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EXCESSIVE WORRY IN ADOLESCENTS AND ADULTS – DEVELOPMENT AND EVALUATION OF THEORY-DRIVEN TREATMENTS

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Excessive worry in adolescents and adults – development and evaluation of theory- driven treatments

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To all of us who worry too much at times.

ABSTRACT

Background: Worry is common among both adolescents and adults, and excessive worry is related to a number of mental health problems. Current pharmacological and psychological treatments for worry are moderately effective, and the processes involved in therapeutic change remain unclear. Building on theories of excessive worry could be a way forward in developing more streamlined and effective treatments. This thesis mainly concerns itself with two theories of worry: the intolerance of uncertainty model and the metacognitive model.

Aim: The overall aim of this thesis was to develop and evaluate streamlined psychological interventions for adolescents and adults, specifically targeting hypothesized causal mechanisms relevant in the maintenance of excessive worry. More specifically, the aims were (1) to develop a streamlined intolerance of uncertainty-focused treatment (IU-CBT) for adolescents with excessive worry, and explore its feasibility and preliminary efficacy in face-to-face and online-delivered formats, (2) to explore the experiences of the adolescents and their parents who had received online IU-CBT with parental involvement, and (3) to develop internet-delivered metacognitive therapy for adult worriers (I-MCT), evaluate its clinical efficacy, and explore the mediating effects of negative beliefs about worry in treatment.

Methods: Four studies (I-IV) were conducted within this doctoral project. To evaluate the feasibility and preliminary efficacy of face-to-face IU-CBT for adolescents, we conducted study I, an uncontrolled pilot feasibility trial (N = 12). The treatment protocol was subsequently transformed into an online version and its feasibility and preliminary efficacy was evaluated in a pilot feasibility study with a multiple-baseline design (N = 13; study II). In study III, eight adolescents and nine parents who had participated in study II were interviewed in a qualitative study and data were analyzed using thematic analysis. Study IV was a randomized controlled trial with mediation analysis where adult excessive worriers (N = 108) were randomized to either I-MCT or a wait-list control condition.

Results: In study I, there were no drop-outs or adverse events, and most families described high treatment satisfaction. The results showed large reductions in self-rated worry and secondary outcomes, and the effects were maintained at three-months follow-up. In study II, all but one adolescent followed through with the online treatment, and treatment module completion rates were high. We found medium to large reductions in self-rated worry, anxiety, depressive symptoms, and impaired functioning at post-treatment and the changes were maintained at one and three-month follow-ups. Study III showed that even though the online format posed challenges to the families and many would have appreciated some additional therapist-support, online IU-CBT for adolescents with excessive worry can

be acceptable for both the adolescents and their parents. Exposure to uncertainty could be difficult but was also experienced as worthwhile and both adolescents and parents described the parental involvement in treatment as important for the adolescents' treatment adherence. In study IV, treatment retention was high and I-MCT appeared to be acceptable to patients. Change in negative beliefs about worry mediated change in worry (more so than did change in depression), and large effects favoring I-MCT were observed. Effects were maintained after six and twelve months.

Conclusions: An IU-focused treatment for adolescents with excessive worry is feasible and potentially effective, when delivered face-to-face as well as online. I-MCT is also acceptable and effective for adults with excessive worry. Change in negative beliefs about worry appear to mediate change in worry outcomes in I-MCT, or put differently: if one does not believe that worry is dangerous or uncontrollable, one worries less. In conclusion, the findings lend further support to intolerance of uncertainty and negative beliefs about worry being promising treatment targets in novel interventions for excessive worry.

SAMMANFATTNING

Bakgrund: Oro är vanligt hos både ungdomar och vuxna och överdriven oro förekommer ofta i samband med psykisk ohälsa. Aktuella farmakologiska och psykologiska behandlingar har måttlig effekt på oro och exakt hur förändring vid psykologisk behandling går till är fortfarande okänt. Att utgå från vetenskapliga teorier om överdriven oro skulle kunna vara ett sätt att utveckla fokuserade och effektiva behandlingar. Denna avhandling utgår i första hand från två teorier för överdriven oro: intolerans för osäkerhetsmodellen och den metakognitiva modellen.

Syfte: Det övergripande syftet med denna avhandling var att utveckla och utvärdera fokuserade psykologiska behandlingar med särskilt fokus på mekanismer som eventuellt bidrar till överdriven oro hos ungdomar och vuxna. Avhandlingens specifika syften var (1) att utveckla en behandling (IU-KBT) som fokuserar på att minska intolerans för osäkerhet hos ungdomar med överdriven oro, och undersöka dess genomförbarhet och preliminära kliniska effekter när behandlingen ges på traditionellt sätt (ansikte-mot-ansikte) samt via internet, (2) att utforska hur ungdomarna och deras föräldrar som genomgått IU-KBT via internet upplevde behandlingen samt (3) att utveckla internetfördlad metakognitiv terapi (I-MCT) för vuxna med överdriven oro, utvärdera dess kliniska effekt samt undersöka om förändring av negativa uppfattningar om oro medierar förändring av oro under behandlingen.

Metod: Fyra studier (I-IV) genomfördes inom ramen för detta doktorandprojekt. För att utvärdera genomförbarheten och den preliminära effekten av IU-KBT ansikte-mot-ansikte genomförde vi studie I, en pilotstudie utan kontrollgrupp (N = 12). Behandlingsprotokollet omvandlades därefter till en internetversion och dess genomförbarhet och preliminära effektivitet utvärderades i en pilotstudie med multipel baslinjedesign (N = 13; studie II). I studie III, en kvalitativ studie, gjordes djupintervjuer med åtta ungdomar och nio föräldrar som hade deltagit i studie II och data analyserades med hjälp av tematisk analys. Studie IV var en randomiserad kontrollerad studie med mediationsanalys där vuxna med överdriven oro (N = 108) randomiserades till antingen I-MCT eller väntelista.

Resultat: Alla patienter i studie I genomförde behandlingen, inga negativa effekter rapporterades och de flesta familjer uppgav att de var nöjda. Resultaten visade stora effekter på självskattad oro och sekundära utfallsmått, och effekterna bibehölls tre månader efter avslutad behandling. I studie II genomförde alla utom en tonåring behandlingen och antalet genomförda behandlingsmoduler var högt för både ungdomar och deras föräldrar. Vi fann medelstora till stora effekter på ungdomarnas oro, ångest, depressiva symtom och nedsatt funktion efter behandlingen och förändringarna bibehölls vid en och tre månaders uppföljning. Studie III visade att även om formatet innebar utmaningar för många, och flera hade önskat

lite mer behandlarstöd, var internetförmiddad IU-KBT acceptabel för både ungdomarna och deras föräldrar. Exponering för osäkerhet beskrevs som utmanande men upplevdes också som värdefull och både ungdomar och deras föräldrar beskrev att föräldrarnas parallella spår i behandlingen var viktigt för att ungdomarna skulle kunna genomföra behandlingen. Även i studie IV genomförde en stor andel av deltagarna behandlingen. Stora behandlingseffekter för I-MCT (jämfört med väntelista) observerades och bibehölls vid sex och tolv månader. Förändring i negativa uppfattningar om oro medierade förändring i oro.

Slutsatser: En IU-fokuserad behandling för ungdomar med överdriven oro tycks vara så väl genomförbar som potentiellt effektiv. I-MCT verkar också vara acceptabel och effektiv för vuxna med överdriven oro. Förändring i negativa uppfattningar om oro tycks mediera förändring i oro, eller annorlunda uttryckt: om man slutar tro att oron är farlig eller okontrollerbar oroar man sig också mindre. Sammanfattningsvis ger resultaten stöd för att fokusera på intolerans för osäkerhet och negativa uppfattningar om oro i nya behandlingar för överdriven oro.

LIST OF SCIENTIFIC PAPERS

- I. Wahlund, T., Andersson, E., Jolstedt, M., Perrin, S., Vigerland, S., Serlachius, E. (2019). Intolerance of uncertainty-focused treatment for adolescents with excessive worry: A pilot feasibility study. *Cognitive and behavioral practice*. doi: 10.1016/j.cbpra.2019.06.002
- II. Wahlund, T., Jolstedt, M., Andersson, E., Vigerland, S., Perrin, S., Öst, L-G., Högström, J., Serlachius, E. (2020). Online cognitive behavior therapy for adolescents with excessive worry: A multiple baseline design feasibility study. *mHealth*. 6(4). doi: 10.21037/mhealth.2019.09.10
- III. Wahlund, T., Wallhem, M., Serlachius, E., Engberg, H. Experiences of online exposure-based treatment with parental support for teenagers with excessive worry. (Manuscript).
- IV. Wahlund, T., Hesser, H., Perrin, S., Johansson, S., Huhn, V., Sörhus, S., Lindskog, V., Serlachius, E., Hedman-Lagerlöf, E., Ljótsson, B., Andersson, E. Are negative metacognitive beliefs driving excessive worry? A randomized controlled trial with mediation analysis. (Manuscript).

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1 INTRODUCTION

Life can be full of reasons to worry, both big and small. Currently, the world is facing great challenges like the impact of climate change, the extinction of species, and social unrest (e.g. Díaz et al., 2019; Evans, 2019; Safi, Tom, & Jones, 2019). Despite the global community agreeing on the Paris Climate Accord and the Global Sustainability Goals in 2015 (the same year I started preparing for this doctoral thesis), most of our common problems are not closer to being solved today (United Nations, 2019; World Meteorological Organization, 2019).

Many of us, both adolescents and adults, worry about the future of the planet (Burke, Sanson, & Van Hoorn, 2018; Leiserowitz et al., 2019; Ojala, 2012), but while worry is a normal human response to uncertainty, challenges, and threats, the worrying itself can become an additional burden. Irrespective of what the worry is about (be it personal matters such as everyday performance and social evaluative stressors, or our global challenges), excessive worrying can impair us, make us paralyzed or hostile, or keep us focused on problems rather than facilitate solutions. It may also lead to suffering and be related to additional mental health problems.

In my clinical practice, I have often found excessive worry to be challenging to treat. The occurrence of worry may not be something the average person (and perhaps some clinicians) would instinctively view as a problem in need of treatment. Excessive worriers often just get on with things, but may do so feeling quite miserable. Others may be so focused on the topics of their worry that they do not identify the worrying itself as the problem. This somewhat peripheral position of worry amongst the anxiety symptoms is largely reflected by standard treatment packages for anxiety that include a broad range of interventions targeting a number of symptoms. These are often moderately effective and can be difficult to work with for both patients and clinicians.

Perhaps a greater focus on worry itself could streamline treatments and facilitate treatment evaluation. If that is in fact the case, how it should be done and if it may further our understanding of excessive worry are some of the questions this thesis aimed to address.

Stockholm, January 2020.

2 BACKGROUND

2.1 What is worry?

Worry is a psychological phenomenon, characterized by intrusive thoughts about potential negative outcomes and accompanied by anxiety (Macleod, Williams, & Bekerian, 1991). The worrier often poses internal “what if”-questions about future threats (Borkovec, 1985), and while worrying can be associated with adaptive problem-focused coping strategies, it often involves both unsuccessful problem-solving attempts, negative intrusive thoughts and somatic anxiety responses (Davey, Hampton, Farrell, & Davidson, 1992; Szabo & Lovibond, 2002). Despite its association with negative affect, worrying seems difficult to dismiss for the worrier (Mathews, 1990), and the process is often perceived as hard to control (Borkovec, Robinson, Pruzinsky, & DePree, 1983; Hirsch & Mathews, 2012; Wells & Carter, 2001).

Worry occurs from early in life, with children as young as five years old reporting worry (Vasey, Crnic, & Carter, 1994). The prevalence of worry increases with age, with older children and adolescents worrying more than younger children (Chorpita, Tracey, Brown, & Collica, 1997; Muris, Merckelbach, Gadet, & Moulaert, 2000). Among children, almost 70% worry about a number of things (Muris et al., 2000; Orton, 1982), and adults without any anxiety disorder have been found to worry daily (Dupuy, Beaudoin, Rhéaume, Ladouceur, & Dugas, 2001). Among older adults in a cross-sectional study, almost 80% reported worrying, and 37% found the worry excessive (Golden et al., 2011). However, older adults have been found to worry less than their younger counterparts (Gonçalves & Byrne, 2013). Women report more worry than men (Dugas, Freeston, & Ladouceur, 1997; Robichaud, Dugas, & Conway, 2003), and data indicate the same for girls compared to boys (Campbell & Rapee, 1994; Muris, Meesters, & Gobel, 2001; Silverman, La Greca, & Wasserstein, 1995).

2.2 The impact of worry

In addition to being common in the general population, worry is also prevalent in a range of mental health problems. Excessive worry about several topics, events, or activities is the core symptom in Generalized Anxiety Disorder (GAD) according to the Diagnostic and statistical manual of mental disorders (5th ed.; DSM-5; American Psychiatric Association, 2013). To fulfill criteria for GAD, the worry must be long lasting, impairing, and be perceived as difficult to control by the individual. It should also be accompanied by physical or cognitive symptoms (e.g., impaired concentration, muscle tension, or sleep disturbance). Children must experience at least one such physical/cognitive symptom, adults three. The 12-month

prevalence for GAD is about 1.0% for 9 to 12 year-olds, 1.5% in adolescence and 2.1% for adults (Copeland, Angold, Shanahan, & Costello, 2014; Grant, Hasin, Stinson, & Dawson, 2005).

Research with children and adolescents finds that those with anxiety disorders (including GAD) do not differ from clinical and normal controls in terms of worry content but for the frequency and intensity of worry (Perrin & Last, 1997). Similarly, adults with GAD tend to worry about the same things as individuals without the disorder (Ruscio & Borkovec, 2004). However, those with GAD worry more often, have more negative thoughts and beliefs about their worry, and are more functionally impaired than those without the disorder (Ruscio & Borkovec, 2004; Wells & Carter, 2001). Importantly, and as described above, individuals without GAD or any other psychiatric disorder also suffer from excessive worry. One study (Ruscio, 2002) found that a majority of high worriers met none or just one of the four major DSM-IV criteria for GAD (APA, 2000). Subthreshold GAD is twice as common as the disorder itself, with subthreshold sufferers experiencing impaired functioning, and frequent use of primary health care services and benzodiazepines (Haller, Cramer, Lauche, Gass, & Dobos, 2014).

Excessive worry is a prominent symptom or associated feature of all the anxiety disorders, trauma and obsessive compulsive-related disorders, depression, and common in individuals suffering from a wide range of psychiatric disorders including autism, psychosis, and eating disorders (to name a few) (Chelminski & Zimmerman, 2003; Olatunji, Wolitzky-Taylor, Sawchuk, & Ciesielski, 2010; Starcevic, 1995). Research points to worry playing a significant role in the development and maintenance of several depressive and anxiety related conditions as well as in persecutory delusions (Calmes & Roberts, 2007; Freeman et al., 2015; Holeva, Tarrier, & Wells, 2001; Hong, 2007; Muris, Roelofs, Meesters, & Boomsma, 2004; Newman & Llera, 2011). Individuals (including adolescents) who report high levels of worry report lower levels of social support (Kertz, Bigda-Peyton, Rosmarin, & Björgvinsson, 2012) and more frequent suicidal thoughts (Boden, Fergusson, & Horwood, 2007). In addition, excessive worry is associated with poorer social adjustment, and increased risk of a range of physical conditions (often beginning in adolescence) including but not limited to, irritable bowel syndrome (Bengtson, Aamodt, Vatn, & Harris, 2015; Gerson et al., 2015), pre-natal distress and pre-eclampsia in pregnant women (Krishnamurti, Davis, & Simhan, 2019), and cardiovascular disease and early mortality (Batelaan, ten Have, van Balkom, Tuithof, & de Graaf, 2014; Kubzansky et al., 1997).

2.3 Previous clinical approaches to excessive worry

Psychosocial treatments that identify worry as the primary problem, and prioritize worry-reduction interventions, have mainly focused on individuals with GAD. Of course, psychosocial treatments for other anxiety or anxiety-related disorders (PTSD, OCD) and depression often included interventions for worry but not as a primary focus of treatment. Therefore, the following (brief) review of the treatment literature covers studies specifically focusing on individuals with GAD.

2.3.1 Pharmacological treatments

While the efficacy of various pharmacological agents has been evaluated in individuals with GAD as a primary or secondary anxiety disorder (Slee et al., 2019), the most frequently evaluated agents are selective serotonin reuptake inhibitors (SSRIs) and selective serotonin norepinephrine reuptake inhibitors (SSNRIs). In respect of children and adolescents, two recent meta-analyses found that such drugs yield effect sizes in the moderate range for clinician-rated GAD severity compared to placebo (Strawn, Welge, Wehry, Keeshin, & Rynn, 2015; Wang et al., 2017). Similar effect sizes relative to placebo are found for these same agents in adults with GAD (Slee et al., 2019; Van Ameringen, Patterson, Turna, Pipe, & Nakua, 2017). Guidelines on the treatment of childhood anxiety disorders (including youth with comorbid GAD) will usually recommend cognitive behavioral therapy (CBT) as the first line treatment but a combination of SSRIs plus CBT for those who do not respond (e.g. Katzman et al., 2014). In adults, SSRI's and CBT are both recommended as first line treatments for GAD in several guidelines (Katzman et al., 2014; National Institute for Health and Care Excellence, 2019; Socialstyrelsen, 2017).

Notably, the evidence for the combination of CBT and antidepressants such as SSRI's as either superior to one single treatment, or as a second-hand alternative for non-responders to either treatment alone is limited (Van Ameringen et al., 2017). For youth, one study compared CBT, SSRI's and the combination of both. Results were comparable for the mono-therapies, and effects of the combination-therapy were better post-treatment (Walkup et al., 2008). However, the combination seemed to benefit especially the most severe cases, the study lacked a placebo-plus-CBT control, and the combination of CBT and SSRI's was not more effective than either mono-therapy at follow-up (Piacentini et al., 2014). For adults, one study offered CBT for patients already receiving anti-depressants and found not additional effect of the combination treatment (Crits-Christoph et al., 2011).

2.3.2 Psychological treatments

The GAD-specific, psychological treatment that has received the most empirical support are various versions of multi-component CBT programs (Cuijpers et al., 2014). These programs will use various interventions to treat excessive worry, muscle tension, sleep disturbances, avoidance behaviors, reassurance-seeking and other interpersonal difficulties, and deficits in problem-solving ability/confidence (among other symptoms) (Clementi & Alfano, 2014; Newman, Llera, Erickson, Przeworski, & Castonguay, 2013).

GAD-specific treatments for use with children and adolescents are relatively new (discussed below). Since the identification of overanxious disorder (the childhood precursor to GAD) in DSM-III (American Psychiatric Association, 1980) and the subsequent modification of the GAD criteria to include children in DSM-IV (APA, 1994), CBT programs have been developed and evaluated for use with youth who have multiple anxiety disorders, including GAD (Kendall, 1994; Rapee, 2000). These “any anxiety” or generic CBT programs for childhood anxiety disorder have been shown to be effective compared to waitlist (59% vs 17% remission rates from one or more of the comorbid anxiety disorders) but with average effect sizes for CBT in the moderate range at post-treatment and follow-up (James, James, Cowdrey, Soler, & Choke, 2015). Few trials have been carried out comparing generic CBT for anxiety programs to another active treatment with little evidence for the superiority of CBT (James et al., 2015).

An advantage of these generic CBT for childhood anxiety programs is that they can be delivered with relatively equal effect in a number of formats (i.e., individual, group, family), as well as in self-help/bibliotherapy and internet formats, i.e. internet-delivered cognitive behavioral therapy (ICBT; Jolstedt, Wahlund, et al., 2018; Rapee et al., 2017; Schwartz, Barican, Yung, Zheng, & Waddell, 2019; Vigerland et al., 2016). However, it is important to point out that outcomes for GAD specifically are not usually reported in trials of generic CBT for childhood anxiety disorder. Instead, outcome is indexed as the change in the average of the clinician severity ratings for the individual comorbid anxiety disorders and/or whether the child has experienced remittance from one or more of their comorbid disorders. Also, scores on continuous measures of trait anxiety, depression, and behavior problems are often assessed, but not so for measures of worry. Hudson et al. (2015) pooled data from several different studies of a generic CBT program for childhood anxiety disorders (Cool Kids) and found that a baseline diagnosis GAD predicted better outcomes than a diagnosis of social anxiety disorder (SAD). However, over 40% of the youth with an initial diagnosis of GAD still met criteria for this condition at follow-up (Hudson et al., 2015). This finding is consistent with those reported for the efficacy of generic programs for remission from ‘any anxiety disorder’, i.e. about 40-50% of treated youth retain one or more of the comorbid anxiety disorders they had at the start of treatment, usually some combination of GAD, SAD and separation anxiety disorder (James et al., 2015).

For adults, a larger number of clinical trials have explored versions of GAD-specific CBT. These treatment packages often include a number of interventions such as cognitive restructuring, exposure, relaxation training and bio-feedback (Cuijpers et al., 2014). Psychological treatments for GAD in adults have been tested in different treatment formats, such as group therapy (Stanley, Beck, & Glassco, 1996; Stanley et al., 2003), self-help interventions (Bowman, Scogin, Floyd, Patton, & Gist, 1997), and via the internet (Andersson et al., 2012; Dahlin et al., 2016; Robinson et al., 2010; Titov et al., 2009). Internet-delivered CBT for adult GAD has shown large effects compared to wait-list controls (Richards, Richardson, Timulak, & McElvaney, 2015). A meta-analysis evaluated the efficacy of CBT for adults with GAD and found that while effect-sizes were large, almost half of patients did not respond to treatment (Cuijpers et al., 2014).

2.4 A complementary approach to excessive worry

Given the central role of worry in GAD and a number of other mental health problems, and the moderate treatment effects of current interventions, there is room for further treatment development. A complementary approach to many of the broad-based CBT packages could be to develop streamlined treatments specifically targeting the worry-process, based on psychological theories for excessive worry. Such an approach has been suggested as a way of increasing our understanding of how psychological treatments work and improve their outreach and efficacy (Holmes et al., 2018; Kazdin, 2007; Kazdin, 2017). In recent years, a number of theories aiming to explain why some people (both adolescents and adults) tend to worry excessively, and what mechanisms are involved in the maintenance of excessive worry have been developed (e.g. Andersson et al., 2017; Behar, DiMarco, Hekler, Mohlman, & Staples, 2009; Newman & Llera, 2011).

This thesis mainly concerns itself with two theories of excessive worry; the intolerance of uncertainty model (Dugas, Gagnon, Ladouceur, & Freeston, 1998) and the metacognitive model of worry (Wells, 1995). At the time of planning this doctoral project, studies had shown promising results for IU-based treatments for adolescents (Léger, Ladouceur, Dugas, & Freeston, 2003; Payne, Bolton, & Perrin, 2011) and one more was underway (Perrin, Bevan, Payne, & Bolton, 2019). Therefore an IU-approach was chosen for work with adolescents. At the same time, studies of metacognitive therapy (MCT) had shown to be effective in reducing worry in adults, and more so than other treatments (van der Heiden, Muris, & van der Molen, 2012; Wells et al., 2010), why that approach was chosen for adult worriers. These theories and their empirical support are described below.

2.4.1 The intolerance of uncertainty model

The *intolerance of uncertainty model* (IUM; see Figure 1) was originally developed to explain excessive worry in individuals with GAD (Dugas et al., 1998). It is based on the proposition that these individuals have an intolerance of uncertainty (IU), meaning that they find uncertain situations stressful and difficult to tolerate, and that they react to uncertainty with excessive worry, however unlikely the negative outcome really is.

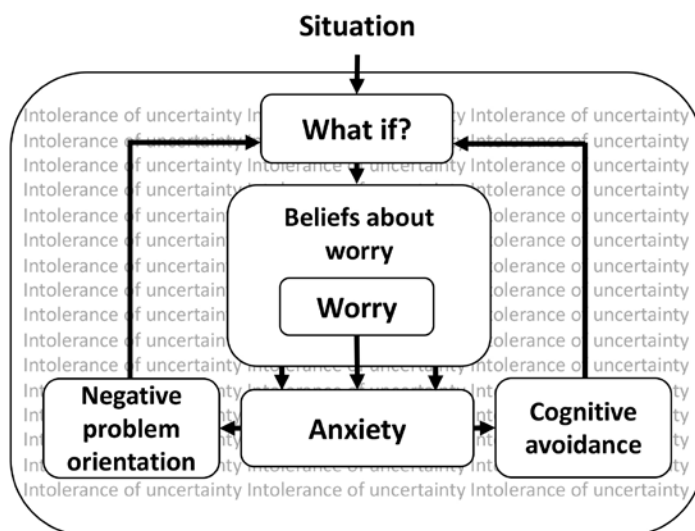


Figure 1. The intolerance of uncertainty model. Adapted from “Generalized anxiety disorder: A preliminary test of a conceptual model”, by Dugas, Gagnon, Ladouceur & Freeston, 1998, *Behaviour Research and Therapy*, 36(2), page 216. Copyright (1998) by Elsevier. Adapted with permission.

The IU model also includes other processes suggested to contribute to excessive worry. According to the model, individuals with GAD hold positive beliefs about worry, meaning they believe that worrying will help them prevent or prepare for negative events. The worry also leads to increased negative affect, which in turn leads to a negative view on problems and one’s ability to solve them (i.e. negative problem orientation), and a tendency to try to suppress or avoid thoughts (i.e. cognitive avoidance), further reinforcing the worry and anxiety.

While IU is not postulated to be a sole causal factor of worry and anxiety, it is suggested to be related to the development of both excessive worry and other mental health problems (Shihata, McEvoy, Mullan, & Carleton, 2016). Meta-analyses have shown strong positive correlations between IU and worry in both children,

adolescents and adults (Gentes & Ruscio, 2011; Kertz & Woodruff-Borden, 2012; Osmanağaoğlu, Creswell, & Dodd, 2018). According to some earlier studies, IU and the other constructs within the IU-model have unique relationships with worry in GAD (Buhr & Dugas, 2006; Dugas et al., 1998), but subsequent research has shown that IU is also strongly related to other psychiatric symptoms and disorders (Carleton, 2012, 2016; Osmanağaoğlu et al., 2018). A number of clinical and experimental studies have explored if IU causally effects a range of mental health problems (for a review, see Rosser, 2019) with findings suggesting that change in IU mediate change in worry in the treatment of adult GAD. Additionally, levels of worry were higher when IU was increased through experimental manipulation (Bomyea et al., 2015; Ladouceur, Gosselin, & Dugas, 2000).

A CBT protocol for adults with GAD is based on the IUM and over the last two decades, this protocol has been evaluated in several studies. The treatment has been shown to be superior to waitlist, (Ladouceur et al., 2000) and equal to or more effective than other active treatments (Dugas et al., 2010; Gosselin, Ladouceur, Morin, Dugas, & Baillargeon, 2006). One study compared IU-CBT to MCT (described below), and found both to be effective, but MCT superior in reducing worry (van der Heiden et al., 2012). IU-CBT has also been delivered in group formats with large effect sizes compared to WL (Dugas et al., 2003). One study compared IU-CBT to MCT (described below), and found both to be effective, but MCT superior in reducing worry (van der Heiden et al., 2012).

As mentioned above, treatments for youth with GAD and/or excessive worry have mainly been generic, targeting a number of symptoms and disorders simultaneously. However, a handful of treatments based on the IU-model have been developed and evaluated for children and/or adolescents. One pilot study evaluated IU-CBT for seven adolescents with GAD, aged 16-18 (Léger et al., 2003). After treatment, one participant had dropped out while three showed clinically significant change. The remaining three were minimally or moderately improved. Based on these results and the authors' suggestions for enhancing the treatment manual, Payne and colleagues replicated the results in a pilot-trial with 16 participants, aged 7-17 years old (Payne et al., 2011). At post-treatment, 81% no longer met diagnostic criteria for GAD and 59% no longer had any comorbid diagnosis. In a randomized pilot trial (n=40), the treatment based on the IU model was compared to waitlist, and large between-group differences for remission and secondary outcomes (e.g. worry) in favor of the IU treatment were found, with 80% no longer meeting GAD criteria post-treatment compared to 0% in the WL-group (Perrin et al., 2019).

2.4.2 The metacognitive model

In the *metacognitive model* of worry (MCM; Wells, 1995, see Figure 2), beliefs about worry (as being dangerous, uncontrollable and/or helpful) are of particular importance to the maintenance of the symptom. The MCM divides the worry into two types; type 1 worries which are general worries about themes such as external situations or physical symptoms (e.g. “what if I make a mistake at work” or “what if I get sick”), and type 2 worry which is worry about the worrying itself, (e.g., “I won’t be able to focus at work if I don’t stop worrying,” or “I will get sick from all this worrying”). According to the MCM, type 2 worry is activated because the individual holds negative beliefs about the worry (i.e., the worry is uncontrollable or dangerous).

According to the MCM, type 2 worry is associated with ineffective strategies such as reassurance seeking, checking behaviors, thought suppression, distraction, and avoidance that aim to avoid worry. The strategies are ineffective in reducing worry and may decrease learning opportunities when individuals do not learn that they can handle both worrisome situations and their own worries, and ultimately lead to reinforced beliefs about worry being uncontrollable and/or dangerous. However, individuals also often hold positive beliefs about the worry (e.g. “worry helps me prepare for negative events”) that also drive the worrying.

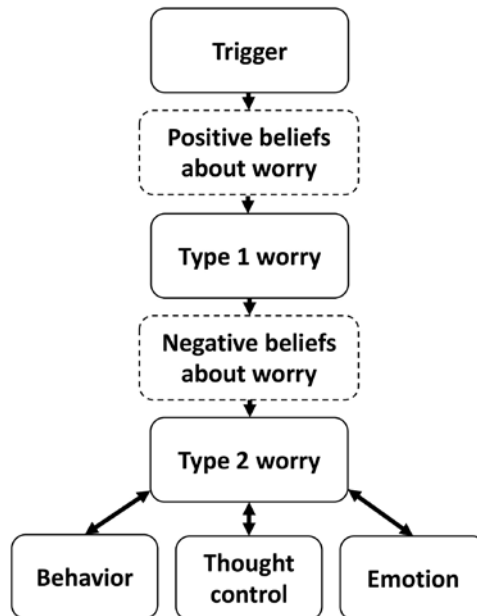


Figure 2. The metacognitive model. Adapted from *Cognitive therapy of anxiety disorders: A practice manual and conceptual guide* (p. 204) by A. Wells, 1997. Copyright (1997) by John Wiley & Sons Inc. Adapted with permission.

Cross-sectional and longitudinal studies of the constructs underlying the metacognitive model have found associations between metacognitive beliefs and excessive worry (Behar et al., 2009). Negative beliefs about worry have been shown to predict worry severity following experimentally induced worry, everyday worry, and anxiety over time (Fergus & Wheless, 2018; Ryum et al., 2017; Thielsch, Andor, & Ehring, 2015). Change in metacognitive beliefs has also been found to precede change in symptoms of both anxiety and depression in a clinical study of mixed anxiety and depression (Newby, Williams, & Andrews, 2014). Some results indicate that these phenomena are specific for individuals with GAD while others have pointed to similar levels of positive and negative beliefs about worry in other psychiatric conditions, e.g. obsessive compulsive disorder and panic disorder (Cartwright-Hatton & Wells, 1997; Wells & Carter, 2001).

Metacognitive therapy (MCT) is based on the MCM and has been evaluated for a number of mental health conditions, among them GAD (Normann & Morina, 2018). The treatment has shown to effectively reduce worry in adults with GAD compared to wait-list and active comparators (Nordahl et al., 2018; van der Heiden et al., 2012; Wells et al., 2010). One pilot study has also evaluated the efficacy of group-based MCT for children aged 7-13 with GAD, with large within group effect-sizes on worry (Esbjørn, Normann, Christiansen, & Reinholdt-Dunne, 2018).

2.5 Conclusions

In conclusion of this brief background, worry is common in the general population and excessive worry is often related to mental health problems. Standard pharmacological and psychological treatments of excessive worry are moderately effective. In order to improve outcomes, we need to further our understanding of the processes involved in excessive worry, and develop effective and scalable treatments.

3 AIMS OF THE THESIS

The overall aim of this thesis was to develop and evaluate streamlined psychological interventions specifically targeting hypothesized causal mechanisms relevant in the maintenance of excessive worry. In this thesis, I have focused on two theoretical approaches; the IUM in the treatment for adolescents with excessive worry, and the MCM in the treatment for adults with excessive worry.

3.1 Study I: Face-to-face pilot study (adolescents)

The aim of study I was to develop a streamlined protocol for an IU-focused psychological treatment for adolescents with excessive worry (IU-CBT; described below) and to evaluate its feasibility and potential efficacy.

3.2 Study II: Online pilot study (adolescents)

The aim of study II was to expand the treatment protocol from study I to a scalable, online format and to evaluate its feasibility and preliminary efficacy. Furthermore, we aimed to evaluate whether changes in self-rated worry occurred only after the introduction of the intervention, thus indicating a causal effect of the intervention.

3.3 Study III: Qualitative interviews (about study II)

The aim of study III was to explore the experiences of the adolescents and parents who had participated in study II. More specifically, we wanted to explore how they experienced the program itself (e.g., the treatment content and working independently with exposure) and the collaborations during treatment (i.e., between the adolescents and the parents, as well as with their therapists).

3.4 Study IV: Randomized trial with mediation analysis (adults)

The aims of study IV were to evaluate the clinical efficacy of internet-delivered metacognitive therapy (I-MCT; described below) for adult excessive worriers, and to explore if change in negative beliefs about worry mediated change in excessive worry, and if such mediation depended on the baseline severity of these beliefs.

4 EMPIRICAL STUDIES

4.1 The treatments

This thesis covers the development and evaluation of two treatment protocols. The first targets excessive worry in adolescents aged 13-17 years old (studies I-III). The second treatment is designed for adults with excessive worry (study IV). The treatments are described below.

4.1.1 Intolerance of uncertainty treatment for adolescents


For adolescents, we developed a treatment based on the IU theory (Dugas et al., 1998), IU-CBT. The treatment was developed in two stages and was evaluated as a face-to-face treatment in study I, and as an online intervention in study II. IU-CBT was directed towards both the adolescent suffering from excessive worry and (at least) one of the adolescent's parents or legal guardians (hereinafter referred to as parents). The treatment was intended to increase the adolescent's tolerance to uncertainty and change their behavioral approach towards uncertainty. That means, helping adolescents see that their usual ways of handling uncertainty through control and/or avoidance was ineffective and reinforced worry, and then encouraged them to expose themselves to uncertain thoughts and situations. The parallel parent program had three main aims: to provide psychoeducation about worry, to change parental behaviors related to worry when needed, and to encourage the parent to support the adolescent through treatment. Interventions specifically targeting processes other than IU, suggested to be of importance to the maintenance of excessive worry (such as negative problem orientation and positive beliefs about worry; Dugas et al., 1998) were not included in IU-CBT. Cognitive avoidance was targeted in treatment, but exposure to thoughts was framed as a way of increasing tolerance to uncertainty rather than as a way of achieving habituation to thoughts related to uncertainty.

In study I, the intervention was provided to the adolescents in-person by a clinical psychologist. The adolescents received up to 12 individual sessions during a 12 week treatment period. During the treatment, the parents worked with an online-delivered parent program consisting of five modules (a new module was opened every other week during the first nine weeks of the treatment). During the treatment period, the parents had contact with a therapist (the same therapist who treated the adolescent) via an encrypted digital platform for support, help with problem solving and clarifications when needed.

For study II, the treatment protocol from study I was transformed into an online version where both the adolescents and the parents received all of the treatment material in ten modules via the internet platform. The intervention can be described

as an online book, with each module similar to a chapter, containing a number of pages with short texts, illustrations, video-clips, and instructions to homework assignments. The modules also included worksheets that the participants filled in and the therapists reviewed and commented on. Both the adolescents and the parents were encouraged to work with one treatment module each week, and after completing one module, they get access to the next. Both the adolescents and the parents had asynchronous (email like) contact with a therapist (the same for the adolescent and the parent) via the internet-platform.


STEG 3 AV 2

FILM 

What if-thoughts

Worry consists of several different pieces. We will start by looking at the first: **"What if?"-thoughts**. On the next couple of pages you will learn all about these thoughts, since they are so important for your treatment.

Start by looking at this film clip about how "What if"-thoughts can trigger the worry cycle.



1:33 / 1:49

Figure 3. Screenshot of a page from module 1 in IU-CBT delivered via the internet (i.e. “BIP Worry”) in study II.

BIP BIP Worry

STEG 2 AV 1

This week's exercise: keep letting go of control

Your first exercise this week is to keep letting go of control behaviors (if you think this would be useful for you). If you are still using control behaviors that aren't helpful for you in the long run, choose one and practice letting go of it this week.

Do you need to let go of control behaviors? If yes, which one will you let go?

Skriv här

How often do you use this control behavior today?

Skriv här

How do you think you are affected by this control behavior?

Skriv här

What can you do instead of your control behavior?

Skriv här

What do you think will happen when you drop the control behavior?

Skriv här

Figure 4. Screenshot of a worksheet from module 7 in IU-CBT delivered via the internet (i.e. “BIP Worry”) in study II. “Skriv här” is Swedish for “Type here”.

4.1.2 Metacognitive treatment for adults

For adults, we developed an internet-delivered metacognitive treatment (I-MCT). The treatment protocol was based on a book chapter about metacognitive therapy for GAD (Wells, 2011). The main aim of the intervention was to change patients’ beliefs about worry (in particular negative beliefs such as worry being dangerous or uncontrollable) in order to reduce excessive worry. I-MCT included a number of exercises and experiments that the participant planned together with a therapist and then conducted and evaluated. Furthermore, the participant practiced attention exercises supposed to help thwart their metacognitive beliefs. Positive beliefs and unhelpful coping behaviors related to worry were also targeted in I-MCT.

The participants worked with eight treatment modules delivered via a secure treatment platform during a ten week period. After having completed one module, they got access to the next. The modules mainly consisted of text material presented in PDF files (about 60 pages) and audio files with instructions to practical exercises. The participants had asynchronous contact with a therapist via the treatment platform, and the therapists normally responded within 24 hours on week days.

4.2 The studies

4.2.1 Study I: Intolerance of uncertainty-focused treatment for adolescents with excessive worry – a pilot feasibility study

4.2.1.1 Methods

Study I was a pilot feasibility study that included 12 adolescents (13-17 years old) with excessive worry. The main inclusion criteria was scoring >21 points on the Penn State Worry Questionnaire for Children (PSWQ-C; Chorpita et al., 1997) and participants were included irrespective of psychiatric diagnosis. Each participant had at least one parent or legal guardian co-participate with them in the study. The adolescents were assessed by a psychologist before and after 12 weeks of IU-CBT and at a three-month follow-up, and they completed self-assessments of worry (the PSWQ-C) and related cognitive processes weekly during the treatment. Parents also reported on the adolescents' levels of worry, anxiety and depression. Patient satisfaction, treatment credibility, adverse events related to the treatment, and parental accommodation to anxiety were also assessed. We calculated within-group effects on worry and secondary measures using ANOVAs with post-hoc analyzes, and calculated clinically significant change and reliable change indexes (Jacobson & Truax, 1991) to assess the number of participants who improved after treatment.

4.2.1.2 Main results

All participants remained in the study, and no serious adverse events were reported. The adolescents attended 9-12 individual sessions ($M = 10.5$) and parents completed 4-5 internet-delivered modules ($M = 4.6$). Most families described high treatment satisfaction and credibility. Of the 12 adolescents, nine achieved a reliable change in self-rated worry at post-treatment and seven did so at follow-up. On a group level, the results showed significant changes in self-rated worry with a large effect size ($d = 2.0$; $p < .001$). Self-reported anxiety and impaired functioning were also significantly reduced after treatment, as were parent-reported worry and impaired functioning. Parents' accommodation to their adolescents' worry was also reduced after treatment. These effects were all maintained at follow-up.

4.2.2 Study II: Online cognitive behavior therapy for adolescents with excessive worry – a multiple baseline design feasibility study

4.2.2.1 Methods

Study II was a multiple baseline design feasibility evaluation of an online version of IU-CBT (“BIP Worry”). It included 13 adolescents (13-17 years old) and at least one of their parents. Before commencing the treatment, the adolescents were randomized to different baseline assessment periods; two, six or ten weeks long. During the baseline periods, the adolescents completed the Brief PSWQ (Topper, Emmelkamp, Watkins, & Ehring, 2014) as a self-assessment of worry every week. The point of using a baseline phase was to insert an element of control over time, maturation and spontaneous recovery in this small feasibility study. The adolescents were assessed by a psychologist before the baseline-phase, after treatment and at one and three-month follow-ups. Pre-baseline, pre- and post-treatment, and at both follow-ups, adolescents also completed the full version of the PSWQ-C (Chorpita et al., 1997). In addition to measuring symptoms of worry, anxiety and depression, we assessed impaired functioning, any negative effects of treatment, treatment credibility and client satisfaction. Multi-level linear mixed models were used to estimate mean effects and we used visual inspection to evaluate how the introduction of BIP Worry affected individual levels of worry.

4.2.2.2 Main results

Of the thirteen adolescents initially included, one dropped out during the first week of treatment and the rest remained in the study. Both the adolescents and their parents who followed through with treatment completed on average 9.8 of the ten treatment modules and client satisfaction and treatment credibility were high. We could not show a casual effect of the intervention through the multiple baseline design but on a group level, we found medium to large reductions in self-rated worry (on the PSWQ-C), anxiety, depressive symptoms, and impaired functioning at post-treatment ($d = 0.69-1.38$; $p = .001$). Similar changes for worry, anxiety and depression were reported by the parents ($d = 0.49-1.76$; $p = .001$) and the changes were maintained at one- and three-month follow-ups. Therapist time averaged 21 minutes per family (adolescent and parent) and week.

4.2.3 Study III: Experiences of online exposure-based treatment with parental support for teenagers with excessive worry.

4.2.3.1 Methods

Study III was a qualitative exploration of adolescents' and parents' experiences of the online version of IU-CBT ("BIP Worry"). We invited all adolescents and parents from study II to participate in qualitative interviews. Of these, eight adolescents and nine parents accepted. Each participant (adolescents and parents alike) received one cinema ticket as compensation for their participation. The interviews were based on an interview schedule and were conducted by a clinical psychologist who had not been involved in study II. All interviews were audio recorded and transcribed verbatim by the interviewer. Based on the transcriptions, we used thematic analysis (Braun & Clarke, 2006) to code the data and categorize the codes into main themes and subthemes.

4.2.3.2 Main results

The data was categorized into two main themes ("Seeing the worry in a new light" and "Freedom with responsibility") which both were divided into three subthemes. The treatment content helped many of the adolescents and parents understand the worrying better. Exposure to uncertainty was experienced as worthwhile even though it was challenging and both adolescents and parents described the parental involvement in treatment as important for the adolescents' treatment adherence. For some families, the parental involvement also had a positive impact on their relationship. Overall, the findings suggested that an online treatment for adolescents with excessive worry can be acceptable for both the adolescents and their parents, even though the online format posed challenges to many and several described having appreciated more therapist support.

4.2.4 Study IV: Are negative beliefs about worry driving excessive worry? A randomized controlled trial of metacognitive therapy with mediation analysis

4.2.4.1 Methods

Study IV was a randomized controlled trial with mediation analysis. We included 108 excessive worriers aged ≥ 18 years who were randomized to either I-MCT or a waitlist control condition (WL). Before inclusion in the study, inclusion/exclusion criteria and diagnostic status were assessed via telephone by a psychology master student under supervision. During the intervention, all contact between the participants and the therapists was via the internet. The participants reported level of worry, negative beliefs about worry and depressive symptoms weekly during I-MCT and WL, at post-treatment and at six and twelve months follow-up. Depression, cognitive avoidance, and emotional contrast avoidance were also assessed pre- and post-treatment, and at follow-up. Occurrences of adverse events during treatment were reported at post-treatment. We used univariate and multivariate latent growth curve models to assess the effects of treatment and the mediators, and participants were assessed as responders at post-treatment if their levels of worry were reduced by at least 9 points on the PSWQ (Meyer, Miller, Metzger, & Borkovec, 1990).

4.2.4.2 Main results

The findings supported our hypothesis that changes in negative beliefs about worry would mediate change in worry post-treatment ($ab = -0.908$, 95% CI [-1.537, -0.458]), and significantly more so than changes in depressive symptoms ($p = .003$). The effect of changes in negative beliefs on worry did not depend on the severity of these beliefs at baseline, meaning that participants with higher levels of negative beliefs about worry did not have a better treatment outcome than those with lower. The analyses showed that participants in the I-MCT group had a significantly larger reduction in worry compared to the WL group ($d = 1.64$), and there was a higher responder rate (74% vs. 7%) in the I-MCT group. The attrition rate was low (3.7% at post-treatment), as were number of reported adverse events.

4.3 Ethical considerations

Ethical considerations must influence researchers on every level of the scientific process. Participation in research should generally not expose participants to greater risk of harm than normal life would, and all research should be considered from the standpoint of the research participants (The British Psychological Society, 2014). The studies included in this thesis were all approved by the regional ethics committee in Stockholm, Sweden, and further steps were taken in order to ensure ethical scientific processes throughout the studies.

Studies I-III involved adolescents (and their parents). Research questions regarding young people are important, as needs of children and adolescents may differ from those of adults (Modi et al., 2014). However, children must never be included in research against their will due to pressure from a parent or other person in a position of power. When recruiting participants to studies I-III, we discussed the importance of the adolescent's consent with each family, and underlined that they could decline participation even if the parent was positive to inclusion in the trial. As previous clinical studies for adolescents with excessive worry are scarce, we did not want to put more participants than necessary through treatment if it showed to be unfeasible for families, or appeared to be ineffective in reducing worry. Therefore, we conducted pilot feasibility trials before initiating any larger trials of IU-CBT.

Furthermore, we conducted a qualitative exploration, (i.e. study III) in order to improve our understanding of the adolescents' perspectives on IU-CBT. Importantly, some ethical aspects specific to qualitative research should be considered. Quotes from the in-depth interviews facilitate understanding of individual experiences of treatment, but because they are rich and descriptive in nature, they may pose a threat to the confidentiality of the informants (Haverkamp, 2005). In order to minimize that risk, we chose the quotes carefully and shortened them when possible so that they would not convey any more information than necessary. Furthermore, participants could potentially feel coerced to participate in study III as they had been given a free (and for some quite effective) treatment by the same people who later asked them to engage in the interviews. While we cannot rule out that this happened, we attempted to decrease the risk of anyone feeling forced to participate by having an independent psychologist being in contact with the informants in study III, rather than someone who had been involved in study II.

Thorough assessments prior to inclusion in the clinical trials were intended to increase safety and minimize harm. It ensured that participants with health care needs not addressed in our trials (e.g. severe depression, eating disorders or suicidality) were referred to other health care providers. We also tracked potential adverse events, and symptoms such as depression and suicidality for all participants in studies I, II and IV.

Studies I, II, and IV all included clinical research via the internet. Participants' personal information should always be treated with confidentiality, but research conducted via the internet places a particular importance on information security (The British Psychological Society, 2017). To ensure the confidentiality of all data, we used double authentication procedures on the internet treatment platforms. In study IV, we did not meet participants face-to-face in initial interviews prior to inclusion as we did in studies I and II, and thus could not detect any non-verbal hesitation or prompt further questions. To ensure valid consent, information about the study was therefore also given by an interviewer during the pre-treatment telephone assessment, and participants were invited to ask questions.

5 DISCUSSION

The overall aim of this thesis was to develop and evaluate streamlined psychological interventions specifically targeting hypothesized causal mechanisms relevant to the maintenance of excessive worry, drawn from the intolerance of uncertainty model (IUM) as applied to adolescents, or from the metacognitive model (MCM) as applied to adults.

5.1 Summary of the findings

Before starting study I, we were not sure that the adolescents and their parents would appreciate the treatment rationale and engage with a treatment focusing narrowly on exposure to uncertainty. Previous research indicated that children and adolescents with GAD could be engaged in face-to-face treatment where exposure to uncertainty was one of several interventions designed to target the four processes in the IU (Dugas et al., 1998) either alone (Leger et al., 2003; Payne et al., 2011; and later Perrin et al., 2019) or alongside interventions targeting perfectionism (Holmes et al., 2014). Clinically, it made sense to hone in on IU, which numerous studies have found to be very strongly correlated with the severity of worry in youth (for a review, see: Osmanağaoğlu et al., 2018). The results from studies I and II suggested that the participants and their parents could engage with both the treatment rationale and the exposure to uncertainty. Furthermore, IU-CBT appeared to be effective in reducing worry, both when delivered in-person and via the internet, with symptoms of anxiety and depression also being significantly reduced at post-treatment, and with uncontrolled effect sizes comparable to previous trials evaluating the efficacy of the full IU model-based treatment with youth (Léger et al., 2003; Payne et al., 2011; Perrin et al., 2019).

In addition to the rationale and primary treatment component, we were uncertain whether the treatment would be acceptable when delivered in an online format. Previous qualitative research has found internet-delivered treatments for youth to be acceptable (for a review, see: McCashin, Coyle, & O'Reilly, 2019), but the evaluated treatments tend to involve multiple components or interventions. If the adolescent or parent could not engage with the IU focus, and there was not many other interventions to work with in the internet-delivered treatment, would they drop-out or be dissatisfied? Informants in study III described the online-treatment as demanding but acceptable, they understood the rationale and felt that it was mostly relevant to them and their experiences. They did not complain about the treatment lacking interventions that were more relevant to their experience of worry, on the contrary, some even found certain parts of the treatment redundant despite our efforts to streamline it. Additionally, we found that many (both adolescents and parents), appreciated the parental involvement, which they thought helped facilitate treatment adherence – specifically facing up to situations involving uncertainty.

Studies I and II did not include control groups, which limits causal inferences about IU-CBT. Instead, we used a multiple baseline design to control for maturation and natural variation in worry in study II, but the findings did not show a causal effect of the intervention. In hindsight, I believe that this could be due (at least in part) to the outcome measure (the Brief PSWQ; Topper et al., 2014). We used it because it only contains five items, and we did not want to burden the participants more than necessary during the baseline and intervention phases. However, the Brief PSWQ is a screening measure and may be insensitive to changes in worry during treatment. Had we used the PSWQ-C (Chorpita et al., 1997), which has been shown to be sensitive to the effects of treatment (e.g., Perrin et al., 2019), during the baseline- and treatment phases, a different set of findings may have emerged in study II. The results of studies I and II are by nature preliminary and need to be replicated, preferably using the PSWQ-C with larger samples and under randomized controlled conditions.

The findings from the mediation analysis in study IV supported the hypothesis that reductions in worry during I-MCT with excessive worriers were at least partly mediated by a reduction in negative beliefs about worry, and more so than by reductions in depressive symptoms as a comparator mediator. Interestingly, the hypothesis that participants with higher levels versus lower levels of negative beliefs about worry would benefit more from I-MCT was not supported. This could be due to restriction of range, i.e. that there were very few participants who did not hold beliefs about worries being dangerous or uncontrollable. However, it might also be true that individuals who do not hold such beliefs are not as bothered by and do not seek treatment for excessive worry, at least via the internet.

The findings from study IV suggest that changes in negative beliefs about worry may be an important change mechanism in I-MCT with excessive worriers. However, mediator effects as tested in study IV are correlational in nature, and while they can point to possible change mechanisms, additional design features and assumptions must be met before inferences about causality can be drawn in clinical trials (Kazdin, 2007). N-of-1 trials with frequent and repeated (daily) measurement of the putative mediators and outcome variable could help to more clearly establish order effects, i.e. that changes in negative beliefs about worry precede changes in worry severity, or with reversals (i.e., reinstatement of negative beliefs about worry), to help establish causality. Future studies could also randomize participants to three conditions, with each providing different dosages of the interventions designed to target the proposed change mechanism (i.e. negative beliefs about worry). If outcomes varied in the expected direction across the three conditions, this would suggest a dose-response relationship, lending further support for the causal impact of these beliefs on excessive worry.

While this is only one trial, the results of study IV suggest that I-MCT was feasible, acceptable, and effective for adults with excessive worry who were recruited online. Importantly, the therapy was delivered with the aid of therapists who were masters-level students, all novices to MCT, and with no financial- or intellectual conflicts of interests (i.e. low level of allegiance effects). Participants completed a relatively high proportion of the treatment modules (mean number of completed modules was 5.6 out of 8) and there were few drop-outs. Both worry and symptoms of anxiety and depression were significantly reduced at post-treatment compared to the participants randomized to the wait-list. The controlled effect sizes were comparable or close to those from previous studies of MCT delivered in the face-to-face format with adults suffering from excessive worry (Nordahl et al., 2018; van der Heiden et al., 2012; Wells et al., 2010). That the treatment was feasible, acceptable, and effective when delivered in an internet format with the aid of MCT-inexperienced therapists, is an important finding given the emphasis placed on the need for advanced training when delivering MCT (Wells, 2011). Again, further studies are needed before firm conclusions can be drawn about the acceptability and efficacy of I-MCT.

5.2 Are the findings important?

Though the effect sizes in the outcome trials in this thesis were mostly in the moderate to large range, the response and remission rates were not significantly greater than previously found using traditional, multi-component, cognitive behavioral interventions for worry. So, in what way are the findings important?

First, the streamlined approach used in study I, II and IV offers what could be termed relatively ‘high-resolution images’ of the patients and their specific trajectories through treatment. That is, instead of providing a large number of different interventions, and hoping that patients would have the time and energy to learn and use them all, we streamlined the treatment to focus on a few major themes, and then evaluated the therapeutic effects of that streamlined treatment. This approach can help guide clinicians and researchers alike to consider what are the necessary or therapeutically active components in standard CBT approaches to excessive worry.

Secondly, the findings in this thesis show that streamlined interventions can be feasible for both participants and their families, and be employed in a time-efficient way, meaning that they can be scalable and delivered to a broader population via the internet. This has been suggested as an important step in future treatment development and improving access to evidence-based treatments (Holmes et al., 2018).

Thirdly, study I, II and IV may help to fill important knowledge gaps in the scientific literature about what factors may trigger and help to maintain excessive worry

in both adolescents and adults. Specifically, these studies with the more narrow focus on a few putative mediators allow us to estimate the relative contributions of individual mediators to worry change in treatment. This can be contrasted to evaluations of standard CBT packages that in addition to providing a model of change (as our treatments do), include multiple interventions designed to reduce arousal levels generally and during worry, to modify appraisals about worry, to improve problem-solving skills and confidence, worry exposures, and imagery techniques. While such treatments have proven to be effective, it remains unclear which interventions are crucial to produce change. Thus, although the clinical effects in the studies included in this thesis are not clearly superior to previous findings, they can contribute to both clinicians and scientists in further understanding excessive worry.

5.3 How streamlined are the treatments?

The aim of this doctoral project was to develop and evaluate streamlined psychological interventions, but how streamlined were the treatments?

Consistent with the IU model of excessive worry and GAD (Dugas et al., 1998), IU-CBT included a modified form of problem solving in addition to exposure to uncertainty. However, it is important to stress that problem solving in IU-CBT was used to elicit specific worries about practical problems, and then, by breaking down the problem into smaller pieces, helping the adolescent to identify the role that uncertainty played in triggering worries, which in turn led problems to be experienced as bigger and less solvable. For instance, when a patient in study I identified worrying about her future math grade, she identified a number of problems related to this worry (e.g. not knowing what her math homework was, not being able to concentrate on math in a crowded classroom). Once these problems were identified, solving them was encouraged as an exposure to uncertainty in itself (as she then started worrying about how her teacher would perceive her when she raised questions about the problems). Thus, while IU-CBT included ‘problem solving’ exercises, their aim (like the rest of the treatment) was to increase awareness about the role of uncertainty in bouts of excessive worry, and that ultimately, it was planned confrontations with uncertainty which would lead to a reduction in worry – not increased problem-solving confidence or skill.

With respect to I-MCT, the treatment included interventions that targeted other constructs than negative beliefs about worry, including attention training and positive beliefs about worry. However, attention training as used in I-MCT was intended to help participants become more aware of their beliefs about the extent to which their own worries were dangerous and uncontrollable, not as a strategy to divert themselves from worrying or to reduce the intensity of worries when they occurred.

Still, it is possible that attention training, separate from any change in appraisals about worry, has by itself a significant impact on the frequency and content of worry, as has been suggested in the literature (Hayes, Hirsch, & Mathews, 2008; Hirsch & Mathews, 2012).

With respect to positive beliefs about worry, it has been suggested that these may be less common and less influential than negative beliefs about worry (Penney, Mazmanian, & Rudanycz, 2013; Ruscio & Borkovec, 2004). Thus, it is arguable whether I-MCT needed to include standard cognitive interventions to modify positive beliefs about worry and/or whether changes in these beliefs also mediated outcomes in study IV. As previously suggested, one recommendation for future trials is therefore to randomize participants to three conditions, and again provide different levels of the intervention targeting the proposed mechanism of change (i.e. either negative or positive beliefs about worry) to each condition to explore the causal impact of positive beliefs about worry. Dismantling trials could also provide important knowledge about the need for interventions targeting positive beliefs about worry in treatment (Kazdin, 2007).

5.4 How should we involve the context?

I personally believe that an important aim in the development of more effective psychotherapies is to streamline (i.e., reduce to absolute minimum necessary) the number of interventions included in the treatment and at the same to define the limits under which these therapies can be effectively delivered. I wanted to take a step in that direction with IU-CBT for adolescents, by developing a treatment that could be delivered online, and included a limited number of interventions aimed at the adolescent, with parallel interventions (modules) for parents. Meta-analyses have not been able to show any incremental effects on anxiety (benefits do accrue in terms of comorbid behavior problems) of parental involvement in the treatment of pediatric anxiety (Breinholst, Esbjørn, Reinholdt-Dunne, & Stallard, 2012; Thulin, Svirsky, Serlachius, Andersson, & Öst, 2014). However, few studies are actually designed to test whether parental involvement adds to the treatment effect (Thulin et al., 2014). Research has also found that accommodation to anxiety symptoms is common in families of children and adolescents with anxiety disorders (Benito et al., 2015; Lebowitz et al., 2013; Thompson-Hollands, Kerns, Pincus, & Comer, 2014), and that it may negatively impact the course of illness and treatment outcomes (Norman, Silverman, & Lebowitz, 2015). Parental accommodation was significantly reduced after treatment with IU-CBT, and in study III, both adolescents and parents highlighted the importance of parental involvement for the adolescents' adherence to treatment. Nevertheless, further studies are needed where internet-based treatments with and without parental involvement are tested, and attempts to identify child- and parent-level moderators that help to explain which treatment approach works best for which patient and parent.

Likewise, research is needed to determine whether treatments like IU-CBT can be feasibly and effectively delivered in primary and specialist care clinics where the organizational structures are built around the delivery of face-to-face treatments. A previous implementation study of internet-delivered CBT for pediatric anxiety within a specialist care clinic in rural Sweden (Jolstedt, Ljótsson, et al., 2018) identified important challenges even though clinicians were positive to the online format. Subsequently, implementation with training and supervision of clinicians needs further investigation. In study III, several adolescents and parents described having experienced a need for more therapist support. Previous studies with adults have shown superior treatment outcomes for therapist-guided compared to unguided internet-delivered treatments (Baumeister, Reichler, Munzinger, & Lin, 2014) but future studies need to further evaluate how the frequency and method of support can be tailored to individual needs, and if that can improve clinical outcomes.

Finally, new research has suggested a streamlined focus on IU as a way of improving treatment outcomes for adults with GAD (Hebert & Dugas, 2019), and that group-MCT can produce effects on worry for adolescents with anxiety and depression similar to those reported in studies I and II in this thesis (Thorslund, McEvoy, & Anderson, 2020). Future studies could build on this new research and the results presented in this thesis and develop streamlined, internet-delivered IU-CBT for adults as well as internet-delivered MCT for adolescents.

6 CONCLUSIONS

Focusing on IU for adolescents with excessive worry is feasible and potentially effective, and both adolescents and their parents found the treatment to be both challenging and valuable. I-MCT appears to be a feasible, acceptable, and effective treatment when delivered in an online format to adults with excessive worry, with changes in negative beliefs about worry mediating changes in worry outcomes (and more so than changes in depression). Future research should aim to replicate the current findings under randomized controlled conditions with adolescents, and with an active control for adults. We also need studies across this age range that include tests of moderation, mediation, and moderated mediation, to better establish causal mechanisms in the treatments and which treatments work best for which patients. If we better understand how treatments work and for whom, even more streamlined, scalable and effective treatments for adolescents and adults can be developed.

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8 REFERENCES

- American Psychiatric Association. (1980). *Diagnostic and statistical manual of mental disorders* (3rd ed.). Washington, DC: Author.
- American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.
- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev). Washinton DC: Author
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washinton DC: Author.
- Andersson, E., Hedman, E., Wadström, O., Boberg, J., Andersson, E. Y., Axelsson, E., . . . Ljótsson, B. (2017). Internet-based extinction therapy for worry: A randomized controlled trial. *Behavior Therapy, 48*(3), 391-402.
- Andersson, G., Paxling, B., Roch-Norlund, P., Östman, G., Norgren, A., Almlöv, J., . . . Cuijpers, P. (2012). Internet-based psychodynamic versus cognitive behavioral guided self-help for generalized anxiety disorder: a randomized controlled trial. *Psychotherapy and Psychosomatics, 81*(6), 344-355.
- Batelaan, N. M., ten Have, M., van Balkom, A. J., Tuithof, M., & de Graaf, R. (2014). Anxiety disorders and onset of cardiovascular disease: the differential impact of panic, phobias and worry. *Journal of Anxiety Disorders, 28*(2), 252-258.
- Baumeister, H., Reichler, L., Munzinger, M., & Lin, J. (2014). The impact of guidance on Internet-based mental health interventions—A systematic review. *Internet Interventions, 1*(4), 205-215.
- Behar, E., DiMarco, I. D., Hekler, E. B., Mohlman, J., & Staples, A. M. (2009). Current theoretical models of generalized anxiety disorder (GAD): Conceptual review and treatment implications. *Journal of Anxiety Disorders, 23*(8), 1011-1023.
- Bengtson, M. B., Aamodt, G., Vatn, M. H., & Harris, J. R. (2015). Co-occurrence of IBS and symptoms of anxiety or depression, among Norwegian twins, is influenced by both heredity and intrauterine growth. *BMC Gastroenterology, 15*, 9
- Benito, K. G., Caporino, N. E., Frank, H. E., Ramanujam, K., Garcia, A., Freeman, J., . . . Storch, E. A. (2015). Development of the pediatric accommodation scale: Reliability and validity of clinician- and parent-report measures. *Journal of Anxiety Disorders, 29*, 14-24.
- Boden, J., Fergusson, D., & Horwood, L. J., (2007). Anxiety disorders and suicidal behaviours in adolescence and young adulthood: Findings from a longitudinal study. *Psychological Medicine, 37*(3), 431-440.
- Bomyea, J., Ramsawh, H., Ball, T. M., Taylor, C. T., Paulus, M. P., Lang, A. J., & Stein, M. B. (2015). Intolerance of uncertainty as a mediator of reductions in worry

- in a cognitive behavioral treatment program for generalized anxiety disorder. *Journal of Anxiety Disorders*, 33, 90-94.
- Borkovec, T. D. (1985). Worry: a potentially valuable concept. *Behaviour Research and Therapy*, 23(4), 481-482.
- Borkovec, T. D., Robinson, E., Pruzinsky, T., & DePree, J. A. (1983). Preliminary exploration of worry: Some characteristics and processes. *Behaviour Research and Therapy*, 21(1), 9-16.
- Bowman, D., Scogin, F., Floyd, M., Patton, E., & Gist, L. (1997). Efficacy of self-examination therapy in the treatment of generalized anxiety disorder. *Journal of Counseling Psychology*, 44(3), 267-273.
- Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, 3(2), 77-101.
- Breinholst, S., Esbjørn, B. H., Reinholdt-Dunne, M. L., & Stallard, P. (2012). CBT for the treatment of child anxiety disorders: A review of why parental involvement has not enhanced outcomes. *Journal of Anxiety Disorders*, 26(3), 416-424.
- Buhr, K., & Dugas, M. J. (2006). Investigating the construct validity of intolerance of uncertainty and its unique relationship with worry. *Journal of Anxiety Disorders*, 20(2), 222-236.
- Burke, S. E. L., Sanson, A. V., & Van Hoorn, J. (2018). The psychological effects of climate change on children. *Current Psychiatry Reports*, 20(5), 35.
- Calmes, C. A., & Roberts, J. E. (2007). Repetitive thought and emotional distress: Rumination and worry as prospective predictors of depressive and anxious symptomatology. *Cognitive Therapy and Research*, 31(3), 343-356.
- Campbell, M. A., & Rapee, R. M. (1994). The nature of feared outcome representations in children. *Journal of Abnormal Child Psychology*, 22(1), 99-111.
- Carleton, R. N. (2012). The intolerance of uncertainty construct in the context of anxiety disorders: theoretical and practical perspectives. *Expert Review of Neurotherapeutics*, 12(8), 937-947.
- Carleton, R. N. (2016). Into the unknown: A review and synthesis of contemporary models involving uncertainty. *Journal of Anxiety Disorders*, 39, 30-43.
- Cartwright-Hatton, S., & Wells, A. (1997). Beliefs about Worry and Intrusions: The Meta-Cognitions Questionnaire and its Correlates. *Journal of Anxiety Disorders*, 11(3), 279-296.
- Chelminski, I., & Zimmerman, M. (2003). Pathological worry in depressed and anxious patients. *Journal of Anxiety Disorders*, 17(5), 533-546.
- Chorpita, B. F., Tracey, S. A., Brown, T. A., & Collica, T. J. (1997). Assessment of worry in children and adolescents: An adaptation of the Penn State Worry Questionnaire. *Behaviour Research and Therapy*, 35(6), 569-581.

- Clementi, M. A., & Alfano, C. A. (2014). Targeted behavioral therapy for childhood generalized anxiety disorder: A time-series analysis of changes in anxiety and sleep. *Journal of Anxiety Disorders*, 28(2), 215-222.
- Copeland, W. E., Angold, A., Shanahan, L., & Costello, E. J. (2014). Longitudinal Patterns of anxiety from childhood to adulthood: The Great Smoky Mountains study. *Journal of the American Academy of Child & Adolescent Psychiatry*, 53(1), 21-33.
- Crits-Christoph, P., Newman, M. G., Rickels, K., Gallop, R., Gibbons, M. B., Hamilton, J. L., . . . Pastva, A. M. (2011). Combined medication and cognitive therapy for generalized anxiety disorder. *Journal of Anxiety Disorders*, 25(8), 1087-1094.
- Cuijpers, P., Sijbrandij, M., Koole, S., Huibers, M., Berking, M., & Andersson, G. (2014). Psychological treatment of generalized anxiety disorder: A meta-analysis. *Clinical Psychology Review*, 34(2), 130-140.
- Dahlin, M., Andersson, G., Magnusson, K., Johansson, T., Sjögren, J., Håkansson, A., . . . Carlbring, P. (2016). Internet-delivered acceptance-based behaviour therapy for generalized anxiety disorder: A randomized controlled trial. *Behaviour research and therapy*, 77, 86-95.
- Davey, G. C. L., Hampton, J., Farrell, J., & Davidson, S. (1992). Some characteristics of worrying: Evidence for worrying and anxiety as separate constructs. *Personality and Individual Differences*, 13(2), 133-147.
- Dugas, M. J., Brillon, P., Savard, P., Turcotte, J., Gaudet, A., Ladouceur, R., . . . Gervais, N. J. (2010). A randomized clinical trial of cognitive-behavioral therapy and applied relaxation for adults with generalized anxiety disorder. *Behavior Therapy*, 41(1), 46-58.
- Dugas, M. J., Freeston, M. H., & Ladouceur, R. (1997). Intolerance of uncertainty and problem orientation in worry. *Cognitive therapy and research*, 21(6), 593-606.
- Dugas, M. J., Gagnon, F., Ladouceur, R., & Freeston, M. H. (1998). Generalized anxiety disorder: A preliminary test of a conceptual model. *Behaviour Research and Therapy*, 36(2), 215-226.
- Dugas, M. J., Ladouceur, R., Léger, E., Freeston, M. H., Langolis, F., Provencher, M. D., & Boisvert, J.-M. (2003). Group cognitive-behavioral therapy for generalized anxiety disorder: Treatment outcome and long-term follow-up. *Journal of Consulting and Clinical Psychology*, 71(4), 821-825.
- Dupuy, J. B., Beaudoin, S., Rhéaume, J., Ladouceur, R., & Dugas, M. J. (2001). Worry: Daily self-report in clinical and non-clinical populations. *Behaviour Research and Therapy*, 39(10), 1249-1255.
- Díaz, S., Settele, J., Brondízio, E. S., Ngo, H. T., Agard, J., Arneth, A., . . . Zayas, C. N. (2019). Pervasive human-driven decline of life on Earth points to the need for transformative change. *Science*, 366(6471).

- Esbjørn, B. H., Normann, N., Christiansen, B. M., & Reinholdt-Dunne, M. L. (2018). The efficacy of group metacognitive therapy for children (MCT-c) with generalized anxiety disorder: An open trial. *Journal of Anxiety Disorders, 53*, 16-21.
- Evans, G. W. (2019). Projected behavioral impacts of global climate change. *Annual Review of Psychology, 70*(1), 449-474.
- Fergus, T. A., & Wheless, N. (2018). Examining incremental explanatory power in accounting for worry severity: negative metacognitive beliefs uniquely predict worry severity following a worry episode. *Anxiety, Stress, & Coping, 31*(5), 514-525.
- Freeman, D., Dunn, G., Startup, H., Pugh, K., Cordwell, J., Mander, H., . . . Kingdon, D. (2015). Effects of cognitive behaviour therapy for worry on persecutory delusions in patients with psychosis (WIT): a parallel, single-blind, randomised controlled trial with a mediation analysis. *The Lancet Psychiatry, 2*(4), 305-313.
- Gentes, E. L., & Ruscio, A. M. (2011). A meta-analysis of the relation of intolerance of uncertainty to symptoms of generalized anxiety disorder, major depressive disorder, and obsessive-compulsive disorder. *Clinical Psychology Review, 31*(6), 923-933.
- Gerson, C. D., Gerson, M. J., Chang, L., Corazziari, E. S., Dumitrascu, D., Ghoshal, U. C., . . . Zali, M. (2015). A cross-cultural investigation of attachment style, catastrophizing, negative pain beliefs, and symptom severity in irritable bowel syndrome. *Neurogastroenterology & Motility, 27*(4), 490-500.
- Golden, J., Conroy, R. M., Bruce, I., Denihan, A., Greene, E., Kirby, M., & Lawlor, B. A. (2011). The spectrum of worry in the community-dwelling elderly. *Aging & Mental Health, 15*(8), 985-994.
- Gonçalves, D. C., & Byrne, G. J. (2013). Who worries most? Worry prevalence and patterns across the lifespan. *International Journal of Geriatric Psychiatry, 28*(1), 41-49.
- Gosselin, P., Ladouceur, R., Morin, C. M., Dugas, M. J., & Baillargeon, L. (2006). Benzodiazepine discontinuation among adults with GAD: A randomized trial of cognitive-behavioral therapy. *Journal of Consulting and Clinical Psychology, 74*(5), 908-919.
- Grant, B. F., Hasin, D. S., Stinson, F. S., & Dawson, D. A. (2005). Prevalence, correlates, co-morbidity, and comparative disability of DSM-IV generalized anxiety disorder in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychological Medicine, 35*(12), 1747-1759.
- Haller, H., Cramer, H., Lauche, R., Gass, F., & Dobos, G. J. (2014). The prevalence and burden of subthreshold generalized anxiety disorder: a systematic review. *BMC Psychiatry, 14*(1), 128-113.
- Haverkamp, B. E. (2005). Ethical perspectives on qualitative research in applied psychology. *Journal of Counseling Psychology, 52*(2), 146-155.
- Hayes, S., Hirsch, C. R., & Mathews, A. (2008). Restriction of working memory capacity during worry. *Journal of Abnormal Psychology, 117*(3), 712-717.
- Hebert, E. A., & Dugas, M. J. (2019). Behavioral experiments for intolerance of

uncertainty: Challenging the unknown in the treatment of generalized anxiety disorder. *Cognitive and Behavioral Practice*, 26(2), 421.

Hirsch, C. R., & Mathews, A. (2012). A cognitive model of pathological worry. *Behavior Research and Therapy*, 50(10), 636-646.

Holeva, V., TARRIER, N., & Wells, A. (2001). Prevalence and predictors of acute stress disorder and PTSD following road traffic accidents: Thought control strategies and social support. *Behavior Therapy*, 32(1), 65-83.

Holmes, E. A., Ghaderi, A., Harmer, C. J., Ramchandani, P. G., Cuijpers, P., Morrison, A. P., . . . Craske, M. G. (2018). The Lancet Psychiatry Commission on psychological treatments research in tomorrow's science. *The Lancet Psychiatry*, 5(3), 237-286.

Hong, R. Y. (2007). Worry and rumination: Differential associations with anxious and depressive symptoms and coping behavior. *Behaviour Research and Therapy*, 45(2), 277-290.

Hudson, J. L., Rapee, R. M., Lyneham, H. J., McLellan, L. F., Wuthrich, V. M., & Schniering, C. A. (2015). Comparing outcomes for children with different anxiety disorders following cognitive behavioural therapy. *Behaviour Research and Therapy*, 72(c), 30-37.

Jacobson, N. S., & Truax, P. (1991). Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. *Journal of Consulting and Clinical Psychology*, 59(1), 12-19.

James, A. C., James, G., Cowdrey, F. A., Soler, A., & Choke, A. (2015). Cognitive behavioural therapy for anxiety disorders in children and adolescents. *Cochrane Database of Systematic Reviews*, 64(2), 333-388.

Jolstedt, M., Ljótsson, B., Fredlander, S., Tedgård, T., Hallberg, A., Ekeljung, A., . . . Vigerland, S. (2018). Implementation of internet-delivered CBT for children with anxiety disorders in a rural area: A feasibility trial. *Internet Interventions*, 12, 121-129.

Jolstedt, M., Wahlund, T., Lenhard, F., Ljótsson, B., Mataix-Cols, D., Nord, M., . . . Vigerland, S. (2018). Efficacy and cost-effectiveness of therapist-guided internet cognitive behavioural therapy for paediatric anxiety disorders: a single-centre, single-blind, randomised controlled trial. *The Lancet Child & Adolescent Health*, 2(11), 792-801.

Katzman, M. A., Bleau, P., Blier, P., Chokka, P., Kjernisted, K., & Van Ameringen, M. (2014). Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. *BMC psychiatry*, 14(1), S1.

Kazdin, A. E. (2007). Mediators and mechanisms of change in psychotherapy research. *Annual Review of Clinical Psychology*, 3, 1.

Kazdin, A. E. (2017). Addressing the treatment gap: A key challenge for extending evidence-based psychosocial interventions. *Behaviour Research and Therapy*, 88, 7-18.

- Kendall, P. C. (1994). Treating anxiety disorders in children: results of a randomized clinical trial. *Journal of Consulting and Clinical Psychology*, 62(1), 100-110.
- Kertz, S. J., Bigda-Peyton, J. S., Rosmarin, D. H., & Björgvinsson, T. (2012). The importance of worry across diagnostic presentations: Prevalence, severity and associated symptoms in a partial hospital setting. *Journal of Anxiety Disorders*, 26(1), 126-133.
- Kertz, S. J., & Woodruff-Borden, J. (2012). The role of metacognition, intolerance of uncertainty, and negative problem orientation in children's worry. *Behavioural and Cognitive Psychotherapy*, 41(02), 243-248.
- Krishnamurti, T., Davis, A. L., & Simhan, H. N. (2019). Worrying yourself sick? Association between pre-eclampsia onset and health-related worry in pregnancy. *Pregnancy Hypertension*, 18, 55-57.
- Kubzansky, L. D., Kawachi, I., Spiro III, A., Weiss, S. T., Vokonas, P. S., & Sparrow, D. (1997). Is worrying bad for your heart? A prospective study of worry and coronary heart disease in the Normative Aging Study. *Circulation*, 95(4), 818-824.
- Ladouceur, R., Dugas, M. J., Freeston, M. H., Léger, E., Gagnon, F., & Thibodeau, N. (2000). Efficacy of a cognitive-behavioral treatment for generalized anxiety disorder: Evaluation in a controlled clinical trial. *Journal of Consulting and Clinical Psychology*, 68(6), 957-964.
- Ladouceur, R., Gosselin, P., & Dugas, M. J. (2000). Experimental manipulation of intolerance of uncertainty: A study of a theoretical model of worry. *Behaviour Research and Therapy*, 38(9), 933-941.
- Lebowitz, E. R., Woolston, J., Haim, Y. B., Calvocoressi, L., Dauser, C., Warnick, E., . . . Leckman, J. F. (2013). Family accommodation in pediatric anxiety disorders. *Depression and Anxiety*, 30(47), 47-54.
- Leiserowitz, A., Maibach, E., Rosenthal, S., Kotcher, J., Bergquist, P., Ballew, M., . . . Gustafson, A. (2019). *Climate Change in the American Mind: November 2019*. Retrieved from New Haven, CT: https://www.climatechangecommunication.org/wp-content/uploads/2019/12/Climate_Change_American_Mind_November_2019b.pdf
- Léger, E., Ladouceur, R., Dugas, M. J., & Freeston, M. H. (2003). Cognitive-Behavioral Treatment of Generalized Anxiety Disorder Among Adolescents: A Case Series. *Journal of the American Academy of Child & Adolescent Psychiatry*, 42(3), 327-330.
- Macleod, A. K., Williams, J. M. G., & Bekerian, D. A. (1991). Worry Is Reasonable: The Role of Explanations in Pessimism About Future Personal Events. *Journal of Abnormal Psychology*, 100(4), 478-486.
- Mathews, A. (1990). Why worry? The cognitive function of anxiety. *Behaviour Research and Therapy*, 28(6), 455-468.
- McCashin, D., Coyle, D., & O'Reilly, G. (2019). Qualitative Synthesis of Young People's Experiences With Technology-Assisted Cognitive Behavioral Therapy: Systematic Review. *Journal of Medical Internet Research*, 21(11), e13540.

- Meyer, T. J., Miller, M. L., Metzger, R. L., & Borkovec, T. D. (1990). Development and validation of the Penn State Worry Questionnaire. *Behaviour Research and Therapy*, 28(6), 487-495.
- Modi, N., Vohra, J., Preston, J., Elliott, C., Van't Hoff, W., Coad, J., . . . Greenough, A. (2014). Guidance on clinical research involving infants, children and young people: an update for researchers and research ethics committees. *Archives of Disease in Childhood*, 99(10).
- Muris, P., Meesters, C., & Gobel, M. (2001). Reliability, validity, and normative data of the Penn State Worry Questionnaire in 8–12-yr-old children. *Journal of Behavior Therapy and Experimental Psychiatry*, 32(2), 63-72.
- Muris, P., Merckelbach, H., Gadet, B., & Moulaert, V. (2000). Fears, worries, and scary dreams in 4- to 12-year-old children: their content, developmental pattern, and origins. *Journal of Clinical Child & Adolescent Psychology*, 29(1), 43-52.
- Muris, P., Roelofs, J., Meesters, C., & Boomsma, P. (2004). Rumination and Worry in Nonclinical Adolescents. *Cognitive Therapy and Research*, 28(4), 539-554.
- National Institute for Health and Care Excellence. (2019). *Generalised anxiety disorder and panic disorder in adults*. Author Retrieved from <https://www.nice.org.uk/guidance/cg113>.
- Newby, J. M., Williams, A. D., & Andrews, G. (2014). Reductions in negative repetitive thinking and metacognitive beliefs during transdiagnostic internet cognitive behavioural therapy (iCBT) for mixed anxiety and depression. *Behaviour Research and Therapy*, 59, 52-60.
- Newman, M. G., & Llera, S. J. (2011). A novel theory of experiential avoidance in generalized anxiety disorder: A review and synthesis of research supporting a contrast avoidance model of worry. *Clinical Psychology Review*, 31(3), 371-382.
- Newman, M. G., Llera, S. J., Erickson, T. M., Przeworski, A., & Castonguay, L. G. (2013). Worry and Generalized Anxiety Disorder: A Review and Theoretical Synthesis of Evidence on Nature, Etiology, Mechanisms, and Treatment. *Annual Review of Clinical Psychology*, 9(1), 275-297.
- Nordahl, H. M., Borkovec, T. D., Hagen, R., Kennair, L. E. O., Hjemdal, O., Solem, S., . . . Wells, A. (2018). Metacognitive therapy versus cognitive-behavioural therapy in adults with generalised anxiety disorder. *BJPsych Open*, 4(5), 393-400.
- Norman, K. R., Silverman, W. K., & Lebowitz, E. R. (2015). Family Accommodation of Child and Adolescent Anxiety: Mechanisms, Assessment, and Treatment. *Journal of Child and Adolescent Psychiatric Nursing*, 28(3), 131-140.
- Normann, N., & Morina, N. (2018). The Efficacy of Metacognitive Therapy: A Systematic Review and Meta-Analysis. *Frontiers in Psychology*, 9(2211).

- Ojala, M. (2012). Regulating worry, promoting hope: How do children, adolescents, and young adults cope with climate change? *International Journal of Environmental and Science Education*, 7(4), 537-561.
- Olatunji, B. O., Wolitzky-Taylor, K. B., Sawchuk, C. N., & Ciesielski, B. G. (2010). Worry and the anxiety disorders: A meta-analytic synthesis of specificity to GAD. *Applied and Preventive Psychology*, 14(1-4), 1-24.
- Orton, G. L. (1982). A comparative study of Children's worries. *The Journal of Psychology*, 110, 153-162.
- Osmanağaoğlu, N., Creswell, C., & Dodd, H. F. (2018). Intolerance of Uncertainty, anxiety, and worry in children and adolescents: A meta-analysis. *Journal of Affective Disorders*, 225, 80-90.
- Payne, S., Bolton, D., & Perrin, S. (2011). A pilot investigation of cognitive therapy for generalized anxiety disorder in children aged 7–17 years *Cognitive Therapy and Research*, 35(2), 171-178.
- Penney, A. M., Mazmanian, D., & Rudanycz, C. (2013). Comparing positive and negative beliefs about worry in predicting generalized anxiety disorder symptoms. *Canadian Journal of Behavioural Science/Revue canadienne des sciences du comportement*, 45(1), 34-41.
- Perrin, S., Bevan, D., Payne, S., & Bolton, D. (2019). GAD-specific cognitive behavioral treatment for children and adolescents: A pilot randomized controlled trial. *Cognitive Therapy and Research*, 43(6), 1051-1064.
- Perrin, S., & Last, C. G. (1997). Worrisome thoughts in children clinically referred for anxiety disorder. *Journal of Clinical Child Psychology*, 26(2), 181-189.
- Piacentini, J., Bennett, S., Compton, S. N., Kendall, P. C., Birmaher, B., Albano, A. M., . . . Walkup, J. (2014). 24- and 36-week outcomes for the child/adolescent anxiety multimodal study (CAMS). *Journal of the American Academy of Child & Adolescent Psychiatry*, 53(3), 297-310.
- Rapee, R. M. (2000). Group treatment of children with anxiety disorders: Outcome and predictors of treatment response. *Australian Journal of Psychology*, 52(3), 125-129.
- Rapee, R. M., Lynham, H. J., Wuthrich, V., Chatterton, M. L., Hudson, J. L., Kangas, M., & Mihalopoulos, C. (2017). Comparison of stepped care delivery against a single, empirically validated cognitive-behavioral therapy program for youth with anxiety: a randomized clinical trial. *Journal of the American Academy of Child and Adolescent Psychiatry*, 56(10), 841-848.
- Richards, D., Richardson, T., Timulak, L., & McElvaney, J. (2015). The efficacy of internet-delivered treatment for generalized anxiety disorder: A systematic review and meta-analysis. *Internet Interventions*, 2(3), 272-282.

- Robichaud, M., Dugas, M. J., & Conway, M. (2003). Gender differences in worry and associated cognitive-behavioral variables. *Journal of Anxiety Disorders, 17*(5), 501-516.
- Robinson, E., Titov, N., Andrews, G., McIntyre, K., Schwencke, G., & Solley, K. (2010). Internet treatment for generalized anxiety disorder: a randomized controlled trial comparing clinician vs. technician assistance. *PLoS one, 5*(6), e10942.
- Rosser, B. A. (2019). Intolerance of uncertainty as a transdiagnostic mechanism of psychological difficulties: A systematic review of evidence pertaining to causality and temporal precedence. *Cognitive Therapy and Research, 43*(2), 438-463.
- Ruscio, A. M. (2002). Delimiting the boundaries of generalized anxiety disorder: differentiating high worriers with and without GAD. *Journal of Anxiety Disorders, 16*(4), 377-400.
- Ruscio, A. M., & Borkovec, T. D. (2004). Experience and appraisal of worry among high worriers with and without generalized anxiety disorder. *Behaviour Research and Therapy, 42*(12), 1469-1482.
- Ryum, T., Kennair, L. E. O., Hjemdal, O., Hagen, R., Halvorsen, J. O., & Solem, S. (2017). Worry and Metacognitions as Predictors of Anxiety Symptoms: A Prospective Study. *Frontiers in Psychology, 8*, 924.
- Safi, M., Tom, P., & Jones, S. (2019). Protests rage around the world – but what comes next? *The Guardian*. Retrieved from <https://www.theguardian.com/world/2019/oct/25/protests-rage-around-the-world-hong-kong-lebanon-chile-catalonia-iraq>
- Schwartz, C., Barican, J. L., Yung, D., Zheng, Y., & Waddell, C. (2019). Six decades of preventing and treating childhood anxiety disorders: a systematic review and meta-analysis to inform policy and practice. *Evidence-Based Mental Health, 22*(3), 103-110.
- Shihata, S., McEvoy, P. M., Mullan, B. A., & Carleton, R. N. (2016). Intolerance of uncertainty in emotional disorders: What uncertainties remain? *Journal of Anxiety Disorders, 41*, 115-124.
- Silverman, W. K., La Greca, A. M., & Wasserstein, S. (1995). What do children worry about? Worries and their relation to anxiety. *Child Development, 66*(3), 671-686.
- Slee, A., Nazareth, I., Bondaronek, P., Liu, Y., Cheng, Z., & Freemantle, N. (2019). Pharmacological treatments for generalised anxiety disorder: a systematic review and network meta-analysis. *The Lancet, 393*(10173), 768-777.
- Socialstyrelsen. (2017). *Nationella riktlinjer för vård vid depression och ångestsyndrom. Stöd för styrning och ledning – Remissversion 2016*. Stockholm, Sweden: Socialstyrelsen.
- Stanley, M. A., Beck, J. G., & Glassco, J. D. (1996). Treatment of generalized anxiety in older adults: A preliminary comparison of cognitive-behavioral and supportive approaches. *Behavior Therapy, 27*(4), 565-581.

- Stanley, M. A., Beck, J. G., Novy, D. M., Averill, P. M., Swann, A. C., Diefenbach, G. J., & Hopko, D. R. (2003). Cognitive-behavioral treatment of late-life generalized anxiety disorder. *Journal of Consulting and Clinical Psychology, 71*(2), 309-319.
- Starcevic, V. (1995). Pathological worry in major depression: a preliminary report. *Behaviour Research and Therapy, 33*(1), 55-56.
- Strawn, J. R., Welge, J. A., Wehry, A. M., Keeshin, B., & Rynn, M. A. (2015). Efficacy and tolerability of antidepressants in pediatric anxiety disorders: a systematic review and meta-analysis. *Depression and Anxiety, 32*(3), 149-157.
- Szabo, M., & Lovibond, P. (2002). The cognitive content of naturally occurring worry episodes. *Cognitive Therapy and Research, 26*(2), 167-177.
- The British Psychological Society. (2014). Code of Human Research Ethics. Retrieved from <https://www.bps.org.uk/news-and-policy/bps-code-human-research-ethics-2nd-edition-2014>
- The British Psychological Society. (2017). *Ethics Guidelines for Internet-mediated Research*. In T. B. P. Society (Ed.). Retrieved from <https://www.bps.org.uk/sites/beta.bps.org.uk/files/Policy%20-%20Files/Ethics%20Guidelines%20for%20Internet-mediated%20Research%20%282017%29.pdf>
- Thielsch, C., Andor, T., & Ehring, T. (2015). Do metacognitions and intolerance of uncertainty predict worry in everyday life? An ecological momentary assessment study. *Behavior Therapy, 46*(4), 532-543.
- Thompson-Hollands, J., Kerns, C. E., Pincus, D. B., & Comer, J. S. (2014). Parental accommodation of child anxiety and related symptoms: Range, impact, and correlates. *Journal of Anxiety Disorders, 28*(8), 765-773.
- Thorslund, J., McEvoy, P. M., & Anderson, R. A. (2020). Group metacognitive therapy for adolescents with anxiety and depressive disorders: A pilot study. *Journal of Clinical Psychology*.
- Thulin, U., Svirsky, L., Serlachius, E., Andersson, G., & Öst, L.-G. (2014). The effect of parent involvement in the treatment of anxiety disorders in children: A meta-analysis. *Cognitive Behaviour Therapy, 43*(3), 185-200.
- Titov, N., Andrews, G., Robinson, E., Schwencke, G., Johnston, L., Solley, K., & Choi, I. (2009). Clinician-assisted internet-based treatment is effective for generalized anxiety disorder: randomized controlled trial. *The Australian & New Zealand Journal of Psychiatry, 43*(10), 905-912.
- Topper, M., Emmelkamp, P. M. G., Watkins, E., & Ehring, T. (2014). Development and assessment of brief versions of the Penn State Worry Questionnaire and the Ruminative Response Scale. *British Journal of Clinical Psychology, 53*(4), 402-421.
- United Nations. (2019). The Sustainable Development Goals Report 2019. Retrieved from <https://www.un-ilibrary.org/content/publication/55eb9109-en>

- Van Ameringen, M., Patterson, B., Turna, J., Pipe, A., & Nakua, H. (2017). The treatment of refractory generalized anxiety disorder. *Current Treatment Options in Psychiatry*, 4(4), 404-417.
- van der Heiden, C., Muris, P., & van der Molen, H. T. (2012). Randomized controlled trial on the effectiveness of metacognitive therapy and intolerance-of-uncertainty therapy for generalized anxiety disorder. *Behaviour Research and Therapy*, 50(2), 100-109.
- Vasey, M. W., Crnic, K. A., & Carter, W. G. (1994). Worry in childhood: A developmental perspective. *Cognitive Therapy and Research*, 18(6), 52-549.
- Vigerland, S., Lenhard, F., Bonnert, M., Lalouni, M., Hedman, E., Ahlen, J., . . . Ljótsson, B. (2016). Internet-delivered cognitive behavior therapy for children and adolescents: A systematic review and meta-analysis. *Clinical Psychology Review*, 50, 1-10.
- Walkup, J. T., Albano, A. M., Piacentini, J., Birmaher, B., Compton, S. N., Sherrill, J. T., . . . Kendall, P. C. (2008). Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety. *The New England Journal of Medicine*, 359(26), 2753-2766.
- Wang, Z., Whiteside, S. P. H., Sim, L., Farah, W., Morrow, A. S., Alsawas, M., . . . Murad, M. H. (2017). Comparative effectiveness and safety of cognitive behavioral therapy and pharmacotherapy for childhood anxiety disorders. *JAMA Pediatrics*, 171(11), 1049-1048.
- Wells, A. (1995). Meta-cognition and worry: A cognitive model of generalized anxiety disorder. *Behavioural and Cognitive Psychotherapy*, 23(03), 301.
- Wells, A. (1997). *Cognitive Therapy of Anxiety Disorders. A Practice Manual and Conceptual Guide*. Chichester: John Wiley & Sons.
- Wells, A. (2011). *Metacognitive Therapy for Anxiety and Depression*. New York: Guilford Press.
- Wells, A., & Carter, K. (2001). Further tests of a cognitive model of generalized anxiety disorder: Metacognitions and worry in GAD, panic disorder, social phobia, depression, and nonpatients. *Behavior Therapy*, 32(1), 85-102.
- Wells, A., Welford, M., King, P., Papageorgiou, C., Wisely, J., & Mendel, E. (2010). A pilot randomized trial of metacognitive therapy vs applied relaxation in the treatment of adults with generalized anxiety disorder. *Behaviour Research and Therapy*, 48(5), 429-434.
- World Meteorological Organization. (2019). *The Global Climate in 2015–2019*. Retrieved from https://library.wmo.int/doc_num.php?explnum_id=9936