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Introduction
The translated lines are part of a children's poem written by a well-known Dutch poet and story-teller (Schmidt, 1987/2007). In a humorous way the poem addresses a topic highly relevant for children, namely the experience of ‘fear’. It shows fear to be a phenomenon from which even the bravest of knights may suffer. The poem continues with a description of the strategy the heroic knight applied to conquer his fear, but alas, his strategy was ineffective. The hero-by-day knight experienced levels of fear beyond normal which may have reflected the presence of an anxiety disorder. Professional help may have been necessary as his own strategy was insufficient to overcome his intense anxiety. But what are the chances that our knight would have recovered from his anxiety if treated by a professional?

That question brings us to the central theme of this dissertation: assessment of the prognostic value of various variables for cognitive behavioral treatment outcome for childhood anxiety disorders. Childhood anxiety disorders can be defined as a limited ability to recover from anxiety levels that prevent or limit developmentally appropriate behavior in children and a limited ability to remain anxiety-free when the anxiety provoking situation is absent (Klein & Pine, 2002). Although the experience of anxiety appears inherent to human beings and childhood, the study of childhood anxiety has not always been that evident. Studies addressing the question ‘what to do’ when confronted with childhood anxiety were longtime rare. Fortunately, a steady increase in the number of studies addressing this topic can be seen in the past decades.

A History of Childhood Anxiety

References to childhood anxiety disorders appeared uncommon in psychiatry and psychology literature in the early nineteenth century (Treffers & Silverman, 2001). It is unlikely however, that children before this period were ‘fearless’. In 1798 Rush published an article ‘On the different species of phobia’. Rush argued that the names of species should have been taken from the names of the objects of the fear (e.g. Rat Phobia, Solo Phobia, Power Phobia, Home Phobia) and said that Blood Phobia and Ghost Phobia are more likely to occur in children. His reference to childhood anxiety is one of the first that can be found in the literature. With regard to the study and implementation of effective and reliable treatments there was still a long way to go, as Rush (1798; in Verhey and Treffers, 2004) explained:

“Blood-letting as a remedy, is defended from being used improperly, by the terror which accompanies its use. This terror rises to such a degree as sometimes to produce paleness and faintness when it is prescribed as a remedy. However unpopular it may be, it is not contrary to nature, … The objections to it (therefore) appear to be founded less in the judgments than in the fears of sick people.” (p. 368)

The scarcity of literature on childhood anxiety disorders in the early nineteenth century can be explained by the then held view that anxiety was mainly a vulnerability factor which could
lead to the development of psychiatric disorders in general (Treffers & Silverman, 2001). In the second half of the nineteenth century anxiety in children acquired the status of a psychiatric symptom and disorder (Treffers & Silverman, 2001, page 2). The first description of an anxiety disorder that is close to our current conception of childhood anxiety can be found in a publication by Chrichton-Brown (1860) on ‘psychical diseases in early life’. Crichton-Browne described that Pantophobia consists in an excited or diseased state of the instinct of self-preservation, which is often accompanied by delusions. He adds that such intense misery may occasion that suicide is resorted to as a means of relief and explains that night horrors, common among young children, are a transient species of Pantophobia (Crichton-Browne, 1860). It was only a couple of decades after Crichton-Brown’s publication that psychologists started to study fear in children and youngsters (more) methodically (Binet, 1896; Hall, 1897). Binet (1896) studied anxiety in school children using a multi-method strategy including teacher questionnaires as well as interviews with acquaintances and observations of children. Approximately 250 teacher questionnaires were distributed of which 110 questionnaires were returned. Interestingly, Binet (1896) reflected on the reliability of his responders observations “… et surtout le caractère moral de l’observateur. Celui-ci n’apprécie le degré de peur d’un enfant que par rapport a ses idées personnelles et a son tempérament. “ (p.238). Binet also highlighted reasons given by teachers and school-boards for non-response (e.g. school teacher’s response: “Je n’ai jamais remarqué de peur chez mes élèves. Au reste, ils auraient peur de quoi? … Ce n’est plus de l’époque. …” (p. 224)). With regard to treatment Binet first posed the question whether it is at all possible to effectively treat all anxious children. Secondly, he differentiated between children with a nervous constitution, children who are anxious due to environmental causes (e.g. accidents, maltreatment) and fears that are normal during childhood and disappear as children grow older. Thirdly, Binet describes that the nature of treatment can either be preventive or curative and makes several suggestions. He suggests that one should not use violence, one should avoid or suppress inadequate role-modeling (peers or parents), one should not over-stimulate children’s imagination, one should ensure that confidence is transferred to the children themselves, and most importantly (according to Binet) training of the children in acts of bravery. The last suggestion is accompanied by the advice to familiarize children gradually with the object of their fear. It is surprising to see how many of his suggestions still hold today.

In the following twentieth century there was a growing attention for, and acceptance of the existence of psychiatric disorders in general. The field of childhood and adolescent psychiatry slowly developed into a professional field in itself. Childhood and adolescent psychiatric disorders were not yet included in the sixth edition of the 1948 version of the International Classification of Diseases, Injuries and Causes of Death (ICD-6; World Health Organization, 1948) nor in the 1952 Diagnostic and Statistical Manual for Mental Disorders (DSM; American Psychiatric Association, 1952). But in the third version of the DSM, published
in 1980, a separate chapter was dedicated to childhood and adolescent disorders (American Psychiatric Association, 1980; Saavedra & Silverman, 2002; Treffers, 2002).

Classification

The first DSM chapter on childhood and adolescent disorders included three separate anxiety disorders (Separation Anxiety Disorder, Avoidant Disorder and Overanxious Disorder) in addition to the anxiety disorders included in the ‘adult section’. In the fourth DSM version only one childhood anxiety disorder was included (i.e., Separation Anxiety Disorder), other anxiety disorders that also apply to children were included in the adult section (American Psychiatric Association, 1994). The taxonomy provided on (childhood) anxiety disorders in this fourth DSM edition (see Appendix 1) led to major advances in understanding and treatment of childhood anxiety (Weems & Stickle, 2005). Nevertheless, the validity of the taxonomy of childhood anxiety disorders continued to be questioned (Ferdinand, Van Lang, Ormel, & Verhulst, 2006) and adjustments to the DSM have been proposed (Ferdinand, Van Lang, Ormel, & Verhulst, 2006; Weems & Stickle, 2005). Though the classification of childhood anxiety disorders may be hindered by several problems (i.e., the high comorbidity of anxiety disorders with each other and with mood disorders; Treffers, 2002), researchers and clinicians appear to agree that childhood anxiety disorders do exist. The utility of classification systems such as the DSM is paramount for the recognition and identification of problem behavior and for facilitating the selection of appropriate treatments with the target problems of clients. In order to reliably assess and discriminate between disorders the use of evidence based assessment methods such as diagnostic interviews are recommended (Silverman & Ollendick, 2005).

Prevalence

In the past decades epidemiological research revealed that childhood anxiety is one of the most prevalent childhood mental problems (Verhulst, 2001). Prevalence rates for childhood anxiety disorders in a USA sample showed that 2-4% of children aged 9 to 16 met DSM criteria for any anxiety disorder (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). Similar results were found in a British survey (age 5-15, 3-4%), a Puerto Rican sample (age 4-17, 2.7-4.6%), a Finnish cohort (age 8-9, 5.2%) and a French sample (age 8-11, emotional disorders 5.9%) (Almqvist et al., 1999; Canino et al., 2004; Fombonne, 1994; Ford, Goodman, & Meltzer, 2003). Prevalence rates vary due to differences in age and gender of the participating youth (Essau, Conradt, & Petermann, 2000). Anxiety disorders tend to be somewhat more prevalent in girls versus boys and more prevalent in older versus younger children (Verhulst, 2001). A recent Dutch study showed that the proportion of children scoring deviant on parent reported internalizing problems increased from 1983 to 2003 (Tick, Van der Ende, & Verhulst, 2007). Unfortunately, media and government attention tends to focus on externalizing problems (e.g. conduct, oppositional behavior) thereby overlooking the negative impact on the well-
being and development of many children with internalizing problems. For instance, between January the 1st 2000 and March the 15th 2008 sixty-three official Dutch government documents were retrieved when searching for ‘anxiety disorders’ combined with ‘children’ whereas a threefold ($n = 190$) of documents was retrieved when searching for ‘conduct disorders’ combined with ‘children’ (http://parlando.sdu.nl/cgi/login/anonymous).

**Developmental Risks Associated with Childhood Anxiety**

Treatment of childhood anxiety disorders (CAD) is of great importance as CAD seriously interfere with the well being of children. CAD have been associated with a lower quality of life, somatic complaints (in girls mostly), school refusal, poor academic performance, peer relationship problems and fewer or poorer friendships than children without emotional disorders (Bastiaansen, Koot, & Ferdinand, 2005; Egger, Costello, Erkanli, & Angold, 1999; Last & Strauss, 1990; Mancini, Van Ameringen, Szatmari, Fugere, & Boyle, 1996; McShane, Walter, & Rey, 2001). These findings illustrate that childhood anxiety disorders affect developmentally important areas such as social functioning and school or academic functioning. Moreover, CAD might be substituted by another (anxiety) disorder some years later (Öst & Treffers, 2001). Children with anxiety problems reported elevated rates of anxiety disorders and major depression during adolescence, young adulthood and adulthood (Goodwin, Fergusson, & Horwood, 2004; Gus Manfro et al., 2003; Reinherz, Paradis, Giaconia, Stashwick, & Fitzmaurice, 2003) and showed an increased risk for developing an avoidant personality disorder or substance use disorder (Compton, Burns, Egger, & Robertson, 2002; Joyce et al., 2003). In general, internalizing problems during childhood or adolescence showed stability over time in both a normal population and a clinically referred population (Heijmens Visser, Van der Ende, Koot, & Verhulst, 2000; Roza, Hofstra, Van der Ende, & Verhulst, 2003). The interference with children’s daily lives and the increased risk these children run for a long-term negative outcome indicate that professional help is needed.

**Treatment of Childhood Anxiety**

Currently, Cognitive Behavioral Therapy (CBT) is one of the most widely used strategies for the treatment of adult anxiety disorders, as behavioral and cognitive behavioral strategies received the label *well-established* (Chambless & Ollendick, 2001) and may be more effective than other treatments (Reisner, 2005). With regard to the treatment of childhood anxiety disorders, the empirical validation of CBT treatments accelerated in 1994 with the publication of a Randomized Clinical Trial (RCT) evaluating the effectiveness of a CBT protocol for children aged 9-13 years with an anxiety disorder (Kendall, 1994). It was hypothesized that children in the active treatment condition ($n = 27$) would show significant change in outcome measures in contrast to the wait-list control condition ($n = 20$). The results supported Kendall’s hypothesis; the post-treatment findings revealed that a significantly higher number of children no longer met criteria for an anxiety disorder in the active treatment condition and
were within normal limits on many outcome measures. Since the publication of this landmark study many RCT’s supporting the effectiveness of CBT for CAD have appeared (e.g., Barrett, Dadds, & Rapee, 1996; Kendall et al., 1997; Shortt, Barrett, & Fox, 2001; Silverman, Kurtines, Ginsburg, Weems, Lumpkin et al., 1999). These studies culminated in such a solid empirical base for the effectiveness of CBT for CAD that CBT received the label probably efficacious (Chambless & Ollendick, 2001). Treatments are awarded this label if there is at least one RCT in which the treatment proved superior to a control condition or other bona fide treatment. The label well-established and specific has not been given due to a lack of studies investigating specificity and superiority to placebo-conditions.

It could be argued that this label might need updating. Several studies showed superiority of CBT over placebo conditions in the treatment of childhood anxiety (Beidel, Turner, & Morris, 2000; Ginsburg & Drake, 2002; Muris, Meesters, & Melick, 2002). Furthermore, a meta-analyses including 24 treatment outcome studies for CAD revealed an overall mean effect of 0.86 (large) based on children’s self-report measures (In-Albon & Schneider, 2007). The mean post-treatment recovery rate for the principal diagnosis was 68.9%; the more clinically relevant rate of recovery from all anxiety diagnoses revealed a more modest percentage of 55.4 in the intent-to-treat sample. Though these results are a promising and hopeful accomplishment, it also indicates that almost half of the treated children do not respond sufficiently to the CBT treatment. Interestingly, four CBT treatment outcome studies on child anxiety included an attention placebo-condition with an average effect-size of 0.58 which is considerably below the effect-sizes of the active treatment condition but not significantly different. One of the factors that might lead to variation in findings between studies is the differential approach to the statistical analysis and description of pre- to post-treatment changes.

Clinically Significant and Meaningful Change

An important issue related to the study of treatment outcome is how to effectively evaluate the nature and degree of change that has occurred as a result of therapy. Effect-sizes are often used to reflect pre- to post-treatment changes, but reporting significant effect-sizes solely might not be representative for the amount of clinical pre- to post-treatment change (Kendall, 1999). A second strategy commonly used in treatment outcome studies to describe pre- to post-treatment change is the use of observed difference scores (difference between the pre- and post treatment measurement for individual clients). However, observed difference scores are influenced by regression to the mean due to errors of measurement. Moreover, observed difference scores do not tell how individuals fared in treatment or whether a clinical significant change was obtained (Wise, 2004). Change should not only be statistically significant, but also clinically meaningful, e.g. a treatment that has proven to be statistically significant but yielded effect-sizes of .15 (Cohen’s $d$) might not be clinically meaningful for individual patients. Conversely, an effect-size of .80 (Cohen’s $d$) which appears considerable is of no value if it is not statistically significant (due for instance to method limitations).
The issue of statistically significant change and clinically meaningful change has been repeatedly discussed (Chambless & Hollon, 1998; Kazdin, 1999; Kendall, 1999) and various sophisticated strategies have been suggested to cope with this issue (Jacobson, Roberts, Berns, & McGlinchey, 1999; Jacobson & Truax, 1991; Kendall, Marrs-Garcia, Nath, & Sheldrick, 1999). The discussion inspired researchers to report on the clinically significant and meaningful change in their research samples (e.g. Shortt, Barrett, & Fox, 2001; Silverman, Kurtines, Ginsburg, Weems, Rabian et al., 1999). Surprisingly, when studying predictors for treatment outcome, researchers tend to fall back on commonly used strategies (e.g. regression analyses with raw scores) (Rapee, 2000; Victor, Bernat, Bernstein, & Layne, 2006) leading to models that account for variance in outcome but not for variance in clinically significant or meaningful change.

A solution is the use of Reliable Change (RC)-scores, the most precise possible estimation of the true pre-post differences (Hageman & Arrindell, 1999). The RC-score is the normal deviate (z-score) of the value 0 within the (conditional) distribution of true difference scores given the observed difference score. For measures with a nearly perfect reliability, the RC-score is nearly a linear function of the observed difference score, as the observed and true differences scores will be almost similar. When the reliability of the measure approaches zero the RC-score will approach a constant, representing the overall mean of the observed difference scores. So, using the RC-score in outcome prediction studies represents a more conservative approach than using the observed difference score, if the outcome measure has a lower than nearly perfect reliability.

The RC-score can be transformed into three categories ($RC_{IND}$ index); improved ($RC_{score} < -1.65$), not reliably changed ($-1.65 \leq RC_{score} \leq 1.65$) and deteriorated ($RC_{score} > 1.65$). Negative RC-scores thus reflect a (reliable) reduction in symptoms. In order to determine which clients have reliably passed the cut-off for ‘normal functioning’, an index for Clinically Significant Change ($CS_{INDIV}$-score) can be computed. The $CS_{INDIV}$-score is, analogous to the RC-score, the normal deviate of the cut-off score within the (conditional) distribution of true post-scores given the observed post-score. A $CS_{INDIV}$-score $<-1.65$ can be used to conclude that the individual client has passed the cut-off for ‘normal’ functioning (a lower score indicates more ‘normal’ functioning with all outcome measures used in this study) (for a detailed description; see Hageman & Arrindell, 1999 and Jacobson & Truax, 1991). A dichotomous variable can be composed from the combination of the RC-categories and the CS-index, differentiating between ‘reliable and clinically significant recovery’ versus ‘not or partially recovered’.

What Works ‘for Whom’?

As already mentioned, not all children have recovered from CAD after CBT. The label ‘not or partially recovered’ might confront both researchers and clinicians with a disappointing fact: not all children benefit sufficiently from treatment. What’s more, the idea that children might deteriorate in the period that they receive treatment is an almost completely ignored
possibility (Mohr et al., 1990). As researchers and therapists we tend to suppress this possibility from our conversations, studies and awareness, or are eager to attribute failure to extra therapeutic conditions such as all too complex family circumstances.

Non-response or partial response evokes (at least) two important questions; (1) what should we offer children who did not benefit (sufficiently) from the treatment and (2) what works for whom? To address issues of non- or partial response researchers have started to develop stepped-care programs, in which more intensive and costly interventions are reserved for those insufficiently helped by an initial intervention (Haaga, 2000). The larger study in which the present dissertation is a part of, offers children who do not respond (sufficiently) to the initial CBT intervention a second treatment ‘step’ or additional treatment phase. The presented findings in this dissertation are based on a 12 session CBT program. The approach of stepped-care treatment will be reported on in a separate manuscript (Van der Leeden, Van Widenfelt, Utens, Liber, & Treffers, In preparation) and dissertation (Van der Leeden, In preparation).

The present dissertation study addresses the second question ‘What works for whom?’ This apparently simple question addresses an intriguing and complex research area. The main focus of this dissertation study will be on these last two words ‘for whom?’; addressing issues that may account for variance in treatment outcome. Investigation of relevant subgroups with particularly good (or poor) treatment response and examination of relevant processes and mechanisms that yield clinically significant change could enrich the investigation of outcome research (Hinshaw, 2007). More rigorously Hinshaw adds "Without the knowledge of which subgroups respond best and worst to any particular treatment, […] research on effective treatments is bound to remain at a relatively primitive, descriptive level." (Hinshaw, 2007, pp 664). Identification of relevant predictors for treatment outcome could therefore be a first step into a further understanding of ‘What works for whom?’.

Predictors for treatment outcome can be selected based either on their theoretical or empirical association with the development or maintenance of increased levels of anxiety. Alternatively, predictors for treatment outcome can also be selected for their previously shown empirical association with treatment outcome. Lambert and Asay (1999) suggested that, in general, variance in treatment outcome in adults can be accounted for by four sets of variables; (1) specific therapeutic techniques (15%), (2) extra-therapeutic change; (2a) factors that are part of the client and (2b) factors that are part of the environment (40%), (3) therapeutic relationship variables (30%), and (4) expectancy (placebo-effects) (15%) (Asay & Lambert, 1999) (see Figure 1.1). The present dissertation study will address several issues from these areas (e.g., family variables, comorbidity, social performance) and explore their impact on treatment outcome for CAD empirically.
Specific Therapeutic Techniques

For the present dissertation study, the category ‘specific therapeutic techniques’ is broadened into a category labeled ‘specific therapeutic techniques, technical factors and treatment modalities’. Technical factors represent the dosage of techniques delivered in this particular treatment. Treatment modalities refer to differences in treatment formats, e.g. individual or group, family or child-focused treatment.

We still know little about the comparative efficacy of alternative treatments to traditional individual CBT for CAD (Cartwright-Hatton, Roberts, Chitsabesan, Fothergill, & Harrington, 2004). One of the factors that might influence the treatment outcome is the format in which the treatment is delivered. Chapter 2 reviews the current empirical support for treating children either in Individual or in Group format and sketches the rationales provided in treatment outcome studies for the choice to treat children in Individual or Group format. Chapter 2 furthermore presents a description of the Randomized Clinical Trial conducted in order to compare the effectiveness of Individual CBT and Group CBT. Subsequently, the results of the Randomized Clinical Trial are presented and its implications discussed.

Evidence with regard to research on specific techniques in child treatment is scarce, but some significant relations between specific therapeutic interventions and child outcomes have been found. Greater use of family focused techniques, for instance, predicted post-treatment improvement in drug use, externalizing and internalizing symptoms in both treatment conditions of a randomized trial investigating individual CBT versus multidimensional family therapy (Hogue, Dauber, Samuolis, & Liddle, 2006). The focus and associated therapeutic techniques of treatments are considered the critical change agents in CBT for
child anxiety (Shadish & Sweeney, 1991). If the technical aspects of CBT do represent change agents, then the level of therapist adherence to the treatment protocol reflects the dose of offered change agents and thus should predict youth outcomes. Adherence checks can be used to assess for variability in the treatment variable, thus creating the means to examine intervention-outcome relations (Doss & Atkins, 2006). Chapter 6 explores the relative contribution of adherence to treatment outcome.

Extra-therapeutic Variables
Lambert and Asay define extratherapeutic change as factors that are a part of the client and part of the environment. The present dissertation study has a strong focus on both aspects of these extratherapeutic factors. Environmental factors herein mainly focus on the child’s home environment, as children are largely depending upon their parents for emotional and daily care.

Environmental factors.
Children spend the majority of their time in the family environment, it is therefore not surprising that this environment has a substantial impact on children’s development (American Academy of Pediatrics, 2003). Chapter 3 includes a short exploration of literature providing empirical support for the impact of parental variables, and more specifically the impact of parental anxiety and depression and parenting styles on the development of childhood anxiety. Consistent relationships between the development of childhood anxiety and especially maternal anxiety, depression and parenting have been reported in reviews and meta-analyses (Chorpita & Barlow, 1998; McLeod, Wood, & Weisz, 2006; Rapee, 1997; Wood, McLeod, Sigman, Hwang, & Chu, 2003). The role of fathers for the development of childhood anxiety and the treatment of childhood anxiety disorders has been largely overlooked. The results of a recent study suggest that the role of fathers with regard to care giving and family involvement may shift over time, adapting to family contexts and life circumstances (Wood & Repetti, 2004). There is some evidence showing differences between fathers and mothers in parenting styles and parental rearing behaviors; these differences suggest that parental rearing of fathers and mothers should not be considered equivalent a priori (Aunola & Nurmi, 2005; Bögels & van Melick, 2004). These new insights underline the importance to explore not only the maternal role but also the paternal role for treatment outcome of CAD, as the role of fathers might shift or change when having an anxious child. So far, researchers tended to focus on the role of mothers for treatment outcome or combined parental data instead of evaluating the differential impact of fathers and mothers. Secondly, chapter 3 includes an exploration of the literature in order to select empirically validated parental predictors for CBT outcome of CAD. The empirical section of chapter 3 carries on with a description of the selection procedure in the present dissertation study of parental predictors for treatment outcome. Furthermore, the discussion on clinically relevant and meaningful change
(Kazdin, 1999) is highlighted, and our solution to determine reliable and clinically significant change is described (Hageman & Arrindell, 1999). Variables that contribute to the prediction of treatment outcome will be described and assessed whether there is consistency in findings across statistical methods and informants. Again, the results on the prognostic value of several parental predictors for treatment outcome will be presented and accompanied by a discussion of the clinical implications and a brief description of the limitations and strengths of the present dissertation study.

Though a previous treatment outcome study did not show a negative effect of social economic status (SES) on treatment outcome (Berman, Weems, Silverman, & Kurtines, 2000) we acknowledge the possibility that the conditions associated with low SES (e.g., adversity and stress) might hinder treatment from being effective. As there is evidence that suggests an impact of SES on the development of emotional disorders in children (Costello, Compton, Keeler, & Angold, 2003) it is assessed whether the SES also impacts upon treatment outcome.

**Client characteristics.**

In the present dissertation study two categories of client characteristics were selected to guide further investigation of differences in treatment outcome; social functioning and comorbidity. The association between social functioning and anxiety symptoms has been examined in several studies (Cartwright-Hatton, Hodges, & Porter, 2003; Chansky & Kendall, 1997; Segrin & Flora, 2000). It has been suggested that anxious children do not necessarily lack social skills, but suffer from a distorted perception of their skills (Cartwright-Hatton, Tschernitz, & Gomersall, 2005). It has also been suggested that social skills deficits may lead to increased levels of anxiety (Segrin & Flora, 2000). Regardless of the chicken and egg question pertaining to social anxiety and social performance (or social skills) difficulties, chapter 4 explores the level of social performance in anxious children and the relation between social performance difficulties and treatment outcome. Those variables that show to contribute significantly to the prediction of treatment outcome will be presented. As social performance difficulties in particular tend to be studied in children or adults with Social Phobia (SOP) (e.g., Rapee & Lim, 1992; Spence, Donovan, & Brechman-Toussaint, 1999), differences between anxiety disordered children with and without SOP will be explored and any differences that might show will be reported. The results on the prognostic value of social performance will be followed by a discussion in which attention is given to the impact of the various social performance aspects on treatment outcome. Again, clinical implications, strengths and limitations of the present dissertation study are addressed.

Chapter 5 examines the hypothesized impact of comorbid conditions and severity on treatment outcome for children with anxiety disorders as comorbidity is a common phenomenon in anxious children (Angold, Costello, & Erkanli, 1999; Chavira, Stein, Bailey, & Stein, 2004). Children with comorbid conditions (e.g. more than one anxiety disorder, depression, ADHD) appear to suffer from more severe clinical phenomenology (Franco, Saavedra, & Silverman,
2007). Comorbidity is assumed to hinder treatment from being effective due to implementation difficulties or as disorders might be mutually maintaining. For instance, children with Social Phobia tend to avoid social situations whereas participation in social situations might be essential in the treatment of (comorbid) Depression in order to activate the clients. Chapter 5 differentiates between two kinds of comorbidity; each including two groups; one including children with a single anxiety disorder and the other a primary anxiety diagnosis and one or more comorbid disorders (labeled ‘total comorbidity’); secondly a differentiation was made between children with one or more anxiety disorders versus children with one or more anxiety disorders and a comorbid disorder other than anxiety (labeled ‘other comorbidity’). Comorbidity appears closely related to the concept of severity which reflects increased symptom levels. Disentanglement of these concepts appears crucial for understanding their unique impact on outcome. It will be assessed whether variance in pretreatment scores and variance in outcome can be accounted for by total comorbidity, other comorbidity and severity.

Differences in the occurrence of anxiety disorders appear related to age and/or gender (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Ford, Goodman, & Meltzer, 2003; Verhulst, 2001). Previous treatment outcome studies did not show an impact of age or gender on treatment outcome (Berman, Weems, Silverman, & Kurtines, 2000; Kendall et al., 1997; Nauta, Scholing, Emmelkamp, & Minderaa, 2003; Shortt, Barrett, & Fox, 2001; Southam-Gerow, Kendall, & Weersing, 2001). Nevertheless, in each of the chapters a differential impact on treatment outcome of these client characteristics is explored for the sake of completeness.

Relationship Variables

A meta-analytic review (Shirk & Karver, 2003) examining relationship variables and treatment outcome in 23 studies on child and adolescent therapy showed a mean correlation between therapist alliance and treatment outcome of .24, with no significant differences between behavioral and non-behavioral treatments, or between research settings and non-research settings. One of these relationship variables concerns therapeutic alliance, which has been defined as the therapist’s ability to develop a warm relationship and engage the client(s) in the therapeutic process (McLeod & Weisz, 2005). Despite these findings others commented that the role of alliance has been less consistent when examined explicitly in the context of specific forms of therapy, such as cognitive therapy, and suggested that the relationship between alliance and outcome may play differing roles across treatment modalities (DeRu- beis, Brotman, & Gibbons, 2005). So far, evidence for the contribution of alliance in CBT for childhood anxiety is scarce and indicates a weak relationship between alliance and outcome (Kendall, 1994; Kendall et al., 1997). Chapter 6 will explore the relative contribution of therapeutic alliance for treatment outcome in the present dissertation study.
Expectancy and Placebo Effects

The fourth category of factors that account for variance in treatment outcome as proposed by Asay and Lambert (1999) concerns placebo-effects. Placebo-effect has been defined as a representative of the factors (e.g., expectancy for improvement) that are related to any benefits observed in the context of a theoretically inert treatment (Herbert & Gaudiano, 2005). It has been estimated that approximately 15% of variance in treatment outcome is attributable to placebo effects (Asay & Lambert, 1999). Placebo-interventions in CBT studies on the treatment of adult anxiety (e.g., Social Phobia (SOP), Obsessive Compulsive Disorder (OCD), Generalized Anxiety Disorder (GAD)) showed significantly better effect-sizes compared to no-treatment conditions but appeared less or equally effective compared to active interventions (Norton & Price, 2007). A mean effect-size of 0.58 [95% CI: -1.6 to 1.3] for attention placebo controlled conditions was found for studies evaluating CBT for childhood anxiety disorders (In-Albon & Schneider, 2007).

The present dissertation study will not address whether placebo-effects or expectancy accounted for variance in treatment outcome. It is beyond our possibilities and statistical desirability's to give a complete assessment of all likely predictors for treatment outcome.

The Present Study and the Larger Study

This dissertation study is part of a larger study on a stepped-care model investigating predictors for treatment outcome of childhood and adolescent anxiety disorders and the effect of an additional treatment protocol for non-responders to a traditional CBT program (Treffers, Van Widenfelt, Ferdinand, & Utens, 2002). To explain the position of this dissertation study with respect to the larger study, a brief description of the overall study design and procedures will be given.

Participants

Eligible for participation were children aged 8-12 years attending primary education and adolescents aged 12-15 years attending secondary education. Children were referred to the anxiety and depression outpatient clinic's of the Child and Adolescent Psychiatry Department, Leiden University Medical Center and Erasmus Medical Center, Sophia Children's Hospital in Rotterdam, in the Netherlands and diagnosed with Separation Anxiety Disorder (SAD), GAD, SOP or Specific Phobia (SP). Exclusion criteria were an IQ below 85, poor command of the Dutch language, Pervasive Developmental Disorder, Selective Mutism, Schizophrenia or other psychotic disorder. Children with OCD, Posttraumatic Stress Disorder and Panic Disorder were excluded because at the time the study was designed there was no empirical evidence that children would benefit more from CBT compared to medical or combined treatment. All youngsters and their parents were interviewed with the ADIS-C/P (Silverman & Albano, 1996). Youngsters with comorbid conditions such as Depression, Dysthymia, Attention Deficit Hyperactivity Disorder (AHDH) or Oppositional Defiant Disorder (ODD) were not excluded from the study. Comorbidity is a common problem presented in general practice; exclusion of
youngsters with comorbid conditions would therefore complicate generalization of the findings to the general practice. The Committees for Medical Ethics of Leiden University Medical Center and of Sophia Childrens Hospital/Erasmus Medical Center approved the conduct of this research.

A total of 142 children and their parents were asked to participate in the present study; 133 subjects gave informed consent to participate, and 132 mothers and 115 fathers participated. The referral rate of adolescents was below that of children; 53 eligible adolescents and their parents were asked to participate. Of these 53 adolescents, 51 adolescents gave informed consent for participation and 51 mothers and 44 fathers participated. Results with regard to the treatment of anxious adolescents were excluded from the analyses in the present study and were therefore not included in this dissertation.

Procedure.

Child participants were randomly assigned in sequences of 6 to either GCBT or ICBT. Six children were excluded from the randomization because they refused assignment to group treatment \((n = 2)\) or were absent at the start of the group \((n = 1)\). Due to location three children were treated at an affiliated outpatient clinic nearby their home. Sixty-two children participated in the GCBT, and 71 children were given ICBT. The intention was to deliver the adolescent treatment in GCBT and ICBT format as well. The referral rate was below expected; it was deemed unethical to have adolescents wait for over four months before group treatment could start. Therefore, it was decided to treat all adolescents individually.

All youngsters and their parents underwent the same procedure, which included 7 assessments spread over a one-year period. Assessments varied in the number of informants and the variety of measurements included (see Table 1.1 for a complete overview). The first assessment \((\text{time 0})\) included the Anxiety Disorders Interview Schedule for Children and Parents interview \((\text{ADIS-C/P}; \text{Silverman & Albano, 1996})\) with the youngster and their parents and completion of the Multidimensional Anxiety Scale for Children \((\text{MASC}; \text{March, 1997})\) and the Children’s Depression Inventory \((\text{CDI}; \text{Kovacs, 1992})\). Additionally, time 0 assessment also included assessment of teacher information on youngster’s behavior problems and youngsters social functioning, as well as information of clinicians on youngsters global functioning \((\text{C-GAS}; \text{Shaffer et al., 1983})\). Time 0 took place at least two weeks prior to the start of the treatment. Directly prior to the start of the treatment time 1 assessment was conducted. After time 1 children and adolescents started the first phase of the treatment-protocol; children were treated with the child-version of the FRIENDS treatment \((\text{Barrett & Turner, 2000})\) and adolescents were treated with the adolescent version of the FRIENDS treatment \((\text{Barrett, Lowry-Webster, & Turner, 2000})\). FRIENDS is a manualized short-term 10-session cognitive behavioral therapy protocol including four additional parent sessions and two additional booster sessions \((\text{relapse prevention})\). One week after the first two parent sessions and five child-sessions \((\text{mid-treatment}; \text{time 2})\) children completed the MASC and CDI. Post-treatment
assessment (time 3) was conducted one-week after the tenth FRIENDS session. Interview (ADIS-C/P) and questionnaire (MASC) information obtained at time 3 was used to determine the short-term treatment outcome. Depending on the outcome of the interview and questionnaire information youngsters were advised either to end the treatment (early responders; remission of all anxiety diagnoses and a self-reported MASC score below the cut-off) and attend booster sessions or to start the second treatment phase (early non-responders; insufficient reduction of anxiety diagnoses and/or MASC score above the cut-off).

The second treatment phase has a strong focus on parent participation in the child treatment (Van Widenfelt, Franswa, Utens, Van der Toorn, & Liber, 2002) and included three more assessments (time 4, time 5 and time 6). The early responders were offered two booster sessions, and non-responders were given five treatment sessions of the second treatment phase. After these five sessions interview and questionnaire information was again obtained and used to advise the youngsters and their parents to either continue the second half of the

### Table 1.1.

**Assessment Information**

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<thead>
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<th>Time</th>
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<td>Pre</td>
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<td>Pre</td>
<td>Mid</td>
<td>Post</td>
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<td>CDI</td>
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<td>c</td>
<td>c</td>
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<td>c</td>
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<td>c/p</td>
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*Note. ADIS-C/P; Anxiety Disorders Interview Schedule for Children and Parents interview (Silverman & Albano, 1996), MASC; the Multidimensional Anxiety Scale for Children (March, 1997), CDI; the Children's Depression Inventory (Kovacs, 1992), CASI; Children’s Anxiety Sensitivity Index (Silverman, Fleisig, Rabian, & Peterson, 1991), EMBU-C; Egna Minnen Beträffande Uppfostran Child version (Markus, Lindhout, Boer, Hoogendijk, & Arrindell, 2003), NASSQ; Negative Affectivity Self-Statements Questionnaire (Ronan, Kendall, & Rowe, 1994), YSR; Youth Self-Report (Achenbach & Rescorla, 2001; Verhulst, 2002a), Social Validity; Social Validity Questionnaire: Parent and Child versions (Barrett, 1999), TRF; Teacher Report Form (Achenbach & Rescorla, 2001; Verhulst, 2002b), SSRS; Social Skills Rating System: Parent and Teacher Versions (Gresham & Elliott, 1990), global functioning scale C-GAS (Shaffer et al., 1983); parent and clinician versions, CBCL; Child Behavior Checklist (Achenbach & Rescorla, 2001; Verhulst, 2002c), EMBU-P; Egna Minnen Beträffande Uppfostran Parent version (Markus, Hoogendijk, & Treffers, 2006), DASS; Depression, Anxiety and Stress Scales (De Beurs, Van Dyck, Marquenie, Lange, & Blonk, 2001). C= child/adolescent, p= mother and/or father, d= diagnostician or therapist, t= teacher. Superscript1= adolescents only, superscript2= was often received either on time 0 or on time 1.*
second treatment phase (phase 2 early non-responders) or end the treatment (phase 2 early responders) in case children no longer met the diagnostic criteria for any anxiety disorder and reported anxiety levels below the cut-off. Children who did not respond (sufficiently) to the first half of phase 2 treatment were again offered 5 treatment sessions. As some children participated in a second treatment after the FRIENDS treatment whereas others did not, we were not able to address follow-up issues with regard to the effectiveness of the first treatment, or with regard to ICBT versus GCBT.

Treatment.
Children were treated with the Dutch translation of the FRIENDS program (Barrett & Turner, 2000; Utens, de Nijs, & Ferdinand, 2001). The FRIENDS program is based on the Coping Cat workbook from Philip Kendall (Kendall, Kane, Howard, & Siqueland, 1990). Results from previous research indicated that FRIENDS is an effective treatment for childhood anxiety disorders (Shortt, Barrett, & Fox, 2001). It is a manualized treatment and based on a theoretical framework with three main target areas for change: physical symptoms, cognitive processes and coping skills. Therapeutic techniques comprise psychoeducation, relaxation and breathing exercises, exposure, problem solving skills training, social support training and cognitive restructuring exercises. Parent sessions comprised mainly psychoeducation. Children are taught coping techniques such as relaxation and breathing exercises to learn to cope with physical symptoms of anxiety. Children are also taught to challenge negative cognitions, irrational beliefs and negative self-talk by changing them into helpful cognitions, realistic beliefs and positive self-talk. Increased awareness of avoidant strategies is stimulated, as well as the development of problem solving skills and coping skills. In the second half of the therapy, gradual exposure to the feared stimulus and underlying fears is more prominent. Attempts to cope are positively rewarded. The FRIENDS treatment is delivered individually and in group format in 10 weekly child sessions and 4 parent sessions. Parent sessions focus mainly on psychoeducation. The treatments of the individual and group format corresponded as much as possible. Differences between formats are inherently related to the formats; the presence or absence of peers and the presence of either one or two therapists.

Sample described in the present dissertation.
The presented findings in this dissertation result from analyses of the sample of children who were invited to participate in the first phase, the FRIENDS treatment. The intent-to-treat sample included 133 children; the sample of treatment completers included 124 children as nine children dropped out of treatment prior to the time 3 assessment. Six children could not be randomized, therefore chapter 1 reports on an intent-to-treat sample of 127 children, eight out of the 127 children dropped out of treatment resulting in a sample of 119 treatment-completers. The majority of children that dropped out of treatment prior to time 3 completed assessment data at time 3.