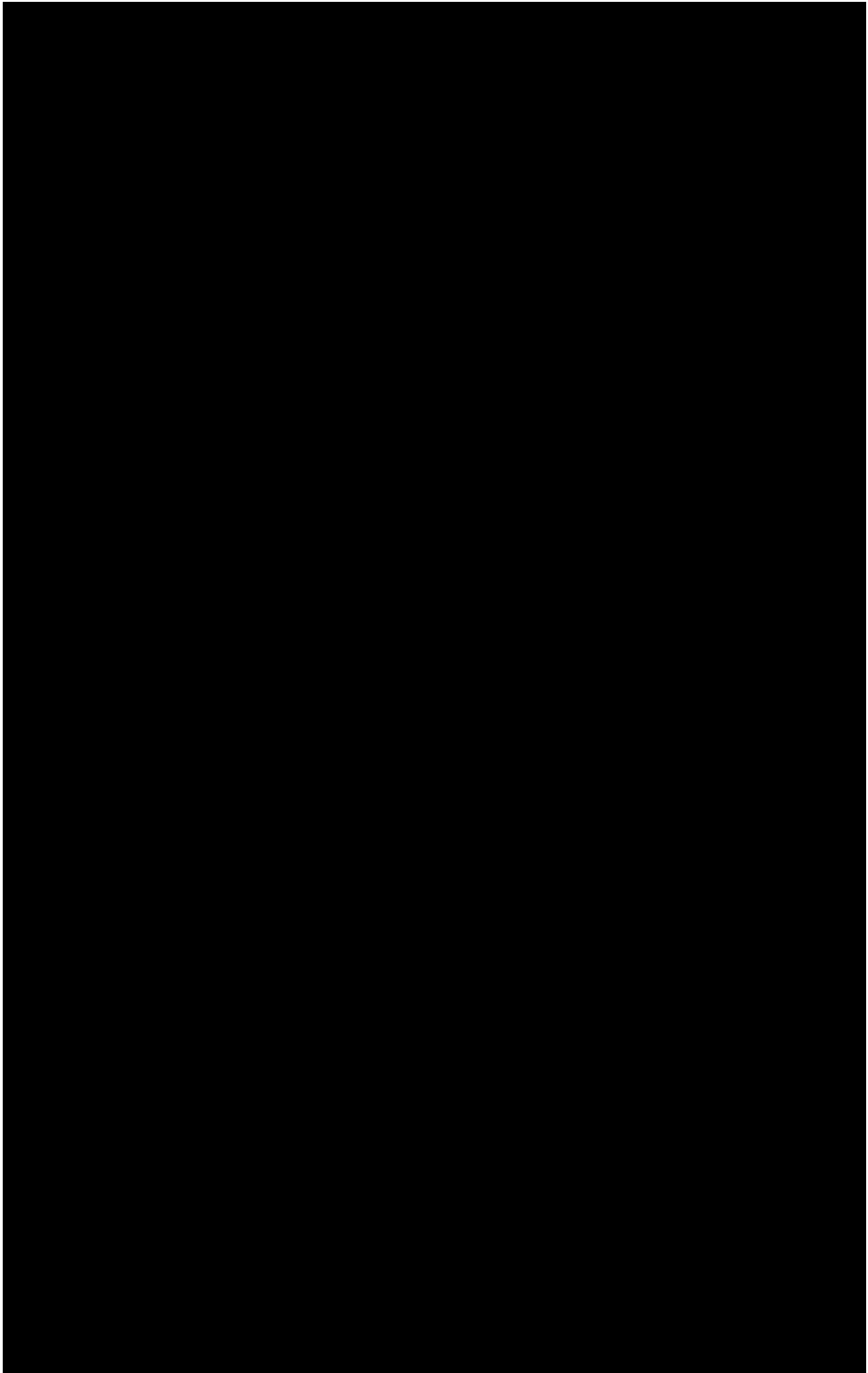














CHAPTER 3

Quality of Life and Relationship Satisfaction of Patients with Obsessive- Compulsive Disorder

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Abstract

Background: Obsessive-compulsive disorder (OCD) affects the life and partner-relationship of patients. Contradictory results were reported on patient characteristics affecting quality of life (QoL). It is unclear whether patients are satisfied with interaction patterns in their relationship that consolidate OCD.

Objective: Identify patient characteristics contributing to QoL and relationship satisfaction of patients with OCD.

Methods: Data of the Netherlands Obsessive-Compulsive Disorder Association (NOCD) were used, including 353 adult patients with a current OCD. The EuroQoL five dimensional questionnaire (EQ-5D) utility score was used to assess QoL. Relationship satisfaction was assessed in a subsample of 213 patients with a partner, using the Relationship Satisfaction Scale (RSS). The examined patient characteristics included sociodemographics, OCD characteristics, psychiatric comorbidity.

Results: QoL was poor (*mean* EQ-5D=0.67; *SD*=0.26) and relationship satisfaction was moderate (*mean* RSS=24.7; *SD*=6.6). Lack of paid employment and more severe comorbid depressive and anxiety symptoms were associated with a poorer QoL. Fewer checking symptoms, more severe comorbid depressive symptoms and the perception that partners lacked emotional support or were irritated were associated with less relationship satisfaction.

Conclusions: To improve QoL and relationship satisfaction, treatment should focus on the perceived interaction with partners, comorbidity and the patients' capacity to work.

Introduction

The quality of life (QoL) of patients with obsessive-compulsive disorder (OCD) is poor. Patients with OCD have significant impairments in well-being and functioning in several life domains, such as social relations, occupation, academic and daily life (Koran et al., 1996; Macy et al., 2013). QoL is reduced in patients who have more severe obsessive-compulsive symptoms and in patients with comorbid depressive and anxiety symptoms (Barahmand et al., 2014; Cassin et al., 2009; Fontenelle et al., 2010; Hollander et al., 2010; Lochner et al., 2003; Subramaniam et al., 2013; Vikas et al., 2011). With respect to other sociodemographic and clinical characteristics affecting QoL contradictory results have been reported. QoL of women with OCD was poorer than that of men (Kugler et al., 2013) but in other studies QoL was equal for both sexes (Hauschildt et al., 2010; Jacoby et al., 2014; Vasudev et al., 2015). Older age (Fontenelle et al., 2010; Hauschildt et al., 2010; Kugler et al., 2013), being married (Eisen et al., 2006) and lower education (Albert et al., 2010; Hauschildt et al., 2010) were associated with a poorer QoL but appeared to be of no influence in other studies (Albert et al., 2010; Fontenelle et al., 2010; Hou et al., 2010; Jacoby et al., 2014; Rapaport et al., 2005; Rodriguez-Salgado et al., 2006). Being in paid employment was related to a better QoL (Fontenelle et al., 2010; Rodriguez-Salgado et al., 2006) but had no association with QoL in another study (Stengler-Wenzke et al., 2007). More severe obsessions but not compulsions were related to a poorer QoL (Eisen et al., 2006; Gururaj et al., 2008; Hou et al., 2010; Masellis et al., 2003), contrasting a study in which it was found that more severe compulsions but not obsessions were related to a poorer QoL (Stengler-Wenzke et al., 2007), while yet other studies found that both obsessions and compulsions were related to a poorer QoL (Hauschildt et al., 2010; Huppert et al., 2009; Rodriguez-Salgado et al., 2006). The OCD subtypes washing, checking and hoarding were related to a poorer QoL (Albert et al., 2010; Fontenelle et al., 2010; Huppert et al., 2009; Moritz et al., 2005), whereas age of onset of OCD was not related to QoL (Masellis et al., 2003; Rodriguez-Salgado et al., 2006).

OCD affects partner-relationships of patients as well. About half of the patients with OCD do not have a partner and those with a partner report significant relationship problems comprising distress, problems with interactional problem solving and trouble with intimacy and self-disclosure (Abbey et al., 2007; P. M. Emmelkamp et al., 1990; Riggs et al., 1992). Partners commonly respond to OCD in two ways: they accommodate (adapt, participate) and/or antagonize (criticize, oppose) (Renshaw et al., 2005). Both responses have a negative impact on the partner and the patient. Accommodation is related to stress, family burden, impaired family functioning and a decreased QoL in family members (Calvocoressi et al., 1995; Cherian et al.,

2014; Kalra et al., 2008; Lebowitz et al., 2016; Lee et al., 2015; Torres et al., 2012). In patients, accommodation is related to more severe obsessive-compulsive symptoms, impaired functioning and poorer treatment results (Cherian et al., 2014; Gomes et al., 2014; Lebowitz et al., 2012, 2016; Strauss et al., 2015; Wu et al., 2016). Antagonism is related to depression, anxiety and a lower QoL in family members (Amir et al., 2000; Cherian et al., 2014) and to impaired functioning and poorer treatment results in patients (Chambless & Steketee, 1999; Leonard et al., 1993; Renshaw et al., 2003; Gail Steketee & Chambless, 2001; Van Noppen & Steketee, 2009).

As far as investigated it appears that patients with OCD are moderately satisfied with their relationship (Staebler et al., 1993; Van Minnen & Kampman, 2000). It could be hypothesized that patients are more satisfied with their relationship when their partners accommodate and not antagonize the obsessive-compulsive symptoms, but research indicates that accommodation of partners is not related to relationship satisfaction of patients with OCD (Boeding et al., 2013). However, another study has reported that patients with anxiety disorders (including OCD) were more satisfied with their relationship when they had the impression that their partner was helping to alleviate their anxiety (Zaider et al., 2010). Remarkably, caregivers of patients with OCD (mostly parents, but also partners) were more satisfied with their relationship with the patient when they experienced a higher level of caregiver burden (Lee et al., 2015). This suggests that patients and their partners are satisfied with interaction patterns that consolidate OCD. It is important to learn more about relationship satisfaction of patients because it might contribute to poor outcome in OCD.

The aim of this study is to examine the QoL and relationship satisfaction of patients with OCD in a large, representative cohort and to explore possible associations with multiple variables, including sociodemographics, OCD characteristics, comorbid psychiatric disorders and perceived level of expressed emotion. More insight in characteristics that influence QoL and relationship satisfaction enables the identification of patients who are most deprived. Also, it might reveal treatment foci to improve treatment for OCD.

Materials and methods

Participants and procedure

Data are derived from The Netherlands Obsessive-Compulsive Disorder Association (NOCDA) study. This is a six-year ongoing longitudinal cohort study to examine the course of OCD. The design of this study has been described in detail elsewhere (Schuurmans et al., 2012). The NOCDA study recruited 419 people of 18 years and

over with a lifetime diagnosis of OCD. All participants provided written informed consent. The OCD diagnosis was verified with the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al., 1995). The present study uses data from the baseline assessment of patients with a current (1-month) OCD diagnosis, which consists of 382 patients. Of this sample, 29 patients were excluded because of missing values on partner status or the dependent variables, resulting in a sample size of 353 patients. Analyses regarding relationship satisfaction were performed on a subsample of OCD patients with a partner (60%; $n=213$).

Primary outcome measures

The self-rated EuroQol five dimensional questionnaire (EQ-5D) was used to assess QoL. This instrument was proven suitable and reliable in the general population and is applicable in patient samples (EuroQol Group, 1990). The EQ-5D contains 5 dimensions: mobility, self-care, daily activities, pain/discomfort and depression/anxiety. Each dimension is rated at three levels: no problems, some problems and major problems. The health states are converted into an index score - the EQ-5D - reflecting the generic overall QoL that can be used to compare QoL in various conditions. The EQ-5D has a value between 1 (best possible health) and 0 (worst possible health).

The Relationship Satisfaction Scale (RSS) was used to assess relationship satisfaction of patients with OCD with a partner. This 9-item self-report inventory was constructed for the NOCDA study. Each item represents a different aspect of the relationship, including 1) daily support from partner, 2) motivation by partner, 3) partners' personality, 4) consideration of partner, 5) sexual relationship with partner, 6) level of intimacy with partner, 7) solutions for differences of opinion, 8) discussing important matters and 9) decision making. Satisfaction on these aspects was assessed on a 5-point scale from 0 (very dissatisfied) to 4 (very satisfied). The internal consistency of the RSS was determined in the current sample and was excellent (Cronbach's $\alpha = 0.91$). In our study the total scores of the RSS were used.

Sociodemographic and clinical characteristics

Sociodemographic and clinical characteristics included age (in years), gender, partner (yes, no), relationship duration (in years), children (yes, no), education (number of years), paid job (yes, no). The severity of OCD was assessed by the Yale Brown Obsessive-Compulsive Scale for Severity (Y-BOCS) (Goodman et al., 1989a; Goodman et al., 1989b). The severity of OCD subtypes was assessed by The Padua Inventory – Revised (PI-R) (Sanavio, 1988; Van Oppen et al., 1995). Age of onset was assessed with the SCID-I as the earliest age at which patients fulfilled the criteria

for OCD. In order to assess the number of current comorbid mental disorders, the ascertained diagnoses on the SCID-I were counted. Comorbid depressive symptoms were measured by the Beck Depression Inventory (BDI) (Beck et al., 1988a; Furlanetto et al., 2005). Comorbid anxiety symptoms were assessed by the Beck Anxiety Index (BAI) (Beck et al., 1988b). The emotional climate in the partner-relationship as perceived by the OCD patient was assessed by the Level of Expressed Emotion (LEE) (Cole & Kazarian, 1988; Gerlsma & Hale, 1997).

Statistical analyses

Characteristics of patients with and without a partner were compared using t-tests for continuous variables and chi-square statistics for categorical variables. We examined the impact of these characteristics on the utility score of the EQ-5D and the total score of the RSS using linear regression analyses. First, associations between potentially associated variables and outcome variables were analysed with simple linear regression analyses. Thereafter, multiple linear regression analyses were conducted including variables showing statistical significance in the simple linear regression analyses ($p < 0.05$). We regarded correlations of 0.80 and above as a sign of multicollinearity (Field, 2009). Furthermore, multicollinearity was checked by means of the Variance Inflation Factor (VIF) and the distribution of variance proportions on eigenvalues. The residuals of the models were normally distributed with some ceiling effect visible in the EQ-5D analyses. A limited number of missing data for some of the variables was present. However, the percentage of missing data was not more than 1%, except for the variables age of onset and relationship duration, each of which had 9% missing data. Missing values of continuous variables were imputed with the mean. Missing values of categorical variables were replaced by the value of the greatest proportion.

Results

Sociodemographic and clinical characteristics

In table 1 the sociodemographic and clinical characteristics are presented. The 213 patients with OCD with a partner (60.3%) were significantly older, were more likely to be female, more likely to have children, had fewer precision symptoms (i.e. doing things in a specific order or in a specific way, compulsions with numbers) and had more frequently a late age of onset compared to patients with OCD without a partner ($n=140$; 39.7%). OCD patients with and without a partner did not differ significantly on presence of schizophrenia, bipolar disorder, hoarding symptoms, tics, attention-deficit hyperactivity disorder and pervasive development disorder (data not shown).

Table 1. Sociodemographic and clinical characteristics of the sample of patients with OCD

	Total sample <i>Mean (SD)</i> or % <i>n=353</i>	With partner <i>Mean (SD)</i> or % <i>n=213</i>	Without partner <i>Mean (SD)</i> or % <i>n=140</i>	t(df) or X²(df); p
Sociodemographics				
Age, years	36.7 (11.0)	38.2 (10.2)	34.4 (11.8)	-3.11(266.5); 0.00*
Gender, female	56.9	63.8	46.4	10.46(1); 0.00*
Partner, yes	60.3	100.0	0.0	
Relationship duration, years	NA	12.0 (9.3)	NA	
Children, yes	35.7	52.1	10.7	63.1(1); 0.00*
Education, years	12.5 (3.2)	12.5 (3.1)	12.5 (3.3)	-0.10(351); 0.92
Paid job, yes	51.8	54.5	47.9	1.5(1); 0.23
OCD characteristics				
Y-BOCS total	21.3 (7.1)	21.2 (7.2)	21.4 (6.9);	0.26(351); 0.79
Y-BOCS obsessions	10.5 (4.0)	10.6 (3.9)	10.4 (4.1);	-0.36(351); 0.72
Y-BOCS compulsions	10.7 (4.3)	10.6 (4.4)	11.0 (4.2)	0.76(351); 0.45
PI-R checking	14.2 (7.6)	14.2 (7.6)	14.2 (7.6)	-0.18(351); 0.86
PI-R impulses	6.1 (6.4)	6.2 (6.6)	6.0 (6.2)	-0.23(351); 0.82
PI-R precision	7.0 (6.1)	6.4 (5.8)	7.9 (6.4)	2.20(276.0); 0.03*
PI-R rumination	23.1 (8.6)	23.0 (8.3)	23.3 (9.0)	0.26(351); 0.80
PI-R washing	11.8 (11.4)	11.7 (11.4)	12.1 (11.4)	0.24(351); 0.81
Age of onset OCD	18.1 (9.0)	18.9 (9.4)	16.7 (8.3)	-2.30(322.6); 0.02*
Comorbidity				
Number of current comorbid psychiatric disorders	2.0 (1.2)	2.0 (1.2)	2.0 (1.1)	-0.04(351); 0.97
Beck Anxiety Index	18.2 (11.9)	18.5 (12.4)	17.8 (11.0);	-0.51(351); 0.61
Beck Depression Inventory	16.0 (9.9)	15.9 (10.0)	16.3 (9.7);	0.36(351); 0.72
Psychological variables				
QoL	0.67 (0.26)	0.68 (0.26)	0.67 (0.27)	-0.27(351); 0.79
Relationship satisfaction	NA	24.7 (6.6)	NA	
Level of Expressed Emotion				
Perceived criticism	NA	8.7 (3.0)	NA	
Perceived intrusiveness	NA	12.0 (5.1)	NA	
Perceived irritation	NA	13.0 (4.7)	NA	
Perceived lack of emotional support	NA	31.1 (11.1)	NA	

Missing values were imputed by the mean

* $p < 0.05$

NA not applicable

Quality of life

The mean EQ-5D utility score was 0.67 ($SD=0.26$), indicating a poor QoL (Szende et al., 2014). The results of the simple and multiple regression analyses of the EQ-5D utility score are presented in Table 2. Being in paid employment was associated with a better QoL. More severe OCD, more severe obsessions, more severe compulsions, more severe symptoms of all OCD subtypes, presence of comorbid psychiatric disorders as well as more severe anxiety and depression, were all associated with a poorer QoL in the simple regression analyses. The Y-BOCS total score was excluded from the multiple regression analyses because of collinearity with the Y-BOCS subscales obsessions and compulsions. In the multiple regression analyses the associations of having a paid job and severity of comorbid anxiety and depressive symptoms with QoL remained significant. The *R square* of this model is 0.42, indicating 42% explained variance. When the Y-BOCS total score was entered in the multiple regression analysis instead of the Y-BOCS obsessions and compulsions subscales, the same result emerged: the associations of having a paid job and severity of comorbid anxiety and depressive symptoms with QoL remained significant (results not presented).

In addition, separate analyses were performed with OCD subscales as assessed with the Y-BOCS Symptom Checklist (Goodman et al., 1989a; Goodman et al., 1989b). In the simple regression analyses aggressive ($stB=-0.152, p=0.00$), contamination ($stB=-0.176, p=0.00$), religious ($stB=-0.143, p=0.01$), symmetry ($stB=-0.120, p=0.02$), somatic ($stB=-0.187, p=0.00$) and miscellaneous obsessions ($stB=-0.119, p=0.03$) and cleaning ($stB=-0.106, p=0.05$), checking ($stB=-0.113, p=0.03$) and miscellaneous compulsions ($stB=-0.117, p=0.03$) were significantly associated with QoL; sexual and hoarding obsessions as well as repeating, counting, ordering and hoarding compulsions were not significantly associated with QoL. When the significantly associated Y-BOCS subscales were entered in the multiple regression analysis along with paid job, severity of obsessions and compulsions, presence of comorbid psychiatric disorders and severity of anxiety and depression only the associations of contamination ($stB=-0.152, p=0.00$) and symmetry obsessions ($stB=-0.088, p=0.05$), having a paid job ($stB=0.103, p=0.02$) and severity of comorbid anxiety ($stB=-0.337, p=0.00$) and depressive symptoms ($stB=-0.372, p=0.00$) with QoL remained significant (*R square*=0.45).

Table 2. Bivariate and multivariate associations between possible associated variables and the QoL of patients with OCD ($n=353$)

EQ-5D utility score	Bivariate associations			Multivariate associations		
	stB	t	p	stB	t	p
Sociodemographics						
Age, years	-0.100	-1.88	0.06			
Gender, female	0.004	0.08	0.94			
Partner, yes	0.014	0.27	0.79			
Children, yes	0.004	0.08	0.93			
Education, years	0.100	1.89	0.06			
Paid job, yes	0.272	5.30	0.00*	0.105	2.42	0.02*
OCD characteristics						
Y-BOCS total	-0.277	-5.39	0.00*			
Y-BOCS obsessions	-0.265	-5.15	0.00*	-0.011	-0.23	0.82
Y-BOCS compulsions	-0.208	-3.99	0.00*	0.025	0.47	0.64
PI-R checking	-0.180	-3.44	0.00*	0.008	0.15	0.89
PI-R impulses	-0.314	-6.20	0.00*	0.008	0.16	0.88
PI-R precision	-0.229	-4.40	0.00*	0.015	0.29	0.78
PI-R rumination	-0.422	-8.72	0.00*	-0.024	-0.39	0.70
PI-R washing	-0.227	-4.37	0.00*	-0.080	-1.74	0.08
Age of onset OCD	0.004	0.07	0.94			
Comorbidity						
Number of current comorbid psychiatric disorders	-0.322	-6.37	0.00*	0.041	0.80	0.43
Beck Anxiety Index	-0.552	-12.39	0.00*	-0.300	-4.97	0.00*
Beck Depression Inventory	-0.590	-13.69	0.00*	-0.368	-5.74	0.00*

Due to collinearity Y-BOCS total score was excluded from the multivariate analyses

* $p < 0.05$

Table 3. Bivariate and multivariate associations between possible associated variables and relationship satisfaction of patients with OCD ($n=213$)

Relationship Satisfaction Score	Bivariate associations			Multivariate associations		
	stB	t	p	stB	t	p
Sociodemographics						
Age, years	-0.130	-1.90	0.06			
Gender, female	0.012	0.18	0.86			
Relationship duration, years	-0.087	-1.26	0.21			
Children, yes	-0.138	-2.03	0.04*	-0.028	-0.53	0.59
Education, years	0.057	0.82	0.41			
Paid job, yes	0.092	1.34	0.18			
OCD characteristics						
Y-BOCS total	-0.068	-0.99	0.32			
Y-BOCS obsessions	-0.071	-1.04	0.30			
Y-BOCS compulsions	-0.048	-0.69	0.49			
PI-R checking	0.161	2.37	0.02*	0.128	2.39	0.02*
PI-R impulses	-0.084	-1.22	0.23			
PI-R precision	-0.086	-1.26	0.21			
PI-R rumination	-0.038	-0.56	0.58			
PI-R washing	0.007	0.10	0.92			
Age of onset OCD	-0.034	-0.49	0.63			
Comorbidity						
Number of current comorbid psychiatric disorders	-0.177	-2.61	0.01*	0.000	0.00	1.00
Beck Anxiety Index	-0.091	-1.33	0.19			
Beck Depression Inventory	-0.284	-4.30	0.00*	-0.158	-2.51	0.01*
Psychological variables						
Level of Expressed Emotion						
Perceived criticism	-0.520	-8.85	0.00*	-0.028	-0.35	0.73
Perceived intrusiveness	-0.246	-3.68	0.00*	-0.022	-0.38	0.71
Perceived irritation	-0.457	-7.46	0.00*	-0.137	-2.11	0.04*
Perceived lack of emotional support	-0.646	-12.28	0.00*	-0.495	-6.24	0.00*

* $p < 0.05$

Relationship satisfaction

The mean score of the RSS (relationship satisfaction) of patients with OCD with a partner was 24.7 ($SD=6.6$), indicating a moderate relationship satisfaction. The results of the simple and multiple regression analyses of associated variables with RSS are presented in Table 3. In the simple regression analyses, having children, fewer checking symptoms, more current comorbid psychiatric disorders, more severe comorbid depressive symptoms and a perceived larger amount of criticism, intrusiveness, irritation and lack of emotional support were all associated with less relationship satisfaction. In the multiple regression analyses, fewer checking symptoms, more severe comorbid depressive symptoms and a perception of irritation and absence of emotional support within relationships continued to contribute significantly to poor relationship satisfaction ($R\ square=0.47$).

In addition, separate analyses were performed with OCD subscales as assessed with the Y-BOCS Symptom Checklist (results not presented). None of the OCD subscales was significantly associated with relationship satisfaction in the simple regression analyses.

Discussion

The QoL of this sample of patients with OCD was poor. Having a paid job was associated with a better QoL while more severe depressive and anxiety symptoms were associated with a poorer QoL. Sixty percent of the patients with OCD had a partner. In general, patients with a partner were moderately satisfied with their relationship. More checking symptoms were associated with more relationship satisfaction. More severe comorbid depressive symptoms and a perceived larger amount of irritation by the partner and a lack of emotional support were associated with less relationship satisfaction. Severity of obsessions and compulsions were not associated with QoL or relationship satisfaction.

The utility score indicating QoL of this sample of patients with OCD (0.67) is substantially lower than that of the general Dutch population (which is 0.89) and comparable to that of patients with schizophrenia (0.68), anxiety disorders in general (0.69) and patients with, for example, rheumatoid arthritis (0.66) (Marra et al., 2004; McCrone et al., 2009; Saarni et al., 2007; Szende et al., 2014). Sixty percent of the patients with OCD had a partner which is a smaller proportion than in the general Dutch population (72%) (CBS, 2009) and also a smaller proportion than in patients with a depressive or anxiety disorder (67%) (Prins et al., 2010). Patients with a partner were more likely to be female, have children and have a later age

of onset of OCD compared to patients without a partner, which is consistent with previous findings (Anholt et al., 2014; Castle et al., 1995). Possibly, early age onset of OCD limits the experience of adolescent romance during teenage years, leading to a decreased competence in interacting romantically in later life. In general, patients with a partner were moderately satisfied with their relationship which is in line with earlier findings (Staebler et al., 1993; Van Minnen & Kampman, 2000). Research also indicates that the marital satisfaction of patients with OCD is worse than those of healthy controls and comparable to those patients who experience panic and depressive symptoms (Staebler et al., 1993; Van Minnen & Kampman, 2000; Whisman, 1999). The perceived level of expressed emotion of this sample of patients with OCD is comparable to a clinical sample of psychiatric patients (Gerlsma & Hale, 1997).

More severe comorbid depressive and anxiety symptoms were associated with a poorer QoL, which is consistent with previous findings (Fontenelle et al., 2010; Huppert et al., 2009). More severe comorbid depressive symptoms were also associated with less relationship satisfaction, corroborating previous research indicating that comorbidity with other mental disorders in general and depression specifically are related to marital discord (Denton et al., 2003). These results stress the importance of treating comorbid depressive and anxiety symptoms.

Having a paid job was associated with a better QoL. Previous findings on this were contradictory (Fontenelle et al., 2010; Rodriguez-Salgado et al., 2006; Stengler-Wenzke et al., 2007). The other sociodemographic variables were not associated with QoL or with relationship satisfaction. Previously, mixed results have been found regarding the association between sociodemographic variables and QoL (Albert et al., 2010; Eisen et al., 2006; Fontenelle et al., 2010; Hauschildt et al., 2010; Huppert et al., 2009; Jacoby et al., 2014; Rodriguez-Salgado et al., 2006). These mixed results may be caused because of small effect sizes by which results may become whether or not significant depending on specific research design, instruments and sample characteristics. Also in our study the effect sizes of the association between sociodemographics and QoL were small, and therefore of limited clinical relevance. Our results indicate that QoL of patients with OCD might be enhanced by increasing the patients' capacity to work.

Severity of OCD was associated with QoL in the univariate regression analysis but this association disappeared in the multiple regression analysis, indicating that other factors are more important. This finding seems contradictory to previous research results (Eisen et al., 2006; Vikas et al., 2011). However, closer inspection

of most studies reveals that only univariate correlations (and not multivariate regression analyses) were used to examine the relationship between severity of OCD and QoL, not allowing for controlling for confounding effects (see also Subramaniam et al., 2013). One could assume that if OCD is mild, severity is not indicative of QoL. However, since the mean severity of OCD of our sample is in the range of that of other studies, our finding cannot be explained by the hypothesis that our sample would only be mildly ill. In our study, the effect of severity of OCD as well as the effect of severity of obsessions and compulsions on QoL are surpassed by the effect of comorbid depressive and anxiety symptoms which suggests that not the severity of OCD in itself affects QoL, but rather the overall burden of depressive and anxiety symptoms. Our finding is in line with a conclusion of a review article that comorbid depression has a stronger effect on QoL than severity of OCD (Subramaniam et al., 2013). In addition, research has indicated that comorbid depressive symptoms mediate the effect of OCD severity on QoL: obsessive-compulsive and depressive symptoms reinforce each other in the withdrawal from daily activities and thus contribute to a poorer QoL (Kugler et al., 2013).

None of the OCD subtypes as assessed with the Padua Inventory - Revised was associated with QoL in the multiple regression analyses. Contamination and symmetry obsessions as assessed with the Y-BOCS symptom checklist appeared significantly associated with QoL in the multiple regression analyses. Our results – derived from two instruments – do not corroborate each other. Indeed, research has demonstrated that the correlation between the Y-BOCS and the Padua Inventory is rather low and that they cover relatively unrelated features of OCD (Anholt et al., 2009). Our study showed mixed results regarding OCD subtype washing which partly confirms research indicating that washing symptom dimensions were related to a poorer QoL (Albert et al., 2010; Fontenelle et al., 2010; Huppert et al., 2009). We did not find a relation between checking and hoarding symptom dimensions and QoL which is not consistent with research indicating that these were related to a poorer QoL (Fontenelle et al., 2010; Hollander et al., 2010; Moritz et al., 2005). More research is needed to understand the relation between OCD subtype and QoL.

The severity of OCD, obsessions and compulsions, was not associated with relationship satisfaction. Previous findings were mixed (Abbey et al., 2007; Emmelkamp et al., 1990; Riggs et al., 1992). Hypothetically, for patients the severity of OCD does not affect their relationship satisfaction directly but rather the extent to which it leads to problems in the relationship. This in turn might indicate that patients are more satisfied when their partners accommodate obsessive-compulsive symptoms. This is important, as accommodation by the partner is not preferable

because it consolidates OCD (Renshaw et al., 2005). However, research has shown contradictory results concerning the last hypothesis (Boeding et al., 2013; Zaider et al., 2010). Our findings that OCD severity does not deteriorate relationship satisfaction or QoL might imply that reducing obsessive-compulsive symptoms in treatment does not improve relationship satisfaction or QoL of patients with OCD. Therefore, decreasing OCD and improving relationship satisfaction and QoL should be addressed as separate goals in treatment.

More checking symptoms as assessed with the Padua Inventory - Revised were associated with more relationship satisfaction. None of the OCD subtypes as assessed with the Y-BOCS symptom checklist appeared significantly associated with relationship satisfaction, also not checking compulsions. Possibly, our result is due to chance. Hypothetically, patients who are satisfied with their relationship check more because they are more anxious about their partner compared to patients who are less satisfied with their relationship. After all, checking symptoms often aim to prevent harm to loved ones. A previous study has shown that some obsessive-compulsive symptoms contribute to more relationship satisfaction, but with other symptoms, namely washing and neutralizing compulsions (Abbey et al., 2007). Not much research is done on this subject and hence, research is necessary to unravel what (and why) specific obsessive-compulsive symptoms contribute to relationship satisfaction of patients.

A larger amount of perceived irritation and lack of emotional support were associated with less relationship satisfaction. The last result is consistent with research on patients with anxiety disorders (Zaider et al., 2010). These may be good foci for treatment: to teach patients with OCD and the partner how to deal with irritation and provide emotional support while not accommodating or antagonizing obsessive-compulsive symptoms as these responses consolidate OCD and are associated with symptoms, impaired functioning in patients and partners and a poorer QoL of partners. Addressing perceived irritation and perceived lack of emotional support in treatment may also improve obsessive-compulsive symptoms as the perceived level of expressed emotion is associated with treatment outcome (Chambless & Steketee, 1999).

This study has several limitations. First, due to cross-sectional analyses we assessed associations and not causal connections between possibly associated variables and dependent variables. Future research should thus examine whether treating the significantly associated variables of our study indeed improves QoL and relationship satisfaction of patients with OCD. A second limitation is that we did not collect data of the partners of the patients, for instance, their relationship satisfaction and

accommodation. This would have provided a more complete picture of the quality of the relationship and interaction styles and, more specifically, the relation between accommodation and relationship satisfaction. Third, our QoL instrument cannot be assorted in subscales, therefore it is not possible to determine the effect of associated variables on subdivided domains of QoL. However, the EQ-5D is a generic instrument that can be reliably applied in various patient populations. Fourth, our results are generalizable to mild to moderately ill patients and not to those with severe OCD. Last, we did not have a control group in our study.

In conclusion, the QoL of patients with OCD in our study was poor and their relationship satisfaction was moderate. These findings underline the importance of identifying patients with OCD at high risk of a very low QoL and low relationship satisfaction and to find treatment foci to improve same. Our study indicated that not severity of OCD but being in paid employment and comorbid depressive and anxiety symptoms were associated with QoL. More checking symptoms were associated with more relationship satisfaction while more severe comorbid depressive symptoms and a perceived larger amount of irritation by the partner and a lack of emotional support were associated with less relationship satisfaction. These results imply that reducing obsessive-compulsive symptoms on the one hand and improving QoL and relationship satisfaction on the other hand should be addressed as separate goals in treatment. Treatment of OCD might be improved by increasing the patients' capacity to work, treating comorbid anxiety and depressive symptoms and couples therapy that focuses on learning how to deal with irritability and how to offer emotional support.

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CHAPTER 4

Four-year Course of Quality of Life and Obsessive-Compulsive Disorder

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Abstract

Objective: Patients with obsessive-compulsive disorder (OCD) have high disease burden. It is important to restore quality of life (QoL) in treatment, so that patients become able to live a fulfilling life. Little is known about the longitudinal course of QoL in patients with OCD, its association with remission from OCD, and about factors that contribute to an unfavourable course of QoL in remitting patients.

Methods: Study on the four-year course of QoL of patients with chronic ($n=144$), intermittent ($n=22$) and remitting OCD ($n=73$) using longitudinal data of the Netherlands Obsessive-Compulsive Disorder Association (NOCDA; complete data: $n=239$; imputed data $n=382$). The EuroQol five dimensional questionnaire (EQ-5D) utility score was used to assess QoL. In patients with remitting OCD, we examined patient characteristics that contributed to an unfavourable course of QoL, including sociodemographics, OCD characteristics, psychiatric comorbidity, and personality traits.

Results: Course of QoL was associated with course of OCD. QoL improved in those who remitted from OCD; however, even in these patients, QoL remained significantly below the population norms. The correlation between QoL and severity of OCD was only moderate: $r=-0.40$ indicating that other factors besides OCD severity contribute to QoL. In remitters, more severe anxiety and depression symptoms were related to a lower QoL. Results were similar in complete and imputed datasets.

Conclusions: Remission from OCD is associated with improvement of QoL but comorbid anxiety and depression symptoms hamper the improvement of QoL. QoL could be improved by reducing OCD symptoms in patients with OCD and by treating comorbid anxiety and depression symptoms in remitting patients.

Introduction

Patients with mental disorders like schizophrenia, major depressive disorder, anxiety disorders and obsessive-compulsive disorder (OCD) experience an impaired quality of life (QoL) compared with the general population. The WHO defines QoL as ‘an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.’ (<https://www.who.int/healthinfo/survey/whoqol-qualityoflife>; page 1). Thus, QoL is a complex concept, dependent of the ability of a person to function in life domains such as his/her physical health, psychological state and social relationships (Lam et al., 2011). It is well known that mental disorders impact on the ability to function in these life domains, and hence, have a strong impact on QoL.

The relationship between psychopathology and QoL, however, is complex. In particular following successful treatment of the index mental disorder, QoL is often not restored to the level of the general population, which implies that remitted patients still may experience problems in their daily physical, psychological, and social functioning (Ardal et al., 2013; Koran et al., 2010). For example, in patients with schizophrenia, it was found that 3-months to 2-years following successful treatment QoL was either improved (Nuttall et al., 2019; Priebe et al., 2011) or had not changed (Bystritsky et al., 2001; Huppert & Smith, 2001; Laws et al., 2018). Fluctuations in QoL in schizophrenia appeared to depend more on severity of comorbid depressive and anxiety symptoms and psychosocial factors than on presence and severity of psychotic symptoms (Priebe et al., 2011; Ritsner et al., 2012), indicating that factors other than the severity of the disorder itself impact on QoL. Likewise, in patients with major depressive disorder and anxiety disorders, QoL improved after treatment, but levels of QoL remained below population norms, even when patients were remitted (Ardal et al., 2013; Davidoff et al., 2012; Hofmann et al., 2014; Moses et al., 2006; ten Doesschate et al., 2010).

OCD is a mental disorder with a tremendous impact on QoL, underlining the need to fully understand the relationship between OCD and QoL (Coluccia et al., 2016; Macy et al., 2013). In the same vein as schizophrenia, in anxiety and depressive disorders, generally, it was shown that QoL was not fully restored following successful treatment (Subramaniam et al., 2013). For example, after treatment with eighteen sessions of exposure in vivo with response prevention, OCD symptom severity and QoL improved significantly although QoL remained below community norms (Endicott et al., 1993; Simpson et al., 2010). Likewise, in a randomized controlled trial comparing the effect of SRI augmentation with eight weeks of either exposure in vivo

with response prevention, risperidone or pill-placebo, QoL improved significantly only in the exposure and response prevention condition; however, it did not reach the level of the general population, even though OCD symptom severity decreased significantly in all conditions (Asnaani et al., 2017). In contrast, QoL did improve up till the level of the general population – and OCD symptom severity decreased – in a study in which patients received escitalopram for 16 weeks (Dougherty et al., 2009).

Although such short-term outcomes are informative to evaluate direct treatment-effects, changes in QoL may require more time. For example, social functioning requires to make contact with other people and to build a social network. Moreover, sustained outcomes may be more important than short-term successes. Data from studies with longer timeframes suggest that over time, OCD severity further decreases and QoL further improves, but also after longer follow-up periods, QoL still remains significantly impaired compared to that of healthy controls. For example, in long-term pharmacological treatment studies, it was found that OCD severity and QoL improved after 24 to 52 weeks of treatment with, respectively, fluvoxamine, fluoxetine, escitalopram, or paroxetine (Hollander et al., 2010; Koran et al., 2010; Srivastava et al., 2011). Albeit improved, in all these three studies, QoL at follow-up remained below community norms. In addition, most aspects of QoL, except social QoL, were significantly improved after 12 months of multimodal inpatient treatment, mainly consisting of exposure in vivo with response prevention but, also in this study, QoL remained below population norms (Hertenstein et al., 2013). Finally, after 3-5 years of treatment with deep brain stimulation, severity of OCD and QoL were improved, except social QoL, but QoL remained below community norms (Ooms et al., 2014).

The general finding that, both in short-term and in longer-term studies, OCD symptom reduction is not equated with regaining QoL suggests that factors other than OCD impact on QoL. Indeed, various longitudinal treatment studies indicate that OCD symptom reduction is not or only weakly related to QoL improvement (Ooms et al., 2014; Srivastava et al., 2011; Subramaniam et al., 2013) and to improvement of depressive symptoms (Hertenstein et al., 2013). Cross-sectional studies examining the factors associated with QoL in OCD report a variety of factors to impact on QoL in OCD patients, including older age, female sex, unemployment, contamination, hoarding and symmetry symptom dimensions, over-responsibility for harm, comorbid anxiety and depression symptoms, low social status and perceived low social support (Coluccia et al., 2016; Fontenelle et al., 2010; Hou et al., 2010; Jahangard et al., 2018; Remmerswaal et al., 2016; Schwartzman et al., 2017; Subramaniam et al., 2013; Velloso et al., 2018). However, due to the cross-sectional design of these studies causal inferences cannot be made.

To get a clear understanding of the long-term course of QoL and its association with OCD, long follow-up periods are needed given the chronic course of OCD and the time required for changes in QoL. A longitudinal design is also required to obtain a clearer view on the factors associated with an unfavourable course of QoL in remitting patients. Malleable predictors may personalize treatment and improve outcome of QoL in patients with OCD.

The goal of the present study was 1) to explore the four-year course of QoL in a large, representative cohort of patients with OCD, 2) to investigate the association between course of QoL and course of OCD and 3) to identify predictors of an unfavourable course of QoL in patients with remitting OCD. For this study, we have selected predictors that have been associated with QoL in OCD or with course and severity of OCD, such as sociodemographic variables, clinical variables, personality traits (Fullana et al., 2004; Stavropoulos et al., 2017) and the quality of the support from the social network (Palardy et al., 2018), which is also determined by need for affiliation and attachment style of the patient (Gillath et al., 2019; Van Tilburg, 1988). We hypothesized that: 1) QoL improves over time but remains lower than the QoL of the general population even after four years; 2) QoL and OCD are weakly correlated; 3) course of QoL is dependent on various factors other than OCD.

Methods

Procedure

Data were derived from The Netherlands Obsessive-Compulsive Disorder Association (NOCDA) study, an ongoing longitudinal cohort study investigating the naturalistic long-term course of OCD in patients referred to mental health care centres and to examine determinants in predicting the course of OCD. The NOCDA study design and baseline characteristics of the study sample are described in detail elsewhere (Schuurmans et al., 2012). The NOCDA study was accredited by the Medical Ethical Committee of the VU-university Medical Centre in 2005.

After intake at one of the contributing mental health clinics, 687 patients aged 18 years and over with a lifetime diagnosis of OCD, as determined by the administration of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al., 1995), were asked to participate in the NOCDA study. Since NOCDA aims to follow a large representative sample of OCD subjects in different stages of the disease and with different degrees of illness severity, the only exclusion criterion was an inadequate understanding of the Dutch language for the purposes of the completion

of interviews and self-report questionnaires. Comprehensive measurements were done at baseline and after two and four years.

Of the 687 patients who were asked to participate in the NOCDA study, 419 (60.9%) gave written informed consent and were enrolled in the study. A comparison on basic demographic characteristics between patients that did ($n=419$) and did not ($n=268$) agree to participate yielded no significant differences.

Baseline measurements took place between 2005 and 2009 and included validated semi-structured interviews and self-report questionnaires to gather information on a broad range of variables related to (amongst others) OCD, comorbidity and psychosocial consequences. The baseline assessment took about five hours. All included participants were contacted after two years and four years for follow-up, irrespectively of their treatment status. The 2-year and 4-year assessments took about 3 hours and in most cases (80%) they were done by the same research assistant. During the follow-up period, participants received treatment as usual that was based on Dutch multidisciplinary guidelines.

Participants in the present study

In the present study only those patients who had a current OCD diagnosis at baseline were included, pertaining to 382 patients at baseline, 278 patients at two-year follow-up (total dropout 27%) and 268 patients at four-year follow-up (total dropout 30%). Of 239 patients complete SCID data at baseline, two and four years were available. Patients with incomplete data did not differ significantly from those with complete data on sociodemographic and clinical characteristics except that they were younger ($F(1,380)=4.16$; $p=0.04$) and less educated ($F(1,380)=23.17$; $p<0.01$).

Patients were divided in three groups: chronic (current diagnosis of OCD at baseline, two- and four-year follow-up; $n=144$), intermittent (current diagnosis of OCD at baseline and four-year follow-up but not at two-year follow-up; $n=22$) and remitting (current diagnosis of OCD at baseline but not at four-year follow-up, irrespectively of diagnostic status at two-year follow-up; $n=73$). This study is reported conform the STROBE statement (2008).

Primary outcome measure: QoL

The self-rated EuroQoL five dimensional questionnaire (EQ-5D) was used to assess QoL. It is a widely used, generic QoL instrument. It is applicable in many populations and can be used to compare QoL in various conditions. The EQ-5D contains 5 dimensions significant for QoL: mobility, self-care, daily activities, pain/discomfort and depression/anxiety. Each dimension is rated at three levels: no problems, some

problems and major problems. These health states are converted into an index score - the EQ-5D - reflecting the generic overall QoL. The EQ-5D has a value between 1 (best possible health) and 0 (worst possible health). The EQ-5D was proven reliable, valid and feasible (EuroQol Group, 1990; Hurst et al., 1997; König et al., 2010; Pitkänen et al., 2012; Van Agt et al., 2005).

Potential predictors of course of QoL in remitting patients

Repeatedly measured variables included severity of OCD, number of current comorbid mental disorders, comorbid anxiety and depressive symptoms, loneliness, need for affiliation, social support and social network. These were assessed at baseline, two- and four-year follow-up. The variable time of remission was determined on the basis of the time-dependent variable current diagnosis of OCD but is not itself a time-dependent variable. All other characteristics were assessed at baseline only: sociodemographics, age of onset, personality characteristics, attachment style and perceived expressed emotion.

Sociodemographic characteristics included age (in years), gender, partner (yes, no), children (yes, no), education (number of years) and employment (yes, no). The severity of OCD was assessed by the Yale Brown Obsessive-Compulsive Scale for Severity (Y-BOCS) (Goodman et al., 1989a; Goodman et al., 1989b). The interrater reliability (ICC=0.96) and test-retest reliability (ICC=0.85) of the Y-BOCS are high (Storch et al., 2010). Age of onset of OCD was assessed with the SCID-I as the earliest age at which patients fulfilled the criteria for OCD. In case of remission, time of remission was defined as early (remission at two-year follow-up) or late (remission at four-year follow-up). In order to assess the number of current comorbid mental disorders, the ascertained diagnoses on the SCID-I were counted. Interrater reliability of the SCID-I is fair to excellent and the test-retest reliability and validity are substantial (Lobbestael et al., 2011; Shankman et al., 2018). Comorbid depressive symptoms were measured by the Beck Depression Inventory (BDI) (Beck et al., 1988; Furlanetto et al., 2005). Comorbid anxiety symptoms were assessed by the Beck Anxiety Inventory (BAI) (Beck et al., 1988). Furthermore, personality characteristics according to the Big Five were assessed with the Five-Factor Personality Inventory (FFPI) (Hendriks et al., 1999). Subscales of the FFPI are: extraversion, agreeableness, conscientiousness, emotional stability and autonomy. Attachment style was assessed with the General Attachment Style Questionnaire (Griffin & Bartholomew, 1994), with the subscales: dismissing, preoccupied, fearful and secure. Loneliness was assessed with the Loneliness Scale (de Jong-Gierveld & Kamphuis, 1985), subscales: emotional loneliness and social loneliness. The need for affiliation was assessed with the Need for Affiliation Scale (Van Tilburg, 1988). Social support was assessed with the Social Support Inventory (Brown et al., 1987). Subscales of the SSI are: emotional support, informative support,

social companionship and instrumental support. Perceived expressed emotion of significant others was assessed with the Level of Expressed Emotion (LEE) (Cole & Kazarian, 1988). Subscales of the LEE are: lack of emotional support, perceived intrusiveness, perceived irritation and perceived criticism. Social network (number of friends) was assessed by an interview designed for the NOCDA study.

Quality aspects of NOCDA

The NOCDA study was coordinated by the academic department at VU Medical Centre/GGZ inGeest Amsterdam and included 7 sites that were specialized OCD mental health clinics spread over the Netherlands. All research assistants had extensive experience with the assessment of OCD. In addition, they received a two-day course, and regular follow-up one-day training sessions in which videos of the SCID were rated, assessor rating scales were practiced and questions and problems raised by the research assistants could be addressed. The first two interviews of all research assistants were audiotaped and monitored by the fieldwork coordinator in order to address any misunderstandings or errors in performing the measurements. All subsequent interviews were audiotaped for future reference. The monitoring of these audiotapes was continuously performed randomly on about 10% of all taped interviews, as well as on the basis of questions raised by the research assistants and the fieldwork coordinator. Assessments were done by around 30 research assistants (profession: psychologist or research nurse).

Power considerations

Differences in QoL between patient groups versus the general population will be evaluated in terms of between-group effect sizes. We expect that the between-group effect sizes will range from medium i.e. Cohen's $d=0.5$, when comparing patients with severe complaints to the general population, to small i.e. $d=0.2$, when comparing patients with mild severity to the general population. Differences in mean QoL scores of patient groups and the general population will be tested using one-sample t-tests. Assuming a total sample size of $n=382$, the minimal detectable effect size will be (Cohen's) $d=0.15$ for the total patient group and $d=0.19$, $d=0.27$ and $d=0.47$ for patient subgroups that consist of 60%, 30% and 10% of the total group, respectively. Restricting the sample to the 239 respondents with complete cases inflates minimal detectable effect sizes slightly to $d=0.18$ for the total sample and $d=0.24$, $d=0.33$ and $d=0.59$ for patient subgroups mentioned earlier.

Statistical analyses

Baseline characteristics of the total sample were summarized. Next, baseline characteristics of the three patient groups were compared using one-way ANOVAs

for continuous variables and chi-square statistics for categorical variables. Post-hoc tests consisted of pairwise t-tests with Bonferroni correction for continuous variables and column proportions z-tests with Bonferroni correction for categorical variables.

Furthermore, the mean QoL of the total sample and the patient groups were compared to the mean QoL of the general Dutch population with one-sample t-tests. We used data from Szende et. al (Szende et al., 2014) to determine the mean EQ-5D of the general Dutch population, which is 0.89. Effect sizes (Cohen's d) within time and between groups were calculated using pooled standard deviations assuming $SD=0.20$ for the general population. A Cohen's d of 0.2 is indicative of a small effect size, $d=0.5$ of a medium effect size and $d=0.8$ of a large effect size. The correlation between QoL and Y-BOCS total score over all measurements was established with Pearson's correlation coefficient r .

We examined the four-year course of QoL using linear mixed models (LMM). LMM was used to correct for the correlation in the data due to the repeated measure design. In a second analysis, we examined the association between course of QoL and course of OCD. In this LMM analysis, time and group (remitting, intermittent and chronic) were added as categorical variables. To examine whether course of QoL differed for the three groups, the group by time interaction terms were entered in the model. Effect sizes between group and between time were calculated using pooled baseline standard deviations.

In a third analysis (using only respondents with remitting OCD) we examined whether change in QoL was associated with the possible predictor variables, using LMM's allowing quadratic development over time. Next, all possible predictor variables were added to the basic model, one at a time. Y-BOCS, number of disorders, BAI, BDI, social network, loneliness (emotional and social), need for affiliation and all subscales of SSI were treated as time-dependent (repeatedly measured) variables. All other variables were treated as time-independent (baseline only) variables. For time-dependent variables it was investigated whether a random slope improved the model. Thereafter, multivariable analyses were conducted in four steps. In step one, all sociodemographic variables showing statistical significance ($p<0.05$) in the univariable analyses were analysed together (model one). Model 2 included all clinical variables showing statistical significance in the univariable analyses and model 3 included all psychosocial variables showing statistical significance in the univariable analyses. The final model (model 4) included all variables showing statistical significance ($p<0.05$) in model one to three. We regarded correlations of .80 and above as a sign of multicollinearity (Field, 2009).

First, statistical analyses were conducted on the complete dataset, including 239 participants. Next, using multiple imputation techniques, a second dataset was created ($n=382$) allowing to investigate potential bias due to missing data. We describe the incompleteness of the data for variables at baseline, 2-year and 4-year follow-up separately (see supplement). The appropriateness of the imputation method relies on the Missing at Random (MAR) assumption, which allows the missingness of data to depend on the observed variables. We applied MI by chained equations (MICE) using predictive mean matching with a single nearest neighbour for all variables used in the analyses to create 100 imputed datasets.

Data analysis was performed with IBM SPSS Statistics version 25 (IBM, 2017). Multiple imputations and analyses on the multiple imputation dataset were performed with Stata version 15.1 (College Station, 2017). Since the analyses with complete data ($n=239$) and imputed data ($n=382$) yielded identical outcomes except for two minor results, we only report the complete data analyses here. Results that differed will be indicated.

Results

Sample characteristics at baseline

In Table 1 the characteristics at baseline of the total sample ($n=239$) and the three OCD groups are presented. Patients with remitting OCD ($n=73$) received significantly more education¹, had more frequently employment and had significantly less severe OCD symptoms compared to patients with chronic OCD ($n=144$). Patients with intermittent OCD ($n=22$) scored in between. Groups did not differ significantly on psychosocial variables including attachment style, personality characteristics, perceived expressed emotion, social network, loneliness, need for affiliation, and social support.

Four-year course of QoL in patients with OCD

Table 2 presents the four-year course of QoL of the total sample and the comparisons with the general population. At all measurements, one samples t-tests indicated that the mean QoL of the total sample was significantly lower than the mean QoL of the general population. QoL improved significantly from baseline to two-year follow-up ($\beta(S.E.)=0.082$ (0.016), $p<0.01$, 95% CI=(0.050, 0.114)) but did not change critically from two-year to four-year follow-up ($\beta(S.E.)=-0.025$ (0.016), $p=0.13$, 95% CI=(-0.057, 0.007)). Correlation (Pearson's r) between QoL and Y-BOCS total score over all measurements was -0.40, which is a modest correlation (Field, 2009).

¹ Remitting patients had as much education as chronic patients in the multiple imputation dataset.

Table 1. Baseline characteristics of OCD patients

	Total sample Mean (SD) or % n=239	n	Chronic (1) Mean (SD) or % n=144	Intermittent (2) Mean (SD) or % n=22	Remitting (3) Mean (SD) or % n=73	test statistic	p-value	post-hoc analysis p<0.05
Sociodemographics								
Age, years	37.3 (10.9)	239	38.0 (11.0)	37.9 (13.4)	35.7 (10.0)	F(2,236)=1.10	0.34	
Gender, female	54%	239	58%	50%	45%	X ² (2)=3.48	0.18	
Partner, yes	64%	234	61%	77%	66%	X ² (2)=2.39	0.30	
Children, yes	38%	239	38%	36%	38%	X ² (2)=0.03	0.99	
Education, years	13.1 (3.1)	239	12.6 (3.1)	13.3 (3.4)	13.9 (3.1)	F(2,236)=4.18	0.02*	1<3
Employment, yes	55%	239	47%	55%	71%	X ² (2)=11.94	<0.01*	1<3
Clinical characteristics								
Y-BOCS total	20.8 (7.1)	236	22.3 (6.8)	19.1 (6.0)	18.3 (7.3)	F(2,233)=8.84	<0.01*	1>3
Late age of onset OCD ^a , yes	36%	217	30%	41%	47%	X ² (2)=5.73	0.06	
Number of disorders ^b	1.9 (1.1)	239	1.9 (1.2)	1.8 (0.8)	1.9 (1.0)	F(2,236)=0.23	0.80	
Beck Anxiety Index	17.4 (11.3)	230	17.8 (11.6)	16.5 (8.9)	17.0 (11.5)	F(2,227)=0.21	0.81	
Beck Depression Inventory	15.6 (9.7)	227	16.2 (9.8)	14.9 (8.9)	14.7 (9.7)	F(2,224)=0.63	0.54	

^a Onset ≥ 20 years^b Number of current comorbid psychiatric disorders

* p<0.05

Table 2. Four-year course of QoL (EQ-5D) of patients with OCD and comparison with QoL of the general population with one sample t-tests¹ and within-time between-group effect sizes of OCD group versus general population²

EQ-5D	Baseline	2-year follow up	4-year follow up
	Mean (SD)	Mean (SD)	Mean (SD)
	<i>n</i>	<i>n</i>	<i>n</i>
	<i>t(df)</i>	<i>t(df)</i>	<i>t(df)</i>
	<i>p</i>	<i>p</i>	<i>p</i>
	ES	ES	ES
Total sample	0.67 (0.28)	0.75 (0.25)	0.73 (0.25)
	228	215	220
	-11.80(227)	-8.09(214)	-9.62(219)
	<0.01*	<0.01*	<0.01*
	0.92	0.58	0.67
Chronic OCD	0.65 (0.28)	0.70 (0.24)	0.66 (0.25)
	137	125	129
	-10.05(136)	-8.93(124)	-10.37(128)
	<0.01*	<0.01*	<0.01*
	1.00	0.79	0.96
Intermittent OCD	0.75 (0.21)	0.85 (0.18)	0.81 (0.14)
	22	21	22
	-3.20(21)	-1.07(20)	-2.74(21)
	<0.01*	0.30	0.01*
	0.68	0.20	0.39
Remitting OCD	0.69 (0.30)	0.83 (0.24)	0.83 (0.24)
	69	69	69
	-5.62(68)	-2.02(68)	-2.20(68)
	<0.01*	0.05*	0.03*
	0.80	0.24	0.24

¹ one sample t-test against test value 0.89

² ES= within-time between-group Effect Size of OCD group versus general population (Cohen's *d*), obtained using pooled standard deviations assuming *SD*=0.20 for the general population

* *p*<0.05

Four-year course of QoL and the association with course of OCD

Table 2 and Figure 1 present the four-year course of QoL in chronic, intermittent and remitting OCD and the comparison with the mean QoL of the general population. At baseline, there was no significant difference in QoL between the patient groups ($F(2,225)=1.17$, $p=0.31$). At all assessments, the mean QoL of the patient groups remained significantly below the mean QoL of the general population, except QoL of patients with intermittent OCD at two-year follow-up, which did not significantly differ from the QoL of the general population. The effect sizes of the difference in QoL of the total sample of patients with the general Dutch population were large (Cohen's *d* between 0.67 and 0.92), indicating that QoL of patients with OCD differs largely from the general population.

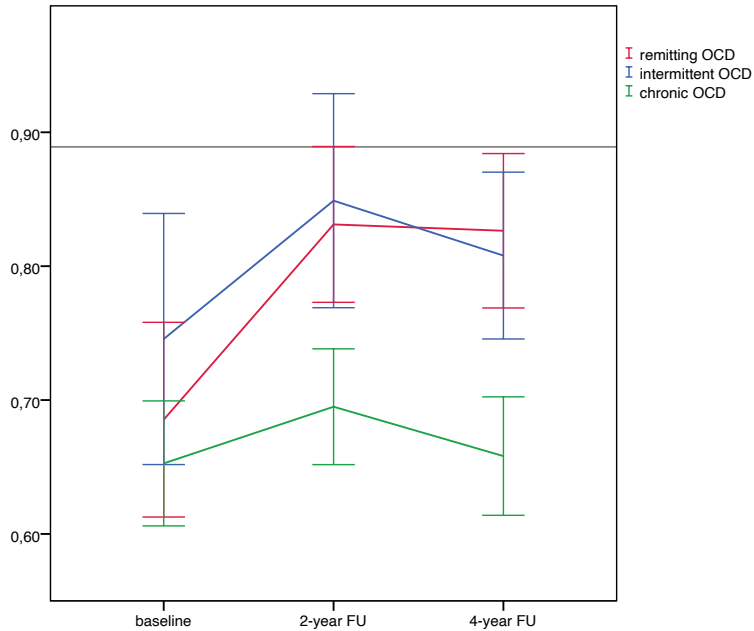


Figure 1. Four-year course of QoL of patients with chronic, intermittent and remitting OCD.

QoL of patients with remitting OCD improved significantly more than patients with chronic OCD from baseline to two-year follow up ($\beta(S.E.)=0.110$ (0.036), $p<0.01$). QoL of patients with chronic OCD was significantly worse than the other two groups on average over time (chronic versus remitting: ($\beta(S.E.)=-0.114$ (0.031), $p<0.01$; chronic versus intermittent: ($\beta(S.E.)=-0.128$ (0.049), $p=0.01$). The reference line displays the QoL of the general population (0.89) (Szende et al., 2014).

Table 3 presents the results of the LMM analyses, investigating the association between course of QoL and course of OCD. The data suggest that course of QoL is significantly associated with course of OCD: QoL of patients with remitting OCD improved significantly more than patients with chronic OCD from baseline to two-year follow-up but not from two-year to four-year follow-up. The effect sizes are moderate (Cohen's $d=0.38$) and small (Cohen's $d=0.14$) respectively, indicating that there is a moderate difference in the improvement of QoL of patients with remitting OCD versus patients with chronic OCD from baseline to two-year follow-up and a small difference from two-year to four-year follow-up. In addition, there was a significant difference between the QoL of patients with chronic OCD and the other two groups on average over time (remitting: ($\beta(S.E.)=0.114$ (0.031), $p<0.01$, 95% $CI=(0.052, 0.175)$; intermittent: ($\beta(S.E.)=0.128$ (0.049), $p=0.01$, 95% $CI=(0.031, 0.225)$).

Table 3. Results of LMM analysis of the four-year course of QoL (EQ-5D) of patients with chronic, intermittent and remitting OCD

OCD group comparison	From Baseline to 2-year follow up			From 2-year to 4-year follow up		
	β (S.E.)	<i>p</i>	95% CI	β (S.E.)	<i>p</i>	95% CI
	ES ¹			ES		
Chronic versus intermittent patients	-0.056 (0.055)			0.002 (0.055)		
		0.31			0.97	
			(-0.165, 0.052)			(-0.106, 0.110)
Chronic versus remitting patients	-0.110 (0.036)			-0.030 (0.036)		
		<0.01*			0.40	
			(-0.180, -0.041)			(-0.099, 0.040)
Intermittent versus remitting patients	-0.054 (0.058)			-0.032 (0.058)		
		0.36			0.59	
			(-0.169, 0.061)			(-0.146, 0.083)
						-0.15

¹ES = Between-group between-time Effect Sizes (standardized using pooled start-time standard deviations)

* $p < 0.05$

Predictors of an unfavourable course in remitters from OCD

Table 4 shows the results of the analyses that investigated whether change in QoL in remitters from OCD was associated with sociodemographic, clinical and psychosocial variables. In the univariable analyses unemployment, late (vs. early) remission, less emotional stability (time independent variables) and more severe OCD, more comorbid mental disorders, more severe comorbid anxiety and depression, a smaller social network, more emotional loneliness and more social loneliness, less emotional support and less social companionship (time-dependent variables) were all significantly associated with an unfavourable four-year course of QoL in remitters from OCD². In the final multivariate model only more severe comorbid anxiety and depression symptoms remained significantly related to an unfavourable course of QoL, suggesting that comorbid anxiety and depression are most strongly associated with course of QoL.

2 Less informative support was significantly related to an unfavourable course of QoL in the univariable analysis on the multiple imputation dataset.

Table 4. Predictors of the four-year course of QoL in remitters from OCD, *n*=73

	Bivariate		Model 1 ^a		Model 2 ^b		Model 3 ^c		Model 4 ^d	
	β (S.E.)	<i>p</i>	β (S.E.)	<i>p</i>	β (S.E.)	<i>p</i>	β (S.E.)	<i>p</i>	β (S.E.)	<i>p</i>
Sociodemographics										
Age, years	-0.002 (0.003)	0.38								
Gender, female	0.016 (0.055)	0.78								
Partner, yes	-0.050 (0.059)	0.40								
Children, yes	-0.016 (0.057)	0.77								
Education, years	0.010 (0.009)	0.27								
Employment, yes	0.126 (0.059)	0.04*	0.126 (0.059)	0.04*					0.038 (0.041)	0.36
Clinical characteristics										
Y-BOCS ^e	-0.008 (0.002)	<0.01*			-0.001 (0.002)	0.67				
Age of onset OCD ^f , late	-0.017 (0.058)	0.78								
Time of remission ^g , late	-0.122 (0.054)	0.03*			-0.034 (0.037)	0.36				
Number of disorders ^h	-0.087 (0.017)	<0.01*			-0.024 (0.017)	0.17				
Beck Anxiety Index ^e	-0.012 (0.002)	<0.01*			-0.005 (0.002)	<0.01*			-0.005 (0.002)	<0.01*
Beck Depression Inventory ^e	-0.019 (0.002)	<0.01*			-0.014 (0.002)	<0.01*			-0.015 (0.002)	<0.01*
Psychosocial variables										
Attachment style/e: dismissing	0.021 (0.014)	0.13								
Attachment style/e: preoccupied	-0.007 (0.013)	0.62								
Attachment style/e: fearful	-0.018 (0.013)	0.19								
Attachment style/e: secure	0.010 (0.015)	0.51								
FFPI ⁱ extraversion	0.021 (0.027)	0.44								

Table 4. Continued

	Bivariate		Model 1 ^a		Model 2 ^b		Model 3 ^c		Model 4 ^d	
	β (S.E.)	p	β (S.E.)	p	β (S.E.)	p	β (S.E.)	p	β (S.E.)	p
FFPI agreeableness	0.002 (0.025)	0.93								
FFPI conscientiousness	0.017 (0.024)	0.48								
FFPI emotional stability	0.076 (0.019)	<0.01*					0.066 (0.019)	<0.01*	0.011 (0.015)	0.46
FFPI autonomy	0.030 (0.025)	0.24								
LEE ^e lack of emotional support	0.000 (0.003)	0.92								
LEE perceived intrusiveness	-0.007 (0.005)	0.21								
LEE perceived irritation	-0.001 (0.007)	0.88								
LEE perceived criticism	-0.007 (0.012)	0.54								
Social network ^e	0.009 (0.004)	0.03*					0.007 (0.004)	0.08		
Loneliness emotional ^e	-0.031 (0.008)	<0.01*					-0.013 (0.011)	0.25		
Loneliness social ^e	-0.025 (0.010)	0.02*					-0.008 (0.012)	0.50		
Need for affiliation ^e	0.007 (0.010)	0.51								
SSI ^h emotional support ^e	0.016 (0.007)	0.02*					0.001 (0.009)	0.92		
SSI informative support ^e	0.015 (0.008)	0.06								
SSI social companionship ^e	0.013 (0.006)	0.04*					0.001 (0.008)	0.91		
SSI instrumental support ^e	0.011 (0.007)	0.12								

^a all sociodemographic variables showing statistical significance ($p < 0.05$) in the univariable analyses analysed together – ^b all clinical variables showing statistical significance ($p < 0.05$) in the univariable analyses analysed together – ^c all psychosocial variables showing statistical significance ($p < 0.05$) in the univariable analyses analysed together – ^d all variables showing statistical significance ($p < 0.05$) in model one to three analysed together – ^e Time-dependent variable (repeatedly measured) – ^f Late onset ≥ 20 years – ^g Late remission (at four-year follow up; $n=31$) vs early remission (at two-year follow up; $n=42$) – ^h Number of current comorbid psychiatric disorders – ⁱ Five-Factor Personality Inventory – ^j Level of Expressed Emotion – ^k Social Support Inventory
* $p < 0.05$

Results using multiple imputed data

The results obtained from using multiple imputed data are deferred to the appendix since they are very similar to the results above that were obtained from complete cases. Missing information was mostly due to drop out. The variables with missing values are displayed in Table A.1. Although information on diagnosis was always available, some missing values occurred in demographic variables (education (1 missing value), having a partner (9 missing values) and clinical measures (20 up to 30 missing values; the maximum number of 39 missing values for age of onset). In total 104 patients missed the 2-year follow-up, while 114 patients missed the 4-year follow-up interview. The missing data pattern was that 239 patients assessed all interviews, 29 patients missed the 2-year follow-up interview only, 39 patients missed the 4-year follow-up interview only, while 75 patients missed both follow-up interviews.

Discussion

The present study underlines the importance of assessing QoL in patients with OCD. We have investigated the four-year course of QoL, its association with remission from OCD and the factors that contribute to an unfavourable course of QoL in remitting OCD patients.

The mean QoL of the total sample of patients with OCD of our study improved from baseline to two-year follow-up and this was maintained at four-year follow-up but it remained substantially lower than the QoL of the general population, which is congruent with previous studies (Hertenstein et al., 2013; Srivastava et al., 2011; Subramaniam et al., 2013). Course of QoL was associated with course of OCD in our study: QoL of patients with remitting OCD improved significantly more than patients with chronic OCD in the first two years; this difference in improvement was moderate. Moreover, QoL of chronic patients was overall poorer than QoL of other patients. Our findings are congruent with research findings that QoL is negatively related to OCD symptom severity (Asnaani et al., 2017; Hollander et al., 2010) and in contrast to findings that there is no or only a modest correlation between them (Ooms et al., 2014; Srivastava et al., 2011; Subramaniam et al., 2013).

In patients with remitting OCD more severe comorbid anxiety and depression symptoms were associated with a lower QoL confirming results from previous cross-sectional studies and a previous longitudinal study, in which depressive symptoms predicted QoL at one-year follow-up (Hertenstein et al., 2013; Subramaniam et al., 2013). Our findings suggest that comorbid anxiety and depression symptoms were

more important for QoL than residual subsyndromal OCD symptoms, implicating that anxiety and depressive symptoms should be given more attention in the treatment of patients with OCD.

Of the sociodemographic variables only unemployment was associated with an unfavourable QoL in remitting patients. This finding might reflect that having a job contributes to a good QoL. Of the psychosocial variables, less emotional stability was associated with an unfavourable QoL and masked the effect of social network, emotional and social loneliness and emotional and social support. Possibly, emotionally instable patients are less able dealing with difficulties arising from OCD. The remaining personality traits were not significantly associated with QoL, which is not congruent with a meta-analysis showing that personality traits and QoL are related (Steel et al., 2008). This discrepancy might be explained by a difference in samples: the current study is based on treatment-seeking patients whereas the meta-analysis is based on convenience samples. Our results might indicate that being extravert, agreeable, conscientious or autonomous does not help coping with the specific limitations arising from OCD. Severity of anxiety and depression symptoms were more important for QoL than unemployment and emotional instability in our study, which might indicate that feeling anxious or depressed overwhelms limitations caused by unemployment or emotional instability. In previous, cross-sectional studies contradictory results were found on the effect of employment on QoL and the effect of emotional stability was not studied before (Remmerswaal et al., 2016; Rodriguez-Salgado et al., 2006; Stengler-Wenzke et al., 2007). Age, gender and perceived lack of support were not associated with course of QoL in our study, contrasting results from previous cross-sectional studies (Coluccia et al., 2016; Fontenelle et al., 2010; Hou et al., 2010). Our study suggests that QoL in remitting patients might be improved by treating comorbid anxiety and depression symptoms, stimulating employment and by developing more emotional stability, for instance by training emotion regulation.

In the literature it has been suggested that a low QoL that remains after remission of a mental disorder may be explained by three hypothetical causes: a trait effect (the low QoL was already present before the onset of the disorder), a scar effect (the low QoL is the result of the disorder) or a state effect (the low QoL is the result of residual mental or somatic symptoms (ten Doesschate et al., 2010)). Although our results suggest a state effect (compared with the normal population, the lower QoL in remitters from OCD is caused by remaining comorbid anxiety and depression symptoms) we cannot rule out that the former presence of OCD has induced a so-called 'scar' since we do not have data on the QoL before the onset of the OCD. A

scar effect might be manifest in for example unemployment, a small social network or not having a partner or a satisfying family life. These scar effects can reinforce each other and further deteriorate QoL, for example OCD can cause low social status by impairing educational achievement and ability to work, and can reduce social support by either alienating family members or by decreasing the likelihood of finding a partner.

Strengths of this study are that we had access to a large, representative sample of treatment-seeking patients with OCD who were followed for a long period of time. Thus, our results are generalizable to clinically referred OCD patients in a specialized setting (Schuurmans et al., 2012). Furthermore, this is the first longitudinal study that examined a broad range of variables possibly associated with course of QoL in patients with remitting OCD, however, future research should examine whether QoL can indeed be improved by targeting the characteristics that were significantly associated with QoL. A limitation of this study is that predictors that are thought to be relatively stable over time (partner, children, education, employment, expressed emotion) were measured at baseline only. The effect of a possible change of these predictors on QoL at 2-year and 4-year follow-up is missing. In addition, a certain amount of overlap between OCD and diminished QoL is to be expected because the DSM diagnosis of obsessive-compulsive disorder incorporates psycho-social dysfunctioning. Likewise, an overlap between anxiety/depression and QoL is not surprising either as psychosocial health is an important aspect of QoL. Nevertheless, our finding that depression and anxiety symptoms are more important for QoL than residual OCD symptoms is important as it underlines the potential opportunity to improve QoL by focusing on depression and anxiety. Furthermore, QoL, as defined by the WHO, encompasses six dimensions: physical health, psychological health, level of independence, social relationships, environment, and spirituality. The EQ-5D does not encompass all of these dimensions. Despite this, the EQ-5D is frequently used and regarded a valid and reliable instrument to assess QoL (Hurst et al., 1997; König et al., 2010; Pitkänen et al., 2012; Van Agt et al., 2005). Last, the group of patients with an intermittent OCD was small, so results on this group need to be verified in future studies.

Historically, clinical research took symptom reduction as an outcome measure with the implicit assumption that patients would be able to resume their life when the disorder was remitted. However, it appears that the relationship between clinical symptoms and QoL is only moderate and remission of symptoms is not sufficient for restoring QoL (McKnight et al., 2016; McKnight & Kashdan, 2009). Moreover, patients place more importance on their ability to live a fulfilling life than on absence

of symptoms (Zimmerman et al., 2006). Nowadays, the importance of taking a broader view on the life of patients and not merely on symptoms is widely accepted. This view is congruent with the definition of mental health of the WHO: “a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community”(World Health Organization, 2005). With QoL outcome measures reflecting QoL aspects such as return to home, work or school, enjoying relationships with family and friends and having a sense of well-being, the perspective of the patient is better taken into account and treatments can be sought that achieve greater effect in these life domains.

Our study indicates that QoL improves in those who remit from OCD, underlining the importance of reducing OCD symptoms in treatment – as an end in itself but also to improve QoL. However, even in remitting patients QoL may remain impaired, suggesting that clinicians should not only focus on remission of obsessive-compulsive symptoms in treatment but on QoL of their patients as well.

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Supplement

Table o. Number of missing observations for all variables in the analyses ($n=382$)

	Baseline	2-year follow-up	4-year follow-up
Baseline characteristics			
Sociodemographic characteristics			
Age	0		
Gender	0		
Partner	9		
Children	0		
Education	1		
Employment	0		
Clinical characteristics			
Age of onset OCD	39		
Psychosocial characteristics			
Attachment style: dismissing	29		
Attachment style: preoccupied	31		
Attachment style: fearful	29		
Attachment style: secure	32		
FFPI ¹ extraversion	19		
FFPI ¹ agreeableness	19		
FFPI ¹ conscientiousness	19		
FFPI ¹ emotional stability	19		
FFPI ¹ autonomy	19		
LEE ² lack of emotional support	20		
LEE ² perceived intrusiveness	20		
LEE ² perceived irritation	20		
LEE ² perceived criticism	20		
Time varying characteristics			
Clinical characteristics			
Current diagnosis OCD	0	104	114
Y-BOCS	5	104	115
Number of disorders ³	0	104	114
Beck Anxiety Index	20	136	138
Beck Depression Inventory	21	134	136

Table o. Continued

	Baseline	2-year follow-up	4-year follow-up
Time varying variables			
Psychosocial characteristics			
Quality of Life	23	135	137
Social network	9	109	119
Loneliness emotional	19	134	137
Loneliness social	18	134	137
Need for affiliation	22	134	140
SSI ⁴ emotional support	19	137	136
SSI ⁴ informative support	19	138	136
SSI ⁴ social companionship	19	137	136
SSI ⁴ instrumental support	22	139	139

¹ Five-Factor Personality Inventory

² Level of Expressed Emotion

³ Number of current comorbid psychiatric disorders

⁴ Social Support Inventory

Table 1. Baseline characteristics of OCD patients, multiple imputations dataset

	Total sample Mean (SE) or % n=382	Chronic (1) Mean (SE) or % n= 222.6 ¹	Intermittent (2) Mean (SE) or % n=44.1 ¹	Remitting (3) Mean (SE) or % n=115.3 ¹	test statistic	p-value	post-hoc analysis p<0.05
Sociodemographics							
Age, years	36.4 (0.56)	37.0 (0.78)	36.5 (2.02)	35.1 (1.12)	$F(2,319.2)=0.80$	0.45	
Gender, female	57%	60%	55%	50%	$F(2,335.2)=1.33$	0.27	
Partner, yes	61%	58%	72%	63%	$F(2,304.5)=0.95$	0.39	
Children, yes	36%	36%	34%	37%	$F(2,323.9)=0.03$	0.97	
Education, years	12.6 (0.16)	12.2 (0.23)	12.6 (0.58)	13.1 (0.34)	$F(2,322.0)=2.17$	0.12	
Employment, yes	52%	47%	49%	63%	$F(2,331.8)=3.25$	0.04*	1<3
Clinical characteristics							
Y-BOCS total	21.2 (0.36)	22.5 (0.50)	20.2 (1.27)	19.2 (0.74)	$F(2,310.1)=5.98$	<0.01*	1>3
Late age of onset OCD ² , yes	38%	33%	43%	46%	$F(2,312.7)=2.20$	0.11	
Number of disorders ³	1.9 (0.06)	1.9 (0.08)	1.9 (0.21)	2.0 (0.12)	$F(2,317.0)=0.04$	0.96	
Beck Anxiety Index	18.2 (0.62)	18.2 (0.90)	18.2 (2.31)	18.3 (1.30)	$F(2,292.4)=0.00$	1.00	
Beck Depression Inventory	16.1 (0.51)	16.1 (0.74)	16.1 (1.89)	15.8 (1.05)	$F(2,300.4)=0.02$	0.98	

¹ sub-sample sizes differ across imputed data sets and were averaged

² Onset \geq 20 years

³ Number of current comorbid psychiatric disorders

*p<0.05

Table 2. Four-year course of QoL of patients with OCD and comparison with QoL of the general population with one sample t-tests¹, multiple imputations dataset, $n=382$

EQ-5D	Baseline	2-year follow up	4-year follow up
	Mean (SE) <i>n</i> <i>t(df)</i> <i>p</i> ES	Mean (SE) <i>n</i> <i>t(df)</i> <i>p</i> ES	Mean (SE) <i>n</i> <i>t(df)</i> <i>p</i> ES
Total sample	0.67 (0.01) 382 -16.36(28856.1) <0.01* 0.92	0.76 (0.02) 382 -8.93(1316.5) <0.01* 0.54	0.73 (0.01) 382 -10.83(1687.2) <0.01* 0.67
Chronic OCD	0.66 (0.02) 222.6 -12.29(2596.2) <0.01* 0.96	0.71 (0.02) 222.6 -9.37(1443.4) <0.01* 0.75	0.68 (0.02) 222.6 -10.95(1285.3) <0.01* 0.88
Intermittent OCD	0.70 (0.04) 44.1 15.92(1264.0) <0.01* 0.93	0.82 (0.04) 44.1 -1.49(1129.3) 0.14 0.34	0.79 (0.05) 44.1 -2.17(624.8) 0.03* 0.49
Remitting OCD	0.68 (0.03) 115.3 26.08(1895.4) <0.01* 0.84	0.82 (0.03) 115.3 -2.79(1929.9) 0.01* 0.28	0.81 (0.03) 115.3 -2.98(1530.9) <0.01* 0.32

¹ one sample t-test against test value 0.89 for the general population

² ES= within-time between-group Effect Size of OCD group versus general population (Cohen's *d*), obtained using pooled standard deviations assuming $SD=0.20$ for the general population

* $p<0.05$

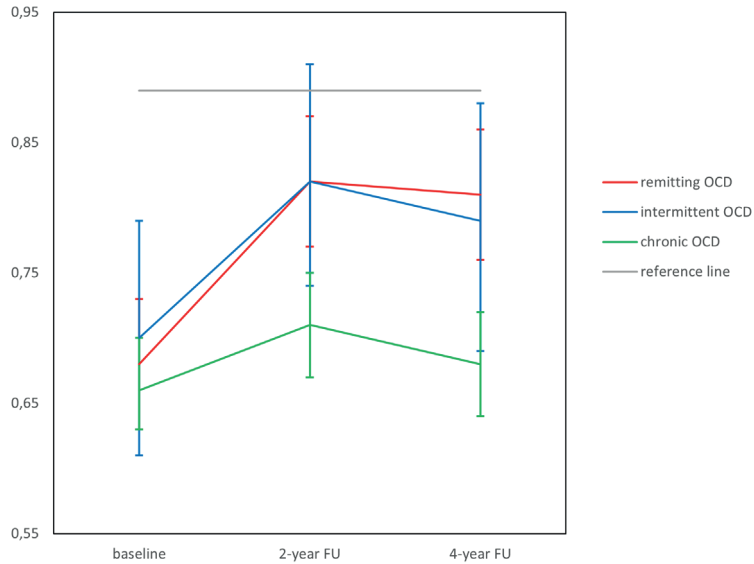


Figure 1. Four-year course of QoL of patients with chronic, intermittent and remitting OCD, multiple imputations dataset, $n=382$.

QoL of patients with remitting OCD improved significantly more than patients with chronic OCD from baseline to two-year follow up ($\beta(S.E.)=0.089 (0.036)$, $p=0.01$). QoL of patients with chronic OCD was significantly worse than the other two groups on average over time (chronic versus remitting: ($\beta(S.E.)=-0.086 (0.025)$, $p<0.01$; chronic versus intermittent: ($\beta(S.E.)=-0.086 (0.039)$, $p=0.01$).

The reference line displays the QoL of the general population (0.89) (Szende et al., 2014).

Table 3. Results of LMM analysis of the four-year course of QoL of patients with chronic, intermittent and remitting OCD, multiple imputations dataset, $n=382$

EQ-5D	From Baseline to 2-year follow up		From 2-year to 4-year follow up	
	β (S.E.)	p	β (S.E.)	p
	95% CI		95% CI	
	ES		ES	
Chronic versus intermittent patients	-0.078 (0.051)	0.13	-0.005 (0.053)	0.92
	(-0.178, 0.023)		(-0.109, 0.099)	
	-0.32		-0.02	
Chronic versus remitting patients	-0.089 (0.036)	0.01*	0.026 (0.036)	0.47
	(-0.159, -0.019)		(-0.044, 0.097)	
	-0.31		0.12	
Intermittent versus remitting patients	-0.012 (0.057)	0.84	-0.032 (0.055)	0.56
	(-0.123, 0.100)		(-0.139, 0.075)	
	-0.05		-0.15	

ES = Between-group between-time Effect Sizes (standardized using pooled start-time standard deviations)

* $p<0.05$

Table 4. Predictors of the four-year course of QoL in remitters from OCD, multiple imputations dataset, n=115.3

	Bivariate		Model 1		Model 2		Model 3		Model 4	
	β (S.E.)	p	β (S.E.)	p	β (S.E.)	p	β (S.E.)	p	β (S.E.)	p
Sociodemographics										
Age, years	-0.002 (0.002)	0.45								
Gender, female	0.005 (0.041)	0.91								
Partner, yes	-0.032 (0.042)	0.45								
Children, yes	0.000 (0.043)	1.00								
Education, years	0.008 (0.006)	0.19								
Employment, yes	0.100 (0.041)	0.02*	0.100 (0.041)	0.02*					0.030 (0.032)	0.35
Clinical characteristics										
Y-BOCS ¹	-0.007 (0.002)	<0.01*			-0.001 (0.002)	0.64				
Age of onset OCD ² , late	0.015 (0.042)	0.72								
Time of remission ³ , late	-0.088 (0.041)	0.03*			-0.035 (0.033)	0.30				
Number of disorders ⁴	-0.071 (0.017)	<0.01*			-0.007 (0.016)	0.67				
Beck Anxiety Index ¹	-0.012 (0.002)	<0.01*			-0.006 (0.002)	<0.01*			-0.006 (0.002)	<0.01*
Beck Depression Inventory ¹	-0.016 (0.002)	<0.01*			-0.011 (0.002)	<0.01*			-0.011 (0.002)	<0.01*
Psychosocial variables										
Attachment style: dismissing	0.008 (0.012)	0.51								
Attachment style: preoccupied	-0.007 (0.012)	0.58								
Attachment style: fearful	-0.016 (0.010)	0.10								
Attachment style: secure	0.015 (0.013)	0.24								
FFPI ⁵ extraversion	0.028 (0.017)	0.11								
FFPI agreeableness	0.009 (0.017)	0.60								

	Bivariate		Model 1		Model 2		Model 3		Model 4	
	β (S.E.)	p	β (S.E.)	p	β (S.E.)	p	β (S.E.)	p	β (S.E.)	p
FFPI conscientiousness	0.012 (0.017)	0.48								
FFPI emotional stability	0.063 (0.015)	<0.01*					0.051 (0.015)	<0.01*	0.008 (0.013)	0.55
FFPI autonomy	0.014 (0.019)	0.45								
LEE ⁶ lack of emotional support	-0.001 (0.002)	0.73								
LEE perceived intrusiveness	-0.005 (0.004)	0.18								
LEE perceived irritation	-0.002 (0.005)	0.68								
LEE perceived criticism	-0.006 (0.008)	0.48								
Social network ¹	0.007 (0.004)	0.04*					0.005 (0.004)	0.17		
Loneliness emotional ¹	-0.031 (0.008)	<0.01*					-0.018 (0.010)	0.06		
Loneliness social ¹	-0.021 (0.010)	0.03*					0.000 (0.011)	1.00		
Need for affiliation ¹	0.009 (0.010)	0.36								
SSI ⁷ emotional support ¹	0.018 (0.007)	0.01*					0.006 (0.009)	0.51		
SSI informative support ¹	0.018 (0.008)	0.03*					0.002 (0.010)	0.81		
SSI social companionship ¹	0.015 (0.006)	0.02*					0.001 (0.008)	0.91		
SSI instrumental support ¹	0.014 (0.007)	0.06								

¹ Time-dependent variable (repeatedly measured)

² Late onset \geq 20 years

³ Late remission (at four-year follow up; $n=31$) vs early remission (at two-year follow up; $n=42$)

⁴ Number of current comorbid psychiatric disorders

⁵ Five-Factor Personality Inventory

⁶ Level of Expressed Emotion

⁷ Social Support Inventory

* $p < 0.05$



CHAPTER 5

Predictors of Intensive Treatment in Patients with Obsessive-Compulsive Disorder

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Abstract

Background: Few studies have investigated which patients with obsessive-compulsive disorder (OCD) do not recover through regular cognitive behaviour therapy or pharmacotherapy and subsequently end up in intensive treatment like day treatment or inpatient treatment. Knowing the predictors of intensive treatment in these patients is significant because it could prevent intensive treatment. This study has identified predictors of intensive treatment in patients with OCD.

Methods: Using 6-year longitudinal data of the Netherlands Obsessive-Compulsive Disorder Association (NOEDA), potential predictors of intensive treatment were assessed in patients with OCD ($n=419$). Intensive treatment was assessed using the Treatment Inventory Costs in Patients with Psychiatric Disorders (TIC-P). Examined potential predictors were: sociodemographics, and clinical and psychosocial characteristics. Logistic Generalized Estimating Equations was used to estimate to what extent the various characteristics (at baseline, 2-year and 4-year assessment) predicted intensive treatment in the following 2 years, averaged over the three assessment periods.

Results: Being single, more severe comorbid depression, use of psychotropic medication, and a low quality of life predicted intensive treatment in the following 2 years.

Conclusions: Therapists should be aware that patients with OCD who are single, who have more severe comorbid depression, who use psychotropic medication, and who have a low quality of life or a drop in quality of life are at risk for intensive treatment. Intensive treatment might be prevented by focusing regular treatment not only on OCD symptoms but also on comorbid depression and on quality of life. Intensive treatment might be improved by providing extra support in treatment or by adjusting treatment to impairments due to comorbid depressive symptoms or a low quality of life.

Introduction

Obsessive-compulsive disorder (OCD) is an impairing disorder, often with a chronic course (Remmerswaal et al., 2020). There are evidence-based treatments for OCD, namely cognitive behaviour therapy (CBT) and psychotropic medication, that can be offered in more or less intensive formats (Lovell & Bee, 2008). Multidisciplinary guidelines recommend determining the designated intensity of treatment according to the principles of so-called 'stepped care' (American Psychiatric Association, 2007; National Institute for Health and Care Excellence, 2005; Van Balkom et al., 2013). In line with stepped care, the least intensive treatment possible is delivered to patients first, taking into account the nature and course of their symptoms. In the case of non-response, treatment may be 'stepped up' to a more intensive level in an effort to meet the treatment goals (Meeuwissen et al., 2019). In the National Institute for Health and Care Excellence (NICE) guideline, the first step in the treatment of OCD consists of awareness, recognition and assessment (National Institute for Health and Care Excellence, 2005). Next step strategies comprise of CBT, antidepressant medication, or a combination of these. In the case of non-response, treatment is stepped up to treatment by a multidisciplinary team with expertise in the management of OCD. Intensive treatment such as day treatment or inpatient treatment may be considered in this latter step for the most severe, impaired, and treatment-resistant patients. In the Netherlands, intensive treatment usually consists of multimodal treatment, with CBT being the main therapy, offered in a group with other patients with anxiety disorders and OCD. It can be offered in a day-care setting or in an inpatient setting. Intensive treatment usually takes several (parts of) days a week up to 5 days a week for a few months to 1 year. Admission may also be necessary when patients are in crisis.

Up till now, no longitudinal studies into the predicting factors of intensive treatment in OCD have been published. However, cross-sectional research exists, describing the characteristics of patients with OCD in intensive residential treatment. These patients were treatment-resistant to antidepressants and/or CBT, suffered from severe OCD symptoms and psychiatric comorbidity (Chase et al., 2015; Falkenstein et al., 2019; Siwiec et al., 2019), had an early age of onset of OCD and a long duration of the disorder (Boschen et al., 2008; Brennan et al., 2014), often did not have a partner or a job (Boschen et al., 2008; Brennan et al., 2014; Veale et al., 2016) and had a low quality of life, with scores of one to 2 standard deviations below the general population (Buchanan et al., 1996; Drummond, 1993; Hertenstein et al., 2013; Stewart et al., 2005; Taube-Schiff et al., 2020).

In populations with other mental disorders, more is known about predictors of hospitalization. A systematic review of 58 papers on predictors of readmission in patients with several mental disorders indicates that previous hospitalization, younger age, being unmarried, having lower financial means, not being satisfied with the index treatment, having more hospital days on the index admission, and a negative attitude towards medication were predicting factors for psychiatric readmission (Donisi et al., 2016). In addition, being male, having psychotic symptoms, a longer duration of untreated psychosis, less social satisfaction, disturbed family dynamics, residing in an urban area, and illegal drugs misuse were found predictive of hospitalization in recent prospective cohort studies involving several mental disorders (Alm et al., 2020; Donisi et al., 2016; Han et al., 2020; Robinson et al., 2019; Tan et al., 2022). A population study combined several survey and register databases of 2,638 individuals born in 1953, including interviews with their mothers. From this study it appeared that poor family relations in adolescence were associated with an increased risk of inpatient psychiatric treatment in the years 1969 until 2008 (Alm et al., 2020).

Knowledge of characteristics that predict future intensive treatment might help to optimize first steps of treatment for patients with OCD to prevent the need for intensive treatment. This is significant because intensive treatment may contribute to stigmatization and the disruption of the lives of patients by hindering work, education, care for children, hobbies or social contacts (Loch, 2014; Wright et al., 2000). In addition, intensive treatment is expensive, which burdens society with costs. Nevertheless, intensive treatment is still the best available treatment for the most severe and impaired patients with OCD. Another significance of predictors of intensive treatment is that they might be used to improve intensive treatment by tailoring it to the characteristics of the patients who need it.

The goal of the present study was to identify predictors of starting with intensive treatment. In the rest of the text, we will refer to this as “predictors of intensive treatment”, for reasons of readability. We have selected potential predictors based on the above presented research findings in other populations. In addition, potential predictors were selected that have been associated with course and severity of OCD, leading to the following potential predictors: sociodemographic variables, clinical variables and psychosocial variables including personality traits (Fullana et al., 2004; Stavropoulos et al., 2017), the quality of the social network (Palardy et al., 2018), and childhood trauma (Gothelf et al., 2004; Semiz et al., 2013; Tibi et al., 2020). We hypothesized that being male, being younger, having more severe symptoms, poor insight in OCD, childhood trauma and a lower quality of social relationships are predictors of intensive treatment.

Methods

The reporting of this study conforms to the STROBE statement (www.strobe-statement.org).

Procedure

Data were derived from the Netherlands Obsessive-Compulsive Disorder Association (NOCDA) study, an ongoing longitudinal cohort study investigating the naturalistic long-term course of OCD in patients referred to mental health care centres. The NOCDA study design and baseline characteristics of the study sample are described in detail elsewhere (Schuurmans et al., 2012). The NOCDA study was accredited by the Medical Ethical Committee of the VU-University Medical Centre in 2005.

After their clinical assessment at one of the contributing mental health clinics, 687 patients aged 18 years and over with a lifetime diagnosis of OCD, as determined by the administration of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First, 1997), were asked to participate in the NOCDA study. Since NOCDA aims to follow a large representative sample of OCD subjects in different stages of the disease and with different degrees of illness severity, the only exclusion criterion was an inadequate understanding of the Dutch language for the purposes of the completion of interviews and self-report questionnaires. Comprehensive measurements were done at baseline and after 2, 4, and 6 years.

Of the 687 patients who were asked to participate in the NOCDA study, 419 (60.9%) gave written informed consent and were enrolled in the study. A comparison on basic demographic characteristics between patients that did ($n=419$) and did not ($n=268$) agree to participate yielded no significant differences.

Baseline measurements took place between 2005 and 2009 and included validated semi-structured interviews and self-report questionnaires to gather information on a broad range of variables related to OCD, comorbidity, and psychosocial consequences. The baseline assessment took about 5 h. All included participants were contacted after 2, 4, and 6 years for assessment, irrespective of their treatment status. The follow-up assessments took about 3 h and in most cases (80%) they were performed by the same research assistant. During the follow-up period, participants received treatment as usual. Three hundred and eleven patients participated in the 2-year assessment (total dropout 26%), 295 patients in the 4-year assessment (total dropout 30%), and 272 patients in the 6-year assessment (total dropout 35%).

Primary outcome measure: TIC-P

Treatment intensity was derived from the Treatment Inventory of Costs in Patients with mental disorders (TIC-P) (Bouwman et al., 2013). This is a 15-item interview assessing health care consumption in the previous 6 months (at baseline) or since the previous interview (at 2-year, 4-year and 6-year). Treatment was scored as “intensive” when patients responded on the TIC-P interview (Bouwman et al., 2013) by stating that they were receiving day-care treatment or inpatient treatment in a psychiatric hospital or a specialized OCD clinic. In all other cases, treatment was scored as “not intensive”.

Potential predictors of intensive treatment in patients with OCD

We studied three categories of potential predictors: sociodemographic, clinical, and psychosocial characteristics.

Sociodemographic characteristics: age (in years), gender, having a partner (yes, no), having children (yes, no), independent living situation (yes (living alone, with partner or children), no (living in a mental health institution or with parents)), education (number of years), paid employment (yes, no) and income (16 categories of increasing income).

Clinical characteristics: Severity of OCD was assessed using the Yale Brown Obsessive-Compulsive Scale for Severity (Y-BOCS) (Goodman et al., 1989a; Goodman et al., 1989b). Age of onset of OCD was assessed using the SCID-I as the earliest age at which patients fulfilled the criteria for OCD. In order to assess the number of current comorbid mental disorders, the ascertained diagnoses on the SCID-I were counted (anxiety-, mood-, post-traumatic stress-, eating-, somatoform- and substance-related disorders, and psychotic disorders). Presence and severity of comorbid anxiety symptoms were assessed using the Beck Anxiety Inventory (Beck, et al., 1988), while comorbid depressive symptoms were measured using the Beck Depression Inventory (BDI) (Beck et al., 1988; Beck et al., 2016; Furlanetto et al., 2005). Psychotropic medication was assessed using the TIC-P (Bouwman et al., 2013), measuring use of all types of psychotropic medication in the previous 6 months (at baseline and follow-up). Insight in OCD was measured using the Overvalued Ideas Scale (OVIS) (Neziroglu et al., 1999).

Psychosocial characteristics: Childhood trauma was assessed using the Structured Trauma Interview (STI) (Draijer, 1989). Traumas on the STI are: 1) early separation from parent; 2 and 3) parental dysfunction of mother or father respectively; 4) witnessing of interparental violence; 5) physical abuse; 6) sexual abuse. Ascertained

childhood traumas were summed. Personality characteristics according to the Big Five were assessed using the Five-Factor Personality Inventory (FFPI) (Hendriks et al., 1999). Subscales of the FFPI are: extraversion, agreeableness, conscientiousness, emotional stability, and autonomy. Social support was assessed using the Social Support Inventory (Brown et al., 1987). The self-rated EuroQol five dimensional questionnaire (EQ-5D) was used to assess quality of life (EuroQol Group, 1990). The EQ-5D contains five dimensions significant for quality of life: mobility, selfcare, daily activities, pain/discomfort, and depression/anxiety.

Stable characteristics like age, gender, age of onset OCD, childhood trauma, and personality characteristics were assessed at baseline only. Characteristics that could vary over time were assessed at baseline, 2-year- and 4-year assessment. These characteristics were: relationship status, children, living situation, education, employment, severity of OCD, number of current comorbid mental disorders, comorbid anxiety and depressive symptoms, use of psychotropic medication, social support, and quality of life. An exception is the characteristic insight in OCD, which was assessed at 2-year- and 4-year assessment.

Quality aspects of NOCDA

The NOCDA study was coordinated by the Department of Psychiatry at the Amsterdam UMC/GGZ inGeest, Amsterdam, and included seven sites that were specialized OCD mental health clinics spread over the Netherlands. All research assistants had extensive experience in assessing OCD. In addition, they received a 2-day course, and regular follow-up 1-day training sessions in which videos of the SCID were rated, assessor rating scales were practiced, and questions and problems raised by the research assistants were able to be addressed. The first two interviews of all research assistants were audiotaped and monitored by the fieldwork coordinator in order to address any misunderstandings or errors in performing the measurements. All subsequent interviews were audiotaped for future reference. The audiotapes were continuously randomly monitored in about 10% of all taped interviews, as well as on the basis of questions raised by the research assistants and the fieldwork coordinator. Assessments were done by around 30 research assistants (profession: psychologist or experienced research nursing staff).

Statistical analyses

Logistic Generalized Estimating Equations (GEE) with an exchangeable correlation structure was used to estimate to what extent the various characteristics (at baseline, 2- and 4-year assessment) predicted intensive treatment in the following period of 2 years, averaged over the three assessment periods (see Figure 1).

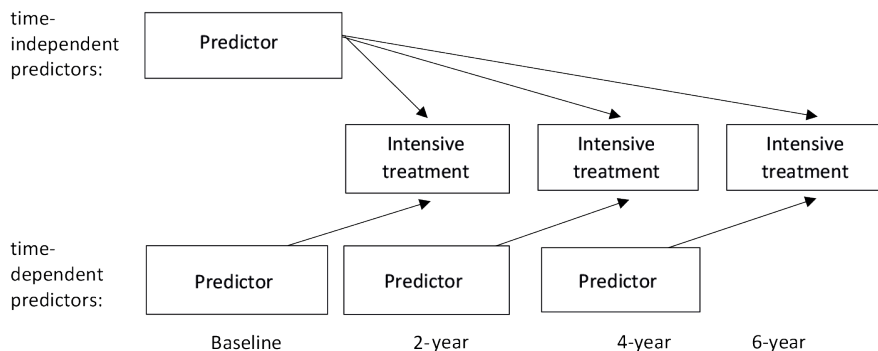


Figure 1. Schematic representation of statistical analyses

The following GEE analyses were performed: 1) univariable analyses in which all potential predictors were analysed separately; 2) multivariable analyses within the three categories of potential predictors in which all variables of a category showing statistical significance in the univariable analyses were analysed together; and 3) a multivariable analysis over the three categories including all variables showing statistical significance ($p < 0.05$) in the multivariable analyses within the three categories of potential predictors. A backward selection strategy was used to obtain the final multivariable models.

As a sensitivity analysis, we repeated the analyses but corrected for Y-BOCS severity. Insight in OCD will be analysed separately using the other characteristics because it was assessed at 2-year- and 4-year assessment only.

Results

Description of potential predictors of intensive treatment

Table 1 presents the description of the potential predictors at baseline, 2-year- and 4-year measurement that may predict whether patients will receive intensive treatment in the following 2 years. The mean severity of OCD and comorbid symptoms decreased from baseline to 2-year measurement. From 2-year- to 4-year measurement, these severity scores stabilized or increased slightly.

Description of 6-year course of intensive treatment

Table 2 presents the description of the intensive treatment variable over the course of 6 years. Over time, fewer patients were treated in mental health care (outpatient care as well as intensive treatment).

Table 1. Descriptives of potential predictors of IT in patients with OCD

Potential predictor	Instrument range <i>min-max</i>	Baseline	2-year	4-year
		measurement <i>Mean (SD) or %</i>	measurement <i>Mean (SD) or %</i>	measurement <i>Mean (SD) or %</i>
		<i>n=419</i>	<i>n=311</i>	<i>n=295</i>
Sociodemographics				
Age, years	18-79 ^a	36.6 (10.9)		
Gender, female		56%		
Partner, yes		62%	69%	66%
Child(ren), yes		37%	40%	55%
Living independently, yes		87%	95%	97%
Education, years	5-18 ^a	12.6 (3.3)	13.2 (3.2)	13.2 (3.3)
Employment, yes		53%	60%	55%
Income	1-16	7.8 (4.2)	8.8 (4.6)	9.0 (4.8)
Clinical characteristics				
Y-BOCS obsessions	0-20	9.9 (4.3)	7.4 (4.8)	7.5 (4.7)
Y-BOCS compulsions	0-20	10.0 (4.8)	7.7 (5.0)	7.9 (5.2)
Y-BOCS total	0-40	19.9 (8.1)	15.1 (9.0)	15.4 (9.2)
Late age of onset OCD, yes ^b		39%		
Insight in OCD ^c	0-10	NA ^d	4.3 (1.5)	4.4 (1.3)
Comorbid disorders ^e	0-7 ^a	1.8 (1.2)	1.2 (1.1)	1.2 (1.1)
Comorbid anxiety ^f	0-63	17.3 (12.0)	13.4 (11.2)	11.6 (9.8)
Comorbid depression ^g	0-40	15.3 (10.1)	11.6 (10.1)	13.6 (10.9)
Psychiatric medication, yes		75%	69%	70%
Psychosocial characteristics				
Extraversion ^h	-5.0-5.0	-0.07 (1.3)		
Agreeableness ^h	-5.0-5.0	2.2 (1.7)		
Conscientiousness ^h	-5.0-5.0	0.9 (1.5)		
Emotional stability ^h	-5.0-5.0	-0.7 (1.2)		
Autonomy ^h	-5.0-5.0	0.9 (1.1)		
Childhood trauma ⁱ	0-6	1.5 (1.2)		
Social support ^j	20-60	50.0 (8.4)	51.2 (9.3)	51.0 (9.2)
Quality of Life ^k	0-1	0.6 (0.3)	0.8 (0.2)	0.7 (0.3)

^a Range in dataset, ^b Onset \geq 20 years, ^c Overvalued Ideas Scale, ^d Not available, ^e Number of current comorbid psychiatric disorders, ^f Beck Anxiety Index, ^g Beck Depression Inventory, ^h Subscale of Five-Factor Personality Inventory (FFPI), ⁱ Structured Trauma Interview, ^j Social Support Inventory, ^k EQ-5D utility score

Table 2. Treatment of patients with OCD over the course of six years

Treatment	Baseline^a	2-year^b	4-year^b	6-year^b
Intensive treatment				
Number of days				
Mean (SD)	55.8 (46.4)	96.3 (103.3)	168.9 (183.5)	78.7 (143.3)
Median	40	55	80	30
<i>n</i>	105 (25%)	76 (24%)	40 (14%)	30 (11%)
Outpatient treatment				
Number of sessions				
Mean (SD)	10.2 (8.7)	30.1 (29.0)	24.9 (26.6)	23.2 (22.0)
Median	7	21	16	18
<i>n</i>	287 (68%)	194 (62%)	166 (56%)	143 (53%)
No treatment				
<i>n</i>	26 (6%)	38 (12%)	88 (30%)	95 (35%)
Missing				
<i>n</i>	1 (0%)	3 (1%)	1 (0%)	4 (1%)
<i>n</i>	419	311	295	272

^a treatment in the previous six months^b treatment in the previous two years

GEE regression analyses: potential predictors of intensive treatment

Table 3 presents the results of the analyses of the potential predictors of intensive treatment 2 years later over a time period of 6 years.

In the univariable analyses, not having a partner, a dependent living situation, fewer years of education, not having a paid job, more severe OCD, more current comorbid diagnoses, more severe comorbid anxiety and depression, use of psychotropic medication, less extraversion, less autonomy, less social support, and a lower quality of life all significantly predicted intensive treatment 2 years later.

In the multivariable analysis of the sociodemographic variables, not having a partner and not having a paid job significantly predicted intensive treatment 2 years later. Predictors in the multivariable analysis of the clinical variables were more severe comorbid depression and use of psychotropic medication, while in the multivariable analysis of the psychosocial variables a lower quality of life predicted intensive treatment 2 years later.

For the final multivariable model, in which all significant predictors from the previous multivariable models were analysed together, severity of comorbid depression and quality of life could not be included together due to high collinearity. Because severity of comorbid depression had a stronger association with intensive treatment, a final multivariable model was made with this variable and quality of life was not included (Table 3 model 1). In this model, not having a partner, more severe comorbid depression and use of psychotropic medication significantly predicted intensive treatment 2 years later. When quality of life was substituted for severity of comorbid depression in the final multivariable model (Table 3 model 2), it appeared that a lower quality of life significantly predicted intensive treatment 2 years later as well as not having a partner and use of psychotropic medication.

From the sensitivity analysis, in which we repeated the analyses but corrected for Y-BOCS severity, it appeared that the same predictors were significantly related to intensive treatment in the final multivariable analysis. Thus these factors predict intensive treatment independently of OCD severity.

Insight in OCD was not significantly related to intensive treatment ($OR=1.07$, 95% CI (0.98, 1.18); $p=0.14$).

Table 3. Results of logistic GEE analyses of potential predictors of intensive treatment two years later over a time-period of six years

	Univariable analyses			Multivariable analyses within categories			Multivariable analyses over categories model 1 ^a			Multivariable analyses over categories model 2 ^b		
	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p
Sociodemographics												
Age, years	0.99	0.98, 1.01	0.30									
Gender, female	1.17	0.83, 1.65	0.38									
Partner, yes	0.54	0.44, 0.68	<0.01*	0.57	0.45, 0.71	<0.01*	0.62	0.51, 0.76	<0.01*	0.62	0.49, 0.77	<0.01*
Child(ren), yes	1.33	0.92, 1.92	0.12									
Living independently, yes	0.51	0.31, 0.84	0.01*									
Education, years	0.93	0.89, 0.98	0.01*									
Employment, yes	0.44	0.30, 0.64	<0.01*	0.50	0.45, 0.71	<0.01*						
Income	0.97	0.93, 1.01	0.12									
Clinical characteristics												
Y-BOCS total	1.10	1.06, 1.14	<0.01*									
Late age of onset(OCD), yes ^c	1.01	0.84, 1.20	0.95									
Comorbid disorders ^d	1.30	1.19, 1.43	<0.01*									
Comorbid anxiety ^e	1.04	1.02, 1.05	<0.01*									
Comorbid depression ^f	1.05	1.04, 1.06	<0.01*	1.05	1.04, 1.06	<0.01*	1.04	1.03, 1.05	<0.01*			
Psychiatric medication, yes	2.75	1.62, 4.68	<0.01*	2.11	1.22, 3.63	0.01*	2.02	1.17, 3.48	0.01*	2.16	1.25, 3.74	0.01*

	Univariable analyses		Multivariable analyses within categories		Multivariable analyses over categories model 1 ^a		Multivariable analyses over categories model 2 ^b		
	OR	95%CI	p	OR	95%CI	p	OR	95%CI	p
Psychosocial characteristics									
Extraversion ^g	0.81	0.70, 0.93	<0.01*						
Agreeableness ^g	0.96	0.80, 1.16	0.70						
Conscientiousness ^g	1.03	0.88, 1.21	0.74						
Emotional stability ^g	0.88	0.75, 1.02	0.10						
Autonomy ^g	0.84	0.72, 0.97	0.02*						
Childhood trauma ^h	1.14	0.99, 1.30	0.07						
Social support ⁱ	0.98	0.96, 0.99	0.01*						
Quality of life ^j	0.23	0.14, 0.38	<0.01*	0.23	0.14, 0.38	<0.01*	0.29	0.19, 0.46	<0.01*

^a Quality of life was omitted in model 1 due to multicollinearity between comorbid depression and quality of life

^b Comorbid depression was omitted in model 2 due to multicollinearity between comorbid depression and quality of life

^c Onset \geq 20 years

^d Number of current comorbid psychiatric disorders

^e Beck Anxiety Index

^f Beck Depression Inventory

^g Subscale of Five-Factor Personality Inventory (FFPI)

^h Structured Trauma Interview

ⁱ Social Support Inventory

^j EQ-5D utility score

* $p < 0.05$

Discussion

We studied potential predictors of intensive treatment in the subsequent 2 years in patients with OCD over the course of 6 years. It appeared that patients with OCD who were single, who had more severe comorbid depressive symptoms, who used psychotropic medication, and who had a low quality of life were significantly more likely to have intensive treatment 2 years later. Our results on being single and more severe comorbid depression resemble the results concerning other mental disorders (Donisi et al., 2016; Han et al., 2020; Tan et al., 2022). Thus, also in patients with OCD, these variables predict future intensive treatment. Quality of life as a potential predictor of intensive treatment has not been studied before. Our result that psychotropic medication predicts future intensive treatment is not congruent with previous research results in which a negative attitude towards medication – and thus likely not using medication – predicted admission (Donisi et al., 2016; Robinson et al., 2019). This difference might reflect the different study populations. While in patients with psychotic disorders or mood disorders medication has a large effect on symptoms and prevents relapse, crisis and hospitalization (Kishi et al., 2021; Leucht et al., 2012), in OCD, medication has only a moderate effect. SSRIs cause a mean reduction of 3.2 points on the Y-BOCS, over placebo, in patients with OCD according to a meta-analysis including 17 studies (3,097 participants) (Soomro et al., 2008). Therefore, patients with OCD not taking medication usually does not lead to severe relapse or crisis, or an increase in the risk of hospitalization. A second explanation for our finding might be that stepped-care principles were followed in the treatment of OCD that indicate prescription of psychotropic medication before stepping up to more intensive treatments (National Institute for Health and Care Excellence, 2005).

Contradictory to our hypotheses, the following potential predictors did not significantly predict intensive treatment. Remarkably, although severity of OCD was associated with intensive treatment in the univariable analysis of our study, this association disappeared in the multivariable models, indicating that other variables were more important in predicting intensive treatment. This might indicate that despair and limitations as a result of OCD are more important reasons for intensive treatment than severity of OCD per se. Next, insight in OCD did not predict intensive treatment in our study. This is not congruent with a previous finding in patients with several mental disorders that better insight was predictive of readmission (Russo et al., 2006). Also, it is not in line with previous findings that patients with poor insight in OCD were less likely to seek mental health care (Beşiroğlu et al., 2004). In addition, poor insight in OCD was previously related to severity and chronicity of OCD (Bellino et al., 2005; Jacob et al., 2014; Visser et al., 2017). Possibly, effects

of insight and help-seeking on intensive treatment cancel each other out. More specifically, patients with poor insight are often severe and chronic patients for whom intensive treatment is indicated. However, they are less likely to seek help. Conversely, patients with good insight do seek help but need intensive treatment less often. Lastly, childhood trauma was not predictive of intensive treatment in our study. To our knowledge, childhood trauma has not been studied as a potential predictor for intensive treatment before. Contradictory results have been found on the association between childhood trauma and severity and chronicity of OCD (Gothelf et al., 2004; Semiz et al., 2013; Tibi et al., 2020; Visser et al., 2014). While childhood trauma is an important predictor of severity and chronicity of depression in patients with depressive disorders, the relationship between childhood trauma and severity and chronicity of OCD is less clear (Nelson et al., 2017).

The predictors of intensive treatment that have emerged from our study might be used to tailor intensive treatment to the characteristics of the patients involved. For instance, single patients obviously lack the support from a partner, which might make it harder for them to stay motivated in the face of setbacks in treatment. Therapists may need to organize or offer extra support to pull these patients through. Next, patients with comorbid depressive symptoms or with a low quality of life may have difficulty following an intensive treatment program. In that case, adapting the treatment to the impairment of the patient may be helpful, and could be done by including activation in treatment or by shortening treatment days.

Our results indicate that intensive treatment might be prevented by improving comorbid depression and quality of life in first-step treatments in addition to treating OCD. In other words, to not focus only on diminishing OCD symptoms in treatment but also on vitality and promoting a fulfilling life with elements that patients want from life, like work, pleasurable activities, a partner, and a social network. We recommend therapists to encourage patients to fulfil life's wishes while allowing them to be hindered by OCD as little as possible. In our clinical experience, patients tend to postpone fulfilling their life's wishes based on the idea that it is better to wait until the OCD symptoms have disappeared. However, this conviction contributes to the notion of being disabled, which drives patients further away from their goals in life and in treatment. Therefore, therapists should educate patients about the importance of working on their life's goals in treatment in addition to working on OCD. Furthermore, therapists can help to find practical solutions to obstacles that may arise.

During the last decade, it has been accepted that recovery from mental disorders does not just entail having fewer symptoms but also regaining functioning and

resuming a meaningful life (Boardman, 2018). Guidelines like the NICE and the APA guidelines recognize the importance of focusing on functioning and quality of life in treatment (American Psychiatric Association, 2007; National Institute for Health and Care Excellence, 2005). Also, treatments are increasingly being evaluated using quality of life outcome measures (Asnaani et al., 2017; Motivala et al., 2017; Winter et al., 2021). Moreover, recovery-oriented treatment programs have been implemented for patients with severe mental illness like schizophrenia, bipolar disorder, major depressive disorder, borderline personality disorder, and substance use disorders. These treatment programs foster adapting to chronic mental illness and movement toward personally meaningful goals like work and education (Burchi et al., 2018; Del Mar Bonnin et al., 2019; White et al., 2017). Recovery-oriented treatment programs help to improve both symptoms and functioning and help reduce hospitalization in these patients with severe mental illness (White et al., 2017). Another treatment that can be effective in improving quality of life is acceptance and commitment therapy (ACT), which aims to accept negative feelings, while moving toward meaningful goals in accordance with personal values (A-Tjak et al., 2015; Arch et al., 2012; Twohig et al., 2010).

A limitation of this study is that although we had a longitudinal study design with potential predictors preceding the outcome measure (intensive treatment) in time, we were unable to establish causal connections between potential predictors and intensive treatment. Future research should thus examine whether treatment of the significantly associated predictors of our study indeed prevents intensive treatment. Another limitation is the attrition rate of 35% over the course of 6 years. To investigate whether dropout was selective, we have compared baseline characteristics of patients who participated in the 6-year assessment with patients who did not participate. Patients did not differ on any of the baseline characteristics except that patients who dropped out had less years of education ($mean=11.7$; $SD=3.3$) compared to patients who participated in the 6-year assessment ($mean=13.1$; $SD=3.2$; $t(416)=-4.2$, $p<0.01$). In previous studies, education was a determinant of attrition as well (De Graaf et al., 2000; Lamers et al., 2012). Presumably, our results were not biased by selective attrition. Last limitation is a potential historical effect due to the fact that the data was collected between 2005 and 2015. However, the intensive treatments that were common in the Netherlands during the NOCDA data collection have largely remained the same to date. This study also had a strength: we had access to a large, representative sample of treatment-seeking patients with OCD who were followed for a long period of time. Thus, our results are generalizable to clinically referred OCD patients in a specialized setting.

In conclusion, therapists should be aware that patients with OCD who are single, who have more severe comorbid depression, who use psychotropic medication, and who have a low quality of life or a drop in quality of life are at risk for intensive treatment. This is significant because knowledge of these predictors might help to optimize first-step treatments for patients with OCD to prevent the necessity of intensive treatment. In addition, the significant predictors of our study might be used to tailor intensive treatment to the characteristics of patients involved. We advise working on comorbid depression and personal goals in treatment in addition to working on OCD. Also, we advise providing extra support in treatment for patients who need it and to adjust treatment to impairments due to comorbid depressive symptoms or a low quality of life.

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CHAPTER 6

Feasibility and Outcome of a Brief CBT Family Intervention for Patients with Obsessive-Compulsive Disorder: a Pilot Study

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https://www.tijdschriftgedragstherapie.nl/inhoud/tijdschrift_artikel/TG-2017-3-3/Een-korte-gedragstherapeutische-familie-interventie-voor-patienten-met-een-obsessieve-compulsieve-stoornis

A summary of the treatment is published in Psychopraktijk, 2014, 2, 11-13.

Research has demonstrated the effectiveness of cognitive behaviour therapy (CBT) for patients with obsessive-compulsive disorder (OCD). However, almost half of the treated patients still meet the criteria for OCD at follow-up. A potential strategy for enhancing CBT is to focus on the family interaction related to obsessive-compulsive symptoms. Family members commonly respond to OCD in two ways: they accommodate (adapt, participate) and/or antagonize (criticize, oppose). These responses are related to unfavourable outcome of CBT and to disability in patients and their family members. Hence, focusing treatment on family responses to OCD may enhance therapy outcome and may improve functioning of patients and family members.

Three controlled studies have examined whether family interventions enhance CBT treatment. Results are positive in two studies (Grunes et al., 2001; Thompson-Hollands et al., 2015) and non-significant in the third (Van Noppen et al., 1997). It is remarkable that only one study has focused on antagonistic responses besides accommodative responses (Grunes et al., 2001), showing positive results. However, this study used a group format and research has indicated superiority of individual family formats (Thompson-Hollands et al., 2014). Therefore, we developed a brief CBT family intervention with an individual family format focusing on both antagonistic and accommodative responses. Moreover, contrasting previous studies, we aimed at normalizing the family relationship by encouraging pleasurable, joint activities. This way we positively and contingently reinforced response prevention of OCD.

We aimed to improve: 1) obsessive-compulsive symptoms and 2) functioning of patients and family members. The protocol was added to regular CBT and offered to a couple consisting of a patient with OCD and the family member most involved in caring for the patient. This pilot study investigated the feasibility and effectiveness of our brief CBT family intervention.

The protocol consisted of five sessions of 90 minutes, planned every other week. Each session consisted of three parts: 1) decreasing antagonistic responses of the family members and patients pleading for accommodation by learning effective communication about OCD; 2) response prevention of accommodation by family members; 3) planning joint activities.

Sixteen patients, 15 partners and 1 mother, were included. The study was conducted at the Academic Outpatient Department for Anxiety Disorders at GGZ inGeest, Amsterdam, The Netherlands.

Inclusion criteria were: 1) OCD of at least moderate severity (Yale Brown Obsessive-Compulsive Scale (Y-BOCS) \geq 16) (Goodman et al., 1989); 2. accommodation of at least moderate severity (Family Accommodation Scale on the family member (FAS) \geq 13) (Calvocoressi et al., 1999) and/or antagonism of significant degree (Perceived Criticism Measure on the patient (PCM) \geq 4) (Hooley & Teasdale, 1989); and 3) medication was allowed but needed to be kept constant during treatment. In addition to the Y-BOCS, FAS and PCM, pre-tests included assessment of functioning with the World Health Organization Disability Assessment Schedule (WHODAS) (Chwastiak & Von Korff, 2003) and assessment of atmosphere at home with a visual analogue scale (0-100, higher scores indicating a better atmosphere). Post-tests included all mentioned instruments plus assessment of satisfaction with the brief CBT family intervention with a visual analogue scale (0-100, higher scores indicating more satisfaction).

Results were examined using two-tailed t-tests in the intent to treat (ITT) sample. Missing values at post-test ($n=5$) were imputed with pre-test scores. The method of Jacobson and Truax (Jacobson & Truax, 1991) was used to determine reliable change (YBOCS decrease \geq 4) and clinically significant recovery (reliable change and post-test YBOCS \leq 16), using data from Frost et al. (Frost et al., 1995).

Patients had a mean age of 39.4 years ($SD=10.8$). Ten patients were female (62.5%), 7 patients had children (43.8%), 6 patients were employed (37.5%), 14 patients lived with their family member (87.5%) and 7 patients used pharmacotherapy (43.8%). The mean duration of OCD was 13.9 years ($SD=7.1$; range 5-31 years). Patients had received on average 2.8 (range 0-5) previous treatments (psychotherapy and pharmacotherapy). The mean duration of the partner-relationship was 14.3 years ($SD=13.6$; $n=15$). We did not assess psychopathology of family members, this is a limit of this study.

Ten couples completed the family treatment. Six couples dropped-out: because their relationship broke up ($n=1$), because of no show ($n=2$) and because of a lack of motivation to change ($n=3$). Sessions were audiotaped; an independent assessor checked a random sample of 50% on patient and therapist compliance to the protocol. Therapists offered core interventions according to protocol, patients adequately conducted most of their homework but were hesitant to practice communication exercises at home.

Table 1 presents the results of the ITT analyses. Results of the ITT and completers analyses were similar. In patients, obsessive-compulsive symptoms significantly decreased; 8 patients achieved a reliable change. Of these, 6 were recovered. The

remaining results of the patients did not change significantly, including antagonism. In family members, accommodation significantly decreased and social functioning (WHODAS subscale Getting Along) and atmosphere at home significantly improved. A non-significant trend of improvement in the overall level of functioning appeared.

Table 1. Family treatment results for patients with OCD and a family member, intent to treat sample

	Pre-test Mean (SD) n=16	Post-test Mean (SD) n=16	t(df); p
Patients			
Y-BOCS total	23.1 (4.5)	18.5 (6.7)	3.43 (15); 0.00*
Perceived Criticism Measure	6.8 (1.6)	6.9 (1.3)	-0.46 (15); 0.65
WHO Disability Assessment Schedule	29.2 (16.5)	27.7 (3.4)	0.41 (15); 0.69
Atmosphere at home	72.7 (22.2)	71.0 (19.5)	0.61 (15); 0.55
Satisfaction with family treatment	NA	83.1 (18.7)	
Family members			
Family Accommodation Scale	19.1 (7.6)	12.5 (11.0)	4.03 (15); 0.00*
WHO Disability Assessment Schedule	14.9 (14.7)	11.6 (14.6)	2.03 (15); 0.06
Getting along ¹	26.6 (20.2)	20.0 (20.4)	2.48 (15); 0.03*
Atmosphere at home	62.1 (19.6)	71.6 (17.4)	-3.41 (15); 0.00*
Satisfaction with family treatment	NA	79.6 (15.6)	

* $p < 0.05$

NA not applicable

¹Remaining WHODAS subscales of patients and family members did not change significantly

Both patients and family members were satisfied with the family intervention. They appreciated getting advice about dealing with OCD in the context of their relationship. Both benefited but in different aspects. Patients, most of whom had received several previous treatments, experienced a clinically significant reduction of OCD. Family members reduced accommodation, whereby they experienced that feared consequences did not occur, possibly due to the coping strategies provided. Stopping with antagonism appeared to be difficult; this implied more emotional contact which appeared to trigger threat. Therefore, patients and family members were hesitant to practice communication exercises at home though they considered them to be helpful. It is possible that five sessions were not sufficient to change antagonistic behaviour patterns; i.e. more sessions are required. The high drop-out might be explained by the impression of therapists that the brief CBT family intervention got to the root cause of OCD and therefore was hard. More effort

is required to inform patients and their family members beforehand about the implications of therapy and to support and motivate them during treatment.

The results of our study indicated a benefit for both patients and family members. Information provided beforehand should address the implications of therapy. Additionally, the protocol should be expanded to elicit antagonistic behaviour change and for motivation and support. Our conclusion is that our treatment package including the brief CBT family intervention is promising and warrants further examination using a controlled design.

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CHAPTER 7

Relieving the Burden of Family Members of Patients with Obsessive- Compulsive Disorder

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Abstract

Objective: Obsessive-compulsive disorder (OCD) burdens family members. Certain responses of family members to OCD augment their burden, namely accommodation and antagonism. Family interventions are successful in reducing severity of OCD but surprisingly, the impact of family interventions on the burden of family members has received little attention.

Method: Sixteen family members of patients with OCD were treated – together with the patient - with our brief CBT family intervention focusing on accommodation, antagonism and normalizing the family relationship. Family burden, accommodation and antagonism were measured before and after the family intervention with: Involvement Evaluation Questionnaire, Impact on Relatives Scale, EuroQol five dimensional questionnaire (EQ-5D), Family Accommodation Scale – Self Report and the Perceived Criticism Measure.

Results: The burden of family members of patients with OCD was considerable and comparable to the burden of family members of patients with schizophrenia. Family burden was diminished after the brief dyadic family intervention and correlated to a decrease in accommodation.

Conclusion: Our brief dyadic family intervention is promising in relieving the burden of family members of patients with OCD.

Introduction

Obsessive-compulsive disorder is an invalidating disorder with a great impact on the life of patients. Patients experience a poor quality of life (QoL) and limitations with working, household activities, social relations and well-being (Eisen et al., 2006). In addition, OCD burdens people close to the patient as well. Caring for a patient with OCD puts a moderate to severe level of burden on family members (Steketee 1997, Laidlaw et al. 1999). OCD disrupts family relations, home management, leisure activities and social life (Stengler-Wenzke et al. 2006, Laidlaw et al. 1999, Gururaj et al. 2008, Cooper 1996). Family members experience distress, anxiety, depression, frustration, anger, guilt and embarrassment as a consequence of the OCD (Albert et al., 2010; Amir et al., 2000; Stengler-Wenzke et al., 2004; Torres et al., 2012). Compared to the general population, family members of persons with OCD have a reduced QoL (Albert et al. 2007, Grover & Dutt 2011, Cicek et al. 2013, Stengler-Wenzke et al. 2006).

Family members are insecure how to deal with OCD (Shafran et al. 1995). They frequently react to the obsessions and compulsions of their relatives by behaviour that is termed 'accommodation' and 'antagonism'. By accommodation is meant the adaptive behaviour of family members to OCD in order to relieve the burden for the patient (Stengler-Wenzke et al., 2004) for instance by participating in performing rituals, giving reassurance to the patient or changing routines because of the demands resulting from obsessions or compulsions. Antagonism means that family members oppose to the OCD, criticize the OCD, or have a rejecting attitude towards the patient. Antagonism is related to the belief that patients are in control of their symptoms (Renshaw et al. 2017). The more family members accommodate, the higher the chance they antagonize the OCD as well (Calvocoressi et al., 1995). In most families with a person with OCD one or both these responses occur; accommodation is present in 90% of the families and antagonism is present in 70% of the families (Calvocoressi et al., 1999; Chambless & Steketee, 1999).

Both family responses to OCD are related to anxiety and depression in relatives, family burden and a reduced quality of life in family members (Amir et al. 2000, Cherian et al. 2014). In addition, accommodation is associated with poor family functioning and antagonism is associated with family conflict (Calvocoressi et al., 1995; Hibbs et al., 1993). In other words, the burden of family members augments as a consequence of their response to OCD. This stresses the importance of helping family members dealing with OCD, to relieve their burden.

In line with this, it has often been advised to help family members dealing with OCD. Family interventions have been developed to learn family members stopping with accommodation and in some cases also with stopping with antagonism (Gomes et al. 2016, Thompson-Hollands et al. 2015, Abramowitz et al. 2013). With these family interventions, positive results have been found for patients: the severity of OCD is reduced and functioning is improved (Thompson-Hollands et al., 2014). Surprisingly, the impact of family interventions on the burden of family members has received much less attention.

In a study of Grunes et al. (2001) the effectiveness of a group therapy for family members of patients with OCD plus individual cognitive behaviour therapy (CBT) for the patient was compared to a control condition existing of individual CBT only; each condition consisted of 14 patient - family member dyads. In the group therapy condition, family members received an 8-week group therapy providing psycho-education, guidance in being a co-therapist, support and coping skills. Subsequently, treatment was individualized: family members learned either reducing accommodation, disentangle from conflict, or how they could contribute to the treatment of the patient, depending on the nature of their response to OCD. Family members in the family group had a greater reduction of depressive and anxiety symptoms than family members in the control condition, who did not participate in the family group. In another study, couples consisting of a patient with OCD and their partner received 16 sessions consisting of psycho-education, partner-assisted exposure, reducing accommodation, and general couple therapy on stressors unrelated to OCD. Partners showed improvements in depressive symptoms after the couple-based treatment, however, this did not maintain at 6-month and 12-month follow-up (Belus et al. 2014).

We have developed a brief dyadic family intervention focusing on accommodation, antagonism and normalizing the relationship between patient and family member. With this intervention we expected to reduce the OCD of the patient as well as to relieve the burden for their family members. The intervention has been tested in a pilot study (Remmerswaal et al., 2016). The brief dyadic family intervention was effective in decreasing severity of OCD of patients and also in decreasing accommodation in family members. However, antagonism did not change after the intervention, apparently because stopping with antagonism generated much anxiety.

The aim of this study is to examine whether the brief dyadic family intervention improves the burden and quality of life of family members of patients with OCD. In addition, we compared the level of burden and quality of life of family members of patients with OCD with relatives of patients with schizophrenia, using data from the literature.

Materials and methods

Subjects

Sixteen couples, consisting of a patient with OCD and the family member most involved in caring for the patient, were included. The study was conducted at the academic outpatient department for anxiety disorders at GGZ inGeest, Amsterdam, the Netherlands. All participants provided written informed consent.

Inclusion criteria for participating in the study were: 1) OCD of the patient of at least moderate severity (Yale Brown Obsessive-Compulsive Scale (Y-BOCS) ≥ 16 ; (Goodman et al., 1989a; Goodman et al., 1989b); 2) accommodation of the family member of at least moderate severity (Family Accommodation Scale on the family member (FAS) ≥ 13 ; Calvocoressi et al. 1999) and/or antagonism of significant degree (Perceived Criticism Measure on the patient (PCM) ≥ 4 ; Hooley & Teasdale, 1989). Psychotropic medication was allowed but should be kept constant during treatment.

Treatment

Our brief dyadic family intervention consisted of five sessions of 90 minutes, planned every other week. Each session consisted of three parts: 1) decreasing antagonistic responses of the family members and decreasing patients pleading for accommodation by learning effective communication about OCD; 2) response prevention of accommodation by family members; and 3) planning pleasurable, joint activities free from OCD. The protocol was added to regular cognitive behaviour therapy of the patient and offered to a couple consisting of a patient with OCD and a family member (Remmerswaal et al., 2016).

Measures

The Involvement Evaluation Questionnaire (IEQ; van Wijngaarden et al. 2000) was used to measure the burden of family members. This instrument is developed for relatives of patients with schizophrenia. We used the scales of the IEQ applicable to relatives of patients with OCD, which were three subscales: 1) tension: strained interpersonal atmosphere between patient and relatives; 2) worrying, for instance about the patient's health and future; and 3) urging: activation and motivation of the patient, for instance stimulating the patient to take care of himself. The IEQ is tested on patients with schizophrenia, the validity and reliability of the IEQ are satisfactory (van Wijngaarden et al., 2000).

The Impact On Relatives Scale (IORS) was used to measure the impact of the OCD symptoms of the patient on the family member. The IORS is an OCD-specific

measurement of family burden that was constructed for the NOCDA study (Schuurmans et al., 2012) and is based on items of the Y-BOCS, adapted to relatives. The IORS consists of five items: How much of your time is occupied with reassuring the person with respect to his obsessive thoughts?, How much of your time do you spend helping the person with performing compulsive behaviours?, How much does the OCD of the person interfere with your functioning?, How much of an effort do you make to resist the OCD symptoms of the person? How much have you helped the person gaining control over his OCD symptoms?.

The self-rated EuroQol five dimensional questionnaire (EQ-5D) was used to assess quality of life. This instrument was proven suitable and reliable in the general population and is applicable in patient samples (EuroQol Group, 1990). The EQ-5D contains 5 dimensions: mobility, self-care, daily activities, pain/discomfort and depression/anxiety. Each dimension is rated at three levels: no problems, some problems and major problems. The health states are converted into an index score - the EQ-5D - reflecting the generic overall QoL that can be used to compare QoL in various conditions. The EQ-5D has a value between 1 (best possible health) and 0 (worst possible health).

The Family Accommodation Scale – Self Report version (FAS-SR; Calvocoressi et al. 1999) was used to measure family accommodation. The reliability and validity of the FAS are good. The FAS has two subscales (accommodation, consequences of not accommodating) and a total score.

The Perceived Criticism Measure (PCM) was used to assess perceived criticism (Hooley & Teasdale, 1989). The instrument consists of one item: 'How critical is your partner of you?' and has a score between 1 and 10. The psychometric properties of the PCM are satisfactory (Chambless & Blake, 2009; Hooley & Teasdale 1989). Antagonism was assessed with the PCM on the patient with OCD, which we reported in a previous paper (Remmerswaal et al., 2016).

Statistical analyses

Results were examined using two-tailed t-tests in the intent to treat (ITT) sample. Missing values at post-test ($n=5$) were imputed with pre-test scores. Furthermore, the pre-test score of quality of life of family members of patients with OCD was compared to the general Dutch population with one-sample t-tests, using data from Szende et al. (2014). The subscales of the IEQ (burden) at pre-test were compared to family members of patients with schizophrenia with one-sample t-tests. We used data from Wijngaarden et al. (2000) to determine the reference values.

Correlations between pre-test scores and difference scores (post-test score minus pre-test score) of accommodation, antagonism and the measurements of family burden were determined with Pearson's correlation coefficient.

Results

Sample characteristics

Table 1 presents the characteristics of family members of patients with OCD. Most family members were partner of the patient (vs parent), well-educated and employed. None of them used psychotropic medication.

Table 1. Characteristics of family members of patients with OCD, $n=16$.

	<i>Mean (SD) or n (%)</i>
Age	41.6 (10.1)
Gender, female	7 (44%)
Children, yes	9 (56%)
Relation to patient	
Partner	15 (94%)
Parent	1 (6%)
Length partner-relationship with patient ¹	14.3 (13.6)
Use of psychotropic medication	0 (0%)
Education, years	13.1 (2.8)
Employed, yes	13 (81%)

¹ $n=15$

Table 2 presents the comparisons of the burden of family members of patients with OCD with family members of patients with schizophrenia. None of the subscales of the IEQ that we measured differed significantly from family members of patients with schizophrenia.

Table 2. Comparison of burden of family members of patients with OCD with family members of patients with schizophrenia with one sample t-tests, ITT sample, $n=16$.

Family burden	Relatives of patients with OCD <i>Mean (SD)</i>	Relatives of patients with schizophrenia ¹ <i>Mean (SD)</i>	<i>t(df)</i>	<i>p</i>
Urging ²	12.4 (3.8)	14.1 (5.6)	-1.84(15)	0.09
Tension ²	13.9 (4.3)	14.3 (4.3)	-0.39(15)	0.70
Worrying ²	13.5 (4.5)	14.3 (5.8)	-0.71(15)	0.49

¹ Data from van Wijngaarden et al. (2000)

² Involvement Evaluation Questionnaire

Change of involvement in OCD of family members after the brief dyadic family intervention

Table 3 presents the results of the ITT analyses. Compared with the pre-test, urging and the impact of the OCD on the life of family members were significantly ameliorated at post-test. A non-significant trend of improvement of consequences of not accommodating appeared after the family intervention. Quality of life of family members of patients with OCD did not significantly differ from the general Dutch population, which is 0.89 (Szende et al., 2014; ($t(15)=1.63$; $p=0.12$).

Table 3. Involvement of family members in OCD, before and after a brief dyadic family intervention, ITT sample, $n=16$.

	Pre-test	Post-test	$t(df)$	p
Urging ¹	12.38 (3.76)	10.63 (3.42)	3.05(15)	0.01*
Tension ¹	13.88 (4.35)	12.88 (3.69)	1.55(15)	0.14
Worrying ¹	13.50 (4.50)	12.25 (3.89)	1.11(15)	0.29
Impact on relatives ²	13.81 (3.54)	11.44 (3.56)	2.73(15)	0.02*
Quality of Life ³	0.93 (0.10)	0.92 (0.10)	0.27(15)	0.79
FAS-SR ⁴				
Accommodation	22.56 (8.23)	20.25 (9.27)	1.29(15)	0.22
Consequences	8.00 (2.85)	6.88 (2.83)	2.09(15)	0.05
Total	33.31 (10.24)	29.50 (11.99)	1.68(15)	0.11
Perceived Criticism ⁵	5.38 (2.36)	5.75 (2.24)	-0.75(15)	0.46

¹ Involvement Evaluation Questionnaire

² Impact on Relatives Scale

³ EuroQol five dimensional questionnaire (EQ-5D)

⁴ Family Accommodation Scale – Self Report

⁵ Perceived Criticism Measure

* $p<0.05$

Relation between family burden measurements and family accommodation and antagonism

Family burden measurements were related to accommodation and antagonism at pre-test: FAS SR accommodation, consequences of not accommodating and the total score were significantly correlated with tension (respectively: $R=0.52$, $p=0.04$; $R=0.71$, $p<0.01$; $R=0.68$, $p<0.01$), while antagonism was significantly correlated with impact on relatives ($R=0.57$, $p=0.02$).

An improvement in accommodation was significantly correlated with an improvement of worrying (FAS SR accommodation: $R=0.64$, $p=0.01$; FAS SR total score: $R=0.57$, $p=0.02$) and an improvement of the impact on relatives (FAS SR

accommodation: $R=0.57$, $p=0.02$; FAS SR consequences: $R=0.78$, $p<0.01$; FAS SR total score: $R=0.66$, $p=0.01$). Change in antagonism was not significantly correlated with change in family burden measurements (IEQ and IORS) or QoL, probably because antagonism did not change significantly from pre-test to post-test.

Discussion

The level of burden of family members of patients with OCD was comparable to the burden of family members of patients with schizophrenia in the areas that we measured, which is considerable. Our result is congruent with previous findings that family burden of patients with OCD, anxiety disorders, depression and schizophrenia is equivalent (Senaratne et al. 2010, Magliano et al. 1996, Angermeyer et al. 2006). This underlines the importance of helping family members how to live with a patient with OCD. It might help patients with OCD as well: previously it was found that the level of experienced family burden and severity of OCD are related (Ramos-Cerqueira et al., 2008), however, another study did not find such a correlation (Gururaj et al., 2008).

Pre-test scores of accommodation and antagonism were significantly correlated to family burden, which is congruent with previous findings that accommodation and antagonism are related to family burden (Amir et al. 2000, Cherian et al. 2014). The burden of family members of patients with OCD was reduced after the brief dyadic family intervention. Not all measurements of burden changed significantly, probably because we had a small sample, however, our intervention is promising in relieving family burden.

QoL of the family members at pre-test was comparable to the QoL of the general Dutch population, which is not congruent with previous findings showing a reduced QoL in family members of patients with OCD (Albert et al. 2007, Grover and Dutt 2011, Cicek et al. 2013, Stengler-Wenzke et al. 2006). Our sample of family members was well-educated and most of them were employed; possibly, this protects their quality of life against the impact of OCD. This is congruent with a research finding that QoL of family members of patients with schizophrenia was higher when family members were unemployed, or had nonqualified occupations (Lua, 2011). Another explanation might be that our quality of life instrument, EQ-5D, is different from quality of life instruments used in other studies (for example SF-36 and WHOQOL), which include domains like social life, environment and role limitations. QoL of family members in our study was not improved after the family intervention, probably because of a ceiling effect.

Perceived criticism of family members was lower than the perceived criticism of their relatives with OCD, which we have reported in our previous paper (*mean (SD)* pre-test: 6.8 (1.6); post-test: 6.9 (1.3); Remmerswaal et al. 2016). It has been reported that the concept of perceived criticism is related to the amount of critical comments made by the other person, but also to the amount of critical comments made by the person himself, both verbal and nonverbal comments, and thus reflects a critical interaction (Gerlsma et al., 2009). Apparently, patients perceive the interaction as more critical than their family members. However, the perceived criticism score of the family members indicates a critical interaction as well. Possibly, interventions on antagonism may be improved by making family members and patients more aware of their verbal and nonverbal critical comments, which contribute to a critical interaction, and by re-appraisal of critical comments by the patient.

To summarize and conclude, living with a patient with OCD burdened the life of family members considerably, even in our sample of family members with a QoL comparable to the general population. Family members were worried about the patient, experienced tension in the relationship with the patient and urged the patient for instance to self-care or to employ activities. In addition, family members accommodated and antagonized the OCD symptoms in a severe degree. A high family burden was significantly correlated with more severe accommodation and antagonism. Family burden was diminished after our brief dyadic family intervention and was correlated to a decrease in accommodation. We presume that family burden diminishes further when family members stop with antagonism. However, family members commonly do not stop with accommodation and antagonism by themselves, because - as they reported in our study - they are afraid it causes quarrels or worsens the mental symptoms (OCD) of the patient. In addition, family members frequently are unsure how to deal with OCD (Shafran et al. 1995). Advice and support during treatment may enable the family to normalize their behaviour and to decrease the burden they experience. Our brief family intervention focusing on accommodation, antagonism and normalizing the family relationship is promising in relieving the burden and the impact of OCD on family members.

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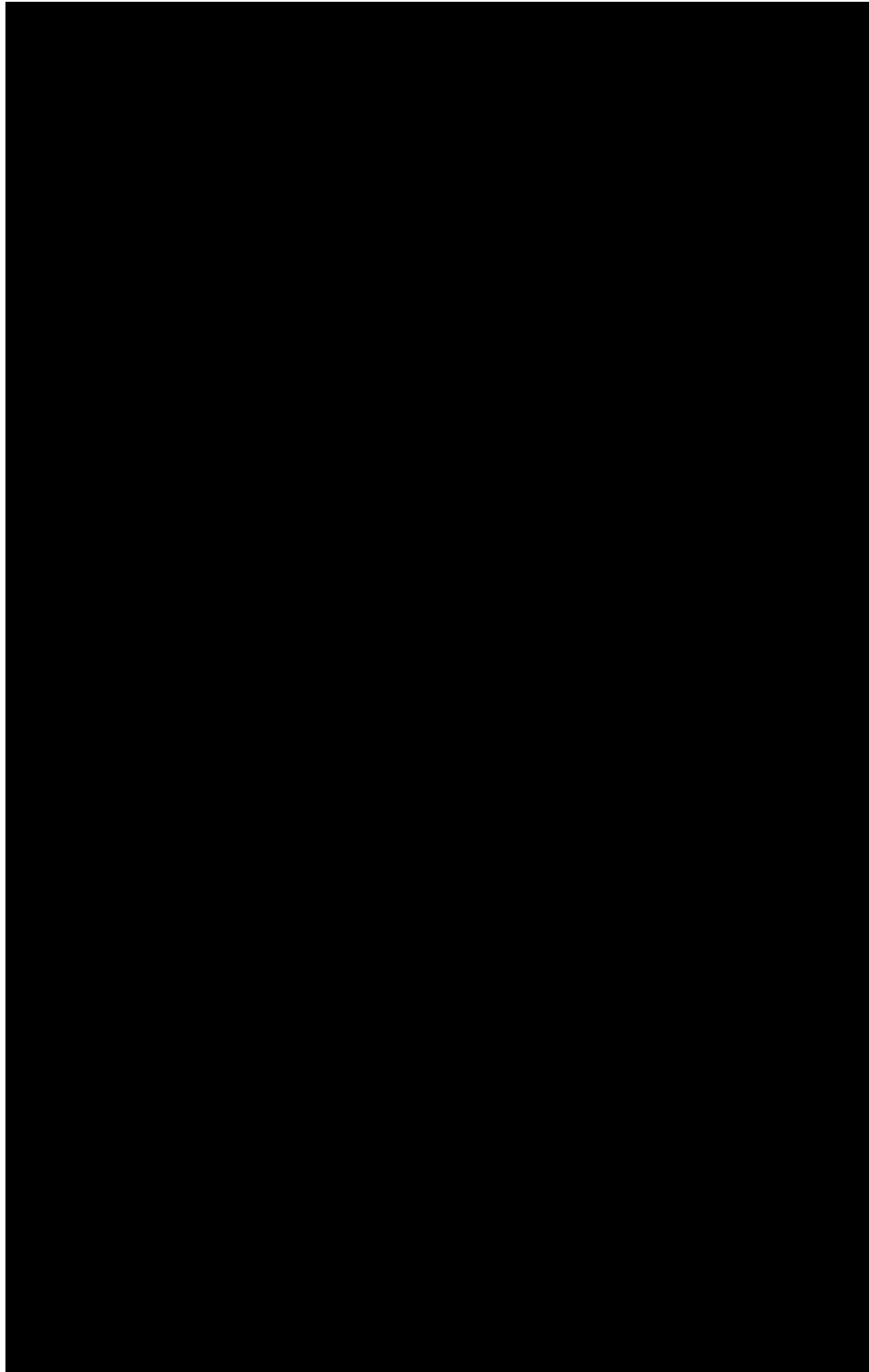


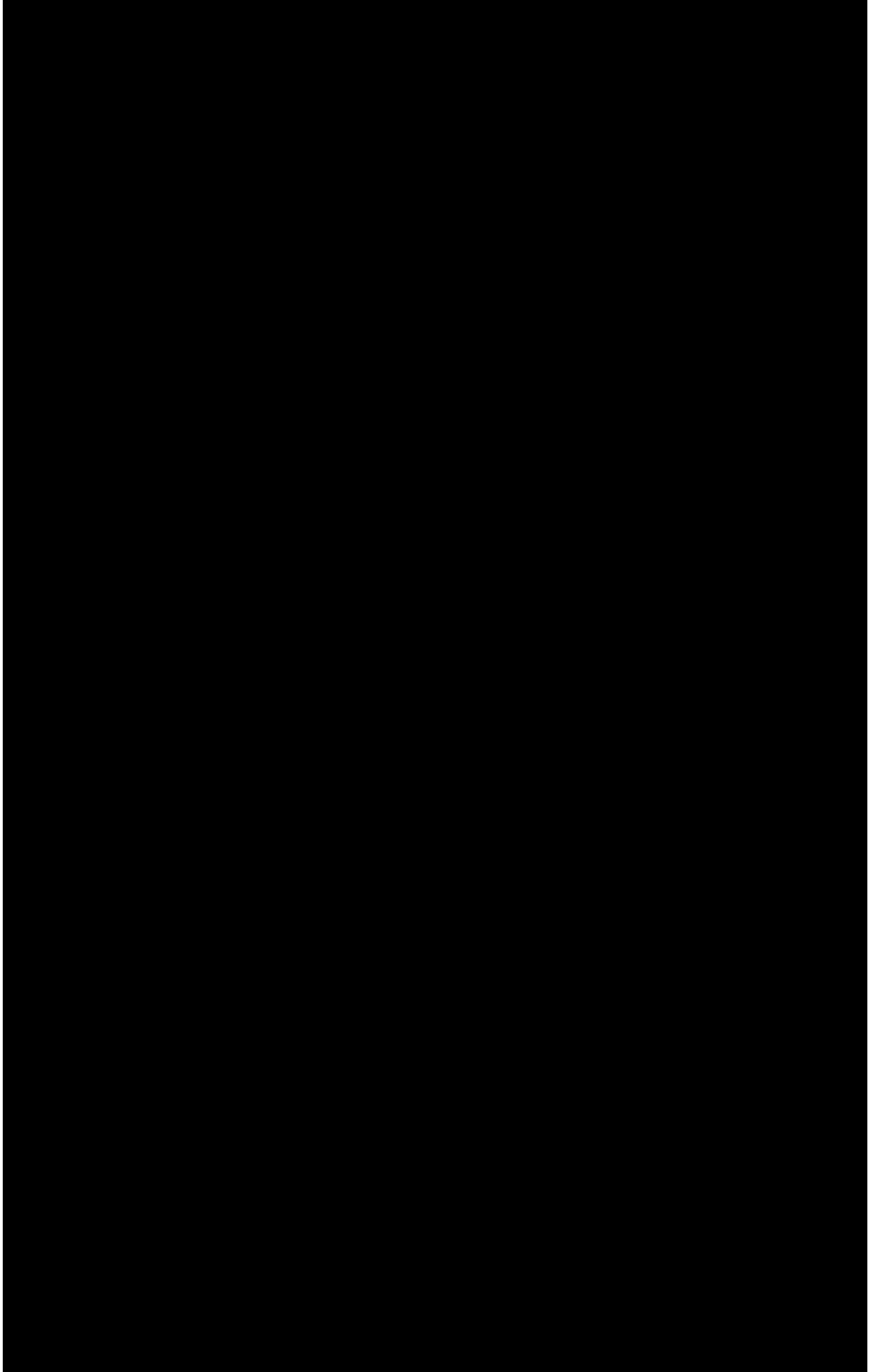
CHAPTER 8

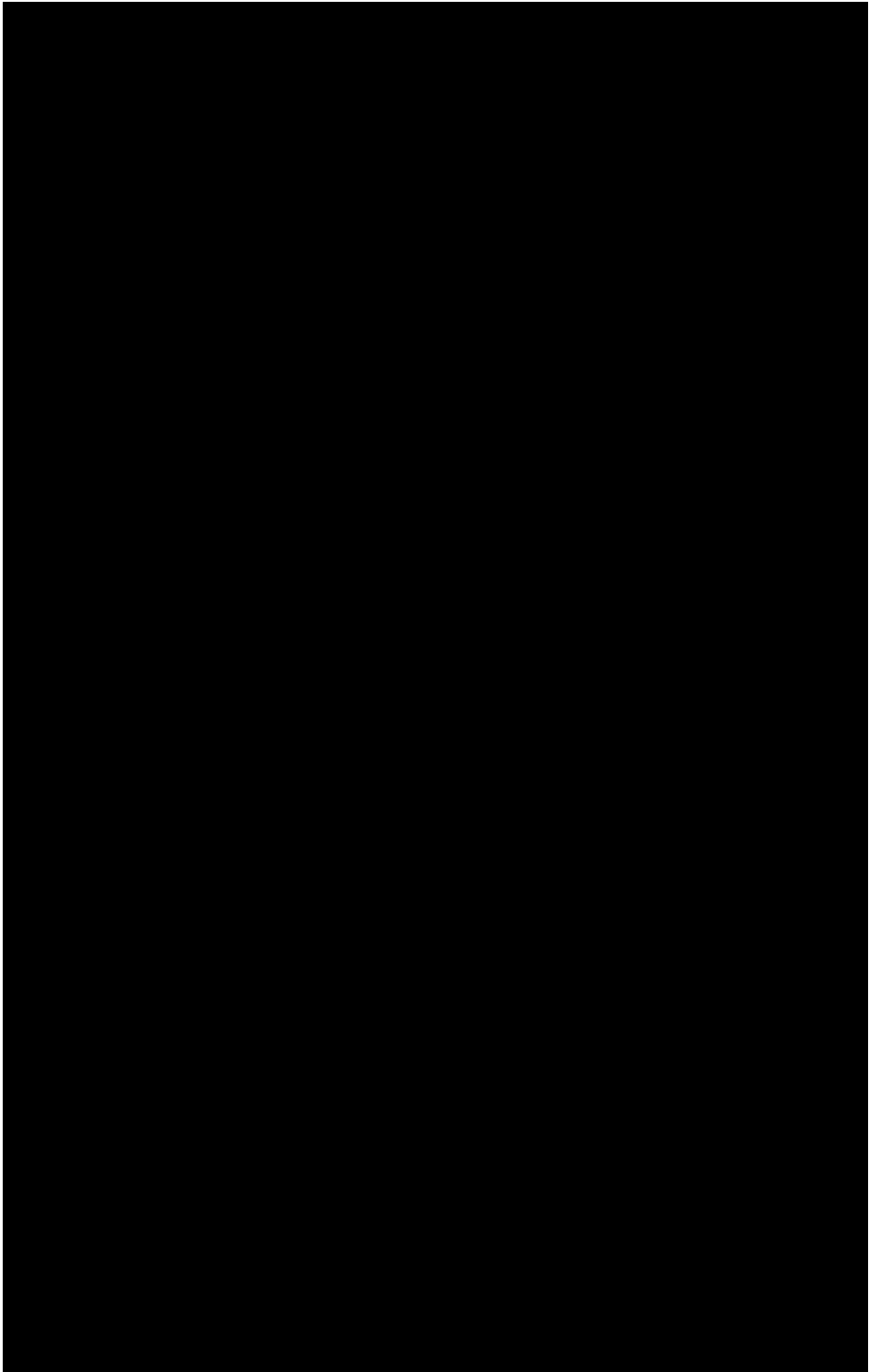
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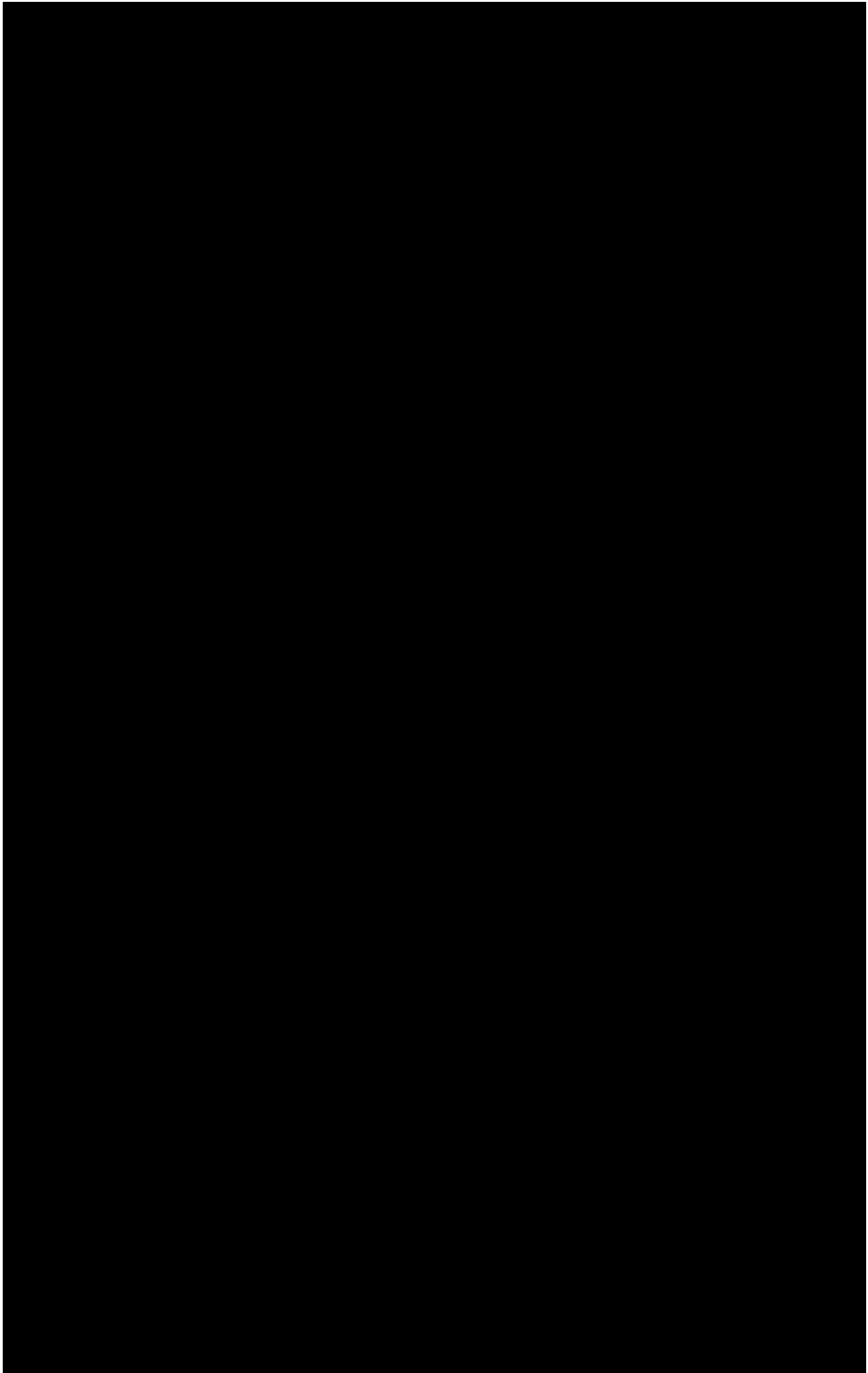
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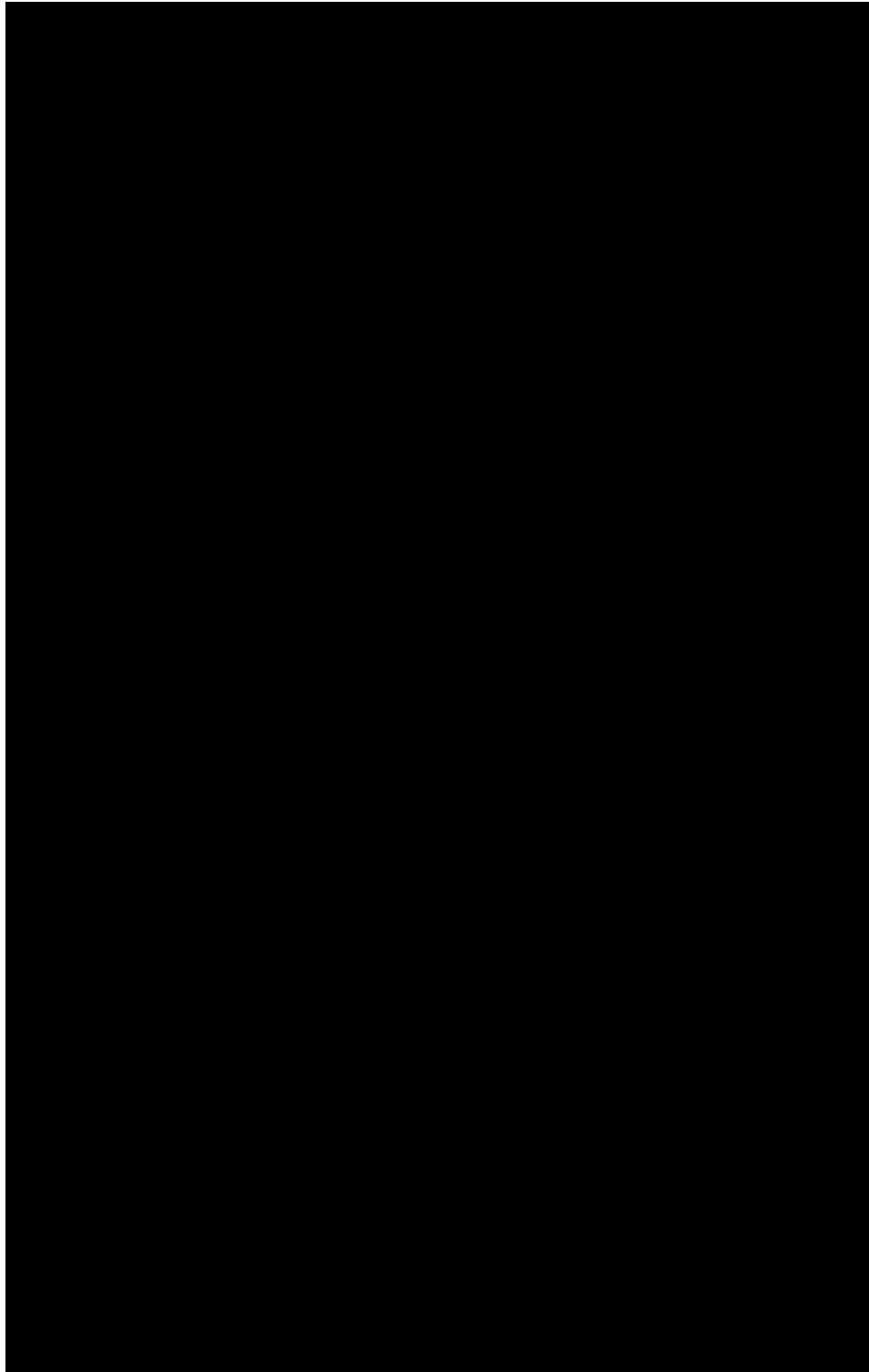
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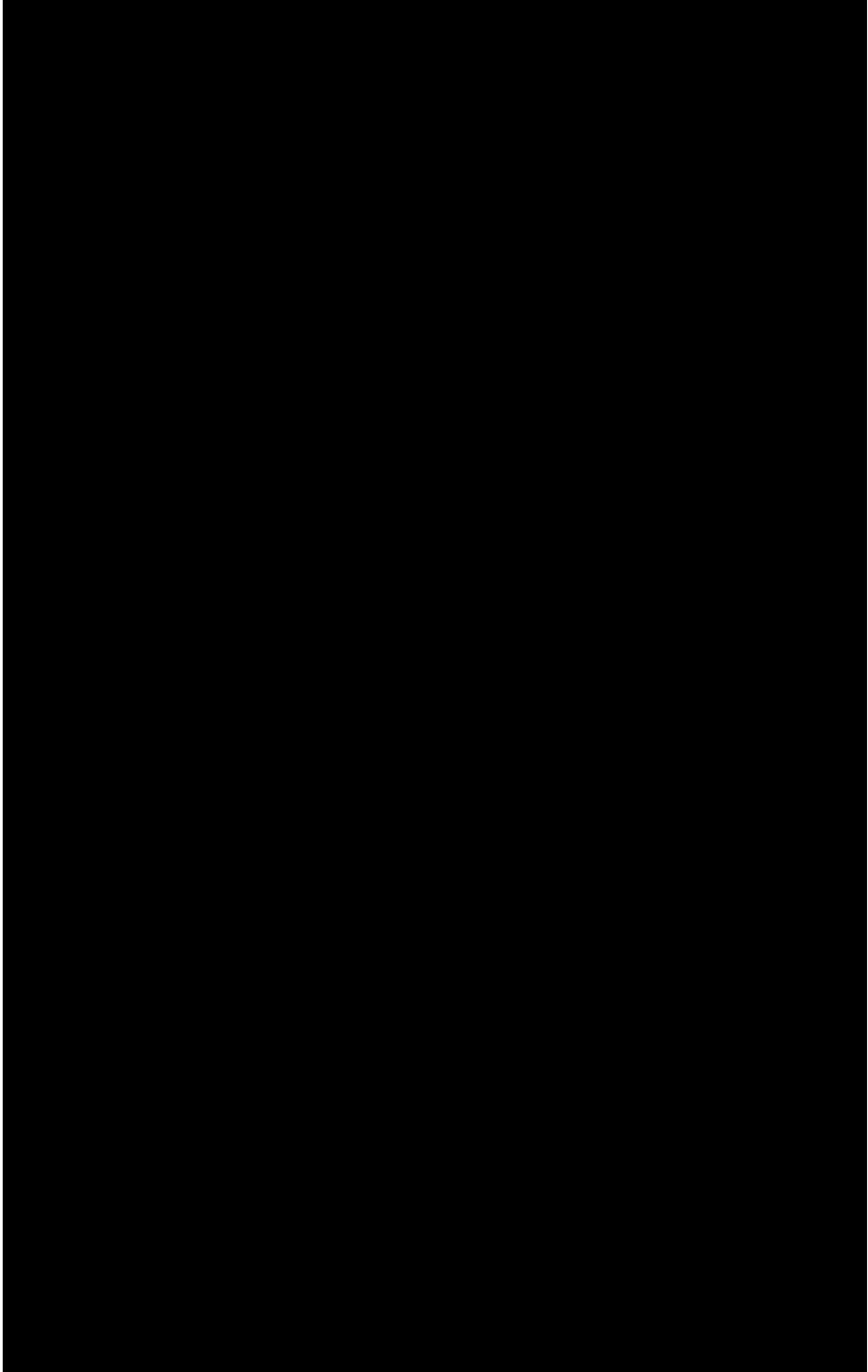


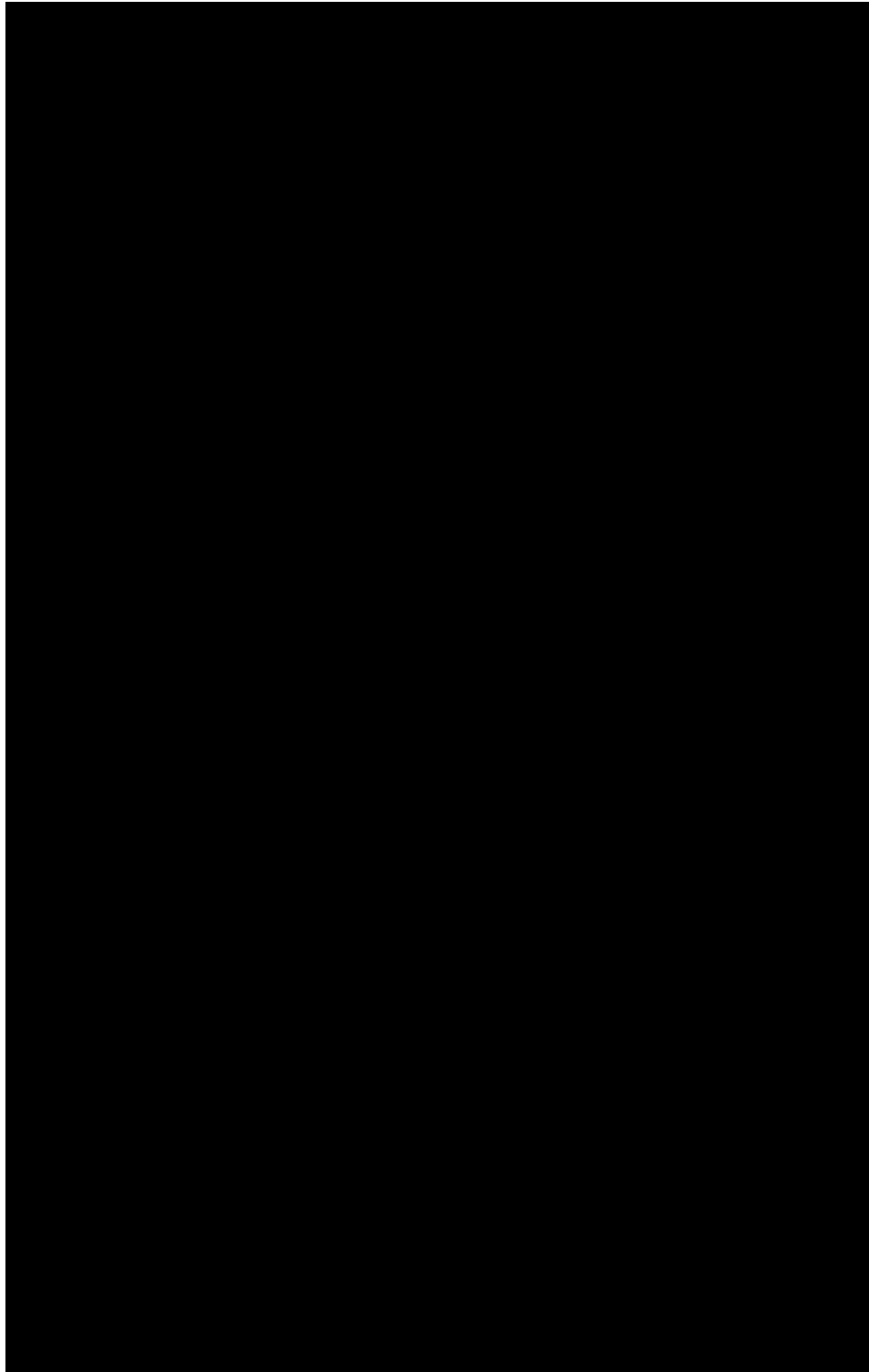


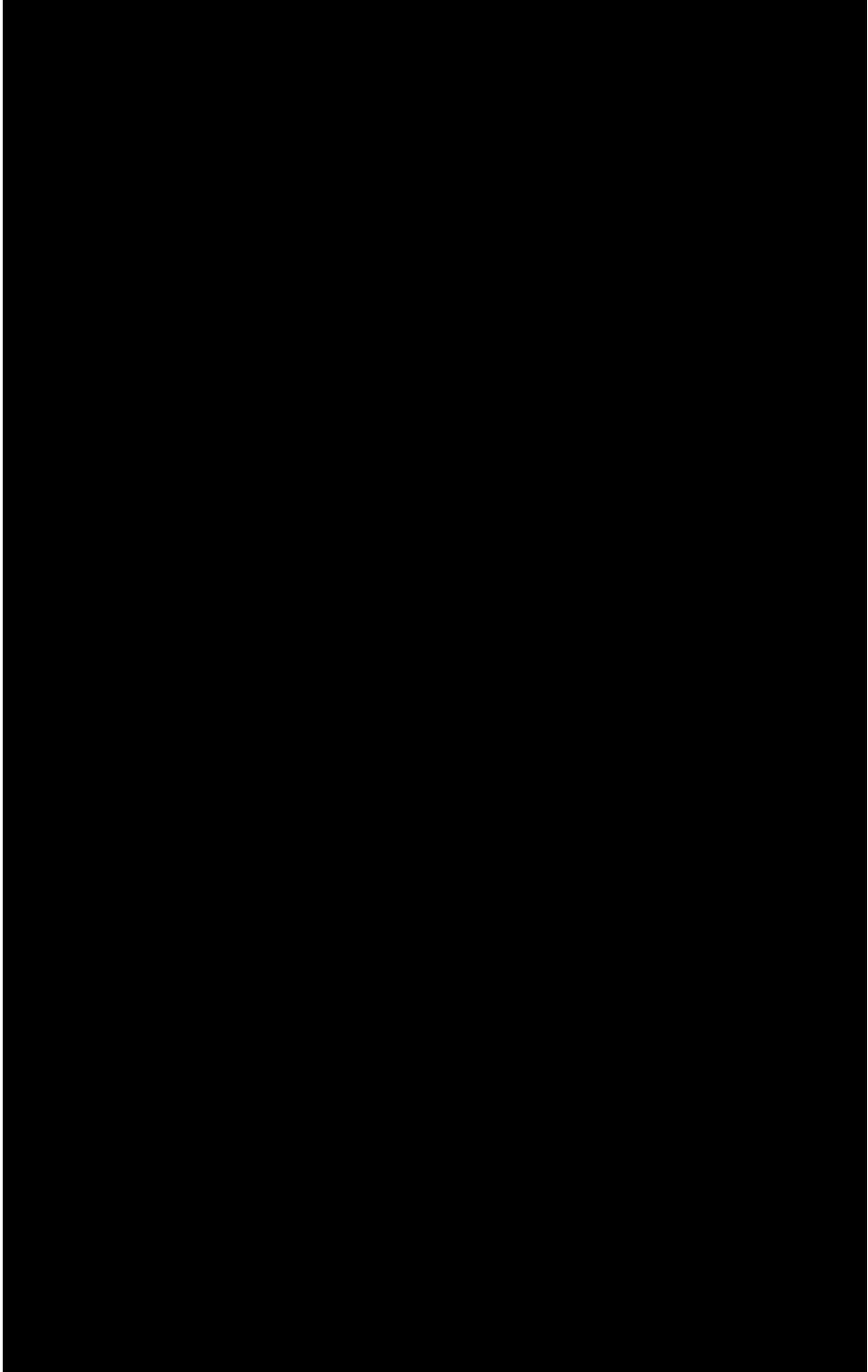


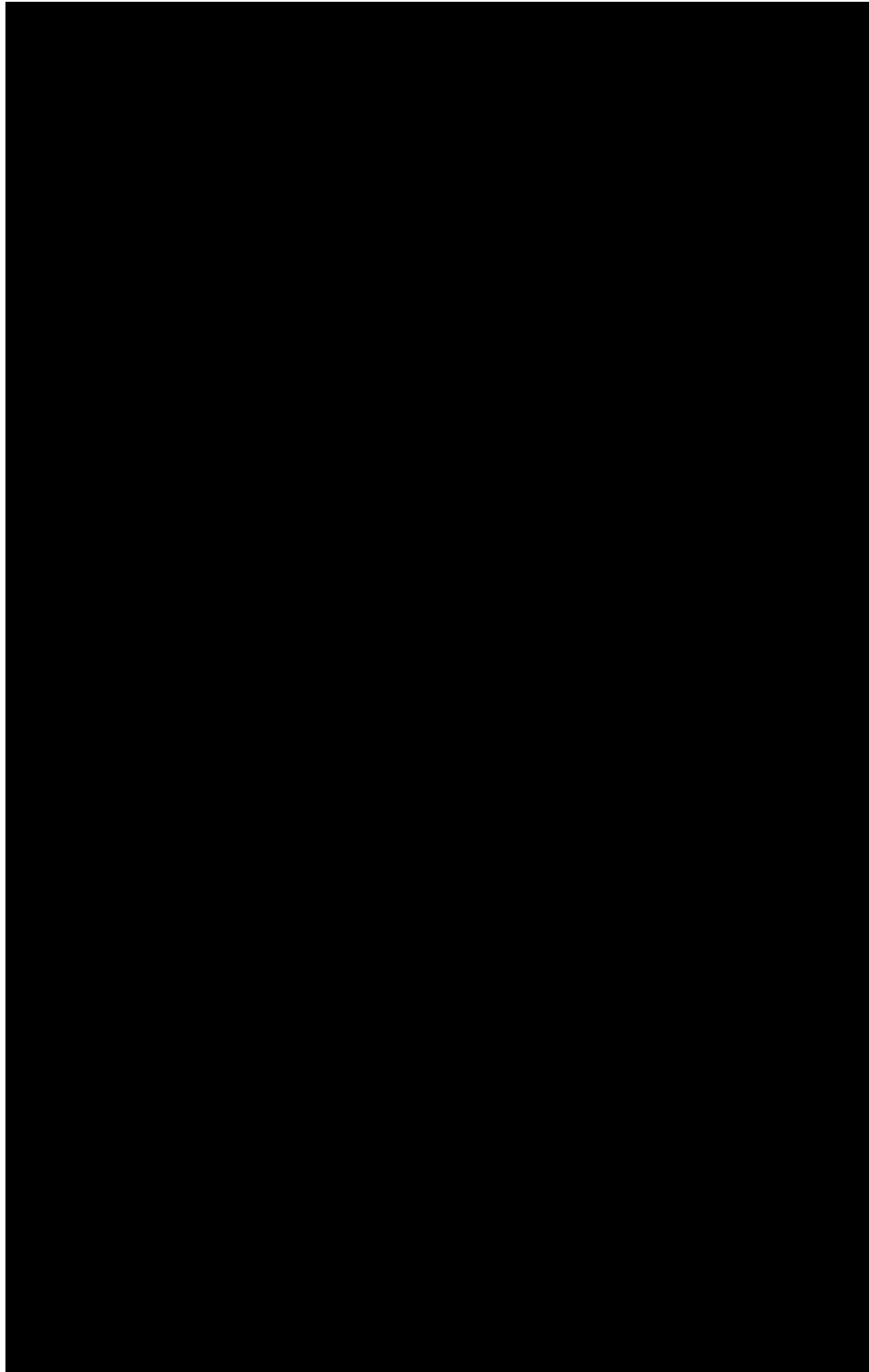


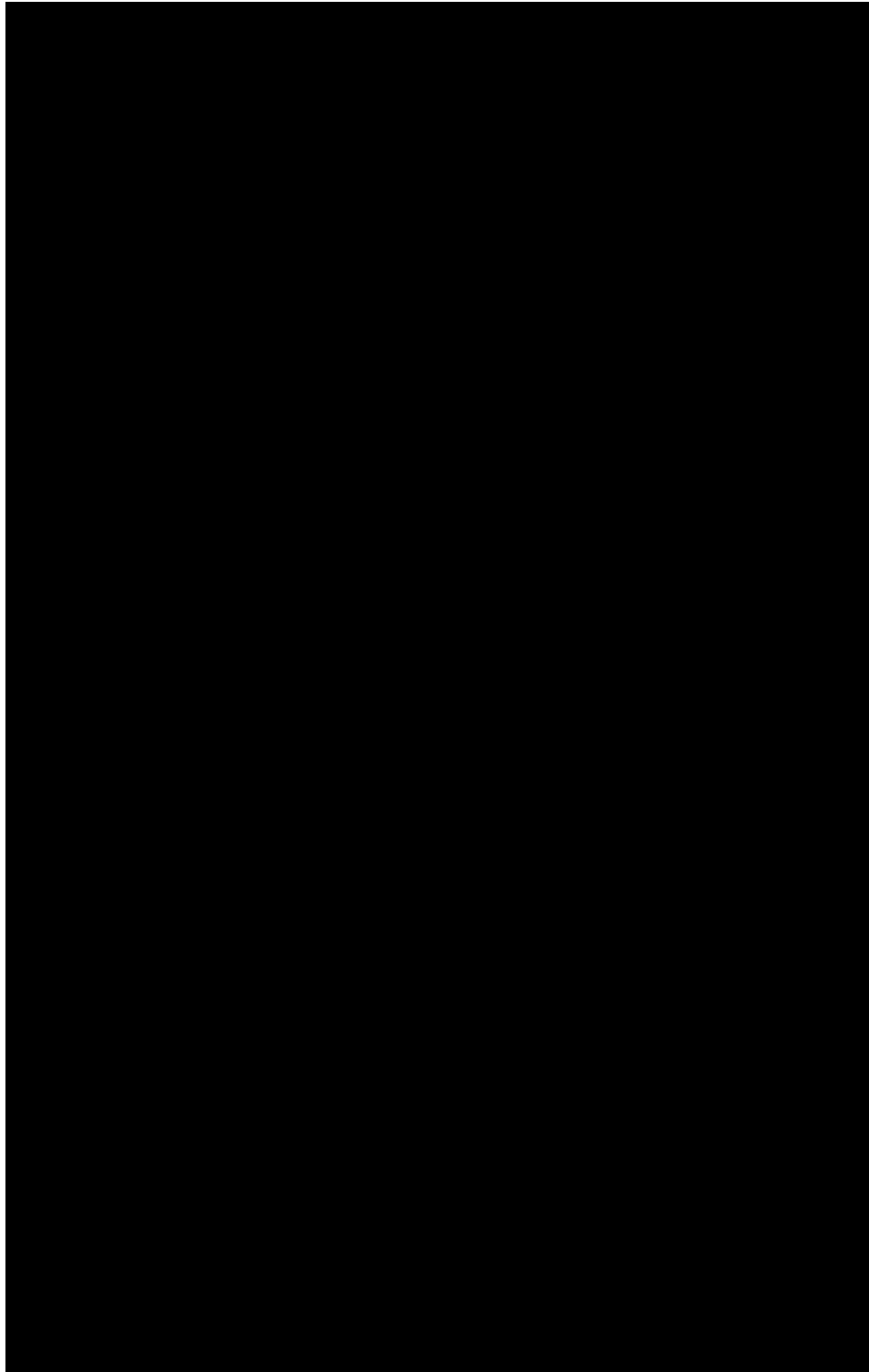


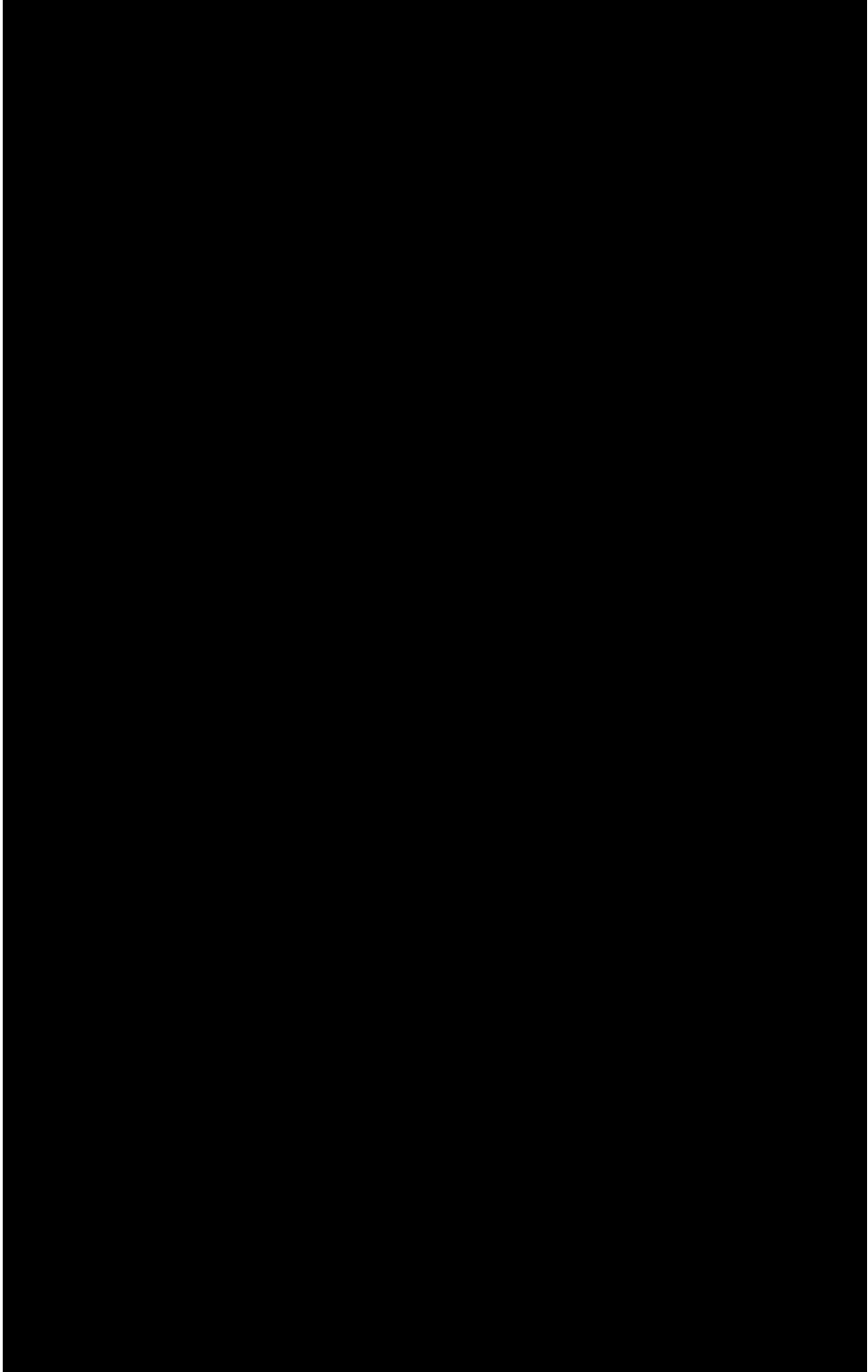


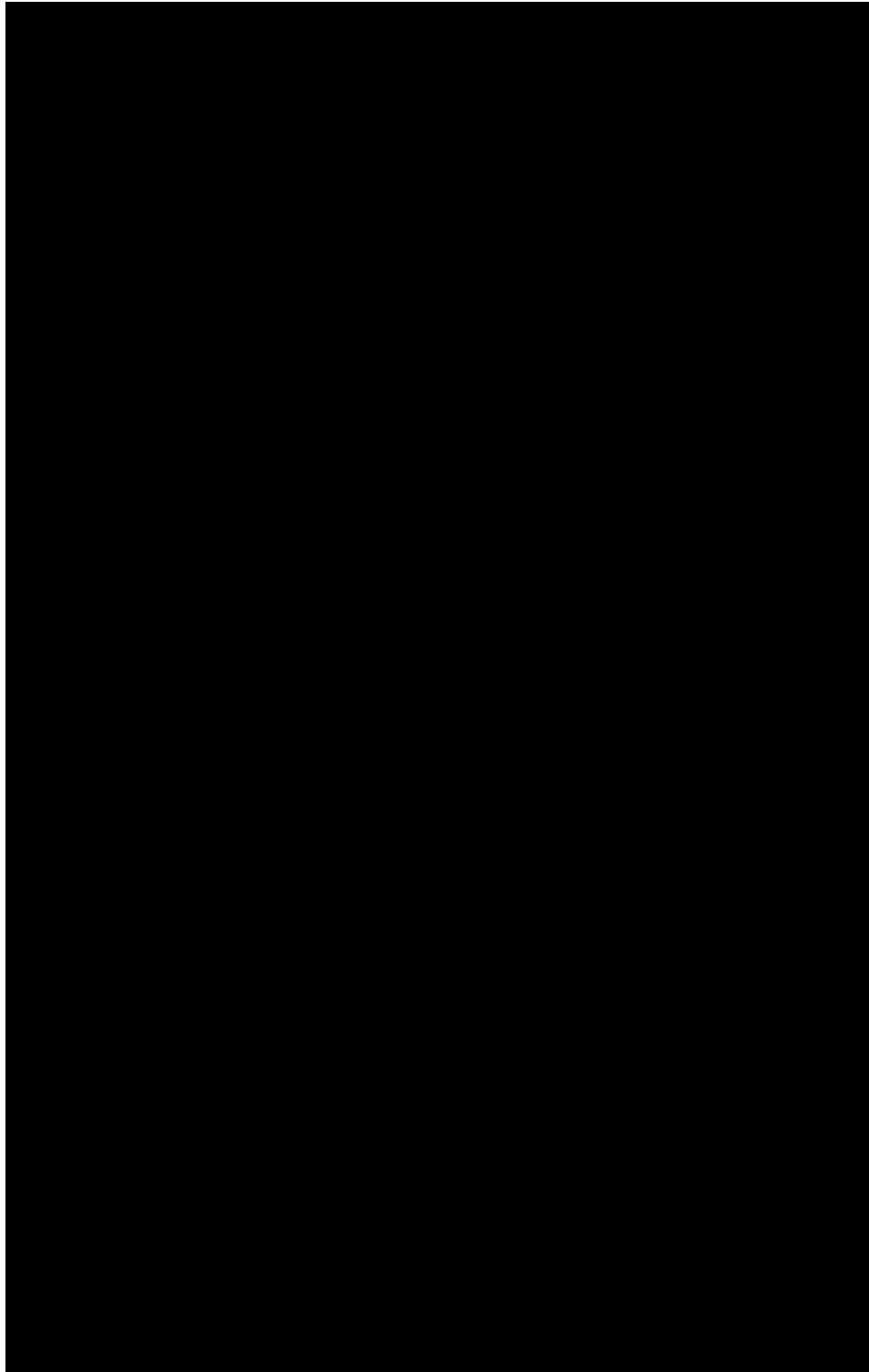


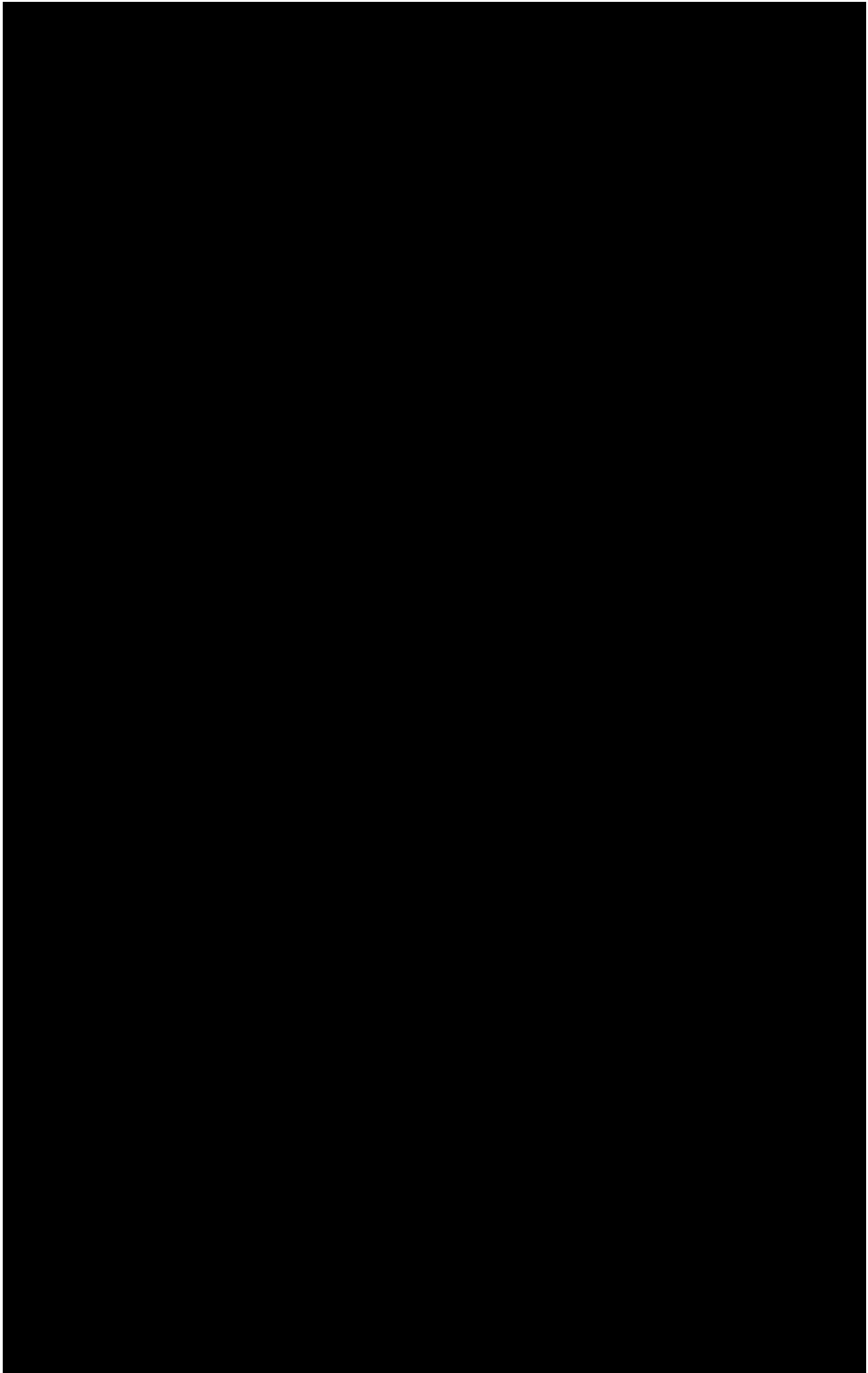


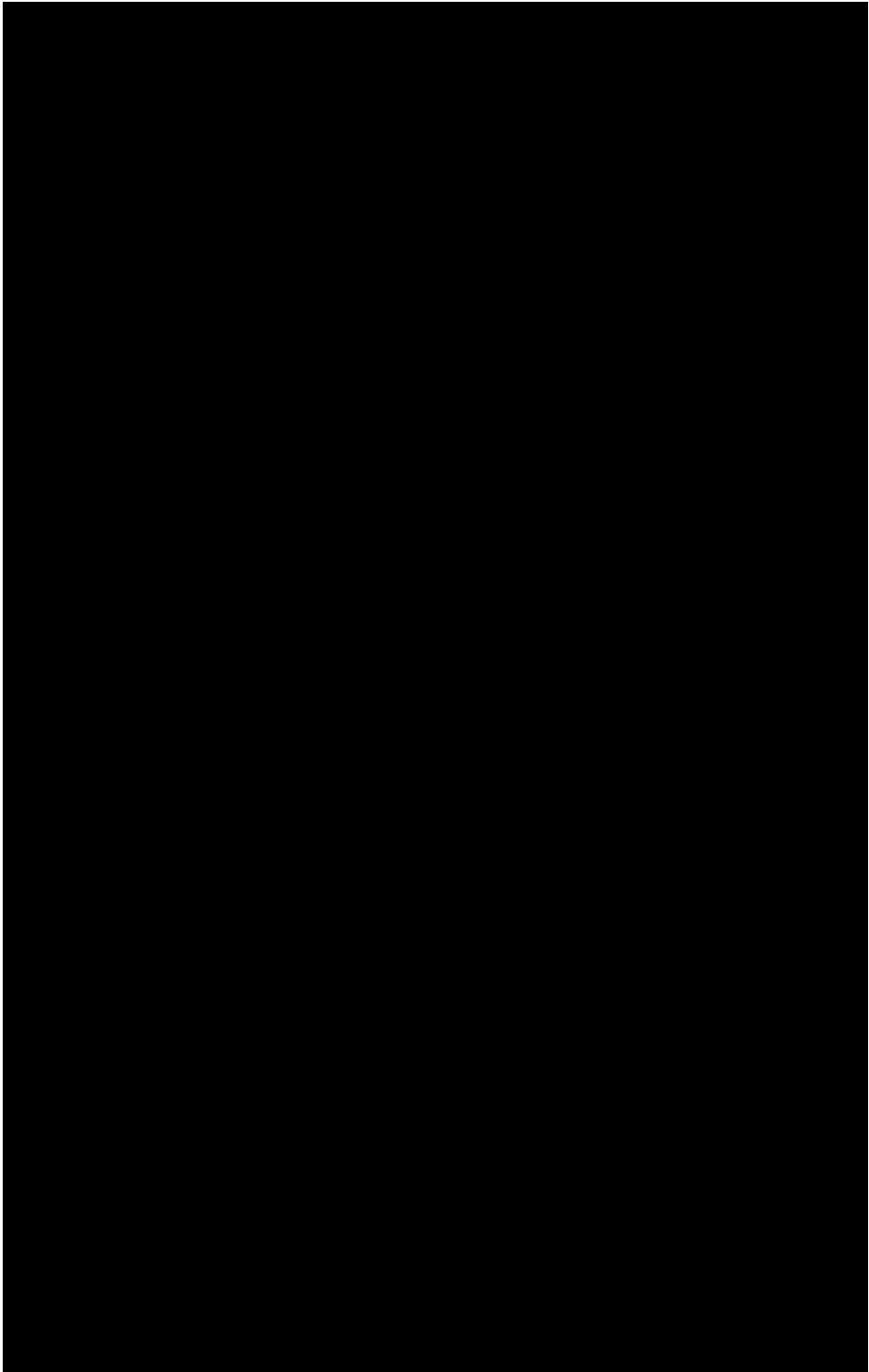


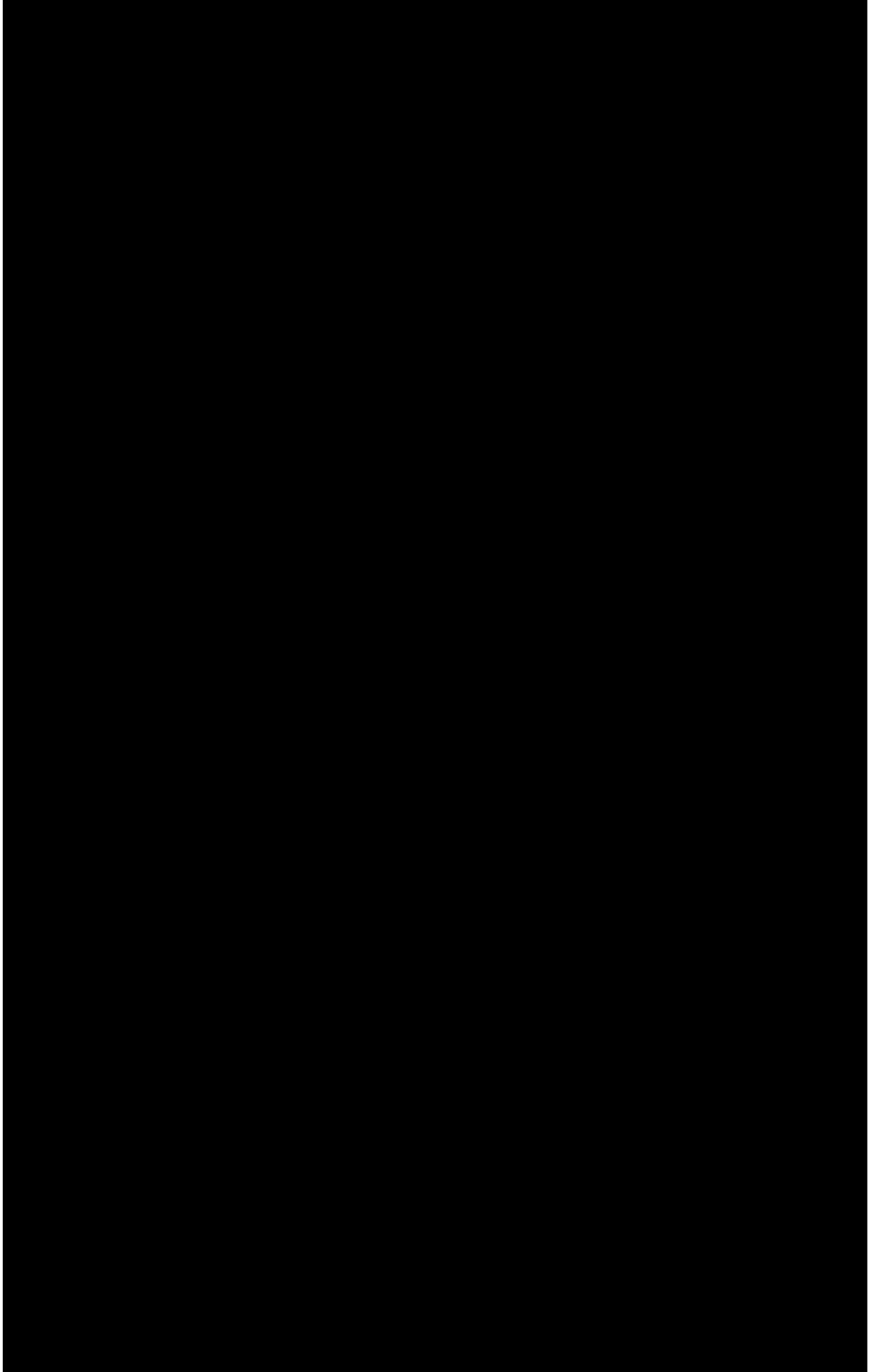


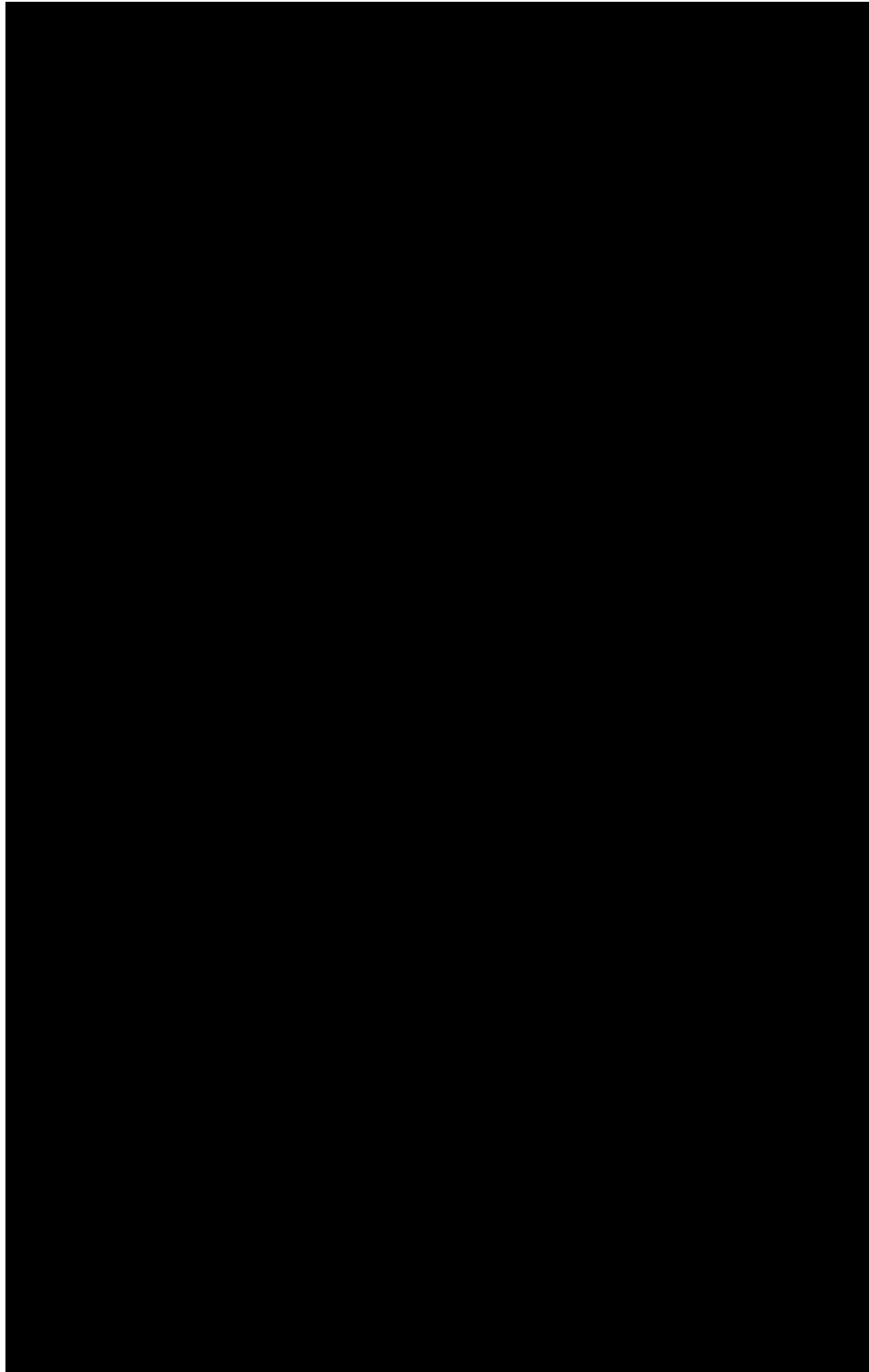


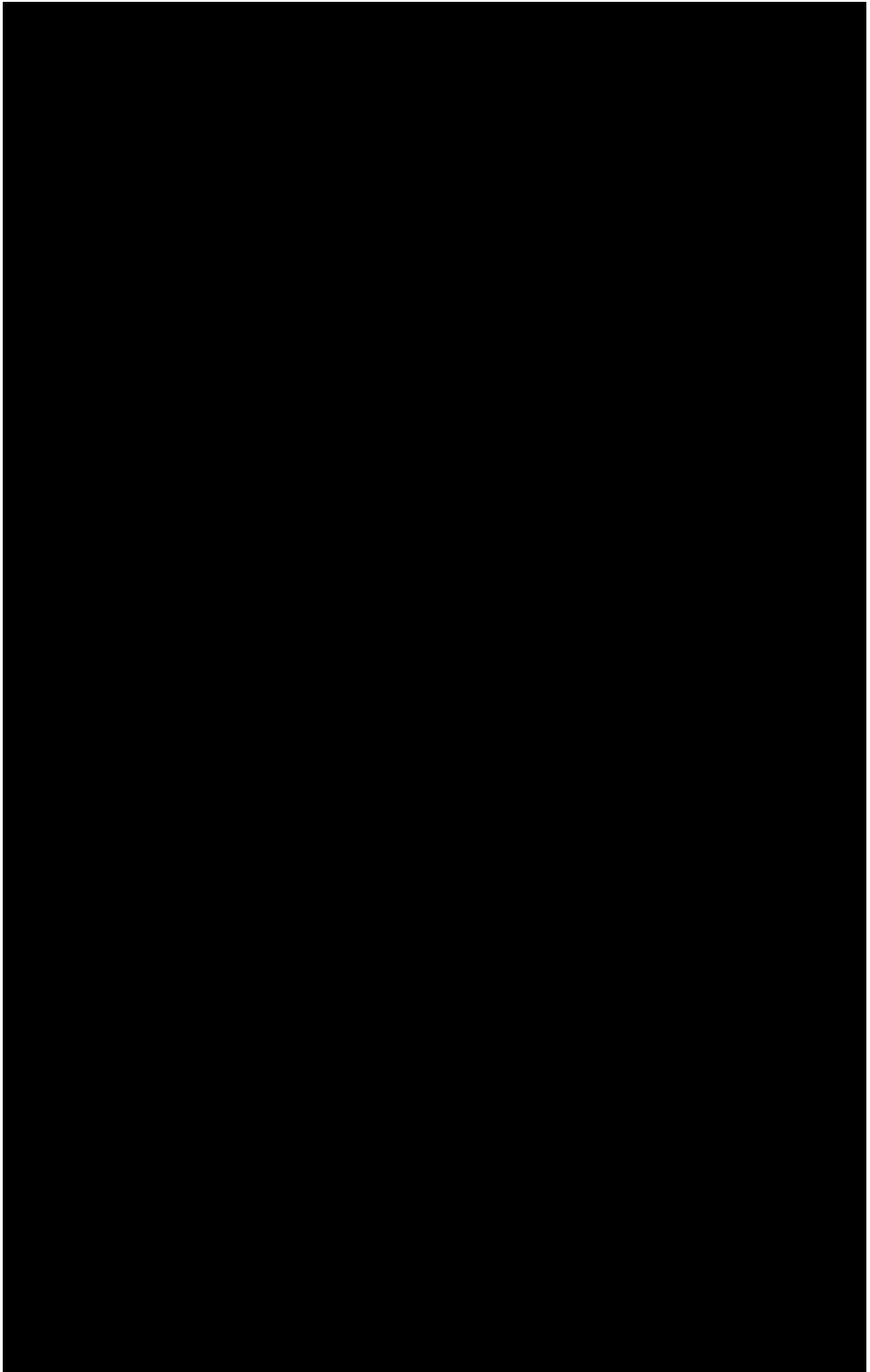


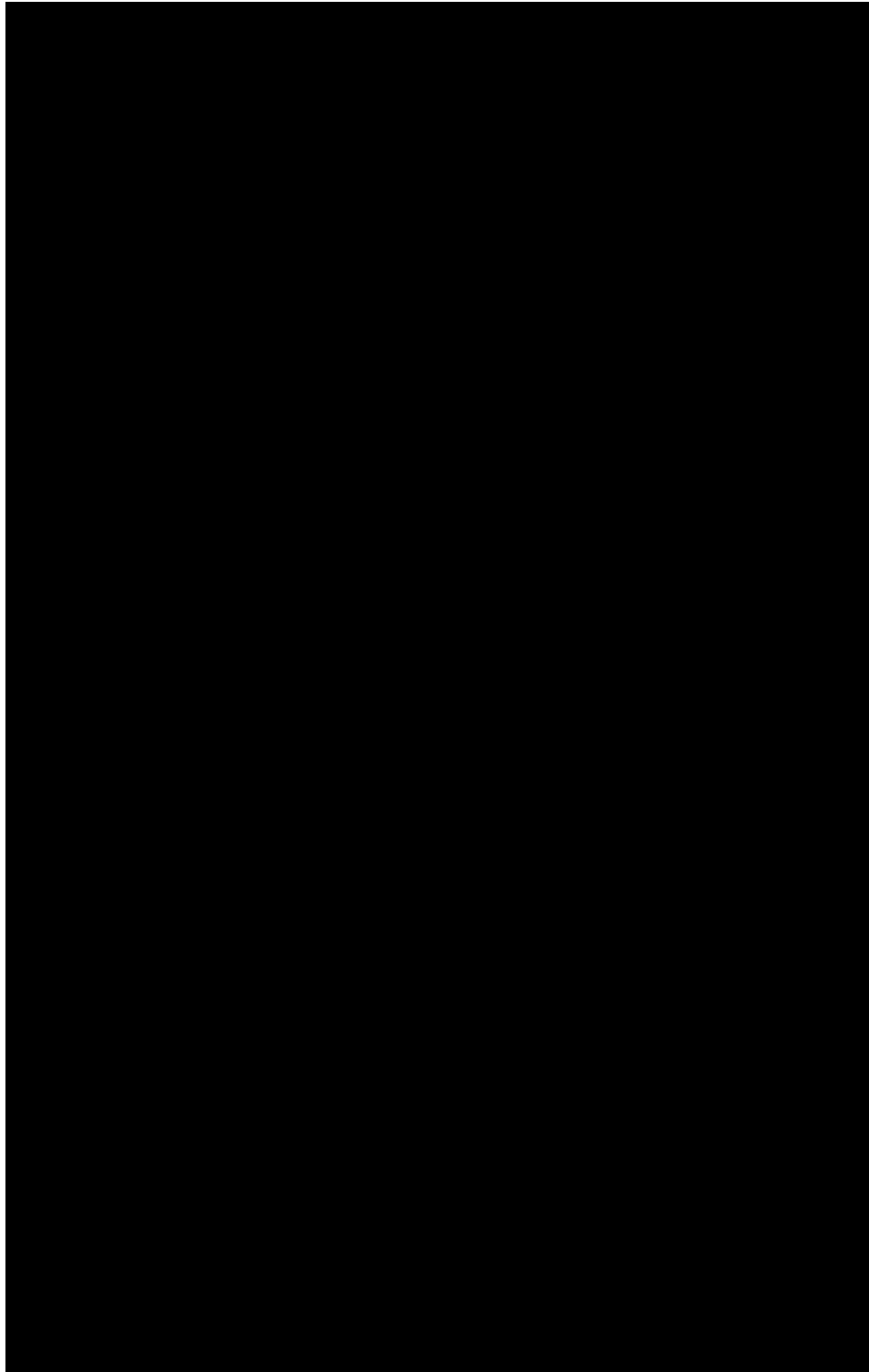


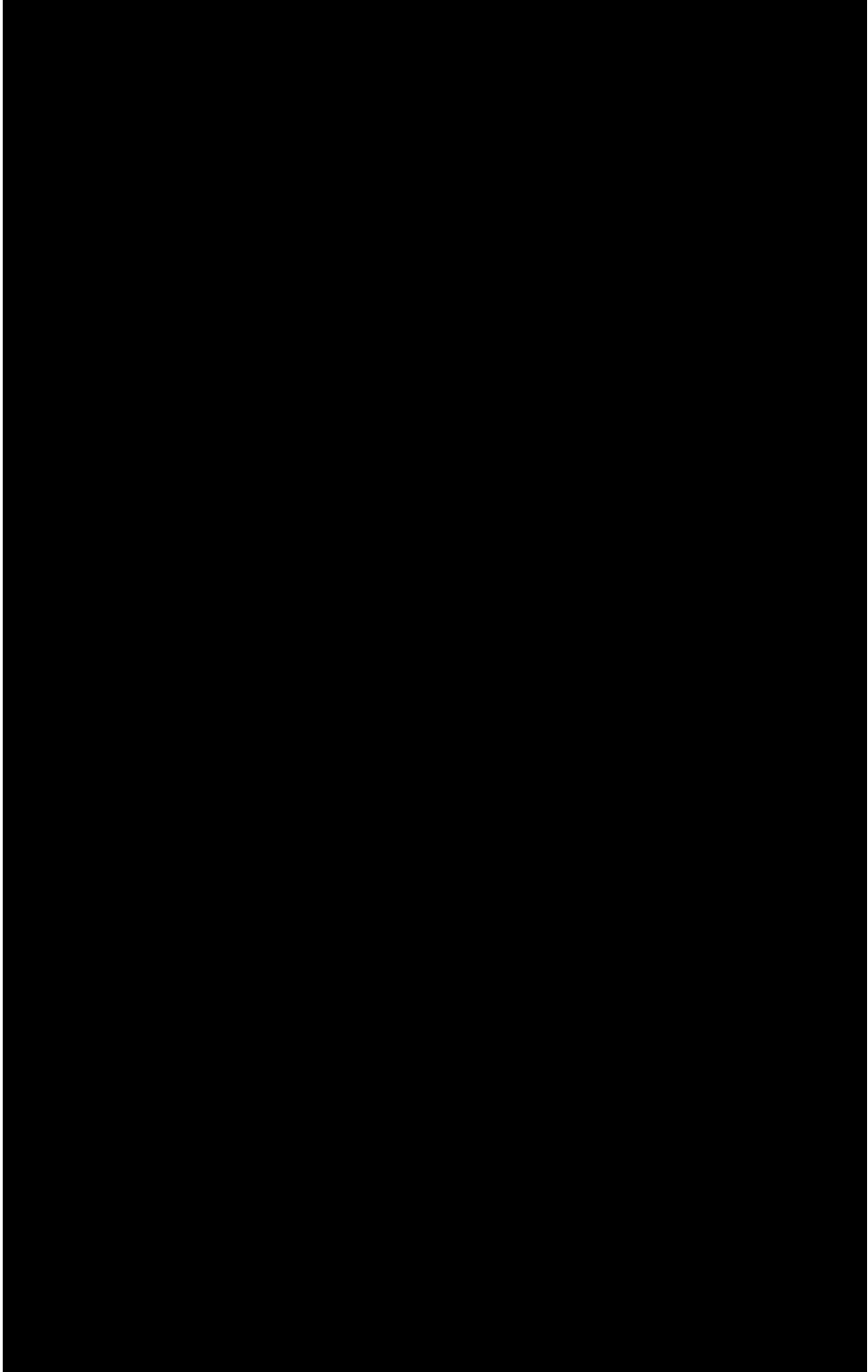


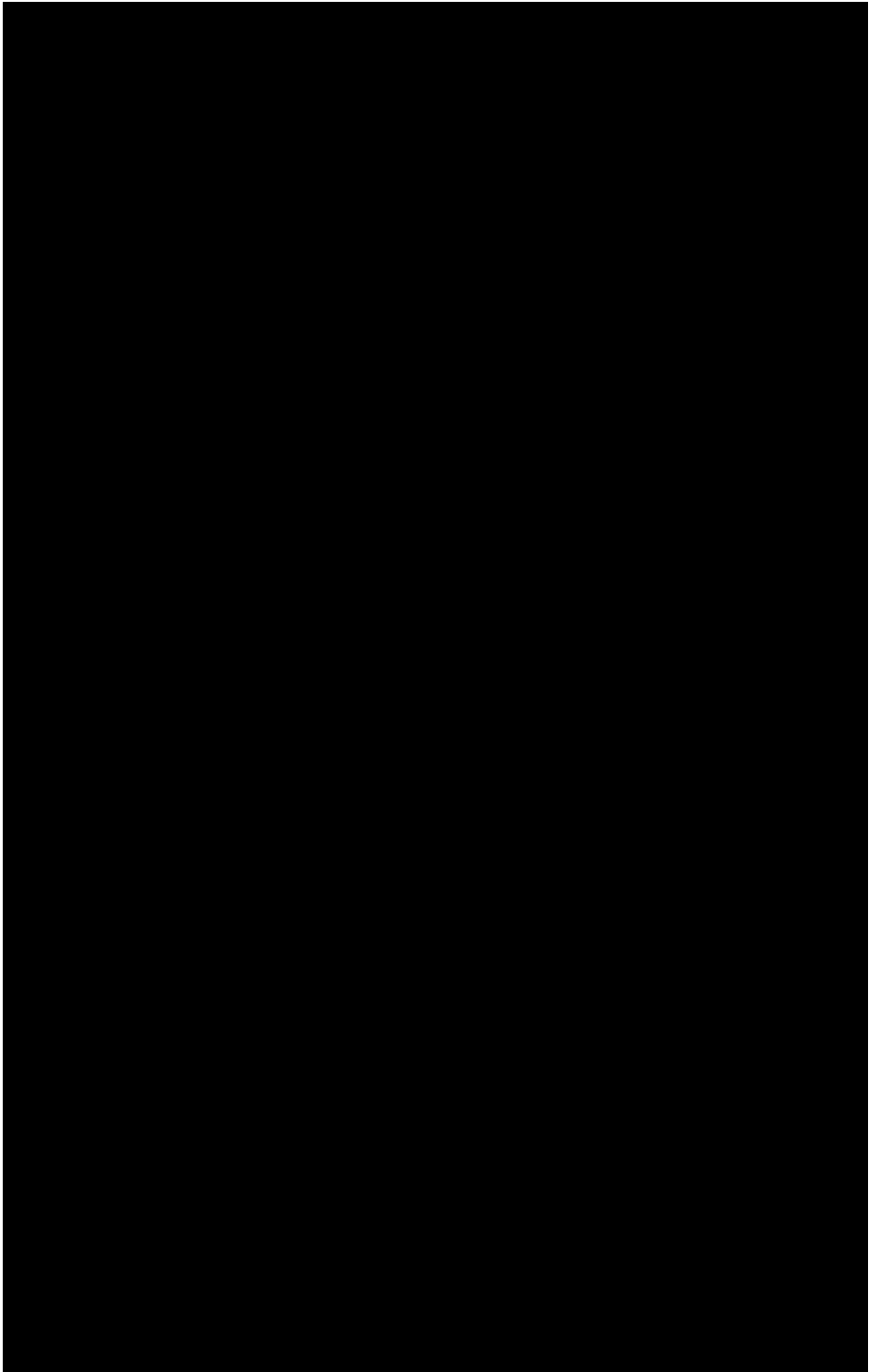


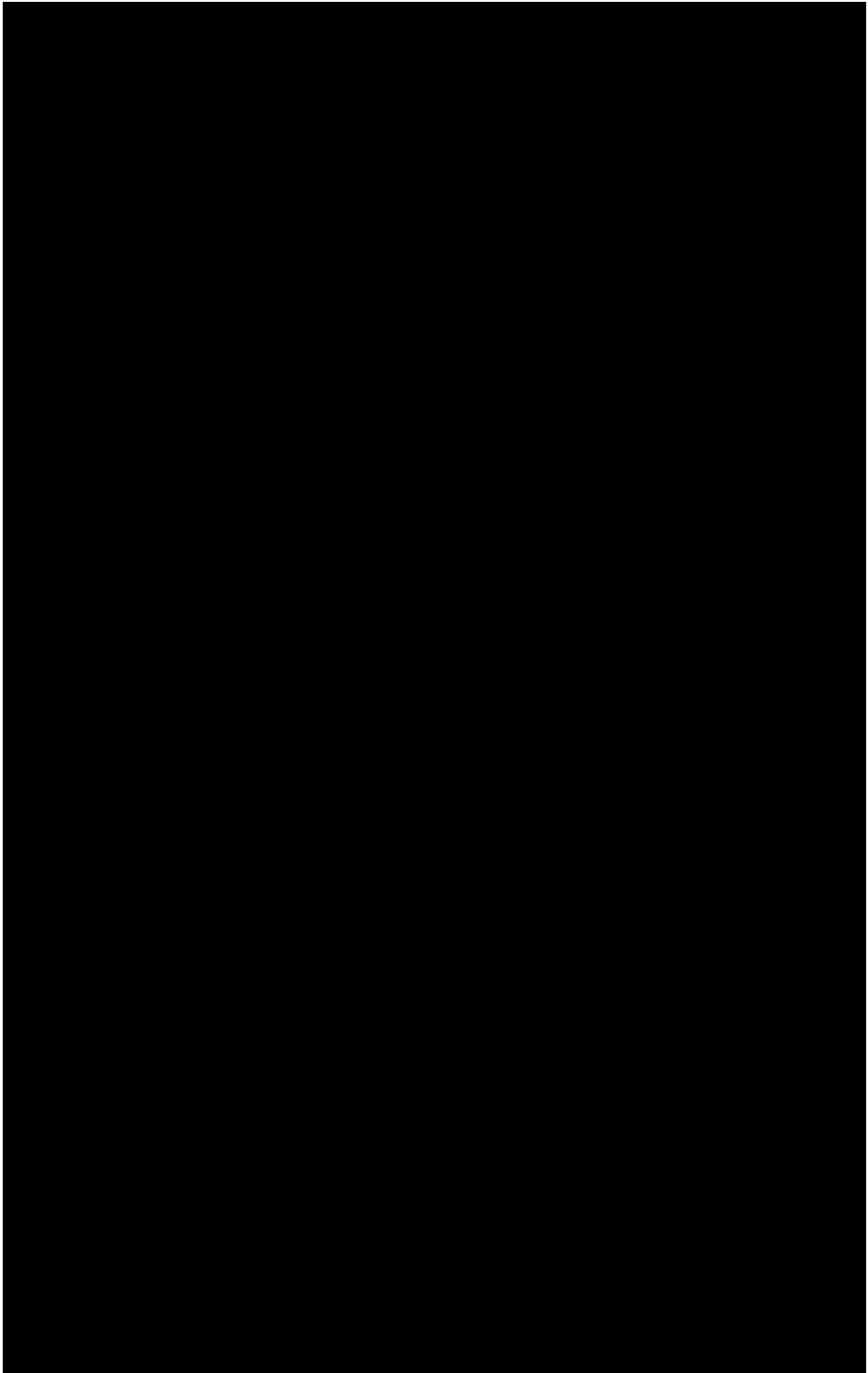


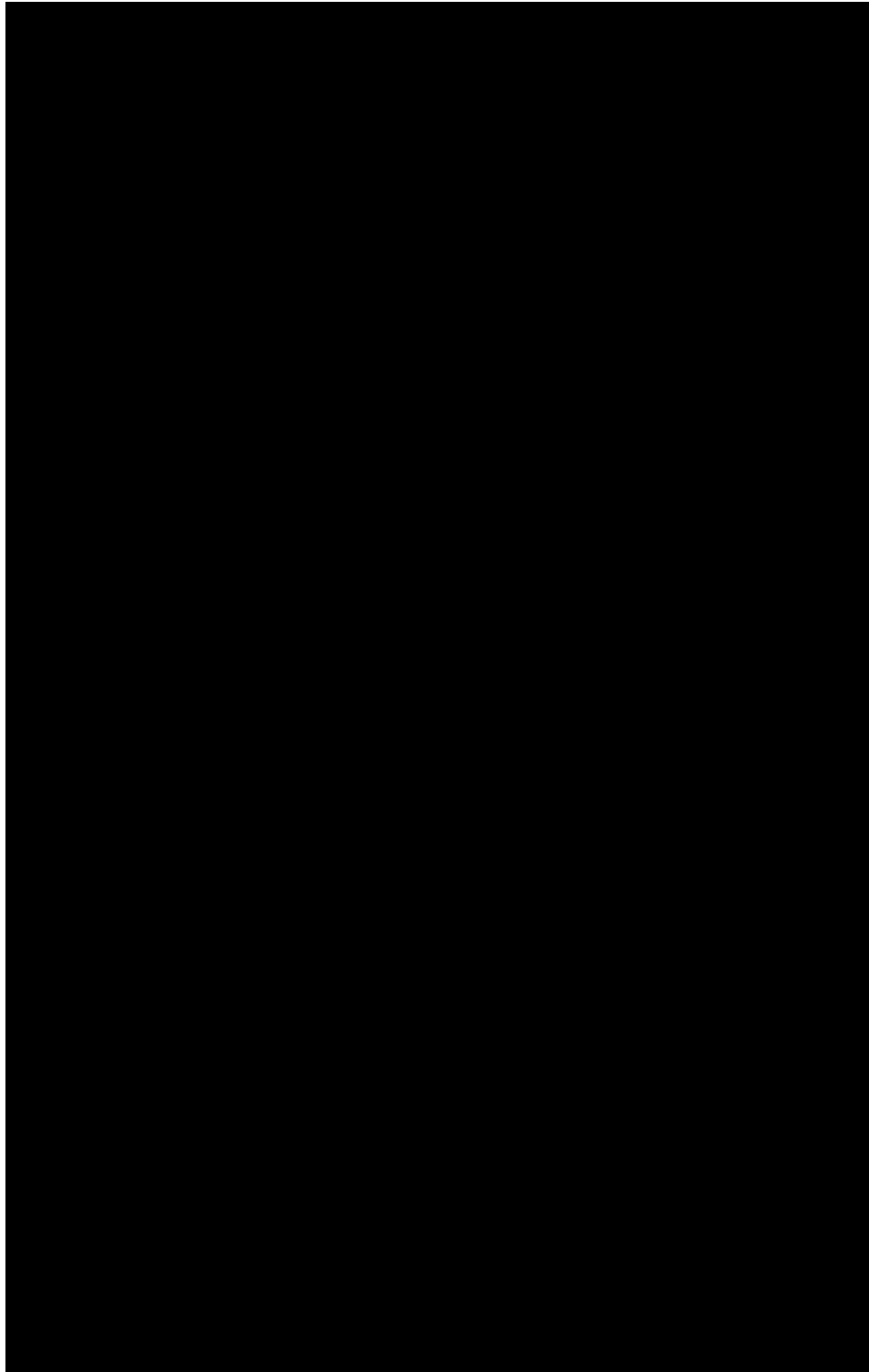


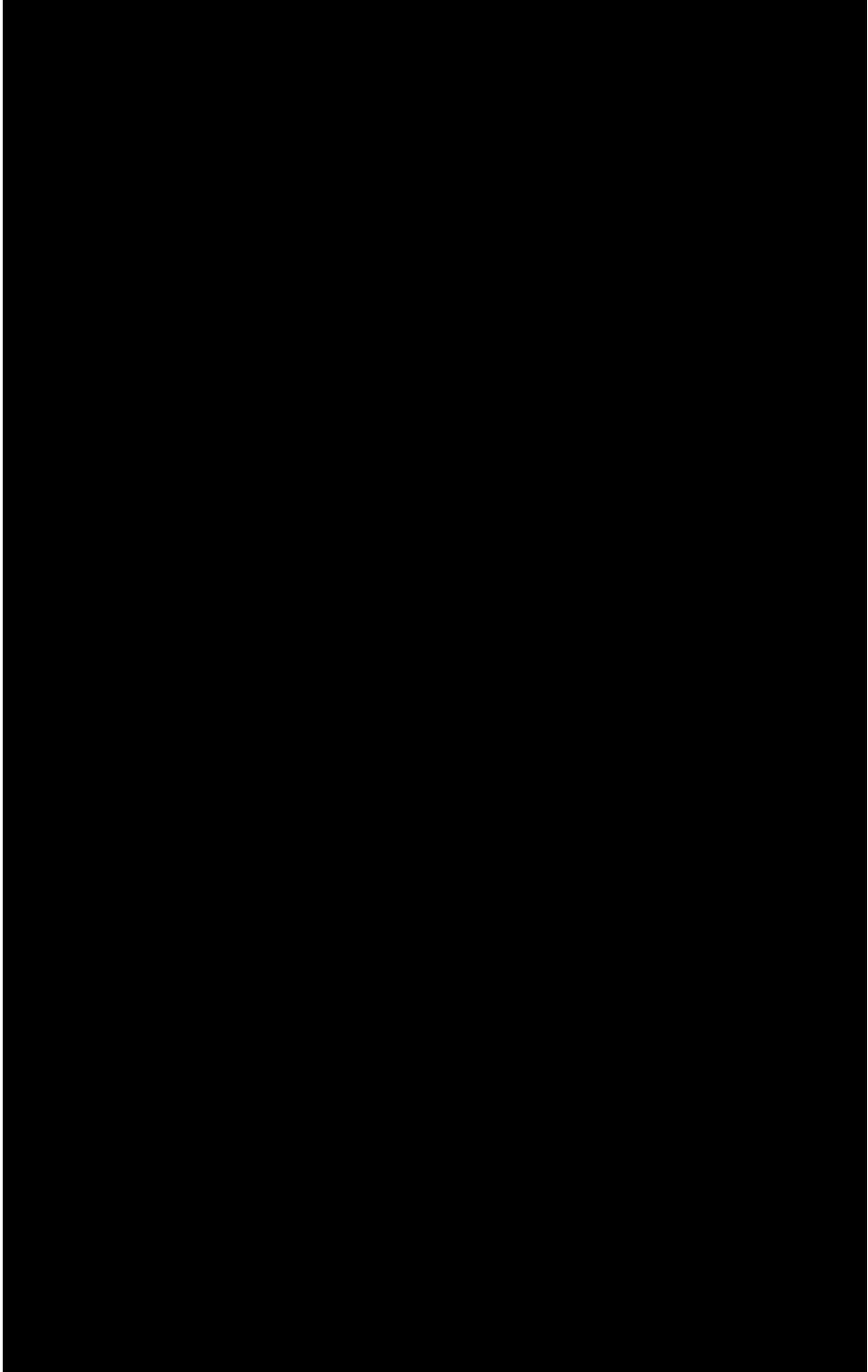


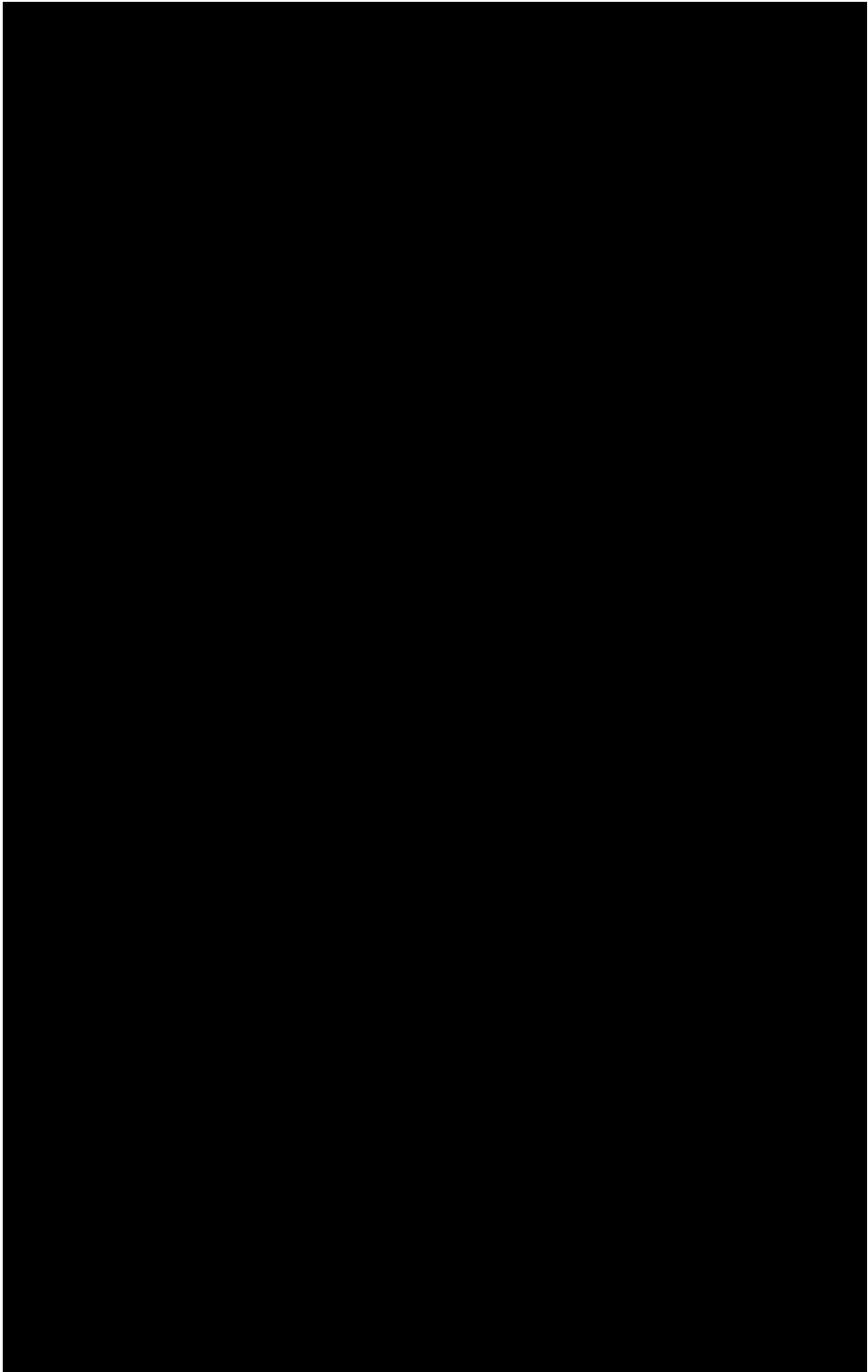


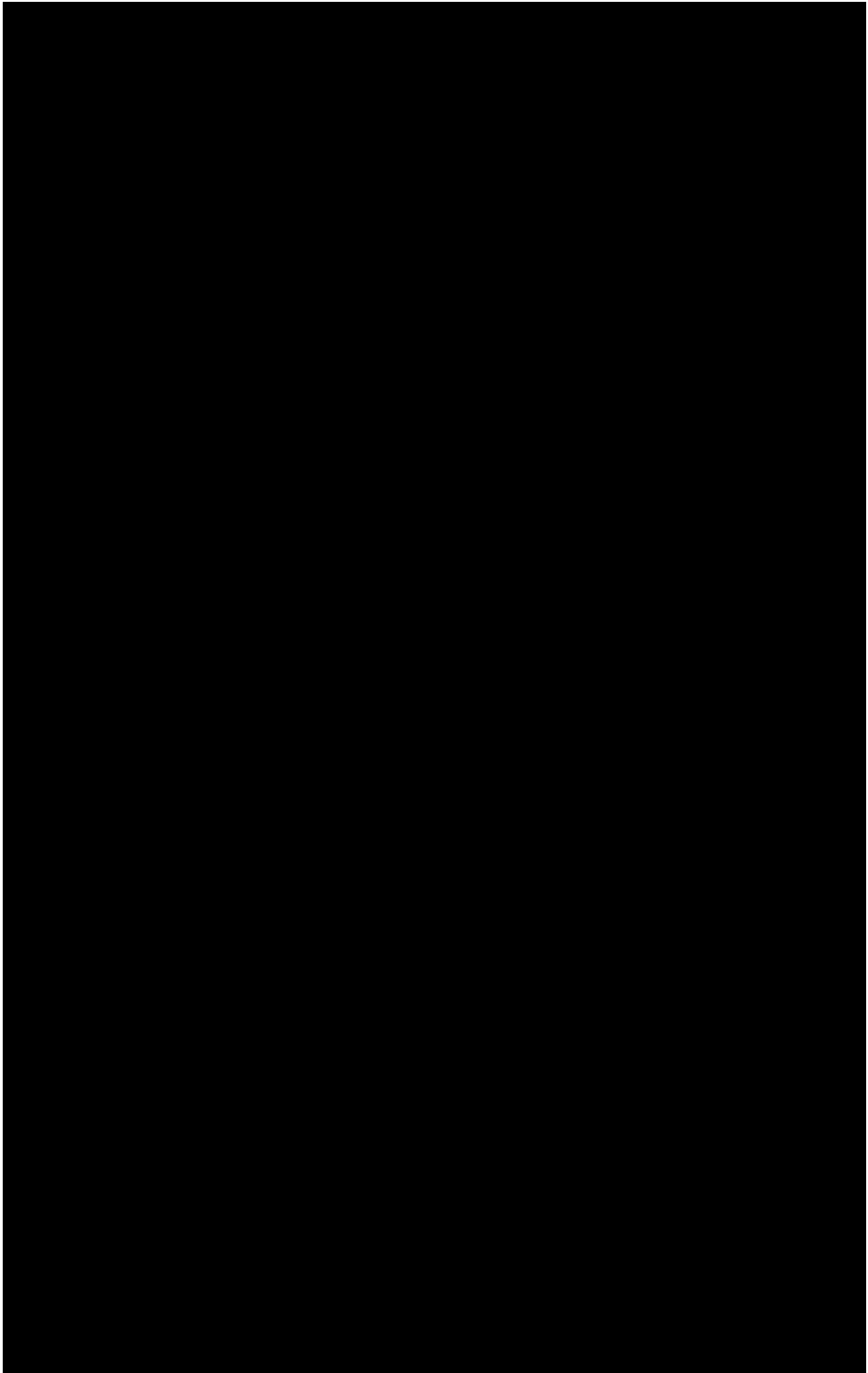




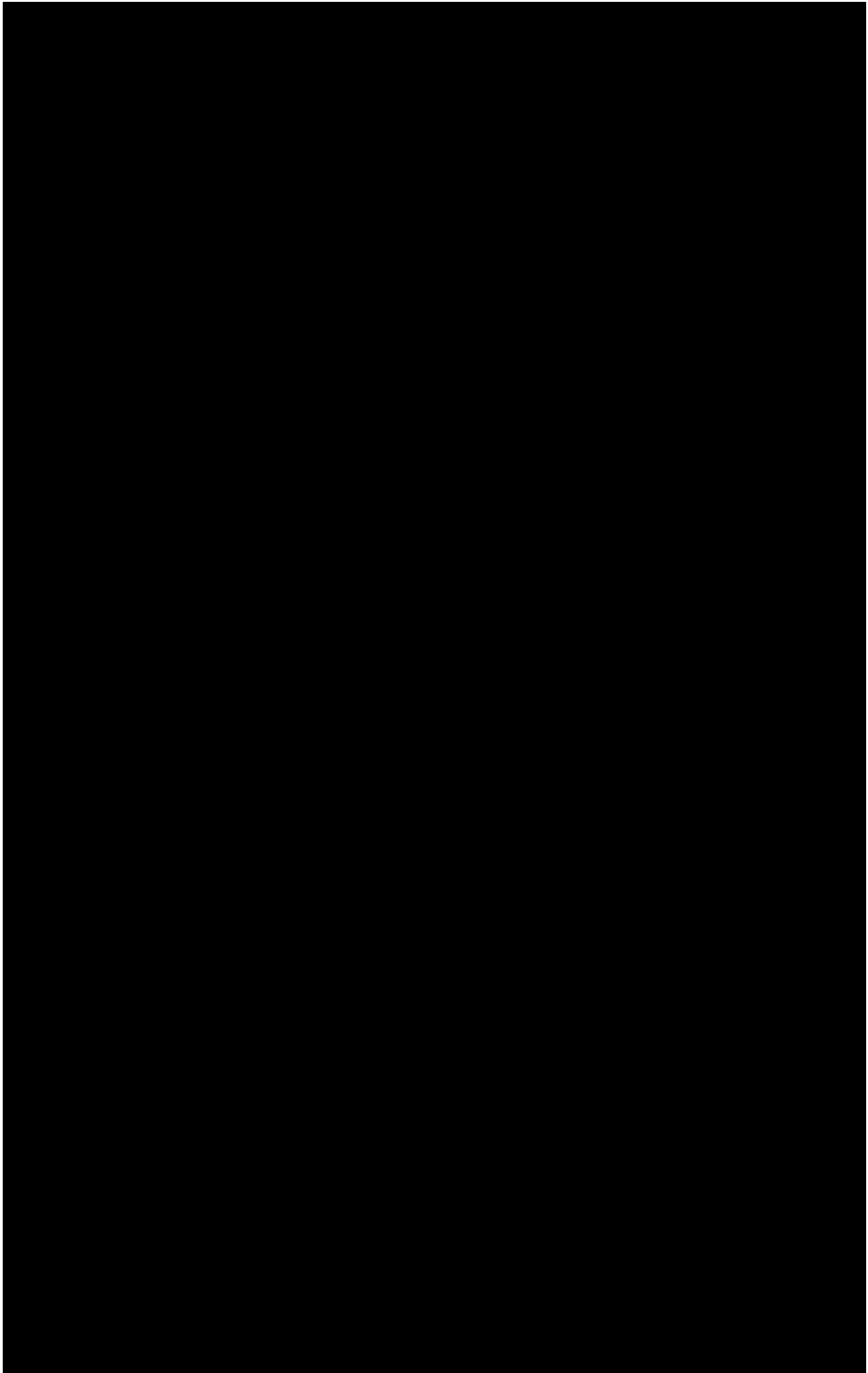


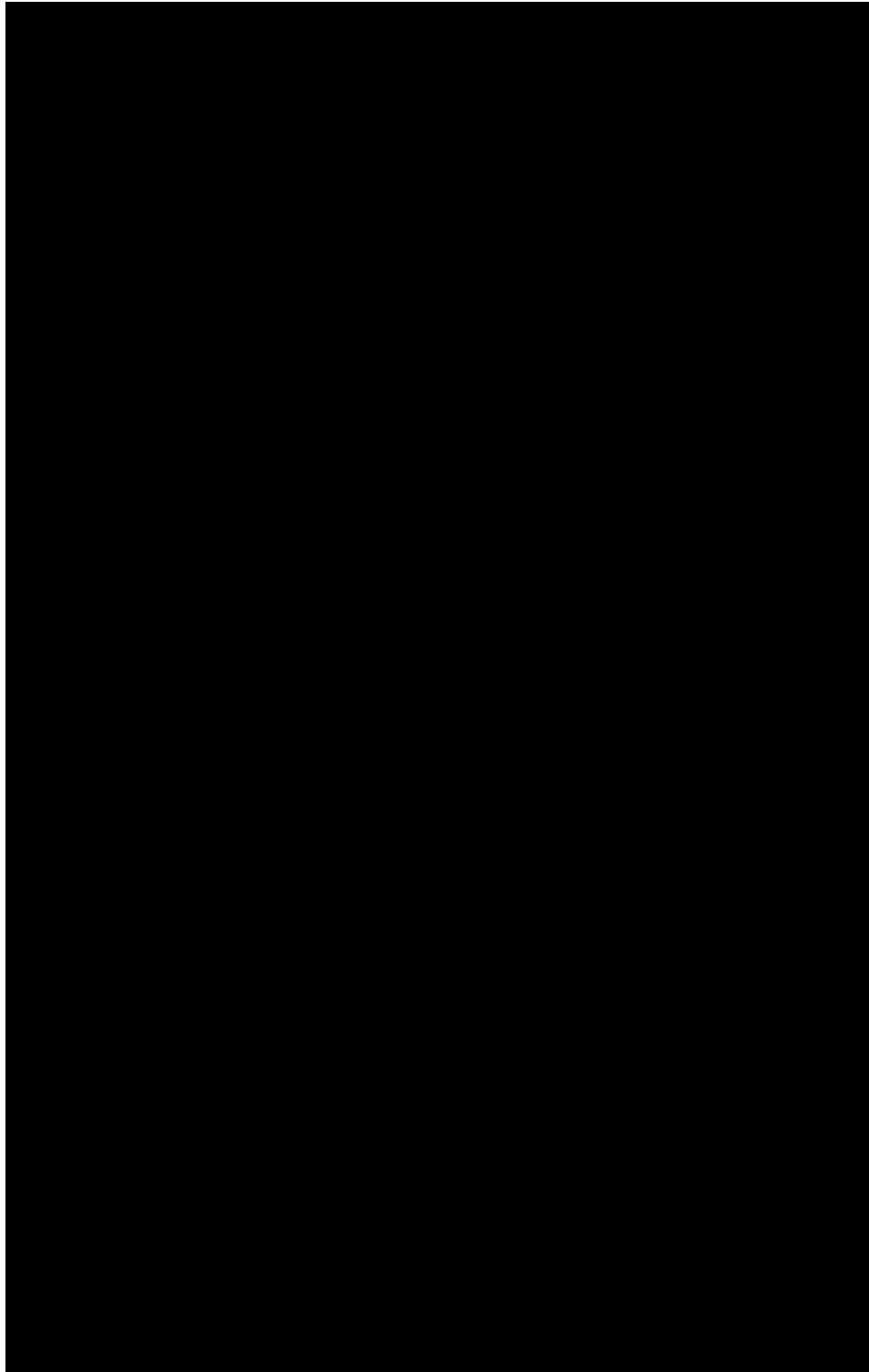














CHAPTER 9

Effectiveness and Feasibility of Intensive versus Regular Cognitive Behaviour Therapy in Patients with Anxiety and Obsessive-Compulsive Disorders: a Meta-Analysis

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Abstract

Background: Since the introduction of cognitive behaviour therapy (CBT), researchers are searching for the optimum schedule of sessions to maximize the effectiveness. In the last decades, short intensive treatments - multiple long sessions in a few weeks - became popular in patients with anxiety disorders and obsessive-compulsive disorder (OCD). However, it is still unknown whether intensive CBT is superior to regular CBT (short weekly sessions for several months).

Methods: This meta-analysis examined whether intensive CBT is superior to regular CBT in patients with anxiety disorders and OCD in reducing anxiety, obsessive-compulsive and comorbid depressive symptoms, and in reducing dropout. A systematic literature search was performed in PubMed, PsycINFO and Embase in which words indicative of an anxiety disorder or OCD were combined with intensive treatment and CBT.

Results: We identified 5012 unique studies. Two randomised controlled trials (RCTs) and four non-RCTs were included in the meta-analysis, pertaining to 398 subjects. Intensive CBT and regular CBT did not statistically differ in reducing anxiety or obsessive-compulsive symptoms from pre- to post-treatment and from post-treatment to follow-up. However, intensive CBT was significantly better in reducing depressive symptoms from pre- to post-treatment ($g=0.25$; 95% CI: (0.04, 0.45)). Dropout was only reported in two studies and could thus not be meta-analysed.

Limitations: The included studies were limited in number and quality.

Conclusions: High-quality RCTs are needed to assess both effectivity and feasibility of intensive CBT. Meanwhile, intensive CBT might be preferable for patients with comorbid depression or for patients who need a fast improvement.

Introduction

Cognitive behaviour therapy (CBT) is a first-choice psychotherapeutic treatment for patients with anxiety and obsessive-compulsive disorders (OCD). Despite its effectiveness, after treatment, roughly half of the patients with anxiety disorders and OCD still fulfil the diagnostic criteria or appear to have disturbing residual symptoms (Springer et al., 2018). In addition, 16 to 20% of the patients with an anxiety disorder or OCD drop out of treatment (Carpenter et al., 2018; Leeuwerik et al., 2019). Since the introduction of CBT, researchers and clinicians have been searching for the optimum dose of CBT to achieve maximum symptom reduction with minimal dropout (Emmelkamp et al., 1989; Foa et al., 1980).

During the early stages of behaviour therapy in the 60's and 70's, one of the main interventions in the treatment of anxiety disorders was 'flooding'. Flooding consisted of exposing patients to their worst fear, and prolonging this situation until they had habituated to it. Duration of flooding sessions appeared crucial: flooding for one to two hours resulted in greater anxiety reduction than shorter flooding of 10 to 30 minutes (Chaplin & Levine, 1981; Rabavilas et al., 1976; Stern & Marks, 1973). In addition, flooding was more effective if it was continued until anxiety was absent for at least one minute as compared to anxiety reduction to approximately 75% of the maximum level in that session (Marshall, 1985). Over time, it appeared that systematic desensitisation was effective in reducing anxiety symptoms as well (Cornish & Dilley, 1973; Everaerd et al., 1973; Gelder et al., 1973; Mealiea & Nawas, 1971; Rudestam & Bedrosian, 1977). Systematic desensitisation is a process in which anxiety stimuli are presented gradually while the patient is in a state of deep muscular relaxation, starting with less fearful situations and working stepwise to the most fearful situation. Advantages of systematic desensitization compared to flooding were that relapse of anxiety symptoms was less frequent after completing therapy, and patients endured lower levels of distress (Everaerd et al., 1973; Gelder et al., 1973; Mealiea & Nawas, 1971; Moor, 1970). Dropout did not differ markedly between systematic desensitisation and flooding (Everaerd et al., 1973; Gelder et al., 1973; Mealiea & Nawas, 1971; Moor, 1970). Later, it also appeared that the relaxation component of systematic desensitisation was not essential for achieving symptom reduction. For all of these reasons, flooding disappeared from clinical practice as did the relaxation component of systematic desensitisation. Consequently, weekly sessions of gradual exposure became the prevailing approach.

In recent decades, clinical research has been published in which gradual exposure sessions were intensified, aiming to find the optimum interval between sessions

(Emmelkamp et al., 1989; Foa et al., 1980). Later, additional reasons for intensifying treatment were presented, such as achieving faster results and increasing access to CBT (Bevan et al., 2010; Mortberg et al., 2007). Many patients were not able to attend weekly sessions of CBT due to work, caregiving or living far from the treatment centre. In intensive CBT, exposure is offered daily for several hours over several days instead of one or two sessions a week over a period of months. Intensive CBT differs from flooding in the aspect of graduality: in flooding, patients are exposed to their worst fear whereas in intensive CBT, patients work stepwise to their worst fear in different contexts. Also, cognitive restructuring is usually part of intensive CBT while it is absent in flooding. Intensive CBT showed significant reduction of anxiety symptoms (Dèttore et al., 2013; Manning et al., 1994; Teng et al., 2015), positive results on patient satisfaction (Bevan et al., 2010; Havnen et al., 2017) and low to average dropout rates between 0 and 22% (Hahlweg et al., 2001; Havnen et al., 2017; Manning et al., 1994; Teng et al., 2015).

Whether intensive exposure is superior over weekly sessions in reducing anxiety and obsessive-compulsive symptoms and dropout is still unknown. In some of the studies comparing both schedules, intensive treatment was superior in reducing anxiety symptoms (Dua, 1972; Foa et al., 1980), whereas in other trials the regular schedule was superior at follow-up (Rowe & Craske, 1998; Tsao & Craske, 2000) and other studies found no difference at all between both schedules (Chambless, 1990; Ning & Liddell, 1991). To date, no meta-analysis has been conducted to examine the effectiveness of intensive exposure versus regular exposure in adults with anxiety disorders. In a meta-analysis in youth and adults with OCD intensive CBT was superior to regular CBT in reducing obsessive-compulsive symptoms from pre- to post-treatment although this difference was no longer present at 3-month follow-up (Jónsson et al., 2015). In a meta-analysis in youth with anxiety disorders, intensive CBT did not significantly differ from regular CBT (Öst & Ollendick, 2017).

Ideas about the optimal schedule of exposure in vivo could also follow from the inhibitory learning theory it is based upon (Bouton, 1993; Craske et al., 2008). This theory poses that the threat association of a CS is not erased during extinction but it remains present next to a new, non-threat association. Thus, the CS becomes an ambiguous stimulus with two associations competing for retrieval when patients are confronted with the CS. An intensive format might exploit the acquisition phase of the inhibitory learning theory better than a regular format because in intensive CBT this phase is less intertwined with the retrieval phase. Therefore, new inhibitory pathways can be formed in more contexts in intensive CBT, before they have to be retrieved in real life when being confronted with feared situations. In regular CBT,

the need to retrieve new inhibitory pathways may come too soon when inhibitory pathways are not yet formed in the context at hand. In that case, old fear pathways may be triggered and reconsolidated instead and remain dominant. Hence, intensive CBT might be superior to regular CBT in acquisition of inhibitory pathways and thus in reducing anxiety symptoms. On the other hand, regular CBT might exploit the (re)consolidation phases of the inhibitory learning theory better. As there is more time in between sessions in regular CBT, new inhibitory pathways can form connections within the memory network and thus grow stronger. (Re)consolidation is facilitated by patients doing homework, usually consisting of repeating exposure exercises in real life. From this perspective, regular CBT might be superior to intensive CBT in (re)consolidation of new inhibitory pathways which might cause less relapse.

Optimal timing schedules for inhibitory learning of anxiety have been studied with rodents in a laboratory setting with mixed results. Some studies have found a regular frequency schedule beneficial (Urcelay et al., 2009), others an intensive schedule (Cain et al., 2003; Rescorla & Durlach, 1987), and still others have found no differences at all (Martasian et al., 1992). Cain et al. (2003) have concluded that separate blocks of intensive exposure perform most effectively, suggesting that the duration of a single exposure session needs to be sufficiently long for extinction learning to occur. However, whenever this threshold is met, consolidation of new information would be optimal within a regular frequency schedule. In sum, data of rodents suggest that timing might matter but it is still inconclusive which schedule is superior and how this translates to human clinical samples.

The objective of this meta-analysis was to investigate whether intensive CBT is superior to regular CBT in patients with anxiety disorders and OCD in reducing: (1) anxiety and obsessive-compulsive symptoms; (2) comorbid depressive symptoms; and (3) dropout. We hypothesised that: (1) intensive treatment is superior in reducing anxiety, obsessive-compulsive and comorbid depressive symptoms from pre- to post-treatment following the principles from the inhibitory learning theory; (2) regular CBT is superior from post-treatment to follow-up in reducing anxiety, obsessive-compulsive and depressive symptoms because relapse might occur less frequently in regular CBT following the principles of inhibitory learning theory; and (3) dropout is not significantly different in intensive and regular CBT analogue to similar dropout rates in systematic desensitisation and flooding.

Methods

This meta-analysis was conducted according to PRISMA guidelines (Moher et al., 2009). Our study was preregistered in PROSPERO (registration number: 2019 CRD42019141694). A systematic literature search was performed and updated on January 22nd, 2021 in PubMed, PsycINFO and Embase by a librarian in collaboration with authors LL and KR. Searches were conducted with free text, MeSH terms and keywords, in which words indicative of an anxiety disorder or OCD were combined with intensive treatment and cognitive behaviour therapy (see supplement for search syntax). Additionally, reference lists of retrieved articles were checked for additional studies.

Inclusion/exclusion criteria

We included randomised controlled trials (RCTs) and non-RCTs in which intensive CBT was compared to regular CBT in patients of 18 years and older with an anxiety disorder or OCD. CBT was defined as an intervention based on cognitive behaviour principles (Beck, 1976), consisting mainly of exposure in vivo and possibly cognitive restructuring as well. We defined a regular frequency of therapy as one or two sessions a week based on the literature and clinical experience (Leeuwerik et al., 2019). An intensive frequency was defined as more than two sessions a week with at least double the therapy hours per week than that of the regular schedule. Total treatment time had to be equal in both conditions. Anxiety disorders (panic disorder (PD), agoraphobia (AG), social anxiety disorder (SAD), generalised anxiety disorder (GAD)) and OCD were included. Specific phobias were excluded as they are considered less disabling than the other anxiety disorders and therefore require limited treatment in most patients (Sancassiani et al., 2019). Only studies published in the English language were included. Publication period was unrestricted.

Study selection and data collection

Two authors (LL and KR) independently screened the titles and abstracts for eligibility. The same authors continued assessing the full text of potentially eligible retrieved references, resolving disagreements via discussion or a third rater (NB). Next, the following data were extracted: type of disorder; standardised assessment instrument with which the diagnosis is established; number of participants; frequency, number and length of sessions; age and gender of participants; psychiatric comorbidity allowed (yes/no); concurrent psychotropic medication allowed (yes/no); number of dropouts; primary and secondary outcome measures regarding anxiety, obsessive-compulsive and depressive symptoms at pre-treatment, post-treatment and follow-up; duration of follow-up. Two authors (LL and KR) independently extracted the data

and compared results. Differences were checked and solved. Since two studies lacked some data needed for this meta-analysis, authors were approached the data was no longer available (Emmelkamp et al., 1989; Foa et al., 1980). Therefore, these studies were excluded from the meta-analysis.

Risk of bias assessment

The validity of the studies was independently rated 'low risk', 'high risk' or 'unclear' by two authors (LL and KR) in accordance with the Cochrane Handbook (Higgins & Altman, 2008) on the following aspects: (1) random sequence generation; (2) allocation concealment; (3) blinding of outcome assessment; (4) incomplete outcome data; (5) selective outcome reporting. As it is impossible to blind patients and therapists in psychological treatment studies, the Cochrane criterion 'blinding of participants and personnel' was not checked. Differences were resolved through discussion or a third rater (NB). The risk of bias plot was created using the robvis tool (McGuinness & Higgins, 2021).

Statistical analysis

The difference in effectiveness of intensive versus regular CBT was calculated as bias-corrected between-group effect sizes (Hedges' g). In the primary analyses, effect sizes were calculated based on symptom severity scores of the index disorder (anxiety symptoms for anxiety disorders, obsessive-compulsive symptoms for OCD) from pre-treatment to post-treatment and from post-treatment to follow-up. As the duration of treatment in intensive CBT was shorter than in regular CBT, post-treatment and follow-up measurements of both schedules were not done at the same time points, but they were aligned to completion and follow-up of the relevant schedule. Also, effect sizes were calculated for depressive symptoms and percentage of dropout. Additionally, all included studies were scanned for adverse events of psychotherapy. We decided on post-hoc secondary subgroup analyses based on diagnosis after noting that only OCD and panic disorder and/or agoraphobia were present in the included studies. Intention-to-treat data was analysed, except for studies that reported completer data only. Effect sizes (Hedges' g) of 0.2, 0.5 and 0.8 indicate a small, moderate and large effect, respectively. Furthermore, 95% confidence intervals (CI) and heterogeneity statistics (Q and I^2 index) were calculated using a random effects model. Data analysis was performed using the Comprehensive Meta-Analysis software package (version 3.3.070; Biostat). A funnel plot was created using CMA software and visually checked for publication bias.

Results

Study inclusion

The study selection process is illustrated in Figure 1. We identified 5012 unique studies and, after title or abstract screening and full text assessment, selected six eligible studies. Most studies were ruled-out because they did not compare intensive with regular CBT. A list of excluded studies is available on request.

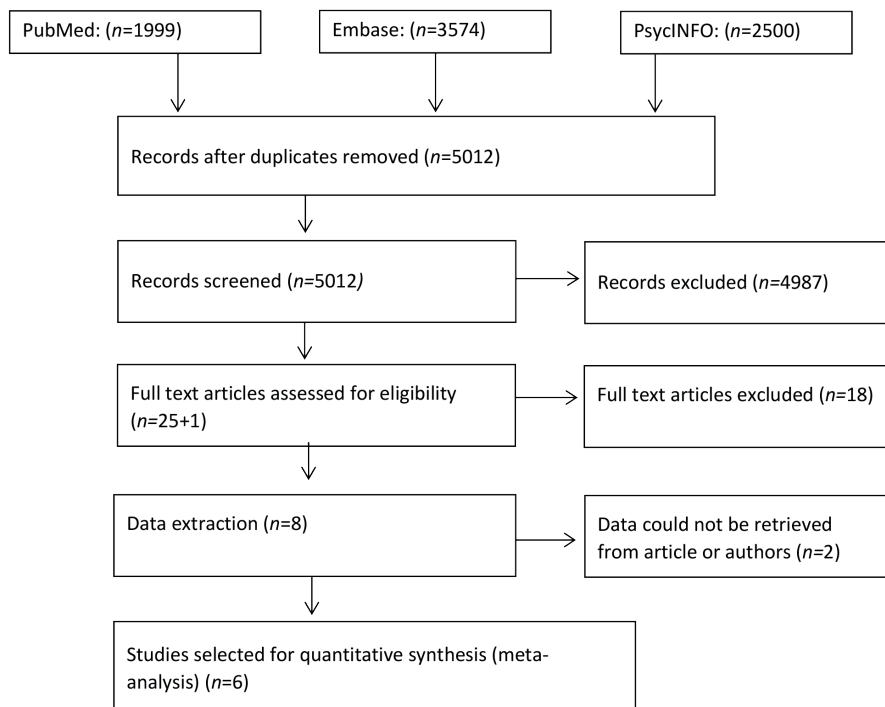


Figure 1. Flowchart of the inclusion of studies

Description of included studies

Characteristics of the six included studies are presented in Table 1. The studies consisted of two RCTs and four non-RCTs, pertaining to 393 subjects (intensive CBT $n=197$, regular CBT $n=196$). The disorders under study were OCD ($n=3$), panic disorder ($n=2$) and agoraphobia ($n=1$). All studies but one (Chambless, 1990) used a standardised instrument to verify the diagnosis. Comorbid psychiatric diagnoses were allowed in all studies. Comorbidity was described in three studies and consisted mainly of mood disorders, other anxiety disorders and personality disorders (Abramowitz et al., 2003; Bohni et al., 2009; Knuts et al., 2015). The number of patients with a comorbid disorder did not differ significantly between the intensive and regular condition in these studies (Abramowitz et al., 2003; Bohni et al., 2009; Knuts et al., 2015). Pharmacological treatment was allowed in all studies. Patients used antidepressant medication, antipsychotic medication, benzodiazepines or beta-blockers. Medication was kept constant during treatment in three studies (Abramowitz et al., 2003; Knuts et al., 2015; Storch et al., 2008), and not described in the remaining three studies (Bohni et al., 2009; Chambless, 1990; Oldfield et al., 2011). Total treatment time varied across studies from 12 to 30 hours. Session duration varied from one to four hours. Intensive CBT was offered in a period ranging from five days to three weeks, while regular therapy was delivered in a period ranging from six to 18 weeks. Next to the outcomes on anxiety or obsessive-compulsive measurements, five studies also reported outcomes on depressive measurements. One study had a follow-up period of six months (Chambless, 1990), while other studies had a follow-up period of three months. In all but one study (Bohni et al., 2009) treatment was delivered in an individual format. Likewise, patients had to do homework in all but one study (Chambless, 1990).

In four studies, treatment consisted of therapist-assisted gradual exposure in vivo (Abramowitz et al., 2003; Chambless, 1990; Knuts et al., 2015; Storch et al., 2008). Two of these studies added cognitive restructuring to the exposure sessions (Abramowitz et al., 2003; Storch et al., 2008), while one study added coping skills such as respiratory control, thought stopping and focusing attention on the environment (Chambless, 1990). In the fifth study, a personalised cognitive model was used as a starting point for cognitive restructuring and behaviour experiments (Oldfield et al., 2011). In the sixth study, participants were treated with unassisted gradual exposure in vivo combined with cognitive restructuring (Bohni et al., 2009).

Table 1. Study characteristics

Study	Design	Disorder	Assessment instrument	Treatment format ¹	n	Intensive		
						Age Mean (SD)	Female %	Psychiatric comorbidity %
Abramowitz et al. (2003)	Matched group	OCD	Semi structured interview	I	20	36.2 (15.6)	40	45
Bohni et al. (2009)	RCT	Panic disorder	ADIS-IV	G	19	36.3 (11.9)	79	47
Storch et al. (2008)	Non-randomised control group	OCD	ADIS-IV	I	32	35.6 (14.8)	47 ³	ND ⁴
Knuts et al. (2015)	Matched historical control group	Panic disorder	MINI	I	96	38.0 (9.1)	76	29
Oldfield et al. (2011)	Matched historical control group	OCD	SCID-IV	I	22	33.5 (8.8)	64	ND ⁴
Chambless (1990)	RCT	Agoraphobia	None	I	9	40.6 (13.5) ³	93 ³	ND ⁴

¹ I=individual; G=group

² dropout after randomisation of total sample (48 patients were randomised), not sufficiently clear described per treatment condition

³ characteristics of total sample

⁴ not described

⁵ not applicable, dropout not possible, historical control group formed from treatment completers

⁶ dropout of total sample was described while in the current study only a subset of agoraphobia patients was used $n=14$ of whom had data

Intensive (continued)			Regular							
Medication %	Dropout n (%)	Therapy	n	Age Mean (SD)	Female %	Psychiatric comorbidity %	Medication %	Dropout n (%)	Therapy	FU in mos
45	4 (20%)	15 x 2h in 3 wks total 30h	20	38.7 (13.6)	45	45	45	4 (20%)	15 x 2h in 8 wks total 30h	3
79	10 (21%) ²	5 x 4h + 3 x 2h in 3 wks total 26h	20	34.3 (10.6)	65	70	80	10 (21%) ²	13 x 2h in 13 wks total 26h	3
79 ³	1 (3%)	14 x 75- 90 min in 3 wks total 17.5-21h	30	27.6 (8.0)	47 ³	ND ⁴	79 ³	5 (17%)	14 x 75- 90 min in 14 wks total 17.5-21h	3
86	ND ⁴	5 x in 1 wk total 23h	98	40.0 (10.9)	70	28	91	NA ⁵	12 x in 6 wks total 23h	3
ND ⁴	ND ⁴	5 x 2-4h in 2 wks total 12-18h	22	35.0 (9.9)	64	ND ⁴	ND ⁴	NA ⁵	12-18 x 1-1.5h in 18 wks total 12-18h	3
33	ND ⁶	10 x 90 min in 2 wks total 15h	10	40.6 (13.5) ³	93 ³	ND ⁴	70	ND ⁶	10 x 90 min in 10 wks total 15h	6

Quality assessment

Figure 2 presents the risk of bias assessment. Four studies scored a high risk on sequence generation and allocation concealment because they were non-randomised studies (Abramowitz et al., 2003; Knuts et al., 2015; Oldfield et al., 2011; Storch et al., 2008). Both RCTs scored unclear on sequence generation because the randomisation process was not clearly described and allocation concealment was either unclear or involved a low risk in these studies (Bohni et al., 2009; Chambless, 1990). In none of the studies the outcome assessors were blinded, except for one study in which it was unclear whether the outcome assessors were blinded (Chambless, 1990). Five studies scored high on incomplete outcome data because dropout was related to treatment condition or dropout was not possible because the control group was formed afterwards from treatment completers (Bohni et al., 2009; Chambless, 1990; Knuts et al., 2015; Oldfield et al., 2011; Storch et al., 2008). None of the studies was pre-registered in a trial database and were therefore scored as unclear on selective outcome reporting.

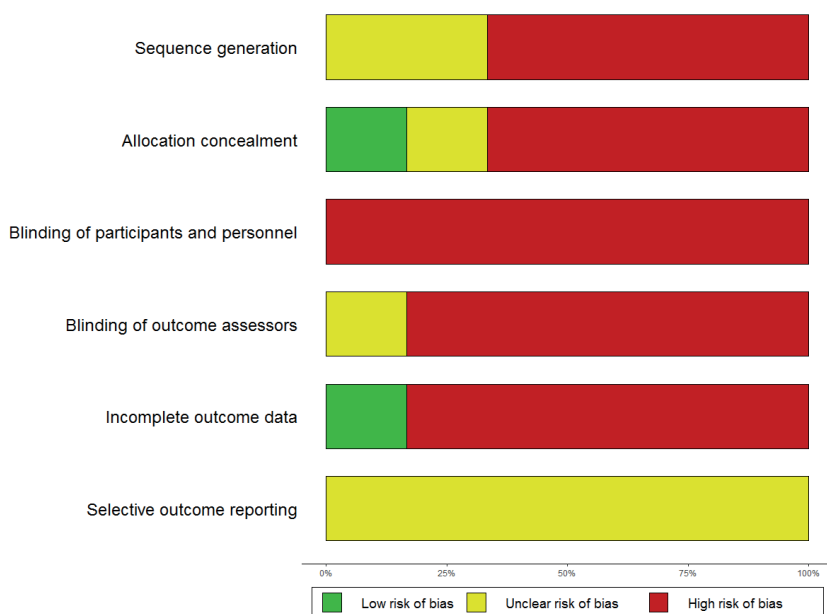


Figure 2. Risk of bias assessment

Effect of intensive versus regular CBT on anxiety or obsessive-compulsive symptoms

The effect sizes of intensive versus regular CBT on anxiety and obsessive-compulsive measures are presented in Table 2 and 3. Neither treatment differed significantly in index symptom reduction from pre-treatment to post-treatment ($g = 0.12$; 95% CI: (-0.08, 0.32) or from post-treatment to follow-up ($g = -0.01$; 95% CI: (-0.22, 0.21)). When studies were split by diagnosis (see supplement Tables S1 and S2), a non-significant trend appeared for patients with OCD, indicating the superiority of intensive over regular CBT in reducing obsessive-compulsive symptoms from pre- to post-treatment ($g = 0.31$; 95% CI: (-0.02, 0.63)). However, this effect was no longer present from post-treatment to follow-up ($g = -0.24$; 95% CI: (-0.59, 0.10)). For panic disorder and/or agoraphobia, neither schedule differed significantly in reducing anxiety symptoms (pre- to post-treatment: $g = 0.02$; 95% CI: (-0.23, 0.26); post-treatment to follow-up: $g = 0.12$; 95% CI: (-0.12, 0.37)). Heterogeneity is presented below the tables and was not significant in any of the analyses.

Effect of intensive versus regular CBT on depressive symptoms

The effect sizes of intensive versus regular CBT on depression measures are presented in Table 4 and 5. Compared to the regular condition, depressive symptoms reduced significantly more in the intensive condition from pre- to post-treatment ($g = 0.25$; 95% CI: (0.04, 0.45)). However, there was no significant difference between intensive and regular CBT from post-treatment to follow-up ($g = -0.00$; 95% CI: (-0.21, 0.20)). When studies were split by diagnosis (see supplement Tables S3 and S4), intensive CBT was superior to regular CBT in reducing depressive symptoms in patients with OCD from pre- to post-treatment ($g = 0.47$; 95% CI: (0.14, 0.81)). However, this effect was not significant from post-treatment to follow-up ($g = -0.14$; 95% CI: (-0.48, 0.21)). In patients with panic disorder with or without agoraphobia, intensive and regular CBT did not significantly differ in reducing depressive symptoms from pre-treatment to post-treatment ($g = 0.15$; 95% CI: (-0.11, 0.40)) and from post-treatment to follow-up ($g = 0.07$; 95% CI: (-0.18, 0.32)). Heterogeneity was not significant in any of the analyses.

Table 2. Forest plot of mean effect sizes (Hedges' g) for intensive versus regular CBT on anxiety and obsessive-compulsive measures from pre-treatment to post-treatment.

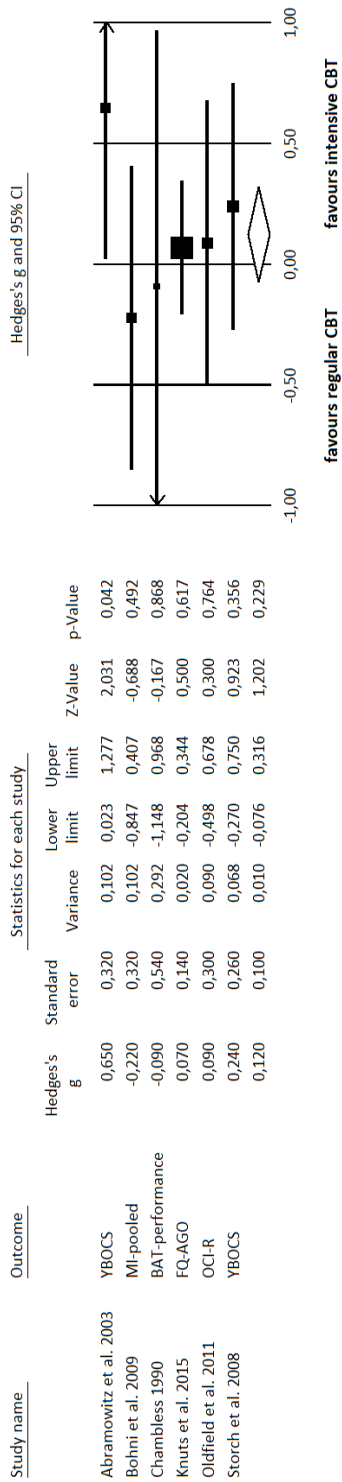


Table 3. Forest plot of mean effect sizes (Hedges' g) for intensive versus regular CBT on anxiety and obsessive-compulsive measures from post-treatment to follow-up.

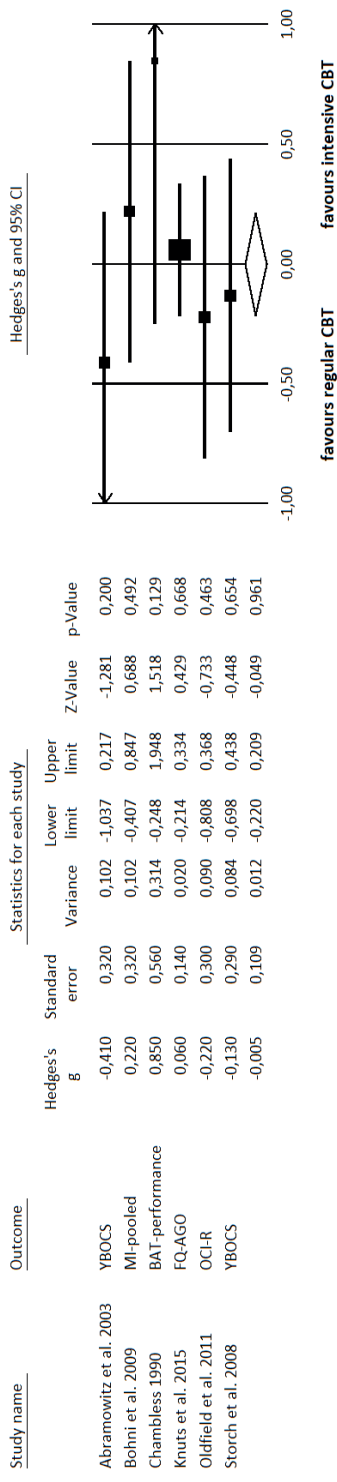


Table 4. Forest plot of mean effect sizes (Hedges' g) for intensive versus regular CBT on depression measures from pre-treatment to post-treatment.

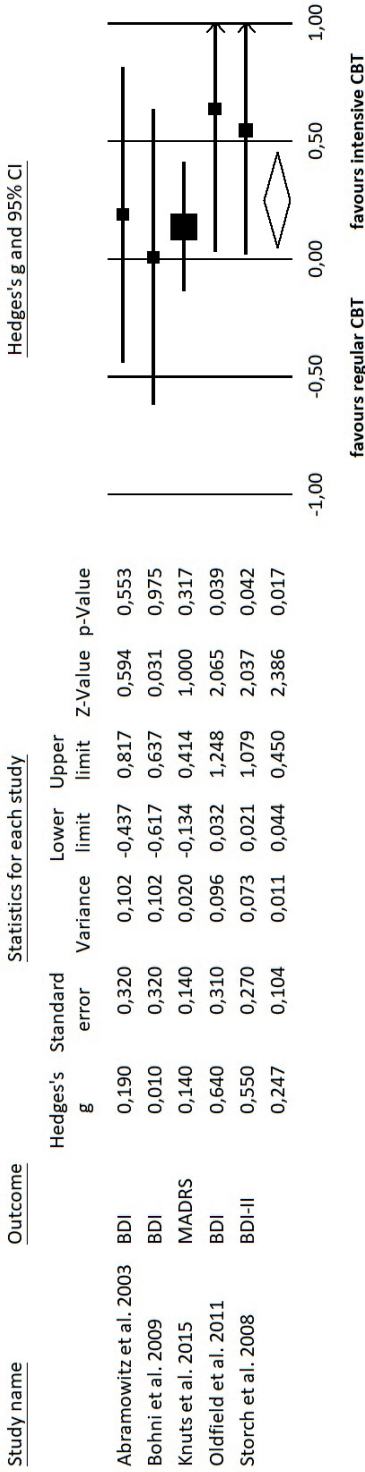
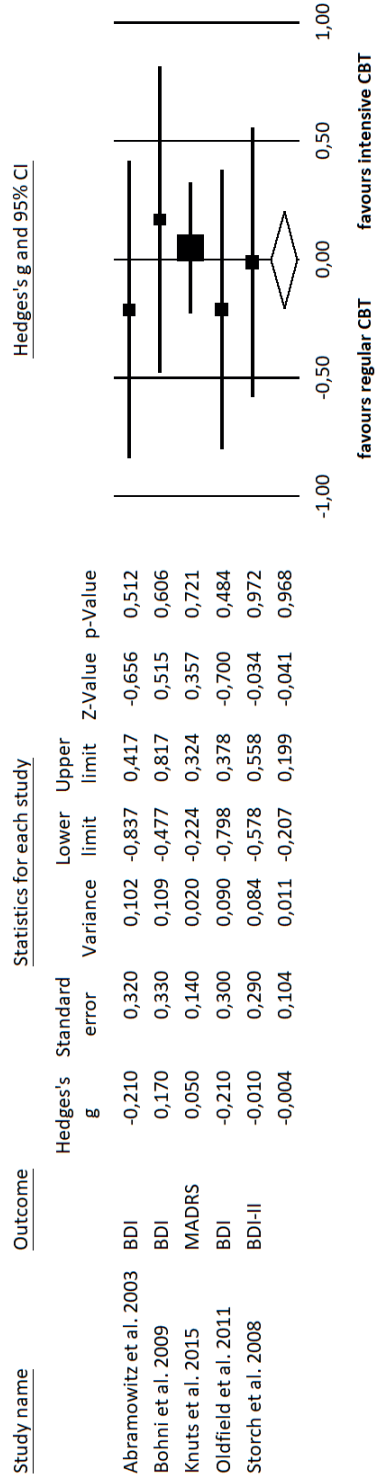


Table 5. Forest plot of mean effect sizes (Hedges' g) for intensive versus regular CBT on depression measures from post-treatment to follow-up.



Dropout in intensive versus regular CBT

Dropout (see Table 1) could not be adequately assessed in four studies: two studies formed a historical control group of patients who completed regular CBT, so dropout was excluded by definition (Knuts et al., 2015; Oldfield et al., 2011); one study did not describe dropout rates in the subgroup of patients that we used (Chambless, 1990); and the fourth study did not clearly describe dropout per condition and excluded patients after randomisation, thus making dropout and exclusion indistinguishable (Bohni et al., 2009). In the remaining two studies, dropout was adequately described (Abramowitz et al., 2003; Storch et al., 2008).

Due to a lack of dropout data, we could not execute our analysis plan and therefore dropout results were evaluated using a chi-square test. Dropout did not significantly differ between intensive CBT (5 of 52 patients; 10%) and regular CBT (9 of 50 patients; 18%; $\chi(1)=1.51$; $p=0.22$). However, dropout results were based on a small number of patients from two non-randomised trials.

Reasons for dropout were described in only one of these studies (Storch et al., 2008): in the intensive condition, one patient dropped out due to limited benefit; in the regular condition, three patients dropped out due to limited benefit, and two patients due to a medication change (Storch et al., 2008). Adverse events were not mentioned in any of the studies.

Publication bias

As no asymmetry was detected in the funnel plot with the studies equally distributed among the funnel plot, there was no evidence for publication bias.

Discussion

The present study investigated whether intensive CBT and regular CBT differ in their effectiveness to reduce anxiety or obsessive-compulsive symptoms, to reduce comorbid depressive symptoms, and in dropout in patients with anxiety disorders and OCD. Two RCTs and four non-RCTs were included in the meta-analysis, pertaining to 393 subjects. Our results showed that intensive CBT and regular CBT did not significantly differ in reducing anxiety or obsessive-compulsive symptoms from pre- to post-treatment or from post-treatment to follow-up. However, intensive CBT was superior in reducing depression symptoms from pre- to post-treatment but this effect disappeared from post-treatment to follow-up. Dropout could be adequately assessed in two non-randomised studies only and was not significantly different in intensive CBT from regular CBT.

Contrary to our expectations, we found that neither CBT schedule differed significantly in reducing anxiety and obsessive-compulsive symptoms from pre-treatment to post-treatment and to follow-up. As the effectiveness of regular CBT in these disorders is already well-established, these results strengthen the evidence that intensive CBT is effective in treating patients with anxiety disorders and OCD. The results are contradictory to both our hypotheses that intensive CBT would be superior to regular CBT from pre- to post-treatment and that regular CBT would be superior from post-treatment to follow-up. As our hypotheses were based on inhibitory learning theory the findings might indicate that inhibitory learning occurs equally well in intensive CBT and regular CBT despite the different utilisation of acquisition and consolidation learning phases in both treatments. This might suggest that learning phases are served sufficiently in both treatment schedules, or that deficiencies of a treatment schedule in one learning phase are compensated by superiority in other learning phases. Another explanation for our findings might be that the intensive treatment schedule differed little from the regular one due to homework. One might argue that patients have more opportunity to do exposure assignments in between therapy sessions in the regular schedule than in the intensive schedule thus levelling the difference in intensity of exposure between both treatment schedules. However, homework does not fully compensate for exposure treatment as therapist-guided exposure leads to more symptom reduction than self-guided exposure e.g. home assignments (Voderholzer et al., 2020).

Our results are congruent with a meta-analysis on intensive treatment in children with anxiety disorders in which intensive CBT and regular CBT did not significantly differ in reducing anxiety symptoms at post-treatment and follow-up up to 12 months after treatment (Öst & Ollendick, 2017). Furthermore, intensity of treatment was not a moderator in a meta-analysis on panic disorder with or without agoraphobia, indicating that intensity of treatment did not predict treatment outcome (Sánchez-Meca et al., 2010). In contrast, intensive CBT was superior to regular CBT in reducing obsessive-compulsive symptoms from pre- to post-treatment in a meta-analysis on intensive CBT for OCD in youths and adults, although this difference was no longer present at 3-month follow-up due to a greater deterioration in patients in the intensive condition (Jónsson et al., 2015). A similar, but non-significant, trend appeared in the OCD subgroup analyses of our meta-analysis, of which two-thirds of the included studies overlap with those of the meta-analysis of Jónsson et al. (2015), highlighting that intensive CBT tended to be superior to regular CBT in reducing obsessive-compulsive symptoms from pre- to post-treatment. Subgroup results for panic disorder with or without agoraphobia of our study revealed no significant difference between either treatment schedule in reducing anxiety symptoms.

Depressive symptoms reduced significantly more in intensive CBT compared to the regular CBT from pre-treatment to post-treatment. Previously, decrease in comorbid depression was related to decrease in OCD symptoms in patients with OCD in residential treatment (Wetterneck et al., 2020). However, our results cannot be explained by this as the decrease in anxiety and obsessive-compulsive symptoms did not significantly differ between both treatment schedules in contrast to the depressive symptoms. In addition, comorbid depression in anxiety disorders and OCD has been related to functional impairment (Abramowitz et al., 2007), interference from obsessions and compulsions (McNally et al., 2017), an early age at onset of OCD (Hong et al., 2004), anxiety sensitivity and worry (Buchholz et al., 2019) and childhood adversities (Chen et al., 2019). Patient differences between the intensive and regular treatment on these characteristics could explain the outcome on depression. However, only some of these characteristics were measured in one of the included studies showing that patients in both treatment schedules did not differ on age at onset, global assessment of functioning and anxiety sensitivity (Bohni et al., 2009). Another explanation is that a fast reduction of anxiety symptoms in the intensive condition leads to more hope and to a sense of self-competence, which subsequently reduces the experience of low mood or depression. This would be in line with research findings that higher treatment outcome expectations predicted improvement in depressive symptoms (Beard et al., 2016) and that a low sense of self-competence is correlated with depression in youth with OCD (Peris et al., 2011). A last explanation for our findings is that intensive therapy is more effective at reducing depression. This would be in line with a finding that patients with depression who received twice weekly sessions showed a greater reduction of depressive symptoms than patients who received weekly sessions (Bruijniks et al., 2020).

Dropout numbers and reasons for dropout could not be adequately derived in most of the included studies of this meta-analysis. Since dropout is a marker of feasibility, unfortunately no conclusions can be made about the feasibility of intensive CBT. Furthermore, reasons for dropout can be used to improve treatment adherence. For instance, by adjusting treatments to practical and life circumstances, comorbid disorders or preferences of individual patients. In addition, none of the included studies mentioned adverse events like deterioration of clinical status, loss of hope, suicidality, fear of treatment stigma or adjustment problems after therapy of the patient or their family (Moritz et al., 2015). Not mentioning adverse events might erroneously suggest that psychotherapy does not have any. We think that assessing adverse events next to benefits of psychotherapy would provide a more objective picture. Dropout was not significantly different in intensive CBT compared to regular CBT. However, being based on a small number of patients from only non-randomised trials, this finding is not robust.

The findings of this study should be interpreted in the light of the following strengths and limitations. The strength of this study is that it is the first meta-analysis comparing intensive CBT to regular CBT in adults with anxiety disorders next to OCD. Also, the heterogeneity of the effect sizes of the included studies was low, indicating that variability across studies was due to chance rather than systematic differences. Effect sizes of the included studies therefore can be used to estimate a combined effect size. A limitation is the low number of included studies. Additionally, as the included studies did not encompass patients with SAD or GAD, our results are not generalizable to SAD and GAD populations. Furthermore, psychopharmacological treatment and psychiatric comorbidities may be confounders. Although in most cases medication was kept constant and psychiatric comorbidity was evenly distributed, it was not described in all studies, so confounding cannot be ruled out. A final limitation is the rather modest quality of the included studies due to non-randomised study designs, a lack of blinding of outcome assessors, dropout related to treatment condition, and a lack of pre-registered study protocols. This warrants caution with respect to the robustness and interpretation of the findings. It might be difficult to conduct a RCT comparing regular CBT to intensive CBT due to practical and ethical reasons. Many patients may not be able to participate in both the intensive and the regular treatment schedule due to work, caregiving or distance to the treatment facility and will therefore not participate in a RCT. However, high-quality studies are needed to substantiate evidence for intensive exposure. When designing future intensive exposure studies, it is recommended to take patient preferences into account. It should be noted that future research on intensive exposure is highly significant. Finding the optimum schedule of exposure may enhance treatment outcome with the same amount of treatment sessions merely by planning them differently. This would lessen the burden for patients without additional costs.

To summarise, intensive CBT and regular CBT did not significantly differ in reducing anxiety symptoms. However, intensive CBT was superior in reducing depression symptoms. Because the number and the quality of the included studies of this meta-analysis were rather modest, conclusions should be considered with caution and further high-quality research is recommended to examine both effectiveness and feasibility (i.e. dropout). Awaiting further high-quality RCTs, intensive CBT might be preferable for patients with comorbid depression or for patients for whom a fast reduction of anxiety or depressive symptoms is desirable since intensive CBT has a shorter lead time. Since our results do not indicate which format is preferable for which patients, it might be best in the meantime to follow patient preferences for intensive or regular CBT, thereby making optimal use of non-specific treatment factors.

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Supplement

Literature search strings

PubMed – 14 January 2020 (1820 records)

Anxiety disorders

“Anxiety disorders” [Mesh] OR anxiety disorder*[tiab] OR mixed anxiet*[tiab] OR generalized anxiet*[tiab] OR generalised anxiet*[tiab] OR social anxiet*[tiab] OR (SAD[tiab] AND anxiet*[tiab]) OR agoraphobi*[tiab] OR panic[tiab] OR social phobi*[tiab] OR obsessive-compulsiv*[tiab] OR neurotic disorder*[tiab] OR hoarding*[tiab] OR OCD[tiab] OR neurotic anxiet*[tiab] OR (GAD[tiab] AND anxiet*[tiab]) OR phobia*[tiab] OR phobic[tiab] OR axis I disorder*[tiab]

Intervention 1

“Behavior Therapy” [Mesh:NoExp] OR “Cognitive Behavioral Therapy” [Mesh] OR “Psychotherapy, Brief” [Mesh] OR “Implosive Therapy” [Mesh] OR “Psychotherapy, Group” [Mesh] OR cognitive therap*[tiab] OR behavior therap*[tiab] OR behavioral intervention*[tiab] OR behavioral therap*[tiab] OR behavioral treatment*[tiab] OR behaviour therap*[tiab] OR behavioural intervention*[tiab] OR behavioural therap*[tiab] OR behavioural treatment*[tiab] OR brief intervention*[tiab] OR brief therap*[tiab] OR CBT[tiab] OR cognition therap*[tiab] OR cognitive behavio*[tiab] OR cognitive psychotherap*[tiab] OR cognitive treatment*[tiab] OR (ERP[tiab] AND exposure[tiab]) OR exposure therap*[tiab] OR group treatment*[tiab] OR hospitalization program*[tiab] OR implosive therap*[tiab] OR interdisciplinary treatment*[tiab] OR interdisciplinary treatment*[tiab] OR prolonged exposure[tiab] OR residential[tiab] OR residential treatment*[tiab] OR response prevention*[tiab] OR ritual prevention*[tiab]

Time

“Inpatients” [Mesh] OR “Day Care, Medical” [Mesh] OR intensive[tiab] OR concentrated[tiab] OR time-intensive[tiab] OR high-intens*[tiab] OR daily[tiab] OR partial[tiab] OR outpatient[tiab] OR inpatient[tiab] OR day-care[tiab]

Intervention 2

intensive group*[tiab] OR concentrated group*[tiab] OR daily group*[tiab] OR partial group*[tiab] OR outpatient group*[tiab] OR inpatient group*[tiab] OR day-care group*[tiab] OR intensive treatment*[tiab] OR concentrated treatment*[tiab] OR time-intensive treatment*[tiab] OR daily treatment*[tiab] OR partial treatment*[tiab] OR outpatient treatment*[tiab] OR inpatient treatment*[tiab] OR day-care treatment*[tiab] OR intensive behavio*[tiab] OR daily behavio*[tiab] OR partial behavio*[tiab] OR outpatient behavio*[tiab] OR inpatient behavio*[tiab]

OR intensive intervention*[tiab] OR daily intervention*[tiab] OR partial intervention*[tiab] OR outpatient intervention*[tiab] OR inpatient intervention*[tiab] OR day-care intervention*[tiab] OR intensive therap*[tiab] OR concentrated therap*[tiab] OR daily therap*[tiab] OR partial therap*[tiab] OR outpatient therap*[tiab] OR inpatient therap*[tiab] OR day-care therap*[tiab] OR flooding[tiab] OR psychiatric hospital outpatient clinic*[tiab]

PubMed Session Results

Search	Query	Items found
#7	Search (#1) AND #6	1820
#6	Search (#4) OR #5	51984
#5	Search (#2) AND #3	17328
#4	intensive group*[tiab] OR concentrated group*[tiab] OR daily group*[tiab] OR partial group*[tiab] OR outpatient group*[tiab] OR inpatient group*[tiab] OR day-care group*[tiab] OR intensive treatment*[tiab] OR concentrated treatment*[tiab] OR time-intensive treatment*[tiab] OR daily treatment*[tiab] OR partial treatment*[tiab] OR outpatient treatment*[tiab] OR inpatient treatment*[tiab] OR day-care treatment*[tiab] OR intensive behavio*[tiab] OR daily behavio*[tiab] OR partial behavio*[tiab] OR outpatient behavio*[tiab] OR inpatient behavio*[tiab] OR intensive intervention*[tiab] OR daily intervention*[tiab] OR partial intervention*[tiab] OR outpatient intervention*[tiab] OR inpatient intervention*[tiab] OR day-care intervention*[tiab] OR intensive therap*[tiab] OR concentrated therap*[tiab] OR daily therap*[tiab] OR partial therap*[tiab] OR outpatient therap*[tiab] OR inpatient therap*[tiab] OR day-care therap*[tiab] OR flooding[tiab] OR psychiatric hospital outpatient clinic*[tiab]	36886
#3	"Inpatients"[Mesh] OR "Day Care, Medical"[Mesh] OR intensive[tiab] OR concentrated[tiab] OR time-intensive[tiab] OR high-intens*[tiab] OR daily[tiab] OR partial[tiab] OR outpatient[tiab] OR inpatient[tiab] OR day-care[tiab]	1396620
#2	"Behavior Therapy" [Mesh:NoExp] OR "Cognitive Behavioral Therapy"[Mesh] OR "Psychotherapy, Brief"[Mesh] OR "Implosive Therapy"[Mesh] OR "Psychotherapy, Group"[Mesh] OR cognitive therap*[tiab] OR behavior therap*[tiab] OR behavioral intervention*[tiab] OR behavioral therap*[tiab] OR behavioral treatment*[tiab] OR behaviour therap*[tiab] OR behavioural intervention*[tiab] OR behavioural therap*[tiab] OR behavioural treatment*[tiab] OR brief intervention*[tiab] OR brief therap*[tiab] OR CBT[tiab] OR cognition therap*[tiab] OR cognitive behavio*[tiab] OR cognitive psychotherap*[tiab] OR cognitive treatment*[tiab] OR (ERP[tiab] AND exposure[tiab]) OR exposure therap*[tiab] OR group treatment*[tiab] OR hospitalization program*[tiab] OR implosive therap*[tiab] OR interdisciplinary treatment*[tiab] OR interdisciplinary treatment*[tiab] OR prolonged exposure[tiab] OR residential[tiab] OR residential treatment*[tiab] OR response prevention*[tiab] OR ritual prevention*[tiab]	147845
#1	"Anxiety disorders" [Mesh] OR anxiety disorder*[tiab] OR mixed anxiet*[tiab] OR generalized anxiet*[tiab] OR generalised anxiet*[tiab] OR social anxiet*[tiab] OR (SAD[tiab] AND anxiet*[tiab]) OR agoraphobi*[tiab] OR panic[tiab] OR social phobi*[tiab] OR obsessive-compulsiv*[tiab] OR neurotic disorder*[tiab] OR hoarding*[tiab] OR OCD[tiab] OR neurotic anxiet*[tiab] OR (GAD[tiab] AND anxiet*[tiab]) OR phobia*[tiab] OR phobic[tiab] OR axis I disorder*[tiab]	110369

Anxiety disorders

'anxiety disorder'/de OR 'anxiety neurosis'/exp OR 'generalized anxiety disorder'/exp OR 'mixed anxiety and depression'/exp OR 'obsessive compulsive disorder'/exp OR 'panic'/exp OR 'phobia'/exp OR 'anxiety disorder*':ab,ti,kw OR 'mixed anxiet*':ab,ti,kw OR 'generalized anxiet*':ab,ti,kw OR 'generalised anxiet*':ab,ti,kw OR 'social anxiet*':ab,ti,kw OR (SAD AND anxiet*):ab,ti,kw OR agoraphobi*':ab,ti,kw OR panic:ab,ti,kw OR 'social phobi*':ab,ti,kw OR 'obsessive compulsiv*':ab,ti,kw OR 'neurotic disorder*':ab,ti,kw OR hoarding*':ab,ti,kw OR OCD:ab,ti,kw OR 'neurotic anxiet*':ab,ti,kw OR (GAD AND anxiet*):ab,ti,kw OR phobia*':ab,ti,kw OR phobic:ab,ti,kw OR 'axis I disorder*':ab,ti,kw

Intervention 1

'cognitive behavioral therapy'/exp OR 'cognitive therapy'/exp OR 'group therapy'/exp OR 'behavior therapy'/de OR 'implosive therapy'/exp OR 'short term psychotherapy'/exp OR 'cognitive therap*':ab,ti,kw OR 'behavior therap*':ab,ti,kw OR 'behavioral intervention*':ab,ti,kw OR 'behavioral therap*':ab,ti,kw OR 'behavioral treatment*':ab,ti,kw OR 'behaviour therap*':ab,ti,kw OR 'behavioural intervention*':ab,ti,kw OR 'behavioural therap*':ab,ti,kw OR 'behavioural treatment*':ab,ti,kw OR 'brief intervention*':ab,ti,kw OR 'brief therap*':ab,ti,kw OR CBT:ab,ti,kw OR 'cognition therap*':ab,ti,kw OR 'cognitive behavio*':ab,ti,kw OR 'cognitive psychotherap*':ab,ti,kw OR 'cognitive treatment*':ab,ti,kw OR (ERP:ab,ti,kw AND exposure:ab,ti,kw) OR 'exposure therap*':ab,ti,kw OR 'group treatment*':ab,ti,kw OR 'hospitalization program*':ab,ti,kw OR 'hospitalization program*':ab,ti,kw OR 'implosive therap*':ab,ti,kw OR 'interdisciplinary treatment*':ab,ti,kw OR 'interdisciplinary treatment*':ab,ti,kw OR 'prolonged exposure':ab,ti,kw OR residential:ab,ti,kw OR 'residential treatment*':ab,ti,kw OR 'response prevention*':ab,ti,kw OR 'ritual prevention':ab,ti,kw

Time

'hospital patient'/exp OR 'day care'/exp OR intensive:ab,ti,kw OR concentrated:ab,ti,kw OR 'time-intensive':ab,ti,kw OR 'high-intens*':ab,ti,kw OR daily:ab,ti,kw OR partial:ab,ti,kw OR outpatient:ab,ti,kw OR inpatient:ab,ti,kw OR 'day-care':ab,ti,kw

Intervention 2

'intensive group*':ab,ti,kw OR 'concentrated group*':ab,ti,kw OR 'time-intensive group*':ab,ti,kw OR 'high-intensive group*':ab,ti,kw OR 'daily group*':ab,ti,kw OR 'partial group*':ab,ti,kw OR 'outpatient group*':ab,ti,kw OR 'inpatient group*':ab,ti,kw OR 'day-care group*':ab,ti,kw OR 'intensive treatment*':ab,ti,kw OR 'concentrated treatment*':ab,ti,kw OR 'time-intensive treatment*':ab,ti,kw OR 'high-intensive treatment*':ab,ti,kw

OR 'daily treatment':ab,ti,kw OR 'partial treatment':ab,ti,kw OR 'outpatient treatment':ab,ti,kw OR 'inpatient treatment':ab,ti,kw OR 'day-care treatment':ab,ti,kw OR 'intensive behavior':ab,ti,kw OR 'concentrated behavior':ab,ti,kw OR 'time-intensive behavior':ab,ti,kw OR 'high-intensive behavior':ab,ti,kw OR 'daily behavior':ab,ti,kw OR 'partial behavior':ab,ti,kw OR 'day-care behavior':ab,ti,kw OR 'outpatient behavior':ab,ti,kw OR 'inpatient behavior':ab,ti,kw OR 'intensive intervention':ab,ti,kw OR 'concentrated intervention':ab,ti,kw OR 'time-intensive intervention':ab,ti,kw OR 'high-intensive intervention':ab,ti,kw OR 'daily intervention':ab,ti,kw OR 'partial intervention':ab,ti,kw OR 'outpatient intervention':ab,ti,kw OR 'inpatient intervention':ab,ti,kw OR 'day-care intervention':ab,ti,kw OR 'intensive therap':ab,ti,kw OR 'concentrated therap':ab,ti,kw OR 'time-intensive therap':ab,ti,kw OR 'high-intensive therap':ab,ti,kw OR 'daily therap':ab,ti,kw OR 'partial therap':ab,ti,kw OR 'outpatient therap':ab,ti,kw OR 'inpatient therap':ab,ti,kw OR 'day-care therap':ab,ti,kw OR flooding:ab,ti,kw OR 'psychiatric hospital outpatient clinic':ab,ti,kw

Embase Session Results

No.	Query	Results
#7	#1 AND #6	3,273
#6	#4 OR #5	76,841
#5	#2 AND #3	25,045
#4	'intensive group':ab,ti,kw OR 'concentrated group':ab,ti,kw OR 'time-intensive group':ab,ti,kw OR 'high-intensive group':ab,ti,kw OR 'daily group':ab,ti,kw OR 'partial group':ab,ti,kw OR 'outpatient group':ab,ti,kw OR 'inpatient group':ab,ti,kw OR 'day-care group':ab,ti,kw OR 'intensive treatment':ab,ti,kw OR 'concentrated treatment':ab,ti,kw OR 'time-intensive treatment':ab,ti,kw OR 'high-intensive treatment':ab,ti,kw OR 'daily treatment':ab,ti,kw OR 'partial treatment':ab,ti,kw OR 'outpatient treatment':ab,ti,kw OR 'inpatient treatment':ab,ti,kw OR 'day-care treatment':ab,ti,kw OR 'intensive behavior':ab,ti,kw OR 'concentrated behavior':ab,ti,kw OR 'time-intensive behavior':ab,ti,kw OR 'high-intensive behavior':ab,ti,kw OR 'daily behavior':ab,ti,kw OR 'partial behavior':ab,ti,kw OR 'day-care behavior':ab,ti,kw OR 'outpatient behavior':ab,ti,kw OR 'inpatient behavior':ab,ti,kw OR 'intensive intervention':ab,ti,kw OR 'concentrated intervention':ab,ti,kw OR 'time-intensive intervention':ab,ti,kw OR 'high-intensive intervention':ab,ti,kw OR 'daily intervention':ab,ti,kw OR 'partial intervention':ab,ti,kw OR 'outpatient intervention':ab,ti,kw OR 'inpatient intervention':ab,ti,kw OR 'day-care intervention':ab,ti,kw OR 'intensive therap':ab,ti,kw OR 'concentrated therap':ab,ti,kw OR 'time-intensive therap':ab,ti,kw OR 'high-intensive therap':ab,ti,kw OR 'daily therap':ab,ti,kw OR 'partial therap':ab,ti,kw OR 'outpatient therap':ab,ti,kw OR 'inpatient therap':ab,ti,kw OR 'day-care therap':ab,ti,kw OR flooding:ab,ti,kw OR 'psychiatric hospital outpatient clinic':ab,ti,kw	55,387
#3	'hospital patient'/exp OR 'day care'/exp OR intensive:ab,ti,kw OR concentrated:ab,ti,kw OR 'time-intensive':ab,ti,kw OR 'high-intens':ab,ti,kw OR daily:ab,ti,kw OR partial:ab,ti,kw OR outpatient:ab,ti,kw OR inpatient:ab,ti,kw OR 'day-care':ab,ti,kw	2,037,638

No.	Query	Results
#2	<p>'cognitive behavioral therapy'/exp OR 'cognitive therapy'/exp OR 'group therapy'/exp OR 'behavior therapy'/de OR 'implosive therapy'/exp OR 'short term psychotherapy'/exp OR 'cognitive therap^{ab,ti,kw} OR 'behavior therap^{ab,ti,kw} OR 'behavioral intervention^{ab,ti,kw} OR 'behavioral therap^{ab,ti,kw} OR 'behavioral treatment^{ab,ti,kw} OR 'behaviour therap^{ab,ti,kw} OR 'behavioural intervention^{ab,ti,kw} OR 'behavioural therap^{ab,ti,kw} OR 'behavioural treatment^{ab,ti,kw} OR 'brief intervention^{ab,ti,kw} OR 'brief therap^{ab,ti,kw} OR cbt:ab,ti,kw OR 'cognition therap^{ab,ti,kw} OR 'cognitive behavio^{ab,ti,kw} OR 'cognitive psychotherap^{ab,ti,kw} OR 'cognitive treatment^{ab,ti,kw} OR (erp:ab,ti,kw AND exposure:ab,ti,kw) OR 'exposure therap^{ab,ti,kw} OR 'group treatment^{ab,ti,kw} OR 'hospitalization program^{ab,ti,kw} OR 'implosive therap^{ab,ti,kw} OR 'interdisciplinary treatment^{ab,ti,kw} OR 'prolonged exposure':ab,ti,kw OR residential:ab,ti,kw OR 'residential treatment^{ab,ti,kw} OR 'response prevention^{ab,ti,kw} OR 'ritual prevention':ab,ti,kw</p>	194,363
#1	<p>'anxiety disorder'/de OR 'anxiety neurosis'/exp OR 'generalized anxiety disorder'/exp OR 'mixed anxiety and depression'/exp OR 'obsessive compulsive disorder'/exp OR 'panic'/exp OR 'phobia'/exp OR 'anxiety disorder^{ab,ti,kw} OR 'mixed anxiet^{ab,ti,kw} OR 'generalized anxiet^{ab,ti,kw} OR 'generalised anxiet^{ab,ti,kw} OR 'social anxiet^{ab,ti,kw} OR (sad:ab,ti,kw AND anxiet^{ab,ti,kw}) OR agoraphobi^{ab,ti,kw} OR panic:ab,ti,kw OR 'social phobi^{ab,ti,kw} OR 'obsessive compulsiv^{ab,ti,kw} OR 'neurotic disorder^{ab,ti,kw} OR hoarding^{ab,ti,kw} OR ocd:ab,ti,kw OR 'neurotic anxiet^{ab,ti,kw} OR (gad:ab,ti,kw AND anxiet^{ab,ti,kw}) OR phobia^{ab,ti,kw} OR phobic:ab,ti,kw OR 'axis i disorder^{ab,ti,kw}</p>	173,865

Embase Session Results - continued

PsycINFO (EBSCO) – 14 January 2020

Anxiety disorders

DE "Animal Hoarding Behavior" OR DE "Hoarding Behavior" OR DE "Hoarding Disorder" OR DE "Generalized Anxiety Disorder" OR DE "Obsessive Compulsive Disorder" OR DE "Panic Disorder" OR DE "Phobias" OR DE "Agoraphobia" OR DE "Anxiety Disorders" OR DE "Social Phobia" OR TI("anxiety disorder*" OR "mixed anxiet*" OR "generalized anxiet*" OR "generalised anxiet*" OR "social anxiet*" OR (SAD AND anxiet*) OR agoraphobi* OR panic OR "social phobi*" OR "obsessive compulsiv*" OR "neurotic disorder*" OR hoarding* OR OCD OR "neurotic anxiet*" OR (GAD AND anxiet*) OR phobia* OR phobic OR "axis I disorder*") OR AB("anxiety disorder*" OR "mixed anxiet*" OR "generalized anxiet*" OR "generalised anxiet*" OR "social anxiet*" OR (SAD AND anxiet*) OR agoraphobi* OR panic OR "social phobi*" OR "obsessive compulsiv*" OR "neurotic disorder*" OR hoarding* OR OCD OR "neurotic anxiet*" OR (GAD AND anxiet*) OR phobia* OR phobic OR "axis I disorder*") OR KW((anxiety Wo disorder*) OR (mixed Wo anxiet*) OR (generalized Wo anxiet*) OR (generalised Wo anxiet*) OR (social Wo anxiet*) OR (SAD AND anxiet*) OR agoraphobi* OR panic OR (social Wo phobi*) OR (obsessive Wo compulsiv*) OR (neurotic Wo disorder*) OR hoarding* OR OCD OR (neurotic Wo anxiet*) OR (GAD AND anxiet*) OR phobia* OR phobic OR (axis W1 disorder*))

Intervention 1

DE "Implosive Therapy" OR DE "Acceptance and Commitment Therapy" OR DE "Behavior Therapy" OR DE "Brief Psychotherapy" OR DE "Cognitive Behavior Therapy" OR DE "Group Psychotherapy" OR DE "Cognitive Therapy" OR TI("cognitive therap*" OR "behavior therap*" OR "behavioral intervention*" OR "behavioral therap*" OR "behavioral treatment*" OR "behaviour therap*" OR "behavioural intervention*" OR "behavioural therap*" OR "behavioural treatment*" OR "brief intervention*" OR "brief therap*" OR CBT OR "cognition therap*" OR "cognitive behavio*" OR "cognitive psychotherap*" OR "cognitive treatment*" OR (ERP AND exposure) OR "exposure therap*" OR "group treatment*" OR "hospitalization program*" OR "hospitalization program*" OR "implosive therap*" OR "interdisciplinary treatment*" OR "prolonged exposure" OR residential OR "residential treatment*" OR "response prevention*" OR "ritual prevention") OR AB(("cognitive therap*" OR "behavior therap*" OR "behavioral intervention*" OR "behavioral therap*" OR "behavioral treatment*" OR "behaviour therap*" OR "behavioural intervention*" OR "behavioural therap*" OR "behavioural treatment*" OR "brief intervention*" OR "brief therap*" OR CBT OR "cognition therap*" OR "cognitive behavio*" OR "cognitive psychotherap*" OR "cognitive treatment*" OR (ERP AND exposure) OR "exposure therap*" OR "group treatment*" OR "hospitalization program*" OR "hospitalization program*" OR "implosive therap*" OR "interdisciplinary

treatment*” OR “prolonged exposure” OR residential OR “residential treatment*” OR “response prevention*” OR “ritual prevention”) OR KW((cognitive Wo therap*) OR (behavior Wo therap*) OR (behavioral Wo intervention*) OR (behavioral Wo therap*) OR (behavioral Wo treatment*) OR (behaviour Wo therap*) OR (behavioural Wo intervention*) OR (behavioural Wo therap*) OR (behavioural Wo treatment*) OR (brief Wo intervention*) OR (brief Wo therap*) OR CBT OR (cognition Wo therap*) OR (cognitive Wo behavio*) OR (cognitive Wo psychotherap*) OR (cognitive Wo treatment*) OR (ERP AND exposure) OR (exposure Wo therap*) OR (group Wo treatment*) OR (hospitalization Wo program*) OR (hospitalization Wo program*) OR (implosive Wo therap*) OR (interdisciplinary Wo treatment*) OR (prolonged Wo exposure) OR residential OR (residential Wo treatment*) OR (response Wo prevention*) OR (ritual Wo prevention))

Time

DE “Partial Hospitalization” OR DE “Outpatient Treatment” OR DE “Psychiatric Clinics” OR DE “Psychiatric Units” OR TI(intensive OR concentrated OR “time-intensive” OR “high-intens*” OR daily OR partial OR outpatient OR inpatient OR “day-care”) OR AB(intensive OR concentrated OR “time-intensive” OR “high-intens*” OR daily OR partial OR outpatient OR inpatient OR “day-care”) OR KW(intensive OR concentrated OR (time Wo intensive) OR (high Wo intens*) OR daily OR partial OR outpatient OR inpatient OR (day Wo care))

Intervention 2

TI(“intensive group*” OR “concentrated group*” OR “time-intensive group*” OR “high-intensive group*” OR “daily group*” OR “partial group*” OR “outpatient group*” OR “inpatient group*” OR “day-care group*” OR “intensive treatment*” OR “concentrated treatment*” OR “time-intensive treatment*” OR “high-intensive treatment*” OR “daily treatment*” OR “partial treatment*” OR “outpatient treatment*” OR “inpatient treatment*” OR “day-care treatment*” OR “intensive behavio*” OR “concentrated behavio*” OR “time-intensive behavio*” OR “high-intensive behavio*” OR “daily behavio*” OR “partial behavio*” OR “outpatient behavio*” OR “inpatient behavio*” OR “day-care behavio*” OR “intensive intervention*” OR “concentrated intervention*” OR “time-intensive intervention*” OR “high-intensive intervention*” OR “daily intervention*” OR “partial intervention*” OR “outpatient intervention*” OR “inpatient intervention*” OR “day-care intervention*” OR “intensive therap*” OR “concentrated therap*” OR “time-intensive therap*” OR “high-intensive therap*” OR “daily therap*” OR “partial therap*” OR “outpatient therap*” OR “inpatient therap*” OR “day-care therap*” OR flooding OR “psychiatric hospital outpatient clinic”) OR AB(“intensive group*” OR “concentrated group*” OR “time-intensive group*” OR “high-intensive group*” OR “daily group*” OR “partial group*” OR “outpatient group*” OR “inpatient group*” OR “day-care group*” OR “intensive treatment*” OR “concentrated treatment*” OR “time-intensive treatment*” OR “high-intensive treatment*” OR “daily treatment*” OR “partial

treatment*" OR "outpatient treatment*" OR "inpatient treatment*" OR "day-care treatment*" OR "intensive behavio*" OR "concentrated behavio*" OR "time-intensive behavio*" OR "high-intensive behavio*" OR "daily behavio*" OR "partial behavio*" OR "outpatient behavio*" OR "inpatient behavio*" OR "day-care behavio*" OR "intensive intervention*" OR "concentrated intervention*" OR "time-intensive intervention*" OR "high-intensive intervention*" OR "daily intervention*" OR "partial intervention*" OR "outpatient intervention*" OR "inpatient intervention*" OR "day-care intervention*" OR "intensive therap*" OR "concentrated therap*" OR "time-intensive therap*" OR "high-intensive therap*" OR "daily therap*" OR "partial therap*" OR "outpatient therap*" OR "inpatient therap*" OR "day-care therap*" OR flooding OR "psychiatric hospital outpatient clinic*") OR KW((intensive Wo group*) OR (concentrated Wo group*) OR (time Wo intensive group*) OR (high Wo intensive Wo group*) OR (daily Wo group*) OR (partial Wo group*) OR (outpatient Wo group*) OR (inpatient Wo group*) OR (day Wo care Wo group*) OR (intensive Wo treatment*) OR (concentrated Wo treatment*) OR (time Wo intensive Wo treatment*) OR (high Wo intensive Wo treatment*) OR (daily Wo treatment*) OR (partial Wo treatment*) OR (outpatient Wo treatment*) OR (inpatient Wo treatment*) OR (day Wo care Wo treatment*) OR (intensive Wo behavio*) OR (concentrated Wo behavio*) OR (time Wo intensive Wo behavio*) OR (high Wo intensive Wo behavio*) OR (daily Wo behavio*) OR (partial Wo behavio*) OR (outpatient Wo behavio*) OR (inpatient Wo behavio*) OR (day Wo care Wo behavio*) OR (intensive Wo intervention*) OR (concentrated Wo intervention*) OR (time Wo intensive Wo intervention*) OR (high Wo intensive Wo intervention*) OR (daily Wo intervention*) OR (partial Wo intervention*) OR (outpatient Wo intervention*) OR (inpatient Wo intervention*) OR (day Wo care Wo intervention*) OR (intensive Wo therap*) OR (concentrated Wo therap*) OR (time Wo intensive Wo therap*) OR (high Wo intensive Wo therap*) OR (daily Wo therap*) OR (partial Wo therap*) OR (outpatient Wo therap*) OR (inpatient Wo therap*) OR (day Wo care Wo therap*) OR flooding OR (psychiatric Wo hospital Wo outpatient Wo clinic*))

PsycINFO Session Results

#	Query	Limiters/ Expanders	Results
S8	S7	Limiters: Academic journals	2,377
S7	S1 AND S6	Search modes - Boolean/Phrase	2,723
S6	S4 OR S5	Search modes - Boolean/Phrase	30,882
S5	S2 AND S3	Search modes - Boolean/Phrase	19,078

#	Query	Limiters/ Expanders	Results
S4	TI("intensive group" sm OR "concentrated group" sm OR "time-intensive group" sm OR "high-intensive group" sm OR "daily group" sm OR "partial group" sm OR "outpatient group" sm OR "inpatient group" sm OR "day-care group" sm OR "intensive treatment" sm OR "concentrated treatment" sm OR "time-intensive treatment" sm OR "high-intensive treatment" sm OR "daily treatment" sm OR "partial treatment" sm OR "outpatient treatment" sm OR "inpatient treatment" sm OR "day-care treatment" sm OR "intensive behavior" sm OR "concentrated behavior" sm OR "time-intensive behavior" sm OR "high-intensive behavior" sm OR "daily behavior" sm OR "partial behavior" sm OR "outpatient behavior" sm OR "inpatient behavior" sm OR "day-care behavior" sm OR "intensive intervention" sm OR "concentrated intervention" sm OR "time-intensive intervention" sm OR "high-intensive intervention" sm OR "daily intervention" sm OR "partial intervention" sm OR "outpatient intervention" sm OR "inpatient intervention" sm OR "day-care intervention" sm OR "intensive therapy" sm OR "concentrated therapy" sm OR "time-intensive therapy" sm OR "high-intensive therapy" sm OR "daily therapy" sm OR "partial therapy" sm OR "outpatient therapy" sm OR "inpatient therapy" sm OR "day-care therapy" sm OR flooding OR "psychiatric hospital outpatient clinic" sm) OR AB("intensive group" sm OR "concentrated group" sm OR "time-intensive group" sm OR "high-intensive group" sm OR "daily group" sm OR "partial group" sm OR "outpatient group" sm OR "inpatient group" sm OR "day-care group" sm OR "intensive treatment" sm OR "concentrated treatment" sm OR "time-intensive treatment" sm OR "high-intensive treatment" sm OR "daily treatment" sm OR "partial treatment" sm OR "outpatient treatment" sm OR "inpatient treatment" sm OR "day-care treatment" sm OR "intensive behavior" sm OR "concentrated behavior" sm OR "time-intensive behavior" sm OR "high-intensive behavior" sm OR "daily behavior" sm OR "partial behavior" sm OR "outpatient behavior" sm OR "inpatient behavior" sm OR "day-care behavior" sm OR "intensive intervention" sm OR "concentrated intervention" sm OR "time-intensive intervention" sm OR "high-intensive intervention" sm OR "daily intervention" sm OR "partial intervention" sm OR "outpatient intervention" sm OR "inpatient intervention" sm OR "day-care intervention" sm OR "intensive therapy" sm OR "concentrated therapy" sm OR "time-intensive therapy" sm OR "high-intensive therapy" sm OR "daily therapy" sm OR "partial therapy" sm OR "outpatient therapy" sm OR "inpatient therapy" sm OR "day-care therapy" sm OR flooding OR "psychiatric hospital outpatient clinic" sm) OR KW((intensive Wo group ^s) OR (concentrated Wo group ^s) OR (time Wo intensive group ^s) OR (high Wo intensive Wo group ^s) OR (daily Wo group ^s) OR (partial Wo group ^s) OR (outpatient Wo group ^s) OR (inpatient Wo group ^s) OR (day Wo care Wo group ^s) OR (intensive Wo treatment ^s) OR (concentrated Wo treatment ^s) OR (time Wo intensive Wo treatment ^s) OR (high Wo intensive Wo treatment ^s) OR (daily Wo treatment ^s) OR (partial Wo treatment ^s) OR (outpatient Wo treatment ^s) OR (inpatient Wo treatment ^s) OR (day Wo care Wo treatment ^s) OR (intensive Wo behavior ^s) OR (concentrated Wo behavior ^s) OR (time Wo intensive Wo behavior ^s) OR (high Wo intensive Wo behavior ^s) OR (daily Wo behavior ^s) OR (partial Wo behavior ^s) OR (outpatient Wo behavior ^s) OR (inpatient Wo behavior ^s) OR (day Wo care Wo behavior ^s) OR (intensive Wo intervention ^s) OR (concentrated Wo intervention ^s) OR (time Wo intensive Wo intervention ^s) OR (high Wo intensive Wo intervention ^s) OR (daily Wo intervention ^s) OR (partial Wo intervention ^s) OR (outpatient Wo intervention ^s) OR (inpatient Wo intervention ^s) OR (day Wo care Wo intervention ^s) OR (intensive Wo therapy ^s) OR (concentrated Wo therapy ^s) OR (time Wo intensive Wo therapy ^s) OR (high Wo intensive Wo therapy ^s) OR (daily Wo therapy ^s) OR (partial Wo therapy ^s) OR (outpatient Wo therapy ^s) OR (inpatient Wo therapy ^s) OR (day Wo care Wo therapy ^s) OR flooding OR (psychiatric Wo hospital Wo outpatient Wo clinic ^s))	Search modes - Boolean/Phrase	15,545

PsycINFO Session Results - continued

#	Query	Limiters/ Expanders	Results
S3	DE "Partial Hospitalization" OR DE "Outpatient Treatment" OR DE "Psychiatric Clinics" OR DE "Psychiatric Units" OR TI(intensive OR concentrated OR "time-intensive" OR "high-intens*" OR daily OR partial OR outpatient OR inpatient OR "day-care") OR AB(intensive OR concentrated OR "time-intensive" OR "high-intens*" OR daily OR partial OR outpatient OR inpatient OR "day-care") OR KW(intensive OR concentrated OR (time Wo intensive) OR (high Wo intens*) OR daily OR partial OR outpatient OR inpatient OR (day Wo care))	Search modes - Boolean/Phrase	288,418
S2	DE "Implosive Therapy" OR DE "Acceptance and Commitment Therapy" OR DE "Behavior Therapy" OR DE "Brief Psychotherapy" OR DE "Cognitive Behavior Therapy" OR DE "Group Psychotherapy" OR DE "Cognitive Therapy" OR TI("cognitive therap*" OR "behavior therap*" OR "behavioral intervention*" OR "behavioral therap*" OR "behavioral treatment*" OR "behaviour therap*" OR "behavioural intervention*" OR "behavioural therap*" OR "behavioural treatment*" OR "brief intervention*" OR "brief therap*" OR CBT OR "cognition therap*" OR "cognitive behavio*" OR "cognitive psychotherap*" OR "cognitive treatment*" OR (ERP AND exposure) OR "exposure therap*" OR "group treatment*" OR "hospitalization program*" OR "hospitalization program*" OR "implosive therap*" OR "interdisciplinary treatment*" OR "prolonged exposure" OR residential OR "residential treatment*" OR "response prevention*" OR "ritual prevention") OR AB(("cognitive therap*" OR "behavior therap*" OR "behavioral intervention*" OR "behavioral therap*" OR "behavioral treatment*" OR "behaviour therap*" OR "behavioural intervention*" OR "behavioural therap*" OR "behavioural treatment*" OR "brief intervention*" OR "brief therap*" OR CBT OR "cognition therap*" OR "cognitive behavio*" OR "cognitive psychotherap*" OR "cognitive treatment*" OR (ERP AND exposure) OR "exposure therap*" OR "group treatment*" OR "hospitalization program*" OR "hospitalization program*" OR "implosive therap*" OR "interdisciplinary treatment*" OR "prolonged exposure" OR residential OR "residential treatment*" OR "response prevention*" OR "ritual prevention") OR KW((cognitive Wo therap*) OR (behavior Wo therap*) OR (behavioral Wo intervention*) OR (behavioral Wo therap*) OR (behavioral Wo treatment*) OR (behaviour Wo therap*) OR (behavioural Wo intervention*) OR (behavioural Wo therap*) OR (behavioural Wo treatment*) OR (brief Wo intervention*) OR (brief Wo therap*) OR CBT OR (cognition Wo therap*) OR (cognitive Wo behavio*) OR (cognitive Wo psychotherap*) OR (cognitive Wo treatment*) OR (ERP AND exposure) OR (exposure Wo therap*) OR (group Wo treatment*) OR (hospitalization Wo program*) OR (hospitalization Wo program*) OR (implosive Wo therap*) OR (interdisciplinary Wo treatment*) OR (prolonged Wo exposure) OR residential OR (residential Wo treatment*) OR (response Wo prevention*) OR (ritual Wo prevention))	Search modes - Boolean/Phrase	144,473

#	Query	Limiters/ Expanders	Results
S1	DE "Animal Hoarding Behavior" OR DE "Hoarding Behavior" OR DE "Hoarding Disorder" OR DE "Generalized Anxiety Disorder" OR DE "Obsessive Compulsive Disorder" OR DE "Panic Disorder" OR DE "Phobias" OR DE "Agoraphobia" OR DE "Anxiety Disorders" OR DE "Social Phobia" OR TI("anxiety disorder*" OR "mixed anxiet*" OR "generalized anxiet*" OR "generalised anxiet*" OR "social anxiet*" OR (SAD AND anxiet*) OR agoraphobi* OR panic OR "social phobi*" OR "obsessive compulsiv*" OR "neurotic disorder*" OR hoarding* OR OCD OR "neurotic anxiet*" OR (GAD AND anxiet*) OR phobia* OR phobic OR "axis I disorder*") OR AB("anxiety disorder*" OR "mixed anxiet*" OR "generalized anxiet*" OR "generalised anxiet*" OR "social anxiet*" OR (SAD AND anxiet*) OR agoraphobi* OR panic OR "social phobi*" OR "obsessive compulsiv*" OR "neurotic disorder*" OR hoarding* OR OCD OR "neurotic anxiet*" OR (GAD AND anxiet*) OR phobia* OR phobic OR "axis I disorder*") OR KW((anxiety Wo disorder*) OR (mixed Wo anxiet*) OR (generalized Wo anxiet*) OR (generalised Wo anxiet*) OR (social Wo anxiet*) OR (SAD AND anxiet*) OR agoraphobi* OR panic OR (social Wo phobi*) OR (obsessive Wo compulsiv*) OR (neurotic Wo disorder*) OR hoarding* OR OCD OR (neurotic Wo anxiet*) OR (GAD AND anxiet*) OR phobia* OR phobic OR (axis W1 disorder*))	Search modes - Boolean/Phrase	94,344

Calculating Hedges' g

First, raw pre-post differences within conditions were calculated as: $X_{\text{diff}} = \bar{X}_{\text{post}} - \bar{X}_{\text{pre}}$. In addition, the pooled standard deviations of these differences over time were calculated for each treatment condition as follows:

$$SD_{\text{pooled}} = \frac{\sqrt{(n_{\text{pre}} - 1)S_{\text{pre}}^2 + (n_{\text{post}} - 1)S_{\text{post}}^2}}{(n_{\text{pre}} + n_{\text{post}} - 2)}$$

Then, the standardized mean pre-post differences between conditions were calculated as:

$$SMD_{\text{diff}} = \frac{X_{\text{diff_intensive}} - X_{\text{diff_regular}}}{SD_{\text{pooled}}}$$

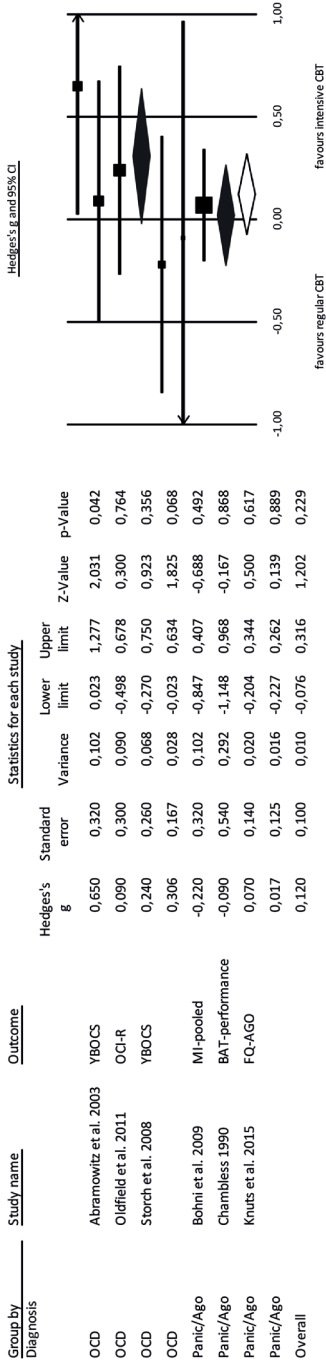
where

$$SD_{\text{pooled}} = \frac{\sqrt{(n_{\text{intensive}} - 1)S_{\text{intensive}}^2 + (n_{\text{regular}} - 1)S_{\text{regular}}^2}}{n_{\text{intensive}} + n_{\text{regular}} - 2}$$

Finally, Hedges' bias correction factor (Hedges & Olkin, 1985) was applied to correct for small samples:

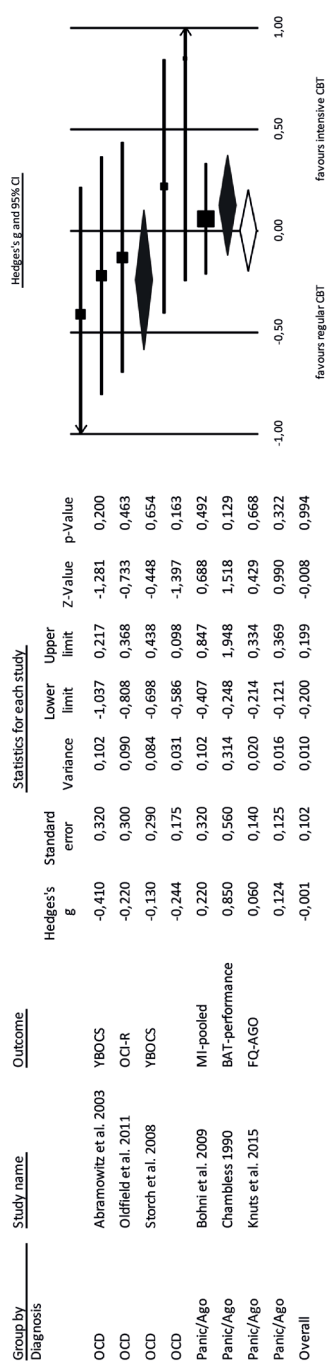
$$g = SMD_{\text{diff}} * \left(1 - \frac{3}{4 df - 1}\right)$$

Table S1. Forest plot of mean effect sizes (Hedges'g) for intensive versus regular CBT on anxiety and obsessive-compulsive measures from pre-treatment to post-treatment, split on diagnosis.



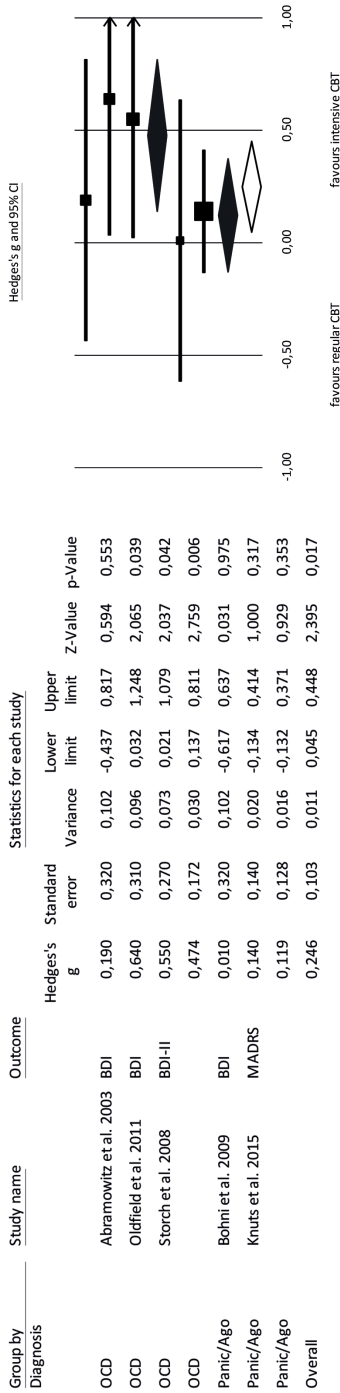
OCD: $Q(2)=1.74$; $p=0.42$; $I^2=0.00$. Panic disorder with/without agoraphobia: $Q(2)=0.73$; $p=0.69$; $I^2=0.00$

Table S2. Forest plot of mean effect sizes (Hedges'g) for intensive versus regular CBT on anxiety and obsessive-compulsive measures from post-treatment to follow-up, split on diagnosis.



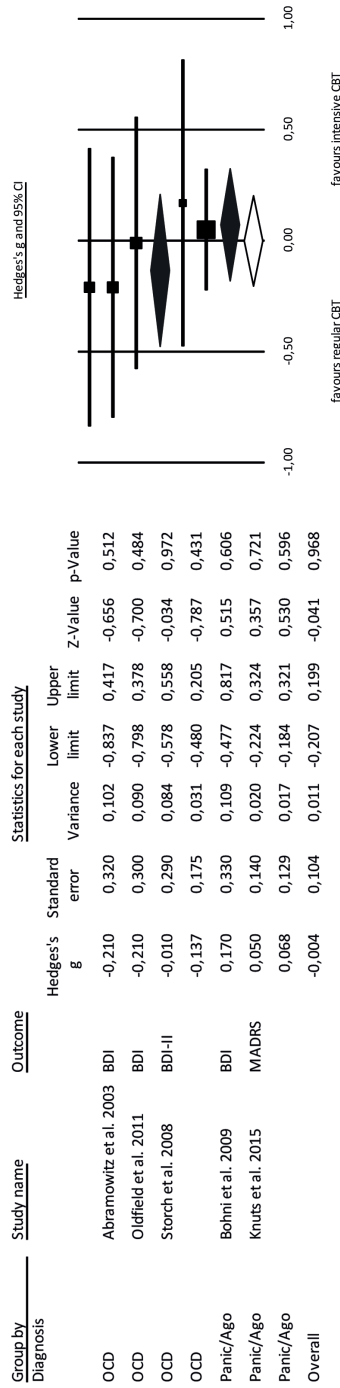
OCD: $Q(2)=0.43$; $p=0.81$; $I^2=0.00$. Panic disorder with/without agoraphobia: $Q(2)=1.98$; $p=0.37$; $I^2=0.00$

Table S3. Forest plot of mean effect sizes (Hedges'g) for intensive versus regular CBT on depression measures from pre-treatment to post-treatment, split on diagnosis.



OCD: $Q(2)=1.15$; $p=0.56$; $I^2=0.00$. Panic disorder with/without agoraphobia: $Q(1)=0.14$, $p=0.71$; $I^2=0.00$

Table S4. Forest plot of mean effect sizes (Hedges'g) for intensive versus regular CBT on depression measures from post-treatment to follow-up, split on diagnosis.



OCD: $Q(2)=0.30$, $p=0.86$; $I^2=0.00$. Panic disorder with/without agoraphobia: $Q(1)=0.11$, $p=0.74$; $I^2=0.00$



CHAPTER 10

Schema Therapy with Cognitive Behaviour Day- Treatment in Patients with Treatment-Resistant Anxiety Disorders and Obsessive- Compulsive Disorder: an Uncontrolled Pilot Study

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Neeltje M. Batelaan

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Abstract

Background: Treatment resistance in patients with anxiety disorders and obsessive-compulsive disorder (OCD) might be caused by dysfunctional personality traits or, more specifically, early maladaptive schemas (EMSs) and schema modes, that can be treated with Schema Therapy (ST).

Aim: To explore possible effectiveness of ST-CBT day-treatment in patients with treatment-resistant anxiety disorders and OCD in an uncontrolled pilot study.

Method: Treatment-resistant patients with anxiety disorders or OCD ($n=27$) were treated with ST-CBT day-treatment for 37 weeks on average including 11.5 therapy hours per week. The Symptom Questionnaire-48, Young Schema Questionnaire-2 and Schema Mode Inventory were completed before and after treatment.

Results: General psychopathology, EMSs and schema modes significantly improved after treatment. Spearman's correlations between pre- to post-treatment difference scores of general psychopathology, EMSs and schema modes were significant and high. The level of pre-treatment EMSs and schema modes did not predict post-treatment general psychopathology.

Conclusions: Symptom reduction was strongly correlated with improvement of EMSs and schema modes. Stronger pre-treatment EMSs and schema modes did not hinder improvement of symptoms. ST-CBT day-treatment is promising for patients with treatment-resistant anxiety disorders and OCD. Further controlled research is needed to substantiate evidence for schema therapy in patients with treatment-resistant anxiety disorders and OCD.

Introduction

Anxiety disorders and obsessive-compulsive disorder (OCD) often run a chronic course. After an evidence-based treatment including pharmacotherapy and cognitive behaviour therapy (CBT) almost half of the patients still fulfil the criteria of the index disorder and lack functional recovery. When patients do not respond to these first-line treatments, guidelines recommend intensive treatment such as day-treatment.

It is believed that dysfunctional personality traits account for treatment resistance in patients with anxiety disorders and OCD. More specifically, early maladaptive schemas (EMSs) and schema modes would result in persistence of symptoms. EMSs are “patterns, developed during childhood or adolescence, consisting of memories, emotions, cognitions, and bodily sensations, regarding oneself and one’s relationship with others” as defined by Young (2003). Schema modes are the emotional states and coping responses arising when EMSs are activated. Indeed, research has provided some evidence that higher levels of EMSs significantly predicted poor response to CBT in patients with OCD (Sunde et al., 2019; Thiel et al., 2014), but this result was not confirmed in a study in patients with depression and anxiety disorders (Halford et al., 2002).

If treatment resistance is associated with EMSs then treating these schemas could help to reduce anxiety and obsessive-compulsive symptoms. One treatment targeting EMSs is Schema Therapy (ST). Schema therapy has been found to be effective in patients with personality disorders. Preliminary evidence exists for the effectiveness of schema therapy in mental disorders such as anxiety disorders, OCD, PTSD, chronic depression and eating disorders (Peeters et al., 2022). Further preliminary evidence comes from a recent pilot study showing that improvement of general psychopathology was correlated to improvement of schema modes in patients with anxiety disorders and OCD; however, EMSs were not measured in this study (Peeters et al., 2021).

To add to previous research, the aim of this exploratory study is to determine: 1) whether symptoms, EMSs and schema modes improve with ST-CBT day-treatment in patients with anxiety and OCD; 2) whether improvement in symptoms correlates with improvement in EMSs and schema modes; and 3) whether the level of EMSs and schema modes at baseline is associated with improvement of symptoms. If no association appears, stronger pre-treatment EMSs and schema modes are not related to symptom improvement. This would be consistent with the hypothesis that treating EMSs and schema modes abolishes treatment resistance.

Methods

Participants

All patients who completed an intensive outpatient ST-CBT treatment between medio 2017 and 2020 were included in the study. To be eligible for the ST-CBT day-treatment, patients had to: 1) have completed at least one previous CBT targeting the primary anxiety disorder or OCD; and 2) use or actively refused psychotropic drugs; and 3) experience severe limitations in daily functioning due to the disorder. The diagnoses were determined by experienced clinicians at the clinical assessment and re-assessed every three months by evaluating the criteria of possible diagnoses, given the symptoms of the patients. Diagnoses were made in accordance with DSM, fifth edition.

Design

Data were collected as part of routine clinical care before and after treatment. This study was approved by the research committee of GGZ inGeest (CWO-2020-013). Because the current study was file research, informed refusal applied. Patients were informed about the study by the clinician/researcher and data from those who objected were not included. This study was conducted in accordance with the Declaration of Helsinki.

ST-CBT day-treatment

The treatment was intensive and combined schema therapy with CBT. For a description, see the extended version of this manuscript in the supplement.

Instruments

To assess severity of general psychopathology, the Symptom Questionnaire-48 (SQ-48) was used. In patients with a primary diagnosis of OCD, severity of OCD was assessed using the Yale Brown Obsessive-Compulsive Scale for Severity – Self-Report (Y-BOCS). To assess presence of EMSs, the Young Schema Questionnaire-2 (YSQ-2) was used. To assess presence of adaptive schema modes (*Happy Child* and *Healthy Adult*) and maladaptive schema modes (all other subscales), the Schema Mode Inventory (SMI) was used.

Statistical analysis

Results were analysed using the Statistical Package for Social Sciences (version 26). To evaluate the level of symptoms, EMSs and schema modes, one-sample t-tests were computed with norm data from the literature. To examine changes between pre- and post-treatment scores, paired samples t-tests were calculated. To determine reliable change and clinically significant recovery, Jacobson and Truax's method was used, see supplement for the critical values.

To examine correlations between pre- to post-treatment difference scores of general psychopathology, EMSs and schema modes, Spearman's correlations were computed. To examine whether the level of EMSs and schema modes at baseline was associated with treatment outcome, regression analyses of pre-treatment level of EMSs and schema modes on outcome of general psychopathology were performed, corrected for severity of pre-treatment general psychopathology.

Results

Sample characteristics

Twenty-seven patients were included in the sample. Most patients (89%) had comorbid mental disorders – mainly other anxiety, mood and personality disorders. Moreover, patients had followed 6.4 previous treatments on average. At admission, 63% of the patients were using psychotropic medication, predominantly SSRIs and SNRIs. The mean treatment duration was 36.8 weeks ($SD=11.2$) including 11.5 treatment hours per week.

The mean level of general psychopathology was significantly higher than a non-clinical population ($t(26)=19.9, p<0.01$) and also compared to a population of patients with clinical disorders ($t(26)=7.3, p<0.01$). Patients with a primary diagnosis of OCD had severe obsessive-compulsive symptoms (Y-BOCS $mean=27.3; n=4$). The level of EMSs was significantly higher than in a non-clinical population ($t(25)=7.9, p<0.01$) and not significantly different from in-patients with personality disorders ($t(25)=-0.8, p=0.42$), indicating severe dysfunctional patterns. The level of schema modes was significantly worse than non-patients (maladaptive: $t(26)=8.0, p<0.01$; adaptive: $t(26)=-11.9, p<0.01$) and patients with clinical disorders ($t(26)=2.8, p=0.01$; $t(26)=-4.2, p<0.01$) but not significantly different from patients with personality disorders ($t(26)=-2.0, p=0.06$; $t(26)=-0.2, p=0.84$), indicating that dysfunctional coping of problems and emotions was frequently used in contrast to healthy coping which was seldom used.

Treatment results

Table 1 presents the treatment results. General psychopathology, EMSs, maladaptive and adaptive schema modes all significantly improved. The severity of OCD improved with 45% from severe to mild symptoms. However, this effect was not significant, probably due to the small subsample. An improvement on the Y-BOCS of 35% and more is considered clinically relevant. A reliable improvement of general psychopathology was present in 74% of the patients. About a third of all patients had a clinically significant recovery.

Spearman's correlation between pre- to post-treatment difference scores of general psychopathology on the one hand and EMSs ($r_s=0.64$; $p<0.01$), maladaptive ($r_s=0.72$; $p<0.01$) and adaptive schema modes ($r_s=-0.80$; $p<0.01$) on the other hand were significant and high, indicating strong correlations between improvement of general psychopathology and improvement of EMSs, and schema modes.

Regression analyses showed that the levels of pre-treatment EMSs ($StB=0.19$; $p=0.42$), maladaptive ($StB=0.01$; $p=0.96$) and adaptive schema modes ($StB=-0.07$; $p=0.74$) did not predict post-treatment level of general psychopathology, corrected for pre-treatment level of general psychopathology.

Table 1. Treatment results

	Pre-treatment	Post-treatment	Paired samples t-test	Reliable improvement	Reliable deterioration	Clinically significant recovery
	Mean (SD)	Mean (SD)	t(df), p	n (%)	n (%)	n (%)
General psychopathology ^a (n=27)	78.6 (16.4)	52.4 (25.7)	5.0 (26), <0.01*	20 (74%)	1 (4%)	10 (37%)
Y-BOCS (n=4)	27.3 (10.1)	15.0 (5.7)	3.1 (3), 0.05			
Early maladaptive schemas ^b (n=26)	48.1 (11.2)	39.5 (11.2)	3.7 (25), <0.01*	14 (54%)	2 (8%)	9 (35%)
Maladaptive schema modes ^c (n=27)	33.9 (6.8)	29.2 (7.2)	3.0 (26), 0.01*	14 (52%)	3 (11%)	9 (33%)
Adaptive schema modes ^c (n=27)	6.5 (1.2)	7.8 (1.6)	-4.3 (26), <0.01*	16 (59%)	1 (4%)	10 (37%)

^a SQ-48 total score without work/study and vitality

^b Young Schema Questionnaire (YSQ-2)

^c Schema Mode Inventory (SMI)

* $p<0.05$

Discussion

General psychopathology improved significantly from pre- to post-treatment, as well as EMSs and schema modes. These results suggest that ST-CBT day-treatment is an effective treatment option in patients with chronic, treatment-resistant anxiety disorders and OCD with many psychiatric comorbidities. Our findings corroborate previous findings in patients with anxiety disorders and OCD treated with a similar day-care treatment (Peeters et al., 2021). More patients in our study were reliably improved and clinically significantly recovered compared with the previous findings (Peeters et al., 2021), possibly because our treatment was of longer duration: 37 weeks of 11.5 therapy hours per week compared with 26 weeks including 10.25 therapy hours, which would be congruent with previous findings that more sessions with schema therapy or CBT lead to better results. Another explanation for the difference from previous findings might be that the mean level of psychopathology before treatment in our sample ($Z=4.28$) was higher than that of Peeters et al. ($Z=3.02$), allowing for a greater reduction of symptoms.

Improvement of general psychopathology was strongly correlated to improvement of EMSs and schema modes in our study. This result is congruent with the hypothesis that treatment-resistance is caused by EMSs and schema modes. We may hypothesize that improved EMSs and schema modes allow for better compliance with CBT and thus may ameliorate anxiety and obsessive-compulsive symptoms resistant to CBT before. However, another interpretation of our result might be that both symptoms and EMSs/schema modes are independently improved by treatment and this is reflected in a correlation. Our result replicates a previous finding on schema modes with even stronger correlations (Peeters et al., 2021). Our finding contributes to an emerging field of research into the effectiveness of schema therapy in patients with treatment-resistant anxiety disorders and OCD.

Pre-treatment level of EMSs and schema modes did not predict outcome of symptoms, indicating that strong, pre-treatment EMSs and schema modes did not hinder improvement of symptoms in our sample of patients with anxiety disorders and OCD. Possibly, treatment of EMSs and schema modes contributed to this result. Congruent with this possible interpretation are two previous findings showing that outcome of CBT – without schema therapy – was worse for patients with OCD with strong EMSs (Sunde et al., 2019; Thiel et al., 2014). This finding, however, was not replicated in a study with patients with depression and anxiety disorders (Halford et al., 2002). While our findings do not demonstrate effectiveness of schema therapy, they suggest that ST-CBT day-treatment may be promising for patients

with treatment-resistant anxiety disorders and OCD. It might offer prospect of improvement and recovery even in the most vulnerable patients.

A strength of this study is that we had a naturalistic sample of patients with treatment-resistant anxiety disorders and OCD. Thus, our results are generalizable to this population. A limitation of our study is the lack of a control treatment. Consequently, it is not known whether ST-CBT day-treatment caused the outcome. In addition, as the treatment was examined as a package, it is not known which elements caused which result. Psychopharmacological treatment may have resulted in improvement as well. Also, it is not known whether ST-CBT day-treatment is superior to other treatments for treatment-resistant anxiety disorders and OCD, such as intensive exposure treatment. Last, diagnoses were clinician-based and personality disorders were not assessed.

To conclude, ST-CBT day-treatment is promising in patients with chronic, treatment-resistant anxiety disorders and OCD with many psychiatric comorbidities. Improvement of general psychopathology was strongly correlated to improvement of EMSs and schema modes, suggesting that treatment of EMSs and schema modes helps to reduce symptoms in these patients. Pre-treatment level of EMSs and schema modes did not predict outcome of symptoms, indicating that stronger EMSs and schema modes that were present before treatment did not hinder symptom improvement. Further controlled research is recommended to substantiate evidence for schema therapy in patients with treatment-resistant anxiety disorders and OCD.

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Supplement

Introduction

Anxiety disorders and obsessive-compulsive disorder (OCD) often run a chronic course (Bruce et al., 2005; Remmerswaal et al., 2020). After an evidence-based treatment including pharmacotherapy and cognitive behaviour therapy (CBT) almost half of the patients still fulfil the criteria of the index disorder and lack functional recovery (Penninx et al., 2011; Visser et al., 2014). When patients do not respond to these first-line treatments, guidelines recommend intensive treatment such as day-treatment (National Institute for Health and Care Excellence, 2014).

It is believed that dysfunctional personality traits account for treatment resistance in patients with anxiety disorders and OCD (Geluk Rouwhorst et al., 2022; Hovenkamp-Hermelink et al., 2021). More specifically, early maladaptive schemas (EMSs), and schema modes would result in persistence of symptoms (Young et al., 2003). EMSs are “patterns, developed during childhood or adolescence, consisting of memories, emotions, cognitions, and bodily sensations, regarding oneself and one’s relationship with others” as defined by Young (2003). Schema modes are the emotional states and coping responses arising when EMSs are activated. Indeed, research has provided some evidence that higher levels of EMSs significantly predicted poor response to CBT in patients with OCD (Sunde et al., 2019; Thiel et al., 2014), but this result was not confirmed in a study in patients with depression and anxiety disorders (Halford et al., 2002).

If treatment resistance is associated with EMSs then treating these schemas could help to reduce anxiety and obsessive-compulsive symptoms. One treatment targeting EMSs is schema therapy (ST). Schema therapy has been found to be effective in patients with personality disorders (Bamelis et al., 2014; Farrell et al., 2009; Giesen-Bloo et al., 2006; Taylor et al., 2017). Preliminary evidence exists for the effectiveness of schema therapy in mental disorders such as anxiety disorders, OCD, PTSD, chronic depression and eating disorders (Cockram et al., 2010; Malogiannis et al., 2014; Peeters et al., 2022; Simpson et al., 2010; Thiel et al., 2016). Further preliminary evidence comes from a recent pilot study showing that improvement of general psychopathology was correlated to improvement of schema modes in patients with anxiety disorders and OCD; however, EMSs were not measured in this study (Peeters et al., 2021).

To add to previous research, the aim of this exploratory study is to determine: 1) whether symptoms, EMSs and schema modes improve with ST-CBT day-treatment

in patients with anxiety disorders and OCD; 2) whether improvement in symptoms correlates with improvement in EMSs and schema modes; and 3) EMSs and schema modes at baseline is associated with improvement of symptoms. If no association appears, stronger pre-treatment EMSs and schema modes are not related to symptom improvement. This would be consistent with the hypothesis that treating EMSs and schema modes abolishes treatment resistance.

Methods

Participants

All patients who completed an intensive outpatient ST-CBT day-treatment between medio 2017 and 2020 were included in the study. To be eligible for the ST-CBT day-treatment, patients had to: 1) have completed at least one previous CBT targeting the primary anxiety disorder or OCD; and 2) use or actively refused psychotropic drugs; and 3) experience severe limitations in daily functioning due to the disorder. Patients with mental retardation or severe mental illness, such as psychosis and bipolar disorder, were not accepted for treatment. The diagnoses were determined by experienced clinicians at the clinical assessment and re-assessed every three months by evaluating the criteria of possible diagnoses, given the symptoms of the patients. Diagnoses were made in accordance with the Diagnostic and Statistical Manual, fifth edition (American Psychiatric Association, 2013).

Design

Data were collected as part of routine clinical care before and after treatment. Approval for this study was obtained by the research committee of GGZ inGeest (CWO-2020-013). Because the current study was file research, informed refusal applied. Patients were informed about the study by the clinician/researcher and data from those who objected were not included. This study was conducted in accordance with the Declaration of Helsinki.

ST-CBT day-treatment

The ST-CBT day-treatment was offered in an open group of up to eight patients with anxiety disorders or OCD. Treatment was intensive, consisting of 11.5 therapy hours per week on three days. The main treatment target was reduction of anxiety and obsessive-compulsive symptoms. Improvement of EMSs and schema modes were considered a secondary, facilitating aim. Experiential interventions such as chair work, roleplay, creative and body oriented exercises were offered for 5 hours per week, next to cognitive interventions (1.5 hours per week) and exposure in vivo with response prevention (5

hours per week). An individual case conceptualization conform schema theory was made in which avoidance from anxiety provoking situations, safety behaviour and compulsions were interpreted as dysfunctional coping modes (*Detached Protector* and *Detached Self-Soother*) and anxiety and obsessions were interpreted as *Vulnerable Child* mode. In addition, an individual exposure exercise list was composed. Patients were treated according to their individual case conceptualization and exposure list. Patients learned to enter anxiety provoking situations without performing safety behaviour or rituals while their *Healthy Adult* mode took good care of the needs of the *Vulnerable Child* mode. Treatment included the following integrated treatment components: schema therapy, drama therapy, art therapy, psychomotor therapy (all offering experiential interventions), exposure in vivo (therapist-guided and self-directed), and cognitive therapy. Schema and CBT jargon was used in each treatment component. In a weekly, joint meeting all therapists geared case conceptualizations, interventions and the therapeutic relationship to one another. In this meeting, improvement of anxiety and obsessive-compulsive symptoms was monitored. Treatment was continued until goals were met with a maximum treatment duration of one year. When a patient finished treatment, a new patient started in the vacant place. Due to Covid-19 measures, therapy was offered online from March 2020 to July 2020. From August 2020 to December 2020 half of the sessions was delivered online and half face-to-face. During treatment, psychotropic medication was optimized according to the multidisciplinary guidelines. Needed benzodiazepines were phased out as these may decrease the effectiveness of exposure in vivo. In addition, relatives were invited for one or two sessions with two therapists and the patient, consisting of psychoeducation about how to deal best with the anxiety and obsessive-compulsive symptoms of the patient in the context of the relationship. That is, not to accommodate (adapt) or antagonize (oppose) the symptoms of the patient. An in-company training lead by a registered schema therapist was provided to all therapists, some of whom additionally took schema therapy courses at training institutes in the Netherlands.

Instruments

To assess the severity of general psychopathology, the Symptom Questionnaire-48 (SQ-48) was used (Carlier et al., 2012; Carlier et al., 2017). It consists of 48 items that are answered on a 5-point Likert scale. A total score was calculated by adding the items of the psychopathology subscales without the Vitality and Work subscales, conform the manual. The thus obtained total score ranges from 0-148. The SQ-48 was found to be valid and reliable with good test-retest reliability and responsiveness to therapeutic change (Carlier et al., 2012; Carlier 2017). Reference data are available for non-patients and for an outpatient population referred for treatment for mood, anxiety or somatoform disorders (Carlier et al., 2012).

In patients with a primary diagnosis of OCD, severity of OCD was assessed using the Yale Brown Obsessive-Compulsive Scale for Severity – Self-Report (Y-BOCS) because presence and severity of obsessive-compulsive symptoms are not captured by the SQ-48 (Goodman et al., 1989a; Goodman et al., 1989b). The Y-BOCS consists of 10 items that are answered on a 5-point Likert scale and has a range of 0-40. The psychometric properties of the Y-BOCS are good and the questionnaire is sensitive to change (Goodman et al., 1989a; Goodman et al., 1989b; Steketee et al., 1996). There are no reference data available for the Y-BOCS. However, the total score can be interpreted with a worldwide accepted classification: a total score of 0-7 subclinical; 8-15 mild; 16-23 moderate severe; 24- 31 severe; 32-40 very severe.

To assess presence of EMSs, the Young Schema Questionnaire-2 (YSQ-2) was used (Rijkeboer et al., 2005; Rijkeboer & van den Bergh, 2006; Young et al., 2003). The YSQ-2 consists of 205 items that are answered on a 6-point Likert scale ranging from 'completely untrue' to 'describes me perfectly'. Sixteen subscale scores are calculated by summation of all scores divided by the number of items in the subscale concerned reflecting the presence of 16 EMSs. A total score was calculated by summation of all subscale scores. The Dutch translated YSQ-2 was found to be valid and reliable (Rijkeboer et al., 2005; Rijkeboer & van den Bergh, 2006). Norm data are available for a non-clinical population, and a clinical population receiving treatment for personality disorders (Rijkeboer & van den Bergh, 2006). Cronbach's alpha in the current sample was 0.982 (pre-treatment) and 0.986 (post-treatment).

To assess presence of schema modes, the Schema Mode Inventory (SMI) was used (Lobbestael et al., 2010; Young et al., 2007). The SMI consists of 118 items that are answered on a 6-point Likert scale ranging from 'never or almost never' to 'always'. Subscale scores are calculated by the mean of the items in the subscale concerned reflecting the presence of 14 schema modes. Next, two total scores are calculated by 1) summation of subscale scores of *Happy Child* and *Healthy Adult* modes (adaptive schema modes); and 2) summation of all other subscale scores (maladaptive schema modes). The Dutch translated SMI-2 is valid and reliable (Lobbestael et al., 2010). Norm data are available for non-patients, patients with clinical disorders such as anxiety, mood, and substance use disorders, and patients with personality disorders (Lobbestael et al., 2010). Cronbach's alpha in the current sample for adaptive schema modes was 0.828 (pre-treatment) and 0.930 (post-treatment) and for maladaptive schema modes 0.961 (pre-treatment) and 0.971 (post-treatment).

Statistical analysis

Results were analysed using the Statistical Package for Social Sciences (version 26) (IBM Corp., 2019). One case was missing on the YSQ and three on the Y-BOCS. Missing values were deleted listwise. There were no outliers.

To evaluate the level of symptoms, EMSs and maladaptive and adaptive schema modes, one-sample t-tests were computed with norm data from the literature (Carlier et al., 2012; Lobbestael et al., 2010; Rijkeboer & van den Bergh, 2006).

To examine changes between pre- and post-treatment scores, paired samples t-tests were calculated. To determine reliable change (SQ-48 decrease ≥ 12 points; YSQ total score decrease ≥ 3.7 ; SMI maladaptive total score decrease ≥ 3.3 ; SMI adaptive total score increase ≥ 0.7) and clinically significant recovery (reliable improvement and post-treatment scores of SQ-48 ≤ 45 ; YSQ ≤ 38.0 ; SMI maladaptive ≤ 27.8 ; SMI adaptive ≥ 7.8), Jacobson and Truax's method was used (Jacobson & Truax, 1991; Wise, 2004). Reliable change was computed with the reliable change index: $RCI = (X_{\text{pre-test}} - X_{\text{post-test}}) / SD_{\text{pre-test}} \sqrt{1 - r_{xx}}$. And the cut-off score for clinically significant recovery with: $c = ((SD_{\text{norm group}} * X_{\text{post-test}}) + (SD_{\text{post-test}} * X_{\text{norm group}})) / (SD_{\text{post-test}} + SD_{\text{norm group}})$ (Wise 2004).

Norm data (standard deviation and Cronbach's alpha of total scores) were calculated with published data and the correlation matrix of subscale scores (Carlier et al., 2012; Lobbestael et al., 2010; Rijkeboer & van den Bergh, 2006).

To examine correlations between pre- to post-treatment difference scores of general psychopathology, EMSs and schema modes, Spearman's correlation coefficients were computed. A power analysis performed beforehand showed that a sample size of 19 participants would be required to obtain correlations of 0.6 and larger beyond a significance level of $p < 0.05$ (two-tailed) with a probability of 80%. No correlation analyses were performed on the Y-BOCS because the subsample of OCD patients was too small. To examine whether the level of EMSs and schema modes at baseline was associated with treatment outcome, regression analyses of pre-treatment level of EMSs, and maladaptive and adaptive schema modes on outcome of general psychopathology were performed, corrected for severity of pre-treatment general psychopathology.

Results

Sample characteristics

Twenty-seven patients were included in the sample. Table 1 presents the baseline characteristics. Most patients (89%) had comorbid mental disorders – mainly other anxiety disorders, mood disorders and personality disorders. Moreover, patients had followed 6.4 previous treatments on average. At admission, 63% of the patients were using psychotropic medication, predominantly SSRIs and SNRIs. The mean treatment duration was 36.8 weeks ($SD=11.2$) including 11.5 hours of treatment per week.

Table 1. Baseline description of sample $n=27$

	<i>Mean (SD) or n (%)</i>
Sociodemographic characteristics	
Age, years	33.4 (7.9)
Gender, female	16 (59%)
Partner, yes	17 (63%)
Child(ren), yes	7 (26%)
Education	
Elementary school, lower vocational education	2 (7%)
General secondary education, secondary vocational education	6 (22%)
Higher professional education, university or university student	16 (59%)
Missing	3 (11%)
Working (paid job), yes	11 (41%)
Clinical characteristics	
Main diagnosis	
Obsessive-compulsive disorder	7 (26%)
Social phobia	6 (22%)
Generalised anxiety disorder	6 (22%)
Panic disorder with or without agoraphobia	5 (19%)
Emetophobia	1 (4%)
Anxiety disorder NOS	2 (7%)
Number of comorbid disorders	1.9 (1.1)
Duration of disorder, years	13.9 (10.5)
Psychotropic medication, yes	17 (63%)
Number of previous treatments	
Psychotherapy	4.1 (3.1)
Psychotropic medication	2.3 (2.1)
Duration of schema-focused day-treatment, number of treatment weeks, including 11.5 therapy hours per week	36.8 (11.2)

Table 2 presents the levels of general psychopathology, EMSs, maladaptive and adaptive schema modes in comparison to general and clinical populations. The mean level of general psychopathology was significantly higher than a non-clinical population and also compared to a population of patients with clinical disorders (Carlier et al., 2012). The severity of OCD symptoms of patients with a primary diagnosis of OCD was severe ($mean=27.3; n=4$) according to the Y-BOCS (Goodman et al., 1989a; Goodman et al., 1989b). The level of EMSs was significantly higher than in a non-clinical population and not significantly different from a population of patients with inpatient treatment for personality disorders (Rijkeboer & van den Bergh, 2006), indicating severe dysfunctional patterns. The level of schema modes was significantly worse than non-patients (maladaptive: $t(26)=8.0, p<0.01$; adaptive: $t(26)=-11.9, p<0.01$) and patients with clinical disorders ($t(26)=2.8, p=0.01$; $t(26)=-4.2, p<0.01$) but not significantly different from patients with personality disorders ($t(26)=-2.0, p=0.06$; $t(26)=-0.2, p=0.84$; Lobbestael et al., 2010). These results on schema modes indicate that dysfunctional coping of problems and emotions was frequently used in contrast to healthy coping which was seldom used.

Table 2. Pre-treatment general psychopathology, EMSs and maladaptive and adaptive schema modes and the comparison with norm groups with one sample t-tests.

	Our sample	Norm data of Non-patients Patients with clinical disorders Patients with personality disorders	One-sample t-test
	Mean	Mean	$t(df); p$
SQ-48 ^a	78.6	15.7 ^b	19.9 (26); <0.01*
		55.6 ^b	7.3 (26); <0.01*
		NA ^c	NA ^c
YSQ ^d	48.1	30.7 ^e	7.9 (25); <0.01*
		NA ^c	NA ^c
		49.9 ^e	-0.8 (25); 0.42
SMI maladaptive ^f	33.9	23.5 ^g	8.0 (26); <0.01*
		30.2 ^g	2.8 (26); 0.01*
		36.4 ^g	-2.0 (26); 0.06
SMI adaptive ^e	6.5	9.1 ^g	-11.9 (26); <0.01*
		7.4 ^g	-4.2 (26); <0.01*
		6.5 ^g	-0.2 (26); 0.84

^a SQ-48 total score without work/study and vitality

^b Norm data from Carlier et al., 2012

^c Not available

^d Young Schema Questionnaire-2

^e Norm data from Rijkeboer & van den Bergh, 2006

^f Schema Mode Inventory

^g Norm data from Lobbestael et al., 2010

The EMSs with the three highest scores were: *Unrelenting Standards* (mean=3.6; the belief that one has to meet very high standards of behaviour and performance), *Failure to Achieve* (mean=3.5; the belief that one is fundamentally inadequate or incompetent and will fail), and *Self-Sacrifice* (mean=3.5; the belief that the needs of others are more important than one's own). The maladaptive schema modes with the three highest scores were: *Demanding Parent* (mean=4.1; imposing high standards and strict rules), *Self-Soother* (mean=3.4; using a substance or behaviour that is numbing or soothing), and *Vulnerable Child* (mean=3.4; vulnerable feelings such as fear, sadness and loneliness) (Young et al., 2003).

Treatment results

Table 3 presents the results of the analyses of pre- to post-treatment change. General psychopathology, EMSs, maladaptive and adaptive schema modes all significantly improved. The severity of OCD improved with 45% from severe to mild symptoms. However, this effect was not significant, probably due to the small subsample. An improvement on the Y-BOCS of 35% and more is considered clinically relevant. A reliable improvement of general psychopathology was present in 74% of the patients, of EMSs in 54%, of maladaptive schema modes in 52%, and of adaptive schema modes in 59%. About a third of all patients had a clinically significant recovery.

Table 3. Treatment results

	Pre-treatment	Post-treatment	Paired samples t-test	Reliable improvement	Reliable deterioration	Clinically significant recovery
	Mean (SD)	Mean (SD)	t(df) p	n (%)	n (%)	n (%)
General psychopathology ^a (n=27)	78.6 (16.4)	52.4 (25.7)	5.0 (26) <0.01*	20 (74%)	1 (4%)	10 (37%)
Y-BOCS (n=4)	27.3 (10.1)	15.0 (5.7)	3.1 (3) 0.05			
Early maladaptive schemas ^b (n=26)	48.1 (11.2)	39.5 (11.2)	3.7 (25) <0.01*	14 (54%)	2 (8%)	9 (35%)
Maladaptive schema modes ^c (n=27)	33.9 (6.8)	29.2 (7.2)	3.0 (26) 0.01*	14 (52%)	3 (11%)	9 (33%)
Adaptive schema modes ^c (n=27)	6.5 (1.2)	7.8 (1.6)	-4.3 (26) <0.01*	16 (59%)	1 (4%)	10 (37%)

^a SQ-48 total score without work/study and vitality

^b Young Schema Questionnaire (YSQ-2)

^c Schema Mode Inventory (SMI)

Correlation between pre- to post-treatment difference scores

Spearman's correlation between pre- to post-treatment difference scores are presented in Table 4. All correlations are significant and high, indicating strong correlations between improvement of general psychopathology and improvement of EMSs, maladaptive and adaptive schema modes.

Regression analyses showed that the levels of pre-treatment EMSs ($StB=0.19$; $p=0.42$), maladaptive ($StB=0.01$; $p=0.96$) and adaptive schema modes ($StB=-0.07$; $p=0.74$) did not predict post-treatment level of general psychopathology, corrected for pre-treatment level of general psychopathology.

Table 4. Spearman's correlation between pre- to post-treatment difference scores

	Early Maladaptive Schemas ^a	Maladaptive Schema Modes ^b	Adaptive Schema Modes ^b
	<i>r</i>	<i>r</i>	<i>r</i>
	<i>n</i>	<i>n</i>	<i>n</i>
General psychopathology ^c	0.64 26	0.72 27	-0.80 27
Adaptive schema modes ^b	-0.57 26	-0.79 27	
Maladaptive schema modes ^b	0.79 26		

^a Young Schema Questionnaire (YSQ-2)

^b Schema Mode Inventory (SMI)

^c SQ-48 total score without work/study and vitality

* $p<0.01$

Discussion

Our sample with treatment-resistant patients with anxiety disorders and OCD had strong pervasive patterns of how they perceive and cope with oneself and others. The strongest present EMSs (*Unrelenting Standards*, *Failure to Achieve*, and *Self-Sacrifice*) and schema modes (*Demanding Parent*, *Self-Soother*, and *Vulnerable Child*) may reflect cluster C personality traits, such as perfectionism, rigidity, feelings of inadequacy and low self-esteem, and anxiety and obsessive-compulsive symptoms. Two of the three EMSs with the highest scores were also in the top three in previous studies in patients with anxiety disorders and OCD, namely *Unrelenting Standards* and *Self-Sacrifice* (Haaland et al., 2011; Henker et al., 2019; Kim et al., 2014; Kwak & Lee, 2015; Thiel et al., 2014; Voderholzer et al., 2013; Wilhelm et al., 2015; Yoosefi et al., 2016).

Strong levels of schema modes were reported in only one previous study, showing overlap of one schema mode with the current study on the three strongest present schema modes, namely *Demanding Parent* (Thiel et al., 2014). Overall, the EMSs and schema modes with the highest levels in our study suggest that patients experienced insufficient fulfilment of specific core emotional needs in childhood, namely expression of emotions, validation of emotions and needs, and autonomy. This might indicate that therapy for treatment-resistant patients with anxiety disorders and OCD should aim to repair these core emotional needs by encouraging autonomy and expression of emotions and needs and by validation of emotions.

General psychopathology improved significantly from pre- to post-treatment, as well as EMSs, and maladaptive and adaptive schema modes. These results may suggest that ST-CBT day-treatment is an effective treatment option in patients with chronic, treatment-resistant anxiety disorders and OCD with many psychiatric comorbidities. Our findings corroborate previous findings in patients with anxiety disorders and OCD who were treated with a similar day-care treatment (Peeters et al., 2021). More patients in our study were reliably improved and clinically significantly recovered on symptoms and schema modes compared to the previous findings (Peeters et al., 2021), possibly because our treatment was of longer duration: 37 weeks of 11.5 therapy hours per week compared to 26 weeks including 10.25 therapy hours per week, which would be congruent with previous findings that more sessions c.q. longer treatment with schema therapy or CBT leads to better results (Craske et al., 2006; Haby et al., 2006; Kool et al., submitted). Another explanation for the difference from previous findings might be that the mean level of psychopathology before treatment in our sample ($Z=4.28$) was higher than that of Peeters et al. ($Z=3.02$), allowing for a greater reduction of symptoms.

The current study showed that improvement of general psychopathology was strongly correlated to improvement of EMSs and schema modes. This result is congruent with the hypothesis that treatment-resistance is caused by EMSs and schema modes. We hypothesize that improved EMSs and schema modes allow for better compliance with CBT and thus may ameliorate anxiety and obsessive-compulsive symptoms resistant to CBT before. However, another interpretation of our result might be that both symptoms and EMSs/schema modes are independently improved by treatment and this is reflected in a correlation. Our result replicates a previous finding on schema modes with even stronger correlations (Peeters et al., 2021). Our finding that reduction of symptoms was strongly correlated to improvement of EMS and schema modes in patients with anxiety disorders and OCD, contributes to an emerging field of research into the effectiveness of schema therapy in patients with treatment-resistant anxiety disorders and OCD.

Pre-treatment level of EMSs and schema modes did not predict the outcome of symptoms, indicating that strong, pre-treatment EMSs and schema modes did not hinder improvement of symptoms in our sample of patients with anxiety disorders and OCD. Possibly, treatment of EMSs and schema modes contributed to this result. Congruent with this possible interpretation are two previous findings showing that outcome of CBT – without schema therapy – was worse for patients with OCD with strong EMSs (Sunde et al., 2019; Thiel et al., 2014). This finding, however, was not replicated in a study with patients with depression and anxiety disorders (Halford et al., 2002). While our findings do not demonstrate effectiveness of schema therapy, they suggest that ST-CBT day-treatment may be promising for patients with treatment-resistant anxiety disorders and OCD. It might offer prospect of improvement and recovery even in the most vulnerable patients.

A strength of this study is that we had a naturalistic sample of patients with treatment-resistant anxiety disorders and OCD. Thus, our results are generalizable to this population. A limitation of our study is the lack of a control treatment. Consequently, it is not known whether ST-CBT day-treatment caused the outcome. In addition, as the treatment was examined as a package, it is not known which elements caused which result. Psychopharmacological treatment may have resulted in improvement as well. Also, it is not known whether ST-CBT day-treatment is superior to other treatments for treatment-resistant anxiety disorders and OCD, such as intensive exposure treatment. Last, diagnoses were clinician-based and personality disorders were not assessed.

To conclude, ST-CBT day-treatment is promising in patients with chronic, treatment-resistant anxiety disorders and OCD with many psychiatric comorbidities. Improvement of general psychopathology was strongly correlated to improvement of EMSs and schema modes, suggesting that treatment of EMSs and schema modes helps to reduce symptoms in these patients. Pre-treatment level of EMSs and schema modes did not predict the outcome of symptoms, indicating that stronger EMSs and schema modes that were present before treatment did not hinder improvement of symptoms. Further controlled research is recommended to substantiate evidence for schema therapy in patients with treatment-resistant anxiety disorders and OCD, comparing the effectiveness of schema therapy with usual care and examining schema therapy with and without CBT. Furthermore, it is recommended to investigate the possible differential effects on EMSs and schema modes in subgroups of anxiety disorders and OCD.

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CHAPTER 11

Summary and General Discussion

For several decades, the treatment of anxiety disorders and OCD has consisted of CBT. Although this is an evidence-based treatment, many patients do not recover with it. The research presented in this thesis aimed to improve the outcome of OCD and anxiety disorders. A synopsis of each study's results is presented at the beginning of this chapter. The key findings will then be discussed in the context of the literature, followed by methodological considerations. Furthermore, implications for clinical practice and public health will be given. This chapter ends with recommendations for future research.

Summary of the main findings

In chapter 2 we examined predictors of course of anxiety and depressive disorders in the general population. Data were used from two waves of the Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2) including 509 respondents with a major depressive disorder or anxiety disorder (panic disorder, social phobia, agoraphobia or generalized anxiety disorder) at baseline. A chronic course of the index disorder – defined as presence of the index disorder during the subsequent three years - was predicted by a higher number of mental disorders and a higher neuroticism score at baseline. The AUC of this model was 0.68, which reflects a small predictive accuracy. The AUC increased to 0.75, a medium size predictive value, with poor overall course as outcome variable, defined as presence of any anxiety, depressive or substance use disorder during the subsequent three years. Now, poor course was predicted by a higher number of mental disorders, a higher neuroticism score, presence of childhood abuse, presence of parental psychopathology, and alcohol use at baseline. Our results support that transdiagnostic risk factors are important in predicting overall course of anxiety and depressive disorders while they cannot accurately predict chronic course of the index disorder. Lifestyle and physical health characteristics did not improve the prediction of course of the index disorder. Alcohol use, one of the included lifestyle indicators, improved the prediction of overall course, albeit modestly. Our results suggest that lifestyle and physical health indicators have little additional value in predicting course of anxiety and depressive disorders in the general population, over clinical and vulnerability characteristics.

Chapter 3 studied relationship satisfaction and quality of life of patients with OCD. Data were derived from The Netherlands Obsessive-Compulsive Disorder Association (NOODA). Patients with OCD with a partner, reported a moderate satisfaction with their relationship ($n=213$). They were significantly less satisfied when they had more severe comorbid depressive symptoms. If they perceived irritation from their partner or absence of their emotional support, relationship satisfaction was lower as well. OCD severity was not independently associated with relationship satisfaction. Our

results imply that not the severity of OCD itself affects the satisfaction of patients with their relationship but rather the extent to which patients feel supported with their symptoms. Quality of life of patients with OCD was poor ($n=353$). Those without a paid job and with more severe comorbid anxiety and depressive symptoms had a significantly poorer quality of life. In the multivariable analyses, severity of OCD was not associated with quality of life. Our findings indicate that paid employment and fewer comorbid anxiety and depressive symptoms contribute more to a better quality of life than fewer obsessive-compulsive symptoms.

In chapter 4, three waves (baseline, 2-year and 4-year follow-up) of the NOCDA study were used to examine the four-year course of quality of life and its association with course of OCD. Additionally, we identified patient characteristics that contributed to an unfavourable course of quality of life in respondents with a remitting OCD. Patients were divided in three groups depending on their course of OCD: those with chronic ($n=144$), intermittent ($n=22$) and remitting ($n=73$) OCD. The mean quality of life of the total sample was significantly lower than in the general population at all measurements. Apparently, OCD deteriorates the quality of life of patients considerably and chronically. Course of quality of life was associated with course of OCD: the quality of life of chronic patients was overall poorer than that of patients in the other groups. Moreover, quality of life of patients with remitting OCD improved significantly more than that of patients with chronic OCD from baseline to 2-year and 4-year follow-up. These results indicate that remission of OCD contributes to improvement of quality of life. However, even in patients with a remitted OCD, the quality of life remained below the community level. Moreover, the correlation between quality of life and severity of OCD was only moderate ($r=-0.40$), suggesting that other factors besides OCD impact on quality of life. Further analyses revealed that comorbid anxiety and depression symptoms are part of the other factors determining quality of life.

Chapter 5 identified patients with OCD who were at risk to start intensive treatment (day-treatment or inpatient treatment) in the subsequent two years. 6-year prospective longitudinal data of the NOCDA study were used ($n=419$). Patients were significantly more likely to start intensive treatment if they were single, had more severe comorbid depression, took psychotropic medication, and experienced a low quality of life. Severity of OCD was not associated with starting intensive treatment in the multivariable analyses. Our results suggest that despair and limitations in daily life as a result of OCD are more important reasons for an intensive treatment than having severe obsessive-compulsive symptoms per se.

Chapter 6 described a pilot study of a brief dyadic family intervention for patients with OCD and a family member. This intervention focused how relatives could cope best with OCD in the context of the relationship without accommodating or antagonizing obsessive-compulsive symptoms. Sixteen patients with OCD and a family member were treated for five sessions, next to CBT for OCD. Patients had received 2.8 previous treatments for OCD on average with insufficient result. In patients, obsessive-compulsive symptoms significantly decreased; eight patients improved reliably. Of these, six could be judged as recovered. Antagonism, functioning and atmosphere at home did not change significantly according to patient-ratings. Possibly, more sessions are needed to change antagonism, allowing extra time and support. In family members, accommodation, social functioning and atmosphere at home significantly improved. Dropout was high: six couples dropped-out because of a relationship breakup, no show and lack of motivation to change. The high dropout rate might be explained by the impression of therapists that breaking with long-term patterns concerning OCD was difficult and triggered much fear in patients as well as family members. In patients, extra fear was triggered by starting exposure exercises and the family intervention at the same time. Therefore, the start of the family intervention may be better postponed until a few weeks after starting CBT. Family members feared for the patient's emotions if they stopped accommodating and antagonizing the obsessive-compulsive symptoms. In addition, dropout might be prevented by providing more detailed information beforehand about the treatment and by paying more attention to motivation and support during treatment. Both patients and family members were satisfied with the family intervention. They felt acknowledged and supported and appreciated getting advice on how to deal best with the OCD. Our results suggest that family involvement is effective and worth investigating further.

Chapter 7 investigated how family members were affected by the patient's OCD and whether the brief family intervention relieved the impact. Data from the pilot study of chapter 6 ($n=16$) were used. Living with a patient with OCD burdened relatives considerably, even in our sample of family members with a quality of life comparable to that of the general population. Family members were worried about the patient, experienced tension in the relationship with the patient and urged the patient for instance to self-care or to employ activities. Family members also accommodated and antagonized the OCD symptoms substantially. When accommodation and antagonism were more severe, relatives experienced significantly more burden. The family burden was diminished after our brief family intervention and was correlated to a decrease in accommodation. Also, relatives activated and motivated the patient significantly less often after treatment, suggesting a more adequate interaction with

the patient. These results indicate that learning how to deal best with OCD relieves the burden of family members of patients with OCD.

Chapter 8 explored a short, intensive exposure treatment at home in patients with OCD who did not respond to regular CBT. We treated 21 patients with this 6-day-treatment. Obsessive-compulsive symptoms, comorbid anxiety and depression symptoms, and quality of life were significantly decreased after treatment, as was accommodating behaviour of family members. 91% of the patients achieved a reliable improvement, while 67% met the criteria for recovery. Results were largely, but not completely preserved at 3-month follow-up. Thus, patients who had not previously benefited from regular CBT, did so after receiving a short, intensive exposure at home. There was only one dropout and both patients and their family members were satisfied with treatment, indicating good feasibility. The response after only two treatment days was associated with a better post-treatment outcome, but not with outcome at 3-month follow-up. The short, intensive exposure treatment may be effective and feasible and needs further investigation with a controlled design.

In chapter 9 it was meta-analysed whether a short, intensive scheduling of CBT sessions is superior to a regular scheduling in patients with anxiety disorders and OCD. Two randomised controlled trials (RCTs) and four non-RCTs were included, pertaining to 393 patients. Short intensive CBT did not statistically differ from regular CBT in reducing anxiety or obsessive-compulsive symptoms from pre- to post-treatment and from post-treatment to follow-up. However, results were obtained faster in the short intensive format due to its shorter lead time. In addition, short intensive CBT was significantly better in reducing depressive symptoms from pre- to post-treatment and this effect persisted at follow-up. Dropout was only reported in two studies and could thus not be meta-analysed. The number and quality of the included studies was limited. Further high-quality research is needed to examine the effectiveness of intensive scheduling of CBT sessions.

In chapter 10 we explored an innovative day-treatment with schema therapy (ST), CBT and creative therapy in an uncontrolled pilot study. 27 patients with treatment-resistant anxiety disorders or OCD were treated with this ST-CBT day-treatment. General psychopathology, early maladaptive schemas (EMSs) and schema modes were significantly improved after treatment. A reliable improvement of general psychopathology was present in 74% of the patients and about a third was recovered. The pre- to post-treatment difference scores of general psychopathology, EMSs and schema modes were significantly and highly correlated, indicating strong interdependence between improvement of general psychopathology and

improvement of EMSs and schema modes. Pre-treatment EMSs and schema modes did not predict outcome of general psychopathology, suggesting that strong dysfunctional patterns and coping did not hinder improvement of symptoms. Our results contribute to an emerging field of research into the effectiveness of schema therapy in patients with treatment-resistant anxiety disorders and OCD.

How this fits in the literature

The predictors of chronic overall course of anxiety and depressive disorders have been studied little before. Most of the identified determinants in chapter 2 (higher number of mental disorders, higher neuroticism, childhood abuse, parental psychopathology and higher alcohol use) corroborated previous preliminary findings of chronic overall course of anxiety and depressive disorders in general and mixed populations (Bokma et al., 2022; Henriksen et al., 2015; Rhebergen et al., 2011; Verhoeven et al., 2020). A chronic course of the index disorder was predicted by baseline number of mental disorders and neuroticism, which is consistent with prior meta-analytic results for depression in general and clinical populations, while a previous meta-analysis in anxiety disorders showed mixed results (Hölzel et al., 2011; Hovenkamp-Hermelink et al., 2021). Congruent with previous preliminary studies, our results indicate that lifestyle and physical health indicators have little value in predicting course of anxiety and depressive disorders (Bokma et al., 2019; Bosman et al., 2020; Verhoeven et al., 2020).

In chapter 3, we found that patients with OCD less often have a partner than people in the community, which corroborated previous research (Koran, 2000). At the moment of our study, the impact of OCD on partner-relationships and how patients with OCD experience their relationship, was not known. Our study revealed that patients with a partner-relationship are moderately satisfied with it. Patients are less satisfied when they have more severe comorbid depressive symptoms and when they perceive irritation and a lack of emotional support in their partner. Our results corroborated earlier findings in patients with other mental disorders, namely anxiety and depressive disorders (Denton et al., 2003; Zaider et al., 2010). Our results were confirmed in later studies in patients with OCD (Kasalova et al., 2020), indicating that OCD damages relationships and that according to patients their partners do not give them enough support.

Our results in chapter 3 and 4 supported previous findings on quality of life in patients with OCD: 1) the quality of life of patients with OCD is poor (Coluccia et al., 2016; Pozza et al., 2018); 2) when OCD improves by treatment, the quality of life improves as well, but remains substantially lower than in the general population (Asnaani et al., 2017; Hertenstein et al., 2013; Huppert et al., 2009; Subramaniam

et al., 2013); 3) the quality of life of patients with OCD is poorer when they have more severe comorbid anxiety and depression symptoms (Fontenelle et al., 2010; Hertenstein et al., 2013; Huppert et al., 2009; Subramaniam et al., 2013; Velloso et al., 2018); and 4) unemployed patients with OCD have a poorer quality of life (Fontenelle et al., 2010; Rodriguez-Salgado et al., 2006; Stengler-Wenzke et al., 2007). Results show that quality of life does not restore automatically when obsessive-compulsive symptoms improve. Treatment for OCD should therefore not be limited to symptom recovery but should also focus on recovery of quality of life, which may include (volunteer) work, meaningful activities, contact with family, social relationships and a satisfactory partner-relationship.

Chapter 5 is the first study on predictors of intensive treatment - such as day-treatment or inpatient treatment - in patients with OCD. Those who are single, have more severe comorbid depressive symptoms, have a low quality of life, and use psychotropic medication, were significantly more likely to end up in intensive treatment in the subsequent two years. Our results corroborated previous findings in other populations, such as patients with mood and psychotic disorders (Donisi et al., 2016; Han et al., 2020; Tan et al., 2022). However, a difference is that use of psychotropic medication predicted future intensive treatment in patients with OCD while in other patient groups not taking medication predicted admission (Donisi et al., 2016; Robinson et al., 2019). This discrepancy probably reflects the different symptoms that can arise in more severe forms of the various disorders.

At the time we conducted the studies in chapter 6 and 7, research was examining the best way to involve family members in the treatment of OCD. For example, by participating in all or some of the patient's sessions, with an individual, or group format and with what type of instructions. Our brief family intervention was delivered in a dyadic format, consisted of five sessions, and was added to CBT of the patient. Results suggested effectiveness and feasibility of this format. A later published meta-analysis showed that family involvement is generally effective, irrespective of the specific format (Stewart et al., 2020). Antagonism was not significantly improved in our pilot study, contrasting results of the later published meta-analysis (Stewart et al., 2020). It might be that we offered too few sessions to stop antagonism. However, surprisingly, greater improvements in antagonism have been found when patients received fewer treatment sessions (Stewart et al., 2020). This unexpected result can probably be explained by confounding by indication: patients with more persistent antagonism need more sessions. Another possible explanation for the persistence of antagonism in our study is that it is a symptom of severe OCD. In the specialized mental health care institution where the current study occurred, patients often have severe and chronic symptoms.

Our finding in chapter 7 that family members experienced considerable burden from the OCD of the patient is congruent with previous results (Cicek et al., 2013; Torres et al., 2012). Family burden was significantly worse when family members accommodated and antagonised the obsessive-compulsive symptoms of the patient more severely which corroborated earlier findings (Amir et al., 2000; Cherian et al., 2014). Surprisingly, little attention was given in the literature to whether family burden improves with family interventions. Our pilot study showed that family burden significantly improved after the brief family intervention. Improvement of family burden was significantly correlated to improvement of accommodation. Both results are consistent with later studies (Stewart et al., 2020). Results indicate that family members are burdened by the OCD of the patient and that their burden decreases when relatives learn how to deal best with the OCD of the patient.

In the last decades, a renewed interest has arisen in short, intensive exposure with response prevention (ERP) for patients with OCD. Advantages of this treatment are faster results and better accessibility to treatment for patients who are not able to attend weekly sessions due to for example work, caregiving or living far from the treatment centre. Previous and more recent studies have suggested effectiveness and feasibility of short, intensive formats (Bevan et al., 2010; Dèttore et al., 2013; Havnen et al., 2017; Pittig et al., 2021). However, our study was the first performed in patients with OCD who did not respond to regular CBT, and showed that short, intensive exposure is also feasible and effective in these patients. In chapter 8 we found that during the short, intensive treatment, which also included family interventions, obsessive-compulsive symptoms, and comorbid anxiety and depression symptoms ameliorated, while accommodation of family members significantly decreased. Results suggested that differential patterns of response to treatment were present, namely a rapid and a slow response pattern. In OCD, response patterns have been studied before, especially sudden gains – defined as a large, rapid and stable decrease in symptoms during treatment – with mixed results, leaving unclear the importance of sudden gains in the treatment of OCD (Aderka et al., 2012; Buchholz et al., 2019; Collins & Coles, 2017).

Chapter 9 contributes to evidence for the effectiveness of short, intensive exposure treatment through a meta-analysis. Reduction of anxiety and obsessive-compulsive symptoms in short intensive CBT did not statistically differ from regular CBT in patients with anxiety disorders and OCD. Results were obtained faster in the intensive schedule, due to its shorter lead time. As the effectiveness of regular CBT in these disorders is already well-established, our result strengthens the evidence that intensive CBT is effective in treating patients with anxiety disorders and OCD. This

finding is in line with a previous meta-analysis in children with anxiety disorders (Öst & Ollendick, 2017), but in contrast to a meta-analysis in youth and adults with OCD in which intensive CBT was more effective at post-treatment (Jónsson et al., 2015). However, in this latter study, at 3-month follow-up intensive CBT was no longer superior to regular CBT (Jónsson et al., 2015). Intensive CBT may be superior in the acquisition of non-threat associations, and in extinction of fear by repetition of non-threat associations, while it may be inferior in memory (re)consolidation, i.e. forming multiple connections of non-threat associations within the memory network, which occurs mainly in real life. When comparing intensive CBT with weekly CBT, the short-term advantages of the former format might be outweighed by the medium-term advantages of the latter format, leaving none of them superior at follow-up. A further important finding was that short intensive CBT was significantly better in reducing depressive symptoms. This is congruent with a previous finding that patients with depression receiving twice weekly sessions showed a greater reduction of depressive symptoms than patients receiving weekly sessions (Bruijnicks et al., 2020). Possibly, the fast reduction of symptoms in an intensive treatment generates hope and a sense of self-competence, which subsequently reduces the experience of low mood or depression.

Schema therapy (ST) has been found to be effective in patients with personality disorders (Bamelis et al., 2014; Farrell et al., 2009; Giesen-Bloo et al., 2006; Taylor et al., 2017). In mental disorders, preliminary evidence for schema therapy is appearing (Peeters et al., 2022). The pilot study in chapter 10 adds to evidence for schema therapy in patients with treatment-resistant anxiety disorders and OCD. ST-CBT day-treatment reduced general psychopathology. Furthermore, the improvement of psychiatric symptoms was significantly correlated to improvement of early maladaptive schemas (EMSs) and schema modes. Our results are in line with a previous study (Peeters et al., 2021). Pre-treatment EMSs and schema modes did not predict outcome of symptoms, indicating that strong, dysfunctional pre-treatment patterns and coping did not hinder improvement of symptoms. Possibly, treatment of EMSs and schema modes contributed to this result. Congruent with this possible interpretation are two previous findings showing that outcome of CBT – without schema therapy – was worse for patients with OCD with strong EMSs (Sunde et al., 2019; Thiel et al., 2014). These findings, however, were not replicated in a study with patients with depression and anxiety disorders (Halford et al., 2002). Our results are in line with the hypotheses that treatment-resistance is caused by EMSs and schema modes and that treatment of EMSs and schema modes enables improvement of symptoms.

Methodological considerations

Study designs

In this thesis, several study designs have been used. Every design has pros and cons which will be discussed in this paragraph.

We used uncontrolled pilot studies to explore innovative treatments (brief family intervention; short, intensive exposure treatment; ST-CBT day-treatment; chapters 6, 7, 8, and 10). Pilot studies are small, exploratory studies aiming to “test the feasibility of methods and procedures and to search for possible effects” (Everitt, 2006). They are conducted prior to randomized controlled trials (RCTs) which are large-scale studies, aiming to demonstrate the effectiveness of an intervention. As RCTs cost much time and resources, pilot studies are conducted as first step. In addition, it is not ethical to investigate an intervention in a controlled design, when not found effective in an uncontrolled study. The results from a pilot thus do not demonstrate the effectiveness of the studied interventions but instead give an impression of feasibility and possible effects.

A cross-sectional study design was used to examine which OCD patients have a poor quality of life and a low relationship satisfaction (chapter 3). In a cross-sectional study, a group of people is measured at a single point in time. This design can be used to investigate whether there is an association between an outcome measure of interest and several characteristics. The nature of the association cannot be established in this type of study, or more specifically, whether it is a causal association, what the direction of a causal connection is, and whether an association is caused by another shared source. Therefore, it cannot be concluded that treatment of the significant determinants of our study would actually improve quality of life and relationship satisfaction.

We used a longitudinal study design to examine 1) trends that are associated with a chronic course of anxiety and depressive disorders in the general population (chapter 2); 2) course of quality of life in patients with OCD (chapter 4); and 3) characteristics of patients with OCD starting with intensive treatment (chapter 5). In a longitudinal study design, a group of people is measured several times. This design examines trends that are associated with a relevant outcome measure. The trends precede change in the outcome measure, which is an important but not sufficient condition for causality. Criteria for establishing a causal connection are described in the Hill's criteria, dating from 1965, and specifically formulated for the link between a pathogen and disease (Hill, 1965). Other examples of these criteria are dose-response relationship (exposure to an increasing amount of pathogen leads to an increased incidence of disease) and plausibility (the association can be explained by a plausible theory or mechanism).

A meta-analysis was used to study whether a short, intensive scheduling of CBT sessions is superior to a regular scheduling of sessions (chapter 9). With this study design, results of several studies are combined which increases the number of participants and the statistical power. Thus, a better estimate of the effect can be obtained. However, the quality of this kind of research depends on the quality of the studies that it is based on ('garbage in, garbage out'). The quality of the studies that made up the meta-analysis of this thesis, was limited. Therefore, results should be interpreted with caution.

Patient samples used in the present thesis

The study in chapter 2 used data from baseline and 3-year follow-up of the Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2). This psychiatric epidemiological cohort study of the Dutch general population aged 18-64 is a large, representative Dutch sample, including 6,646 participants. Mental disorders were assessed with a valid, standardized instrument (Composite International Diagnostic Interview). The NEMESIS-2 sample has a non-response of 34.9% of all people who have been requested to participate. However, to correct for different response rates in different population groups, a weighing factor was applied. After correction, the demographic characteristics of the sample matched those of the general population. Furthermore, NEMESIS-2 has an attrition rate of 20% at 3-year follow-up. Attrition occurred significantly more often in respondents who were younger, had less education, no paid job and who were not born in the Netherlands but was not related to any mental disorder under study (De Graaf et al., 2012). To conclude, NEMESIS-2 is a valid and reliable database with which psychiatric epidemiology in the Dutch general population can be studied. An sample from the general population contains a wide variation, for example in the severity of mental disorders, which is an advantage.

For the studies described in chapter 3, 4 and 5 data from baseline, 2-year, 4-year, and 6-year follow-up of the Netherlands Obsessive-Compulsive Disorder Association (NOCDA) were used. NOCDA is a naturalistic cohort study designed to examine determinants of chronicity in a clinical sample. Strength of NOCDA is the large, representative sample ($n=419$) of treatment-seeking patients with lifetime OCD who were followed for a long time. Furthermore, a broad range of putative risk factors were measured. The sample was recruited from patients who were referred for treatment to mental health care centres specialized in OCD. Therefore, chronic and severe cases may be overrepresented. Of all patients who received an intake in one of the affiliated institutions, 39.1% did not give informed consent and refused to participate in the NOCDA study (Schuermans et al., 2012). Refusers did not differ

significantly from participants on sex, age and education (Schuurmans et al., 2012). However, whether they differed on clinical characteristics is unknown because these data were unavailable for refusers. The NOCDA sample, however, roughly resembles other large, clinically referred OCD samples from Europe and the United States on demographic and clinical characteristics, suggesting its representativeness (Schuurmans et al., 2012). In addition, NOCDA has an attrition rate of 35.1% over the course of 6 years. Attrition occurred significantly more in those with less education (du Mortier et al., 2021), suggesting that results of follow-up measurements are less generalizable to patients with lower educational level. To conclude, NOCDA is a suitable database for studying determinants of chronicity in OCD.

Measurements and definitions used in the present thesis

We used standardized clinical interviews and questionnaires with good reliability and validity. As with all retrospective measurements, they carry a risk of state-dependent bias or general recall bias, especially with measurements covering a longer period of time. In addition, in longitudinal designs, retesting a participant is prone to test artefacts such as practice of the participant and interrater differences. However, instruments can be robust to retesting artefacts, expressed in the test-retest reliability and interrater reliability. Although these psychometric properties are not known for all instruments, the test-retest reliability is good for the EQ-5D, and the Y-BOCS and SCID-I also have good interrater reliability.

In chapter 3 and 4 quality of life was assessed with the EuroQol five-dimensional questionnaire (EQ-5D). The EQ-5D contains five dimensions significant for QoL: mobility, self-care, daily activities, pain/discomfort, and depression/anxiety. Ratings of each dimension are converted into an index score – the EQ-5D – reflecting the generic overall quality of life. A limitation of the EQ-5D is that it lacks environmental and spiritual aspects of quality of life. These are part of quality of life according to the definition of the WHO, besides physical health, psychological health, level of independence, and social relationships. Nevertheless, the EQ-5D is frequently used and regarded a valid and reliable instrument to assess quality of life.

Problematic is the overlap of quality of life with two predictors from our studies, being ‘comorbid anxiety’ and ‘comorbid depression’, as the level of anxiety and/or depression is a dimension of quality of life on the EQ-5D. In addition, quality of life overlaps with the diagnosis of OCD because both concepts include impairment of daily functioning. These overlaps are present in the following results in this thesis: 1) in patients with OCD and with remitting OCD, quality of life is lower with more severe comorbid anxiety and depression, and 2) quality of life is lower in patients

with chronic OCD compared to individuals with remitting OCD. However, a certain amount of overlap between anxiety/depression and quality of life is unsurprising as psychological health is an important aspect of quality of life. Likewise, overlap between OCD and quality of life is inevitable because poor functioning is important in both concepts. Moreover, the concepts of quality of life, comorbid anxiety and depressive symptoms, and OCD differ considerably. For all these reasons, despite the limitations, our results are informative and relevant.

Implications for clinical practice and public health

Despite evidence-based treatments, anxiety disorders and OCD often run a chronic course. Anxiety and obsessive-compulsive symptoms interfere with daily functioning and quality of life. Many patients are limited in pursuing their personal goals in life for a long time. With the use of the results of this thesis, outcome of anxiety disorders and OCD can be improved.

First, we aimed to identify people with anxiety disorders or major depressive disorder in the general population at risk of a chronic course. Chronic course was mainly predicted by clinical and vulnerability characteristics. More specifically, people with whom the disorder is accompanied by other mental disorders, higher neuroticism, childhood abuse, parental psychopathology and more alcohol use were at risk of a chronic course. These people should be informed about the high risk to relapse or to develop another mental disorder even after remission of the index disorder by, for example, mental health literacy interventions by the government, health professionals and patient organisations. In addition, people at high risk should be encouraged to seek help. Our results further suggest that mental health may be enhanced by adopting a broader perspective on mental disorders, including focus on comorbid mental disorders and aetiological or vulnerability factors, such as childhood abuse, dysfunctional personality characteristics and dysfunctional coping.

Furthermore, our studies have shown that remission of obsessive-compulsive symptoms is not sufficient for restoring relationship satisfaction and quality of life. This is in contrast with previous views that patients would be able to resume their lives when the OCD is remitted. So, it is important to take a new, broader view on recovery. Therapists therefore should make sure that they address quality of life and relationship satisfaction as separate goals in treatment besides reduction of obsessive-compulsive symptoms. This might be done with treating of comorbid anxiety and depressive symptoms, and encouraging patients to resume their lives with for instance meaningful relationships, activities and (volunteer) work. The latter intervention may encounter difficulties with patients. In our clinical

experience, patients tend to postpone (volunteer) work, social and/or love life based on the idea that it is better to enter society when the psychiatric symptoms have disappeared. However, this conviction of patients may reinforce the notion of being disabled, which drives patients further away from recovery. Therapists can help patients by explaining and motivating why it is better to find their way in life with (residual) symptoms. This may increase the quality of life and satisfaction with their relationship and may also prevent intensive treatment.

OCD affects those living with the patient as well. Family members experience considerable burden, consisting of worrying about the patient, tension in the relationship with the patient, and urging the patient. Therefore, therapists should involve family members in treatment to learn them dealing best with the OCD of the patient. Therapists should educate family members not to accommodate or antagonize the obsessive-compulsive symptoms of the patient. In addition, couples therapy focusing on dealing with irritability and offering emotional support without accommodating or antagonizing the OCD may decrease the family burden and improve the relationship. Involving family in treatment is often omitted, which is regrettable because it may help to improve obsessive-compulsive symptoms of the patient as well.

This thesis has explored several innovative treatments. Awaiting controlled evidence for their effectiveness, therapists may consider these treatments when patients do not benefit from evidence based treatments such as CBT and serotonergic antidepressants. If patients are not recovered after sufficient sessions, therapists can follow two treatment strategies: 1) extending the treatment at hand, or 2) switch to another treatment. Support has been found for both strategies, however, research does not show when best to follow which strategy. Meanwhile, therapists should work with patients to assess the reasons for non-response and base their decision on further treatment accordingly, taking into account the patient's preferences. Non-response may for example be due to clinical characteristics of the disorder, psychiatric and medical comorbidity, stressors, childhood abuse, and noncompliance (Bystritsky, 2006). In the event that patients do respond to the treatment but have not yet recovered, extending treatment is a logical choice. In other cases, change of treatment is indicated. The following innovative treatments from this thesis may be considered: the brief family intervention added to CBT may be effective in patients with OCD who have family members accommodating and/or antagonizing the obsessive-compulsive symptoms; and a short, intensive scheduling of CBT sessions may be effective in patients with OCD, panic disorder and agoraphobia who avoid many situations. In addition, intensive treatment such as the ST-CBT

day-treatment may be considered for patients with chronic, treatment-resistant anxiety disorders and OCD with comorbid clinical and personality disorders, and a low quality of life. The characteristics of patients ending up in intensive treatment may impede treatment of the index disorder, but can be adequately addressed in the intensive treatment. For example, passivity, demoralization, fatigue, and a limited ability to concentrate or socialize, make it more difficult to commit to therapy. All the more so because many patients lack a partner or a social network that can support and motivate them. In the treatment ward, the team of therapists and fellow patients can offer support and hope, and guide with activation and socializing until patients function better and are able to get support in their own environment. Finally, a recovery approach may be considered as well, which places less emphasis on remission of anxiety and obsessive-compulsive symptoms and more emphasis on improvement of quality of life. For instance, with Acceptance and Commitment Therapy (ACT), in which patients learn to accept negative feelings and symptoms while moving towards personal, meaningful goals in life. This approach may be considered for patients in whom no significant further improvement is expected from treatment of the psychiatric symptoms.

Suggestions for future research

Up to date we are insufficiently able to accurately predict which patients are at risk of a poor course. This is a major gap in current knowledge. With precise prediction models, we would be able to allocate the limited financial resources available for mental health care to those who need it the most. Thus, public health would then be fostered the best possible way. In addition, the predictors making up these prediction models may indicate how best to help people so that a poor course is prevented. Anxiety disorders may become temporary episodes, not chronic life-disrupting conditions, that people can put behind them at some point.

Future research should examine the best way to predict a poor course of anxiety disorders and OCD. It is recommended to mention the predictive accuracy in studies on prediction models, such as the area under the curve (AUC) or the c statistic. This draws attention to the predictive capability of models and will invite researchers to enhance it. It is best to use broad outcome measures in which presence of other disorders in addition to the index disorder are included, because they reflect the nature of mental disorders best. To study broad outcome, future research should use measuring instruments to general psychopathology.

Furthermore, research should focus on the choice of predictors. Up to date, clinical characteristics predict a poor course of the index disorder best. However, with

broad outcome measures transdiagnostic predictors might perform better, such as personality traits, and social and vulnerability characteristics. Our results support that transdiagnostic risk factors are important in predicting overall course of anxiety and depressive disorders, while they cannot accurately predict chronic course of the index disorder. This result needs to be replicated in other studies and samples.

Our result implies that the worldwide used classification system for mental disorders – the Diagnostic and Statistical Manual of Mental Disorders (DSM) – falls short as it describes delineated disorders while ignoring the frequent occurrence of comorbidity and the probable common aetiology with the index disorder. To overcome these shortcomings of the DSM, it is recommended to develop new systems that classify symptoms according to their underlying aetiology. For example, the subdivision of disorders in internalizing and externalizing disorders, described in the introduction of this thesis.

Currently, it is not known exactly what the causes of mental disorders are. Widely used is the biopsychosocial model of mental health (Engel, 1977), stating that mental health conditions develop not due to a single cause but by interaction of several biological, psychological, and socio-environmental factors. For example, genetic vulnerabilities, neurochemistry, physical health, temperament, self-esteem, social and coping skills, family relations, social network, and socioeconomic circumstances. Because it is infeasible to construct a prediction models with all possible predictors, science should strive to construct a model with factors relevant to clinical practice that predicts as accurately as possible.

Future research should also examine effectiveness of treatments. Clinical practice will become more efficient and more professional when several evidence-based treatments are available in addition to a decision tool indicating which treatment is offered best to which patient. This is also known as personalized medicine. Due to lacking knowledge, personalized medicine is not yet available. In the meantime, it is recommended to using measurement-based care as this optimizes treatment outcome (Duncan et al., 2021; Guo et al., 2015). In measurement-based care, patient data that are collected frequently during treatment, guide clinical decision making. In addition, it is advisable to follow multidisciplinary guidelines as this improves outcome compared to treatment as usual (van Dijk, 2014).

As the importance of quality of life is stressed in this thesis, it is highly recommended to include a quality of life outcome measure in future research as this is an important aspect of recovery. Patients place even more importance on quality of life than on

reduction of symptoms which may influence the choice of treatment. Therefore, information about the effect of treatments on quality of life should be included in the future treatment decision tool. In addition, it is recommended to explore treatments aiming to improve quality of life. For instance with a pilot study to quality of life enhancing interventions such as rehabilitation, expanding the social network, and expanding pleasurable and meaningful activities.

We explored three innovative treatments in this thesis: 1) a brief family intervention; 2) a short, intensive exposure treatment at home; and 3) ST-CBT day-treatment. The tentative results of these pilot studies suggested feasibility and positive effects of these treatments. In future research, effectiveness needs to be demonstrated in randomized controlled trials (RCT). If family interventions are offered, they are added to the CBT of the patient, and as the effectiveness of CBT already has been established, an additional effect of the family intervention besides the effect of CBT needs to be demonstrated. A design with two arms, each with the same number and length of sessions, one arm including family interventions, and the other not, could prove superior effectiveness of adding family interventions. A non-inferiority design can also be chosen, with which it can be demonstrated that a new treatment is not less effective than the standard therapy. However, both designs need a large amount of participants ($n=788$ and $n=620$ respectively) to be able to demonstrate an effect with statistical significance. For such a large study, a consortium of multiple treatment centres is required. A consortium could be established through existing partnerships such as TOP-GGZ and NedKAD. Evidence for additional effects may also be gathered with other research designs, such as a multiple case series design and a meta-analysis. Meta-analyses benefit if researchers practice uniformity in the use of instruments, so that results are easier to combine.

To conclude, this thesis has argued that to improve mental health, we need to take a broader view. A broader view of mental disorders that takes into account the common aetiology of the index and comorbid mental disorders. A broader view in treatment, so that clinicians not only treat the index disorder, but also include comorbid symptoms, the social environment, and aetiological factors, such as dysfunctional personality traits. Last, a broader view on recovery which includes restoring the quality of life besides remission of symptoms. With such a broader view, a future in which anxiety disorders and OCD are episodes that do not interfere with quality of life, and are easy to treat, approaches. To achieve this future goal, research into strategies to end chronicity is crucial, including research at outpatient clinics such as GGZ inGeest.

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CHAPTER 12

Appendix

Nederlandse samenvatting

Dankwoord

Publicaties

Curriculum Vitae

Dissertation series

Nederlandse samenvatting

Sinds enkele decennia bestaat de behandeling van angststoornissen en de obsessieve-compulsieve stoornis (OCS) uit antidepressiva en cognitieve gedragstherapie (CGT). Hoewel de effectiviteit van deze behandelingen aangetoond is met wetenschappelijk onderzoek, herstellen veel patiënten er niet mee. Het onderzoek dat in dit proefschrift wordt gepresenteerd, was gericht op het verbeteren van de behandeluitkomst en het langetermijnbeloop van OCS en angststoornissen.

Introductie

Angst is een nuttige emotie die ons beschermt tegen gevaar. Angst brengt het lichaam in een staat van paraatheid om met gevaar om te kunnen gaan, bijvoorbeeld met een vlucht-, vecht-, of bevroeringsreactie. Het brengt lichamelijke sensaties met zich mee zoals een versnelde hartslag, zweten, trillen, duizeligheid en het plotseling warm of koud krijgen. Wanneer iemand buitensporige angst heeft terwijl er geen gevaar dreigt en deze angst het dagelijks functioneren belemmert, bijvoorbeeld door vermijdingsgedrag, spreken we van een angststoornis. In de 'Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition' (DSM-5) worden verschillende angststoornissen onderscheiden, waarvan de volgende in dit proefschrift zijn onderzocht: paniekstoornis, agorafobie, sociale angststoornis en gegeneraliseerde angststoornis. Tevens is de OCS onderzocht die in eerdere versies van de DSM was ingedeeld onder de groep 'angststoornissen' maar nu in een apart hoofdstuk is ondergebracht.

De paniekstoornis wordt gekenmerkt door terugkerende, onverwachte paniekaanvallen die gepaard gaan met zorgen over het krijgen van nog meer paniekaanvallen, zorgen over de gevolgen van de paniekaanvallen of een duidelijke gedragsverandering gerelateerd aan de aanvallen. Agorafobie bestaat uit vrees om een paniekaanval te krijgen in situaties van waaruit vluchten niet goed mogelijk of schaamtevol is. Deze situaties worden vaak vermeden of doorstaan met intense angst. De sociale angststoornis, of sociale fobie, wordt gekenmerkt door een overmatige vrees voor sociale situaties. Patiënten zijn bang voor een negatieve beoordeling door andere mensen vanwege hun gedrag of angstsymptomen, zoals blozen. De gegeneraliseerde angststoornis bestaat uit overmatige angst en zorgen die moeilijk te beheersen zijn over verschillende situaties en problemen, zoals ziekte, financiële problemen, werk en rampen. Mensen met OCS hebben obsessies (ook wel dwanggedachten genoemd) en/of compulsies (of dwanghandelingen). Obsessies worden gedefinieerd als terugkerende, opdringerige gedachten of beelden die spanning of angst veroorzaken. Dwanghandelingen zijn repetitief en geritualiseerd

gedrag of mentale handelingen gericht op het verminderen van angst. Een voorbeeld van OCS is angst voor besmetting met een ernstige ziekte in combinatie met overmatig wassen (smetvrees).

Angststoornissen komen vaak voor terwijl OCS relatief minder vaak voorkomt. Ongeveer 30% van de volwassenen in de algemene bevolking krijgt op een bepaald moment in hun leven een angststoornis terwijl 2,5% OCS ontwikkelt. In verreweg de meeste gevallen hebben mensen naast de angststoornis of OCS ook nog andere psychische stoornissen; dit wordt comorbiditeit genoemd. De meest voorkomende comorbide psychische stoornissen zijn andere angststoornissen en stemmingsstoornissen.

Het beloop van angststoornissen is minder gunstig dan op het eerste gezicht lijkt. Vier op de vijf mensen met een angststoornis in de algemene bevolking herstelt binnen drie jaar. Terugval komt echter vaak voor, soms in de vorm van dezelfde angststoornis, soms ook in de vorm van een andere angststoornis of depressie. Het beloop van OCS is alleen in klinische steekproeven onderzocht vanwege de geringe prevalentie, waaruit bleek dat OCS in 60% van de gevallen chronisch verloopt. Het is momenteel nog niet goed te voorspellen bij welke mensen het beloop van hun angststoornis of OCS ongunstig zal zijn.

Angststoornissen veroorzaken het grootste, niet-dodelijke gezondheidsverlies in Nederland van alle fysieke en psychische aandoeningen. De mate van gezondheidsverlies kan uitgedrukt worden met het begrip 'kwaliteit van leven', wat het vermogen aanduidt om te kunnen functioneren in verschillende levensdomeinen. Patiënten met angststoornissen en OCS hebben een slechte kwaliteit van leven. Ernstigere angst- of obsessieve-compulsieve symptomen en de aanwezigheid van comorbide psychische stoornissen verlagen de kwaliteit van leven nog verder. Als de symptomen verminderen door behandeling, verbetert de kwaliteit van leven. Meestal blijft deze echter onder het niveau van de algemene bevolking, zelfs wanneer de angststoornis of OCS volledig in remissie is. Naast de ernst van de symptomen en de aanwezigheid van comorbide psychische stoornissen, is weinig bekend over risicofactoren van een slechte kwaliteit van leven.

Angststoornissen en OCS hebben een negatieve invloed op intieme relaties. Patiënten met deze stoornissen hebben minder vaak een partnerrelatie dan mensen in de algemene bevolking. Degenen die wel een partner hebben, melden meer huwelijksproblemen en minder tevredenheid met hun relatie dan mensen in de algemene bevolking. De stoornis van de patiënt heeft bovendien impact op partners

en andere familieleden. De belasting van een psychische stoornis voor de omgeving is vaker bij OCS onderzocht dan bij angststoornissen. Uit deze onderzoeken blijkt dat familieleden van patiënten met OCS kampen met angst- en depressieve symptomen en een verminderde kwaliteit van leven. Familieleden raken vaak in de OCS verstrikt, doordat ze zich aanpassen aan de dwangstoornis van de patiënt. Dit zogenaamde accommoderen kan bijvoorbeeld bestaan uit het meehelpen met uitvoeren van dwanghandelingen. Daarnaast komt het regelmatig voor dat familieleden hun geduld verliezen en de patiënt bekritisieren of fysiek weerhouden van het uitvoeren van dwanghandelingen. Dit wordt 'antagoneren' genoemd. Accommoderen en antagoneren verhogen de ervaren belasting van familieleden van de OCS. Bovendien houden deze reactiepatronen de obsessieve-compulsieve symptomen van de patiënt in stand.

Bewezen effectieve behandelingen voor angststoornissen en OCS bestaan uit serotonerge antidepressiva en CGT. De laatste behandeling richt zich op het veranderen van cognities (gedachten, overtuigingen) en gedrag om negatieve emoties te verminderen. Cognitieve therapie bij angststoornissen en OCS bestaat uit het leren veranderen van een angstige interpretatie van situaties in een niet-angst interpretatie. Gedragstherapie bestaat uit 'exposure in vivo' (lijfelijke blootstelling), waarbij patiënten leren om situaties te betreden die ze normaal gesproken zouden vermijden uit angst of vrees. Bij OCS wordt de exposure aangevuld met responspreventie, wat betekent dat er geen geruststellende dwanghandelingen mogen worden uitgevoerd tijdens en na de exposure oefeningen. CGT is effectief in het verminderen van angst- en obsessieve-compulsieve symptomen. Ongeveer 60%-80% van de patiënten met angststoornissen heeft baat bij CGT. Dit betekent echter ook dat een significante groep patiënten geen profijt heeft van CGT. Bij OCS voldoet bijna de helft van de patiënten na een adequaat gegeven bewezen effectieve behandeling nog steeds aan de diagnostische criteria.

Wanneer CGT en psychotrope medicatie niet effectief zijn en daarbij de symptomen het dagelijks functioneren van de patiënt ernstig verstoren, adviseren richtlijnen intensivering van de behandeling, bijvoorbeeld door te starten met een dagbehandeling of een klinische behandeling. Gewoonlijk is het een multimodale behandeling, waarbij CGT de belangrijkste therapie is, naast vaktherapie en psychotherapie. De behandeling wordt aangeboden in een groep met andere patiënten met angststoornissen en OCS.

Onderzoeksvragen

Het onderzoek in dit proefschrift beoogt de behandeluitkomst en het langetermijnbeloop van angststoornissen en OCS te verbeteren. We hebben risicofactoren van een slecht

beloop onderzocht zodat deze patiënten beter geïdentificeerd kunnen worden en de zorg beter op hen kan worden afgestemd. Een slecht beloop is op de volgende manieren geoperationaliseerd: 1) een chronisch beloop van angst- en depressieve stoornissen in de algemene bevolking, 2) een slecht beloop van de kwaliteit van leven en van de tevredenheid met de partnerrelatie bij patiënten met OCS en 3) het starten met een intensieve behandeling bij patiënten met OCS.

Daarnaast zijn een drietal innovatieve behandelingen onderzocht in ongecontroleerde pilotstudies en een meta-analyse, te weten 1) een familie-interventie, 2) een korte, intensieve exposure met responspreventie behandeling en 3) schematherapie met CGT dagbehandeling. Met deze onderzoeken sluiten we aan bij recente ontwikkelingen die gericht zijn op het vergroten van de effectiviteit van CGT. Het is niet bekend of deze innovaties inderdaad de effectiviteit van CGT verbeteren. De eerste innovatie die in dit proefschrift wordt geëvalueerd betreft het betrekken van familieleden bij de behandeling van OCS. Omdat bepaalde interactiepatronen (accommoderen en antagoneren) de OCS mede in stand houden, kan het aanleren van een adequatere interactie rondom OCS mogelijk helpen om de obsessieve-compulsieve symptomen te verminderen. De tweede innovatie is om CGT-sessies anders te plannen, namelijk om ze te concentreren. Gewoonlijk worden sessies eenmaal per week gepland gedurende enkele maanden. In een kort intensief format worden dezelfde hoeveelheid sessies (bijna) dagelijks gepland in een periode van enkele weken. Een korte, intensieve planning zou beter kunnen zijn dan een reguliere planning omdat patiënten minder gelegenheid hebben om beangstigende situaties tussen de sessies door te vermijden. Hierdoor kunnen niet-angstige interpretaties en gedragspatronen zonder vermindering mogelijk sterker groeien voordat ze in de dagelijkse praktijk moeten worden toegepast. Een derde innovatie is het aanpakken van persoonlijkheidsproblemen in de behandeling naast de angststoornis of OCS. Er wordt wel gedacht dat disfunctionele persoonlijkheidstrekken zorgen voor therapieresistentie bij patiënten met angststoornissen en OCS. Een behandeling die zich richt op disfunctionele persoonlijkheidstrekken is schematherapie. Schematherapie, of elementen ervan, wordt tegenwoordig daarom wel toegevoegd aan CGT.

Samenvatting van de belangrijkste bevindingen

In hoofdstuk 2 zijn de voorspellers onderzocht van een chronisch beloop van angst- en depressieve stoornissen in de algemene bevolking. Er zijn gegevens gebruikt van de basismeting en de meting na drie jaar van de Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2). Dit is een longitudinale studie die het vóórkomen van psychische stoornissen in de algemene Nederlandse bevolking in kaart brengt. Een chronisch beloop van de stoornis die aanwezig was bij de

basismeting (indexstoornis) werd geoperationaliseerd als de aanwezigheid van eenzelfde soort stoornis bij de driejaarsmeting. Dit beloop werd voorspeld door een hoger aantal comorbide psychische stoornissen en een hogere neuroticisme score op de basismeting. De voorspellende nauwkeurigheid van dit model was echter klein. De predictieve precisie steeg naar gemiddeld als er in plaats van de indexstoornis naar een algeheel chronisch beloop werd gekeken, gedefinieerd als de aanwezigheid van een angst- of depressieve stoornis of van middelenmisbruik of -afhankelijkheid na drie jaar. In dit laatste model werd een chronisch beloop voorspeld door een hoger aantal comorbide psychische stoornissen, een hogere neuroticisme score, mishandeling in de kindertijd, psychopathologie bij de ouders en de mate van alcoholgebruik op de basismeting. De resultaten geven aan dat transdiagnostische (stoornis-overstijgende) kenmerken belangrijk zijn bij het voorspellen van het beloop van angst- en depressieve stoornissen in de algemene bevolking, zoals persoonlijkheidskenmerken, kindermisbruik en coping stijl. Leefstijl en fysieke gezondheidsindicatoren hebben weinig toegevoegde waarde bij de beloopspredictie.

In hoofdstuk 3 werd de relatietevredenheid en de kwaliteit van leven van patiënten met OCS onderzocht. De gegevens zijn afkomstig van de basismeting van de Nederlandse Obsessieve-Compulsieve Stoornis Associatie (NOCDA). In deze studie wordt een groot aantal patiënten die hulp zoeken voor OCS voor langere tijd gevolgd. Patiënten met OCS die een partner hadden, rapporteerden een matige tevredenheid over hun relatie. Ze waren significant minder tevreden wanneer ze ernstigere comorbide depressieve symptomen hadden. Ook als patiënten irritatie van hun partner ervaren of een gebrek aan emotionele steun, was de relatietevredenheid lager. De ernst van OCS was niet onafhankelijk geassocieerd met relatietevredenheid. Onze resultaten impliceren dat niet de ernst van OCS op zich de tevredenheid van patiënten met hun relatie beïnvloedt, maar eerder de mate waarin patiënten zich ondersteund voelen met hun symptomen. We maten ook de kwaliteit van leven van patiënten met OCS en die bleek slecht. Degenen zonder een betaalde baan en met ernstigere comorbide angst- en depressieve symptomen hadden een aanzienlijk slechtere kwaliteit van leven. De ernst van OCS was niet onafhankelijk gerelateerd aan de kwaliteit van leven. Onze bevindingen geven aan dat betaald werk en minder comorbide angst- en depressieve symptomen meer bijdragen aan een betere kwaliteit van leven dan minder obsessieve-compulsieve symptomen.

In hoofdstuk 4 werden gegevens van drie metingen (basismeting, tweejaar en vierjaar follow-up) van de NOCDA-studie gebruikt om het beloop van de kwaliteit van leven en de associatie met het beloop van de OCS te onderzoeken. Daarnaast onderzochten we welke patiëntkenmerken bijdroegen aan een ongunstig beloop van de kwaliteit van

leven bij respondenten bij wie OCS in remissie ging. Patiënten werden verdeeld in drie groepen, afhankelijk van het beloop van hun OCS: chronische, intermitterende en in remissie gaande (remitterende) OCS. De gemiddelde kwaliteit van leven van de totale steekproef over alle metingen was significant lager dan in de algemene populatie. Blijkbaar verslechtert OCS de kwaliteit van leven van patiënten aanzienlijk en langdurig. Het beloop van de kwaliteit van leven was gerelateerd aan het beloop van de OCS: de kwaliteit van leven van chronische patiënten was over het algemeen slechter dan die van patiënten uit de andere twee groepen. Bovendien verbeterde de kwaliteit van leven van patiënten met een remitterende OCS significant meer dan die van patiënten met een chronische OCS. Bij patiënten met een remitterende OCS waren ernstigere angst- en depressiesymptomen gerelateerd aan een slechter beloop van de kwaliteit van leven. Deze resultaten geven aan dat remissie van OCS bijdraagt aan een verbetering van de kwaliteit van leven. Maar zelfs bij patiënten met een OCS in remissie bleef de kwaliteit van leven onder het niveau van de algemene bevolking. Blijkbaar zijn andere factoren naast de OCS van invloed op de kwaliteit van leven. Comorbide angst- en depressiesymptomen spelen daarin een belangrijke rol.

Met het onderzoek in hoofdstuk 5 werden patiënten met OCS geïdentificeerd die in de daaropvolgende twee jaar een intensieve behandeling (dagbehandeling of intramurale behandeling) zouden starten. Gegevens van alle meetmomenten van de NOCDA-studie werden gebruikt, namelijk de basismeting en tweejaar, vierjaar en zesjaar follow-up. Patiënten hadden significant meer kans om binnen twee jaar met een intensieve behandeling te starten als ze alleenstaand waren, ernstigere comorbide depressiesymptomen hadden, psychotrope medicatie gebruikten en een lagere kwaliteit van leven ervaarden. De ernst van OCS was niet onafhankelijk geassocieerd met het gaan starten met een intensieve behandeling. Onze resultaten suggereren dat wanhoop en beperkingen in het dagelijks leven als gevolg van OCS belangrijker redenen zijn voor een intensieve behandeling dan het hebben van ernstige obsessieve-compulsieve symptomen op zich.

Hoofdstuk 6 bevat een pilotstudie van een korte familie-interventie voor patiënten met OCS en een familielid. Deze interventie leerde hen hoe ze goed kunnen omgaan met de OCS in de context van hun relatie zonder dat de obsessieve-compulsieve symptomen geaccommodeerd of geantagoneerd worden. Zestien patiënten met OCS en een familielid werden met vijf sessies behandeld. Deze behandeling werd toegevoegd aan de CGT van de patiënt, voor OCS. Patiënten hadden gemiddeld al 2,8 behandelingen voor OCS achter de rug met onvoldoende resultaat. Bij patiënten namen de obsessieve-compulsieve symptomen aanzienlijk af na de korte familie-interventie. Antagonisme, functioneren en de sfeer thuis veranderden niet

significant volgens de patiëntbeoordelingen. Mogelijk zijn er meer sessies nodig om antagonisme te veranderen. Volgens de familieleden zijn het accommoderen, hun sociale functioneren en de sfeer thuis aanzienlijk verbeterd na de behandeling. Relatief veel patiënten en hun familieleden stopten voortijdig met de behandeling. Dit kan mogelijk verklaard worden door de indruk van therapeuten dat het doorbreken van langetermijn-interactiepatronen over de OCS moeilijk was en veel angst veroorzaakte bij zowel patiënten als familieleden. Meer aandacht voor motivatie en ondersteuning tijdens de behandeling zou deze uitval kunnen voorkomen. Patiënten waren tevreden over de familie-interventie, evenals de familieleden. Onze resultaten suggereren dat het betrekken van de familie bij de behandeling effectief is en de moeite waard om verder te onderzoeken.

In hoofdstuk 7 werd onderzocht hoe het leven van familieleden werd beïnvloed door de OCS van de patiënt en of de korte familie-interventie deze impact verlichtte. Er is gebruik gemaakt van gegevens uit de pilotstudie van hoofdstuk 6. Het leven met een patiënt met OCS belastte familieleden aanzienlijk. Familieleden maakten zich zorgen om de patiënt, ervaarden spanning in de relatie met de patiënt en spoorden de patiënt aan om bijvoorbeeld zichzelf te verzorgen of activiteiten te ondernemen. Familieleden accommodeerden en antagoniseerden de OCS-symptomen in aanzienlijke mate. Hoe meer er geaccommodeerd en/of geantagoneerd werd, hoe meer belasting familieleden ervaarden. De belasting was verminderd na onze korte familie-interventie en was gecorreleerd met een afname van het accommoderen. Ook activeerden en motiveerden familieleden de patiënt aanzienlijk minder vaak na de behandeling, wat suggereert dat de interactie adequater was. Deze resultaten geven aanwijzingen dat het leren omgaan met OCS de last van familieleden van patiënten met OCS verlicht.

In hoofdstuk 8 onderzochten we een korte, intensieve exposure behandeling bij patiënten met OCS die geen profijt hadden gehad van een eerdere reguliere CGT. We behandelden 21 patiënten met deze zesdaagse behandeling. Familieleden werden bij de behandeling betrokken. Obsessieve-compulsieve symptomen, comorbide angst- en depressiesymptomen, evenals het accommoderende gedrag van familieleden waren na de behandeling significant verminderd. De kwaliteit van leven was verbeterd. De resultaten bleven bestaan bij follow-up na drie maanden. Hieruit blijkt dat patiënten die eerder geen baat hadden bij een reguliere CGT, wel kunnen profiteren van een korte, intensieve exposure behandeling. Er was slechts één dropout en zowel patiënten als hun familieleden waren tevreden over de behandeling. De korte, intensieve exposure behandeling kwam als effectief en goed uitvoerbaar naar voren in deze pilot studie en moet verder onderzocht worden in een gecontroleerd onderzoeksdesign.

In hoofdstuk 9 werd met een meta-analyse onderzocht of een korte, intensieve planning van CGT-sessies superieur is aan een reguliere planning van dezelfde hoeveelheid sessies bij patiënten met angststoornissen en OCS. Twee gerandomiseerde, gecontroleerde studies (RCTs) en vier niet-RCTs werden geïncludeerd in de meta-analyse, met in totaal 393 patiënten. Korte intensieve CGT verschilde statistisch niet van reguliere CGT in het verminderen van angst- of obsessieve-compulsieve symptomen. De resultaten werden echter sneller verkregen in het korte intensieve format vanwege de kortere doorlooptijd. Bovendien was de korte intensieve CGT significant beter in het verminderen van depressieve symptomen. Dropout werd slechts in twee geïncludeerde studies vermeld en kon dus niet worden gemeta-analyseerd. Het aantal en de kwaliteit van de geïncludeerde studies was beperkt. Verder hoogkwalitatief onderzoek is nodig om de effectiviteit van een intensieve planning van CGT-sessies te onderzoeken.

In hoofdstuk 10 onderzochten we een innovatieve dagbehandeling met schematherapie (ST), CGT en vaktherapie in een ongecontroleerde pilotstudie. 27 patiënten met therapieresistente angststoornissen of OCS werden behandeld met deze ST-CGT dagbehandeling. Algemene psychopathologie en disfunctionele persoonlijkheidskenmerken, in de vorm van vroege maladaptieve schema's en schemamodi, waren na de behandeling aanzienlijk verbeterd. Daarnaast was de verbetering van psychiatrische symptomen significant en sterk gecorreleerd met de verbetering van schema's en schemamodi, wat een sterke onderlinge afhankelijkheid suggereert tussen verbetering van algemene psychopathologie en verbetering van disfunctionele persoonlijkheidskenmerken. De sterkte van de schema's en schemamodi voor de behandeling voorspelde de uitkomst van algemene psychopathologie niet, wat suggereert dat sterkere disfunctionele persoonlijkheidskenmerken de verbetering van de symptomen niet belemmerden. Mogelijk heeft schematherapie bijgedragen aan dit resultaat, maar dat kan op grond van dit onderzoek niet vastgesteld worden. Onze resultaten dragen bij aan een opkomend onderzoeksveld naar de effectiviteit van schematherapie bij patiënten met therapieresistente angststoornissen en OCS.

Conclusies

De resultaten van dit proefschrift kunnen worden gebruikt om de behandeluitkomst en het langetermijnbeloop van angststoornissen en OCS te verbeteren. Tot op heden weten we deels bij welke patiënten de angststoornis of OCS een ongunstig beloop krijgt maar onvoldoende om het nauwkeurig te voorspellen voor een individuele patiënt. Dit is een belangrijke lacune in de huidige kennis. Als we dit wel zouden weten, dan zou de geestelijke gezondheidszorg beter ingericht kunnen worden. De risicofactoren van

een chronisch beloop van een angst- of depressieve stoornis in de algemene bevolking bestaan met name uit klinische en kwetsbaarheidskenmerken (comorbide psychische stoornissen, neuroticisme, mishandeling in de kindertijd, psychopathologie bij de ouders en alcoholgebruik). De betreffende mensen zouden geïnformeerd moeten worden over het hoge risico op terugval of het ontwikkelen van een andere psychische stoornis, zelfs na remissie van de index stoornis, door bijvoorbeeld gezondheidszorg-professionals, patiëntenorganisaties of overheidscampagnes. Daarbij zouden mensen met een hoog risico geadviseerd moeten worden om hulp te zoeken voor hun psychische klachten. Onze resultaten suggereren eveneens dat de mentale gezondheid verbeterd zou kunnen worden door een breder perspectief op psychische stoornissen aan te nemen waarbij ook oog is voor comorbide psychische stoornissen en etiologische of kwetsbaarheidsfactoren zoals kindermishandeling, disfunctionele persoonlijkheidskenmerken en disfunctionele coping.

De remissie van obsessieve-compulsieve symptomen brengt niet vanzelf herstel van de kwaliteit van leven en de relatietevredenheid van patiënten met zich mee. Dit weerspreekt eerdere visies dat patiënten in staat zijn om hun leven te hervatten zodra de OCS in remissie is. Het is dus belangrijk om herstel breder te definiëren en niet alleen te kijken naar het herstel van de OCS. Dit betekent onder andere dat in een behandeling de kwaliteit van leven en relatietevredenheid als aparte doelen gesteld moeten worden, naast het verminderen van obsessieve-compulsieve symptomen. Mogelijk kan hieraan gewerkt worden door het behandelen van comorbide angst- en depressieve symptomen en het aanmoedigen van patiënten om hun leven op te pakken met bijvoorbeeld betekenisvolle relaties, activiteiten en (vrijwilligers)werk.

Het is belangrijk om familieleden van patiënten met OCS bij de behandeling te betrekken. Vaak wordt dit achterwege gelaten en dat is een gemiste kans omdat het de belasting die familieleden van de OCS ervaren, kan verminderen. Bovendien kan het helpen om de obsessieve-compulsieve symptomen van de patiënt te verbeteren. Therapeuten kunnen familieleden leren hoe ze het beste kunnen omgaan met de OCS van de patiënt en daarbij de obsessieve-compulsieve symptomen niet te accommoderen of te antagoneren. Bovendien kan het helpen om te leren omgaan met irritatie en het bieden van emotionele steun, ook weer zonder de OCS te accommoderen of te antagoneren.

De innovatieve behandelingen die in dit proefschrift zijn onderzocht, kunnen overwogen worden als patiënten geen baat hebben bij bewezen effectieve behandelingen zoals CGT en serotonerge antidepressiva. De korte familie-interventie additief aan CGT – in deze context nogmaals genoemd – kan effectief zijn bij patiënten

met OCS die familieleden hebben die gebukt gaan onder de OCS en die de obsessieve-compulsieve symptomen accommoderen en/of antagoneren. Een korte, intensieve planning van CGT-sessies kan effectief zijn bij patiënten met OCS, paniekstoornis en agorafobie die veel situaties vermijden. Daarnaast kan een intensieve behandeling met schematherapie, zoals de ST-CGT dagbehandeling, overwogen worden voor patiënten met chronische, therapieresistente angststoornissen en OCS met comorbide psychische en persoonlijkheidsstoornissen en een slechte kwaliteit van leven. Tenslotte kan ook een herstelbenadering worden overwogen, die minder nadruk legt op remissie van angst- en obsessieve-compulsieve symptomen en meer nadruk legt op verbetering van de kwaliteit van leven. Bijvoorbeeld met Acceptance and Commitment Therapy (ACT), waarbij patiënten leren om negatieve gevoelens en symptomen te accepteren terwijl ze persoonlijke, betekenisvolle doelen in het leven nastreven. Deze aanpak kan worden overwogen voor patiënten bij wie geen significante verdere verbetering wordt verwacht van de behandeling van de psychiatrische symptomen.

In dit proefschrift werd betoogd dat de geestelijke gezondheid verbeterd kan worden met een bredere visie op psychopathologie en herstel. Dat wil zeggen, een kijk op psychische stoornissen die rekening houdt met de gemeenschappelijke etiologie van de index- en comorbide psychische stoornissen. Een bredere kijk op de behandeling, zodat klinici niet alleen de indexstoornis behandelen, maar ook comorbide symptomen, de sociale omgeving en etiologische variabelen meenemen, zoals disfunctionele persoonlijkheidskenmerken. Tenslotte een bredere kijk op herstel, waarbij de kwaliteit van leven in ogenschouw genomen wordt naast remissie van symptomen. Met zo'n bredere kijk komt een toekomst dichterbij waarin angststoornissen en OCS episodes zijn die de kwaliteit van leven minder verstoren en die beter te behandelen zijn. Om dit toekomstige doel te bereiken, is onderzoek naar strategieën om chroniciteit te beëindigen cruciaal, waaronder onderzoek op poliklinieken zoals GGZ inGeest.

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Curriculum Vitae

Karin Remmerswaal is in 1968 geboren in Leiden. Na haar VWO eindexamen aan het Bonaventuracollege te Leiden ging ze psychologie studeren aan de Universiteit Utrecht alwaar ze in 1992 afstudeerde in de richting experimentele functieleer. Haar eerste baan was als onderzoeksmedewerker op het Max Planck Instituut voor Psycholinguïstiek in Nijmegen. Naast deze baan volgde ze de studie klinische psychologie aan de Universiteit Utrecht. Vervolgens heeft ze twaalf jaar als therapeut, projectmanager en vestigingsmanager gewerkt bij HSK, een GGZ instelling voor werkgerelateerde problematiek, en bij Altrecht. De opleiding tot gedragstherapeut rondde ze af in 2005. Haar registratie als Gezondheidszorgpsycholoog BIG behaalde ze in 2007 en die als supervisor bij de Vereniging voor Gedrags- en Cognitieve therapieën (VGCT) in 2010. Zes jaar lang heeft ze een psychologie praktijk gehad. In 2010 kwam ze in dienst bij GGZ inGeest op de polikliniek voor angst- en dwangstoornissen als behandelverantwoordelijke voor de deeltijdbehandeling en daar werkt ze nu nog steeds. Karin startte in 2014 met een promotie onderzoek dat als doel had het beloop van angst- en dwangstoornissen te verbeteren. Naast haar therapeutische werk geeft Karin supervisie aan psychologen en psychiaters in opleiding en maakt ze deel uit van het onderzoeksnetwerk Angst, Dwang en Trauma van TOP-GGZ.

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