But I am scared…

Impact, transmission, and effectiveness of treatment of childhood anxiety disorders

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Liesbeth Telman

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COLOFON

But I am scared… Impact, transmission, and effectiveness of treatment of childhood anxiety disorders, Liesbeth Telman
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Impact, Transmission, and Effectiveness of Treatment of Childhood Anxiety Disorders

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Faculteit:	Faculteit der Maatschappij- en Gedragswetenschappen	

Eerlijk waar, ik wil niet bang zijn
En ik doe ook best mijn best
Maar zodra ik alleen in bed lig
Wordt mijn dapperheid getest
Door wel duizend gekke piepjes
Door gekraak en soms gezang
En dan weet ik dat het nep is
Maar dan ben ik toch weer bang

Kinderen voor Kinderen – Bang, hoezo bang

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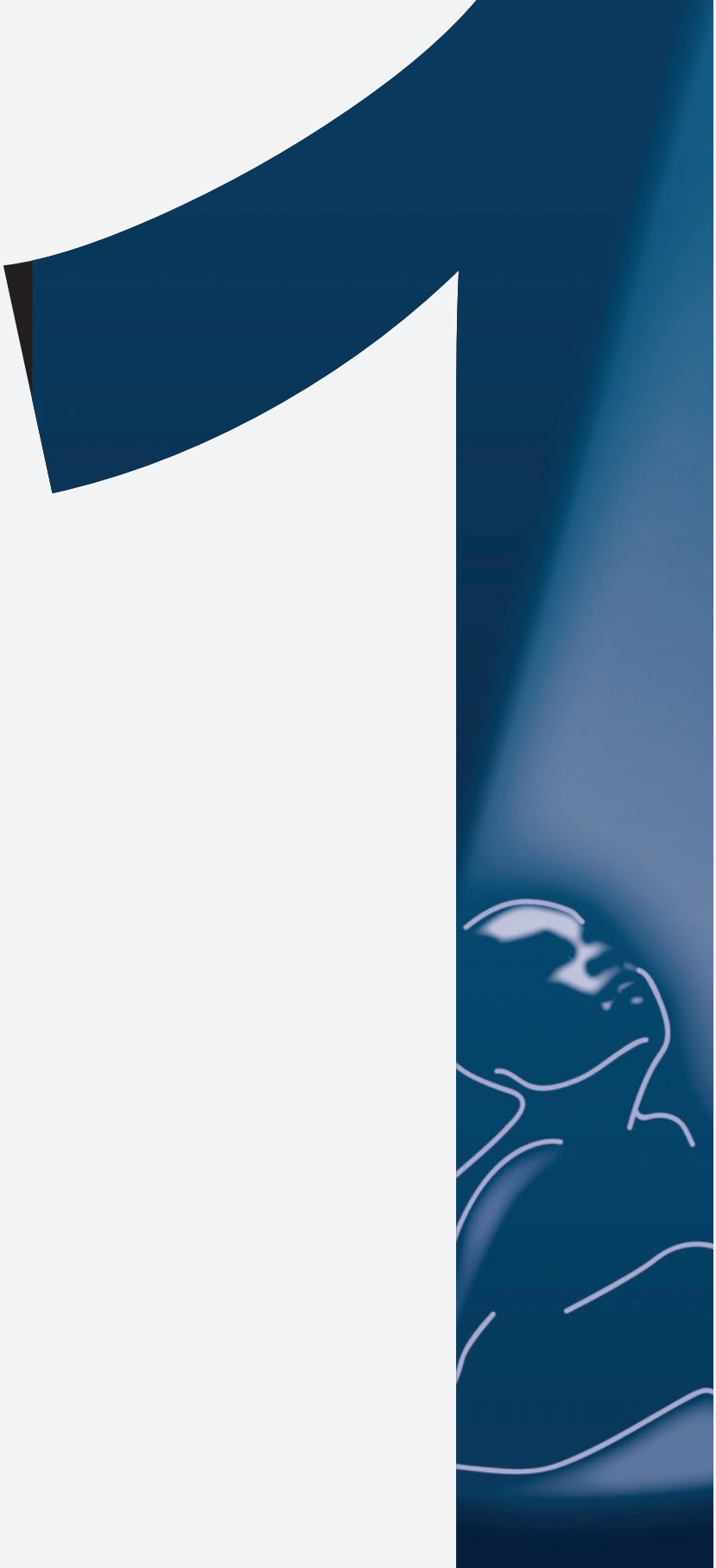

INTRODUCTION


BATHROOM
BATHROOM
I need to pee but I'm afraid to go alone
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INTRODUCTION

Anxiety Disorders in Children and Adolescents

Anxiety is a healthy response to a threatening situation, in order to make one aware of danger. All children experience feelings of anxiety and these are often related to a developmental period, for example experiencing symptoms of separation anxiety when the child is 6-9 years old (Weems & Costa, 2005). However, when the anxiety persists in the absence of a threatening situation, and impairs the child's daily functioning, the child can be classified as having an anxiety disorder (American Psychiatric Association, 2013). The Diagnostic and Statistical Manual of mental disorders fifth edition (DSM-5; APA 2013) separates seven types of anxiety disorders: separation anxiety disorder, selective mutism, specific phobia, social anxiety disorder, panic disorder, agoraphobia, and generalized anxiety disorder.

Anxiety disorders are by far the most prevalent mental disorders in children and adolescents, with prevalence estimates up to 20% (APA, 2013; Costello, Egger, & Angold, 2005; Wittchen et al., 2011). In comparison, other childhood psychiatric disorders such as ADHD are prevalent in 5% of children and autism spectrum disorders in 1% of children (Wittchen et al., 2011). Comorbidity among anxiety disorders is high (19%-80%, Chavira, Stein, Bailey, & Stein, 2004; Curry, March, & Hervey, 2004), as well as with other disorders, for example, children with anxiety disorders are more than eight times likely to suffer from depression compared to children without anxiety disorders (Costello et al., 2005). Although highly prevalent, not all children with anxiety disorders are receiving help to overcome their anxiety. That is, only 31% of them are referred to mental health care (Chavira et al., 2004), while it is known that children hardly recover from their anxiety disorder on their own (Keller et al., 1992). This implies that there is a need for treatment of anxiety disorders, as well as adequate diagnosis.

Impact of Anxiety Disorders

Most children that are referred to mental health care centers are the ones with high levels of interference and/or multiple anxiety disorders (Jongerden, Simon, Bodden, Dirksen, & Bögels, 2015). In addition, treatment use is found to be related to the perceived burden of the child's problem by their family (Angold et al., 1998). Somewhat surprisingly, the percentage of children with anxiety disorders seeking help (31%) is lower than children with ADHD (79%) and depression (40%) (Chavira et al., 2004). This raises the question whether the impact of having an anxiety disorder is lower than other disorders. When looking at the burden of

having an anxiety disorder, the literature reports about a variety of problems that are associated with having an anxiety disorder. That is, most children experience difficulties in social functioning, school functioning and family functioning (Bögels & Brechman-Toussaint, 2006). For example, children with anxiety disorders often show withdrawn behavior, tend to be shy and struggle with social interactions. With regards to family life, children with anxiety disorders can impair their family functioning by avoiding going to family visits (social anxiety disorder), not willing to go out because there could be dogs (specific phobia), or by responding with panic in a situation that appears threatening to them (panic disorder). In addition, untreated anxiety disorders in children are associated with negative consequences such as subsequent anxiety, depressive, and substance use disorders. Moreover, untreated anxiety disorders may lead to impairment in interpersonal functioning, loneliness, school refusal and drop-out, and lower educational level (e.g., Beidel, Turner, & Morris, 1999; Burstein et al., 2011; Kendall, Safford, Flannery-Schroeder, & Webb, 2004; Wittchen & Fehm, 2003). Finally, anxiety disorders usually persist in adulthood and are related to reduced quality of life (Detweiler, Comer, Crum, & Albano, 2014; Pine, Cohen, Gurley, Brook, & Ma, 1998).

Next to the individual or family impact of anxiety disorders, childhood anxiety disorders are associated with additional costs for society. That is, a cost of illness study on childhood anxiety disorders estimated that anxiety disorders cost the Dutch population more than 20 million euros a year (Bodden, Dirksen, & Bögels, 2008b). The study also reported that anxiety disorders are accompanied with 21 times higher costs compared to the normal population. This is mainly expressed in mental health care use, but also in loss of leisure time and school absence (Bodden et al., 2008b).

Thus, it is evident that anxiety disorders have impact on the child's and family's life and come along with societal costs. The question that remains is: to what extent are anxiety disorders more or less impairing than other common psychiatric disorders? Although studies have compared several clinical groups (ADHD, ASD, anxiety) to a group of typically developing children, studies comparing different clinical groups to each other are scarce and warrant further investigation (see introduction Chapter 2).

Anxiety in Families

There is quite some evidence that anxiety tends to run in families. That is, top-down studies found children from anxious parents to have more anxiety disorders than children from non-anxious parents (Beidel & Turner, 1997; Hettema, Neale, & Kendler, 2001; Merikangas, Dierker, & Szatmari, 1998), and bottom-up studies found parents of anxious children to have more anxious disorders (Cooper, Fearn, Willetts, Seabrook, & Parkinson, 2006; Hughes, Furr, Sood, Barmish, & Kendall, 2009) (also see introduction Chapter 3). Such findings indicate that parents may be important in the etiology (and maintenance) of childhood anxiety disorders. There are two pathways through which parents may contribute to their child's anxiety: there is a genetical transmission from parent to child, and an environmental transmission of anxiety disorders (Murray, Creswell, & Cooper, 2009). For example, parenting strategies and anxious modeling are part of the environmental transmission: parents may use parenting strategies that enhance and maintain anxiety in their children, such as overprotective parenting and warning children for danger (Bögels & Brechman-Toussaint, 2006; Ollendick & Benoit, 2012). Moreover, parents' own anxiety disorders could play a role in the maintenance of childhood anxiety disorders, by avoiding situations or by anxious modeling (Rapee, 2012).

In addition, research suggests that the role of mothers and fathers in the maintenance and etiology of childhood anxiety differ (Bögels & Phares, 2008). For example, fathers are important for the development of social competence and social fears (Kashdan & Herbert, 2001); whereas mothers might be more important in transmitting worry as a coping strategy (Aktar, Nikolic, & Bögels, 2017). These different roles have been supported by research in young children, which showed that specifically fathers' anxiety is related to the development of anxiety in young children (Möller et al, 2015). Moreover, fathers' role seems to have specific relevance to the development and maintenance of social anxiety disorder (Knappe et al., 2012).

As evident from above, parents may contribute to their child's anxiety in a number of ways and there is evidence for the different roles of fathers and mothers. However, research regarding the transmission between mother-child and especially between father-child is scarce, as well as research studying the entire family (including fathers, mothers, and *all* children) (also see introduction of Chapter 3). Examining the presence of anxiety disorders in the entire family and looking at specific relations between mother-child and father-child may provide additional insights in: (1) the similarities and/or differences between fathers and mothers

in the child-parent transmission of anxiety disorders, and (2) whether anxiety disorders really tend to run in the family (suggesting 'family shared factors' to be involved) or whether a specific child within a family is vulnerable for developing anxiety (suggesting individual susceptibility).

Treatment of Anxiety Disorders

Cognitive Behavioral Therapy (CBT) is the most efficacious treatment of anxiety disorders in children and adolescents (James et al., 2015; Reynolds, Wilson, Austin, & Hooper, 2012). CBT is also the first treatment of choice according to the Dutch guidelines of mental disorders in children (Nederlands Jeugd Instituut, 2017). In general, CBT consists of psycho-education, cognitive restructuring (i.e. replacing anxious thoughts with helping thoughts), and exposure exercises (i.e. gradual exposure towards anxious stimulus). Over 50 years of research on treatment of childhood anxiety disorders has shown that CBT is an effective treatment (Higa-McMillan, Francis, Rith-Najarian, & Chorpita, 2016). Meta-analyses have shown that up to 67% of the children are free of their primary anxiety disorder after treatment (In-Albon & Schneider, 2007; James et al., 2015). CBT is usually manual-based and carried out by trained psychologists. The research in this dissertation will focus on the manual Discussing+Doing=Daring (Bögels, 2008). The original manual consists of 12 sessions, 9 with the child and 3 including the parent, and there are 3 additional sessions for parents only if needed. Its efficacy has been established in previous research (Bodden et al., 2008), as well as in group format (Jongerden, 2015), and for children with comorbid autism spectrum disorders (Van Steensel & Bögels, 2015). Nevertheless, the percentage of children that are not free of their primary anxiety disorder remains about one third of the cases at three months follow-up (67% free of primary anxiety disorder, Bodden et al., 2008; 72% free of primary anxiety disorder, Van Steensel & Bögels, 2015). Thus, instead of looking if therapy works, we need to move forward to examine for whom therapy works (not) and why.

Modular Therapy. It has been acknowledged that treatment does not work equally well for each individual; therefore, we should seek to find ways to improve treatment outcome of these non-responders (or 'less good' responders). One way to do this is by targeting therapy to the individual by choosing elements of a treatment protocol that fits the child. For example, children with specific phobias are more likely to need exposure exercises to overcome their anxiety whereas children with generalized anxiety disorder may need cognitive restructuring. In addition, a study in clinical practice showed that therapists tend to use parts of

treatment protocols instead of the entire protocol (Chu et al., 2015). Therefore, a modular CBT program fits the current trends in clinical work by letting therapists choose specific parts of a treatment manual.

Modular CBT is essentially an evidence-based CBT program that is divided into self-contained modules, in order to adapt the intervention to the individual (Ng & Weisz, 2016). By doing so, the therapist is equipped with a structured approach, while at the same time having possibilities to adapt treatment to the individual. Treatment of two different children with the same manual may look different because of the chosen modules or the order of the modules. Thus far, effects of modular therapy have been encouraging, with 60.0% of youth with anxiety, depression, trauma, and/or conduct problems being clinically improved after modular treatment compared to 36.7% of youth in the standard evidence-based treatments (Chorpita et al., 2013). Also, modular treatment included more evidence-based content than care as usual (Weisz et al., 2012); and youth showed faster improvements after modular therapy compared to standard evidence-based treatments (Chorpita et al., 2013; Weisz et al., 2012). Modular CBT is therefore a promising way to improve treatment outcome.

In order to fit with the current trends and wishes of clinical practice, a modular Discussing + Doing = Daring (DDD) protocol has been developed and its effectiveness is examined in this dissertation. The modular DDD treatment was based on the original manual (Bögels, 2008), and extended with additional mindfulness exercises. It contains the following modules: psycho-education, cognitive restructuring, coping (i.e. task concentration tasks), dealing with feelings (i.e., relaxation exercises, mindfulness exercises), exposure and experiments, parental guidance, and relapse prevention. Therapists were obliged to start with psycho-education and to end with a summary and relapse prevention, the other modules could be used when necessary and appropriate. The manual is structured, but the modular use enables therapists to work with a "structured flexibility" approach. The use of the workbook for children was also flexible, therapists were encouraged to create individual workbooks by only sharing those exercises that were necessary.

For whom therapy works (better). One way to optimize treatment outcome is by improving our understanding of which child and parent characteristics are related to treatment effectiveness. For example, if we know that for some children with specific characteristics (e.g., gender, age, type of anxiety disorder, parental

psychopathology) treatment works better or worse, then this provides directions how to target treatment to the right child.

Children. Child demographics such as gender and age are not (consistently) found to be related to treatment effectiveness (Crowe & McKay, 2017; Nilsen, Eisemann, & Kvernmo, 2013). Type of anxiety disorder, however, has been linked to treatment effectiveness and cumulating evidence seems to suggest that children with social anxiety disorder benefit less from CBT than children with other anxiety disorders (e.g., Hudson et al., 2015). One explanation for this is that there is a high level of comorbidity with affective disorders, leading to higher symptom severity (Kendall, Settipani, & Cummings, 2012). Moreover, therapy might not address the core symptoms of social anxiety disorder sufficiently, leading children to still being focused on themselves after treatment and entering social situations with negative expectations (Spence & Rapee, 2016). Programs specifically targeting social anxiety disorders exist for adults but are hard to translate to children as other maintaining mechanisms may play a role, such as the family environment (Halldorsson & Creswell, 2017). Moreover, initial studies examining treatment aimed at children with social anxiety disorders by adding social skills training elements, focusing on reducing self-focused attention, and processing of social tasks, did not show improved outcome compared to general CBT (Spence, Donovan, March, Kenardy, & Hearn, 2017).

Parents. Next to child factors, parent factors might also play a role in treatment effectiveness. The associations between parental anxiety, parenting, and child anxiety have been established, which implies – from a theoretical perspective – that it would make sense to involve parents in child therapy. However, research thus far has shown that the involvement of parents does not seem to improve treatment outcome over and above the effects of individual CBT (e.g., In-Albon & Schneider, 2007). This is somewhat counterintuitive, especially for clinicians, and asks for a further examination. Up till now, parental involvement has been studied mostly by randomizing children to either family CBT (which may vary from including the whole family, adding additional sessions for the parents, or combined child-parent sessions) or child CBT. Similar to examining for which child CBT works (better), it may be relevant to consider examining for which child parental involvement is necessary and/or more beneficial in terms of treatment outcomes. For example, for children with comorbidity (ASD- and ADHD-problems) involving parents is found to be related to higher treatment gains (Van Steensel, Zegers, & Bögels, 2015; Maric, Van Steensel, & Bögels, 2018). Similar, child age and parental anxiety

may interact with parental involvement in a way that parental involvement is more important for younger children, and when parents are anxious themselves (also see introduction Chapter 5).

Dissertation Outline

Taken together, childhood anxiety disorders are highly prevalent but not always visible. In contrast to other childhood disorders (e.g. ADHD, oppositional defiant disorders, and depressive disorders), children with anxiety disorders are less likely to receive help (Chavira et al., 2004; Costello & Janiszewski, 1990). This questions the impact of childhood anxiety disorders, relative to other childhood disorders. Moreover, anxiety seems to run in families; however, we do not know whether this holds for the whole family (i.e., mothers, fathers, siblings), and if this is specific for some types of anxiety disorders. CBT for childhood anxiety disorders is effective in most cases; however, not for everyone, and with recent developments regarding increased demand for mental health care and the need to reduce costs there is a need to provide effective treatment in less time. Modular therapy seems a promising way to improve treatment outcome and reduce treatment time and costs. Finally, providing more insight into the predictors of treatment effectiveness such as parental involvement could contribute to a better understanding for whom treatment works better. Therefore, the aims of this dissertation are to gain understanding in the impairment and transmission of anxiety disorders in children, as well as to examine the (predictors of) effectiveness of a modular treatment protocol.

Chapter 2 focuses on the extent to which anxiety disorders are impairing for children with regard to their quality of life, and parental stress and parental psychopathology, in comparison to other clinical groups. Data is collected at UvA minds (academic treatment center for children and parents), partly collected by the author of this dissertation, and includes 228 children that received treatment at UvA minds, and their parents, and a control group of 42 typically developing children and their parents recruited for the purpose of this study.

Chapter 3 examines the widely used claim that 'anxiety disorders run in the family'. We do not yet know whether this holds for all family members, and for all types of anxiety disorders. This chapter will examine the prevalence of anxiety disorders in children, mothers, fathers, and siblings. Moreover, this chapter examines whether specific anxiety disorders are transmitted in the family. Data was collected previously (Bodden, Bögels, & Muris, 2009) and included 144 families of which one

child was referred for treatment for its anxiety problems, as well as a control group of 49 families with typically developing children.

Chapter 4 focuses on children with social anxiety disorders in specific, who usually benefit less from CBT than children with other anxiety disorders. This chapter aims to examine the effectiveness of a modularized cognitive behavioral therapy (CBT) for children with SAD, including mindfulness. This will inform us if and how this treatment works for this target group. Data consisted of 10 case studies that were pooled from a larger dataset that was collected by the author of this dissertation and falls under the project 'working mechanisms in the treatment of childhood anxiety disorders' (ZonMw grant 729101010).

Chapter 5 focuses on treatment effectiveness and predictors of outcome in usual clinical practice. This study takes into account an innovative modular CBT protocol and examines child and parent predictors of treatment effectiveness. Data was collected by the author of this dissertation and was part of the project 'working mechanisms in the treatment of childhood anxiety disorders' (ZonMw grant 729101010). The sample consists of 116 children, and their parents, who were referred to 20 different mental health care centers throughout the Netherlands because of anxiety problems.

1

Are Anxiety Disorders in Children and Adolescents Less Impairing Than ADHD and Autism Spectrum Disorders?

Associations with Child Quality of Life and Parental Stress and Psychopathology

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ABSTRACT

We compared clinically referred children with Anxiety Disorders (AD; *n* = 63) to children with Autism Spectrum Disorder (ASD; *n* = 39), ADHD Combined (ADHD-C; *n* = 62), ADHD Predominantly Inattentive (ADHD-I; *n* = 64), and typically developing children (*n* = 42) on child quality of life (QOL), paternal and maternal psychopathology and parental stress. Diagnoses were based on DSM-IV-TR criteria. Multilevel analyses showed that QOL in AD was higher on school and social functioning, compared to respectively ADHD and ASD, and lower compared to normal controls on all five domains. Fathers reported their AD children higher QOL than mothers. Also, AD appears to be associated with less parental stress and parental psychopathology than other child psychopathology. Therefore, parental factors may need to be considered more in treatment of children with ADHD/ASD than AD.

Keywords: anxiety disorders, quality of life, parental stress, parental psychopathology

ARE ANXIETY DISORDERS IN CHILDREN AND ADOLESCENTS LESS IMPAIRING THAN ADHD AND AUTISM SPECTRUM DISORDERS? ASSOCIATIONS WITH CHILD QUALITY OF LIFE AND PARENTAL STRESS AND PSYCHOPATHOLOGY

Anxiety disorders (AD) are by far the most prevalent mental disorders in childhood, with prevalence estimates ranging from 10-20% (Chavira, Stein, Bailey, & Stein, 2004; Costello, Egger, & Angold, 2005; Wittchen et al., 2011). Interestingly, despite its prevalence, only 31 % of AD children receive treatment (Chavira et al., 2004). Nevertheless, societal costs of childhood AD have been estimated high, with nine to twenty times more costs than the normal population (Bodden, Dirksen, & Bögels, 2008; Van Steensel, Dirksen, & Bögels, 2013). Taking into account the high prevalence and societal costs, but low treatment usage, the question has raised whether AD might be less disturbing for the child and their parents than other common childhood mental disorders such as attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). To provide more insight into this issue, this study compared families of clinically referred children with AD to children with ADHD, ASD, and a non-clinical control group on child quality of life, parental psychopathology, and parental stress, in order to examine the functional impairment of childhood AD with respect to child and parental factors.

Currently, studies focusing on child psychiatric disorders have increasingly used quality of life as an assessment of functional impairment. The concept quality of life encompasses multiple domains, such as physical well-being, psychological well-being, and social functioning (Bastiaansen, Koot, & Ferdinand, 2005). Comparisons of quality of life in various clinical groups have been scarce, even though it has been suggested that children who are diagnosed with a psychiatric disorder generally have a considerably poorer quality of life than children from the general population (Bastiaansen et al., 2005; Watson & Keith, 2002). Bastiaansen, Koot, Ferdinand & Verhulst (2004) compared the quality of life between 310 clinically referred children referred to outpatient child psychiatric clinics with AD, ADHD, ASD, mood disorders, and other disorders, and showed that children with AD had a poorer quality of life in the domain of emotional functioning than children with ADHD, whereas the impact of AD on other aspects of quality of life was equal to children with ADHD, disruptive behavior disorders, and mood disorders (Bastiaansen et al., 2004). Moreover, Thaulow and Jozefiak (2012) found no significant differences between quality of life of clinically referred children with ADHD and children with anxiety/depression. Van Steensel, Bögels, & Dirksen (2012) found no differences

between clinically referred children with ASD and comorbid AD and children with AD only in both parent and child reported quality of life; however, a lower quality of life was related to a higher anxiety severity and more severe autistic behavior. Thus, quality of life studies of clinically referred children with AD versus other mental disorders indicate that children with AD are at least as impaired as their counterparts with other disorders, but research is still sparse, and a comparison of several clinical groups with a control group seems to be missing.

Parental psychopathology has often been found to be elevated in parents of children with behavioral problems; however, it is unclear to what extent parents of children with AD have more or less psychopathology themselves than other parents, and how specific this relationship is. Moreover, likely heritability plays a role in the relationship between child and parental psychopathology, with heritability estimates of 30-40% for AD (Hettema, Neale, & Kendler, 2001), and even stronger evidence for the heritability of ASD (>90%; Freitag, 2007) and ADHD (around 76%; Johnston & Mash, 2001). For AD, it has been found that (a) parental anxiety functions as a risk factor for child AD (e.g., Bögels & Brechman-Toussaint, 2006); (b) children with AD are more likely to have parents with AD as compared to other children (Bögels & Brechman-Toussaint, 2006; Beidel & Turner, 1997); and (c) parental anxiety is related to child anxiety and depression, but not to child externalizing symptoms (Burstein, Ginsburg, & Tein, 2010). Moreover, a recent study showed that maternal anxiety symptoms were associated with all childhood problems, while paternal anxiety was only associated with childhood internalizing problems (Middeldorp et al., 2016). Research in other clinical groups found that parental depression was specifically associated with child internalizing problems, whereas parental ADHD was related to child psychopathology in general (Humphreys, Mehta, & Lee, 2012). Thus far, different relations between child and parental psychopathology were found, and research is inconclusive whether these relations are specific or not and whether parents of one clinical group referred to mental health care appear to have more or less behavioral problems than other parents. Above all, most studies have examined the relation between child and parental psychopathology by measuring symptoms, instead of relying on childhood DSM-IV-TR disorders to define groups.

Parenting a child with a clinical diagnosis often raises parental stress, which can be defined as the distress that arises from the demands of parenting (Deater-Deckard, 1998), and which may contribute independently to the clinical portrait of clinic-referred families (Costa, Weems, Pellerin, & Dalton, 2006).

The available evidence for differences in parental stress between children with different clinical diagnoses is scarce. The study of Costa et al. (2006) showed that parental stress concerning dysfunctional interactions predicted child internalizing symptoms specifically; whereas parental stress concerning raising a difficult child predicted externalizing symptoms as well. In line, a comparison of children in a school-based system of care showed that parents of children with both high internalizing and externalizing symptoms reported more parental stress than children with low symptom levels (Vaughan, Feinn, Bernard, Brereton, & Kaufman, 2013). Moreover, parents of children with internalizing problems reported comparable parental stress in parent-child interactions compared to parents of children with both internalizing and externalizing symptoms (Vaughan et al., 2013). In addition, previous studies found that parents of children with ADHD combined subtype showed more parental stress than parents of ADHD inattentive subtype (Tzang, Chang, & Liu, 2009). Finally, some studies have shown that parental stress was specifically associated with children's anxiety symptoms (Rodriguez, 2011). Thus, both children's internalizing and externalizing problems seem to be related to parental stress; however, little consideration has been given to the association between the types of child psychiatric diagnosis and parental stress. Knowledge about the role of parental stress in different child psychopathology is the first step to shed light on the role of parental stress in the etiology, maintenance, and treatment of child psychopathology.

The different roles of fathers and mothers in the development and maintenance of childhood AD have received more attention over the last decade (Möller, Majdandžić, de Vente, & Bögels, 2014). Nevertheless, fathers still tend to be underrepresented in research (Bögels & Phares, 2008). However, fathers may be important informants as they may have a different perspective on their child's problems (i.e., they tend to report less internalizing problems; Duhig, Renk, Epstein, & Phares, 2000) and they may evaluate the burden of parenting a clinical child differently than mothers (Theule, Wiener, Tannock, & Jenkins, 2013). In addition, child internalizing problems have been found to be more closely related to internalizing symptoms of mothers than fathers (Connell & Goodman, 2002). Therefore, the current study included reports from both mothers and fathers, in order to examine possible differences between their reports.

In sum, research suggests that clinically referred children with AD are impaired in terms of quality of life; however, it is unclear whether this impairment is similar to other mental disorders. Parental impairment in children with AD was also found:

parents of children with AD were more anxious themselves, and parents of children with internalizing problems experienced different parental stress than parents of children with externalizing problems. Parental impairment studies examined child anxiety symptoms instead of diagnosis and therefore no conclusions can be drawn about which childhood disorders are more or less associated with parental psychopathology or parental stress. The aim of this study was to investigate whether children with AD differ from children with different psychiatric disorders (i.e. ASD, ADHD) and a control group of children without a clinical diagnosis on a range of variables: quality of life of the child, parents' internalizing and externalizing psychopathology, and parental stress, using both mother and father reports. Examining these possible differences is important because it may lead to further insight into the impact of childhood AD and may lead to the identification of possible treatment targets. Based on the above literature, we hypothesized that (1) children with AD would be at least as impaired in quality of life as children with ASD and ADHD (Bastiaansen et al., 2004; Thaulow & Jozefiak, 2012), and have a lower quality of life than children in the control group (Watson & Keith, 2002), (2) tentatively, parents of children with AD would have more internalizing and less externalizing problems than parents of children in the other clinical groups (Bögels & Brechman-Toussaint, 2006; Beidel & Turner, 1997; Burstein et al., 2010), and (3) parents of children with AD would likely experience similar levels of parental stress as parents of children in other clinical groups, but lower levels of stress compared to the control group (Vaughan et al., 2013).

METHOD

Participants

Participants eligible for this study were children and adolescents aged 6-21 years consecutively referred for clinical treatment to UvA minds, a community academic child mental health center in Amsterdam. Participants were included in this study when (1) children had a clinical diagnosis of AD, ASD, ADHD combined subtype (ADHD-C), or ADHD inattentive subtype (ADHD-I), (2) at least one of the parents had completed one of the questionnaires, and (3) had no comorbid clinical diagnosis. In addition, a control group of typically developing children without a clinical diagnosis was added. In total, 270 children (M = 11.70, SD = 2.92) were included, of which 264 (97.8%) mothers and 231 (85.6%) fathers participated (98.8% biological parents; 21.1% of the families were divorced). In 225 (83.3%) cases, both parents completed the questionnaires.

Of the 270 children, 63 (23.3%) children were diagnosed with AD, 39 (14.4%) with ASD, 62 (23.0%) with ADHD-C, 64 (23.7%) with ADHD-I, and 42 (15.6%) children in the control group. Table 1 displays the demographics of the five groups. Groups differed in child age (F (4, 265) = 4.44, p = .002) and gender (χ^2 (4, N = 270) = 18.53, p = .001): children in the ASD and control group were significantly older than children in the ADHD-C group, and there were relatively more girls in the AD group than in the other groups. Groups did not differ in ethnicity (χ^2 (20, N = 270) = 16.54, p = .683) or parental age (mothers: F(4, 259) = 1.694, p = .152; fathers: F(4, 226) = 0.743, p = .563). Fathers did not differ in educational background, but mothers did (F (4, 253) = 9.030, p < .001): mothers of the control group had a lower educational background than mothers of the other groups (p values < .001).

Table 1 Demographics of Sample Categorized by Diagnosis

	TOTAL (N=270)		AD (n=63)		ASD (n=39)		ADHD-C (n=62)		ADHD-I (n=64)		Control (n=42)	
Gender boys (n, %)	182	67.4	31	49.2	32	82.1	50	80.6	42	65.6	27	64.3
Age child (M, SD)	11.70	2.92	11.73	0.33	12.49	0.57	10.60	0.33	11.58	0.38	12.71	0.39
Age mother (M, SD)	44.95	5.15	45.73	0.63	45.10	0.76	43.67	0.70	45.63	0.71	44.44	0.68
Age father (M, SD)	47.03	5.70	47.48	0.75	47.09	0.85	45.96	0.79	47.68	0.85	46.83	0.93
Ethnic background (n, % Dutch)	207	76.7	45	71.4	30	76.9	46	74.2	47	73.4	39	92.9
Educational level mother[a] (M, SD)	5.56	1.34	5.63	0.17	6.08	0.15	5.69	0.16	5.68	0.18	4.41	0.19
Educational level father[a] (M, SD)	5.59	1.45	5.48	0.23	5.91	0.19	5.90	0.18	5.39	0.23	5.26	0.22

[a]Range 1-7: 1 = Primary school; 7 = University

Procedure

Data was collected from May 2012 to May 2014 using online questionnaires that are part of the intake procedure of the treatment center. All participants were informed about the study, and ethical approval for the study as well as informed consent was obtained. Only children with an IQ > 70 are admitted at the treatment center. Children were excluded when a) their parents did not give informed consent; b) they were re-admitted and already participated in the study; c) one of their siblings participated in the study; d) diagnosis was not (yet) confirmed; e) they had a primary diagnosis other than AD, ASD, ADHD-C, or ADHD-I. Figure 1 shows the flow chart of the recruitment process. Moreover, when more than two parents were involved, only data from the biological parents was used. 356 children were eligible for this study based on their primary diagnosis of AD, ASD, ADHD-C, or ADHD-I. It was chosen to only include children without comorbid diagnoses because we wanted to be able to tease apart the possible differences between the disorders and the variables of interest (quality of life, parental psychopathology and parental stress). That is, if we allowed comorbidity in the groups, we could no longer make inferences about children with a particular disorder having a lower quality of life, or parents of children with a particular disorder having higher levels of stress or psychopathology, which was the main aim of this study. Therefore, 126 (35.6%)

children were excluded from analyses (38 AD, 29 ASD, 33 ADHD-C, 26 ADHD-I) because they had a comorbid diagnosis (AD, ADHD, ASD, mood disorders or oppositional defiant disorders). The excluded group did not differ from the included group in age, gender, parental psychopathology or parental stress. The groups did differ in terms of child psychopathology as reported by the father (included group had less total and internalizing problems on the CBCL, resp. $t(292) = 2.32$, $p = .021$; $t(293) = 3.02$, $p = .003$), and psychological wellbeing as reported by the father (included group had better psychological wellbeing, $t(285) = -2.24$, $p = .026$), but did not differ on any of the measures according to mother report (p-values > .10). Of the included children, 4.8% used medication at time of intake (methylphenidate, atomoxetine or dexamphetamine, used by 5.2% of the children with ASD; 4.8% ADHD-C; 9.4% ADHD-I), compared to 16.7% of the excluded children.

DSM-IV-TR diagnoses were made by a multidisciplinary team within the treatment center and were based on diagnostic assessments (including for example records on developmental history, observations, diagnostic interviews and psychological and/or psychiatric evaluations). In addition, a standardized interview was administered in nearly half of the cases (n=103); i.e. the ADIS-C/P (Silverman & Albano, 1996) for anxiety disorders and ADHD, and the ADOS (Lord, Rutter, Dilavore, & Risis, 1999) and/or ADI-R (Lord, Rutter, & Le Couteur, 1994) for ASD, that confirmed the diagnosis of the multidisciplinary team. In line with the clinical classification of subtypes of ADHD as defined in the DSM-IV-TR and DSM-5 (APA, 2000; APA, 2013, the ADHD group was divided into a group with children with both hyperactivity and inattention problems (ADHD-C) and a group with predominantly inattention problems (ADHD-I). Due to small sample size, children with ADHD predominantly hyperactive/impulsive type were excluded from the study.

Next to the clinical diagnosis assessment, we compared clinical groups on the Child Behaviour Checklist (CBCL) (Achenbach & Rescorla, 2001) to confirm their diagnosis by clinical profile. Differences on the CBCL subscales were examined using the same technique as the analyses described in the statistical analyses section. Table 2 shows the means on the different subscales. Children with AD had more anxiety problems and withdrawn behavior than children with ADHD and control children. Children with ASD showed more withdrawn behavior and social problems than AD children, while children with ADHD (and ASD) showed more attention problems as well as more externalizing behaviors (rule-breaking and aggressive behaviors) than AD children. Children in the control group were found to have lower scores than each of the clinical groups on every subscale. These findings

support the (DSM-IV-TR-based) distinction that is made in this sample between the four clinical groups and the control group.

Typically developing children were recruited by graduate students via schools, day care facilities, and convenience sampling. Children were excluded from the control group when their parents reported that they had a psychiatric diagnosis (DSM-IV-TR; (APA, 2000), or when they received (or had received) support or treatment from a child mental health care center in the past year. Low scores on the CBCL of the control group, comparable to those found in the general population (Bongers, Koot, van der Ende, & Verhulst, 2003), further supported the representativeness of the control sample.

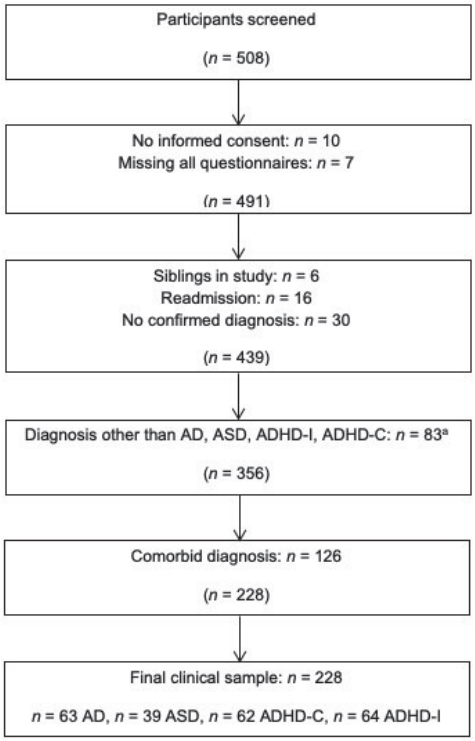

Figure 1. Flow chart of recruitment process clinical groups.

[a]Other diagnoses included: ADHD not otherwise specified (*n* = 23), ADHD predominantly hyperactive subtype (*n* = 7); oppositional defiant disorder (*n* = 5); mood disorders (*n* = 10); other disorder of infancy, childhood, or adolescence (*n* = 26); adjustment disorder (*n* = 2); other disorder (*n* = 10), including: body dysmorphic disorder (*n* = 1); dissociative disorder (*n* = 1), learning disorder not otherwise specified (*n* = 2), eating disorder (*n* = 1), tic disorder not otherwise specified (*n* = 4), undifferentiated somatoform disorder (*n* = 1).

Table 2 Means (M) and Standard Deviations (SD) of scores on CBCL and KIDSCREEN, Classified by Diagnosis

	AD	ASD	ADHD-C	ADHD-I	Control
	M (SD)	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*
CBCL					
Anxious	9.03 (5.25)	7.93 (4.42)	5.18 (3.61)$_a$	4.85 (3.83)$_a$	1.44 (2.32)$_a$
Withdrawn	4.35 (3.29)	7.07 (3.56)$_b$	2.28 (2.05)$_a$	3.37 (2.57)$_a$	1.18 (1.53)$_a$
Somatic	4.25 (3.29)	3.60 (3.08)	2.43 (2.41)$_a$	3.17 (3.02)	0.97 (1.40)$_a$
Social	4.51 (3.62)	7.16 (3.87)$_b$	5.35 (3.17)	3.80 (3.18)	0.96 (1.38)$_a$
Thought	5.39 (4.26)	6.41 (3.70)	4.54 (3.05)	4.19 (3.34)	1.24 (1.83)$_a$
Attention	5.58 (3.89)	8.70 (3.78)$_b$	11.20 (2.59)$_b$	10.75 (3.73)$_b$	3.58 (3.13)$_a$
Rule-breaking	2.02 (1.92)	3.82 (3.13)$_b$	4.64 (3.10)$_b$	2.81 (2.60)$_b$	0.85 (1.15)$_a$
Aggressive	6.30 (5.77)	10.27 (6.29)$_b$	12.56 (5.48)$_b$	7.00 (5.59)	2.42 (2.76)$_a$
KIDSCREEN					
Physical Well-being	49.41 (12.94)	46.52 (11.30)	54.87 (11.12)	51.13 (11.75)	57.77 (11.48)$_b$
Psychological Well-being	44.25 (11.77)	39.76 (9.69)	46.21 (10.03)	46.87 (7.24)	54.08 (9.16)$_b$
Autonomy and Parent Child Relations	52.57 (9.32)	50.40 (8.55)	50.46 (8.54)	50.52 (6.74)	56.24 (9.13)$_b$
Social Support and Peers	50.64 (11.44)	43.34 (11.47)$_a$	51.49 (8.44)	53.70 (8.70)$_b$	55.66 (6.76)$_b$
School Environment	49.57 (10.57)	45.14 (9.25)	43.01 (8.54)$_a$	43.01 (7.47)$_a$	54.15 (9.13)$_b$

Note. Groups are compared to the reference group of AD children. Subscripts indicate which group differs from the AD group: [a]Group has significantly lower score than AD; [b]Group has significantly higher score than AD.

Table 3 Means (M) and Standard Deviations (SD) of scores on ASR and NOSI, Classified by Diagnosis and Respondent

	AD		ASD		ADHD-C		ADHD-I		Control	
	M	F	M	F	M	F	M	F	M	F
	M (SD)	*M (SD)*	*M (SD)*	*M (SD)*	*M* (SD)	*M* (SD)	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*
ASR										
Total	33.74 (25.14)	28.54 (25.08)	28.97 (17.47)	32.85 (17.19)	37.39 (20.02)	32.87 (22.20)	42.37 (24.99)$_b$	33.35 (17.92)$_b$	22.78 (20.61)$_a$	13.73 (14.10)$_a$
Internalizing	12.24 (10.42)	10.10 (10.60)	9.28 (6.79)	9.45 (7.14)	11.93 (7.48)	9.33 (8.71)	14.24 (9.15)	9.35 (7.23)	7.87 (8.36)$_a$	3.36 (4.58)$_a$
Externalizing	7.11 (5.93)	6.04 (5.76)	6.36 (4.98)	9.06 (6.73)	9.03 (5.80)	8.54 (6.10)	8.65 (6.91)	9.33 (5.06)	4.26 (4.22)$_a$	3.29 (3.14)$_a$
NOSI										
Stress	54.66 (23.28)	53.22 (23.60)	72.71 (22.96)$_b$	75.63 (25.85)$_b$	74.10 (21.22)$_b$	64.46 (22.66)$_b$	59.18 (21.04)	51.82 (19.71)	43.54 (19.48)	39.87 (17.74)

Note. M=Mother; F=Father. Groups are compared to the reference group of AD children. Subscripts indicate which group differs from the AD group: [a]Group has significantly lower score than AD; [b]Group has significantly higher score than AD.

Instruments

Quality of life. Quality of life was measured with the KIDSCREEN-27 quality of life questionnaire (Ravens-Sieberer et al., 2006). This study used the proxy report, designed for parents. The KIDSCREEN-27 measures five dimensions: Physical Well-being (5 items); Psychological Well-being (7 items); Autonomy and Parent Child Relations (7 items); Social Support and Peers (4 items); and School Environment (4 items). An example item is: 'Did your child have the chance to talk to his/her parents when he/she wanted to?' (item of the Autonomy and Parent Child Relations scale). The items are scored on a 5-point scale ranging from 1 = *never/not at all* to 5 = *always*. Internal consistency values in this study range between .73 and .92 for mother reports, and between .78 and .89 for father reports.

Parental psychopathology. Parental psychopathology was assessed with the Adult Self Report (ASR) (Achenbach & Rescorla, 2003). The ASR measures a broad range of behavioral problems in adults and contains 123 items which are rated on a 3-point scale (0 = *not at all*, 1 = *sometimes*, 2 = *often*). An example item is: 'I cannot get along with other people'. A total problem scale is created by summing the score of all items. This study also used the two broad-band syndrome scales: internalizing and externalizing problems. Internal consistency values in this study range between .85 and .96 for mother reports and between .84 and .95 for father reports. Means and standard deviations are shown in Table 3.

Parental stress. Parental stress was assessed with the Nijmeegse Ouderlijke Stress Index Kort (NOSI-K) (De Brock, Vermulst, Gerric, & Abidin (1992), a short version of the Dutch version of the Parenting Stress Index (PSI). The NOSI-K consists of 25 items, which are rated on a six-point scale, ranging from 1 = *I completely disagree* to 6 = *I completely agree*. The NOSI-K is a short version of the NOSI (123 items) and is constructed by combining the 25 items with the highest factor loadings on the scale 'general parenting stress'. An example item: is 'My child is more demanding to me than most other children'. Internal consistency values in this study are .94 (mothers) and .95 (fathers). Means and standard deviations are shown in Table 3.

Statistical analyses

Multilevel analyses using maximum likelihood estimation procedures were used to examine group differences in child quality of life, parental psychopathology, and parental stress. Multilevel data analysis is used when data is nested, in this case mothers and fathers reported about the same child. Their reports were treated as repeated measures. An advantage of multilevel data analysis is that it does not

require complete data over measures, nor is there a need for equal numbers of cases in each group (Tabachnick & Fidell, 2012). Therefore, all available data is used in analysis, including those cases of which one parent did not participate. Moreover, multilevel analysis takes into account dependency among respondents, as both respondents in this study are nested within one child (grouping variable).

Each (sub)scale of the different measures (KIDSCREEN-27, ASR, NOSI-K) was used separately as a dependent variable in analyses. Prior to analysis, several univariate outliers were detected for each dependent variable ($-3.29 > z > 3.29$, $p < .001$). Outliers were trimmed to acceptable z-scores, and analyses were run with the original and adjusted data. There were no differences in outcomes; therefore, it was decided to report results of the analyses including outliers. No multivariate outliers were detected using Mahalonobis distance at $\alpha = .001$. Assumptions were checked for the residuals of the different models. Not all variables approached a normal distribution; however, transformations did not improve normality thus the original distributions were used.

Clinical groups were treated as dichotomous measures, by creating dummy variables, and the dummy variables of ASD, ADHD-C, ADHD-I, and the control group were used as predictors. The reference group in each analysis is the group of children with AD. The continuous variables were transformed into standardized scores. In this way the parameter estimates of the dummy variables can be interpreted as a measure of effect size (Cohen's *d*). Child age, child gender, and maternal education were added as covariates in analyses, in order to account for existing differences between the groups. Respondent (father versus mother) was added as a predictor as well, and interactions between respondent and clinical group were added to the model. When a significant interaction was found, additional analyses were run within the AD group and within the concerning other group with respondent as a single predictor, in order to interpret the interaction effect.

RESULTS

Quality of Life

Results indicated that (a) children with AD had a higher quality of life in school functioning compared to children with both types of ADHD, (b) children with AD had a higher quality of life in social functioning than children with ASD, but had a lower social functioning than children with ADHD-I, and (c) no significant

differences between AD and the other clinical groups on the other three domains (physical well-being, psychological well-being, and autonomy and parent child relations). In addition, children in the control group were reported to have a higher quality of life than all other children on all five dimensions except on the subscale social functioning where children in the control group did not differ from children with ADHD-I.

A significant interaction effect between respondent and ASD (compared to reference group AD) was found for the two domains psychological well-being and autonomy and parent-child relation, showing that fathers reported a higher quality of life for children with AD than mothers (resp. $\beta = .39$, $p = .006$ and $\beta = .41$, $p = .015$), but mothers and fathers reported comparable scores for children with ASD. Table 4 shows the parameter estimates, which indicate differences of the groups compared to the AD group: a positive parameter indicates a higher quality of life than the AD group, while a negative parameter indicates a lower quality of life than AD children.

Table 4 Parameter Estimates of the Models Concerning the KIDSCREEN Quality of Life Dimensions

	PHY	PSY	AUT	SOC	SCH
Predictors	*β (SE)*	*β(SE)*	*β (SE)*	*β (SE)*	*β (SE)*
Intercept	1.07** (.31)	-.49(.33)	.45 (.32)	.19 (.33)	.83* (.33)
ASD	-.22 (.19)	-.20 (.19)	-.07 (.19)	-.74** (.20)	-.29 (.19)
ADHD-C	.13 (.16)	.28 (.17)	-.17 (.16)	-.03 (.18)	-.64** (.16)
ADHD-I	.11 (.16)	.30 (.16)	-.18 (.16)	.39* (.18)	-.62** (.16)
Control	.84** (.20)	1.05** (.20)	.70** (.20)	.57** (.22)	.66** (.20)
RES	-.00 (.12)	.38** (.11)	.39* (.15)	.00 (.12)	.14 (.12)
AGE	-.09** (.02)	-.02 (.02)	-.03 (.02)	.00 (.02)	-.05** (.02)
GENDER	-.49** (.11)	-.24* (.12)	-.26* (.11)	-.27* (.12)	.16 (.12)
MEDU	-.01 (.04)	-.11* (.04)	-.01 (.04)	-.03 (.04)	-.02 (.04)
ASD*RES	-.21 (.19)	-.46** (.18)	-.50* (.24)	-.05 (.20)	-.12 (.18)
ADHD-C*RES	.24 (.17)	-.28 (.16)	-.32 (.22)	.15 (.18)	.02 (.16)
ADHD-I*RES	-.05 (.17)	-.14 (.16)	-.17 (.21)	-.23 (.17)	.01 (.16)
Control*RES	-.04 (.20)	-.51** (.19)	-.33 (.26)	-.17 (.21)	-.18 (.19)

*$p < .05$; **$p < .01$

Note. PHY = Physical Well-being; PSY = Psychological Well-being; AUT = Autonomy and Parent Child Relations; SOC = Social Support and Peers; SCH = School Environment; RES = Respondent: 0 = mother, 1 = father; Gender: 0 = boy, 1 = girl; MEDU = Maternal Education

Parental Psychopathology and Parental Stress

No differences in total parental psychopathology were found between parents of children with AD and parents of children with ASD and ADHD-C. However, parents of children with AD reported less psychopathology than parents of children with ADHD-I, and reported more psychopathology than parents of control children.

With respect to specific forms of parental psychopathology, parents of children with AD reported similar levels of internalizing and externalizing problems as parents of children with ASD and both types of ADHD. Furthermore, a significant interaction effect between respondent and ASD was found; additional analyses showed that fathers of children with ASD showed borderline significant more externalizing problems than mothers (β = .46, p = .061), whereas fathers and mothers of children with AD reported similar amounts of problems.

Parents of children with AD reported lower parental stress than parents of children with ADHD-C and parents of children with ASD. No differences in parental stress were found between parents of children with AD, ADHD-I and normal control children. Finally, a significant interaction effect between respondent and ADHD-C was found; additional analyses showed that fathers of children with ADHD-C showed less parental stress than mothers (β = -.40, p = .009), whereas fathers and mothers of children with AD reported similar amounts of parental stress. Parameter estimates are shown in Table 5, positive parameters indicate higher levels of parental psychopathology and stress compared to parents of the reference group of AD children, and negative parameters indicate lower levels of parental psychopathology and stress than parents of AD children.

Table 5 Parameter Estimates of the Models Concerning ASR Total Problems, Internalizing, and Externalizing Problems, and NOSI Parental Stress

	TOTAL	INT	EXT	STRESS
Predictors	*β*(SE)	*β*(SE)	*β* (SE)	*β*(SE)
Intercept	-.19 (.32)	.36 (.33)	-.15 (.30)	-.77* (.31)
ASD	-.16 (.21)	-.28 (.20)	-.11 (.20)	.77** (.18)
ADHD-C	.22 (.18)	.03 (.18)	.34 (.18)	.84** (.16)
ADHD-I	.40* (.18)	.25 (.18)	.27 (.17)	.18 (.16)
Control	-.56* (.23)	-.57** (.22)	-.53* (.22)	-.25 (.20)
RES	-.18 (.16)	-.18 (.15)	-.16 (.17)	-.06 (.13)
Age	.01 (.02)	.02 (.02)	.01 (.02)	-.02 (.02)
Gender	.12 (.11)	.12 (.11)	.02 (.10)	.14 (.11)
MEDU	-.06 (.04)	-.07 (.04)	-.05 (.04)	.12** (.04)
ASD*RES	.40 (.25)	.25 (.23)	.62* (.28)	.15 (.20)
ADHD-C*RES	.00 (.22)	-.09 (.21)	.09 (.25)	-.36* (.18)
ADHD-I*RES	-.21 (.22)	-.37 (.20)	.27 (.24)	-.20 (.18)
Control*RES	-.16 (.27)	-.31 (.25)	.02 (.29)	-.09 (.22)

*$p < .05$; **$p < .01$

Note. TOTAL = Total problems; INT = Internalizing Problems; EXT = Externalizing Problems; STRESS = Parental Stress; RES = respondent: 0 = mother, 1 = father; Gender: 0 = boy, 1 = girl; MEDU = Maternal Education

DISCUSSION

The goal of this study was to compare families of children with AD to families of children with ASD, ADHD-C, ADHD-I, and a control group on child quality of life, parental psychopathology and parental stress. Most important findings can be summarized as follows: (a) Children with AD had a lower quality of life than typically developing children, a higher quality of life than children with ASD on the domain social functioning, and a higher quality of life than children with both types of ADHD on the domain school functioning, but did not differ from the other clinical groups on physical well-being, psychological well-being and autonomy and parent-child relation; in addition, fathers of AD children reported higher quality of life than mothers on the domains psychological well-being and autonomy and parent-child relation; (b) parents of children with AD had less psychopathology than parents of children with ADHD-I, but more than parents of typically developing children, and did not differ in psychopathology from parents of children with ADHD-C and ASD; (c) no evidence for specificity was found: parents of children with AD reported similar levels of internalizing and externalizing problems as parents of children with

ASD and both types of ADHD; (d) parents of children with AD experienced less parental stress than parents of children with ASD and ADHD-C, but did not differ in parental stress from parents with ADHD-I and parents of the control group; and (e) mothers and fathers of AD children reported comparable levels of parental stress, in contrast to fathers of ADHD-C children who reported less parental stress than mothers.

First, this study showed that clinically referred children with AD are as impaired in parent-reported quality of life as children with other clinical diagnoses in three out of five domains. However, for two domains a significant difference was found, which contrasts the findings of Bastiaansen et al., (2004) and Thaulow and Jozefiak (2012) that AD children do not seem to differ from children with ADHD, except for emotional functioning (Bastiaansen et al., 2004). This may have to do with the lack of comorbid disorders in the current sample and/or the different instrument used to measure quality of life. Although not reflected in quality of life, these studies did find lower academic performance in ADHD compared to AD (Bastiaansen et al., 2004; Thaulow & Jozefiak, 2012), which could explain the difference in school functioning between these groups that was found in the current study. More specific, we found that children with AD had higher scores with respect to their school functioning than children with both types of ADHD and children with ASD. It is interesting that problems of children with AD seem to interfere less with their school functioning when compared to other clinical groups (however, note that the control group had a significantly higher quality of life in the domain of school functioning than children with AD). This is in line with the finding of Weitkamp, Daniels, Romer, & Wiegand-Grefe (2013) that externalizing, but not internalizing, psychopathology was associated with low functioning at school. Moreover, our findings are also in line with the finding that children with AD are found to be impaired in school functioning, although children with a comorbid externalizing disorder show the greatest impairment (Mychailyszyn, Méndez, & Kendall, 2010). In addition, children with AD had a better social functioning than children with ASD, which is in line with the clinical presentation of ASD (APA, 2013) and the finding that children with ASD have a poorer quality of life than children with other clinical diagnoses (Bastiaansen et al., 2004). Concluding, AD children are impaired in quality of life compared to normal controls, but show fewer impairments in school and social functioning than children with ADHD-C and ASD respectively. It may be that the severity of the disorder (or the severity of particular symptoms of the disorder) plays a role in how well children function in each quality of life domain. For example, severity of attention problems (especially seen in ADHD; Barry, Lyman,

& Klinger, 2002) may account for larger impairments in school, while more social skills problems (often seen in ADHD and ASD; Luteijn et al., 2000) may be related to more social functioning impairments. Indeed, severity of anxiety and autistic problems were related to a lower quality of life in the study of Van Steensel et al. (2012). In this respect, it may be interesting for future studies to measure disorder severity and/or symptom severity and investigate how it relates to each domain of quality of life.

Although no differences between the AD group and the other clinical groups were found, an interesting finding was that fathers of children with AD reported a higher quality of life compared to mothers on both psychological well-being and autonomy and parent relations. Earlier research into informant agreement on quality of life among children with different psychiatric disorders using the KIDSCREEN-27 found moderate correlations between father-mother agreement, but did not find fathers and mothers to differ in their child reports (Weitkamp, Daniels, Rosenthal, Romer, & Wiegand-Grefe, 2013). However, they did not examine agreement for each separate clinical group. It is possible that the same mechanism for the difference in reports of internalizing problems is underlying the difference in quality of life, that is, mothers spending more time with their child and thus being more aware of internalizing problems (Treutler & Epkins, 2003). Alternatively, father involvement in raising children has increased and it could also be that fathers' perception of their child differs from mothers' perception (Bögels & Phares, 2008; Krain & Kendall, 2000). Tentatively, viewing the child as less impaired may serve fathers' role of helping their child overcome anxiety by challenging the child (e.g., Bögels & Perotti, 2011). That is, if fathers would view their child as highly impaired they would have more difficulty challenging the child to explore new territory and cross their own borders. However, more research into the (different) perspective of mothers and fathers regarding their child's quality of life and whether it is dependent on the child's clinical diagnosis is necessary before firm conclusions can be drawn.

With respect to parental psychopathology, this study does not support a specific link between child and parental internalizing problems as parents of children with AD reported no elevated levels of internalizing problems themselves compared to parents of the other clinical groups, which is in contrast with previous studies (Beidel & Turner, 1997), but in line with a recent study that found little evidence of specificity in offspring mental disorders (McLaughlin et al., 2012). This study also found that parents of children with AD experience more psychopathology themselves than parents of typically developing children, suggesting that child and

parental psychopathology are related. Moreover, no differences were found in parents own psychopathology reports between fathers and mothers from each clinical group. This is in line with earlier research (Middeldorp et al., 2016), and underlines the importance of both fathers' and mothers' contribution to child psychopathology and/or the child's psychopathology affecting both fathers and mothers equally in terms of their own psychopathology.

This study found that levels of parental stress are lower among parents of children with AD as compared to ASD and ADHD-C. In addition, parents of AD children did not differ in parental stress from parents of children with ADHD-I and the control group. Thus, in contrast to previous findings (Vaughan et al., 2013), it seems that the externalizing behavior of children with ASD and ADHD-C is more associated with parental stress than the internalizing behavior of the children with AD. Research to date indicates that maternal stress (paternal stress was not investigated) is associated with children's both anxious and depressive symptoms (Rodriguez, 2011) as well as externalizing problems (Barry, Dunlap, Cotton, Lochman, & Wells, 2005), but does not provide enough evidence for differences in parental stress between internalizing and externalizing disorders. However, it is possible that stress levels experienced by parents may include different domains; e.g., parenting a child with internalizing problems may lead to parental stress concerning parent-child interactions, while parenting a child with externalizing problems may lead to parental stress concerning raising a difficult child (Vaughan et al., 2013). Finally, this study did not find differences between both parents' reports regarding parental stress, which implies that fathers experience equal levels of stress as mothers while raising children with psychopathology, and thus suffer as much, and/or affect their children as much with their stress.

Strengths of this study were that (a) this study was one of the first to estimate the impact of childhood AD associated with child and parental factors, in comparison to other diagnostic groups and a control group of children without a clinical diagnosis, (b) reports from both mothers and fathers on each of the measures were included, (c) this study included clinically referred children and thus groups were based on DSM-IV-TR diagnoses instead of symptomatology, and (d) multilevel data analysis was used to address the dependent structure of the data. Limitations of this study also need to be addressed. First, as parents were the sole reporters about their child's quality of life, their own emotional-behavioral problems and their levels of stress, it might be that the relations between these variables are overestimated because of distortion: parents' own symptoms (and/or parental concern) influence

their reports of their child's behavior and can account for discrepancies between parents' reports (Treutler & Epkins, 2003). Moreover, the lack of an independent measure of quality of life potentially biased this study's results, because results are now solely based on parental perception of the child's quality of life. Future studies should include objective quality of life indicators in order to account for this bias. In addition, the difference in recruitment procedures between the clinical and control group potentially biased the current results; i.e., it is possible that the control group had a higher quality of life because they were not treatment-seekers. Next, this study included children with a single diagnosis, in order to avoid measuring shared symptoms due to comorbidity and to be able to state which diagnoses differed from each other in terms of quality of life, parental psychopathology, and parental stress. Nevertheless, differences in CBCL scores still showed comorbidity on a symptom level, indicating overlap in symptoms between clinical diagnoses. Moreover, comorbidity on a diagnosis level is frequently present in clinical practice, and excluding this group makes the generalizability of our findings to routine clinical practice limited. At the same time, note that (1) comorbidity in symptoms is different from comorbidity in diagnosis (e.g., not impairing for daily functioning, no target for treatment), (2) the CBCL scores for the different clinical groups followed the expected clinical profile (see Table 2), indicating valid differences in symptom profiles between diagnoses, and (3) the excluded comorbid group did not differ in (mother-reported) child psychopathology, quality of life, parental stress and psychopathology. Finally, considering the cross-sectional design of this study, no conclusions can be drawn on the direction of the association between child psychiatric diagnosis and parents' problems. Therefore, it is not possible to disentangle to what extent higher reports of behavioral problems among parents of the clinical groups reflect the burden of parenting a child with a psychiatric disorder, or to what extent more psychopathology in parents causes more child problems in general. Likely, the relation is bidirectional: parents with behavior problems influence their child's behavior, next to heritability (Hettema et al., 2001), and children with behavioral problems influence parents' behavior problems and stress; however, more research is needed.

Despite these limitations, this study points out that the quality of life of children with AD is less impaired on school and social functioning compared to children with ADHD and ASD; although their quality of life is lower than typically developing children. Moreover, childhood AD are associated with less parental psychopathology and stress than children with ADHD and ASD. By selecting subjects based on diagnosis, we were able to examine impairments in daily life and

family functioning specific to each diagnostic group. This information could help the community to better understand the impact of different diagnoses on children and their families and could help clinicians adjust child interventions and parental guidance. Although dimensional measurement of psychopathology is becoming more popular (see DSM-5; APA, 2013), treatment decisions and reimbursement are still mostly guided by categorically measured diagnoses rather than symptoms, which is why we chose diagnosis rather than symptoms as our selection criterion. It could be that parental factors are less associated with children with AD compared to children with neurobiological or externalizing disorders, and/or that having a child with AD is less severe compared to having a child with ADHD-C or ASD. Future research should disentangle the bidirectional relation between parent factors and children referred with mental disorders, comparing different mental disorders. Our findings may also suggest that parental factors need to be considered in child treatment (e.g., focus on parental stress management), and perhaps may need to be considered more in children with ADHD/ASD than in children with AD.

SUMMARY

Anxiety Disorders (AD) in children are associated with functional child and parental impairment; however, the severity of AD, compared to other common child mental disorders, is unclear. This study compared children referred with AD to children with ASD, ADHD-C, ADHD-I, and a control group on both child and parental factors. It was found that the quality of life of children with AD is less affected in school and social functioning than children with other clinical diagnoses; however, their quality of life is lower than typically developing children on all domains. In addition, parental psychopathology of children with AD was higher than typically developing children, but lower than children with ADHD-I. Interestingly, parental stress of parents of AD children did not differ from parents in the control group and parents of ADHD-I children, and was lower than that of parents of children with ASD and ADHD-C. The direction of the findings remains to be investigated, that is, childhood AD impacts parental functioning less, is less caused/maintained by parental functioning, or both. Parental factors may need to be considered more in treatment of children with ADHD/ASD than AD.

What are the Odds of Anxiety Disorders Running in Families?

A Family Study of Anxiety Disorders in Mothers, Fathers, and Siblings of Children with Anxiety Disorders

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ABSTRACT

This family study investigated (1) the prevalence of anxiety disorders (ADs) in parents and siblings of children (*n* = 144) aged 8-18 years with ADs compared to control children (*n* = 49), and (2) the specificity of relationships between child-mother, child-father, and child-sibling ADs. Clinical interviews were used to assess current DSM-IV-TR ADs in children and siblings, and lifetime and current ADs in parents. Results showed that children with ADs were two to three times more likely to have at least one parent with current and lifetime ADs than the control children (odds ratio (OR) = 2.04 and 3.14). Children with ADs were more likely to have mothers with current ADs (OR = 2.51), fathers with lifetime ADs (OR = 2.84), but not siblings with ADs (OR= 0.75). Specific relationships between mother-child ADs were found for Social Anxiety Disorder (SAD, OR = 3.69) and Generalized Anxiety Disorder (OR = 3.47). Interestingly, all fathers and siblings with SAD came from families of children with SAD. Fathers of children with SAD were more likely to have lifetime ADs themselves (OR = 2.86). Findings indicate that children with ADs more often have parents with ADs, and specifically SAD is more prevalent in families of children with SAD. Influence of parent's (social) ADs should be considered when treating child ADs.

Keywords: Anxiety disorders; Children; Parents; Siblings; Family

WHAT ARE THE ODDS OF ANXIETY DISORDERS RUNNING IN FAMILIES?
A FAMILY STUDY OF ANXIETY DISORDERS IN MOTHERS, FATHERS, AND SIBLINGS OF CHILDREN WITH ANXIETY DISORDERS

One of the well-examined features of anxiety disorders (ADs) is that they tend to 'run in families' and are transmitted from parents to children (Murray, Creswell, & Cooper, 2009). So far, evidence is available that this can partly (30-40%) be attributed to biological/genetic markers (Hettema, Neale, & Kendler, 2001). However, a recent study in a large sample of children of twins found evidence for direct environmental transmission of ADs from the parent to the child, which could imply that parental anxiety shapes the way for a parenting style that contributes to the development of ADs in children (Eley et al., 2015). One of these parenting styles is over-controlling behavior, which limits children's autonomy, and could maintain their inhibition and anxiety. Moreover, children's anxious behavior could also evoke parents over-controlling parenting behavior in order to prevent distress in their child (Bögels & Brechman-Toussaint, 2006). In addition, parents' anxious behavior and expressed anxiety could also promote and maintain child anxiety through modeling, i.e. catastrophizing and over-attribution of threat (Bögels & Brechman-Toussaint, 2006; Murray et al., 2009; Rapee, 2012). Together this shows that the development and maintenance of ADs in children are a result of genetic, environmental and parenting factors.

In order to inform our understanding of the etiology, prevention and treatment of child ADs, it is important to know to what extent parents of children with ADs have ADs themselves. It has been shown that children with ADs did less well in treatment when their mothers had ADs (Cooper, Gallop, Willets, & Creswell, 2008), and CBT for children with AD is less effective when parents have an AD themselves (Bodden et al., 2008). Numerous studies have examined the familial risk of ADs; however, most used a top-down approach (i.e., examining the presence of ADs in the offspring of parents with ADs; Beidel & Turner, 1997; Hettema et al., 2001; Merikangas, Dierker, & Szatmari, 1998). Another way to examine transmission of ADs is to use a bottom-up approach: evaluating the presence of ADs in parents of children that are diagnosed with ADs.

Bottom-up studies have shown increased rates of ADs in parents of children referred with ADs compared to parents of typically developing children, with lifetime prevalence rates ranging between 46-83% in mothers, and between

30-45% in fathers (Liberman & Öst, 2016; Cooper, Fearn, Willetts, Seabrook, & Parkinson, 2006; Hughes, Furr, Sood, Barmish, & Kendall, 2009; Last, Hersen, Kazdin, Francis, & Grubb, 1987), compared to 15-38% in parents of typically developing children. While these initial studies were valuable in terms of examining the associations between child and parental ADs, it should also be noted that some of these studies included participants diagnosed with DSM-III disorders (Last et al., 1987; Last, Hersen, Kazdin, Orvaschel, & Perrin, 1991), had low father participation and/or did not use a diagnostic instrument to assess fathers' clinical status (Liberman & Öst, 2016; Cooper et al., 2006; Last et al., 1987), or lacked a control group (Liberman & Öst, 2016). In addition, an important aspect that was not addressed in these studies is the prevalence of ADs in siblings.

To determine familial transmission of ADs and to understand the mechanisms behind it, it is important to include the whole family. Recently, fathers are more often included in child anxiety research, and it has been suggested that fathers' ADs contribute differently to the development of child anxiety than mothers, for example father's role in physical play may be affected more by his own anxiety (disorders) than mother's role of caring (Bögels & Phares, 2008; Bögels & Perotti, 2011). Nevertheless, associations between mother-child ADs seem to be stronger than father-child ADs, with odds ratios of lifetime ADs found between 3.40 – 4.44 for mothers and odds ratios between 2.33 – 3.17 for fathers (Cooper et al., 2006; Hughes et al., 2009). However, Last et al. (1991) found twice as many ADs in fathers and brothers (male relatives combined) of children with ADs than in control children, and no difference in mothers' prevalence, but note that father participation was low in the group of children with ADs (38%). To conclude, the relative risks of mothers versus fathers of children referred with ADs being affected by own ADs need to be established in studies in which no more fathers are missing than mothers, in order to draw valid conclusions, as missing fathers are likely to be systematically missing (e.g., because of divorce, anxiety disorders, or busy in the outside world; Bögels & Perotti, 2011).

Next to the increased prevalence of ADs in mothers and fathers, siblings of children with mental health problems are at risk of developing psychopathology themselves (Ma, Roberts, Winefield, & Furber, 2015). However, it is unclear whether they develop an AD more often than siblings of typically developing children. Only a few studies examined the prevalence of ADs in siblings of anxious children (Dia & Harrington, 2006; Helenius, Munk-Jørgensen, & Steinhausen, 2014; Last et al., 1991; Li, Sundquist, & Sundquist, 2011). The study of Dia and Harrington (2006)

showed that 12% of siblings of children with ADs had a (mostly mother-reported) diagnosis of AD, but this study did not include a control group and two other studies examining anxiety in siblings lacked a DSM-based diagnostic assessment (Helenius et al., 2014; Li et al., 2011). One study did use a control group and a diagnostic instrument (but based on DSM-III), and found that siblings of children with ADs were about twice as likely to have ADs as siblings of typically developing children (Last et al., 1991).

In addition to the intergenerational transmission of ADs, it is interesting to examine to what extent there is diagnostic specificity in this transmission. Diagnostic specificity suggests that children of anxious parents are at greater risk of developing the same AD as their parents, because their parents, next to heritability aspects (Hettema et al., 2001), model or communicate their specific anxieties to their children (Hughes et al., 2009). A better understanding of the specificity of the transmission of ADs could inform child treatment or preventive interventions. In previous studies, some evidence has been found for specificity of social anxiety disorder, separation anxiety disorder and panic disorder between child and mother, but not between child and father (Cooper et al., 2006; Hughes et al., 2009). Otherwise, other studies found strong associations between parental social phobia and social phobia in their adolescent children (odds ratio = 4.7; Lieb et al., 2000). In addition, specificity in siblings was found for agoraphobia and social phobia (Li et al., 2011), although those ADs were not measured with a diagnostic instrument but based on clinical judgment. In contrast, other studies did not find evidence for specificity, thus providing support for a transmission of anxiety in general and not for specific ADs, which implies that ADs have shared etiology (Eley et al., 2015; Cooper et al., 2006). Thus, only few studies have studied specificity of ADs between family members and those studies that did, found contrasting results.

Finally, considering the comorbidity between ADs and depressive disorders (Brown, Campbell, Lehman, Grisham, & Mancill, 2001), parents of children with ADs may be more likely to have depressive disorders than parents of children without ADs. Bottom-up studies have found mixed results, as Cooper et al. (2006) found that children with ADs were more likely to have mothers with current and lifetime depressive disorder than children without anxiety disorders, whereas Last et al. (1991) and Hughes et al. (2009) did not find that parents of children with ADs were at increased risk for lifetime mood disorders. In addition, stronger associations have been found between ADs in children and parents than between ADs in children and depressive disorders in parents (Beidel & Turner, 1997). Moreover, it remains

unclear whether children with ADs have an elevated risk of having parents with depressive disorder, or that this is mainly due to an elevated risk of ADs in parents with comorbid depressive disorder (Hirshfeld-Becker et al., 2012). Thus, it is important to consider comorbid depressive disorder in parents when examining ADs in parents of children with ADs.

The main aim of the current study was to examine the transmission of ADs in the family using a bottom-up approach, in order to understand to what extent children with ADs grow up with parents and siblings with ADs. Establishing the risk for ADs in mothers, fathers, and siblings of referred children with ADs is important for our understanding of the etiology, prevention, and treatment of child ADs. In this study, we examined the association between ADs in a clinically referred sample of children with ADs, their mothers, fathers, and siblings, using diagnostic interviews, and we compared these rates to a control group of typically developing children. We hypothesized that mothers, fathers, and siblings of children with ADs would be more likely to have ADs than families of typically developing children. Additionally, given that parental depression has been associated with the development of child ADs, we examined the association between depressive disorder in parents of children with AD and parents of children in the control group. Finally, we examined specificity of transmission, i.e. whether a specific AD in the child (e.g., SAD) would be associated with the same AD (SAD) in the parent or not; and familial risk of specific ADs, i.e. whether children with a specific AD (e.g., SAD) would be more likely to have parent(s) and/or siblings with any AD, compared to children with other ADs.

METHOD

Participants and procedure

In total, 193 children participated: 144 children with ADs and 49 typically developing children (further referred to as controls). Reports were present from 191 (99.0%) mothers and 172 (89.1%) fathers. In total, 162 families (83.9%) had more than one child (total number of siblings = 239). Out of the 239 siblings, 168 siblings from 123 (75.9%) families participated; of those who did not participate, 33 siblings (13.8%) did not fulfill the age range of 7-23 years, 4 siblings (1.7%) did not live at home anymore, and 44 siblings (14.2%) did not want to participate or were unable to be reached. Table 1 shows the characteristics of both groups.

Participants were drawn from a sample of children recruited for a study on the relation between anxiety and parental rearing (Bögels, Bamelis, & van der Bruggen, 2008), and most were enrolled in a study on the efficacy of CBT (see Bodden et al., 2008 for inclusion criteria). A community sample of control children was recruited through advertisements in journals and magazines and received a €50 fee (Bodden et al., 2008). Children were included if they did not receive any support from a child mental health care center. Note however that eight controls (16.3%) met the criteria for an AD on the Anxiety Disorders Interview Schedule-Child and Parent Versions (ADIS-C/P; Silverman & Albano, 1996) (see Table 2). It was decided to keep these children in the control sample, as this percentage does not deviate from prevalence rates found in other studies of typically developing children (Costello, Egger, & Angold, 2005). Moreover, in practice only 30% of children that have an AD are referred to mental health care centers and referral is associated with the impairment of the child (Chavira, Garland, Yeh, McCabe, & Hough, 2009; Jongerden, Simon, Bodden, Dirksen, & Bögels, 2015). Of note, analyses were performed with and without these children and are reported in the results section.

Clinical interviews were carried out by trained psychology research assistants, who had received 2 days training from the authors of the Dutch translation of the ADIS-C/P (Siebelink & Treffers, 2001). Their diagnostic ratings had to match those of experienced interviewers from Temple University. Moreover, each research assistant videotaped four of her own interviews, which were rerated by two trained students. The total interrater agreement for all ADIS diagnoses (κ) was based on the presence or absence of the specific anxiety disorder; ADIS-Child report 0.89, ADIS-Parent about child report 0.83, and ADIS-Adult report 0.94. The interviewer was blind to the goals of this study. Medical-ethical approval was obtained, and all participants signed informed consent.

Table 1 Demographics of Participants

	Children with ADs (n = 144)	Controls (n = 49)
Age (M, SD)	12.38 (2.71)	12.44 (2.63)
Number (%) of boys	57 (40.6%)	21 (44.7%)
Married families (n, %)	113 (78.5%)	35 (71.4%)
Parental age (M, SD)		
Mother	41.95 (4.92)	42.58 (5.51)
Father	44.97 (5.04)	44.77 (5.40)
Parental educational level[1] (M, SD)		
Mother**	5.06 (1.96)	6.17 (1.81)
Father*	5.69 (2.03)	6.44 (2.02)
Siblings	n = 130	n = 38
Age**	13.90 (4.16)	11.86 (2.83)
Number (%) of boys*	62 (48.1%)	25 (67.6%)

*$p < .05$, **$p < .01$

[1] On a scale of 1 (no education) to 9 (university).

MEASURES

Anxiety disorders children and siblings. Anxiety disorders for children and siblings were assessed with the ADIS-C/P (Silverman & Albano, 1996), which follows criteria of the DSM–IV (APA, 2000). The interview was conducted separately with the child and with both parents together when the parents reported about their child(ren). Father and mother reported separately about their own ADs. The interview starts by examining symptoms of ADs, and when this symptom criterion is fulfilled, the respondent is asked to rate the impairment for daily functioning on a 0 – 8 point scale. When a score of 4 or higher is given, then an AD is assigned. Child and parent interview scores were aggregated based on recommendations of the manual in which the aggregated rating consisted of a composite score of the combined parent and child interview (Silverman & Albano, 1996). Psychometric properties of the ADIS-C/P are good (Silverman, Saavedra, & Pina, 2001). Interrater reliability for this sample was high, total interrater agreement (kappa) was .89 for child report, and .83 for combined parent report (Bögels et al., 2008).

Anxiety disorders parents. Parents' ADs were assessed with the ADIS-IV-L (DiNardo, Brown, & Barlow, 1994) which is a structured interview that assesses DSM-IV disorders. Both current and life-time diagnoses were gathered from the

interview. In the interview, symptoms of disorders are checked, and when all criteria were met an impairment rating (on a scale 0-8) was given. A rating of 4 or higher indicates a diagnosis. Psychometric properties of the ADIS-IV-L are good (Brown, DiNardo, Lehman, & Campbell, 2001) and interrater reliability for this sample was high (0.94; Bögels et al., 2008).

Statistical analyses

First, odds ratios for the clinically anxious children against controls were calculated for the risk of (1) having a parent (father and/or mother) with AD(s), (2) having a mother with AD(s) (3) having a father with AD(s), and (4) having a sibling with AD(s). Siblings were assigned to have an AD when one or more of the siblings had at least one AD (due to the small number of children with 2 or more siblings, data for siblings from the same family were collapsed). Second, odds ratios for the clinically anxious children against controls were calculated separately for having a mother or father with lifetime or current depressive disorder. Logistic regression was used to estimate the odds ratios, with group (children with ADs versus controls) as predictor and mother, father, or sibling AD as the dichotomous dependent variable. Parental education level was used as a covariate in the analyses because parents of children with ADs were found to have a lower educational level than parents of controls, and sibling age in the comparison of siblings of both groups. Wald test was used to evaluate predictors, and, in line with our hypotheses, *p*-values were divided by two because of one-sided testing (Ludbrook, 2013). Odds ratios were calculated to examine the strength of the effect; the closer the odds ratio is to 0, the smaller the effect (Tabachnick & Fidell, 2012).

Second, following the study of Hughes et al. (2009), the hypothesis of specific AD in families was tested within the group of children with ADs. Two approaches were used. In favor of the specificity hypothesis (Hughes et al., 2009), odds ratios for each specific AD was calculated using logistic regression with the parent/sibling AD as the dependent variable, and the specific child AD as the predictor (e.g. child GAD versus no GAD predicting parent GAD). In favor of a more familial risk of ADs, odds ratios for the risk of parents/siblings having ADs was calculated using logistic regression with the presence of ADs as the dependent variable, and the specific child AD (e.g., SAD, GAD) as the predictor. Wald test was used to evaluate predictors using two-sided testing, as specificity of ADs was an explorative question.

For the specificity analyses, maternal, paternal and sibling anxiety was assessed within the group of anxious children for five groups with the most prevalent child AD: Social Anxiety Disorder (SAD), Generalized Anxiety Disorder (GAD), Specific Phobia (SP), Separation Anxiety Disorder (SEP), and Panic Disorder/Agoraphobia (PAG). Due to high comorbidity among ADs (Brown et al., 2001; Costello et al., 2005), which was also seen in the present study (see Table 2), odds ratios were calculated regardless of comorbidity. Thus, for example, the risk of SAD in mothers of children with SAD was calculated, regardless whether the child or mother had other ADs. In a few cases, one of the cells contained zero and therefore odds ratios could not be calculated. In those cases, a description of the prevalence rate instead of an odds ratio is given.

Table 2 Prevalence of Lifetime Anxiety Disorders of Families of Children Referred with ADs and Typically Developing Children

	Children referred with ADs (n = 144)								Typically Developing Children (n = 49)							
	Child		Mother (n = 134)		Father (n = 124)		Siblings (n = 130)		Child		Mother (n = 49)		Father (n = 38)		Siblings (n = 38)	
	N	%	N	%	N	%	n	%	n	%	n	%	N	%	n	%
Any AD	144	100	73	54.5	36	29.0	34	26.2	8	16.3	20	40.8	4	10.5	12	31.6
SAD	99	68.8	37	27.6	15	12.1	15	11.5	2	0	8	16.3	4	10.5	6	15.8
GAD	74	51.4	28	20.9	18	14.5	13	10.0	1	4.1	8	16.3	1	2.6	3	7.9
SP	83	57.6	48	35.8	14	11.3	17	13.1	6	12.2	4	8.2	0	0	8	21.1
PAG	32	22.2	30	22.4	14	11.3	2	1.5	0	0	4	8.2	0	0	0	0
SEP	62	43.1					4	3.1	0	0					0	0
OCD	7	4.9	3	2.2	2	1.6	3	2.3	0	0	1	2.0	0	0	0	0
PTSD	8	5.6	15	11.2	3	2.4	2	1.5	0	0	2	4.1	0	0	0	0
Average number of ADs	M 2.53	SD 1.28	M 0.95	SD 1.06	M 0.5	SD 0.92	M 0.44	SD 0.75	M 0.18	SD 0.44	M 0.49	SD 0.68	M 0.03	SD 0.16	M 0.48	SD 0.64

Note: AD = Anxiety Disorder, SAD = Social Anxiety Disorder, GAD = Generalized Anxiety Disorder, SP = Specific Phobia, PAG = Panic Disorder and Agoraphobia, SEP = Separation Anxiety Disorder, OCD = Obsessive Compulsive Disorder, PTSD = Posttraumatic Stress Disorder

RESULTS

Odds ratios for ADs running in the family

The prevalence of ADs for mothers, fathers and siblings is shown in Table 2. Having ADs as a child raised the odds of having at least one parent with (1) lifetime AD(s) (OR = 2.04, 95% CI = 1.02–4.06, p = .022), and (2) current ADs (OR = 3.14, 95% CI = 1.34–7.35, p = .005). Inspecting fathers and mothers separately, children with AD were not more likely to have mothers with lifetime AD(s) than controls (OR = 1.29, 95% CI = 0.63–2.63, p = .244), but more likely to have mothers that met criteria for current AD(s) (OR = 2.51, 95% CI = 1.01–6.21, p = .024). Children with ADs were significantly more likely to have fathers with lifetime AD(s) (OR = 2.84, 95% CI = 0.92–8.75 p = .035) and borderline more likely to have fathers with current AD(s) (OR = 4.12, 95% CI = 0.51–33.31, p = .092) compared to controls. Finally, children with ADs were not more likely to have siblings with AD(s) than controls (OR = 0.75, 95% CI = 0.29–1.93, p = .273).

Additionally, the prevalence of depressive disorder in the parents was examined. Lifetime depressive disorder was present in 29.9 % of the mothers and 13.7% of the fathers in the clinical group; in the control group 26.5% of the mothers had depression and 13.2% of the fathers. Results showed that children with ADs were not more likely to have mothers with lifetime depressive disorder (OR = 1.00, 95% CI = 0.45–2.21, p = .499), and also not more likely to have fathers with lifetime depressive disorder (OR = 1.15, 95% CI = 0.38–3.44, p = .403) than controls. For current depressive disorder, a trend towards significance was found for mothers of children with AD compared to children of the control group (OR = 5.35, 95% CI = 0.67–42.65, p = .057), and no difference between children with ADs and controls was found for fathers (OR = 0.26, 95% CI = 0.03–1.99, p = .097).[1]

1 Additionally, the same analyses were performed with the 41 children of the control group without ADs. When leaving the children with ADs out of the control group, results did not change for having at least one parent with lifetime AD(s): (OR = 2.18, 95% CI = 1.03–4.62, p = .022), having at least one parent with current AD(s) (OR = 3.27, 95% CI = 1.25–8.55, p = .008), mothers' lifetime AD(s) (OR = 1.40, 95% CI = 0.64–3.07, p = .200), mothers' current AD(s) (OR = 2.84, 95% CI = 1.00–8.05, p = .025), fathers' current ADs (OR = 3.17, 95% CI = 0.39–25.91, p = .141), and siblings' AD(s) (OR = 0.74, 95% CI = 0.27–1.99, p = .274). The only change observed was for fathers' lifetime AD(s), which became a trend to significance (OR = 2.37, 95% CI = 0.76–7.41, p = .070). When leaving the children with ADs out of the control group, results did not change for mothers' lifetime depressive disorder (OR = 1.13, 95% CI = 0.47–2.74, p = .393), fathers' lifetime depressive disorder (OR = 0.99, 95% CI = 0.32–3.01, p = .491), mothers' current depressive disorder (OR = 4.17, 95% CI = 0.51–34.03, p = .092), and fathers' current depressive disorder (OR = 0.20, 95% CI = 0.03–1.59, p = .064).

Specificity and familial risk

Table 3 displays the results regarding parents' and siblings' risk for a specific (same) AD as predicted by the child's specific AD. It was found that family members of children with SAD were more likely to have SAD themselves, that is (1) children with SAD were more likely to have mothers with lifetime SAD than children with other ADs (OR = 3.69, 95% CI = 1.20–11.40, p = .023), (2) odds ratios could not be calculated for father-child SAD because all fathers with lifetime SAD (17.4%, n = 15) had children with SAD, and (3) no odds ratios could be calculated for sibling-child SAD because all siblings with SAD (22.4%, n = 15) were from families with children with SAD. Finally, there was evidence of specificity for GAD: children with GAD were more likely to have mothers with lifetime GAD compared to children with other ADs (OR = 3.47, 95% CI = 1.28–9.41, p = .014). No specific risk was found for specific phobia, panic disorder and/or agoraphobia, and separation anxiety disorder.

Table 4 displays the results for parents' and siblings' familial risk of having any AD as predicted by the child's specific AD. It was found that children with GAD were more likely to have mothers with lifetime ADs than children with other ADs (OR = 2.48, 95% CI = 1.23–4.98, p = .011). Children with SAD were more likely to have fathers with lifetime ADs (OR = 2.86, 95% CI = 1.07–7.60, p = .035), but children with specific phobia were less likely to have fathers with lifetime ADs (OR = 0.41, 95% CI = 0.19–0.90, p = .027).

Table 3 Results of Specificity Analyses: Odds ratio and 95% Confidence Interval of Child AD Compared to Lifetime Mother, Father, and Current Sibling AD

	Specificity					
	Mother AD[1]		Father AD[1]		Sibling AD[1]	
Child	OR	95% CI	OR	95% CI	OR	95% CI
SAD	**3.69***	**1.20–11.40**	∞[a]		∞[a]	
GAD	**3.47***	**1.28–9.41**	0.93	0.33–2.65	3.42	0.88–13.31
SP	1.11	0.50–2.49	0.61	0.19–1.92	3.11	0.91–10.59
PAG	2.43	0.91–6.45	1.28	0.25–6.60	∞[a]	
SEP					1.49	0.20–11.03

*$p < .05$
Note: AD = Anxiety Disorder, SAD = Social Anxiety Disorder, GAD = Generalized Anxiety Disorder, SP = Specific Phobia, PAG = Panic Disorder/Agoraphobia, SEP = Separation Anxiety Disorder, OR = Odds Ratio. 95% CI = 95% confidence interval. No specificity could be calculated for parents' SEP because SEP was not measured with the ADIS-IV-L for parents.
[1]Each column represents the odds ratio of having the same AD as the child
[a]∞ = not applicable: odds ratio could not be calculated because one of the cells contained zero: all fathers/siblings with SAD came from families with children with SAD; all siblings with PAG came from families without children with PAG.

Table 4 Odds Ratio and 95% Confidence Interval of Specific Child AD Compared to Lifetime Mother, Father, and Current Sibling AD

	Any Anxiety Disorder					
Child AD	Mother Any AD		Father Any AD		Sibling any AD	
	OR	95% CI	OR	95% CI	OR	95% CI
SAD	1.60	0.77–3.33	**2.86***	**1.07–7.60**	1.28	0.49–3.35
GAD	**2.48***	**1.23–4.98**	0.57	0.26–1.25	0.83	0.35–1.98
SP	1.65	0.83–3.29	**0.41***	**0.19–0.90**	1.69	0.71–4.07
PAG	2.03	0.84–4.90	1.76	0.68–4.54	0.53	0.18–1.61
SEP	0.57	0.29–1.14	0.99	0.45–2.16	1.43	0.60–3.44

*$p < .05$

Note: AD = Anxiety Disorder, SAD = Social Anxiety Disorder, GAD = Generalized Anxiety Disorder, SP = Specific Phobia, PAG = Panic Disorder/Agoraphobia, SEP = Separation Anxiety Disorder, OR = Odds Ratio. 95% CI = 95% confidence interval.

DISCUSSION

The aims of the current study were to examine whether (I) children with ADs referred to community mental health care centers were more likely to have mothers, fathers, and siblings with ADs than typically developing children, and (II) children with specific ADs were more likely to have parents and siblings with

the same AD (specificity) and/or parents and siblings with any AD (familial risk). Regarding (I), as compared to controls, children with ADs were respectively two and three times more likely to have at least one parent with lifetime and current ADs; two-and-a-half times more likely to have a mother with current ADs; nearly three times more likely to have a father with lifetime ADs, and – although borderline significant – four times more likely to have fathers with current ADs. Children with ADs were not more likely to have siblings with ADs. Regarding (II), specificity was found for mother-child SAD, all fathers with lifetime SAD had children with SAD, and all siblings with SAD were siblings from children who had SAD. In addition, specificity was revealed for mother-child GAD. At the same time, there were indications of a familial risk for some child ADs: (1) children with SAD were nearly three times more likely to have fathers with lifetime AD, and (2) children with GAD were two-and-a-half times more likely to have mothers with lifetime AD, compared to children with other ADs. Each of these findings is discussed in more detail below.

In line with our hypothesis and previous research (Cooper et al., 2006; Hughes et al., 2009), we found that children with ADs were more likely to have mothers and fathers with ADs than controls. Results of the current study showed comparable sizes of odds ratios for mothers and fathers, whereas previous research mainly found stronger associations for internalizing problems between mother-child than father-child (Connell & Goodman, 2002; Cooper et al., 2006). Therefore, our findings could suggest that both mothers and fathers are important to consider when assessing transmission of ADs in families. Moreover, we have found no heightened prevalence of depressive disorder in mothers and fathers of children with ADs compared to controls, which adds to the evidence that ADs are running in families. In contrast to our hypothesis, we did not find that siblings of children with ADs were more likely to have ADs which could be explained by the child susceptibility hypothesis. That is, some children, who are genetically susceptible for the development of an AD, because of an anxious temperament, are more likely to be affected by the consequences of living in a family with parental ADs than siblings who are not genetically-burdened, based on gene-environment interaction (Barrett, Fox, & Farrell, 2005; McLeod, Wood, & Weisz, 2007). In addition, anxious parents may be differentially susceptible for the anxious temperament of their child (for example experiencing the child as highly vulnerable), and consequently treat their anxious child different from their non-anxious children, for example by overprotecting their anxious child, which could influence parents' risk of developing pervasive ADs (Eley et al., 2015). Another, methodological, explanation for the lack of heightened risk of ADs in siblings of children with ADs, is the elevated

prevalence of ADs in siblings of both groups (26.2% in the AD-group and 31.6% in the control group) when compared to the general prevalence of childhood AD (8.3-27%, Costello et al., 2005), as well as when compared to previous studies on siblings of children with AD (21.7%, Last et al., 1991; 12%, Dia & Harrington, 2006). It is remarkable that these rates are this high, and they are higher than would be expected in this sample. One explanation could be that the siblings that were interested in participating in our study were more familiar with anxiety symptoms. Moreover, the siblings of the control group were younger and consisted of more girls compared to the group of children with ADs, which could have affected prevalence rates (Costello et al., 2005). Larger child and sibling samples are needed, as well as full participation of siblings to prevent systematic missing data, in order to examine the prevalence of AD in siblings.

Strong evidence was found for the specificity of mother-child SAD, for an elevated risk of SAD in fathers and siblings of children with SAD. These findings are interesting as they suggest that something specific is happening with the (familial) transmission of SAD. Next to heritability of an inhibited temperament (although only moderately; Spence & Rapee, 2016), it could be that mothers and fathers of children with SAD are lacking certain social skills, which are modeled to the children and thus leading to childhood SAD. Previous studies have found that mother-child SAD is related (Hughes et al., 2009), but the finding that all fathers of children with SAD have SAD themselves is interesting. This could be explained by the finding that socially anxious fathers show less challenging parenting behavior, which is a risk factor for the child developing social anxiety (Majdandžić, Möller, de Vente, Bögels, & van den Boom, 2014). This indicates that fathers do have a different role in the development of ADs in their offspring than mothers (as suggested by Bögels and Phares, 2008), and that father's role may be particularly important for children with SAD (Bögels & Perotti, 2011; Knappe, Beesdo-Baum, Fehm, Lieb, & Wittchen, 2012). Interestingly, there are indications that children with SAD respond less well to treatment (Hudson et al., 2015). This could be related to the finding that SAD runs in the family and perhaps SAD needs a more family-oriented treatment approach than other ADs. In sum, it seems that SAD runs in the family, and as SAD is the most common AD (Knappe, Sasagawa, & Creswell, 2015), more research towards the mechanisms of family transmission of SAD in specific is necessary.

Next to SAD, specificity was found for mother-child GAD, that is, children with GAD were more likely to have mothers with lifetime GAD than children with other ADs. This is interesting as previous research suggested that avoidance in GAD is

less observable and therefore less easily transmitted through modeling (Hughes et al., 2009). Thus, it seems that GAD is transmitted through another mechanism, and it has been proposed that mothers transmit the cognitive styles associated with GAD, for example that worry helps to cope with uncertainty (Aktar, Nikolic, & Bögels, 2017). Next to this environmental transmission of GAD, it could be that genetic transmission of a certain trait or physiological marker is more important in GAD than in other ADs (Hettema et al., 2001). Furthermore, the specificity of both mother-child SAD and GAD could indicate a shared etiology or trans-diagnostic perspective, for example the tendency to worry that is present in both disorders (Hearn, Donovan, Spence, March, & Holmes, 2017). Nevertheless, we cannot rule out that there are specific or common pathways in the transmission of SAD and GAD between mothers and children and vice versa. These effects should be examined bi-directionally in order to understand which mechanisms account for the specificity and to understand to what extent the worrying child affects maternal worry and maternal feelings of uncertainty.

Finally, we have found indications of a more familial risk of certain ADs, because children with GAD were more likely to have mothers with ADs, whereas children with SAD were more likely to have fathers with ADs, compared to children with other ADs. It could be that the mechanisms of transmission from father to child are different from transmission from mother to child, and/or that mothers and fathers respond differently to an anxious subtype in the child, i.e. a child with GAD evokes more anxiety in the mother while a child with SAD evokes more anxiety in the father. Previous studies have shown that fathers of socially anxious children show less emotional warmth and more rejection [(Knappe et al., 2012) and this relation is likely to be bidirectional, i.e. fathers show less warmth because their child is socially anxious, and/or their child becomes more socially insecure because fathers show less warmth and more rejection (Bögels & Phares, 2008). Concerning GAD, it could be that mothers of children with GAD are transmitting their anxious thoughts and behaviors through specific and non-specific pathways (see Aktar, Nikolic, and Bögels (2017) for a review of the literature), and/or that mothers of children with GAD feel more anxious when their child is worrying and expressing uncertainty. Experimental studies need to be carried out in order to understand the mechanisms behind the transmission of SAD and GAD between father, mother and child, as well as the direction of effect (parent to child, child to parent or both). Next to the possibility of a different transmission from mother and father to the child, the child's gender could also play a role in the transmission of ADs. It has been found that rates of ADs between mothers and daughters were higher than between

fathers and sons (Last et al., 1991). A more recent study did not find gender effects between sons and daughters (Ranøyen, Klöckner, Wallander, & Jozefiak, 2015). Thus, in order to get a better understanding of the transmission of ADs, future studies should not only consider the specificity of ADs for mothers and fathers, but also whether this differs between daughters and sons.

As with all studies, the current study is not without limitations. First, although the clinical sample size was large, not all odds ratios could be calculated. This study provided important information (i.e. no SAD fathers had children without SAD), but this issue should be examined further, for example by including a larger sample of children with SAD. Second, due to the large number of children meeting criteria for several ADs, the interpretation of the current findings concerning the specific disorders is somewhat limited. Thus, in order to improve internal validity, only children with a single AD should participate; however, this will limit the generalizability to the field of child and adolescent psychiatry where comorbidity is the rule rather than the exception (Costello et al., 2005). Third, the design of this bottom-up study only examined children with AD and not children with other types of psychopathology, which limits the findings of specificity only to this AD sample, and it would be interesting to compare these rates to parents of children with other disorders. Fourth, the control group included children that met criteria for an AD, which raises the question whether this is a true control group. We have decided to keep the children with ADs in the control group, in order to support the external validity of our study. Nevertheless, the control group was smaller than the group of children with ADs, and it could be that the control group is less representative due to the recruitment through newspaper advertisements. Finally, the study design does not allow conclusions about the mechanisms that are underneath the observed transmission of anxiety (i.e. genetic and/or environment), nor about the direction of transmission.

Despite its limitations, this study represents a comprehensive evaluation of prevalence of ADs and specificity in mothers, fathers, and siblings of children referred with ADs. The study was one of the first to systematically include fathers and siblings, which adds to the existing knowledge of ADs running in families. Another strong point is that this study used structured diagnostic interviews for all family members and combined child and parent report for the child diagnoses. We have found that children with ADs are over twice as likely to have mothers and/or fathers with lifetime and/or current ADs. We have also found evidence for specificity of SAD and specificity of mother-child GAD. It has been shown that

children of parents with ADs do less well in treatment than children of parents without ADs (Bodden et al., 2008); and, in specific, children of mothers with social anxiety disorder tend to do poorly compared to children of mothers without ADs (Cooper et al., 2006). In addition, this study showed that fathers and siblings of children with SAD reported high rates of SAD themselves. Siblings of children with ADs usually are not included in treatment and research (compared to siblings of children with special needs; Ma et al., 2015), but it may be important to screen them for ADs as well and to consider involving them in treatment. Finally, treatment of SAD in children has been mentioned as least effective compared to other ADs (Hudson et al., 2015). Possibly, treatment of childhood SAD is less effective because parents' social anxiety disorder functions as a maintaining factor and parents are for example not able to facilitate social exposures because they lack certain social skills. Thus, it should be examined whether parents will also change when their child is treated or vice versa, especially regarding SAD.

Modular CBT for Childhood Social Anxiety Disorder: A Case Series Examining Initial Effectiveness

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ABSTRACT

Cognitive Behavioral Therapy (CBT) is the most efficacious treatment for childhood anxiety disorders. At the same time, several studies showed that for children and adolescents with social anxiety disorder (SAD), standard protocolized CBT seems to be less efficacious than for youth with other types of anxiety disorders, suggesting that children with SAD need a different approach. The purpose of this study was to examine the effectiveness of a modularized cognitive behavioral therapy (CBT) for children with SAD, including mindfulness. Ten children and adolescents (50% girls, aged 8-17 years) referred for SAD were measured at pretreatment, posttreatment and 10 weeks follow-up. Results showed that 5 youths (50%) were free of their SAD posttreatment, and 8 (80%) at follow up. Clinically meaningful improvements from pretest to follow-up were found in 90% and 60% of the cases, for the total anxiety symptom score and social anxiety symptom score, respectively. Pre-post-follow/up group analyses revealed significant improvements in SAD severity (parent and child report) and social anxiety symptoms across child, mother, and father report. The remission rate of 80% and substantial social anxiety symptom decline is promising, providing a starting point for improving treatments of youth with SAD.

Keywords: CBT, social anxiety disorder, children and adolescents, modular treatment

MODULAR CBT FOR CHILDHOOD SOCIAL ANXIETY DISORDER: A CASE SERIES EXAMINING INITIAL EFFECTIVENESS

Social anxiety disorder (SAD) is one of the most common mental disorders and anxiety disorders in children and adolescents, with prevalence rates reaching 10% in adolescence (Burstein et al., 2011; Kessler et al., 2012; Merikangas et al., 2010). The DSM-5 [American Psychiatric Association (APA), 2013] characterizes SAD as a persistent, intense fear of social situations in which the individual may be negatively evaluated by others. In children, this fear must occur in peer settings and not just in interactions with adults (APA, 2013). SAD is a typical childhood onset disorder, as first incidence after the age of 21 is very low (Bögels et al., 2010; Burstein et al., 2011). Untreated SAD in children and adolescents leads to negative consequences such as impairments in interpersonal functioning, loneliness, school refusal and dropout, lower educational level, subsequent anxiety, depressive, and substance use disorders (e.g., Beidel, Turner, & Morris, 1999; Burstein et al., 2011; Kendall, Safford, Flannery-Schroeder, & Webb, 2004; Wittchen & Fehm, 2003). If untreated, SAD generally persists in adulthood, relates to reduced quality of life, and does not remit until up to 40 years after onset (Comer & Olfson, 2010). Thus, there is a clear need for effective treatment of SAD early in development.

Cognitive Behavioral Therapy (CBT) is the most efficacious treatment for anxiety disorders (ADs) in children and adolescents, with moderate to large effect sizes compared to other therapies (Reynolds, Wilson, Austin, & Hooper, 2012) and approximately 50-70% of children being free of their primary AD after treatment (e.g., Bodden et al., 2008; Hudson et al., 2015a; In-Albon & Schneider, 2007). CBT for childhood ADs generally consists of a 'skill-building' phase in which children acquire skills that reduce anxiety (e.g., psycho-education, cognitive restructuring, coping skills), and an 'exposure' phase in which children are gradually exposed to their feared situation and practice new skills (Detweiler et al., 2014). Nevertheless, a large number of studies from multiple sites have shown that delivery of this general form of CBT is less successful for SAD than for other types of ADs in both children and adults (e.g., Crawley, Beidas, Benjamin, Martin, & Kendall, 2008; Ginsburg et al., 2011; Hudson et al., 2015a; Hudson et al., 2015b; Wergeland et al., 2016); even at long-term follow-up (Kodal et al., 2018).

One strategy to enhance therapy outcomes that is recently gaining in popularity (Ng & Weisz, 2016) is to deliver therapy in a more individualized way. In general, this means tailoring the selection and implementation of therapy techniques to the

personal needs of the clients (Crawley et al., 2008; Hudson et al, 2015b; Kendall et al., 2012). With regard to CBT manuals, these are individualized by dividing it into separate self-contained modules (e.g., cognitive therapy, problem-solving) that can be matched to the individual strengths and needs, and that can be used multiple times or not at all (Ng & Weisz, 2016). Such modular therapies for children with anxiety disorders, depression, trauma, and/or conduct problems have shown to offer incremental benefit over usual care and standard therapy, and a steeper decrease in child's anxiety symptoms than the standard treatment (Chorpita, Taylor, Francis, Moffitt, & Austin, 2004; Chorpita et al., 2013; Weisz et al., 2012). For children with SAD, modular therapy could, for example, provide therapists with more time to invest in challenging common cognitive biases and in building the therapeutic alliance (Crawley et al., 2008). Moreover, modular therapy also supports trends in usual clinical practice, in which therapists – possibly due to time constraints – tend to use parts of treatment manuals instead of the whole manual (Chu et al., 2015). Thus, modular therapy appears to have the potential to improve treatment outcomes for children dealing with psychopathology, and may be a promising strategy for improving effectiveness in particular for children with SADs.

Another recent line of thinking regarding treatment of psychopathology has focused on implementation of innovative therapy techniques, such as mindfulness approaches. With regard to adult and youth anxiety (disorders), it has been suggested that these clients could benefit from mindfulness interventions, especially when integrated with existing CBT protocols (Maric, Willard, Wrzesien, & Bögels, 2019; Van Bockstaele & Bögels, 2014). Mindfulness as a method implies welcoming daily hassles and stressors with attention and acceptance. By increasing awareness for the present moment and encouraging the individual to divert its attention to internal experiences and environmental stimuli, mindfulness may be a method to target (distorted) cognitive processes (Van Bockstaele & Bögels, 2014). This may sound paradoxical as CBT models for SAD (e.g., Clark & Wells, 1995) view the tendency to focus on internal experiences as one of the key mechanisms that keeps the problem going. However, Bögels and Mansell (2004) proposed six different change mechanisms of attentional processes training in SAD: reducing hypervigilance by focusing on broader aspects of self and environment; reducing attentional avoidance; reducing self-focused attention; increasing mindfulness to counter mindless ruminating; increasing attention control; and increasing self-esteem through enhanced concentration (also called 'flow'). In line with this reasoning, treatment of SAD in adults with mindfulness (i.e., mindfulness-based stress reduction, mindfulness and acceptance-based group treatment, and

mindfulness-based task concentration training) was found to be more effective than waitlist in decreasing social anxiety symptoms (Bögels, Sijbers, & Voncken, 2006). In addition, the mindfulness groups demonstrated similar improvements when compared to (group) CBT (Goldin et al., 2016; Kocovski, Fleming, Hawley, Huta, & Antony, 2013). At this moment, empirical evidence regarding the efficacy of mindfulness in children and adolescents with SAD is lacking.

In the present study we incorporated these recent suggestions in the treatment of youth with anxiety disorders. We implemented a modular CBT (adapted from the Dutch CBT manual Discussing+Doing=Daring; Bögels, 2008) that included general modules such as cognitive therapy and exposure; and additional elements of mindfulness therapy. In the current study, we examined this manual in 10 children and adolescents referred with SAD (8-17 years, 50% girls). Accordingly, we aimed to explore: (i) the effectiveness of modularized CBT (including mindfulness) in these 10 youths; and (ii) which modules and treatment components were used in each participant. The expectation is that exploration of these questions in children and adolescents with SAD on a single-case level will provide us with initial information about the utility of a modular CBT approach for treating SAD in youth.

METHOD

Participants and procedure

This study is part of a larger study examining working mechanisms of modularized CBT for childhood ADs. The inclusion criteria for the current study were a) primary diagnosis of SAD based on DSM-5 criteria (APA, 2013); b) no comorbid pervasive developmental disorder; c) having completed at least a pretest and posttest measure; and d) IQ > 80. After the final assessment point, families received a gift card of 20 euros. Participants gave active informed consent, and ethical approval was obtained from the Ethical Committee of the University of Amsterdam.

Initially, 16 participants were selected based on their SAD. Six participants dropped out of research because of the incomplete assessments at post-treatment and follow-up. In comparison to the 10 study completers, the six drop-outs had on average the same diagnosis severity at pretest, were one year older, and received fewer treatment sessions. None of the 10 cases were suicidal or housebound, however, all participants did avoid one or more situations (ranging from e.g., not daring to play with other kids to not going to school) and rated their anxiety as severely impairing (using CSR) for their daily functioning.

The children and adolescents were aged 8-17 years (mean age = 11.70, SD = 2.69), 50% girls. Both parents were included in the study, the majority was married (90%), and their educational levels were average (distribution of respectively low-middle-high educational level for mothers: 11%-44%-44%; for fathers: 30%-30%-40%). Participants were treated by eight different therapists (participants 2 & 8, and 6 & 7 had the same therapist). All therapists were female, had a master's degree in psychology, their ages ranged from 23-59 years (M = 35.63, SD = 11.64), and experience as a mental health care professional ranged from 1 - 40 years (*M* = 12.38, *SD* = 13.35).

Measures

Anxiety diagnosis. SAD and comorbid disorders were assessed with the Dutch version of the Structured Clinical Interview for DSM-5 Disorders for Children (SCID-junior, Braet, Vandevivere, & Wante; *unpublished manuscript*). Parent and child reports were combined based on standard procedures used in the SCID-junior. The SCID-junior was used instead of the commonly used Anxiety Disorders Interview Schedule – Child/Parent Versions (ADIS-C/P; Silverman & Albano, 1996) because the SCID-junior is based on DSM-5 instead of DSM-IV criteria. In order to compare severity of diagnoses to previous studies, we additionally determined an impairment score between 0 and 8, comparable to the Clinical Severity Rating (CSR) of the ADIS-C/P. Research investigating the psychometric properties of the SCID-junior is ongoing (C. Braet, personal communication, July 12, 2017). In the ongoing study, interrater agreement (kappa) based on the presence or absence of the anxiety disorder was high; SCID-junior child report $\kappa = 0.82$, SCID-junior parent report $\kappa = 0.72$. The assessment interview pre- and post-treatment was conducted by the first author or a research assistant, who were independent from the therapists and who were blind about the moment of assessment and which treatment modules were used with that specific client.

Anxiety symptoms. The 71-items Screen for Child Anxiety Related Emotional Disorders (SCARED-71; Bodden, Bögels, & Muris, 2009), child and parent report, was used to assess child anxiety symptoms, rated on a three-point scale (0 = (almost) never; 1 = sometimes; 2 = often). The total scale and social anxiety subscale were used (9 items), which have good psychometric properties (total scale: $\alpha > .94$; social anxiety subscale $\alpha > .85$) for both child and parent report (Bodden et al., 2009).

Therapist flexibility. In line with modularized approaches, we assessed therapist flexibility by coding audiotapes of the treatment sessions (N = 82) with the

Discussing + Doing = Daring Adherence Checklist-Flexibility Scale (DDDAC-F). The DDDAC-F is based on the Coping Cat Adherence Checklist-Flexibility Scale and manual (CCPAC-F and CCPAC-F manual; Chu & Kendall, 1999; Southam-Gerow, Jensen Doss, Gelbwasser, Chu, & Weisz, 2001). Because of the modular character of the Discussing + Doing = Daring protocol, the fixed session format of the CCPAC-F could not be used. Therefore, a list of all possible session elements (= subparts of the different modules; e.g., discuss normal anxiety versus anxiety disorder in the psycho-education module and explain the rationale of exposure in the module of exposure) was created. Coders identified the used techniques from each session and scored these on the DDDAC-F form. In line with the manual (Southam-Gerow et al., 2001), therapist flexibility was rated on a 6-point scale ranging from 0 (not at all flexible) to 5 (extremely flexible) and functional appropriateness of the flexibility on a 6-point scale ranging from 0 (not at all appropriate) to 5 (extremely appropriate). For each session, a mean flexibility score was calculated from flexibility scores of the subparts of that session. All 82 available therapy sessions were randomly distributed among the two coders, and 25% randomly selected sessions were coded by both coders. A two-way random effects single-measures ICC showed a fair agreement (ICC = .48) which is not unreasonable in the exploratory phase of the research and is even somewhat higher than the .40 found in the study of Chu & Kendall (2009).

Modular CBT

The modular approach of this treatment is based on the original 12-session manual and three optional parent sessions ('Discussing + Doing = Daring'; Bögels, 2008). The original manual consists of various CBT elements (e.g., psycho-education, cognitive restructuring, experiments, exposure, task concentration, relaxation, relapse prevention) and the optional parent sessions concern parental modeling, child-parent communication and parental guidance. The original manual contains detailed information about each session and its goals (e.g., in the session psycho-education: 'explain normal anxiety versus anxiety disorder'; in the exposure session: 'address the rationale for doing exposure'). To facilitate individually-tailored treatment and therapist flexibility, the modularized version consists of seven modules with ten techniques: psycho-education, cognitive restructuring, coping skills, task concentration, dealing with feelings, mindfulness exercises (body scan, meditation), experiments, exposure, parental guidance, and relapse prevention.

All therapists in this and the larger study had at least a master's degree and were qualified to diagnose and treat children and adolescents (under the supervision

of a post-master healthcare psychologist). CBT in general is well implemented in the master and post-master educational system in the Netherlands, as well as in the community mental health care centers. According to the national guidelines, CBT is the treatment of choice for childhood anxiety disorders (van Rooijen, 2018). Therapists were all working in different community mental health care centers. Therefore, they received supervision following the guidelines of the center they worked in (which varies from once in two months to multiple times a week).

Of the eight therapists, four had a post-master healthcare psychology registration, one had completed a PhD program, and three were post-master psychologists trained in CBT.

The therapists received an initial 4-hour training in the use of the modular protocol provided by the first, second and/or last author. Therapists were instructed to choose from the optional modules, based on their theoretical knowledge (e.g., all therapists also received written information including a summary of the current knowledge around (treatment of) childhood anxiety disorders), clinical experience and patient information. Moreover, therapists decided on treatment dosage (number of sessions) and number and length of homework assignments. Having the opportunity to choose from the optional modules facilitated the therapist to tailor the treatment to the individual needs of the child and family, and to include components that she thought may improve the treatment of youth with SAD. The therapist could for example give more attention to mindfulness, or to experiments, or additional parental guidance. Therapist affinity with mindfulness, cognitive restructuring and exposure were registered and ranged from 5 to 10 (M = 7.60, SD = 1.26) for the mindfulness module, from 7 to 10 for the cognitive module (M = 8.40, SD = 1.07), and from 6 to 10 for the exposure module (M = 8.40, SD = 1.58).

Data Testing and Exploration

The effectiveness of modularized CBT was investigated through inspection of percentages of cases that improved regarding diagnosis (SCID) and symptoms of social anxiety (SCARED-71) from pre- to posttest, and to follow-up measurement points. Further, for each case, the Reliable Change Index (RCI; Jacobson & Truax, 1991) was calculated. The RCI facilitates investigation of clinically meaningful change in the severity of SAD diagnosis (SCID) and levels of (social) anxiety symptoms (SCARED-71) pre- to post-treatment, and pre- to follow-up treatment.

An RCI > 1.96 or < -1.96 indicates clinically reliable change (Jacobson & Truax, 1991).

Following Jarrett and Ollendick (2008), nonparametric Friedman tests and Wilcoxon tests were carried out for the whole group to analyze pre-post and pre-follow up differences on severity ratings of SAD (CSR scores) and anxiety symptoms (SCARED-71).

To provide answers to our other questions regarding specific modules and treatment techniques implemented and participants' characteristics, the data was inspected qualitatively.

RESULTS

Effectiveness of Modularized CBT for SAD

Results from the SCID interview with parents and children showed that 50% of the children and adolescents were free of their SAD diagnosis at posttest, and 80% at follow-up. Combined results from the parent and child report of SAD symptoms (SCARED-71) revealed slightly lower percentages of children and adolescents scoring below the clinical threshold of social anxiety symptom severity, namely 30% and 60% at posttest and follow-up respectively (see Table 1). Clinically meaningful improvements were found from pretest to follow-up on combined results (more than 1 reporter) for 90% of children and adolescents for the total anxiety score (SCARED-71), and for 60% of children and adolescents with regard to social anxiety subscale of the SCARED-71.

Additionally, in Table 2 percentages of social and total anxiety symptom reduction per reporter (child, mother, father) from posttest to follow-up are presented.

Table 1 Summary of Participant Characteristics, Clinical Outcomes, and Session Content

C	Sex	Age	Comorbidity	SCID pre-test	Free of diagnosis Post-test/ FU	Below cut-off social anxiety	Sig RCI total Scared-71	Sig RCI social Scared-71	#s	Exp Gen	Exp Anx	Aff cog	Aff exp	Aff mnf	PE	CR	F	MFN	TCT	CS	E	ES	PG	SR
1	F	8	-	6	N/Y	N/N	*	-	7	3	10	8	10	5	14.3%	14.3%	0%	0%	0%	14.3%	57.1%	0%	0%	14.3%
2	M	12	GAD	7	Y/Y	Y/Y	*	*	7	10	30	8	9	7	28.6%	28.6%	14.3%	0%	0%	14.3%	42.9%	0%	0%	14.3%
3	F	9	-	6	N/N	Y/Y	*	*	12	5	10	9	9	8	16.7%	16.7%	8.3%	0%	0%	8.3%	75%	0%	8.3%	8.3%
4	M	13	-	8	Y/Y	N/N	*	*	6	25	> 50	10	10	8	25%	25%	25%	0%	25%	25%	50%			
5	F	14	SpP	7	Y/Y	N/Y	-	-	15	8	8	8	7	10	20%	26.7%	6.7%	26.7%	6.7%	33.3%	46.7%	13.3%	20%	20%
6	M	11	SEP, SpP, GAD, ADHD, MD	8	Y/Y	Y/Y	*	*	10	1	0	7	6	8	10%	40%	10%	0%	10%	10%	50%	0%	0%	20%
7	M	8	-	7	N/N	N/N	*	-	14	1	0	7	6	8	7.1%	92.9%	7.1%	14.3%	0%	57.1%	71.4%	64.3%	0%	14.3%
8	M	17	-	6	N/Y	N/Y	*	-	11	10	30	8	9	7	18.2%	54.5%	0%	63.6%	9.1%	45.5%	54.5%	18.2%	18.2%	36.4%
9	F	12	SpP, GAD	6	Y/Y	N/N	*	*	11	7	20	9	8	8	9.1%	18.2%	18.2%	18.2%	9.1%	18.1%	18.1%	36.4%	0%	9.1%
10	F	13	GAD, MD, ADHD-I, Ins	7	N/Y	N/Y	*	*	23	40	> 50	10	10	7	34.8%	52.2%	0%	4.3%	4.3%	34.8%	4.3%	8.7%	8.6%	13.0%

Note. C = Client; F = Female, M = Male; GAD = Generalized Anxiety Disorder, SpP = Specific Phobia, SEP = Separation Anxiety Disorder, MD = Mood Disorder, ADHD-I = ADHD predominantly inattentive subtype, Ins = Insomnia; N = No, Y = Yes; Below cut-off social anxiety symptoms as reported by > 1 reporter; * = significant RCI change pretest to follow-up, reported by > 1 reporter; #s = number of sessions; Exp Gen = clinical experience in general (number of years), Ex Anx = experience with treating anxiety in children (number of treated cases), Aff cog = affinity with cognitive module (measured on a scale 1-10), Aff exp = affinity with exposure module (measured on a scale 1-10), Aff mnf = affinity with mindfulness module (measured on a scale 1-10); PE = Psycho-education, CR = Cognitive Restructuring, F = dealing with feelings, MFN = Mindfulness, TCT = Task Concentration Training, CS = Coping Skills, E = Exposure, ES = Experiments, PG = Parental Guidance, SR = Summary + Relapse Prevention. Note that when PG is 0%, parents could still be involved in therapy, but not for separate sessions; *note:* Percentages do not sum to 100% because often several modules were used in one session.

Table 2 Percentages of SCARED-71 Symptom Reduction Reported by Child, Mother, and Father

	Child report		Mother report		Father report	
	Post-test	FU	Post-test	FU	Post-test	FU
Social anx symptoms below cutoff	44.4	60	25	44.4	33.3	50
Social anx symptoms improved RCI	50	50	37.5	87.5	37.5	44.4
Total anx symptoms below cutoff	33.3	50	50	66.7	22.2	70
Total anx symptoms improved RCI	50	66.7	62.5	100	62.5	77.8

Note. SAD = social anxiety disorder; RCI = reliable change index; FU = follow-up.

Non-parametric Friedman tests were carried out to examine if participants showed a significant decline over time. For CSR scores we found a significant effect for both reporters. Parent report: $\chi^2(2, N = 8) = 12.00$, $p = .002$, and child report: $\chi^2(2, N = 7) = 9.54$, $p = .008$. Wilcoxon tests showed significant improvement for parent report from pretreatment to posttreatment, $Z(2, N = 8) = -2.38$, $p = .018$, and from pretreatment to 10-weeks follow up $Z(2, N = 8) = -2.04$, $p = .041$. For child report the same was found: $Z(2, N = 7) = -2.04$, $p = .042$, and from pretreatment to 10-weeks follow up $Z(2, N = 7) = -2.39$, $p = .017$.

For child anxiety symptoms (as measured with the SCARED-71) over time, Friedman tests showed a significant decrease in symptoms over time for all three reporters: mother report: $\chi^2(2, N = 8) = 13.00$, $p = .002$, father report: $\chi^2(2, N = 9) = 16.22$, $p < .001$, and child report: $\chi^2(2, N = 6) = 9.65$, $p = .008$. Post-hoc Wilcoxon tests showed significant improvement for mother report from pretreatment to posttreatment, $Z(2, N = 8) = -2.52$, $p = .012$, and from pretreatment to 10-weeks follow up $Z(2, N = 8) = -2.53$, $p = .011$. For father report, comparable results were found: from pretreatment to posttreatment, $Z(2, N = 9) = -2.67$, $p = .008$, and from pretreatment to 10-weeks follow up $Z(2, N = 9) = -2.67$, $p = .008$. For child report comparable results were found: $Z(2, N = 5) = -2.02$, $p = .043$, and from pretreatment to 10-weeks follow up $Z(2, N = 6) = -2.21$, $p = .027$.

Modules and treatment components used with each participant

Based on the (82) audiotapes that were coded, therapists had an average score of 2.18 (scale 0 - 5; SD = 0.65; range 0.80 - 3.67) on the flexibility scale. Thus, it seemed that therapists showed a medium amount of flexibility (flexibility score of 2 out of 5 = content adaptation of the manual, for example through including relevant examples to the interest of the child into treatment lessons), and they used it in a functional way (functional flexibility: M = 2.88, SD = 0.44; range = 2 -

3.80; functional flexibility score of 3 out of 5 = moderately appropriate, the child responded positively to the modifications the therapist made to the session).

An overview of therapy content for each individual participant is shown in Table 1. In addition, the number of sessions varied largely between the clients, with an average of 11.60 sessions of therapy, ranging between 6 and 23 sessions. The length of sessions ranged between 40 and 70 minutes, with an average of 58 minutes. Moreover, the participants with the same therapist (2 and 8; 6 and 7) did not show similarity in treatment content, which could be an indication of the flexibility of the therapist as well as an indicator of a personalized approach.

For the majority of cases (80%), most time in each therapy trajectory was spent on exposure (including preparation of tasks, execution, and evaluation). The younger participants (aged between 8 and 12; participants 1, 2, 3, 6 and 7) seemed to have received more exposure (addressed in 50% - 75% of the sessions) than the adolescent participants (4% - 55%). Further inspection of the session content showed that half of the participants received mindfulness exercises, and this was always used next to the general 'core' CBT practices such as cognitive restructuring and exposure, thus not replacing these modules. The younger participants (aged between 8 and 12; participants 1, 2, 3, 6 and 7) seemed to have received less mindfulness (addressed in 0 -14% of the sessions) than the adolescent participants (4%-64%). Task concentration training was used in 6 of 10 treatments. Interestingly, most of the younger participants (aged between 8 and 12; participants 1, 2, 3, 6 and 7) did not receive task concentration (addressed in only once case in 10% of the sessions) while all of the adolescent participants received some extent of task concentration (4.3% - 25.0%). Parent sessions were added in 4 out of 10 cases.

DISCUSSION

This study evaluated a modularized CBT program with additional inclusion of mindfulness exercises for a random selection of children and adolescents with social anxiety disorder (SAD) referred to community mental health care. Results showed that a relatively short (average 11 sessions) modular CBT was effective with 50% of the children and adolescents being free of their SAD diagnosis post-treatment and 80% at 10-weeks follow-up. Taken over the whole group, substantial improvements in SAD diagnosis and social anxiety symptoms were found directly after the treatment and at follow-up. The effects were consistent across child, mother, and father report. However, some youths still showed (sub)clinical levels

of social anxiety symptoms at posttest and follow-up. It appears that the adapted protocol is feasible and promising in improving treatment outcomes of youth SAD.

Our results that 50% of the children and adolescents were free of SAD immediately after treatment and 80% at follow-up, is larger than reported in previous CBT trials specifically aimed at treating children and adolescents with SAD (30%; Melfsen et al., 2011; Spence et al., 2017) as well as CBT trials including children with different ADs (30.7%-40.6%; Ginsburg et al., 2011; Hudson et al., 2015a). Also, children in this study received a lower number of sessions (11 on average) as compared to most studies using 10-16 sessions of manualized CBT (e.g., Bodden et al., 2008; Kendall et al., 2004), and lower than SAD-specific CBT (e.g., 20 sessions, Melfsen et al., 2011). This could be explained by the way in which therapy was delivered: therapists were instructed to tailor the treatment to the individual client and could choose which modules to use. In line with our results, Weisz et al. (2012) showed that a modular protocol outperformed general CBT for children with ADs, and children showed faster improvements than youth in care as usual. Our results showed indications of a personalized approach, in that: (i) the therapists were offered a training in the modularized treatment, so the therapists were aware (and 'allowed') to vary the treatment based on the needs of the client, and (ii) our finding that the same therapists provided treatments based on different combination of modules to different clients. Moreover, therapists frequently used the novel module of mindfulness. Although we cannot state which adaptation led to the enhanced effectiveness rates, it appears that modular CBT with inclusion of mindfulness does benefit youth with SAD when looking into anxiety outcomes.

With respect to the use of the modules, it became evident from these 10 cases that therapists varied in the number of sessions that were used in the treatment and the dosage of each module. Furthermore, it was found that (on average) therapists used a medium level of flexibility in their sessions (2 out of 5) and this flexibility was moderately adaptive and functional (3 out of 5). The treatments included many exposure sessions which may explain (part of) the high effectiveness as studies including adults with SAD have shown that a larger number of exposure sessions led to better results (Feske & Chambless, 1995). With respect to mindfulness, we found that in 50% of the cases this module was implemented in treatment and was implemented next to (one of) the "core" elements of CBT (cognitive restructuring and exposure). We consider this percentage of 50% quite high given that this is – to our knowledge – the first study that added mindfulness to a modular CBT for youth, and that the majority of the therapists who participated in this study were

not mindfulness trainers. Interesting, mindfulness – and task concentration training – seemed to be used more in adolescents than in younger children. These modules may be used to target the self-focused attention that is suggested to play a role in SAD (e.g., Clark & McManus, 2002; Heimberg, Brozovich, & Rapee, 2010; Rapee & Heimberg, 1997), which may become more apparent in adolescence. Another interesting finding was that in 40% of the cases parent sessions were added to the treatment. This percentage is quite high given the findings of several meta-analyses (In-Albon &Schneider, 2007; Ishikawa, et al., 2007; Reynolds, Wilsen, Austin, & Hooper, 2012; Thulin, Svirsky, Serlachius, Andersson, & Öst, 2014) that adding parent sessions to child CBT does not improve treatment effectiveness of CBT for childhood anxiety disorder. It may be that parent sessions are important, especially in treatment of youth social anxiety disorder. Note however that we cannot compare our 40% to what therapists do with CBT for other types of childhood anxiety disorders.

Future Recommendations and Limitations

Although this study provides preliminary evidence for the effectiveness of modularized CBT for youth SAD, the study is limited because of the uncontrolled design and small sample size. Therefore, we cannot state which adaptation of the CBT led to the high effectiveness in this sample; whether it was the modular therapy, the inclusion of mindfulness, or that other therapist, client, or therapy (e.g., exposure) characteristics have played a role. Future studies using for example multiple baseline procedures (Nakamura, Pestle, & Chorpita, 2009) or RCTs need to be carried out in order to examine active ingredients that need to be implemented in therapy for youth SAD. Also, cognitive constructs such as mindful attention (Brown, West, Loverich, & Biegel, 2011) and its relation to social anxiety outcomes should be investigated. Another limitation is the lack of long-term follow-up measurement, and it is unclear whether the prolonged effects still hold at longer-term follow-up, as previous research has shown that children with SAD are less likely to further recover during a longer follow-up periods, compared to children with generalized anxiety disorder and separation anxiety disorder (Kodal et al., 2018). Finally, this study included some adaptations to benefit children with SAD (i.e., modular therapy, mindfulness training), but other disorder-specific adaptations could also be of interest, such as social skills training (Beidel, Turner, & Morris, 2000) or more intensive parent education training (Öst, Cederlund, & Reuterskiöld, 2015).

Clinical Implications

This study showed that therapists are able to implement a modular CBT, by choosing elements out of the evidence-based therapy that could fit the individual child. Moreover, most children and adolescents in this study received many sessions of exposure, which has been suggested to be less successful for children with SAD due to the possibility of strengthening their fear belief in case of failed exposure tasks (Hudson et al., 2015b), and are often left out by therapists when treating child ADs in general (Chu et al., 2015). Results of the current study imply that it is feasible to use exposure for children with SAD, for example through roleplay, preparing a speech task for a public recruited at the treatment center, or conducting exposure tasks in the city environment. In addition, it seems that it is possible to treat children referred with SAD in relatively few sessions with a modular approach. Previous research concerning children with ADs has shown that relaxation training had a limited effect on anxiety improvement, compared to exposure and cognitive restructuring (Peris et al., 2015). However, mindfulness is not the same as relaxation, and tentatively, mindfulness may be a good addition to CBT for childhood social anxiety disorder.

CONCLUSIONS

Youth with SAD tend to respond less well to general CBT than youth with other ADs, and modular CBT (including the possibility to add mindfulness next to the core elements of CBT) seems to be one way to improve outcomes. A next step would be to examine whether the modular and adapted protocol used in this study outperforms general and non-modular CBT for children and adolescents with SAD, and whether the inclusion of mindfulness adds to treatment effectiveness. In this study, therapist flexibility was moderately adequate which further strengthens the use of modular therapy, as one of the goals of modular therapy is to enable therapists to adhere to the manualized protocol and at the same time facilitate flexible application of the protocol (Weisz et al., 2012). However, further investigations of therapist flexibility in modular treatment, as well as how therapists choose from the different modules is necessary and could lead to a better understanding of how to deliver modular CBT for children and adolescents with SAD.

Modular CBT for Childhood Anxiety Disorders: Evaluating (predictors of) Treatment Effectiveness

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ABSTRACT

Aim. This study examined (1) the effectiveness of a modular CBT for children with anxiety disorders (ADs) in a real-life clinical setting, and (2) predictors of treatment effectiveness. **Method.** Participants were 116 anxiety-disordered children aged 7-17 years (mean age = 11.13, SD = 2.51), their mothers (n = 109) and fathers (n = 89). Children received a modular CBT to treat their anxiety problems. Anxiety was measured with a DSM-5 diagnostic interview (SCID junior) and a questionnaire (SCARED-71) at pre-, mid-, post-test, and 10 weeks after treatment (follow-up). Predictors of treatment effectiveness (measured pre-treatment) were child characteristics (gender, age, type of AD, comorbid disorders), fathers' and mothers' anxious/depressive symptoms, and parental involvement based on parents' presence during treatment sessions. **Results.** Modular CBT was highly effective with 56% (based on intent-to-treat analyses) to 68% (based on completer analysis) of children being free of their primary anxiety disorder at follow-up. A significant decrease in anxiety symptoms was found with an effect size of 0.97 at follow-up. Multilevel analyses showed that children with Generalized AD had higher treatment gains at follow-up compared to children with other anxiety disorders. Children's comorbid symptoms were positively associated to their anxiety scores, but comorbidity was not associated with treatment effectiveness at post-test or follow up. Higher parental involvement was related to lower child anxiety at follow-up, but only for children with comorbid disorders. **Discussion.** Results show that the use of a modular CBT protocol is effective for childhood ADs. Parental involvement seems beneficial for treatment effectiveness when children have comorbid disorders. However, the fact that parental involvement was not randomized hampers more definite conclusions.

Keywords: anxiety disorders; children; modular CBT; effectiveness; predictors

MODULAR CBT FOR CHILDHOOD ANXIETY DISORDERS: EVALUATING (PREDICTORS OF) TREATMENT EFFECTIVENESS

Cognitive Behavioral Therapy (CBT) is effective for treating anxiety disorders in children (e.g., effect size of CBT compared to no therapy: $d = 0.76$; Crowe & McKay, 2017). This is promising, yet there is still room for improvement. For example, about one third of children is not free from their primary anxiety disorder after treatment (e.g., Silverman, Pina, & Viswesvaran, 2008). One way to optimize outcome is to adjust treatment to the individual child, for example through the use of a modular CBT. Modular CBT is an innovative way of adapting CBT intervention to the individual, by dividing an evidence-based treatment into self-contained modules (Ng & Weisz, 2016). In this way, modular CBT provides a structured approach while at the same time the therapist is able to choose which modules to use, and in what order. Therefore, treatment of two different children with the same manual may look different because of the chosen modules or the order of the modules. Support for the use of modular treatment comes from a study of Weisz et al. (2012). In this study, 174 youths with anxiety, depression, trauma, and/or conduct problems received intervention for their problems. Therapists were randomized by providing either modular treatment, standard evidence-based care (manual), or usual care. Youth showed faster improvements after modular therapy compared to both usual care and standard evidence-based treatments (Chorpita et al., 2013; Weisz et al., 2012). A limitation to that study was that sample sizes were too small to conduct separate analyses for the specific target groups (e.g., children with anxiety disorders). In addition, modular CBT for anxiety disorders has been applied in school-based settings and demonstrated positive results in terms of treatment effectiveness and treatment response (Chiu et al., 2013; Galla et al., 2012; Ginsburg, Becker, Drazdowski, & Tein, 2012).

Another way to improve our understanding about treatment effectiveness is examining for whom treatment (does not) work or for whom treatment works best. Several child and parental characteristics have been examined as predictors of treatment outcome in standardized (non-modular) CBT for anxiety disorders. Consistently, reviews and meta-analyses did not find that child gender or age predicted treatment outcome (Crowe & McKay, 2017; Nilsen, Eisemann, & Kvernmo, 2013). In contrast, other child pre-treatment characteristics such as type of AD or comorbidity have been found to predict treatment outcome. Several studies indicated that having a diagnosis of social anxiety disorder (SAD) is a predictor of less favorable outcomes compared to children with for example generalized anxiety

disorder (GAD), separation anxiety disorder or specific phobias (e.g., Compton et al., 2014; Hudson et al., 2015). In addition, comorbid depressive symptoms are found to be a predictor of less favorable CBT outcome for children with anxiety disorders (Compton et al., 2014; Walczak, Ollendick, Ryan, & Esbjørn, 2017), whereas no negative treatment effect was found for hyperactivity symptoms (Manassis et al., 2002) or autism spectrum traits (Puleo & Kendall, 2011; Van Steensel & Bögels, 2015).

Next to child factors, parent's own anxiety symptoms and parental involvement has been associated with treatment effectiveness. However, for both factors evidence is inconsistent. That is, Bodden et al. (2008) found parents' own anxiety (disorders) to be associated with worse treatment outcome, while others did not find a relation between parental anxiety and treatment outcome (Lundkvist-Houndoumadi, Hougaard, & Thastum, 2014; Podell & Kendall, 2011). In addition, some studies point to the relevance of studying fathers' and mothers' anxiety separately. For example, Legerstee et al. (2008) found that maternal (but not paternal) anxiety symptoms were associated with better treatment outcome in adolescents, while it has also been found that fathers' (but not mothers') anxiety symptoms were predictive of worse treatment outcome (Liber et al., 2008; Rapee, 2000). With respect to parental involvement, involving parents does not seem to enhance treatment outcomes (see the (meta-analytical) reviews of Breinholst, Esbjørn, Reinholdt-Dunne, & Stallard, 2012; Crowe & McKay, 2017; In-Albon & Schneider, 2007; Manassis et al., 2014; Thulin, Svirsky, Serlachius, Andersson, & Öst, 2014). However, when children are young, parents have anxiety problems themselves, and/or when a child has comorbid problems, parental involvement may be related to beneficial treatment outcomes. For example, previous research did show that family CBT – in which parents were involved – was more effective for younger children (and girls) compared to older children (Barrett, Dadds, & Rapee, 1996). In addition, for children with high attention deficit problems family CBT was more beneficial than child CBT (Maric, Van Steensel, & Bögels, 2015), and similar results were found for children with high autistic traits (Puleo & Kendall, 2011). Further, parental involvement may be differentially related to child therapy outcome, dependent on parents' own psychopathology, although inconsistent findings have been found in this regard. For example, Bodden et al. (2008) found that when parents had anxiety disorders themselves, child CBT was more beneficial than family CBT, while Pereira et al. (2016) did not find that parental involvement interacted with mothers' and fathers' anxiety in the prediction of therapy outcome.

Summing up, CBT is highly effective for children with ADs, but about one third is not recovered after treatment. The current study tried to address this variability in outcome by using a modularized CBT program in order to enhance CBT outcomes for children with ADs. Thus, we studied the effectiveness of modular CBT and examined predictors of treatment effectiveness, in a sample of children who were referred to several community mental health care clinics. We hypothesized that treatment effectiveness was large, and that child characteristics such as age, gender, type of AD, and comorbidity would not necessarily predict treatment effectiveness, as modular therapy may be more personalized and therefore not differentially related to these child factors. However, we did expect parents' own anxiety/depression symptoms to lead to less favorable outcomes. Considering the large amount of evidence that family CBT does not outperform child CBT (at least on the short term), we did not expect that the level of parental involvement would contribute to a better outcome; however, we did expect that parental involvement would interact with child age, child comorbidity and parents' anxiety/depression symptoms in a way that parental involvement is beneficial for younger children, children with comorbidity and, tentatively, when parents are anxious/depressed themselves.

METHOD

Participants

Participants were 116 children referred with anxiety disorders (56 boys; 48.3%) aged 7-17 years (mean age = 11.13, SD = 2.51), and their parents. Of the parents, 109 mothers (93.9%) and 89 fathers (76.7%) participated. Their mean age was 43.92 (SD = 4.89) and 46.38 (SD = 5.97) respectively. Parents filled in their highest educational level which was divided in five categories: (1) primary school (0% of the mothers / 1.4% of the fathers) (2) secondary school (8.2% of the mothers / 10.1% of the fathers), (3) middle level vocational school (37.1% of the mothers / 27.5% of the fathers), (4) bachelor degree (27.8% of the mothers / 34.8% of the fathers), and (5) master degree or higher (26.8% of the mothers / 26.1% of the fathers).

Of the 116 children, 106 were administered a semi-structured clinical interview (SCID-junior) at pre-test to establish the presence of DSM-5 disorders (n = 10 did not complete the interview assessment prior to treatment). All 106 children were found to have at least one anxiety disorder; most common being generalized anxiety disorder, social anxiety disorder and specific phobia (see Table 1). Most children had more than one anxiety disorder (mean number of anxiety disorders = 2.03,

SD = 0.95; 69 children (65.1%) had a comorbid anxiety disorder. In addition, 62 children (58.5%) had a comorbid disorder other than an anxiety disorder (see Table 1).

Table 1. Overview of the types of anxiety disorders and comorbid disorders based on the semi-structured interview for DSM-5 disorder (SCID-junior)

	N = 106*	%
Anxiety disorder (AD)		
Generalized anxiety disorder	67	63.2
Social anxiety disorder	56	52.8
Specific phobia	53	50.0
Separation anxiety disorder	29	27.4
Panic disorder	8	7.5
Agoraphobia	1	0.9
Selective Mutism	1	0.9
Comorbid disorder (not AD)		
Attention Deficit Hyperactivity Disorder	34	32.1
Insomnia	26	24.5
Mood Disorder	12	11.3
Obsessive Compulsive Disorder	7	6.6
Autism Spectrum Disorder	5	4.3
Illness Anxiety Disorder	5	4.7
Post-Traumatic Stress Disorder	3	2.8
Oppositional Defiant Disorder	3	2.8
Tourette's Disorder	1	0.9
Disruptive Mood Dysregulation Disorder	1	0.9

* SCID missing n = 10

MEASURES

Treatment effectiveness was measured by the presence (yes/no) of the (primary) anxiety disorder (as measured by the SCID-Junior) and by the amount of anxiety symptoms (as measured by the SCARED-71). Child predictors were gender and age (as measured by a demographical questionnaire), type of anxiety disorder (as measured by the SCID-junior), and comorbidity (as measured by the SCID-junior and the BPM). Parent predictors were mothers' and fathers' anxiety/depression symptoms (as measured by the anxiety/depression subscale of the ASR), and parental involvement in treatment (yes/no) as indicated by the questionnaire that

therapists filled in about each treatment sessions (i.e., who was present during the session, how long did the session last, which module(s) did you use).

SCID-Junior. DSM-5 disorders were assessed with the Structured Clinical Interview for DSM-5 Disorders for Children (SCID-junior, Braet, Wante, Bögels, & Roelofs, 2015). The SCID-junior integrates parent and child reports to obtain a combined diagnosis. Results regarding the psychometric properties of the SCID-junior are expected in 2020 (C. Braet/L. Wante, personal communication, October 9, 2019). Psychometric properties of the previous version (KID-SCID) have been evaluated (Roelofs, Muris, Braet, Arntz, & Beelen, 2015). Results demonstrated reasonable to good agreement between children's and parent's report, and satisfactory to good internal consistencies. In the current study, 10% of the interviews were double coded by an independent rater and interrater agreement based on the presence or absence of the anxiety disorder was high; SCID-junior child report $\kappa = 0.82$, SCID-junior parent report $\kappa = 0.72$.

SCARED-71. The Screen for Child Anxiety Related Emotional Disorders (SCARED-71; Bodden, Bögels, & Muris, 2009) was used to assess child anxiety symptoms. Child and both parent reports were used. The SCARED-71 consists of 71 items which are rated on a three-point scale (0 = (almost) never; 1 = sometimes; 2 = often). The total scale of the SCARED-71 was used for the current study. The SCARED-71 has good psychometric properties (with high internal consistencies with α's above > .90 for the total score and good construct and discriminant validity; Bodden et al. 2009; Van Steensel, Deutschman, & Bögels, 2013). In the current study, high internal consistency was found for all reporters at all measurements (α > .89 for mothers; α > .92 for fathers; α > .92 for children).

BPM. The Brief Problem Monitor (BPM; Achenbach, McConaughy, Ivanova, & Rescorla, 2011) was used to assess comorbid symptoms in children. The BPM consists of 19 items which are drawn from the CBCL (Achenbach & Rescorla, 2001) and can be summed to three subscales (internalizing, externalizing and attention problems) or a total score. The total score was used in the current study. Each item is rated on a 3-point scale (0 = not true, 1 = somewhat true, 2 = very true) by the mothers and fathers. The BPM has demonstrated good test-retest reliability, validity and internal consistency (Achenbach & Rescorla, 2001; Piper, Gray, Raber, & Birkett, 2014). In the current study, internal consistency was good (α > .80 for mothers; α > .77 for fathers).

ASR. The subscale anxiety/depression of the Adult Self-Report Form for Ages 18-59 (ASR 18-59; Achenbach & Rescorla, 2003) was used to measure anxiety/depression symptoms in both parents. The subscale anxiety/depression consists of 18 items that are rated on a 3-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true). In the current study, the subscale score obtained at pretest was used. The reliability and validity of the ASR and the anxiety/depression subscale is good (Achenbach & Rescorla, 2003). In the current study, internal consistency of the anxiety/depression subscale was high ($\alpha > .83$ for mothers; $\alpha > .82$ for fathers).

Parental involvement. Therapists completed a treatment rating form in which they filled in for each session who was present during the session (child, mother, father) and which module was used (e.g., psycho-education, cognitive restructuring, exposure, etc.). Parental involvement was expressed as the percentage of total number of sessions that at least one parent was present during treatment.

Procedure

Mental health care centers and therapists were asked to participate in the study. The mental health care centers were typical community centers not specifically specialized in treating anxiety disorders. No in- or exclusion criteria were set for a mental health care center or therapist to join the study. In addition, no in- or exclusion criteria were set for the participants other than (1) having an anxiety disorder, (2) having a least one parent who wanted to participate in the research, and (3) the therapist/multidisciplinary team indicated anxiety treatment. Thus, children with anxiety problems were referred to one of the 20 participating mental health care centers and were asked to participate in the study when the multidisciplinary team decided that anxiety treatment was needed. When families agreed to participate, the researcher was informed, and families were contacted for their first measurement. There were four assessments: before treatment started (pre), after 5 sessions (mid), directly after treatment (post) and 10 weeks after treatment (follow-up). Families gave informed consent and ethical approval was obtained from the ethical committee of the University of Amsterdam. Families received a 20 euro gift card after they finished all measurements.

All children received a modular CBT to treat their anxiety problems. This modular CBT is an adapted version of the protocol Discussing + Daring = Doing (Bögels, 2008) which consists of 12 child sessions and additional 3 parent sessions, and is proven effective to treat anxiety disorders in children (Bodden et al., 2008;

Jongerden, 2015; Van Steensel & Bögels, 2015). The adapted modular CBT consists of the following modules: (1) psycho-education, (2) coping skills (including task concentration), (3) think (cognitive restructuring), (4) feel (relaxation + mindfulness), (5) do (experiments + exposure), (6) parental guidance, and (7) relapse prevention. In this study, the modules psycho-education and relapse prevention were compulsory in respectively the first and last session. For the remaining sessions, therapists (together with clients) were free to choose any module which they thought (based on intake and pre-treatment information, and clinical experience) would be helpful to overcome the child's anxiety problems. In addition, therapists (together with clients) decided on the number and length of the sessions, as well as on homework assignments.

Data analyses

Percentages were calculated for the number of children being free from their primary anxiety disorder and for the number of children being free from all anxiety disorders. Two approaches were used. First, we calculated the percentages based on completer analyses. Second, we calculated the percentages based on intent-to-treat analyses where the approach of last observation carried forward was used to estimate the outcomes of the participants who dropped out (or of which their measurement was missing).

Hierarchical multi-level analyses were used to calculate the treatment effect on anxiety symptoms and to examine which child and parent predictors were related to treatment effectiveness. Standardized scores were used in all analyses. Therefore, parameter estimates can be interpreted as Cohen's *d* (dichotomous predictors) or *r* (continuous predictors). Standardized Z-scores were used to check for outliers (Z-scores > (-)3.29). Outliers were identified for parental involvement and were trimmed when used in analysis. In the first multi-level analysis, we evaluated treatment effectiveness by adding mid-, post- and follow-up to the model as predictors (as contrasted against pre-assessment). In the second set of multi-level analyses, child and parent predictors were added for their main effects, and interactions between the child/parent predictors and assessments (mid, post and follow-up) were added to evaluate the predictors' effect on treatment effectiveness. Separate analyses were run for each predictor (child gender, child age, child type of anxiety disorder, child comorbidity, parental anxiety/depression and parent involvement). In the third set of multi-level analyses, models were run to examine whether the effect of parental involvement on treatment effectiveness is associated with (1) child age, (2) child comorbidity, and (3) parental anxiety/

depression. To investigate this, three-way interactions (between assessments, parental involvement and child age/ child comorbidity/ parental anxiety/depression) were added to the models.

RESULTS

Prior to analyses, data of the clinical information provided by parents and therapists were inspected. It turned out that 20 children were using medication (14 for ADHD-related problems, and 6 for anxiety/mood related problems) during the study trial, and that 27 families received additional treatment next to or after CBT (additional treatment was most often parental or family guidance for other problems than anxiety). The use of medication interacted with treatment effectiveness in a way that anxiety scores were higher at mid-, post, and follow-up assessments (less decrease in anxiety symptoms over time) for children who used medication compared to children who did not use medication (*parameter estimates* for mid-, post-, and follow-up assessment were respectively 0.47, p = .009; 0.37, p = .064; 0.57, p = .007). Children who received additional treatment next to modular CBT for anxiety disorders did not have higher anxiety levels, nor was additional treatment found to be related to treatment effectiveness.

Based on the completed session forms by therapists (N = 93, 80.2%), the mean number of sessions was 9.64 (SD = 4.40; range = 3-26; 14% received 1-5 sessions; 50% received 5-10 sessions, 30% received 10-15 sessions, and 7% received 15-26 sessions). It was examined whether treatment duration (i.e., number of sessions) was related to treatment effectiveness, however, this was not found to be the case. Because of the modular approach and therapists decided about which modules to use, treatment content varied.

In 83 (89%) of the 93 cases for which the session forms were completed by therapists, at least one parent was involved in treatment in (at least) one session. If parents were involved, both parents were involved in 53% of the cases, mothers only were involved in 40% of the cases, and fathers only were involved in 8% of the cases. In addition, when parents were involved in treatment, there was large heterogeneity in presence; from one session being present (7%) to every session being present (100%).

Treatment effectiveness

Table 2 displays the percentage of children being free from their (primary) anxiety disorder at pre-, mid-, post-, and follow-up assessment. Based on completer analyses, 68% of the children were free from their primary anxiety disorder at 10 week follow-up, and 60% free of all anxiety disorders. Based on intent to treat analyses, these percentages were 56% and 50% respectively (see Table 2).

Table 3 gives the results of the multi-level analyses examining treatment effectiveness. Compared to pre-assessment, anxiety symptoms at mid-, post- and follow-up are significantly decreased with an effect size of almost 1 for the follow-up (Table 3).

Table 2. Treatment effectiveness based on % free of (primary) anxiety disorder (AD)

	Completer analyses		Intent to treat analyses (LOCF)	
	Primary AD	Any AD	Primary AD	Any AD
Pre	0.0	0.0	0.0	0.0
Mid	19.7	11.3	12.1	6.9
Post	60.2	45.5	47.4	35.3
Follow-up	67.7	60.4	56.0	50.0

Table 3. Treatment effectiveness based on decrease in anxiety symptoms (measured by the SCARED-71) since pre-measurement

	Parameter estimate (SE)*	t	p
Mid	-0.29 (0.07)	-4.04	<.001
Post	-0.78 (0.08)	-10.24	<.001
Follow-up	-0.97 (0.08)	-11.62	<.001

* Interpretable as Cohen's *d* (0.3 = small, 0.5 = medium, 0.8 = large)

Predctors of treatment effectiveness

Results of the predictor analyses are displayed in Table 4. Child predictors (i.e., gender, age, type of anxiety disorder, presence of a comorbid disorder, and comorbid symptoms) were not found to be related to treatment effectiveness (i.e., non-significant interactions between predictors and measurements) with two exceptions. First, anxiety symptoms of boys were lower than girls at mid-assessment (NB. note that boys already had the tendency to have lower anxiety scores than girls, and that the gender difference in treatment effect was no longer evident at post-assessment or follow-up). Second, the anxiety scores of children

who had a Generalized Anxiety Disorder at pre-treatment were decreased more at follow-up than the anxiety scores of children with other anxiety disorders. (NB. note that children with Generalized Anxiety Disorder had higher anxiety levels than children without Generalized Anxiety Disorder to begin with). Children with comorbid disorders (other than AD) had higher anxiety levels than children without comorbidity, and relatedly, children's comorbid symptoms (measured with the BPM) were positively associated to their anxiety scores, but comorbidity was not associated with treatment effectiveness.

Maternal (but not paternal) anxiety/depression scores were found to be related to child anxiety scores in the direction that higher anxiety/depression scores in mothers are associated with higher anxiety levels in their children. However, maternal as well as paternal anxiety/depression scores were not related to treatment effectiveness. Higher level of parental involvement in treatment was related to a higher decrease in anxiety scores at follow-up.

Three-way interactions between level of parental involvement, measurements (mid- post- and follow-up against pre-assessment) and (1) child age, (2) child comorbidity, and (3) parental anxiety/depression scores were examined. No significant three-way interactions with child age or parental anxiety/depression scores were found, however, a significant three-way interaction between time (follow-up), child comorbidity (yes/no comorbid non-anxiety disorder based on SCID), and parental involvement was found (*parameter estimate* = -0.30, p =.048). Post hoc analyses revealed that at follow-up the level of parental involvement was not associated with better treatment effectiveness for children without comorbid disorders (*parameter estimate* = 0.05, p = .666), but for children with comorbid disorders higher parental involvement in treatment was associated with less anxiety symptoms at follow-up (*parameter estimate* = -0.35, p = .006).

Table 4. Results of the multi-level analyses examining predictors of treatment effectiveness.

	Parameter estimate (SE)*	t	p
Gender (0 = girl; 1 = boy)	-0.29 (0.17)	-1.75	.083
Gender*Mid	**-0.33 (0.14)**	**-2.44**	**.017**
Gender*Post	-0.20 (0.15)	-1.29	.199
Gender*Follow-up	-0.23 (0.17)	-1.38	.171
Age	0.08 (0.08)	0.94	.350
Age*Mid	0.03 (0.07)	0.38	.703
Age*Post	0.08 (0.08)	1.01	.317
Age*Follow-up	0.07 (0.09)	0.84	.404
Separation AD (0 = no; 1 = yes)	0.21 (0.20)	1.07	.288
Separation AD*Mid	0.17 (0.15)	1.12	.267
Separation AD*Post	-0.22 (0.16)	-1.36	.176
Separation AD*Follow-up	-0.27 (0.19)	-1.46	.149
Social AD (0 = no; 1 = yes)	0.20 (0.18)	1.11	.268
Social AD*Mid	0.03 (0.15)	0.19	.853
Social AD*Post	-0.01 (0.15)	-0.04	.967
Social AD*Follow-up	-0.09 (0.17)	-0.51	.611
Generalized AD (0 = no; 1 = yes)	**0.74 (0.17)**	**4.46**	**<.001**
Generalized AD*Mid	0.16 (0.15)	1.08	.285
Generalized AD*Post	-0.23 (0.15)	-1.57	.120
Generalized AD*Follow-up	**-0.36 (0.17)**	**-2.10**	**.039**
Specific phobia (0 = no; 1 = yes)	0.14 (0.17)	0.80	.425
Specific phobia*Mid	-0.12 (0.15)	-0.86	.395
Specific phobia*Post	-0.23 (0.14)	-1.56	.122
Specific phobia*Follow-up	-0.09 (0.17)	-0.56	.576
Comorbid non-anxiety disorder (0 = no; 1 = yes)	**0.39 (0.17)**	**2.27**	**.025**
Comorbid disorder*Mid	-0.13 (0.15)	-0.88	.386
Comorbid disorder*Post	-0.11 (0.15)	-0.76	.452
Comorbid disorder*Follow-up	0.04 (0.17)	0.23	.817
Comorbid symptoms (BPM total score)	**0.40 (0.08)**	**5.00**	**<.001**
Comorbid symptoms*Mid	0.02 (0.07)	0.28	.784
Comorbid symptoms*Post	-0.03 (0.08)	-0.36	.722
Comorbid symptoms*Follow-up	0.02 (0.09)	0.27	.787
Maternal anxiety/depression (ASR)	**0.21 (0.09)**	**2.41**	**.018**
Maternal anxiety/depression*Mid	-0.04 (0.08)	-0.57	.569
Maternal anxiety/depression*Post	-0.06 (0.08)	-0.71	.480
Maternal anxiety/depression*Follow-up	-0.06 (0.09)	-0.66	.511

Table 4. Continued

	Parameter estimate (SE)*	t	p
Paternal Anxiety/depression (ASR)	0.17 (0.10)	1.77	.080
Anxiety/depression*Mid	-0.04 (0.07)	-0.53	.595
Anxiety/depression*Post	0.04 (0.09)	0.42	.674
Anxiety/depression*Follow-up	-0.00 (0.11)	-0.00	.998
Parental Involvement	0.03 (0.10)	0.35	.729
Parental involvement*Mid	-0.08 (0.08)	-0.92	.359
Parental involvement*Post	-0.17 (0.08)	-1.99	.050
Parental involvement*Follow-up	**-0.20 (0.09)**	**-2.32**	**.023**

DISCUSSION

The current study examined the effectiveness of a modular CBT for childhood ADs in a community clinics sample, as well as predictors of treatment outcome. Main findings can be summarized as follows: 1) the modular therapy with an average amount of sessions of less than 10 (M = 9.64, SD = 4.40) was highly effective, with an effect size of almost 1 and 56% (intent-to-treat analysis) to 68% (completer analysis) of the children being free from their primary anxiety disorder at 10 week follow up; and 2) treatment effectiveness was not predicted by child age, gender, comorbidity, or parental anxiety/depression symptoms; however, having a generalized anxiety disorder (GAD) was associated with better treatment effectiveness at follow-up comparted to having other anxiety disorders; and higher parental (maternal) involvement was associated with better treatment effectiveness at follow-up, but only for children with comorbid disorders.

The effectiveness of the modular CBT protocol in this sample was found to be in line with previous reported effects of non-modular CBT for child anxiety disorders (e.g., see meta-analyses of In-Albon & Schneider, 2007; Ishikawa, Okajima, Matsuoka, & Sakano, 2007; Reynolds, Wilson, Austin, & Hooper, 2012; Thulin et al., 2014). This finding may raise questions about the merit of modularization concerning that it was our study's aim to enhance CBT effectiveness by using a modular approach. However, our sample received on average approximately 10 sessions (9.64), which is quite low compared to non-modularized CBT protocols (standard CBT for childhood anxiety ranges between 12 and 16 sessions; e.g., Bodden et al., 2008; Kendall, Safford, Flannery-Schroeder, & Webb, 2004; mean number of sessions of 13.1 reported in the review of James, James, Cowdrey, Soler, & Choke, 2015, which included 41 treatment studies on childhood anxiety), and particular

when considering that 64% of the sample received between 1-10 sessions, this form of treatment may potentially be highly cost-effective. In addition, our study was performed in usual clinical practice with no in- or exclusion criteria for participants, therapists' education level or mental health care centers, and could therefore be regarded as a real-life effectiveness – instead of efficacy – study. Viewed in this light, our results may be even more promising. Although we cannot draw any conclusions towards the effects of modular CBT above and beyond standardized CBT based on this study, and RCT's comparing costs and effects of modular versus standardized treatment are needed, it seems at least plausible that using a modular approach is beneficial for children with ADs. In addition, although we have not examined this specifically in the current study, the acceptability of modular CBT in clinical practice may be higher compared to manualized CBT due to practical concerns (e.g., limited number of sessions allowed within certain systems of mental health care) as well as clinical considerations (e.g., shared decision making in treatment, therapeutic relationship, being able to adjust treatment to the individual needs). In support, the study by Chorpita et al. (2015) demonstrated that therapists' satisfaction was higher in the modular condition than in the standard evidence-based (manual) condition.

In agreement with most studies examining non-modularized CBT, we did not find evidence for child age or gender predicting treatment effectiveness (e.g., Herres et al., 2015). We did find some evidence that type of AD is associated with treatment effectiveness. That is, anxiety scores of children with Generalized AD were decreased more at follow-up than anxiety scores of children with other ADs. However, also note that children with generalized AD had higher anxiety scores to begin with, perhaps leaving more room for improvement. On the other hand, generalized AD has been linked to better treatment effectiveness in previous studies as well (e.g., Hudson et al., 2015; Wergeland et al, 2016). With respect to type of AD, it is somewhat remarkable that we did not find that children with social AD benefit less from treatment, as this is quite a robust predictor in many studies (Hudson et al., 2015; Wergeland et al., 2016). An explanation could be the use of a modular treatment approach in the current study which deviated at some points from other (non-modular) CBT. That is, not only could therapists decide how many sessions were spent on what content (modules) and in which order, they were also able to choose modules including task concentration and mindfulness, which helps the child become less self-focused (e.g., heightened self-focused attention is regarded as an important maintaining mechanism in social anxiety in adults as

well as in children; e.g., Bögels & Mansell, 2004; Maric, Willard, Wrzesien, & Bögels, 2019; Rapee & Heimberg, 1997).

With regards to parental involvement, we found that higher parental involvement was associated with higher treatment effectiveness at follow-up but only for children with comorbid disorders. It is important to note here that parental involvement was not a random factor, but it was deliberately chosen by therapists based on their clinical intuition. Thus, the result may reflect that therapists have chosen (in)correctly whether or not to involve parents, and at what time (e.g., involve parents on forehand, or when treatment stagnated). A further complication is that we do not know the nature of parental involvement in the treatment sessions: e.g., involving parents as collaborators or as co-clients, targeting parenting behaviors such as controlling or autonomy-granting, or supporting parents to do exposures with their child at home. Despite these uncertainties about the type of parental involvement, we did find that parental involvement appeared beneficial for children's anxiety scores at follow-up in the presence of child comorbidity other than anxiety disorders which is in line with previous research findings demonstrating that parental involvement for children with comorbid ASD- or ADHD-problems is more important (Maric et al., 2015; Puleo & Kendall, 2011; Van Steensel et al., 2017).

The main strength of this study is that it evaluated treatment effectiveness, and its predictors, in a large sample of clinically referred children who were treated for their anxiety problems in 'real-world' clinical practice. Therapists from multiple treatment centers participated, they could receive a short (2 hours) training in the modular treatment protocol, and were not supervised by the researchers during the delivery of treatment. In addition, the use of the modular protocol comes close to how clinicians use protocols in their daily work, thus contributing to the external validity of this study. However, some limitations also need to be addressed. First, there was no comparison group (receiving non-modular CBT), so there is no way of knowing whether modular CBT would outperform manualized CBT for childhood ADs. Second, no random assignment of parental involvement was made, and we also do not know in what way parents were involved. Although such an approach contributes to the external validity of the study, it is difficult to draw firm conclusions as to what extent parental involvement does or does not contribute to treatment effectiveness. Third, parental anxiety/depression symptoms were based on a self-reported questionnaire, and there was no measure for parental anxiety disorder. In addition, important to note is that parental anxiety/depression can

change during the course of treatment, and it may be that the change – rather than the anxiety/depression at baseline – is related to treatment effectiveness. Finally, a longer-term follow-up assessment is lacking, which is unfortunate as it has been suggested that the influence of parental involvement leads to more remission in the (long-term) period following treatment (Walczak, Esbjørn, Breinholst, & Reinholdt-Dunne, 2017).

To conclude, this study provides evidence that modular CBT can be highly effective for the treatment of childhood ADs. Recovery rates of ADs and effect sizes in this study are comparable to those of efficacy studies but in (on average) less treatment sessions. Although the benefits of involving parents in CBT for children with ADs have been – and still are – subject to debate, this study suggests that it appears beneficial to involve parents when the child has comorbid problems (in this study most common comorbid disorders were ADHD, insomnia, and mood disorders). However, the fact that parental involvement was not randomized hampers more definite conclusions regarding the role of parental involvement for children with comorbidity.

DISCUSSION

DISCUSSION

The aims of this dissertation were to gain understanding in the impairment and transmission of anxiety disorders in children, as well as to examine the effectiveness and the predictors of effectiveness of a modular treatment protocol. Following the results of the chapters in this dissertation, several points will be more thoroughly reflected upon.

Impact of Childhood Anxiety Disorders

First, results of Chapter 2 showed that (family) impact of childhood anxiety disorders is present and comparable to the impact of developmental disorders such as ADHD and ASD. Mothers and fathers do report similar levels of parental stress for children with anxiety disorders, compared to parents of children with ADHD and ASD. In addition, the psychopathology of parents of children with anxiety disorders was comparable to those of parents of children with ADHD and ASD, and was heightened compared to parents of typically developing children. Finally, quality of life of children with anxiety disorders was affected, as it was lower than typically developing children, and comparable to quality of life of children with ASD and ADHD on the domain psychological functioning.

These findings indicate that the impact of childhood anxiety disorders on children and their parents should not be underestimated. That is, taking into account our results and those of other studies, anxiety disorders are definitely impairing and thus require adequate treatment in order to improve quality of life. Nonetheless, only 31% of children with anxiety disorders are seeking help (Chavira, Stein, Baily, & Stein, 2004). This shows that we might miss out on children who suffer from their anxiety (disorder) while not receiving help. On the other hand, the study of Jongerden et al. (2015) showed that impairment was associated with referral, indicating that the most severe cases do get help. This calls for a better awareness of the presence of anxiety disorders among significant others in the environment of the anxious child, such as parents and teachers. However, distinguishing children with moderate and severe anxiety disorder may not always be straightforward for teachers (Headley & Campbell, 2011) and parent-child agreement about referral problems is generally low and even lower for internalizing problems (Yeh & Weisz, 2001). It is known that parents have several barriers when seeking help, such as beliefs that the child's anxiety will disappear over time, and ignorance about available professional support (Reardon, Harvey, & Creswell, 2019). In addition, childhood anxiety may not always be recognized due to anxiety disorders being

less visible than behavioral disorders because of their internalizing nature and the avoidance strategies of the children. Thus, more information about presence and development of anxiety disorders should become accessible to parents, for example through the child monitoring system (Dutch: *consultatiebureau*). In addition, when teachers are more sensitive to the symptoms of anxiety disorders as well as the possibilities to treat anxiety disorders, they could have a signaling function and inform parents or direct the child to school care. This asks for a thorough approach, and one could think of distributing information packages regarding anxiety disorders, or providing lectures in schools about anxiety disorders. Some regions in The Netherlands already use screening instruments in order to examine youth mental health at primary and secondary schools (i.e. Hart en Ziel, GGD Amsterdam; Jij en Je Gezondheid, GGD Amsterdam, GGD Drenthe). This could be extended by adding a specific screening instrument for anxiety disorders and referring children that are above a certain level of symptoms to the general practitioner or a (school) psychologist. When there is more specialized help needed, children should be referred to specialized mental health care in order to prevent negative consequences related to untreated anxiety disorders (Kendall, Safford, Flannery-Schroeder, & Webb, 2004).

Anxiety in Families

Main findings of Chapter 2 were that children with anxiety disorders are two to three times more likely to have a parent with anxiety disorders compared to children without anxiety disorders. This confirms the existing claim that anxiety disorders do run in families. However, we did not find that siblings of children with anxiety disorders were at higher risk of developing anxiety disorders themselves. This is interesting, as it has been shown that there is evidence for both a genetic and a direct environmental transmission of parent anxiety to offspring anxiety (Eley et al., 2015). Possibly, this indicates that children are differentially susceptible in developing anxiety disorders. That is, the anxious child responds differently to its environment than its siblings, i.e. the child is more negatively affected by its anxious parent (through modeling or overprotection, e.g., Barrett, Rapee, Dadds, & Ryan, 1996). If anxious children truly are differentially susceptible, this would also mean that they would flourish more than their non-anxious sibling when they are in a positive and stimulating environment (Belsky & Pluess, 2009). Moreover, the finding that siblings do not have an anxiety disorder while the referred child has, could be an indication that it is not only the parents that play a role in the transmission of anxiety disorders (either through genes or environment (parenting practices), but that the non-shared environment is important as well as individual

factors. It is known that individual factors within the child are important markers of the development of anxiety disorders. Some of these are already known such as an inhibited temperament, and interpretation biases (the tendency to interpret neutral or ambiguous situations as negative or threatening; Miers, Blöte, Bögels, & Westenberg, 2008). It is important to examine these factors in order to prevent anxiety disorders. Future research needs to be carried out in order to examine the individual susceptibility more into detail. Recently, the attention for genes has already spread to the treatment studies, examining whether children are differentially susceptible for the effectiveness of treatment (Keers et al., 2016; Lester & Eley, 2013). In this way, combining knowledge of the transmission and origins of anxiety disorders can be used to improve treatment outcome.

One remarkable finding from Chapter 3 was that all fathers with social anxiety disorders had children with social anxiety disorders themselves. Tentatively, this suggests that specifically social anxiety disorders run in families; and, it might be that fathers in particular have an important role in the transmission of social anxiety disorders. It has been proposed that socially anxious fathers show less challenging behavior, and this in turn is related to the development of social anxiety in their children (Majdandžić, Möller, de Vente, Bögels, & van den Boom, 2014). Therefore, it could be that specifically social anxiety in fathers impacts their child, as it might be conflicting with fathers' evolutionary role (Bögels & Perotti, 2011). However, do keep in mind that the current study had a cross-sectional design and we cannot state the direction of effect; that is, it could also be that the socially anxious child evokes social anxiety symptoms in their father, more so than in their mother. Longitudinal designs involving fathers with and without social anxiety disorders, and preferably a comparison group, may provide additional insights. Results of Chapter 3 further stress the importance of including both parents in research and examine the possible different influences of mother versus father, as well as the influence of parents on different children in the family.

Treatment

Treatment studies can be placed on an efficacy-effectiveness continuum (Weisz & Jensen, 1999), considering three dimensions: treated individuals, treatment setting, and therapists. In short, efficacy is characterized by carefully controlled conditions, whereas effectiveness is based on the real-world clinical practice. This dissertation is a follow-up in a series of studies that examined the efficacy and effectiveness of the treatment protocol Discussing + Doing = Daring (DDD; Bögels 2008). The efficacy of DDD has been established in 2008, following an RCT

comparing group CBT vs individual CBT (Bodden et al, 2008). The effectiveness of DDD was also partially established in that study, given that the RCT took place in real world clinical centers under partially real-world clinical conditions. Following that study, the treatment program was published and consisted of 12 individual sessions and 3 optional parent sessions. It became well-known in The Netherlands and is included in the NJI database of effective interventions. Table 1 summarizes the studies that have been carried out to examine the effectiveness of the DDD program. The current study (Chapter 5) contributed to this research line. Results regarding treatment effectiveness are consistent with those of the previous studies (see Table 1). Although no direct comparison was made, it seems like the flexible (modular) approach did not lead to better results. However, it was found that the average number of sessions used in the current study was lower (10 sessions versus 12-15 sessions), making this approach potentially cost-effective. In addition, two other results are noteworthy:

First, the modular treatment protocol seems to have a beneficial effect for children with social anxiety disorders (see Chapter 4), and treatment was not found to be less effective for the children with social anxiety disorders compared to the children with other anxiety disorders (Chapter 5). This is in contrast to previous studies which have consistently shown that children with social anxiety disorders benefit less from treatment than children with other anxiety disorders (Baartmans, Van Steensel, Klein & Bögels, submitted; Hudson et al., 2015; Wergeland et al., 2016). This contradictory finding makes it particularly interesting to speculate why our modular treatment may be beneficial for treating social anxiety disorders in specific. One explanation is that the modular version provides more time for relaxation exercises, mindfulness, and/or task concentration tasks. Although previous studies have shown that relaxation exercises do not benefit children with all sorts of anxiety disorders over and above cognitive restructuring and exposure (Ale, McCarthy, Rothschild, & Whiteside, 2015); it could be that for children with social anxiety disorders these exercises are of particular use. Specific characteristics of children with social anxiety disorders are their attention bias towards anxious stimuli, self-focused attention, and post-event processing (negative evaluation of a social situation) (Spence & Rapee, 2016). Mindfulness does target these attention processes by focusing on the here and now in a non-judgmental way. Future research incorporating mindfulness as an additional module and comparing treatment with and without mindfulness- or task-concentration training, may provide additional insights whether mindfulness is beneficial for children with social anxiety disorders.

The second result concerns parental involvement. Although contrary to clinical expectations (e.g. parents are important in guiding exposures in order to let their child practice in different situations), previous studies have shown that the involvement of parents in treatment does not have additional benefit over and above individual child therapy (see the meta-analyses of Breinholst, Esbjørn, Reinholdt-Dunne, & Stallard, 2012; In-Albon & Schneider, 2007; and, Thulin, Svirsky, Serlachius, Andersson, & Öst, 2014). It has been speculated that parents are less effective than therapists in supporting their child due to an existing pattern of overprotective behaviors (Thulin et al., 2014), or because parents simply identify and empathize with their anxious children, and/or that the parental involvement is too time consuming and distracts from the core elements of therapy (Breinholst et al., 2012). Interestingly, our study showed that parental involvement predicts a better outcome at follow-up, but only for children with comorbid disorders, such as externalizing disorders. Thus, it seems that for some children, involvement of parents is of importance, and for others not. Therefore, we may need to approach parental involvement bottom-up: which child with which characteristics benefits from parental involvement in treatment. Possibly, children with comorbid disorders benefit from parental involvement as they need not only anxiety treatment, but also need to deal with their comorbid problems. For example, a child with ADHD may have problems with planning exposures, a child with depression may need to be stimulated by its parents to actively engage in exposures, and a child with ASD may need its parents to translate exposures to daily practice. Or, as these children are not only anxious, they elicit a different response from their parents than children who are anxious only, possibly making their parents better co-facilitators of therapy. Future research needs to be carried out in order to provide therapists with the right tools to inform their decision in (the amount of) parental involvement, and in this way tailor treatment to the individual.

In sum, the modular treatment program of DDD is potentially cost-effective due to the lower mean number of sessions, limited training, and supervision of therapists. The modular treatment is also beneficial to children with specifically social anxiety disorder, a disorder found to be more difficult to treat with standard CBT. In addition, the decision for parental involvement should be based on the child's characteristics. Building upon previous research regarding DDD, the modular treatment is a next step in trying to find answers to 'what works for whom' in treatment of childhood anxiety disorders.

Table 1 Studies Examining Effectiveness of the 'Discussing + Doing = Daring' Treatment Program

Author	Type of study	Treatment protocol	Participants	Effect size*	Percentage free of primary AD
Bodden et al., 2008	RCT	Individual vs family DDD	Clinically referred children with ADs	High: *d* = 1.2	At 3 month follow-up 73% (indiv. DDD) versus 61% (family DDD)
Jongerden (2015)	Effectiveness	Real world vs controlled research trial	Children with an anxiety disorder according to the ADIS-C/P, no ASD	Posttest: *d* = .85; follow-up: *d* = .94	At 3-months follow-up: 50% below cutoff SCARED (research-child report) - 56% (real world – child report)
Van Steensel & Bögels, 2015	Effectiveness	Individual DDD	Clinically referred children with ASD + AD versus ADs	*d* = 1.45	At 3 months follow-up, 65% of the children with and 72% without ASD were free of their primary anxiety disorder
Maric, Van Steensel, & Bögels, 2015	Efficacy	Individual CBT vs Family CBT	Children with an anxiety disorder and comorbid ADHD symptoms	Posttest: *d* = 0.91; follow-up: *d* = 0.94	Not available
Van Doorn, Jansen, Bodden, & Lichtwarck-Aschoff, & Granic, 2017	Efficacy	Manualized (DDD) vs Treatment-as-Usual	Children with an DSM-IV anxiety disorder and exclusion criteria, no ASD or specific phobia	Child-rated symptoms posttest DDD: *d* = 0.96; follow-up: *d* = 1.53. TAU: posttest: *d* = 0.63; follow-up: *d* = 1.06	Not available
Van Steensel, Telman, Maric, & Bögels, 2019	Effectiveness	Modular	Clinically referred children with ADs, no exclusion other disorders	Posttest: *d* = 0.78; 3-months Follow-up: *d* = 0.97	At 3-months follow-up: 68% (completer analysis)

*Interpretable as Cohen's *d* (0.3 = small, 0.5 = medium, 0.8 = large).

Note: DDD= Discussing + Doing = Daring; AD = anxiety disorder; ASD = autism spectrum disorder

Limitations and future directions

Despite its strengths, the studies discussed in this dissertation are not without limitations. The most important limitations are addressed below, followed by some suggestions for future research.

First, we did not address comorbidity in Chapter 2. That is, we only selected children with a single diagnosis in order to make pure comparisons between children with different psychiatric diagnoses. However, in real world clinical practice, children are often facing comorbid diagnosis; for example, children with anxiety disorders suffering from depression (Costello, Egger, & Angold, 2005), and children with ASD suffering from anxiety disorders (Van Steensel, Bögels, & Perrin, 2011). This makes it hard to generalize our findings to real world clinical practice. Therefore, it is recommended to examine the impact of anxiety disorders, over and above other disorders. For example, by comparing various clinical groups with and without comorbid anxiety disorders. A study by Van Steensel, Dirksen and Bögels (2012) did this for children with ASD. In that study children with ASD and anxiety disorders were compared to children with anxiety disorders without ASD. They found that anxiety disorders had a negative impact on the quality of life over and above the ASD-related problems. A similar comparison could be made with other groups; for example by comparing children with ADHD with and without comorbid anxiety disorders. This way, we may have a more clinically representative sample, while still being able to disentangle the impact of anxiety disorders.

Second, the design of Chapters 2 and 3 was cross-sectional and therefore we cannot state the direction of the associations between parent and child variables. A longitudinal design would be able to indicate the temporal sequence: does child anxiety disorder affect the parent, does parent anxiety disorder affect the child, or are associations bi-directional (i.e. parent and child influence each other over time). As we know, children and parents are constantly changing and influencing each other, and trying to capture relations in one moment in time (cross-sectional design) ignores the dynamic interplay and hampers more definite conclusions. Moreover, the studies do not indicate which mechanisms are underneath the observed associations (i.e. genetic and/or environmental).

Third, Chapters 4 and 5 examined the preliminary efficacy of a modular treatment manual, but did not compare this to a standard manualized treatment, treatment as usual, or a waitlist control condition. Interesting in this respect is the study of Chorpita et al. (2015) which showed that therapists valued both effectiveness and responsiveness of the modular treatment over and above standard manualized treatment and treatment as usual (Chorpita et al., 2015; Weisz et al., 2012). We did not compare the modular DDD to manualized DDD or treatment as usual directly; however, it does not seem that the modular approach (Chapter 5) led to higher effects than the manualized approach (Table 1), which is in contrast to the study

of Chorpita et al. (2015). Possible explanations for the differences between our study outcomes and Chorpita et al. (2015) might be that our follow-up was too short (i.e., Weisz et al., 2012, included a one year follow-up), or that our sample was more specific (treatment of anxiety disorders only while the study of Chorpita et al. also included treatment of depression and conduct problems), or that the broad range of inclusion criteria in our study resembled the real world clinical practice more. However, do note that our effect sizes of manualized DDD are high, and our modular therapy was on average shorter than manualized DDD. Further research directly comparing modular anxiety treatment to manualized treatment and to treatment as usual is needed, as well as research on how and why therapist choose a particular module for a specific client.

Fourth, we relied mainly on parent and child reported measures in this dissertation. We did administer structured diagnostic interviews in order to provide an objective measure for treatment effectiveness, but still parents and children answer the questions. Objective measures of child anxiety disorders, such as behavioral approach tests (e.g., Klein et al., 2015), provide a different and important type of information about child anxiety improvement.

Finally, there is a large variability in the samples used in Chapters 4 and 5. This was a goal of the study, to examine treatment effectiveness in a sample that is close to the 'real world of clinical practice'; however, at the same time, this could have led to a (too) large variation which makes it hard to find differences or possible predictors. In addition, predictors such as parental involvement were not randomized, which hampers more definite conclusions about when or how to involve parents if their child has comorbid disorders. Moreover, increasing external validity usually leads to a decrease in internal validity. Indeed, therapies differed in length as therapists were not restricted to a number of sessions, and therapists were not asked about why they decided to choose a particular module, on which information they based their decision, or what their motivation was to structure the treatment. Such information is important to better understand the treatment process, and to find out if it is really the treatment that has driven the effect. Another possibility to gain insight into the treatment process and its efficacy, is to examine when change takes place during treatment. This could be examined using *sudden gain analysis* (Tang & DeRubeis, 1999; Wiedemann, Thew, Scott, & Ehlers, 2019). A sudden gain is a sudden reduction in symptoms between two consecutive sessions (Tang & DeRubeis, 1999). In practice, the child could fill out a short screening list of anxiety symptoms after each session. Sudden gain analysis could then examine

when change takes place (Wiedemann et al., 2019) and connect this to the therapy techniques that possibly contributed to that change.

Final considerations

Taken together, this dissertation shows that childhood anxiety disorders are impairing, parents of anxiety disordered children more often suffer from anxiety disorders themselves, and modular CBT seems a feasible and potentially cost-effective way of treatment of childhood anxiety disorders. For clinical practice the implications of this dissertation's findings are quite simple and straightforward: (1) be aware and screen for childhood anxiety disorders, (2) know that anxiety tends to run in families – which seems specifically the case for social anxiety disorders in fathers and children, (3) consider the role of mothers *and* fathers, (4) know that there is a highly effective modular treatment for childhood anxiety disorders and use it, (5) consider the involvement of parents in childhood treatment for anxiety disorders when the child has comorbid disorders, but (6) also know that treatment predictors and moderators still need to be examined to determine which children benefit from which treatment, and the answer to the question 'for whom therapy works (and why)' is still a very relevant one (Maric, Prins & Ollendick, 2015).

Does this dissertation raise more questions than it answers? Probably. When having answers to some questions, those answers almost immediately address other questions leading to new and other research questions. However, this dissertation hopes to add to the field of childhood anxiety disorders some starting points in order to tailor treatment to the individual. It would be naïve to think that – with the right information – we can prevent anxiety disorders from developing; however, when we are able to intervene in time with the right intervention, we can prevent anxiety disorders from worsening, treat them effectively, and hopefully make them less impairing for the child and its family.

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SUMMARY

SUMMARY

Impact, Transmission, and Effectiveness of Treatment of Childhood Anxiety Disorders

Anxiety is a healthy response to a threatening situation, in order to make one aware of danger. However, when anxiety persists in the absence of a threatening situation, and impairs the child's daily functioning, the child can be classified as having an anxiety disorder. Anxiety disorders are by far the most prevalent mental disorders in children and adolescents. Comorbidity among anxiety disorders is high (i.e., children with one anxiety disorder are often suffering from another anxiety disorder), as well as comorbidity with other disorders such as depression or ADHD. Anxiety disorders can lead to difficulties in social functioning, school functioning and family functioning. Moreover, untreated anxiety disorders may lead to impairment in interpersonal functioning and school refusal, as well as a reduced quality of life in adulthood.

Although anxiety disorders are found to be highly prevalent and have been associated with negative consequences, not all children with anxiety disorders are receiving help to overcome their anxiety. This questions the impact of childhood anxiety disorders; are (families of) children with anxiety disorders better off (less interference) compared to children with other disorders? In **Chapter 2** the (family) impact of anxiety disorders was compared to children with ADHD, ASD and a control group of typically developing children. Quality of life of these children, as well as parental psychopathology and parental stress were examined. Results showed that the impact of childhood anxiety disorders is present and comparable to the impact of developmental disorders such as ADHD and ASD, especially in the domains physical and psychological well-being. Moreover, the psychopathology of parents of children with anxiety disorders was comparable to that of parents of children with ADHD and ASD, and higher than the psychopathology of parents of typically developing children. Mothers and fathers of children with anxiety disorders showed comparable levels of parental stress but did not differ in parental stress from parents of typically developing children. The direction of findings remains to be investigated, that is, childhood anxiety disorders impact parental functioning, cause/maintain parental functioning, or both. It was concluded that the impact of childhood anxiety disorders on children and their parents should not be underestimated, and parents and teachers need to be informed about the presence and development of anxiety disorders.

Next, there is quite some evidence that anxiety tends to 'run in families', that is, parents with anxiety disorders often have children with anxiety disorders. Evidence is available that this transmission is partly attributed to genetic markers, as well as to direct environmental factors. In **Chapter 3** it was examined to what extent anxiety runs in families from a bottom-up approach: are children with anxiety disorders more likely to have parents with anxiety disorders and siblings with anxiety disorders? In this study, the association between ADs in a clinically referred sample of children with ADs, their mothers, fathers, and siblings was examined, using diagnostic interviews, and these rates were compared to a control group of typically developing children. Results showed that children with anxiety disorders were two to three times more likely to have at least one parent with an anxiety disorder (current or lifetime). Interestingly, children were not more likely to have siblings with anxiety disorders. Evidence was found for the specificity of generalized anxiety disorders between mothers and children and it was found that social anxiety disorder in specific tends to run in families (mothers, fathers, children, and siblings). As social anxiety has been associated with worse treatment outcomes in previous studies and this research showed that social anxiety does seem to run in families, more research towards the mechanisms of family transmission in social anxiety disorders as well as the role of these parents in treatment is necessary.

In Chapter 4 and 5 the effectiveness of a modularized Cognitive Behavioural Therapy (CBT) for children with anxiety disorders was examined. It is known from previous studies that CBT is the most effective treatment of anxiety disorders in children, with up to two-third of the treated children overcoming their primary anxiety disorder. Nevertheless, treatment does not work for everyone and this asks for a more thorough examination of treatment adaptations in order to improve treatment outcome. A modular treatment program is one way to adapt treatment to the individual and in this way possibly improving treatment outcome.

In **Chapter 4** the effectiveness of a modularized CBT for children with social anxiety disorders was examined in 10 cases that were pooled from a larger dataset. To facilitate individually tailored treatment and therapist flexibility, the modularized CBT consisted of seven modules: (1) psycho-education, (2) think (cognitive restructuring), (3) coping skills (including task concentration), (4) dealing with feelings (relaxation and mindfulness exercises), (5) do (experiments + exposure), (6) parental guidance, and (7) relapse prevention. Results showed that 5 children were free of their social anxiety at posttest, and 8 at follow-up. Clinically meaningful improvements from pretest to follow-up were found. This study showed that

therapists are able to implement a modular CBT, by choosing elements out of the evidence-based therapy that could fit the individual child, and that in particular social anxiety disorder a modular approach works well. Possibly, the modular version provides more time for relaxation exercises, mindfulness, and/or task concentration tasks. However, future research examining these specific treatment ingredients may provide additional insights about which modules are beneficial for children with social anxiety disorders in specific.

Finally, **Chapter 5** examined treatment effectiveness and predictors of outcome of a modular treatment protocol used in usual clinical practice. This study examined 116 children with anxiety disorders. Predictors of effectiveness were child characteristics (gender, age, type of AD, comorbid disorders), fathers' and mothers' anxious/depressive symptoms, and parental involvement based on parents' presence during treatment sessions. Main results showed that the modular treatment was effective but not more effective when compared to the outcomes of other studies. In contrast to previous research, it was found that the treatment was not less effective for children with social anxiety disorders compared to children with other anxiety disorders. Next, results showed that parental involvement predicts a better treatment outcome at follow-up, but only for children with comorbid disorders. Thus, the involvement of parents might be beneficial for some children, but not all. However, parental involvement was not randomized, and future research needs to be carried out in order to provide therapists with the right tools to inform their decision in (the amount of) parental involvement, and in this way tailor treatment to the individual.

Taken together, this dissertation first shows that childhood anxiety disorders are impairing, and that the impact is comparable to the impact of developmental disorders such as ADHD and ASD. Second, parents of anxiety disordered children more often suffer from anxiety disorders themselves, but siblings of children with anxiety disorders are not at higher risk of developing anxiety disorders themselves. There seems however to be a specific tendency of social anxiety disorder to run in families. Third, modular CBT seems a feasible way of treatment of childhood (social) anxiety disorders and is potentially cost-effective due to the relatively low mean number of sessions, limited training and supervision of therapists.

SAMENVATTING

Angststoornissen bij kinderen: Invloed op het dagelijks leven, overdracht en de effectiviteit van behandeling

In een bedreigende situatie is angst een gezonde reactie van het lichaam om te waarschuwen voor dreigend gevaar. We spreken van een angststoornis als de angst aanwezig is in een situatie die niet bedreigend is en als het kind zodanig last heeft van de angst dat het dagelijks leven beïnvloed wordt. Angststoornissen zijn de meest voorkomende psychische stoornissen bij kinderen en adolescenten. De comorbiditeit tussen angststoornissen is hoog (verschillende angststoornissen komen tegelijkertijd voor bij één kind), net zoals de comorbiditeit met andere stoornissen zoals depressie of ADHD. Angststoornissen kunnen leiden tot problemen met het dagelijks functioneren, zoals sociaal, op school en thuis. Bovendien kunnen onbehandelde angststoornissen leiden tot beperkingen op latere leeftijd, waaronder schoolweigering, vermindering van sociale contacten en een verminderde kwaliteit van leven.

Hoewel angststoornissen veelvoorkomend zijn en geassocieerd worden met negatieve consequenties, krijgen niet alle kinderen met angststoornissen hulp voor het behandelen van hun angsten. Dit roept de vraag op in hoeverre een angststoornis invloed heeft op het (gezins)leven van het kind: zijn (gezinnen van) kinderen met angststoornissen beter af dan kinderen met andere stoornissen? In **Hoofdstuk 2** is een vergelijking gemaakt tussen kinderen met angststoornissen en kinderen met ADHD, autismespectrumstoornissen (ASS), en een controlegroep van normaal ontwikkelende kinderen. Deze groepen werden vergeleken op kwaliteit van leven, ouderlijke psychopathologie en opvoedingsstress. De resultaten toonden aan dat het hebben van een angststoornis wel degelijk impact heeft, en dat deze vergelijkbaar is met de impact van ontwikkelingsstoornissen zoals ADHD en ASS, met name in de domeinen fysiek en psychologisch welbevinden. Daarbij was de psychopathologie van ouders van kinderen met angststoornissen vergelijkbaar met die van ouders met kinderen met ADHD en ASS, en hoger dan de psychopathologie gemeten bij ouders van de controlegroep. Moeders en vaders van kinderen met angststoornissen lieten even hoge niveaus van opvoedingsstress zien, maar verschilden niet van kinderen van de controlegroep. Het is nog onduidelijk in welke richting we deze resultaten kunnen interpreteren: is het zo dat angststoornissen bij het kind de ouderlijke psychopathologie beïnvloeden, veroorzaken, of hieruit voortvloeien. We concludeerden uit deze studie dat de impact van angststoornissen op zowel het kind als op hun ouders niet moet worden onderschat. Het is daarom

belangrijk dat ouders en leraren goed op de hoogte zijn van de aanwezigheid en de ontwikkeling van angststoornissen bij kinderen, zodat zij op tijd hulp kunnen inschakelen.

Er is aantoonbaar bewijs dat ouders met angststoornissen vaak ook kinderen met angststoornissen hebben; de appel valt niet ver van de boom. Deze overdracht kan deels door de genen worden verklaard, maar ook door omgevingsfactoren (bijvoorbeeld door een bepaalde opvoedingsstijl of angstig voorbeeld van ouders). In **Hoofdstuk 3** is onderzocht hoe vaak angst voorkomt binnen gezinnen, waarbij wordt beredeneerd vanuit het kind: hebben kinderen met angststoornissen vaker ouders en/of broers/zussen met angststoornissen vergeleken met kinderen zonder angststoornissen? De resultaten toonden aan dat een kind met een angststoornis twee tot drie keer vaker een ouder met een angststoornis heeft. Opvallend was dat dit niet geldt voor de broers/zussen, daarbij werd geen verschil gevonden met de controlegroep. Daarnaast werd gevonden dat een sociale angststoornis vaker voorkomt binnen het gezin: als het voorkwam bij het kind was de kans groter dat ook de moeder, vader, en/of broer/zus last had van een sociale angststoornis. Uit de literatuur is bekend dat sociale angststoornissen vaak moeilijker te behandelen zijn dan andere angststoornissen bij kinderen. Het is daarom van belang dat er meer onderzoek gedaan wordt naar hoe deze angststoornissen worden overgedragen binnen gezinnen en waarom de sociale angststoornis vaker voorkomt binnen gezinnen. Op deze manier kunnen er mogelijk aanknopingspunten gevonden worden om de behandeling van sociale angststoornissen bij kinderen te verbeteren.

Vervolgens is de effectiviteit onderzocht van een modulaire Cognitieve Gedragstherapie (CGT) voor kinderen met angststoornissen. CGT is de meest effectieve behandeling voor kinderen met angststoornissen, waarbij ongeveer twee derde van de kinderen na afloop van behandeling vrij is van zijn/haar angstklachten. Toch blijft er ook een groep kinderen over voor wie de behandeling minder goed werkt en daarom richt de wetenschap zich op het bieden van handvatten om ook deze laatste groep goed te kunnen ondersteunen. In hoofdstukken 4 en 5 wordt onderzoek naar een modulair behandelprotocol beschreven; hierbij wordt het bestaande behandelprotocol ‘Denken + Doen = Durven’ opgedeeld in losse modules waar de therapeut uit kan kiezen. Op deze manier kan de behandeling worden toegespitst op het individuele kind, wat bovendien goed aansluit bij het werken in de klinische praktijk.

In **Hoofdstuk 4** zijn de effecten van de modulaire CGT voor 10 kinderen met sociale angststoornissen onderzocht. Het behandelprotocol bestond uit 7 modules die naar wens konden worden toegepast: (1) psycho-educatie, (2) denken (cognitieve herstructurering), (3) copingvaardigheden (waaronder taakconcentratie), (4) omgaan met gevoelens (ontspanningsoefeningen en mindfulness), (5) doen (experimenten en exposure), (6) ouderbegeleiding en (7) terugvalpreventie. Resultaten lieten zien dat 5 kinderen vrij waren van hun sociale angststoornis op de nameting, en 8 kinderen bij follow-up. Deze resultaten zijn veelbelovend en het is mogelijk dat er door de modulaire versie meer tijd is voor ontspanningsoefeningen, mindfulness en/of taakconcentratie; elementen die verband houden met het verplaatsen van de aandacht van de angst naar een neutrale situatie. Er is echter meer en gestandaardiseerd onderzoek nodig om te onderzoeken welke modules nu zorgen voor een vermindering van de sociale angst van het kind.

In **Hoofdstuk 5** zijn de voorspellers van behandeluitkomsten en behandeleffectiviteit onderzocht van het modulaire. Dit onderzoek werd uitgevoerd in de klinische praktijk onder 116 kinderen met een angststoornis. De predictoren die werden onderzocht waren kindkenmerken (geslacht, leeftijd, type angststoornis, comorbiditeit), ouderkenmerken (angstig/depressieve klachten) en ouderbetrokkenheid (aanwezigheid bij de behandelsessies). De resultaten toonden aan dat de modulaire behandeling effectief is in het verminderen van angstklachten van voor- naar nameting en follow-up. De uitkomsten lijken overeen te komen met studies naar de behandeleffectiviteit van 'gewone' CGT. In tegenstelling tot eerder onderzoek werd in deze studie geen verschil gevonden in de effectiviteit voor kinderen met sociale angststoornissen ten opzichte van andere angststoornissen. Ten tweede werd gevonden dat de betrokkenheid van ouders een beter behandelresultaat voorspelde op follow-up, maar alleen voor kinderen met comorbide stoornissen. Dit kan inhouden dat de aanwezigheid van ouders bij de behandeling nuttig is voor sommige kinderen. Toekomstig onderzoek zou dit verder moeten onderzoeken om zo aanknopingspunten te vinden voor therapeuten over het al dan niet betrekken van ouders bij de behandeling.

Samenvattend toont dit proefschrift aan dat angststoornissen bij kinderen leiden tot beperkingen in het dagelijks leven, op sommige gebieden vergelijkbaar met de impact van ontwikkelingsstoornissen zoals ADHD en autismespectrumstoornissen. Ten tweede hebben ouders van kinderen met angststoornissen zelf vaker ook last van angststoornissen, maar broers/zussen van angstige kinderen lijken geen verhoogd risico te hebben op het ontwikkelen van een angststoornis. Er is

tegelijkertijd wel een aanwijzing dat sociale angst vaker voorkomt binnen gezinnen. Tot slot lijkt de modulaire CGT een wenselijk alternatief voor het behandelen van angststoornissen bij kinderen en is deze mogelijk kosten-effectief doordat het minder sessies vergt en gepaard gaat met relatief weinig training en supervisie van therapeuten. Toekomstig onderzoek zal zich moeten richten op de vraag 'wat werkt voor wie onder welke omstandigheden' zodat behandeling nog meer kan worden toegespitst op het individuele kind.

CONTRIBUTIONS OF CO-AUTHORS

Chapter 2 is published as: Telman, L. G. E., Van Steensel, F. J. A., Maric, M., & Bögels, S. M. (2017). Are Anxiety Disorders in Children and Adolescents Less Impairing Than ADHD and Autism Spectrum Disorders? *Child Psychiatry and Human Development*, *48*, 891-902.
LT contributed to the design and data collection of this study, wrote the draft of the manuscript and conducted the statistical analyses. FvS designed the study. FvS, MM, and SM commented on the draft of the manuscript. SB was project leader of this study.

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When the dog bites, when the bee stings, when I'm feeling sad
I simply remember my favorite things
And then I don't feel
So bad

Julie Andrews – My favorite things

Anxiety disorders in children are the most common child mental health disorders; however, their impact on children seems to be understood. In addition, anxiety tends to run in families, but it is unclear to what extent this holds for mothers, fathers, and siblings, as well as for specific anxiety disorders. Finally, treatment of childhood anxiety disorders leads to improvement, but not for every child. This dissertation aims to shed light on these issues by examining the impact of childhood anxiety disorders, the transmission of anxiety disorders within families, and the initial effectiveness of a modular approach of cognitive behavioral

Liesbeth Telman (1989) grew up in Pijnacker with her parents, brother and sister. After obtaining her gymnasium diploma in Delft, she moved to Amsterdam for studying European Studies and Pedagogical Sciences. Her main interest was in the abnormal development of children and she specialized in clinical treatment studies. From her passion to help children overcome and/or learn to deal with their problems, she started this research. Liesbeth lives with her husband and two daughters in Houten.