

From the Department of Clinical Neuroscience
Karolinska Institutet, Stockholm, Sweden

FEAR AND MISSING OUT: INTERNET-TREATMENT FOR SOCIAL ANXIETY DISORDER IN YOUTH

Martina Nordh



**Karolinska
Institutet**

Stockholm 2020

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Printed by Arkitektkopia AB, 2020
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ISBN 978-91-7831-758-5

Fear and missing out: Internet-treatment for social anxiety disorder in youth

THESIS FOR DOCTORAL DEGREE (Ph.D.)

To be defended in public in the Gustaf Retzius lecture hall,
Karolinska Institutet, Stockholm, Sweden

Friday May 8, 2020, 9 am

By

Martina Nordh

Principal Supervisor:

Dr. Jens Högström
Karolinska Institutet
Department of Clinical Neuroscience
Centre for Psychiatry Research

Co-supervisors:

Associate Professor Eva Serlachius
Karolinska Institutet
Department of Clinical Neuroscience
Centre for Psychiatry Research

Professor David Mataix-Cols
Karolinska Institutet
Department of Clinical Neuroscience
Centre for Psychiatry Research

Opponent:

Professor Ron Rapee
Macquarie University, Sydney, Australia
Department of Psychology
Faculty of Human Sciences

Examination Board:

Associate Professor Ewa Mörtberg
Stockholm University, Sweden
Department of Psychology

Associate Professor Raziye Salari
Uppsala University, Sweden
Department of Public Health and
Caring Sciences

Associate Professor Lisa Thorell
Karolinska Institutet, Sweden
Department of Clinical Neuroscience

In loving memory of my father Åke,
who taught me to explore the world and enjoy life.

SAMMANFATTNING

Bakgrund

Social ångest, tidigare kallat social fobi, är vanligt förekommande, funktionsnedsättande och associerat med omfattande kostnader för samhället. Social ångest uppstår vanligen i barndomen och tenderar att bli kroniskt om ingen behandling erbjuds. Få individer med social ångest har tillgång till effektiv behandling och behovet är stort av nya metoder för att förmedla behandling som kan nå fler som är i behov av behandling. Den pågående covid-19 pandemin har ytterligare understrukt behovet av behandling som ges på distans. Internet-förmedlad kognitiv beteendeterapi (IKBT) skulle kunna öka tillgängligheten till evidensbaserad behandling men kunskapen om dess effekt och kostnadseffektivitet för unga med social ångest är begränsad. Ytterligare kunskap behövs även om faktorer som vidmakthåller social ångest hos unga. Selektiv uppmärksamhet till sociala stimuli har föreslagits vara en sådan faktor, men studier som undersökt området har visat blandade resultat.

Syfte och metod

Det övergripande syftet med den här avhandlingen var tvådelat. Det första syftet var att utveckla och utvärdera ett IKBT-program för barn och ungdomar med social ångest. Det andra var att undersöka selektiv uppmärksamhet hos ungdomar med social ångest. Tre specifika frågeställningar var: 1) om IKBT är en genomförbar, acceptabel och potentiellt effektiv behandling, 2) om IKBT är en effektiv och kostnadseffektiv behandling, och 3) om ungdomar med social ångest uppvisar selektiv uppmärksamhet mot socialt hotfulla stimuli. Dessa frågeställningar undersöktes i tre studier: Studie I var en genomförbarhetsstudie där IKBT (i kombination med tre gruppträffar) erbjöds till 30 ungdomar med social ångest, Studie II var en randomiserad kontrollerad studie som jämförde IKBT (i kombination med tre videosamtal) med en aktiv kontrollbehandling, ISTÖD, för 103 barn och ungdomar med social ångest och Studie III var en experimentell studie som använde ögonrörelseteknologi (eyetracking) för att jämföra social uppmärksamhet bland 25 ungdomar med social ångest och 22 ungdomar utan ångest från allmänheten.

Resultat

Studie I visade att majoriteten av deltagarna var nöjda med IKBT, upplevde att behandlingen var enkel att förstå och skulle rekommendera den till en vän med liknande problem. Deltagarna genomförde i genomsnitt två tredjedelar av IKBT-modulerna och deltog i de flesta gruppträffarna. Barn- och föräldraskattningar samt klinkerbedömningar av social ångest visade på symtomreduktion motsvarande stora inomgruppseffekter (Cohen's $d=0.85$, 0.79 respektive 1.17). Studie II visade att IKBT minskade symtom på social ångest signifikant mer än ISTÖD, en skillnad

som motsvarade en medelstor mellangrupps effekt (Cohen's $d=0.66$). Signifikant förbättring till fördel IKBT observerades också på sekundära utfallsmått såsom symptom på depression och funktionsnedsättning med medelstora mellangrupps-effekter. Deltagarna slutförde i genomsnitt 75% av IKBT-modulerna och deltog i 85% av videosamtalen. IKBT var mer kostnadseffektiv än ISTÖD med besparingar av samhällskostnader som huvudsakligen berodde på minskad användning av mediciner och ökad produktivitet i skolan för de som fick IKBT-behandling. Studie III visade att både ungdomar med social fobi och ungdomar i kontrollgruppen reagerar snabbare på, och sedan undviker, arga ansikten i jämförelse med neutrala eller glada ansikten. De ungdomar med social ångest som uppvisade mer undvikande förbättrades mer av IKBT.

Slutsats

Studierna som ingår i avhandlingen ger stöd för att IKBT är en genomförbar, effektiv och kostnadseffektiv behandling för unga med social ångest. Deltagarna var engagerade i behandlingen, genomförde större delen av modulerna och tyckte att IKBT var en trovärdig behandling. Resultaten bygger vidare på tidigare studier som visat lovande resultat för IKBT för unga med social ångest. Ytterligare utvärderingar behövs för att fastställa hur utfallet av IKBT kan förbättras för de unga som inte svarade på behandlingen. Unga med social ångest uppvisar selektiv uppmärksamhet vid socialt hotfulla stimuli och ett liknande mönster noterades bland kontroller utan ångest. Dessa resultat är i linje med studier som undersökt selektiv uppmärksamhet hos barn, men skiljer sig delvis från resultat som visats för ungdomar. Det behövs fler ögonrörelsestudier, med fler deltagande unga med social ångest, för att fastslå om vissa aspekter av selektiv uppmärksamhet är specifikt för social ångest. Sammanfattningsvis så kan IKBT öka tillgängligheten till evidensbaserad behandling för unga med social ångest och ytterligare kunskap om selektiv uppmärksamhet skulle kunna generera hypoteser om vidmakthållande av social ångest samt hur psykologisk behandling för social ångest kan förbättras genom tillägg av komponenter som syftar till att minska vidmakthållandet.

ABSTRACT

Background

Social anxiety disorder (SAD) is common, highly impairing and associated with severe effects on functioning and with increased monetary costs for the society. The disorder typically emerges during childhood and tends to follow a persistent and chronic course if left untreated. Currently, a minority of individuals with SAD have access to effective treatment and new approaches to treatment delivery are needed. In addition, the current covid-19 pandemic crisis further highlights the need for remotely delivered therapies. Internet-delivered cognitive behavioral therapy (ICBT) could increase availability of evidence-based treatment but little is known about its efficacy and cost-effectiveness for youth with SAD. Further knowledge is also needed regarding maintaining factors of SAD in youth. Attention bias has been suggested as one of those factors but studies evaluating attention bias in youth with SAD have showed mixed results.

Aims and methods

The overall aim of this thesis was twofold. First, to develop and evaluate an ICBT program for children and adolescent with SAD. Second, to examine attention bias in adolescents with SAD. Three specific research questions were: 1) to examine if ICBT is feasible, acceptable and potentially efficacious, 2) to examine if ICBT is efficacious and cost-effective and, 3) to examine if adolescents with SAD show attention bias to social threat. These research questions were examined in three studies: Study I being a feasibility trial where ICBT (supplemented with three group-exposure sessions) was offered to 30 adolescents with SAD, Study II being a randomized controlled trial comparing ICBT (supplemented with three video-call sessions) with an active control treatment, ISUPPORT, for 103 children and adolescents and, Study III being an eye-tracking study examining attention bias in 25 adolescents with SAD compared to 22 non-anxious controls from the general population.

Results

Study I showed that the vast majority of the participants were satisfied with ICBT, found the treatment easy to understand and would recommend it to a friend with similar problems. On average, participants completed two thirds of the ICBT modules and attended most of the group-exposure sessions. Child-, parent- and clinician-reported measures of social anxiety showed symptom reduction with large within-group effects sizes (Cohen's $d=0.85$, 0.79 and 1.17 , respectively). Study II showed significantly more reduction of social anxiety in the ICBT group compared to the ISUPPORT group corresponding to a moderate between-group

effect size (Cohen's $d=0.66$). Significant improvement in favor of ICBT was also observed on most secondary outcomes such as depressive symptoms and functional impairment, with moderate between-group effect sizes. Participants completed on average 75% of ICBT modules and participated in 85% of the video call sessions. ICBT was deemed more cost-effective than ISUPPORT with societal cost savings mainly driven by reduction in medication use and increased school productivity. Study III found support for a vigilant and avoidant gaze pattern to angry faces, compared to neutral or happy faces, in youth with SAD as well as in controls. Adolescents with SAD who showed more avoidance of social stimuli improved more after ICBT.

Conclusions

The studies included in this thesis support ICBT as a feasible, efficacious and cost-effective treatment for youth with SAD. Treatment completion was high and participants found ICBT to be a credible treatment. These results build on and further extend results from previous studies that have shown promising results for ICBT for youth with SAD. Further evaluations are needed to determine how clinical outcomes can be improved for youth who do not respond to ICBT. Youth with SAD show attention bias to social threat and similar patterns are shown in non-anxious controls. These results are in line with previous eye-tracking studies that have examined attention bias in children but is partly inconsistent with those found for adolescents. Future eye-tracking studies with larger samples of youth with SAD are needed to determine if aspects of attention bias are specific to SAD. In summary, ICBT could increase access to evidence-based treatment for youth with SAD and further knowledge about attention bias could generate hypotheses about the maintenance of social anxiety as well as how psychological treatment for social anxiety could be improved to target those maintaining factors.

LIST OF SCIENTIFIC PAPERS

- I. **Nordh, M.**, Vigerland, S., Öst, L.G., Ljótsson, B., Mataix-Cols, D., Serlachius, E., & Högström, J. (2017). Therapist-guided internet-delivered cognitive-behavioural therapy supplemented with group exposure sessions for adolescents with social anxiety disorder: a feasibility trial. *BMJ open*, *7*(12), e018345.
- II. **Nordh, M.**, Wahlund, T., Jolstedt, M., Sahlin, H., Bjureberg, J., Ahlen, J., Lalouni, M., Salomonsson, S., Vigerland, S., Lavner, M., Öst, L.G., Lenhard, F., Hesser, H., Mataix-Cols, D., Högström, J., & Serlachius, E. Therapist-guided internet-delivered cognitive behavioural therapy versus internet-delivered supportive therapy for children and adolescents with social anxiety disorder: a randomised controlled trial. Unpublished manuscript.
- III. Högström, J., **Nordh, M.**, Lindal, M. L., Taylor, E., Serlachius, E., & Kleberg, J. L. (2019). Visual attention to emotional faces in adolescents with social anxiety disorder receiving cognitive behavioral therapy. *PloS one*, *14*(11) e0225603.

CONTENTS

1	Introduction	1
2	Background	3
2.1	What is social anxiety disorder?	3
2.2	Etiology: How does social anxiety develop?	3
2.2.1	Temperament	4
2.2.2	Genetics	4
2.2.3	Environmental factors	5
2.2.4	Impairment and related problems	5
2.3	How is social anxiety disorder maintained?	6
2.3.1	Psychological models	6
2.3.2	Attention bias	8
2.4	What is the health-related cost of social anxiety disorder?	10
2.5	Treatment for social anxiety disorder	11
2.5.1	Pharmacological treatment	11
2.5.2	Cognitive behavioral therapy	13
2.5.3	Parental involvement	14
2.5.4	Barriers to seeking treatment	14
2.5.5	Internet-delivered CBT	15
2.6	Conclusions	16
3	Aims of the thesis	17
3.1	Study I	17
3.2	Study II	17
3.3	Study III	17
4	The empirical studies	18
4.1	The research setting	18
4.2	The treatment	18
4.3	Study I	20
4.3.1	Method	20
4.3.2	Results	20
4.4	Study II	20
4.4.1	Method	20
4.4.2	Results	21
4.5	Study III	21
4.5.1	Method	21
4.5.2	Results	22
4.6	Additional evaluations	22
4.7	Ethical considerations	23

5	Discussion	26
5.1	The feasibility of ICBT for youth with social anxiety disorder	26
5.2	The efficacy of ICBT for youth with social anxiety disorder	27
5.3	The cost-effectiveness of ICBT for youth with social anxiety disorder	28
5.4	Attention bias in adolescents with social anxiety disorder	29
5.5	Where do we go from here?	31
6	Conclusions	34
7	Acknowledgements	35
8	References	38

LIST OF ABBREVIATIONS

ADIS-C	Anxiety Disorders Interview Schedule – Child version
BI	Behavioral inhibition
BIP	Barninternetprosjektet (eng. the child internet project)
BIP SOFT	Barninternetprosjektet Social Fobi Tonår (eng. social phobia teenage)
CAMHS	Child and adolescent mental health services
CBT	Cognitive behavioral therapy
CGAS	Children’s Global Assessment Scale
CGI-S	Clinical Global Impression – Severity
CSR	Clinician Severity Rating
ICBT	Internet-delivered cognitive behavioral therapy
ISUPPORT	Internet-delivered supportive therapy
LSAS-CA	Liebowitz Social Anxiety Scale – Child and Adolescent version
M.I.N.I KID	Mini International Neuropsychiatric Interview for Children and Adolescents
RCT	Randomized controlled trial
SAD	Social anxiety disorder
SET-C	Social Effectiveness Therapy for Children
SNRI	Serotonin-norepinephrine reuptake inhibitors
SSRI	Selective serotonin reuptake inhibitors
TiC-P	Trimbos/iMTA questionnaire for Costs associated with Psychiatric Illness – Parent version
QALY	Quality-adjusted life years

1 INTRODUCTION

Children and adolescents with social anxiety disorder are not the ones standing first in line to our mental health clinics, but they certainly suffer severely. Already at an early age, many of these young individuals are so fearful of social situations that they miss out on activities and experiences that are associated with typical development at their age. They are less oriented towards relationships outside the family, such as friendships or love relations, and they hesitate to become independent from their parents. Since almost any facet of everyday life can be potentially socially threatening, many of these youths have already worked out sophisticated ways of reducing contact with peers, teachers, relatives, and staff in stores, restaurants and cafés. From the patients I have met during my clinical work and doctoral studies, I have learned that even though some indeed have friends, many struggle to ‘show who they really are’ or to ‘speak their minds’ and that they often feel lonely even when being around peers.

As will be described in this thesis, youth with social anxiety disorder have fewer close relationships and more self-reported loneliness than their non-anxious peers (Beidel et al., 2019), and importantly, loneliness in youth does not only mediate reduction of social anxiety during treatment (Alfano et al., 2009) but also mediates the relationship between social anxiety and suicidal ideation (Gallagher et al., 2014). That means that the experience of loneliness plays an important role in social anxiety. Social isolation is harming and belongingness is protecting (Asher & McDonald, 2010). To me, this highlights the urgency to identify and treat social anxiety disorder in young people. If we can help them form at least one close relationship outside the family and develop a basic concept about how to orient independently in social situations and in society, that might make all the difference for a young person who is suffering from social anxiety disorder. Therefore, this group needs to be identified early and the interventions we develop should provide them with a toolbox that put them on the path to independence and social belongingness.

This thesis aimed to further our understanding of social anxiety in youth and explore if internet-delivered cognitive behavioral therapy can help those affected overcome some of their fears and instead of missing out, helping them join in.

Stockholm, March 2020



Illustration by: Johanna Henriksson

2 BACKGROUND

2.1 What is social anxiety disorder?

Social anxiety disorder (SAD) is characterized by fear of scrutinization and negative evaluation in social or performance situations (American Psychiatric Association, 2013). Socially anxious individuals fear exhibiting unacceptable behaviors and to show signs of anxiety, such as blushing or trembling and may therefore avoid social situations or endure them under great distress. The disorder is one of the most common mental disorders among children and adolescents with a 12-month prevalence of 3.4% (Lawrence et al., 2015). More than 8% of the adolescent population have been shown to fulfill diagnostic criteria at some point between the age of 13 and 18 (Burstein et al., 2011). Most cases of SAD have an age of onset during late childhood or in adolescence (Kessler et al., 2005) and onset after mid-twenties is rare (Chavira & Stein, 2005). Younger age of onset has been associated with a more persistent development of the disorder into adulthood (Wittchen & Fehm, 2003). In general, SAD is persistent and 40-60% retain the disorder for as long as 40 years following onset (Ruscio et al., 2008). The disorder is more common among girls with a female to male odds ratio reported to be 1.58 among youth (Burstein et al., 2011) and 1.35 among adults (Xu et al., 2012). Although studies on SAD with transgender populations are scarce, the prevalence in a gender dysphoric youth sample was reported to be 9% (De Vries et al., 2011), and in an adult sample as high as 31.4% (Bergero-Miguel et al., 2016).

2.2 Etiology: How does social anxiety develop?

Several factors contribute to the development of SAD and growing evidence supports an interactional model (Spence & Rapee, 2016). The model suggests that intrinsic elements (the child's temperament and genetic or biological predisposition) interact with environmental risk factors such as peer victimization and parental style (e.g., overprotection or hesitation during social interactions) in the development in SAD. A large body of research highlights the interplay between individual and interpersonal factors such as peer acceptance in the development of social withdrawal and anxiety (Gazelle & Rubin, 2019). In addition, recent epigenetic studies add evidence to the environmental impact on the expression or suppression of genetic predispositions in the development of anxiety disorders such as SAD (Nieto et al., 2016). In summary, presence of one risk factor is not enough to trigger SAD. Rather it is the concurrence of several factors that puts young persons on the developmental path towards SAD (Ollendick & Hirshfeld-Becker, 2002).

2.2.1 Temperament

One of the more prominent temperamental traits that has been associated with the development of SAD is behavioral inhibition (BI), which in its more severe form is found in 15% of toddlers and children (Clauss & Blackford, 2012). BI is a tendency to react with cautiousness and abstention to novel stimuli, such as unfamiliar persons or contexts (Kagan et al., 1984). This has been linked to both physiological arousal including higher cortisol levels, atypical heart rate responses and pupil dilation (for a review see, Hirshfeld-Becker et al., 2014), as well as behavioral withdrawal including impaired eye contact, limited verbal interaction and avoidance of novel persons and situations (Rapee, 2002). BI has been proposed as one of the major risk factors for developing SAD and signs of BI in early childhood has been associated with a sevenfold risk to develop SAD later in childhood and adolescence (Clauss & Blackford, 2012).

2.2.2 Genetics

Genetic research has up until recently mainly focused on finding specific risk genes for mental disorders, including SAD. However, more refined techniques have resulted in the possibility to conduct genome wide analyzes and research is now pointing to a complex combination of multiple locations on the chromosomes, that through interaction with one another, increases the risk of developing SAD (M. B. Stein et al., 2017). Even though the discovery of multiple risk loci on the genetic map are just emerging, familial aggregation of SAD has been suggested to be mainly attributable to genetic factors rather than the shared environment (for a review see, Spence & Rapee, 2016). Studies with different methods such as twin-studies (Scaini et al., 2014), register based studies (Isomura et al., 2015) and, genome wide-association analyses (M. B. Stein et al., 2017) corroborate evidence that social anxiety at both subclinical and clinical levels have a genetic base. The genetic contribution in SAD has been estimated to range from 20% to slightly above 55% (e.g., Isomura et al., 2015) and several studies show that SAD is at least two to three times more common in persons with a first-degree relative with SAD compared to relatives to healthy-controls (e.g., Coelho et al., 2007; Merikangas et al., 2003; Tillfors et al., 2001). In terms of epigenetics, the oxytocin system has been suggested to play an important role in SAD as studies have indicated decreased methylation in oxytocin receptor genes in persons with SAD (e.g., Christiane et al., 2015). A further description of this complex system is beyond the scope of this thesis but studies revealing an epigenetic relationship between the oxytocin system and SAD have, for instance, pointed to an improved clinical response to psychological treatment after intranasal application of oxytocin (Guastella et al., 2009).

2.2.3 Environmental factors

Temperamental and genetic risk factors contribute in the development of SAD, as described above. However, not all individuals with these risk factors develop SAD. For young persons, parents and peers play an important role in everyday life and hence can serve as either risk or protective factors. Parenting styles characterized by overprotection or overcontrol and, parental modelling of overconcerns with others' opinions or hesitation during social interactions, has been suggested to be associated with SAD (for an overview, see Wong & Rapee, 2015). However, several of these factors have been associated with anxiety disorders in general, and most studies have not examined the association with social anxiety specifically (Ollendick et al., 2014). Even though the evidence is somewhat limited, models of the association between parental behaviors and social anxiety in children stresses a reciprocal relationship where the inhibited child activates overprotective parenting, such as speaking on behalf of the child, which leads to a gradual increase of the child's social anxiety and subsequent more compensating behaviors from the parent (Spence & Rapee, 2016). Also, more recent studies suggest that constraining parental factors such as overprotection specifically contribute to SAD when they interact with biological predispositions such as child cortisol reactivity (Poole et al., 2018) or genetic variation in the oxytocin system (Nelemans et al., 2019). Overall, shared environmental factors within families is only thought to account for a small part of the variation in SAD (Scaini et al., 2014). Non-shared environmental factors such as peer relations and peer victimization, on the other hand, have been reported to explain a relatively large proportion of the variance and will also be described briefly.

Acceptance among peers and the ability to form friendships is associated with several protective factors, such as school adjustment, increased self-esteem and lower risk of mental health issues (Asher & McDonald, 2010). For youth with social anxiety, studies repeatedly show an association with low peer acceptance, fewer close friendships, more overall negative interactions with peers and higher risk for peer victimization (for a review see, Beidel et al., 2019). The association between SAD and poor peer relations seem to be bi-directional and evidence points to a vicious circle where poor social performance or inhibited social behavior contribute to negative responses from peers, which in turn leads to higher risk of failure in social interactions and increased risk of social anxiety (Spence & Rapee, 2016).

2.2.4 Impairment and related problems

Almost two thirds of young individuals who suffer from SAD report moderate to severe impairment in several important life domains such as school and friendships due to the disorder (Lawrence et al., 2015). In school, for instance, performance can be negatively affected by fear of giving presentations, hesitation to ask the

teacher for help, or due to high absenteeism (Beidel et al., 1999). Persons with SAD have more experiences of academic failure, from an early age up to young adulthood, than persons without the disorder (Vilaplana-Pérez et al., 2020). In terms of friendships, socially anxious children are more often excluded from peer interactions, have fewer close friends (Gazelle & Faldowski, 2019) and report more feelings of loneliness (Beidel et al., 1999). Impairment from SAD has been shown to correlate with age and adolescents generally have more difficulties due to SAD than children, regardless of severity level (Hoff et al., 2017).

SAD commonly presents with other mental health problems and up to 80% of all SAD cases fulfill lifetime diagnostic criteria for at least one other mental disorder (D. J. Stein et al., 2017). Studies exploring the developmental trajectories of mental health problems indicate that SAD tends to have an earlier onset than many of the related problems and hence, could be a possible precursor for other severe problems (Ruscio et al., 2008). Such problems include increased risk of depression (Beesdo et al., 2007), substance- and alcohol dependence (Buckner et al., 2008) and, an increased degree of suicidality and suicide attempts (Katzelnick et al., 2001). For instance, a large population based American study showed that among adolescents with SAD, 20-30% also fulfilled diagnostic criteria for other anxiety disorders, 20% for major depressive disorder and, around 20% for alcohol- or substance-use disorders (Burstein et al., 2011). Furthermore, in a large sample of adolescents with a history of suicidal ideation and behaviors, 20% fulfilled diagnostic criteria for SAD (Nock et al., 2013).

In summary, genetic, temperamental, peer and parental factors are some of the main etiological factors contributing to the development of SAD. Once the disorder is developed, the majority of young persons living with SAD have substantial impairments in important life domains such as school and friendships and a large proportion also suffers from other psychiatric disorders.

2.3 How is social anxiety disorder maintained?

2.3.1 Psychological models

For adults, there are two prevailing models that describe the *maintenance* of SAD once it is manifested, namely the cognitive model by Clark and Wells (1995) and the cognitive-behavioral model by Rapee and Heimberg (2014; 1997). In both models, maintaining factors are thought to facilitate fear learning in social and performance situations. The Clark and Wells model (1995) particularly highlights increased internal attention, the use of safety seeking behaviors and, atypical anticipatory and post-event information processing as important maintaining factors. The model by Rapee and Heimberg (2014; 1997) focuses rather on a more interactive relation between internal and external focus of attention, avoidance

rather than safety seeking behaviors and, fear of evaluation of any valence and not only fear of negative evaluation.

For children and adolescents no such clear model exists but attempts have been made to summarize knowledge about early maintaining factors. Halldorsson and Creswell (2017) reviewed studies on maintaining factors for pre-adolescent children (7-12 years of age) with SAD in relation to the abovementioned maintaining models for adults. Cross-sectional support was found for *perceived danger*, *self-focus*, *anticipatory processing* and *parental styles* but not specific for SAD. This indicates that these factors indeed are associated with, and may contribute to, the maintenance of SAD in children, however they do also exist in children with other anxiety disorders or, to some extent are shown in non-anxious children. For *safety seeking behaviors* and *post-event processing*, support was found for the association with SAD, however no studies had examined the association in relation to other anxiety disorders and hence the specificity for SAD remains unclear. Two factors were found to be specifically associated with SAD and no other disorder: *social skills deficits* as well as *negative peer interactions*. The authors note that social skills deficits tend to vary over different situations, so that children with SAD are able to perform and interact adequately under certain circumstances which indicates that these ‘deficits’ may not be firm underlying factors. The authors conclude that the strongest support for maintenance of SAD in pre-adolescent children to date comes from social skills deficits and negative peer interactions. Additionally, the authors point out that there is evidence to believe that socially anxious children indeed make more threat interpretations of their surrounding world, use more safety behaviors and experience high levels of self-focused attention, even though the specificity of the disorder is not fully understood.

In another review, Leigh and Clark (2018) examined the potential application of the cognitive model by Clark and Wells (1995) on adolescents with SAD, based on results from 25 previously conducted studies. The majority of the included studies had participants from community samples, hence, most of the evidence for the suggested factors come from adolescents without a clinical diagnosis of SAD. Over all, some support was found for most of the potentially maintaining factors: *negative cognitions and perceived social danger*, *processing of the self as a social object*, *safety behaviors*, *social skills deficits* and, *pre- and post-event processing*. However, the authors suggest that more research is needed with clinical samples and with methodology that allows conclusions to be drawn about the causality of these factors on the maintenance of SAD.

In summary, there is promising support for several maintaining factors in child and adolescent SAD. However, the results are still limited by cross-sectional designs and a majority of studies conducted with non-clinical samples or samples that

include several anxiety disorders. Hence, more longitudinal studies are needed with clinical samples of children and adolescents with SAD to determine the causal effects of specific maintaining factors.

2.3.2 Attention bias

SAD has been suggested to be associated with an atypical perception of the surrounding world with atypical interpretations and atypical attention processing of threat-related information, which is stressed in the theoretical models of SAD mentioned above (Clark & Wells, 1995; Heimberg et al., 2014; Rapee & Heimberg, 1997). For instance, the Rapee and Heimberg model (2014; 1997) highlights that persons with SAD have selective attention towards any cues of possible negative evaluation by others. This is suggested to activate biased appraisals of potential social threat and negative self-evaluations, which in turn may fuel vigilance towards threat even more. The Clark and Wells model (1995) suggests that individuals with SAD use safety behaviors to self-regulate internal distress when a potential social threat is present, which actively directs attention away from potentially threatening interactions and hence negative appraisals are avoided.

The tendency to direct the attention towards or away from threatening social stimuli (e.g., angry faces) has been studied as *vigilance-avoidance* biases or *attention bias*. Studies of attention bias in individuals with SAD are aiming to delineate how the direction of attention is characterized, if attention biases are present and if these observations are different in samples of individuals without SAD (Chen & Clarke, 2017). Most studies of attention bias have been conducted with experimental methods where the study subject is placed in front of a screen where threatening or non-threatening stimuli are presented. Threat stimuli is often presented as angry faces and non-threat stimuli can for instance be happy or neutral faces or non-social objects. Within the widely used *dot-probe* paradigm, the individual is pushing a button to indicate the position of a visual cue as either being located where a threat stimulus was previously displayed or where a non-threat stimulus was previously shown. Faster reaction time towards a threat stimulus is interpreted as *vigilance* to threat whereas longer responses can be interpreted as *avoidance* of threat.

Studies on adults have found that anxious individuals orient faster towards threat compared to non-anxious individuals (Bar-Haim et al., 2007). For children, a meta-analysis by Dudeny and colleagues (2015) found that although anxious children showed a stronger bias towards threat over neutral stimuli than the non-anxious youth, both of the groups showed attention biases towards threat. The reported effects were also smaller than those reported for adults. Even though reaction-time methods, including the dot-probe task, has been used in the vast majority of attention bias-studies, the task has been questioned (Clarke et al., 2013). For children,

the results can be specifically confounded by variation in motor response, in other words how fast the button is pushed after the detection of the visual cue. Also, most often either vigilance *or* avoidance is measured even though research suggests that they can occur dynamically within the same trial (Chen & Clarke, 2017).

Therefore, gaze-location methods such as *eye tracking* have been increasingly used to measure attention (Armstrong & Olatunji, 2012). In such studies, the study subject attend to stimuli on a screen and the direction of attention is measured directly with a camera specifically designed to track eye movements. Hence, no manual or verbal responses are required. Eye tracking measures the time between fixation at one stimulus to fixation at another stimulus. Vigilance is commonly defined as the tendency to fixate the first gaze faster to threat stimuli compared to the first gaze at non-threat stimuli. Avoidance on the other hand is defined as the tendency to move the gaze faster, or more often, to non-threatening stimuli compared to threatening stimuli. A recent meta-analysis evaluated eye-tracking studies on anxious children and adolescents (Lisk et al., 2019). The results indicated some support for avoidance bias in samples with mixed anxiety disorders, compared to controls, but no support was found for vigilance bias among anxious youth compared to controls. To date, only a few eye-tracking studies with homogenous samples of youth with SAD have been conducted and the results are inconclusive.

For instance, Schmidtendorf and colleagues (2018) included children aged 9-13 with a SAD diagnosis ($n=37$) and healthy controls ($n=42$) in a free-viewing task where pairs of stimuli were presented as face-face or face-object pairs (angry-happy, angry-neutral, angry-house). In addition, half of the sample in both groups were subjected to induced social anxiety (being told that they would be evaluated in a speech task following the eye-tracking task). The results showed that both socially anxious and healthy controls initially oriented faster to angry faces when they were paired with houses (non-social stimuli). A similar pattern was observed in both of the groups that were subjected to stress induction, however an absolute bias (significantly different from chance) was surprisingly only found for the control group. When the authors explored later stages of attention beyond first fixation (*dwell time* during up to 5000 ms) no support was found for relocation to angry faces or avoidance. Lastly, the authors found that initial vigilance towards angry faces compared to houses in both of the stress induced groups was followed by avoidance of angry faces in the stress induced SAD group. Although the results are somewhat inconclusive, children with SAD and non-anxious controls had a similar vigilance bias towards threat compared to non-social stimuli with potential avoidance bias among stress induced youth with SAD at later stages of attention.

In another eye-tracking study, adolescents aged 12-16 with SAD ($n=25$) and healthy controls ($n=25$) observed face pairs of angry and neutral faces (Capriola-Hall et al., 2020). Initial fixation and dwell time for first fixation was evaluated as measures

of vigilance and disengagement/maintenance, respectively. Adolescents with SAD were faster to direct the attention to angry faces as well as fixating attention longer to angry faces than the healthy controls. However, this was also true for neutral faces, and hence the authors conclude that they did not find support for a specific attention bias. The authors speculate that this may be because youth with SAD may interpret neutral faces as threatening. The study did not include faces with other emotions such as happy faces, and did not compare faces to non-social stimuli. The authors also highlight that their methodology might not have captured disengagement ideally and propose that future trials should include tasks where participants more actively have to shift the attention.

In conclusion, attention bias seems to be present in adults with SAD where faster apperception of treat-stimuli is associated with SAD and not controls (Armstrong & Olatunji, 2012). For adolescents, limited data shows that those with SAD orient faster towards and maintain attention longer to angry and neutral faces compared to healthy controls (Capriola-Hall et al., 2020). For children, both those with SAD and healthy controls orient faster to angry faces compared to non-social stimuli and, when children with SAD is subjected to induced anxiety, they tend to avoid angry faces at later stages of attention (Schmidtendorf et al., 2018).

2.4 What is the health-related cost of social anxiety disorder?

Alongside the personal distress for persons suffering from SAD, several studies in the adult literature point to long-term societal costs associated with the disorder, so called *cost-of-illness* (e.g., Patel et al., 2002; Stuhldreher et al., 2014). *Indirect costs* of the disorder accumulate when there is a loss of productivity due to for instance sick-leave from work or early retirement and, *direct costs* arise through resource use such as health care visits and medication use (Konnopka et al., 2009). SAD has foremost been associated with the former rather than the latter, due to higher rates of work absenteeism and lower frequency of health care utilization compared to groups without the disorder (e.g., Acarturk et al., 2009). Two recent German population-based studies calculated the total cost-of-illness for SAD. The first study found that the total 6-month cost of SAD was 4802€ (SE ± 623€; Stuhldreher et al., 2014) and indirect costs unsurprisingly constituted the largest proportion of the total cost. The main driver of the indirect cost was *presenteeism*, which means that an individual attend work but have reduced productivity due to the disorder. The second study found a lower 6-month total cost of 963€ (SE ± 222€; Dams et al., 2017). This study did not include costs of presenteeism, medication use or, disability pension which may explain the difference in total costs. In the second trial individuals from the general population without an anxiety diagnosis was included and this group had a significantly lower 6-month cost (512€, SE ±

89€) than the SAD group. Hence SAD was associated with a significantly higher excessive cost of 451€ (95% CI: 199€–703€). The total costs in both studies were explained to 70-80% by indirect costs and to 20-30% by direct costs of SAD and, most costs increased with SAD severity.

To my knowledge only one study has been published on the cost-of-illness for youth with SAD. Dams and colleagues (2019) included 103 adolescents with SAD in a randomized controlled trial (RCT) and used baseline data to calculate direct costs. The 6-month direct cost was estimated to 809€ (SE ± 508€), with the main drivers of the cost being outpatient clinic visits and psychiatric hospital stays. Indirect costs were not measured and therefore it remains unknown if adolescents had similar reductions in school productivity as seen in work productivity for adults. In addition, no control group from the general population was included and hence the excessive cost of SAD could not be calculated.

In summary, considering the substantial distress for youths suffering from SAD and the burden on their families, paired with long-term societal costs (e.g., Acarturk et al., 2009; Patel et al., 2002), early identification and treatment of SAD is imperative.

2.5 Treatment for social anxiety disorder

Treatment for SAD can include psychological and/or pharmacological interventions, with cognitive behavioral therapy (CBT) and selective serotonin-reuptake inhibitors (SSRIs) being the most supported interventions in the literature (Mayo-Wilson et al., 2014; Walkup et al., 2008). For youth with SAD in Sweden, the combination of CBT and SSRIs is the first-line treatment recommendation (the National Board of Health and Welfare, 2016). However, psychological evidence-based interventions are seen as less invasive than pharmacological interventions, due to for instance lower risk of side effects (the National Institute for Health and Care Excellence; NICE, 2014) and pediatric physicians in Sweden are recommended to be cautious when prescribing, as there are no approved SSRIs for children with SAD (the National Board of Health and Welfare, 2016).

2.5.1 Pharmacological treatment

A recent systematic review and meta-analysis evaluated the effectiveness of pharmacotherapy and CBT for childhood anxiety disorders (Wang et al., 2017). Several of the included trials had samples with social anxiety or where social anxiety was one of the treated anxiety disorders. The meta-analysis concludes that SSRIs, such as sertraline or fluoxetine, are significantly more effective than pill placebo in reducing anxiety symptoms, including social anxiety symptoms,

when symptoms are reported by a clinician or parents. SSRIs were also found to be more effective than pill placebo in terms of remission (loss of all anxiety disorders) and response (loss of principle anxiety disorder) to treatment. Compared to pill placebo, SSRIs were however not associated with reduced child reported anxiety symptoms. A large RCT included in the meta-analysis lend support to the superiority of combined of SSRIs and CBT over mono-therapy with either SSRIs *or* CBT (Piacentini et al., 2014; Walkup et al., 2008). However, in a later review by Creswell and colleagues (2020) it is stated that follow-ups of these results have showed similar effects for all three active treatments (SSRIs vs CBT vs SSRIs+CBT) up to 12 years after treatment and the authors suggest that future trials include a CBT+pill placebo condition to fully understand the effects of combined treatments. In terms of other types of medication, the meta-analysis by Wang and colleagues (2017) found support for reduction in clinician reported anxiety symptoms after treatment with serotonin-norepinephrine reuptake inhibitors (SNRIs), but not for child or parent reported symptoms. No support was found for significant clinical improvement after treatment with benzodiazepines, and limited support was found for tricyclic antidepressants (Wang et al., 2017).

In terms of studies focusing specifically on SAD in youth, the efficacy of SSRIs and SNRIs are supported in comparison with pill placebo (Schneier et al., 2014). One trial has to date examined the relative effect of SSRIs compared to CBT (Social Effectiveness Therapy for Children, SET-C) and pill placebo (Beidel et al., 2007). Both active treatments improved social anxiety symptoms and functioning significantly more than to pill placebo and SET-C was deemed more effective than SSRIs on most outcome measures. Within the same study, the quality of social skills associated with the different treatment arms were evaluated and the results indicated that no improvement of social skills was observed for the fluoxetine group (Scharfstein et al., 2011). The authors conclude that even though SSRIs were efficacious in reducing social anxiety symptoms, compared to pill placebo, pharmacological treatment may not target the full presentation of SAD.

Few studies have investigated the long-term effects of psychotropic medication for SAD. In the adult literature the results from a few trials lend support to continuation of medication use for 3-6 months after response, due to high relapse when medication is discontinued earlier (for a review see Baldwin et al., 2014). No such recommendations exist for children and adolescents with SAD and the long-term effects of psychotropic medication are still unknown (Blanco et al., 2013).

In summary, psychopharmacological treatment with specifically SSRIs are considered effective for anxiety disorders including SAD in children and adolescents. However, evidence for the long-term effects is yet to be systematically evaluated.

2.5.2 Cognitive behavioral therapy

CBT for SAD is effective for adults (Hofmann & Smits, 2008) as well as for children and adolescents (Scaini et al., 2016; Segool & Carlson, 2008) and is considered the first-line treatment according to international clinical guidelines (Pilling et al., 2013). CBT trials with anxious youth has either included SAD as one of several anxiety disorders (Flannery-Schroeder & Kendall, 2000; Hudson et al., 2009; Kendall et al., 2008; Rapee, 2000; Walkup et al., 2008; Wergeland et al., 2014) or specifically focused on SAD in children (Beidel et al., 2000; Melfsen et al., 2011) or adolescents (Albano et al., 1995; Hayward et al., 2000; Herbert et al., 2009; Ingul et al., 2014; Olivares et al., 2002). All with results lending support to CBT as an effective treatment for youth with SAD.

Common treatment components in CBT for children and adolescents include psychoeducation, graded exposure in vivo, cognitive restructuring, social skills training, problem solving, coping strategies such as relaxation and, relapse prevention (Rapee et al., 2009). Generic CBT treatment protocols for youth with anxiety disorders, such as the well-studied *Cool kids program*, have been associated with significant improvement of overall anxiety levels and global functioning (Hudson et al., 2009; Rapee et al., 2006). Other well-researched generic CBT programs for anxious youth are the *Coping Cat Program* (Kendall & Hedtke, 2006a, 2006b; Kendall, 1994; Kendall et al., 1997), the *BRAVE program* (Spence et al., 2006), as well as the prevention program *FRIENDS* (Anticich et al., 2013; Barrett, 2005). In one trial evaluating the contribution of different treatment components in such generic CBT, cognitive restructuring and exposure tasks were specifically shown to accelerate improvement of clinical symptoms whereas relaxation training did not alter the course of anxiety to any significant extent (Peris et al., 2015). In addition, anxious youth who are treated with CBT have been shown to be four times more likely to remit from their anxiety diagnosis compared with youth in non-active control conditions (Ewing et al., 2015). The overall effect size for generic CBT for youth with anxiety disorders is moderate to large compared to passive control conditions such as waitlist or no treatment control groups (Ale et al., 2015) and mixed results has been reported regarding active control conditions. One meta-analytic review reported small effect sizes when CBT was compared to active control conditions such as supportive counseling, drug placebo or relaxation (Reynolds et al., 2012), whereas two later reviews did not report any significant difference between CBT conditions and active control conditions (Ale et al., 2015; James et al., 2013).

Unfortunately, in studies that include youth with different anxiety disorders, analyses that compare treatment outcome between the different anxiety disorders are rarely reported (Walkup et al., 2008). However, an increasing number of prediction studies have shown that youths with SAD show lower recovery rates after generic CBT compared to youth with other anxiety disorders (Hudson et al., 2015; Waters et al., 2018; Wergeland et al., 2016).

Therefore, SAD has been described as a challenging disorder to treat. However, when treatment has been tailored with SAD-specific components, the reported effects have been large (Beidel et al., 2000; Beidel et al., 2007) and comparable to those seen in the treatment of other anxiety disorders. The strongest support for specific CBT-methods for SAD in youth comes from SET-C where social skills training and exposure in vivo are emphasized (Beidel et al., 2000). In addition, social skills training has been found to be a significant moderator of improvement in social anxiety as described in a meta-analysis that included 13 different studies on CBT for SAD in children and adolescents (Scaini et al., 2016).

2.5.3 Parental involvement

Parents are often included in CBT treatments to some extent, even though the level of participation can vary from basic information about the condition and treatment program, to active participation as a ‘co-therapist’ with training in behavior management (Rapee et al., 2009). Active parental involvement in CBT treatment of child anxiety does not seem to generate superior effects compared with an entirely child-directed treatment condition (Thulin et al., 2014). However, parental involvement seems to moderate treatment outcome when it has emphasis on teaching parents to change the child’s behavior through contingency management (systematically reinforcing desired behaviors), as well as a focus on gradual transfer of treatment control from the therapist to the parent (Manassis et al., 2014).

2.5.4 Barriers to seeking treatment

Despite effective treatments and the high level of impairment caused by the disorder, it has been reported that only 13% of young persons with SAD have ever talked to a professional about their social anxiety, 10% have received any kind of treatment and, of those seeking help, only 9% have received treatment specifically targeting SAD (Zarger & Rich, 2016). Adults with the disorder has been found to seek help for SAD for the first time when they are approaching 30 years of age with an average of 11 years after onset (Xu et al., 2012). The nature of the social anxiety symptoms as being characterized by fear of meeting or talking to new persons may act as a barrier to seek treatment (Dalrymple & Zimmerman, 2011) and stigma or embarrassment also contribute to higher thresholds to seek help for young persons (Chandra & Minkovitz, 2006). Along with this, structural barriers to receiving evidence-based and effective treatment include limited availability of trained therapists (Comer & Barlow, 2014), long waiting times, long travelling distances between home and clinic, and having to take time off from school or work to attend treatment at clinics that are generally only open during office hours (Anderson et al., 2017).

2.5.5 Internet-delivered CBT

Internet-delivered CBT (ICBT) has been suggested as a possible solution to some of these barriers as this modality of delivery can offer the same treatment components as standard CBT but with the patients working with the online material from home or wherever suitable. In addition, the current covid-19 pandemic crisis urgently highlights the need for remotely delivered therapies, such as ICBT (Wind et al., 2020). In ICBT, a therapist commonly guides the patient through telephone, e-mail or, equivalent online communication. Treatment becomes more accessible as the therapist and patient does not have to work with the treatment at the same time, and thereby can communicate asynchronously. Furthermore, ICBT may increase overall treatment capacity, as therapist time per patient is lower compared with face-to-face CBT (Titov et al., 2018). For adults with SAD, ICBT is already considered an evidence-based and cost-effective treatment with at least two trials showing that ICBT is non-inferior to face-to-face CBT (Andrews et al., 2011; Hedman et al., 2011).

For youth, ICBT is an effective treatment for different psychiatric and psychosomatic conditions (Vigerland, Lenhard, et al., 2016). For anxiety disorders in youth, there is growing evidence that ICBT is effective when compared to a waitlist control (Donovan & March, 2014; March et al., 2009; Stjerneklar et al., 2019; Vigerland, Ljótsson, et al., 2016), to an active comparator (Jolstedt et al., 2018) and, when it is publicly offered as open-access without therapist support (Eysenbach et al., 2018). The results from this increasing body of knowledge suggests that ICBT could be a suitable treatment for youth with SAD. However, there are still very few studies focusing solely on ICBT for youth with SAD.

One Swedish RCT (Tillfors et al., 2011) adapted an ICBT program, developed for university students (Tillfors et al., 2008), to treat high school students ($n=19$, 15-21 years of age) with SAD and public-speaking fear. The program consisted of nine modules with limited therapist support and was compared to a wait-list control. The between-group effect size at post-treatment for the social anxiety measures were $d=1.48$ on the fear subscale of Liebowitz Social Anxiety Scale (LSAS-SR Fear; Liebowitz, 1987) and $d=1.28$ on the Social Phobia Screening Questionnaire (SPSQ-C; Gren-Landell et al., 2009). Even though the sample size was small, the results indicated that ICBT might be an effective treatment for young persons with SAD. Another RCT conducted in Australia compared 12 weeks of a SAD-specific ICBT (CBT-SAD) to generic ICBT (CBT-GEN) and a wait-list condition for 125 youth (8-17 years of age) with SAD (Spence et al., 2017). In addition to the 5-10 minutes spent on giving personalized feedback through e-mail after each session, the therapist support included a 15-minute telephone call halfway through the treatment. Automated computer-generated feedback was also sent through e-mail on behalf of the therapist. At post-treatment, 12.8% (CBT-SAD) and 14.6% (CBT-

GEN) were free from their SAD diagnosis (compared with 3.3% in the waitlist group). The results improved to the 6-month follow-up, to 29.8% (CBT-SAD) and 35.4% (CBT-GEN) respectively. Significant clinical improvement was observed on several measures for both of the active treatments with moderate to large effect sizes compared to the waitlist control. No difference was observed between the two active treatments. In summary, ICBT is a promising treatment for anxiety in youth, but research specifically focusing on youth with social anxiety is limited. There is a need for studies that include active or placebo control conditions (Tillfors et al., 2011), as well as several assessment points of both outcome and potential mediating variables to enable examination of potential causal effects of ICBT on anxiety reduction (Spence et al., 2017).

2.6 Conclusions

SAD is frequent among children and adolescents. The complex interaction of several etiological and maintaining factors contribute to the emergence and chronicity of SAD. The early onset, the severe impact on the lives of the affected and, the societal costs associated with the disorder, calls for early identification and treatment of SAD. Effective treatment such as CBT and SSRIs exist, but does not reach enough of the affected children and adolescents. ICBT may bridge the gap between treatment demand and available resources, but there is not enough evidence of its efficacy and cost-effectiveness.

3 AIMS OF THE THESIS

The overall aim of this thesis was to evaluate the efficacy and cost-effectiveness of internet-delivered CBT for youth with SAD, as well as to investigate attention bias in relation to healthy controls. This project contributes by evaluating a new ICBT protocol that combines ICBT with group-exposure sessions or video call sessions, as well as by evaluating attention bias with eye-tracking technology. The project also adds knowledge in preparation for the future process of implementing ICBT into regular psychiatric care for children and adolescents.

3.1 Study I

The aim of Study I was to test the feasibility and preliminary efficacy of ICBT supplemented with group-exposure sessions for adolescents (13-17 years of age) with SAD. The main hypothesis was that ICBT with group-exposure would be acceptable and feasible for the participants, as well as lead to significant reduction of social anxiety symptoms and improvement in global functioning and quality of life.

3.2 Study II

Study II tested the efficacy and cost-effectiveness of ICBT for children and adolescents (10-17 years of age) with SAD compared to an active control treatment (internet-delivered supportive therapy; ISUPPORT) by using a randomized controlled design. ICBT was expected to result in significantly more reductions in social anxiety and improvement in other clinical outcomes as well as being more cost-effective than ISUPPORT.

3.3 Study III

Study III investigated attention bias in youth with SAD and the association with outcome from ICBT. We hypothesized that adolescents with SAD would be more vigilant towards socially threatening stimuli and quicker to disengage attention from such stimuli, compared to happy or neutral stimuli and significantly more so than non-anxious controls. The study also examined if vigilance or disengagement latency predicted the outcome of ICBT for adolescents with SAD.

4 THE EMPIRICAL STUDIES

4.1 The research setting

All three studies included in this thesis were conducted at the Child and Adolescent Psychiatry Research Unit within the Child and Adolescent Mental Health Services (CAMHS) in Stockholm, Sweden. The unit is a clinical research unit, where psychiatric patients are included in research which applies several research methods concerning a range of psychiatric conditions.

4.2 The treatment

The development of the ICBT protocol used in Study I and II, called BIP SOFT, started from the generic ICBT protocol for children, called BIP Anxiety, that have been used in other trials at our clinic (Jolstedt et al., 2018; Vigerland, Ljótsson, et al., 2016). As we aimed to develop a program more tailored to SAD, we included specific components previously found to have effect on SAD symptoms in young persons. The main components *exposure training* and *reduction of avoidance and safety behaviors* were kept, and *social skills training*, *focus shifting* and *adaptive thinking* were added. Between Study I and II the protocol was updated, which led to removal of anxiety management strategies (such as breathing exercises) and more emphasis were put on exposure training, focus shifting and social skills training.

The online material comprised of texts, audio clips, short video clips and written exercises for the participants to complete (see example screenshots in figure 1). The material was presented as one module per week in a predefined order, and each module had to be completed before the next was made available. The structure and delivery of the treatment is in many aspects similar to BIP Anxiety (Jolstedt et al., 2018, Vigerland, Ljótsson, et al., 2016) which is described in detail in Högström and Vigerland (2019).

The three group exposure-sessions in Study I built on the group-CBT manual by Albano and DiBartolo (2007). The focus for the group sessions were exposure to talk in front of a group, either by telling something about oneself or by giving a short presentation about a topic suggested by the group leaders. In addition, each session included a coffee break where the participants could practice social and conversation skills with each other and the group leaders. The last session targeted social mishaps and exposure was conducted outside the clinic. For instance, after modelling of the group leaders, participants asked silly questions to staff in a grocery store or did a silly walk on the side walk.

Let's start!

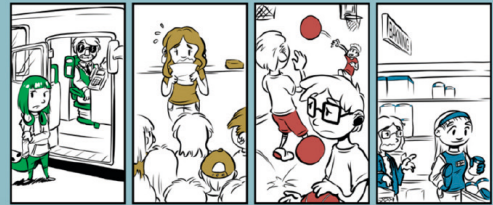
Now that you know how the program works we will move on to the first step. You will learn more about emotions, worry and anxiety, and the connection between thoughts, feelings and behaviours. And of course about social anxiety. Let's start with a film about social anxiety!



Social situations

Social situations that are experienced as challenging can differ from person to person, but some of them are more common than others.

Below are some examples of common challenging social situations: riding the bus, presenting in front of the class, participating in sports and asking about something in a store.



This weeks exercise

Think of a challenging social situation from the last week and fill out the circle.



Figure 1. Screen shots from the online material in BIP SOFT; an educative video clip about SAD and maintaining factors, illustrated examples of challenging social situations and, a written exercise about the functional analysis of anxious thoughts, feelings and behaviors.

4.3 Study I

4.3.1 Method

In the first study, 30 adolescents (13-17 years of age) with a principal diagnosis of SAD were included in a feasibility trial with an open design (no control group). All participating adolescents were offered 12 weeks of CBT-treatment, consisting of nine online modules in the BIP SOFT treatment, supplemented with three group-exposure sessions at the clinic. Parents were offered five parallel online modules of ICBT. Mini International Neuropsychiatric Interview for Children and Adolescents (M.I.N.I. KID; Sheehan et al., 1998) was used to establish SAD diagnosis and comorbid conditions. The main outcome measure was the clinician-rated Clinician Global Impression – Severity (CGI-S; Guy, 1976) and secondary outcome measures included adolescent- and parent-reported measures of social anxiety, comorbid anxiety and depression as well as level of global functioning. Measures of feasibility included number of completed modules, attendance to group-exposure sessions, as well as adolescent reported acceptability and satisfaction. Participants were assessed pre treatment, post treatment and, at 6-months follow-up.

4.3.2 Results

Participants were in general satisfied with the treatment, e.g., would recommend it to a friend and found the treatment easy to understand. Adolescents completed on average 5.7 ($sd=2.1$) of the nine online modules. Attendance at group-exposure sessions was high, with two-thirds of the participants attending two or three sessions out of the three. Therapists spent on average 19.5 minutes per family and week giving feedback on the online modules. When time for group-exposure sessions was added each family got 29.5 minutes of therapist support per week. At post-treatment, a significant improvement was observed for the primary outcome measure CGI-S, with a large within-group effect of Cohen's $d=1.17$. This pattern was also observed for most of the secondary outcome measures, with moderate to large within-group effects. These results were maintained, and for some measures further improved, to the 6-month follow-up. At the post-treatment assessment and the 6-month follow-up respectively, 47% and 57% of the participants no longer fulfilled diagnostic criteria for SAD.

4.4 Study II

4.4.1 Method

In Study II, 103 children and adolescents (10-17 years of age) with a principal diagnosis of SAD were randomly assigned to 10 weeks of either ICBT ($n=51$) or internet-delivered supportive therapy (ISUPPORT; $n=52$). Regardless of treatment arm participants were offered 10 consecutive online modules and three

video-call sessions. Parents were offered five corresponding online modules. The main outcome measure was the clinician-rated Clinician Severity Rating (CSR) derived from the Anxiety Disorders Interview Schedule – Child Version (ADIS-C; Albano & Silverman, 1996) and the primary endpoint was set to three months after treatment termination. Secondary outcomes included clinician rated global level of functioning, as well as child- and parent-reported measures of social anxiety, comorbid anxiety and depression. Health related costs were calculated from the Trimbos/iMTA questionnaire for Costs associated with Psychiatric Illness – Parent version (TiC-P; Bouwmans et al., 2013). Cost-effectiveness was evaluated from both a societal perspective, where all health-related costs were included, and from a health-care provider perspective, where only treatment costs were included. Participants who received ISUPPORT was offered 10 weeks of ICBT after the primary endpoint.

4.4.2 Results

Intent-to-treat analyses showed that ICBT reduced symptoms of social anxiety significantly more than ISUPPORT. At the primary endpoint (3-month follow-up), the between-group effect size was Cohen's $d=0.66$ for the primary outcome measure CSR, favoring ICBT. The same pattern was observed for most secondary outcome measures, with between-group effect sizes in the moderate range. For instance, there was a 26% reduction in child-reported social anxiety in the ICBT group, compared to 2% in the ISUPPORT group, corresponding to a moderate between-group effect on the LSAS-CA. In the ICBT group and the ISUPPORT group respectively, 30.6% and 18% no longer met diagnostic criteria for SAD at the primary endpoint. The difference in proportions approached but did not reach significance ($p=0.86$). Cost-effectiveness analyses indicated ICBT to be more cost-effective than ISUPPORT in terms of improvement in social anxiety, but not in quality of life. The cost-effectiveness analysis with a societal perspective showed that ICBT was associated with cost-savings compared to ISUPPORT, mainly driven by reduction in medication use and increase in school-productivity. From a health-care provider perspective the results indicated an additional cost for ICBT that was associated with higher probability of being free from SAD in the ICBT group. Analysis of participants who crossed over to ICBT after ISUPPORT showed significant reductions in clinician-, child- and parent-reported social anxiety from pre-treatment to the 3-months follow-up.

4.5 Study III

4.5.1 Method

In Study III participants from Study I were asked if they wanted to participate in an additional trial investigating visual attention through eye-tracking technology. Twenty-five adolescents consented to participate and constituted the clinical

group (adolescents *with* SAD). Another 22 adolescents (13-18 years of age) were recruited from the general population and constituted the group of healthy controls (adolescents *without* SAD). During the eye-tracking task participants were instructed to visually attend to a set of pictures that were presented on a computer screen. The trial used a modified version of the gap-overlap paradigm that has been widely used in basic neurocognitive research on attention (e.g., Elsabbagh et al., 2013; Van der Stigchel et al., 2017). The aim was to measure vigilant and avoidant gaze patterns. Vigilance was defined as the time it took for a participant to move the eye-gaze *towards* a social stimuli and avoidance was defined as the time it took for the participant to move the eye-gaze *away* from a social stimulus. Both groups conducted the experiment for 20 minutes at pre-treatment. In addition, adolescents with SAD repeated the eye-tracking procedure at post-treatment and at 6-months follow-up.

4.5.2 Results

In both of the study groups participants moved the attention faster towards (*vigilance*) angry faces in comparison to happy or neutral faces. In addition, both groups were faster to move the attention away (*avoidance*) from angry faces. Participants in the clinical group who disengaged faster from social stimuli had less symptoms of social anxiety after treatment.

4.6 Additional evaluations

In addition to the three studies included in this thesis, some participants were also included in two master's theses in psychology. The results from those two theses will therefore be described briefly below.

Participants who were included in Study I were also asked if they wanted to participate in a master's thesis in psychology, evaluating the experiences of going through the ICBT treatment and group-exposure sessions (Hanqvist & Juselius, 2016). Ten participants agreed to be interviewed and thematic analysis was conducted to distill the participants' answers into three overarching themes. The first theme was *Not alone* and included experiences of feeling supported by the therapists, other group-members and the parents and, by reading case examples throughout the online treatment. Many adolescents felt that the therapists were available and easy to contact thorough the online platform and most found the group-exposure sessions very supporting as they enabled contact with other adolescents with the same problem. In addition, many found the continuous case examples as supportive as they made the adolescents feel validated and less lonely with their problems. The second theme was *Freedom under responsibility* and included experiences of freedom and independence but also demands related to working with the treat-

ment. Many adolescents appreciated the flexibility, accessibility and variation in the treatment material. At the same time many experienced high thresholds to initiate treatment engagement, such as working with the online modules or conducting exposures. For some, reading comprehension interfered with the ability to concentrate on the online material, while others felt that the content was easy to understand. The third theme was *The treatment is helpful*, which included experiences of the outcomes of the treatment. Most adolescents described that they learned a lot about SAD and how they could manage their social fears and that they generally felt better after the treatment. Even though many experienced that it was hard to challenge themselves, and that some felt worse during the initial part of the treatment, most described that over time they had learned to master the social fears and improved their functioning in many situations in life. Many also felt helped by learning more about social anxiety and that they reflected more about thoughts, feelings and behaviors related to the social fears after treatment.

Another master's thesis in psychology evaluated cost-of-illness of SAD by using data from 50 of the 103 participants in Study II (Lavner, 2018). The results indicated a yearly total mean cost of 7386€ (95% CI 4841, 9931) for SAD, which was not significantly different from the mean total cost in the general population of 7157€ (95% CI 4846, 9467). However, sub-total cost analysis showed a significant mean difference in educational loss between the two groups. Educational loss included costs generated by school absenteeism and school productivity loss and accounted for 30% of the mean total costs in the SAD group. The cost for educational loss was 2225€ (95% CI 1263, 3188) in the SAD group and 841€ (95% CI 648, 1033) in the general population, which reflects 2.5 times significantly higher yearly costs for SAD. Cost-of-illness data has now been collected for the whole sample in Study II and a manuscript presenting the results will be submitted for publication shortly.

4.7 Ethical considerations

Study I had a within-group design with the purpose to inform us about the acceptability, feasibility and preliminary effects of the ICBT protocol. This was ethically important due to the fact that a large number of participants were to enter this new treatment in the RCT and we wanted to first confirm that the treatment was feasible, acceptable and sufficiently efficacious. We also wanted to see that the treatment was not associated with any harmful effects and adolescents and parents were asked to report adverse events. Around a fifth of the participants reported a negative event during the course of the treatment. Many of the events were expected, such as increased social anxiety when exposure was initiated, which is a natural cause of exposure to feared situations. In general, the data on adverse events informed us that the treatment did not seem to generate long-term negative or adverse events.

In Study II, data on adverse events were collected during treatment and through a child- and parent-reported scale at the post-treatment assessment. About one third of the participants reported negative effects due to increased symptoms during the course of the treatment. Such symptoms included increased difficulty to sleep and increased anxiety symptoms. Around 10% reported suicidal ideation during the treatment, but only one participant associated that to the treatment. Whenever suicidal ideation was reported this was addressed with the family by the therapist who followed a predefined protocol for steps of action.

All participants included in this thesis were assessed at the clinic before entering the trial to confirm that all inclusion criteria and no exclusion criteria were fulfilled. All youth and their parents were interviewed with a semi-structured diagnostic interview. This procedure ensured that patients in need of more extensive care (for example those with severe depression or suicidality) were not included in the studies and were referred to more suitable treatments. The youths were also shortly interviewed without the presence of the parents to capture any potential sensitive information such as occurrence of abuse in the family.

Before and during the pre-treatment assessment, the families were provided with written and verbal information about the study and were given several opportunities to pose questions. The written information was provided in a parent version as well as in a child version. The child version of the information used child-adapted language and children were asked if they wanted the parent to read the information for them. Youth aged 15 and above provided written consent while participants aged 10-14 provided verbal assent. All caregivers/legal guardians provided written consent. Youths were explicitly informed that they had the right to decline participation in the study, even if their parents consented to participate. All families were informed that participation was voluntary and that they at any time could withdraw from the study without further explanation.

Monitoring of the fluctuation of severity of symptoms throughout the treatment by youth- and parent-reports about every third week, increased the possibility to detect participants who deteriorated. Participants who deteriorated (e.g., who experienced increased symptoms of depression or suicidality) were contacted by their therapist for a telephone assessment and had the possibility to be referred to other treatments. All families had weekly contact with their therapist through the online platform and three times through group-exposure sessions (Study I) or video-call sessions (Study II), which also increased the possibility to detect such deterioration. Study I and II followed routine documents written by the doctoral student and the main-supervisor, which for example included specific action plans in the case of increased depression or suicidality among participants. All therapists involved in the trials meet weekly to discuss clinical considerations and assessments to further ensure patient safety.

In Study II supportive therapy (ISUPPORT) was used as the control condition. Even though we believed ICBT to be more effective for youth with SAD, we did not know the effect of the ISUPPORT on social anxiety symptoms. The control condition was developed as an internet-delivered version of what we believed many children and adolescents receive in primary mental health care, in school counseling or even at the CAMHS. The participants were given written information about the two treatment conditions and were informed that CBT was considered the first-line treatment. With supportive therapy as a control treatment we had the possibility to move the primary endpoint to the 3-months follow-up, without having the ethical problem of letting patients wait longer than three months without any therapist support. The possible risk of offering an inferior treatment to the controls was weighted against the valuable gains of a deeper understanding about the effects of ICBT beyond general therapy effects.

Group-exposure sessions (Study I) might pose specific ethical considerations in terms of confidentiality between patients participating in the group. All participants in the groups were therefore asked to provide verbal consent to an agreement about ‘code of conduct’, including keeping personal information within the group.

Lastly, technological security, and thereby patient integrity, was ensured in several ways. First, through a two-factor authentication (individual password and a single-use code sent to the participants mobile phone) that was used for participants to access the online platform. Second, sensitive material such as video recordings of the baseline assessments, audio recordings from the video-call sessions and assessment material (case report forms and diagnostic interview schedules) were stored in locked cabinets (similarly secure as those used for medical records). Third, collected child-, parent-, and clinician-reported measures and treatment ‘chat-logs’ were saved in two secure databases respectively, that both use two-factor authentication. In addition, the independent Karolinska Trial Alliance (KTA) monitored Study II, and the regional ethical board approved Study I-III. This further ensured that the studies were conducted in an ethically sound way.

5 DISCUSSION

The overall aim of this thesis was to develop and evaluate an internet-delivered CBT program for SAD in children and adolescents, as well as to evaluate attention bias in adolescents with SAD.

5.1 The feasibility of ICBT for youth with social anxiety disorder

When we started planning for an internet-delivered treatment for youth with SAD, the high frequency and severe personal and societal impact of the disorder were well documented, as was the gap between the need for treatment and the proportion of patients who actually seek and receive help for their social fears (e.g., Lawrence et al., 2015; Stuhldreher et al., 2014; Zarger & Rich, 2016). ICBT had shown to be effective for adults with SAD (Hedman et al., 2011) and promising results were emerging for youth with mixed anxiety disorders (Vigerland, Ljótsson, et al., 2016), but ICBT studies for youth with SAD were scarce. Back in 2015, only one study had evaluated ICBT specifically for youth with SAD: a small trial by Tillfors and colleagues (2011) including 19 high-school students. That study showed promising results in terms of efficacy and patient satisfaction but completion of treatment modules was very low. Thus, when planning Study I, relatively little was known about the feasibility of an online treatment for adolescents with SAD.

We created the BIP SOFT program to be primarily delivered online in but in order to increase therapist support we also added three group-exposure sessions at the clinic. We believed that the face-to-face sessions could serve to help the adolescents start practicing the skills they learned online, as well as to address and resolve more challenging aspects of the treatment. The results showed that the adolescents completed a majority of the online modules and that the attendance rate at the group-exposure sessions was high. The vast majority of adolescents were satisfied with the treatment and would recommend it to a friend with similar problems. As shown in the qualitative evaluation of the intervention, many adolescents expressed that they felt very supported both by the group-sessions as well as by the online communication with the therapists (Hanqvist & Juselius, 2016). In addition, we observed significant clinical improvement of social anxiety, functional impairment and comorbid symptoms with large within-group effects on most outcomes. Taken together, Study I showed that ICBT supplemented with group-sessions is feasible for youth with SAD, and that the clinical effects were promising. The findings encouraged us to further develop and test the intervention in a larger trial (Study II). However, the overall aim of this doctoral project was to increase access to CBT for this patient group and face-to-face sessions in the original version of BIP SOFT demanded that participants sometimes travelled long

distances to the clinic and took time off from school, both documented barriers to treatment (Anderson et al., 2017). In order to further increase the access and the scalability of the treatment (and over time reach more patients) we made some adaptations to the treatment, before commencing Study II. The group-exposure sessions used in Study I were replaced by individual video-call sessions with a therapist. Other adaptations included earlier introduction of exposure training and, information about coping strategies, such as breathing techniques, where removed. This change was based on the results from meta-analyses suggesting that exposure should be introduced early in treatment and that anxiety management strategies do not improve outcomes of CBT for youth anxiety disorders (Ale et al., 2015; Whiteside et al., 2020). We also decided to broaden the age range from previously 13-17 to 10-17 years of age as onset of SAD is not uncommon in pre-adolescent children (Kessler et al., 2005).

5.2 The efficacy of ICBT for youth with social anxiety disorder

Previous research has shown face-to-face CBT for SAD to be more effective than wait-list controls (Scaini et al., 2016) and during this doctoral project one study showing ICBT to be superior to a wait-list control was also published (Spence et al., 2017). However, CBT for anxiety disorders in youth have for a long time struggled to show superior effects when compared to active control treatments (Warwick et al., 2017). From that perspective, producing yet another trial that compared (internet-delivered) CBT to a waitlist control condition would have left many questions unanswered. More rigorous designs testing novel treatments against active comparators are also generally recommended in current psychological research (Holmes et al., 2018). Study II was therefore designed to put ICBT to a real test: would the treatment effectively reduce symptoms of SAD, and more so than an active control condition? To be able to determine treatment effects beyond treatment components that are common in most forms of therapies (e.g., getting attention from a therapist, talking about one's symptoms), we designed Study II as a comparison between ICBT and an active comparator: internet-delivered supportive therapy (ISUPPORT). In ISUPPORT, we attempted to mimic ICBT in terms of format, length and therapist support without including any of the active components in CBT. This meant that if the findings would show ICBT to be more effective than ISUPPORT, it would be more likely that the difference in effect would actually stem from the different treatment components and not from other, general factors.

Our results did show significantly larger improvements in social anxiety and functional impairment measures for the ICBT group compared to the ISUPPORT group, and the differences were reflected in clinician-, youth- and parent-reported

measures. Given the rigorous design, very low attrition and minimal data loss, these findings further support the importance of incorporating active components such as exposure, social skills training and focus shifting in the treatment of SAD, as those interventions were only administered in ICBT. Clinical outcomes of face-to-face CBT have recently also shown to be increased when exposure and social skills training are included (Scaini et al., 2016; Whiteside et al., 2020). Results from both Study I and Study II also indicated further improvement from post treatment to follow-up. Currently, the long-term effects of BIP SOFT in Study II is being evaluated in a 1-year follow-up. Even though those results are outside the scope of this thesis they will further inform us about the robustness of the results over time, which has not been reported in previous ICBT trials for youth with SAD.

5.3 The cost-effectiveness of ICBT for youth with social anxiety disorder

This project aimed to increase the access to CBT for youth with SAD by increasing the scalability of treatment. For a treatment to be scalable, it also needs to be evaluated in terms of cost-effectiveness, as such evaluations may guide health-care providers and policy makers in how health-care resources should be distributed (Saha et al., 2001). In Study II, we found that ICBT was more cost-effective than ISUPPORT in terms of societal cost-savings while also producing a higher rate of participants being free from SAD diagnosis at the primary endpoint. The difference in sub-total costs was driven by reduction in medication use and increased school productivity among children and adolescents in the ICBT group.

Specifically, the increase in school productivity is an interesting finding. Productivity loss due to a disorder, as mentioned in the background, is also called *presenteeism* (i.e. producing worse due to a disorder when being present in school or at work), has been shown to be one of the more expensive aspects in cost-of-illness studies for SAD in adults (Stuhldreher et al., 2014). If this is true also for young persons with SAD is yet to be examined as no published trials to date have evaluated the indirect costs of SAD among youth. Preliminary results from a master's thesis by Lavner (2018), using data from Study II, indeed indicated that educational loss was one of the main parts of total cost-of-illness for SAD. The cost of educational loss was also found to be more than two times significantly higher compared to the general population. If presenteeism is responsible for societal costs for SAD already in the young age groups and ICBT has the potential to reduce such costs, this would further strengthen the case for making ICBT available as a treatment option for youth with SAD. Over all, our results align with the results from two recently published studies showing that ICBT compared to an active control condition (Jolstedt et al., 2018) and, computerized CBT compared to face-to-face CBT

(Chatterton et al., 2019) are cost-effective treatments for anxiety disorders in youth, including SAD. Furthermore, similarly as shown in Study II both mentioned trials indicated cost-effectiveness in terms of clinical improvement in anxiety, but no difference was found for quality-adjusted life years (QALY). Since it is unlikely that symptom change is unrelated to quality of life this rather indicates that the current measures of quality of life among youth with anxiety disorders are not sensitive enough to change and may not be well suited for evaluations of cost-effectiveness.

5.4 Attention bias in adolescents with social anxiety disorder

Study III was designed to add to the understanding of SAD by examining if adolescents with SAD attend to emotional stimuli in atypical ways. Theoretical models of SAD suggest that atypical attention to social stimuli may maintain SAD (Clark & Wells, 1995; Heimberg et al., 2014; Rapee & Heimberg, 1997), but limited research has examined this association in children and adolescents (Lisk et al., 2019). In addition, few studies have used eye-tracking technology to evaluate attention patterns in youth with SAD (Capriola-Hall et al., 2020; Schmidtendorf et al., 2018), even though this method is suggested to more directly capture attention bias than other available methods, such as the dot-probe task (Clarke et al., 2013). Hence, in Study III we used eye-tracking technology with the gap-overlap paradigm aiming to study vigilant and avoidant gaze behavior in youth with SAD, compared to non-anxious controls.

The results from Study III showed that adolescents with SAD had a bias to attend faster to threatful stimuli as well as a bias to avoid threat faster, relative to neutral or positive stimuli. However, the same bias related to threatful stimuli was also found in the non-anxious control group. As the study sample size was small, post-hoc analyses using Bayesian statistics were conducted and the results indeed supported the finding that the groups did not differ. The limited but existing evidence from eye-tracking studies of attention bias in youth with SAD indicate a vigilant-avoidant gaze pattern during exposure to threatening stimuli but the results are mixed. Our results are in line with a meta-analysis of eye-tracking studies that found no difference in vigilance or avoidance between SAD cases and non-anxious controls in studies with homogenous samples of youth with SAD (Lisk et al., 2019). A recent study did, however, find that adolescents with SAD oriented faster to and maintained attention longer on social stimuli than controls (Capriola-Hall et al., 2020). It has been suggested that attention bias is moderated by age, in samples with mixed anxiety disorders, due to developmental differences between youths who develop anxiety disorders and those who do not (Dudeny et al., 2015). Infants and young children have been suggested to have an innate attentional bias to threat

regardless of anxiety levels, something that with age is gradually more and more controlled by top-down regulating processes as the involved brain regions mature (Field & Lester, 2010). Individuals with anxiety, however, have been suggested to ‘fail’ to develop this attentional/inhibitory control (Kindt & Van Den Hout, 2001). Even though this is a feasible explanation that also fits with evidence of attention bias in anxious adults (Armstrong & Olatunji, 2012; Bar-Haim et al., 2007), our results did not support this theory. The adolescents in Study III were on average 15 years old, which could be considered a sufficiently high mean age to detect a difference between those with SAD and non-anxious controls. Nevertheless, the findings partly contradicted the developmental theory. Hence, there is still a need for additional studies to examine the developmental trajectory of attention bias from childhood and adolescence into adulthood. The mixed findings in previous studies could be attributed to differences in samples (mixed vs. homogenous), differences in methodology (e.g., dot-probe vs. eye-tracking), specificity of paradigms (ability to detect vigilance and avoidance), differences in emotional stimuli and differences in stimuli presentation time. Larger samples with a broader age range could also provide a better understanding of attention bias in SAD over a longer developmental span.

Study III also explored if ICBT treatment is associated with changes in vigilant or avoidant attention. We found no changes in attention bias over the course of treatment which might indicate that attention biases are rather stable traits. Interestingly, we found that those participants who were faster to disengage from faces (regardless of emotion) at baseline improved more after ICBT. This could imply that ICBT is specifically beneficial for those more prone to avoid social stimuli. The treatment includes several components aiming to reduce avoidance, such as exposure exercises, exercises to direct attention towards the surrounding environment, as well as exercises of social skills including seeking and maintaining eye contact with others. Hence, assessments of attention bias could potentially contribute to detect subgroups of patients that may be specifically responsive to treatment.

Currently, the majority of children and adolescents in Study II are participating in a replication and extension of Study III where eye-tracking assessments are conducted before and after treatment and, at 3- and 12-months follow-up. Data is also collected from age- and gender matched controls from the general population. This larger study, which includes a broader age range (10-17 years), may provide important information about differences between youth with SAD and controls, with sufficient power to examine a potential moderating effect of age on vigilant and avoidant attention biases.

5.5 Where do we go from here?

This last part of the discussion covers a few hypotheses and questions that were generated from the results in Study I-III. These may guide future research on further evaluations of ICBT to deepen the understanding of SAD in youth and to improve clinical outcomes after treatment.

ICBT in Study I and II was deemed feasible in terms of satisfaction and acceptability, but also in the sense that completion rates were high. In both studies, the completion rate of online modules was higher than those reported in other trials: 2.9 out of 9 (32%) in the Tillfors trial and 4.4 out of 10 (44%) in the Spence trial versus 5.9 out of 9 (66%) in Study I and 7.5 out of 10 (75%) in Study II. However, we do not know why so many of the participants completed such large proportions of the treatments. One hypothesis is that it could be related to the amount of therapist support. Study I and II included more therapist support in terms of therapist support provided on the online modules, as well as the additional support provided by the group-exposure sessions and the video-call sessions, than reported in previous ICBT trials for youth with SAD (Spence et al., 2017; Tillfors et al., 2011). The authors in the previous two trials reasoned that stand alone ICBT may not be enough for youth with SAD to engage with treatment and suggested future trials to identify additional support as a means to increase treatment compliance. In the qualitative master's thesis by Hanqvist and Juselius (2016) some participants requested more (face-to-face) therapist support and in a qualitative study by Olsson and colleagues (2014) adults with SAD had a wish to get in contact with other participants. Maybe a flexible approach can be used in the future, where face-to-face components or additional therapist support can be added based on patients' preferences. In addition, further interaction between participants could be enabled through online chat forums, video calls or even group meetings in virtual reality (VR) environments. Future studies should evaluate if children and adolescents with SAD have different needs of therapist support in ICBT, and if the level of support could be tailored individually in order to optimize treatment outcome while retaining the scalability and cost-effectiveness of internet-delivered treatment.

The next future consideration concerns that, despite the promising findings from Study II, there appears to be further room for treatment development and improvement in remission rates. Even though we observed large improvements in clinician-, child- and parent-reported levels of SAD, these results were not entirely reflected in the proportion of participants being free from SAD diagnosis after treatment. Just above 30% in the ICBT group no longer fulfilled diagnostic criteria for SAD at the primary endpoint (a non-significant difference from the corresponding 18% in the ISUPPORT group). This is comparable to the proportions in the study by Spence and colleagues (2017), where about one third of the participants no longer fulfilled diagnostic criteria for SAD at the follow-up after ICBT. The proportion

of participants being free from SAD in these two ICBT trials (Study II and Spence et al., 2017) are lower compared to those reported in studies evaluating face-to-face CBT, which report around half of participants being in remission immediately after CBT (Beidel et al., 2007; Öst et al., 2015). However, we do not know if face-to-face treatment is superior to ICBT for youth with SAD. To my knowledge two studies on adults with SAD have confirmed a non-inferior relationship between face-to-face CBT and ICBT (Andrews et al., 2011; Hedman et al., 2011). Looking at remission rates in Hedman et al (2011), 40% in the ICBT group and 34% in the face-to-face CBT group no longer fulfilled diagnostic criteria for SAD at 6-months follow-up. Future trials designed to test non-inferiority between ICBT and face-to-face CBT for youth with SAD may answer if the differences in remission rates between different studies represent actual differences in clinical effects between the face-to-face and the internet-delivered treatment format.

Furthermore, more work is needed to analyze change mechanisms during ICBT treatment that may be associated with treatment outcome. In Study II we collected data on potential mediators of outcome during delivery of ICBT and ISUPPORT. These included measures of potential maintaining factors, such as post mortem rumination, safety behaviors, self-focused attention and parents' accommodation to the child's anxiety. Those results may guide decisions on how treatment can be tailored further to target maintaining factors in order to improve symptom reduction and remission rates. In addition, increased number of sessions and treatment weeks could be considered in ICBT as this has been shown to be associated with better outcomes in face-to-face CBT for SAD (Scaini et al., 2016). Future trials could also evaluate better ways to detect patient deterioration early during treatment. In Study II, we successfully used LSAS-CA to track changes in child- and parent-reported social anxiety symptoms at three occasions during the treatment, but a shorter version of the scale would facilitate monitoring symptoms with shorter time intervals and patients who don't improve (or deteriorate) could be detected faster and offered more intensive interventions earlier. In Study II, non-responding participants were offered face-to-face CBT three months after ICBT.

Lastly, the results from Study III showed that those participants who were more avoidant during the eye-tracking task were also those who showed larger reductions in social anxiety after ICBT. Additional studies are needed to determine the ecological validity of these findings, in other words how this avoidance in an experimental environment translates to avoidance in everyday life for individuals with SAD. In most eye-tracking studies, static pictures have been used as social stimuli and the use of more dynamic stimuli would potentially add to the field (Claudino et al., 2019). For instance, wearable eye trackers could be used to capture eye gaze in more 'real life' situations. Another possibility would be to use eye tracking in virtual or augmented reality settings. Eye-tracking studies using

VR environments have indicated that adults with SAD or high levels of social anxiety (Jonas et al., 2020; Mühlberger et al., 2008) show attention biases and that eye-tracking in VR environments can successfully be used to distinguish high socially anxious individuals from low socially anxious individuals (Dechant et al., 2017). These methods could also add further knowledge about maintaining factors beyond self-reported measures or behavioral assessments in real world settings, as virtual or augmented environments can be created to simulate specific aspects of everyday life that would otherwise be difficult to capture.

6 CONCLUSIONS

ICBT is a feasible treatment for youth with SAD as reflected by high treatment completion and acceptability. ICBT is also significantly more efficacious in reducing social anxiety and functional impairment, when compared to internet-delivered supportive therapy. In addition, ICBT is a cost-effective treatment contributing to reduced societal costs.

Adolescents with SAD show attention biases when exposed to socially threatening stimuli and similar patterns are shown in non-anxious controls. Those with SAD who are more prone to avoid social stimuli before ICBT also shows larger reductions in social anxiety after treatment.

Further evaluations are needed to determine how clinical outcomes can be improved for youth who do not respond to ICBT and future eye-tracking studies with larger samples of youth with SAD are needed to determine if aspects of attention bias are specific to SAD and if these contribute to the maintenance of SAD.

In summary, ICBT could increase access to evidence-based treatment for youth with SAD and further knowledge about attention bias could generate hypotheses about the maintenance of social anxiety as well as how psychological treatment for social anxiety could be improved to target those maintaining factors.

7 ACKNOWLEDGEMENTS

First of all, my warmest gratitude to all children, adolescents and parents who participated in the studies included in this thesis. Thank you for being so active in the treatments, for answering our questions and for giving us valuable feedback!

The biggest thank you to my main-supervisor *Jens Högström*. What a journey this has been! I am deeply grateful for everything you have taught me and proud to be your first PhD student! You have been present and engaged in every step of the SOFT-project and at the same time you have let me try my own wings. I remember us sitting by your kitchen table sometime in the beginning of my PhD studies, discussing the first study and at the same time listening to this awesome Swedish rapper that we had just discovered (clue: *suedi*). For me, that is the perfect symbol for our years together: digging into science while sharing some sweet beats.

Eva Serlachius, the godmother of BIP, my co-supervisor. Thank you so much for giving me this crazy opportunity! You have taught me three of the most important things during these years: the importance of a great team, how to build research muscles and to celebrate everything. I look forward to share more champagne and ideas!

David Mataix-Cols, my co-supervisor, the master mind of study design and scientific writing. Thank you for your support to aim high and for your realistic eye in challenging times!

Thank you to my mentor *Linda Jüris*. Going to Uppsala a couple of times during these years was a sweet escape. I really appreciated our talks about life and academia!

Kristina Aspvall, *Tove Wahlund* and *Maral Jolstedt* my co-PhD students and champagne brains: nothing of this would have happened without you. Kristina my dear! Going through similar things in life gave us a fast track towards a strong friendship. Even though we are different in many ways (which I love that we can make fun of) I actually think we are increasingly regressing to the mean. I will always remember our trip to Lofoten in the summer of 2017 as the kick-off for our friendship. Tove liebe, liebe! We have shared the same room for 5 years now. I don't think any space can ever compete with the *tyska rummet* in terms of discussions about life. Five years of laughing and crying at the same time – I love you for being so silly and at the same time having that stroke of existential *svärta* that makes room for whatever life brings! Maral *käraste vän!* We have known each other for 13 years now, all the way from studies in Uppsala, via BUP Solna to BIP – with the last years really making us close friends. You are one of the craziest and bravest persons I know. You pave the way for big things to happen and I am so happy to have shared the PhD studies with you. You convinced me to apply for this position in the first place and for that I am forever grateful!

Thank you *Rebecca Grudin* for holding on to the working units: coffee breaks with talks about hikes and skiing have been invaluable energy boosts. I am so happy you joined the crew, you will make a big difference for the teens in your studies! *Per Andrén, Klara Lauri, Lie Åslund* and *Eva Hesselmark* thank you for sharing different parts of the PhD journey with me! I have enjoyed to share scientific (and not so scientific) discussions with you and to sing together on the power ballad Fridays!

Sarah Vigerland the first BIP PhD, thank you for being so awesome in both SOFT pilot and SOFT RCT! You are the queen of anxiety assessments and I am so grateful to have learned from the best!

Thank you to my fantastic, present and former, PhD colleagues at G22 for collaborations, lunch discussions and work outs (or talks about work outs): *Erik Andersson, Martin Bellander, Johan Lundin Kleberg, Fredrik Enocson, Marianne Bonnert, Hedvig Engberg* and *Fabian Lenhard*. Thank you, *Vera Wachtmeister, Moa Holmsved, Helene Ringberg* and other members of the BIP-crew for bringing positive energy to the projects! Also, thank you to everyone in, and related to, the *Serlachius* and *Mataix-Cols* research groups; so many sharp brains in one place!

Thank you *Pia Ahrgren, Claes-Henrik Molin, Karin Liv* and the admin staff for chats and laughs and for keeping everything at work running – G22 would be nothing without you!

Lorena Fernández de la Cruz tack för all pepp och för att du är den absolut bästa randomization queen (and yes I am still speaking Swedish to you 😊).

Karin Sundström, Viktor Eriksson, Malin Lavner and *Malin Burman* thank you is not enough. Each and every one of you deserves a prize for best professional first aid kit (and continuous aid kit) in BIP SOFT RCT. I am so grateful that you joined the team and I am so impressed and proud of the incredible work you did for the families and the trial!

Thank you, *Hanna Sahlin, Sigrid Salomonsson, Johan Åhlén, Johan Bjureberg, Mathilde Annerstedt* and *Maria Lalouni* (the best group leader!) for excellent assessments in the BIP SOFT RCT and for a positive spirit in a challenging trial! Thank you *Hugo Hesser* for explaining, suggesting and conducting statistics on the rct data!

Many thanks to *Cornelia Hanqvist* and *Jon Juselius* for participating as group leaders, and writing a really neat qualitative master's thesis, in BIP SOFT pilot! Thank you, *Martin Persson*, for excellent diagnostic assessments in the same trial!

Dimitar Krastev, Karin Edh, Erica Sundqvist (snus!), *Johanna Aleus, Julia Martinis, Simon Åberg* and many others in OCD-gänget. Without you there is no reasonable fika or lunch break. Thank you for chats, laughs and support when office hours

were long and energy low! Also, the biggest thank you to *Johanna Henriksson* for the fantastic illustrations to this thesis!

Vide Ohlsson Gotby I am so happy we made friends at G22. Thank you for fun late nights and for being such a cool dancer!

Johanna Ekdahl thank you for always being the genuine you! No time or distance can keep us apart – you will always be my beloved stjärnsyster.

To my dear best friends; *Sophie, Maria, Emma, Johanna* and *Caroline*, my Malmslätt-crew, thank you for your love for more than two decades. You are my best friends and you know me inside out. I am always longing for our next yearly weekend!

Axetfamiljen, Stockholmsfamiljen: *Moa, Rebecka, Emma* and *Ebba*. And *Karin* and *Märta* at distance. Words are not enough to describe the love and importance. You are my sisters, my partners, my soul mates. Without your love and support this work would never have happened. Jag älskar er, jag älskar er, jag älskar er!

Familjen! Tack mamma *Bettan* and pappa *Åke*, I love you for always having my back no matter what, for teaching me to stand up for what is right and to remember what is important in life. *Loisan* and *Vigge*, thank you for being the most loving siblings, I always laugh the hardest with you, have the most internskämt with you and get the most dishen with you. Mormor *Siv* och morfar *Lasse*, ni har alltid funnits där med kärlek i sin enklaste form och full närvaro. Alltid hemlagat, hemstickat, hemsnickrat. Mormor med ditt snabba steg och morfar med din värme och glimt i ögat. Jag älskar er! Och tack farmor *Vivi-Anne* för lusten till att skriva och berätta sagor, brevväxla och rimma – jag saknar dig och älskar dig! To *Adde* and to *Maria* thank you for being the best for my siblings, I am so happy to have you in my life. Tack *Ludwig* och *Ewelin* älskade gullungar, ni gör mig så lycklig! Familjen Appelberg; *Henkan, Oskar, Emma* och *Amanda*, thank you for being such an awesome extended family! I am so grateful for all dinners and hang outs and silly discussions and laughs!

Finally, *Anders*, älskling! We met in my apartment at my halftime party (!), which was right before all I managed to do was sleeping. I am so incredibly happy that you saw something in that exhausted person and stayed in my life. Every day is a better day with you by my side and I am so looking forward to explore the future with you. Jag älskar dig!



March 30, 2020

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