On the Diagnosis, Assessment, and Treatment of Generalized Anxiety Disorder

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Chapter 1

General introduction

1.1 | Background

Generalized anxiety disorder (GAD) is increasingly recognized as a prevalent anxiety disorder with a chronic course and significant impairment (APA, 2000; Ballenger et al., 2001; Weisberg, 2009). In the Netherlands, according to the second Netherlands Mental Health Survey and Incidence Study (NEMESIS-2; De Graaf, Ten Have, & Van Dorsselaar, 2010) GAD was found to have a 4.5% lifetime prevalence rate, and the 12-month prevalence rate was reported to be 1.7%. GAD is a long-term illness with a high likelihood of recurrence. For instance, during the 12 years of a large longitudinal study, the Harvard-Brown Anxiety Research Project (HARP; Bruce et al., 2005), the average amount of time that patients met diagnostic criteria of GAD was 74%. Further, GAD was found to have a probability of recovery of 0.58 in the 12 years the study lasted, and the probability of recurrence in patients who recovered was 0.45. GAD has been found to be associated with considerable impairment and severity. For instance, in one study GAD was the anxiety disorder with the highest rate of moderate to severe disability (Sanderson & Andrews, 2002). Further, lifetime and current GAD were found to be associated with decreased overall well-being (Stein & Heimberg, 2004) and with impairment that was equivalent in magnitude to the impairment caused by major depressive disorder (Kessler, Dupont, Berglund, & Wittchen, 1999).

GAD was defined for the first time in the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III; APA, 1980), when the older category of anxiety neurosis was divided into panic disorder and GAD. The disorder was characterized by generalized, persistent anxiety for at least one month, that was accompanied by an unspecified number of symptoms from the following categories: apprehensive expectation, motor tension, autonomic hyperactivity, or vigilance. By definition, GAD was considered to lead to rarely more than mild impairment in social and occupational functioning. Finally, GAD was not to be diagnosed if other Axis I conditions were present, leaving it a residual category.

Since then, the definition of the disorder underwent considerable modification in the successive editions of the DSM (APA, 1987; APA, 1994; see Table 1.1). The essential feature of the disorder has been changed from persistent anxiety to excessive and uncontrollable worry about more than one life circumstance, and the required symptom duration has changed from one month to six months. Further, in the DSM-IV (APA, 1994) ancillary symptoms were reduced, involving only three of six symptoms from the categories of motor tension and vigilance, impairment was no longer considered as 'only mild', but as 'producing significant distress or impairment', and GAD could be diagnosed in the presence of another mental disorder, thereby changing GAD from a residual problem to a primary diagnostic entity. The primary goal of the modifications was to '*modify the definition of the disorder to reflect*

Table 1.1 | Shift in diagnostic criteria for generalized anxiety disorder in the *Diagnostic and Statistical Manual of Mental Disorders,* since 1980.

Criterion	DSM-III (1980)	DSM-III-R (1987)	DSM-IV (1994)
Anxiety	Generalized, persistent anxiety	Unrealistic or excessive anxiety and worry about two or more life circumstances, more days than not	Excessive anxiety and worry about a number of events or activities that is difficult to control, more days than not
Duration	1 month	6 months'	6 months
Ancillary symptoms	Unspecified number of symptoms from 3 of the categories: 1. motor tension 2. autonomic hyperactivity 3. apprehensive expectation 4. vigilance	≥ 6 symptoms from 3 categories: 1. motor tension (4 symptoms) 2. autonomic hyperactivity (9 symptoms) 3. vigilance (5 symptoms)	≥ 3 of 6 specified symptoms: 1. restlessness or feeling keyed up 2. being easily fatigued 3. poor concentration 4. irritability 5. muscle tension 6. sleep disturbance
Impairment in social and occupational functioning	Rarely more than mild	Rarely more than mild	Significant distress or impairment
Exclusions	Not due to another mental disorder	Symptoms: 1. are unrelated to another disorder 2. do not occur exclusively during a mood disorder or psychotic disorder 3. are not organic 4. are not related to substance abuse	Symptoms: 1. are unrelated to another disorder 2. do not occur exclusively during a mood disorder or psychotic disorder 3. are not organic 4. are not related to substance abuse

anxiety symptoms unique to it and try to exclude features that overlapped with other anxiety disorders' (p. 232, Klein, Kaplan-Tencer, & Werry, 1997).

Unfortunately, GAD is still one of the more controversial anxiety disorders in the current edition of the DSM (APA, 2000). Nosologic controversies continue to surround the criteria for excessive worry, symptom duration, the relationship between GAD and major depressive disorder, and the required number of associated symptoms (see Weisberg, 2009). Therefore, in order to better determine the nosology of GAD, research is required into the phenomenology and the etiology of GAD. Another problem that was not solved by changing the diagnostic criteria, is that in clinical practice the diagnosis of GAD is frequently missed (Beesdo et al., 2009), not only because of the debatable diagnostic criteria, but also as a result of the symptom presentation and high comorbidity. Fewer than 20% of GAD patients present themselves in primary care with psychological complaints. The majority of the patients complains about somatic symptoms, such as fatigue or restlessness, whereas other GAD sufferers may complain about feeling under stress (Ballenger et al., 2001). Further, around two thirds of patients with GAD will be found to have other conditions at the time of presentation or later in their course, including physical illness and other psychological disorders (Ballenger et al., 2001). Both symptom presentation and comorbidity complicate the diagnosis of GAD. For instance, of the people with GAD that seek professional help, only 50-65% are identified as 'psychiatric cases' by their general practitioner (Hoyer, Krause, Hofler, Beesdo, & Wittchen, 1998; Weiller, Bisserbe, Maier, & Lecrubier, 1998).

In addition to diagnostic interviews, screening instruments can be used to arrive at a diagnosis, such as the Penn State Worry Questionnaire (PSWQ: Meyer, Miller, Metzger, & Borkovec, 1990). This self-report instrument for measuring worry is also very useful in both monitoring individual treatment effects and studying the effectiveness of treatments for GAD. However, although frequently used in GAD studies, the factor structure of the PSWQ remains unclear. Although originally developed as a unifactorial measure, several investigators have noted that a two-factor solution might provide a better fit to the data (e.g., Fresco, Heimberg, Mennin, & Turk, 2002), whereas others question the substantive meaning of the second factor. This second factor, called 'absence of worry', consists of the five reverse-worded items of the PSWQ, and might only be a so-called method factor without substantive meaning (Brown, 2003; Hazlett-Stevens, Ullman, & Craske, 2004). Further, normative data for the PSWQ that can be used to describe individual treatment effects in clinical practice are hardly available.

GAD is responsive to treatment, especially cognitive-behavioral therapy and pharmacotherapy (Ballenger et al., 2001). However, in a reanalysis of data from eleven CBT outcome studies, Fisher (2006) reported a recovery rate across all treatments of 40% overall based on worry and trait-anxiety scores. These data show that there is a need for more effective treatments. Progress might be made by basing treatment on a model of the

mechanisms and factors underlying pathological worry, the hallmark of this disorder (Wells & King, 2006). Further, as most studies were so-called efficacy studies, in which patients with concurrent disorders have been routinely eliminated and therapists used explicit treatment manuals with high supervision frequency, there is a need for studies that reflect clinical practice, in which GAD is frequently comorbid with major depressive disorder or other anxiety disorders and practitioners have different supervision intensity.

1.2 | Aim and outline of the current thesis

The first aim of our studies was to provide diagnostic guidelines for improving the recognition of GAD, and for effectively distinguishing GAD from other conditions in clinical practice (Chapter 2), and to improve the understanding of the etiology of GAD, by examining a hierarchical model for the relationships between general and specific vulnerability factors and symptom manifestations of GAD. More specifically, in this model the basic personality dimensions of neuroticism and extraversion acted as higher order vulnerability factors. Two constructs that are hypothesized to contribute to GAD, intolerance of uncertainty and metacognitive beliefs about worrying, served as second-order vulnerability factors. At the symptom level worry served as the specific manifestation of GAD and depressive symptoms as a co-morbid manifestation (Chapter 3).

The second aim was to improve the usefulness of the PSWQ, by investigating the factor structure (Chapter 4) and by providing normative data to assist clinicians in assessing treatment progress (Chapter 5).

The third and final aim was to evaluate the effectiveness of two new forms of cognitive-behavioral therapy that are both based on specific theoretical models of GAD, metacognitive therapy (MCT) and intolerance-of-uncertainty-therapy (IUT). So far, there is preliminary evidence supporting the efficacy of both treatments (see Dugas & Robichaud, 2007; Wells, 2009). In Chapter 6 MCT and IUT are described using case examples. In Chapter 7 the results are presented of a randomized controlled trial into the effectiveness of MCT and IUT in the treatment of GAD. The final Chapter 8 contains a general discussion and the conclusions of the findings. It ends with recommendations for future research.

Chapter 2

Generalized anxiety disorder: Clinical presentation, diagnostic features, and guidelines for clinical practice

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Abstract

Generalized anxiety disorder (GAD) is a prevalent and disabling disorder characterised by persistent worrying, anxiety symptoms, and tension. General practitioners and mental healthcare professionals frequently misdiagnose the presenting symptoms. This chapter addresses the clinical presentation of GAD and provides guidelines for discriminating GAD from other disorders, based on theoretical considerations and clinical experience. Debate relating to the validity of the definition of GAD is discussed, and suggestions are made for improving the criteria for GAD, which may guide future versions of classification systems such as the Diagnostic and Statistical Manual.

2.1 | Introduction

In 1980 generalized anxiety disorder (GAD) was first defined as an independent disorder in the DSM-III (APA, 1980). It was characterized by persistent anxiety and an unspecified number of ancillary symptoms, such as apprehensive expectation and motor tension, which had to be present for at least one month. After the introduction of GAD in the DSM-III, nosologic issues and controversies have persisted. In an effort to improve the specificity and validity, the diagnostic criteria for GAD underwent important changes in the composition and number of required symptoms, and their minimum duration, in successive editions of the DSM (APA, 1987, 1994, 2000). In the current edition, the DSM-IV-TR (APA, 2000), excessive anxiety and uncontrollable worry about a number of events for at least six months, are the main features of GAD. At least three out of six of the following additional symptoms are required for a diagnosis: restlessness/mental tension, fatigue, poor concentration, irritability, muscle tension, and sleep disturbance. Finally, the symptoms have to lead to significant distress and impairment.

Despite the remarkable changes in the diagnostic criteria, GAD still is the anxiety disorder with the lowest diagnostic reliability (Brown, DiNardo, Lehman & Campbell, 2001) and the diagnostic criteria continue to be debated (Weisberg, 2009). Current debate centers on the duration criterion, the addition of the qualification ‘excessive’ to the levels of anxiety and worrying, the number of associated symptoms required for a diagnosis of GAD, and the relationship between GAD and major depressive disorder (MDD). Apart from the poor reliability and the continuing controversies about the definition, GAD is also still poorly recognized in clinical practice (Beesdo et al., 20009). Of the people who meet the diagnostic criteria for GAD that seek professional help for their symptoms, only 50-65% are identified by their general practitioner (GP) as ‘psychiatric cases’, and only 34% of the latter group

is recognized as GAD patients (Hoyer, Krause, Hofler, Beesdo, & Wittchen, 1998; Weiller, Bisserbe, Maier, & Lecrubier, 1998). This may be due to the fact that patients with GAD often do not seek help for their anxious apprehension (Kessler, Lloyd, Lewis, & Gray, 1999), but rather present to their GP with general, vague, and non-specific somatic complaints, such as sleeping problems, fatigue, nervousness, or pain in the neck and shoulders (Culpepper, 2002; Wittchen et al., 2002b). Therefore, unstructured clinical interviews in which clinicians gather information based on the main complaint presented by the patient are definitely not suitable as a diagnostic tool for GAD (Kessler et al., 1999; Wittchen et al., 2002b). Yet, clinicians have disposal of structured clinical interviews such as the Structured Clinical Interview for DSM-IV-TR Axis-I Disorders (SCID-I; First, Spitzer, Gibbon & Williams, 2001) or the Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV; Brown, DiNardo & Barlow, 1994), which may guide them to make the appropriate diagnosis.

The recognition of GAD is further complicated by a high prevalence of comorbidity with other psychiatric disorders as well as with general medical conditions, both of which lead to a complex clinical presentation. Comorbity rates range from 90% for people with lifetime GAD meeting criteria for an additional axis I disorder in general population studies (Carter, Wittchen, Pfister, & Kessler, 2001) to 45-98% of patients with GAD having one or more lifetime comorbid disorders in clinical studies (Holaway, Rodebaugh, & Heimberg, 2006). Among individuals with current GAD, 66% had at least one concurrent psychiatric disorder (Wittchen, Zhao, Kessler, & Eaton, 1994). GAD is frequently comorbid with major depressive disorder (MDD) and other anxiety disorders, and is also strongly associated with chronic pain conditions, medically unexplained somatic symptoms, and sleep disorders (Nutt, Argyropoulos, Hood, & Potokar, 2006). Highest among these comorbidities is MDD (Simon, 2009).

Given the high rates of comorbidity it has been questioned whether GAD is an independent disorder, or rather a prodrome, a residual or severity marker of other anxiety or mood disorders (Kessler, 2002). However, for several reasons there seems to be a basis for retaining GAD as a diagnostic category. First, GAD has established reliability and validity in its own right (see Mennin et al., 2008), and noncomorbid GAD has been found to occur more frequently than assumed (Wittchen et al., 2002b). Of patients who visit their GP 5.3% meet the criteria of GAD. In 72% of these cases GAD is the only disorder (i.e., 3.8% of patients who visit their GP). As comorbidity was also found to be a powerful predictor of help-seeking rtefact in GAD patients, it seems that comorbidity is an rtefact of a 'help-seeking bias' rather than a characteristic inherent to GAD (Kessler, 2002; Kessler, Chiu, Demler, Merkikangas, & Walters, 2005b).

However, as a result of the strong relationship between GAD and MDD at both genotypic and phenotypic levels, the substantial loadings on a higher-order negative affectivity factor

that both disorders demonstrate, and substantial symptom overlap between them (Watson, 2005; Mennin, Heimberg, Fresco, & Ritter, 2008), there have been a number of calls to reclassify GAD in the upcoming DSM-V (expected in 2013). Proposed changes for DSM-V include (1) placing GAD together with MDD, dysthymia, and PTSS in a category of 'distress disorders', one of the subclasses of the overarching class of 'emotional disorders' (Watson, 2005), (2) recategorizing GAD as a mood disorder (Vollebergh et al., 2001), (3) categorizing GAD as a subtype of MDD (Kendler, Neale, Kessler, Heath, & Eaves, 1992), or (4) using a higher-order factor such as neuroticism to capture both disorders (Andrews, 1996). However, removing GAD from the anxiety disorders seems to be premature because such a reclassification (1) does not fully reflect the complex relationship of GAD with both mood and anxiety disorders (e.g., despite overlapping genetic factors, GAD and MDD differ with regard to environmental factors and temporal presentations), and (2) does not fully account for the relationship between mood disorders and anxiety disorders other than GAD (e.g., MDD also has strong relationships with other anxiety disorders) (Mennin et al., 2008). Thus, given available data, this issue will be a topic of further discussion for the architects of DSM-V.

The poor recognition of GAD is a major problem for several reasons. First, based on the current DSM-IV-TR criteria, GAD is a highly prevalent disorder. With a current prevalence of 1.5-3% and lifetime prevalence estimations ranging from 4-7% (Kessler & Wittchen, 2002), GAD is one of the most frequently observed psychological disorders in epidemiologic studies (Lieb, Becker, & Altamura, 2005). GAD is generally considered to have a fairly chronic course (Wittchen, 2002), although recent longitudinal studies demonstrate a recurrent course for the disorder, with a chronicity rate of under 20% and even remission in a significant proportion of the participants (Angst, Gamma, Baldwin, Ajdacic-Gross, & Rössler, 2009; Bruce et al., 2005). The disorder is associated with high severity and impairment. For instance, it was found that no other anxiety disorder had a rate of severity as high as that of GAD, including having impairment in occupational or social functioning (Kessler et al., 2005b; Sanderson & Andrews, 2002). Further, GAD was found to be associated with an impairment in life satisfaction and well-being that is (at least) comparable to that of patients suffering from other prevalent psychological disorders (Wittchen, Beesdo, & Kessler, 2002; Lieb et al., 2005). Without treatment the prognosis is poor (Yonkers, Massion, Warshaw, & Keller, 1996; Yonkers, Dyck, Warshaw, & Keller, 2000).

Consequently, unrecognized GAD results in intensive use of healthcare facilities for a long period (e.g., Lieb et al., 2005), in which patients with GAD are confronted with unnecessary, often costly and ineffective medical examinations and treatments (Wittchen, 2002; Dugas & Robichaud, 2007). As effective treatments for GAD are available (Fisher, 2006) and a shorter time elapsing between the onset of GAD and the first treatment seems to be associated with a larger treatment effect (Altamura et al., 2008), a better recognition would allow for earlier

and adequate treatment of GAD. This is an important consideration given that GAD is a strong predictor of later depressive disorder and other secondary disorders (Bruce, Machan, Dyck, & Keller, 2001; Kessler, 2002) and of therapy resistance in comorbid depression (Petersen et al., 2001). GAD also worsens the prognosis of chronic physical conditions (Ballenger, et al., 2001), while successful treatment of GAD leads to a considerable reduction of comorbid symptoms (Borkovec, Abel, & Newman, 1995; Newman, Przeworski, Fisher, & Borkovec, 2010). Hence, earlier identification and treatment of GAD may not only alleviate the impairment and distress caused by this disorder and reduce the considerable claim made by GAD patients on healthcare facilities, but may also have a preventive effect on other problems and increase the effectiveness of treatments for other (comorbid) disorders. For instance, Goodwin and Gorman (2002) showed that pharmacological treatment of GAD significantly decreased the risk for subsequent onset of major depression.

This chapter aims to provide diagnostic guidelines for improving the recognition of GAD, and for effectively distinguishing GAD from other conditions in clinical practice. These guidelines are mainly based on theoretical considerations and clinical experience. However, as it has been shown that anxiety disorders and comorbid disorders are difficult to detect when evaluating patients if the diagnostic process does not include a structured clinical interview, these guidelines should be used to arrive at a diagnosis in addition to, not instead of, such clinical interviews (Simon, 2009; Zimmermann & Mattia, 1999; Zimmermann & Chelminski, 2003b). After a description of the clinical presentation of GAD, differential diagnostic issues will be addressed and illustrated with a case example. Moreover, the validity of the diagnostic criteria of GAD is discussed. In addition, implications for the forthcoming DSM-V are addressed, and suggestions for further research are provided to determine whether the suggested guidelines should be built into future diagnostic interviews.

2.2 | Clinical presentation

‘Last night we went to bed and my boyfriend had a sore throat. He soon fell asleep and I listened to him snoring, and that’s when it started. I was thinking, what if he falls ill and can’t go to work tomorrow. Then he’ll have to call in sick. But what if his throat is so sore that he can’t speak, then I’ll have to make the call. But who do I call? Do I call the company he’s deployed at now, or do I call the company he actually works for? And what if I call the wrong company? He might get fired. And my own contract will end in two months … so what if they don’t renew it… then we’ll end up with no money and won’t be able to pay for this house anymore.’

The quotation above is the answer a patient gave when asked to describe a recent worrying episode. On further questioning, it turned out that such a chain of thoughts was not a one-off incident. It was typical for her way of thinking; everyday problems (here: a partner suffering from a sore throat) result in a series of 'what-if' thoughts, which eventually lead to a 'disastrous' prediction (in this case: 'We're going to lose our house').

Because individuals with GAD are highly sensitive to threat in general, particularly when it has personal relevance, they frequently observe possible threats (Aikins & Craske, 2001; Barlow, 2002). In response to these anticipated 'dangers', fight-or-flight reactions are activated. In most anxiety disorders (such as specific phobias or social anxiety disorder) it is generally clear what needs to be escaped or avoided (e.g., spiders or social situations), but in GAD there is no clear threat from which to escape or to attack, due to the often common nature and the low likelihood of occurrence of the worrying themes that bring about anxiety (Aikins & Craske, 2001). One of the few remaining coping resources that GAD patients deploy to deal with the observed risks is to use their cognitive capabilities to find ways to avoid the anticipated danger (Borkovec, 2002). This mental strategy of trying to prevent catastrophes from happening by worrying about them is reinforced in two ways. Worrying is positively reinforced as it results in a decreased physiological and emotional response (Vrana, Cuthbert, & Lang, 1986; Borkovec & Hu, 1990), and negatively as the feared catastrophes generally do not come true, i.e., not many disasters actually occur on a day-to-day basis (Borkovec, Hazlett-Stevens, & Diaz, 1999). Consequently, beliefs about worrying as a helpful strategy can arise, which result in an increased use of worrying as a strategy to cope with anticipated danger. Finally, GAD patients may continuously anticipate possible problems in their mind as a result of which they seem to 'live in the future' instead of living in the present (Borkovec, 2002).

Contrary to the (supposed) benefits of worrying, there is some evidence that this cognitive activity serves the same maladaptive purpose in patients with GAD as avoidance does for patients with phobias. For instance, patients with GAD mainly talk to themselves when they are worrying and are less likely to engage in imagery, at rest as well as during worry episodes (Freeston, Dugas, & Ladouceur, 1996; Rapee, 1993; Borkovec & Inz, 1990). As the process of creating images of potential danger would elicit more substantial negative affect and autonomic activity, it has been suggested that a verbal-linguistic kind of thinking about upcoming problems serves to avoid the negative affect associated with the threat (Borkovec, Alcaine, & Behar, 2004). As such, like any avoidance response, worry precludes emotional processing of the anxiety reaction (Borkovec, 1994). Moreover, it might lead to a strengthening of the tendency to worry (Borkovec, Robinson, Pruzinsky, & DePree, 1983), and possibly contributes to a spreading of anxious meanings to previously neutral stimuli (Thayer, Friedman, Borkovec, Johnsen, & Molina, 2000). Further, GAD patients lack the experience

that the 'catastrophes' they try to prevent from happening by worrying, would also not have occurred if they had not worried about it. GAD patients will thus remain more or less trapped in 'living in an illusion' (Borkovec, 2002): i.e., much time is spent thinking about things that only exist in their own mind, because they are convinced that negative events are prevented by worrying about them, and no or little attention is paid to real life because there is always a new danger that needs to be anticipated.

2.3 | Differential diagnosis: A case example and general guidelines

Linda (identifying information was changed to ensure confidentiality) is a 39-year-old woman, working as a high-school teacher. She is married and has two children. She is referred to a psychologist after she called in sick at work. Linda reports being sad and hopeless. She feels tense and nervous, has problems with sleeping and is tired all the time. She has difficulty in enjoying things and is not very interested in daily life. She worries about anything and everything, and calls herself 'a real 'doom and gloom' type of a person who sees danger lurking everywhere'. Examples of recent worry themes are the possible negative consequences of her calling in sick, her personal health, her upcoming 40th birthday party, and her younger brother moving house. Her complaints have increased in the last two years as a result of the reorganisation at her work and her own change of house two years ago. However, Linda reports that she was often nervous and worried when she was a child. Three months before she went to consult her GP Linda called in sick at work, 'because otherwise all I'll do is worry in case I said or did something wrong.' When asked whether she avoids things or does things to deal with her anxiety and worry, she reports keeping track of the schedules of seven people that are close to her. She telephones her parents, brother, sister and two friends very often, and then casually asks them about what they will be doing in the near future. She records these activities in a diary, along with the upcoming activities of her partner, who is the other person whose schedule she tracks closely.

This example was taken from an intake interview at an outpatient treatment center. It illustrates how complicated the differential diagnosis of GAD can be. Based on this preliminary information several diagnoses could be considered. The worrying, nervousness, feelings of tension, sleeping problems, and tiredness could be indicative of GAD, but the sad mood, fatigue, diminished interest, and lack of joy could be indicative of a depressive episode or dysthymia as well. The worries about saying or doing the wrong thing and her own health could be an example of GAD worrying, but might also be indicative of social anxiety disorder or hypochondriasis. Further, keeping track of the schedules of seven people is a reason to screen for the presence of obsessive-compulsive disorder (OCD). However,

Linda was diagnosed with only GAD. Before addressing the considerations related to this, we first continue to discuss the differences between GAD, 'normal' worrying, and various other psychological disorders. Table 2.1 summarizes the differential-diagnostic guidelines[1].

Table 2.1 | Differential-diagnostic considerations for generalized anxiety disorder (GAD).

GAD	Normal worrying
1. Persistent symptoms resulting from the worrying 2. Functioning severely impaired by the worrying	1. No persistent symptoms 2. Functioning not (severely) limited
GAD	**Other anxiety disorders in general**
1. Worrying about minor, everyday life events 2. Worrying about transient, shifting issues.	1. Worrying about one or some major issues 2. Worrying largely about an invariant stimulus, mostly concerning the specific disorder
GAD	**Adjustment disorder**
1. Symptoms have been present for at least 6 months 2. Worrying is perceived as uncontrollable	1. Symptoms have lasted for less than 6 months 2. Worrying is perceived as controllable
GAD	**Panic disorder**
1. Anxiety attacks interpreted as indication that worrying is threatening/harmful 2. No agoraphobic avoidance behavior	1. Symptoms interpreted as indicative of fainting, losing one's mind, heart attack, loss of control or dying 2. Often agoraphobic avoidance behavior
GAD	**OCD**
1. Compulsive behavior focused on relational situations and achievement 2. Compulsive behavior serves to prevent worrying 3. Concerns about realistic, common issues 4. Worrying mainly verbal-linguistic 5. Worrying is perceived as egosyntonic; often an ambivalent attitude towards worrying 6. Content of worrying is dynamic	1. Compulsive behavior focused on objects 2. Compulsive behavior serves to avert danger 3. Obsessions often considered as strange or inappropriate 4. Obsessions also in images 5. Obsessions are perceived as obtrusive, undesirable and egodystonic 6. Obsessions have a static content
GAD	**Social phobia**
1. Focus of worrying varies 2. Little to no avoidance of (social) situations 3. Functioning impaired as a result of the worrying	1. Focus of worrying is always negative assessment and/or embarrassing behavior 2. Avoidance of social situations as much as possible 3. Functioning hampered as a result of the avoidance behavior
GAD	**PTSD**
1. Sometimes associated with exposure to a traumatic event 2. No re-experiencing symptoms	1. By definition caused by a traumatic event 2. Presence of re-experiencing of the traumatic event

1 These differential-diagnostic considerations are partly based on Dugas and Robichaud (2007).

GAD	Hypochondriasis
1. Fear of contracting a disease 2. Worrying pertains to ever-changing, common issues 3. Alerted to physical sensations only periodically 4. Little to no monitoring of the body, and if so, only periodically 5. Medical examination reassures	1. Convinced of having a disease 2. Worrying always pertains to health 3. Alerted to physical sensations continuously 4. Monitoring of the body. 5. Medical examination will reassure briefly if at all
GAD	**Insomnia**
1. Worrying may be present at any time 2. Worrying about transient, shifting issues 3. Complaints are perceived as the result of worrying	1. Worrying typically in the evening 2. Worrying about the sleeping problems, or consequences of these problems 3. Complaints are perceived as the result of not sleeping
GAD	**Somatization disorders**
1. Predominance of anxiety 2. Worrying about transient, shifting issues	1. No, or mild, anxiety 2. Recurrent thinking about causes and consequences of physical complaints
GAD	**Mood disorders**
1. Muscular tension complaints in neck and shoulders 2. Worrying concerns future events 3. Aimed at avoiding or preventing danger ('what if?') 4. Predominance of feelings of anxiety 5. Absence of anhedonia	1. Little to no muscular tension complaints in neck and shoulders 2. Ruminating on the past 3. Aimed at establishing understanding and meaning ('why?') 4. Predominance of depressed mood 5. Presence of anhedonia

Many people worry from time to time, often about issues that are comparable to the themes that GAD patients worry about (Craske, Rapee, Jackell, & Barlow, 1989; Roemer, Orsillo, & Barlow, 2002). Thus, it has first to be determined whether the worrying is normal or pathological, by examining whether the worrying results in persistent symptoms and influences daily functioning.

In case the worrying is pathological, the mere presence of it is not sufficient for classifying GAD, as many patients who report clinically significant symptoms and functional impairments related to their worrying fail to meet the full criteria for GAD, particularly the associated symptoms criterion (Lawrence & Brown, 2009). Such 'subsyndromal' cases are under the current DSM-criteria classified as Anxiety Disorder, Not Otherwise Specified. Further, worrying is not unique to GAD, but a feature of several psychological disorders (a so-called transdiagnostic process; Harvey, Watkins, Mansell, & Shafran, 2004). Compared to other disorders in which worry is prominent, the process characteristics of worrying seem to define the distinction, e.g., the frequency, number and kind of issues, and the perceived uncontrollability of the worrying. As such, assessment should be directed at these

characteristics. To examine the number of issues involved, patients can be asked whether they think their worries will be over once the topic they currently worry about is resolved. When patients reply in the affirmative, GAD is likely not warranted, as the worrying of GAD is by definition concerned with more than one topic. In clinical practice patients with GAD typically reply to this question by stating that they expect there will soon be another thing to worry about, once their current worry issue is over. In such cases, further GAD symptoms must be probed for, to either confirm or rule out the diagnosis.

The kind of themes patients worry about can be helpful in distinguishing GAD from other anxiety disorders. More specifically, worrying about minor, everyday life events is very characteristic of GAD patients, as almost all of them respond 'yes' to the question: 'Do you worry excessively about minor things?', compared to approximately 50% of patients diagnosed with another anxiety disorder (Sanderson & Barlow, 1990). Thus, a negative reply to this question is an indication that GAD might be ruled out. A final process characteristic that should be screened for is the perceived uncontrollability of the worrying. As the uncontrollability of worrying is a defining characteristic of GAD (APA, 2000), the diagnosis is ruled out when patients think of their worries as controllable. However, this does not imply that in other disorders worrying is simply viewed as annoying, but controllable (see Harvey et al., 2004). Hence, when patients report having difficulty in controlling their worrying, further screening is needed to arrive at the diagnosis at hand. Therefore, specific guidelines for distinguishing GAD from other diagnosis are provided below.

2.4 | Differential diagnosis: Specific guidelines

When structured clinical interviews are used, in clinical practice most DSM-IV-TR Axis-I disorders (APA, 2000) can be reliably distinguished from GAD by their defining characteristics, and the process characteristics described above (see Scott & Sembi, 2006; Zimmermann & Mattia, 1999). But even if structured interviews are used, in cases where worry is prominent it still can be difficult to assess whether a patient suffers from GAD, from another psychological disorder, or from comorbid GAD. Therefore, specific guidelines are described that are based on clinical experience and on theoretical considerations from the published literature.

First, in response to a clear stressor (such as a conflict at work or an argument with a relative) patients may present with being nervous and worried, and feeling tense. Such symptoms are defining characteristics of an adjustment disorder, but are also very similar to symptoms that define GAD. The difference with GAD is that the symptoms of an adjustment disorder by definition may not exist for longer than six months after the stressor (or the consequences of the stressor) has (have) disappeared, whereas the GAD symptoms have to

be present for at least six months (although this criterion has been debated, as will be further discussed in the Discussion). However, in some cases this time criterion does not provide clarity, particularly if it takes a long time for the stressor (or its consequences) to subside. For example, the stressor 'being in debt' can lead to debt support with payment schemes continuing for many years, which may result in the patient having to live on a limited budget for a long time. This in turn may lead to years of worrying about various common issues, e.g., whether there will be enough food, whether the children can go on their school's outing, or whether bills can be paid on time. In addition to the fact that all these concerns can be traced back to the consequences of one and the same stressor, patients with an adjustment disorder do not (or hardly) perceive the worrying as uncontrollable.

Further, as with other anxiety disorders, GAD can result in anxiety/panic attacks. These attacks may in fact be the reason for patients to seek professional help, as a result of which a diagnosis of panic disorder seems obvious. The main difference seems to be the focus of the fear. Whilst patients with a panic disorder are afraid of passing out, losing control, going crazy, getting a heart attack and/or dying, patients with GAD think of the anxiety attacks mainly as an indication that the worrying is not good for them and that (in the future) they may get heart problems as a result of the continuous worrying. Further, patients with panic disorder often show agoraphobic avoidance, whereas patients with GAD do not (or hardly ever) show such behavior.

The distinction between OCD and GAD can be complicated by the obsessions as well as the compulsions. In most cases, compulsive behavior is indicative of OCD. However, patients with GAD are also known to engage in checking behaviors. A main difference is the focus of the checking behavior. Patients with OCD tend to focus their checking on objects, whereas GAD patients tend to focus their checking on relational situations and achievement (Coleman et al., in press). Furthermore, in OCD the behavior is performed to avert danger (e.g., contamination), whereas GAD patients seem to use checking behavior as a strategy to avoid (1) triggers that might start the worrying process, or (2) affective experiences (Schut, Castonguay, & Borkovec, 2001). Obsessions more often complicate the differential diagnosis between GAD and OCD, especially in the absence of compulsions. A number of guidelines may be useful to distinguish obsessions from worrying (Dugas & Robichaud, 2007). The worrying of GAD patients often concerns realistic, everyday matters (e.g., health, performance at work, the household, and relationships), whereas patients with OCD often think of their obsessive thoughts as strange or inappropriate, especially if these pertain to aggressive, blasphemous or sexual themes. As a result, obsessions are often considered to be undesired, as opposed to worrying which is seen as more egosyntonic and as less undesirable. Morever, many GAD patients have an ambivalent attitude towards their worrying, as is reflected in the positive and negative beliefs they hold about worrying (Wells, 1995). Another difference is that obsessions

may occur as vivid images, whereas worrying is mainly verbal-linguistic in nature (Borkovec, 1994). Perhaps the most distinctive item is the static content of obsessions as opposed to the dynamic content of worrying. Whereas OCD patients report that they experience the same intrusion over and over again, GAD patients worry about a wide variety of issues, and the worrying is perceived more as a developing scenario.

Patients with social anxiety disorder (SAD) may also present with anxiety and concerns about various situations, such as parties, meetings, hobbies and sports clubs, lively places and face-to-face conversations (Heimberg, 1995). The concerns and the multitude of situations appear to be similar to GAD. Probing for the underlying fear can be helpful to distinguish GAD from SAD. In the case of SAD the focus will always be the fear of being judged negatively or behaving in an embarrassing or humiliating manner (Dugas & Robichaud, 2007). Although GAD patients may have similar concerns from time to time, they also report various other concerns. A final distinctive feature concerns the avoidance behavior: patients with SAD avoid the situations that they fear as much as possible, and it seems to be primarily this avoidance behavior that disrupts their social and/or professional functioning. Patients with GAD at times report that they also try to avoid (social) situations or events that could lead to worrying, but their suffering is mainly the result of their excessive and uncontrollable worrying.

Worry-like processes, such as dwelling on past traumatic event(s), are a feature of posttraumatic stress disorder (PTSD) and have been conceptualized as a factor in the escalation and persistence of this disorder (Wells & Mathews, 1994). A first distinction is that PTSD is by definition caused by exposure to a traumatic event, whereas GAD is not. However, several studies indicate that exposure to trauma, particularly assaultive trauma, is associated with GAD (Brawman-Mintzer, Monnier, Woliztzsky, & Falsetti, 2005; Ghafoori et al., 2009; Roemer, Molina, Litz, & Borkovec, 1997). Inquiring about the presence of re-experiencing symptoms, the second main characteristic of PTSD, is therefore indicated when patients report that they have experienced a trauma and are worrying about the trauma and future negative events.

Although patients suffering from hypochondriasis tend to worry about illness-related topics but not about general issues (Bouman & Meijer, 1999), their persistent concerns for their own health of can be reminiscent of GAD (Wells & Hackmann, 1993). Based on clinical experience, the main distinction seems to be whether patients fear that they will get a serious disease (GAD) or whether they are convinced they already suffer from it (hypochondriasis). Further, patients with hypochondriasis seem to be inclined to pay attention to slight physical changes, which are considered to be evidence of a serious disease, and to regularly check their body for indications of a serious disease. Like patients with hypochondrias, people with GAD also regularly visit their GP, but mainly to discuss physical symptoms that result from

their worrying rather than to seek reassurance about whether or not they have a serious disease. Moreover, if the concerns of GAD patients pertain to their health they often report that medical examination leads to reassurance, whereas most hypochondric patients do not.

People with insomnia often contribute their sleep disturbance to intrusive thoughts or a racing mind (Harvey, 2000, 2001). As it has been found that the pre-sleep cognitive activity of patients with insomnia is focused on several topics, such as solving problems and general worries, and as sleeping problems are a diagnostic feature of GAD (APA, 2000), it may be difficult to distinguish GAD from insomnia. However, three characteristics may be helpful in defining the difference in clinical practice. First, the worrying of patients with insomnia typically starts in the evening, when patients think of going to bed. Further, the focus of the worrying is almost always the sleeping problems, or is related to that topic. For example, when worrying about unsolved problems, patients with insomnia often report that they are afraid that they cannot sleep if they do not solve the problem at hand, whereas GAD patients think of all kinds of 'disasters' that can happen if they do not solve such a problem. A final difference is that patients with insomnia think their complaints are the result of not sleeping, whereas GAD patients see the worrying as their main problem.

Somatization disorders, particularly undifferentiated somatoform disorder, may overlap with GAD as well and be difficult to distinguish diagnostically. The main difference is the presence and particularly the predominance of anxiety symptoms in GAD, which is not typical of somatization disorders (Rickels, Rynn, & Khalid-Khan, 2002). Further, when somatization patients report problems of recurrent thinking, they mainly ruminate about the (possible) causes of their physical complaints and/or worry about their possible consequences.

As already mentioned in the introduction, given their high rate of lifetime comorbidity, shared genetic factors, and the overlap in diagnostic criteria, debate is ongoing about whether GAD and major depressive disorder (MDD) should be classified as distinct disorders in the upcoming DSM-V. As a result of these commonalities, MDD may be the most difficult disorder to distinguish from GAD. In clinical practice, especially the overlap in somatic symptoms, the tendency to ruminate, which resembles the worrying of GAD patients, and the presence of a depressed mood complicate the differential diagnosis. As for the somatic symptoms, only the experience of muscle tension (in particular in neck and shoulders) has been found to be specific to GAD (Joormann & Stöber, 1999).

More important with respect to the differential diagnosis is the thinking style, as worrying is one of the main features of GAD. A first distinction is the focus in time of the repetitive thoughts. GAD patients usually focus on negative things that might happen in the future with the aim to avoid or prevent danger, whereas depressive patients predominantly ruminate about negative things that have happened in the past in an attempt to establish understanding and meaning (Wells, 2009). Stated in a different way, the thinking of worriers is characterized by a

chain of 'what if…?' questions and that of depressive patients by 'why?' questions (Watkins & Baracaia, 2001). However, this difference can be misleading, as sometimes worrying also concerns negative past events (Dugas & Robichaud, 2007). An example of this would be a patient who is continuously worrying about a mistake he made at work some time ago. Although it is about a negative event that actually did take place, the question is whether the patient ruminates about the event as (yet) another example of his failure ('why?'), or whether he worries about the possible negative consequences of his mistake in the future, e.g., a negative job appraisal or dismissal ('what if?').

A final differential diagnostic problem is the presence of a depressed mood, because GAD patients often also report that they feel sad. However, the key characteristic of GAD with respect to mood is feelings of anxiety. Thus, when patients report to become depressed as a result of their negative thinking, this seems indicative of a mood disorder. Further, when patients report to feel both anxious and depressed, it may be helpful to find out whether patients are anhedonic, as low positive affect has been found to be characteristic of MDD, but not of GAD (Krueger, 1999). Furthermore, the clinician can ask whether patients think their worrying about future negative events is the problem or their sad mood. Patients with GAD commonly report that they think that if their worrying would be treated successfully, their sadness will be over.

In Linda's case the diagnosis of GAD was established. A mood disorder was ruled out for several reasons. The worrying turned out to mainly concern negative events that might occur in the future, even in the case of worrisome thoughts she had about mistakes or wrong comments she made at work. She was not ruminating on how silly she had been and why she acted this way, but rather what the consequences of such an error or comment might be: 'I'll be reprimanded by my boss and miss out on my salary raise, or my colleagues might think I'm stupid ... and what if my mistake caused damage for my employer … then I'll be fired!'. Further, she felt that her sleeping problems appeared to be related to her worrying, which started as soon as she relaxed. Finally, she did not meet other important criteria of MDD. Her feelings of sadness and her difficulty to enjoy things were only periodically present. Further, her appetite was unchanged, her weight remained stable, and she reported no significant feelings of guilt or worthlessness. Finally, Linda did not think of death or suicide, and had no suicidal ideation. Although some of Linda's scenarios concerned the fear of being judged negatively by others, one reason for not diagnosing her with SAD was that she hardly avoided social situations. Linda did call in sick at work, but she did this in order not to worry about (mistakes she made at) work and not so much to prevent a possible negative judgement by her colleagues. Moreover, her calling in sick led to further worries about its potential consequences. Another reason for not diagnosing her with a social phobia was the fact that Linda did not view social situations as problematic *per se*. Although she was concerned

about social situations at the time of the intake interview, she thought that when these worries were over she certainly would find something else to worry about, as was always the case. Further, although she reported worries about her health, hypochondriasis was excluded as Linda did not prove to be preoccupied with having a serious disease or illness. She was only sometimes afraid of getting a serious disease, and could be reassured about not having such a disease relatively easily. OCD could be ruled out by tracing the function of her behavior. Linda reported that if she would not keep track of the schedule of those seven people, she would worry about what might have happened to them if she would not be able to reach them on the phone or at home one day. As long as she knew where everyone was, she could prevent ending up in a scenario of catastrophic thinking. Finally, Linda did not report to have experienced a traumatic event, and as such the diagnosis of PTSD was ruled out.

2.5 | Controversies surrounding the diagnostic criteria of GAD

It should be noted that the guidelines described above emerged from the GAD criteria as presented in DSM-IV-TR (APA, 2000), the validity of which is still questioned despite considerable modifications in the criteria since the introduction of GAD in the DSM-III (APA, 1980). Current controversies predominantly relate to the criteria for duration and excessive worry. With regard to the first, several studies could not confirm the 6-month criterion as being clinically meaningful (Bienvenu, Nestadt, & Eaton, 1998; Kessler et al., 2005a; Angst et al., 2006). No significant differences in work impairment, distress, and comorbidity were found between groups of patients with generalized anxiety syndromes defined by varying duration (Angst et al., 2006). This suggests that the DSM-V classification could identify a clinically significant GAD even if the duration threshold is lowered (Andrews et al., 2010). However, future research is needed to investigate whether such a reduced duration will reduce the discriminant validity of GAD relative to normative anxious reactions to life events, or to adjustment disorders. As for the excessive worry criterion, excessiveness is a rather ambiguous term and there is no clear guidance on defining worry as excessive (Ruscio et al., 2005). The elimination of the additive ‘excessive’ from the criteria could be associated with an increase in inter-rater reliability, and does not seem to substantially change the type of person identified as having GAD, as excessive and non-excessive worriers who meet all other DSM-IV-TR criteria for GAD have only been shown to differ in terms of the onset and the severity of the symptoms (Wittchen, Kessler, Zhao, & Abelson, 1995). In the meantime, if the excessiveness criterion would be omitted from the GAD definition in DSM-V, the classification would identify a milder form of the disorder, and the prevalence of the disorder would increase substantially (Andrews et al., 2010). Therefore, it seems most beneficial for

the classification of GAD to provide further details on what excessive actually means (e.g., an operationalization in terms of the amount of time per day spent on worrying).

The debate is further concerned with the number of associated symptoms that are needed for making the diagnosis. Currently, three out of six symptoms are required, but it is not well-established whether or not this is the optimal subthreshold (Weisberg, 2009). Although several authors have suggested that a change in the number of symptoms could improve the specificity of the diagnosis (Bienvenu et al., 1998; Rickels & Rynn, 2001), it was recently found that requiring only two associated symptoms had little effect on the prevalence of GAD in community samples (Ruscio et al., 2007). If changing the number of associated symptoms has little effect on the prevalence of the disorder, there seems little point in retaining this criterion for diagnosing GAD. It may be preferable to focus on the presence of certain symptoms, such as restlessness, feeling keyed up, and muscle tension, which seem to be endorsed by most people who meet the DSM-IV-TR-criteria for GAD (Andrews et al., 2010). However, it remains to be investigated whether these specific symptoms indeed increase or at least maintain the discriminant validity of the GAD diagnosis as compared to other anxiety or mood disorders.

A final point of debate pertains to the supposed hierarchy in the DSM-IV-TR-criteria of GAD (APA, 2000), which is likely a conceptual remnant of GAD's residual status in DSM-III (Andrews et al., 2010). Recent studies could not confirm the validity of the criterion that GAD may not occur exclusively during the course of a mood disorder, as no differences could be found between patients with MDD and comorbid GAD, and patients with GAD exclusively within the course of MDD (Lawrence, Liverant, Rosellini, & Brown, 2009; Zimmermann & Chelminski, 2003a). Moreover, instead of promoting diagnostic parsimony, the hierarchical exclusion criterion seems to result in the false exclusion of patients from the GAD diagnosis (Lawrence et al., 2009). Therefore, it has been suggested to reconsider the utility of the hierarchical criteria for DSM-V.

Interestingly, the second main criterion of GAD, i.e. having difficulties controlling the worrying, has been hardly questioned. The perception of control over worry is negatively associated with anxiety, i.e., the more control individuals perceive over their worry, the fewer anxiety symptoms they report (Rapee, Craske, Brown, & Barlow, 1996). Moreover, rather than the worrying itself negative beliefs about worrying appear to be a distinguishing characteristic of GAD (Ruscio & Borkovec, 2004). In terms of their beliefs about the uncontrollability of their worrying, GAD patients were found to be significantly different from non-anxious and anxious individuals who do not worry. Further, negative beliefs about worrying seem to determine the difference between worriers who do and worriers who do not meet the GAD criteria (Tallis, Davey & Capuzzo, 1994; Ruscio & Borkovec, 2004; Davis & Valentiner, 2000). As such, it has been suggested that this subjective interpretation of worrying might be the most

important feature of GAD (Ruscio & Borkovec, 2004). As negative beliefs about worrying do not exclusively concern the uncontrollability of worrying but also the harmful consequences of worrying (Wells, 1995), this criterion might be extended as follows: 'the person finds it difficult to control the worry *and/or thinks worrying is harmful or dangerous*.' However, it should be noted that the contribution of the difficult-to-control criterion to the classification of GAD might be explained by the excessiveness criterion, as it appears that a worry cannot be excessive but still controllable. Further, it has recently been found that if this criterion was omitted in DSM-V, it would have little impact on the prevalence rates in community samples (see Andrews et al., 2010). As data on this issue are sparse, it needs to be examined whether this criterion can be omitted, needs to be altered (e.g., adding beliefs about the dangers of worrying, or replacing the beliefs about uncontrollability by beliefs about the dangers), or has to be left unchanged in DSM-V. An important consideration with respect to this decision should be whether the beliefs about the uncontrollability and/or dangerousness of worrying do help distinguish GAD from other anxiety and mood disorders and from healthy controls.

The difficulties in diagnosing GAD may also reflect the limitations of a categorical diagnostic system such as the DSM, in which cut-points are provided on dimensional data. As several researchers have noted that many patients fail to meet full criteria for GAD, but nevertheless experience clinically significant symptoms and have similar levels of functional impairment to those with the disorder (Kessler et al., 2005a; Lawrence & Brown, 2009), the current DSM criteria for GAD might be too restrictive, and therefore fail to provide adequate coverage for the range of symptom presentations associated with worry. As this threshold problem is not unique to GAD (Pincus, Davis, & McQueen, 1999; Lawrence & Brown, 2009), and several other diagnostic categories might also be excessively restrictive (e.g., Stein, Walker, Hazen, & Forde, 1997), it has been suggested that dimensional elements (e.g., clinical severity ratings) should be adopted in future editions of the DSM, in order to acknowledge the dimensional nature of disorder features and to improve diagnostic reliability (Brown & Barlow, 2005). However, as yet it has to be investigated at what level such elements should be incorporated in the current diagnostic system (e.g., dimensional severity ratings for the existing DSM disorder constructs or dimensional assessment of higher-order constructs, which are not currently recognized by the DSM, such as temperament, personality, and genetics; Brown & Barlow, 2005).

2.6 | Discussion

GAD is a highly prevalent disorder, which is associated with persistent suffering and considerable impairments. If left untreated, the prognosis is poor. Unfortunately, because the diagnosis of GAD is poorly recognized, GAD patients do not receive adequate treatment. As effective treatments are available (Fisher, 2006), the misdiagnosing of GAD contributes to unnecessary suffering and claims on mental healthcare facilities. One problem is the high comorbidity, which significantly lowers the probability that GAD is successfully diagnosed and treated (Wittchen et al., 2002b). Therefore, in this chapter clinical guidelines are provided, which may contribute to the successful identification of GAD. However, these guidelines emerged from the DSM-IV-TR (APA, 2000) criteria for GAD, which are currently surrounded by considerable debate. These controversies are described in this chapter, as well as suggestions to solve them. However, based on the currently available evidence none of these issues can be solved, so further research is needed to assess whether these suggestions will improve the specificity, validity and reliability of the diagnosis of GAD, or whether it may prove better to leave the criteria for GAD unchanged. The same is true for the diagnostic guidelines as provided in this chapter. As most of them are based on clinical experience, these guidelines should be examined prior to the publication of the DSM-V to determine whether they should be adapted into future versions of structured diagnostic interviews (e.g., the SCID-I) instead of supplementing them, as suggested in the introduction. For instance, future research could examine whether absence of anhedonia is in fact an important factor in distinguishing GAD from depressive disorders.

Chapter 3

A hierarchical model for the relationships between general and specific vulnerability factors and symptom levels of generalized anxiety disorder

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A hierarchical model for the relationships between general and specific vulnerability factors and symptom levels of generalized anxiety disorder.

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Abstract

The present study examined a hierarchical model for the relationships between general and specific vulnerability factors and symptom manifestations of generalized anxiety disorder (GAD). A clinical sample of patients with GAD (*N* = 137) completed a set of self-report questionnaires for measuring neuroticism, extraversion, intolerance of uncertainty, metacognitive beliefs, and symptoms of generalized anxiety (i.e., worry) and depression. A bootstrapping analysis yielded support for a model in which the relation between the general vulnerability factor of neuroticism and symptoms of GAD were mediated by the specific vulnerability factors of intolerance of uncertainty and negative metacognitions. Implications for the classification and treatment of GAD are discussed.

3.1 | Introduction

As stated in Chapter 2, generalized anxiety disorder (GAD) is among the most common mental health problems, and leads to severe distress and functional impairments (Yonkers, Warshaw, Massion, & Keller, 1996). Some authors have referred to GAD as the 'basic anxiety disorder', suggesting that a better understanding of the etiological factors for GAD may also increase our knowledge about the origins of other anxiety disorders, and perhaps unipolar mood disorders as well (Mineka, Yovel, & Pineles, 2002; Roemer, Orsillo, & Barlow, 2002).

As to the etiology of GAD, it has been proposed that the general vulnerability factor of neuroticism plays a prominent role (Mineka, Watson, & Clark, 1998). This notion is mainly based on research that examined the relationship between neuroticism and emotional disorders, which has demonstrated that there are clear-cut positive associations between this personality trait and all anxiety disorders (Brown, Chorpita, & Barlow, 1998; Clark & Watson, 1991; Watson, 2005), with the link to GAD emerging as the strongest (Kotov, Watson, Robles, & Schmidt, 2007). However, critics have argued that neuroticism can better be viewed as a universal concomitant of abnormal functioning that by itself has little explanatory value (Claridge & Davis, 2001; Ormel, Rosmalen, & Farmer, 2004). Further, it has been pointed out that (high) neuroticism and GAD seem to refer to a similar construct (Hettema, Prescott, & Kendler, 2004), which is supported by studies indicating that neuroticism is hardly distinguishable from chronic worry, the key feature of GAD (Kotov et al., 2007; Mineka et al., 1998; Watson, 1999; Watson, Gamez, & Simms, 2005). Thus, although it is generally assumed that neuroticism is involved in various emotional problems, little is known about the precise mechanisms by which neuroticism exerts its influence on specific syndromes. The

examination of such mechanisms can be justified because their identification might lead to the development of more effective treatment methods.

In an attempt to conceptualize the role of neuroticism in GAD and other emotional disorders in a more satisfactory way, several authors have proposed hierarchical models for the vulnerability of these problems. Such models imply that neuroticism should be regarded as a higher-order vulnerability factor, while there are more specific second-order factors that intermediate between this basic personality trait and various manifestations of emotional problems (Taylor, 1998). Empirical tests of such models have yielded interesting results. For example, Norton and Mehta (2007), Norton, Sexton, Walker, and Norton (2005), and Sexton, Norton, Walker, and Norton (2003) tested a hierarchical model in which anxiety sensitivity (AS), the tendency to be afraid of physical anxiety symptoms based on the belief that they have negative consequences (McNally, 1999), and intolerance of uncertainty (IU), a dispositional characteristic which results from a set of negative beliefs about uncertainty and its implications (Dugas & Robichaud, 2007), were included as second-order factors. They found AS and IU to differentially mediate between the higher-order factor of neuroticism, and symptoms of various anxiety and mood disorders. With regard to GAD, IU but not AS was found to partially mediate between neuroticism and worry, the core symptom of this anxiety disorder. Interestingly, IU also emerged as a partial mediator in a model explaining depressive symptoms (Norton & Mehta, 2007; Norton et al., 2005). Further, results indicated that another higher-order factor, i.e., extraversion, made a significant direct contribution to the model of depressive symptoms, but not to the model explaining worry, which suggests that this basic personality factor might play a differential role in the etiology of GAD and depression (Clark, Watson, & Mineka, 1994; Goldberg, 2008; Mineka et al., 1998).

Although previous studies have provided insight in the hierarchical model of vulnerability for anxiety disorders and depression (Norton & Mehta, 2007; Norton et al., 2005; Sexton et al., 2003), no definitive conclusions can be drawn with regard to GAD because the research conducted so far suffers from a number of limitations. First of all, few clinical patients with GAD have been included in these studies. That is, Norton and Mehta (2007) and Sexton et al. (2003) relied on non-clinical samples of psychology students, while Norton et al. (2005) used 125 outpatients diagnosed with various emotional disorders, with only 8% of the participants meeting the DSM-IV-criteria of GAD (APA, 2000). Therefore, the extent to which the results of these studies hold for specific clinical samples is unclear, and should be further addressed.

Second, the studies of Norton et al. (2005) and Sexton et al. (2003) assessed the unique contributions of various vulnerability factors by means of a series of multiple regression analyses, which may lead to biased estimates due to the omitted parameter problem (Judd & Kenny, 1981). In response to this latter critique, Norton and Mehta (2007) carried out a formal mediation analysis using structural equation modeling (SEM) in order to investigate

to what extent disorder-specific vulnerability factors account for the relationship between general vulnerability factors (i.e., high neuroticism and low extraversion) and symptom levels. Because the sample size in Norton and Mehta's study was quite large (*N* = 650), SEM allowed for assessing whether a predictor variable affects a dependent variable indirectly through one or more mediator variables (Sobel, 1982, 1986). However, a disadvantage of this analytic strategy was that it was not possible to determine (1) to what extent specific mediators accounted for the effect of the predictor on the outcome variable, and (2) the relative magnitudes of the specific indirect effects associated with each of the mediators. To address these problems, the current study employed a bootstrapping method for testing multiple mediation effects (Preacher & Hayes, 2008). This method will be discussed in more detail in the further course of this chapter.

A third and final shortcoming of previous studies examining the hierarchical vulnerability model with regard to GAD is that they have only focused on IU as a specific vulnerability factor. In recent years, metacognitive beliefs about worry have been described as another specific variable that may be involved in the vulnerability to GAD (Borkovec & Roemer, 1995; Davis & Valentiner, 2000; Wells, 1995; Wells & Carter, 1999, 2001). Briefly, such metacognitions can be defined as trait-like ideas and appraisals about worrying (Wells, 1999) and in patients with GAD two broad classes of metacognitive beliefs can be identified: positive metacognitions, which refer to the conviction that worrying can be used as a means of coping with threat (e.g., 'Worrying helps me cope with problems'), and negative metacognitions, which pertain to the problematic aspects of worrying (e.g., 'Worrying will make me go crazy').

The present study was conducted to replicate and extend previous work (Norton & Mehta, 2007; Norton et al., 2005; Sexton et al., 2003) by examining a hierarchical model of the vulnerability for GAD in a sample of patients suffering from this particular anxiety disorder. Apart from IU, metacognitive beliefs were included in the model as a second potential mediating variable. The main purpose of the study was to investigate the relationships between the general higher-order vulnerability factors of neuroticism and extraversion, the specific second-order vulnerability factors of IU and metacognitive beliefs, and symptoms of generalized anxiety (i.e., worry) in clinically referred GAD patients. To investigate the specificity of various general and specific vulnerability factors for GAD, their links to symptoms of depression (which is a common comorbid problem in patients with GAD) were also explored. First and foremost, it was investigated to what extent the expected relation between the higher-order factor of neuroticism and worry would be mediated by the second-order factors of IU and metacognitive beliefs. Further, in the case of depression, both the higher-order factors of neuroticism and (low) extraversion were expected to be associated with symptom levels, and here it was explored whether these links were also mediated by the second-order factors of IU and metacognitive beliefs (see Figure 3.1).

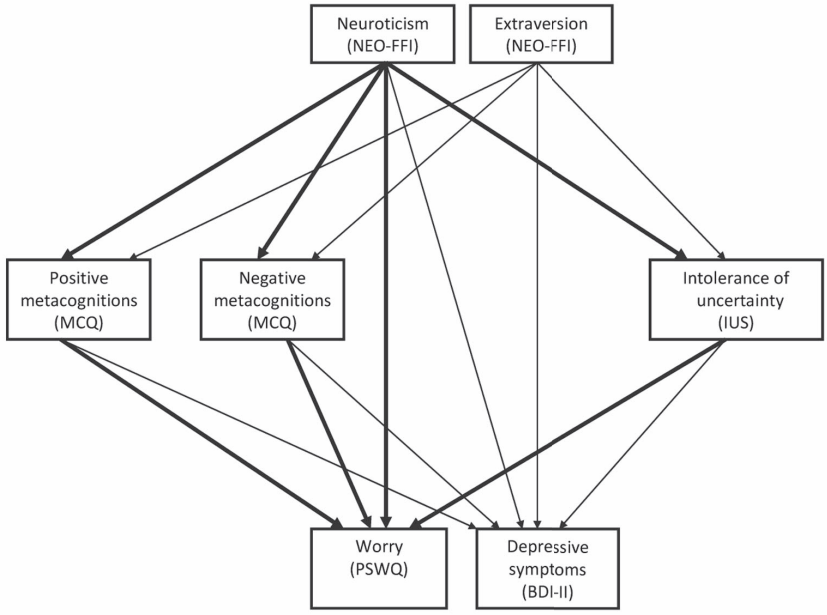

Figure 3.1 | Hypothesized hierarchical model of the vulnerability for GAD (bold lines) and comorbid depressive symptoms (regular lines).

3.2 | Method

3.2.1 | Participants

Participants were 137 patients with a primary diagnosis of GAD (101 women and 36 men; mean age = 35 years, range 19-66 years) who were referred for treatment to PsyQ, a community mental health center in Rotterdam, the Netherlands. The diagnosis of GAD was established by means of a semi-structured DSM-IV-based clinical interview (SCID-I; First, Spitzer, Gibbon, & Williams, 1994), which was administered by a trained psychologist. Most participants were married (32.1%) or living together (35.8%), 22.6% were single, and 8.0% were divorced or living separately from their partner. Three-quarter of the participants were full-time employed, 12.4% had a part-time job, and 8.8% were unemployed. The sample breakdown in terms of educational level was as follows: 19.7% had a low level of education, 41.6% an average level of education, and 38.7% a high level of education. More than half of the participants (57.8%) met the DSM-IV criteria for at least one comorbid axis-I diagnosis. The most common comorbid diagnoses were depressive disorder (21.8%), panic disorder (13.6%), social phobia (10.2%), somatoform disorder (8.8%), obsessive-compulsive disorder

(4.1%), dysthymic disorder (3.4%), specific phobia (2.7%), and insomnia (2%). Patients were not screened for DSM-IV axis-II disorders.

3.2.2 | Questionnaires and procedure

After patients had provided informed consent, they completed a number of questions pertaining to demographic characteristics along with a set of self-report scales, which were presented in random order to minimize possible order effects. For all questionnaires, the Dutch translations were used.

The *neuroticism* and *extraversion* scales of the *NEO Five Factor Inventory* (NEO-FFI; Costa & McCrae, 1992), a 60-item self-report scale for measuring the 'Big Five' personality factors: neuroticism, extraversion, openness, agreeableness, and conscientiousness. Both the original English and the Dutch version of the NEO-FFI have been demonstrated to possess sound reliability and validity in both clinical and community samples (Costa & McCrae, 1992; Hoekstra, Ormel, & De Fruyt, 1996). In the present study, Cronbach's alpha values were .87 for neuroticism and .82 for extraversion.

The *Intolerance of Uncertainty Scale* (IUS; Freeston, Rheaume, Letarte, Dugas, & Ladouceur, 1994) is a 27-item self-report measure which intends to assess 'emotional, cognitive and behavioral reactions to ambiguous situations, implications of being uncertain, and attempts to control the future' (Dugas, Freeston, & Ladouceur, 1994; p.56). The original French version (Freeston et al., 1994), the English version (Buhr & Dugas, 2002), and the Dutch version of the IUS (De Bruin, Rassin, Van der Heiden, & Muris, 2006) all have demonstrated comparable, adequate psychometric properties. In the current study, Cronbach's alpha of the IUS was .80.

The *Meta Cognitions Questionnaire* (MCQ; Cartwright-Hatton & Wells, 1997) is a 65-item self-report scale for assessing individual differences in positive beliefs about worry, negative beliefs about worry, beliefs about the need to control thoughts, metacognitive monitoring of thoughts, and the judgment of cognitive effectiveness. In the present study, we only employed the two subscales that are considered as most relevant to GAD (Wells, 1999), namely positive beliefs about worry (e.g., 'Worrying helps me to cope') and negative beliefs about worry (e.g., 'Worrying is dangerous for me'). The MCQ has been shown to possess good psychometric properties (Cartwright-Hatton & Wells, 1997), and this seems also true for the Dutch translation of the scale (Hermans, Crombez, Van Rijsoort, & Laeremans, 2002). In the present sample, Cronbach's alphas were .89 for the positive metacognitions and .93 for the negative metacognitions subscales.

The *Penn State Worry Questionnaire* (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990) is a widely used 16-item self-report scale for measuring the intensity and uncontrollability of worry, which is regarded as the key symptom of GAD. The PSWQ assesses a construct that

is separate from both anxiety and depression, and is capable of discriminating GAD from other anxiety disorders (Brown, Anthony, & Barlow, 1992; Meyer et al., 1990). Various studies have reported adequate psychometric qualities for the English (Startup & Erickson, 2006) and the Dutch version of the PSWQ (Van der Heiden, Muris, Bos, Van der Molen, & Oostra, 2009; Van Rijsoort, Emmelkamp, & Vervaeke, 1999). In the current study, a Cronbach's alpha value of .83 was found.

The second edition of the *Beck Depression Inventory* (BDI-II; Beck, Steer, & Brown, 1996) is a 21-item self-report index to assess the affective, cognitive, behavioral, somatic, and motivational components of depression, as well as suicidal ideas. This scale has been shown to possess sound psychometric properties (Beck et al., 1996), and this is also true for the Dutch BDI-II (Van der Does, 2002). The Cronbach's alpha value in the current study was .92.

3.3 | Results

3.3.1 | Data screening and outlier analysis

Prior to carrying out the main statistical analyses, the data were screened to determine whether statistical assumptions were met (see Tabachnick & Fidell, 1996). Assumptions for linearity, normality, and homogeneity of variance were met for all measures. Second, data were screened for univariate and multivariate outliers. Again, no violations were identified. Means and standard deviations for the questionnaires, and the correlations among them are provided in Table 3.1.

Table 3.1 | Means, standard deviations, and intercorrelations among the main variables in this study.

	M (SD)	1	2	3	4	5	6
1. NEO-FFI Neuroticism	44.07 (7.25)						
2. NEO-FFI Extraversion	35.97 (7.23)	-.46**					
3. IUS Intolerance of uncertainty	81.14 (21.15)	.63**	-.47**				
4. MCQ Negative metacognitions	50.76 (7.93)	.49**	-.22*	.47**			
5. MCQ Positive metacognitions	33.06 (10.92)	.34**	-.09	.35**	.17*		
6. PSWQ Worry	67.62 (8.27)	.57**	-.30**	.53**	.62**	.23**	
7. BDI-II Depression	23.18 (12.15)	.62**	-.41**	.63**	.57**	.31**	.45**

Note. **NEO-FFI** = NEO-Five Factor Inventory; **IUS** = Intolerance of Uncertainty Scale; **MCQ** = MetaCognitions Questionnaire; **PSWQ** = Penn State Worry Questionnaire; **BDI-II** = Beck Depression Inventory, 2nd edition.
* $p < .05$, ** $p < .01$.

3.3.2 | Bootstrapping

To test the hypothesis of mediation by multiple variables, multiple mediation is the appropriate analytic strategy (Preacher & Hayes, 2008). In multiple mediation models not only the total direct effect of the independent variable *X* on the dependent variable *Y* is assessed, but also the specific indirect effect of each potential mediator *M* (West & Aiken, 1997). As the present sample was not that large, the assumption of normality of the sampling distribution for the indirect effect could not be met (Preacher & Hayes, 2008). In such cases, bootstrapping provides the most powerful and reasonable method for obtaining confidence intervals of specific indirect effects. An advantage of using this nonparametric re-sampling procedure is that it is possible to draw conclusions about (a) the extent to which mediators mediate the effect of the independent variable on the outcome variable (conditional on the presence of other mediators in the model), and (b) the relative magnitudes of the specific indirect effects associated with each of the mediators (Preacher & Hayes, 2008). Bootstrapping involves at least a thousand times of repeatedly sampling from the original data and estimating the indirect effect in each re-sampled data set. As such, an empirical approximation of the sampling distribution of the indirect effect of *X* on *Y* through multiple *M*'s can be obtained. This approximation is then used to construct percentile bootstrap confidence intervals (CIs) for the total and specific indirect effects. As this procedure results in estimation inaccuracy and problems with Type I error and power when used in hypothesis testing, percentile bootstrap CIs are improved by an adjustment to the percentage values of the sorted distribution of bootstrap estimates used for determining the boundaries of the interval (bias-corrected CI; Efron & Tibshirani, 1993; Preacher & Hayes, 2008). To test the mediation hypotheses in the current study, data were analyzed using a SPSS-macro for estimating a bias-corrected 95% CI, as developed by Preacher and Hayes (2008).

We first tested the relations between the higher-order factors of neuroticism and extraversion, the second-order factors of positive metacognitions, negative metacognitions, and intolerance of uncertainty, and the symptom variable worry. The higher-order and second-order factors together explained 39.8% of the variation in worry, $F(5,115) = 15.18$, $p < .0001$. After controlling for neuroticism no significant relationship between extraversion and worry was found ($b = -.10$, SE = .09, $t = -1.06$, $p > .05$): both the direct effect ($b = -.04$, SE = .09, $t = -.45$, $p > .05$) and total indirect effect ($b = -.06$, SE = .05, *bootstrapped 95% CI* = -.17 to .05) were not significant. After controlling for extraversion, the link between neuroticism and worry appeared to be significant ($b = .46$, SE = .10, $t = 4.59$, $p < .01$). The direct effect of neuroticism on worry was not significant ($b = .17$, SE = .11, $t = 1.53$, $p > .05$). However, the total indirect effect was significant ($b = .29$, SE = .08, *bootstrapped 95% CI* = .13 to .45). Within the indirect effect, both negative metacognitions ($b = .20$, SE = .05, *bootstrapped 95%*

CI = .11 to .31) and intolerance of uncertainty (*b* = .10, SE = .05, *bootstrapped 95% CI* = .01 to .21) made significant contributions.

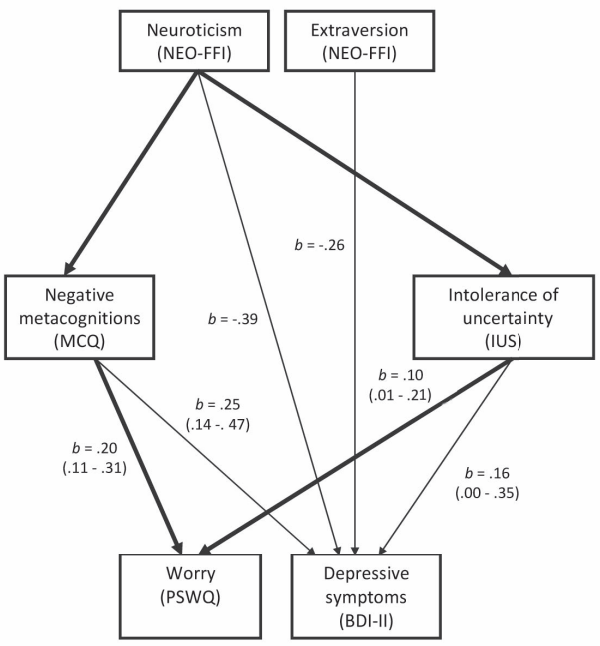

Figure 3.2 | Hierarchical model of the vulnerability for GAD (bold lines) and comorbid depressive symptoms (regular lines). *Note*: Only significant ($p < .05$) pathways are shown. Values in parentheses represent *bootstrapped 95%* confidence intervals.

A similar procedure was performed to study the link between the higher-order and second-order vulnerability factors and depressive symptoms. Results indicated that 48.8% of the variation in depressive symptoms was explained by all variables together, $F(5,115) = 21.92$, $p < .0001$. After controlling for extraversion, the link between neuroticism and depressive symptoms appeared to be significant (*b* = .85, SE = .15*, t* = 5.82, $p < .001$). Both the direct effect (*b* = .39, SE = .16, *t* = 2.43, $p < .05$) and the total indirect effect (*b*= .46, SE =.11, *bootstrapped 95% CI* = .25 to .67) of neuroticism on depressive symptoms were significant. Within the indirect effect, negative metacognitions (*b* = .25, SE = .08, *bootstrapped 95% CI* = .14 to .47) and intolerance of uncertainty (*b* = .16, SE = .09, *bootstrapped 95% CI* = .00 to .35) both made a significant contribution. After controlling for neuroticism, the link between extraversion and depressive symptoms appeared to be significant (*b* = -.34, SE =

.13, t = -2.52, p < .02). The direct effect was significant (b = -.26, SE = .13, t = -2.01, p < .05), but the indirect effect was not (b = -.08, SE = .08, *bootstrapped 95% CI* = -.26 to .06).

From these results, it can be concluded that the variation in worry was, as expected, mainly explained by neuroticism. This relationship between neuroticism and worry was fully mediated by both negative metacognitions and intolerance of uncertainty. Furthermore, contrary to expectations positive metacognitions were not found to have a mediating effect in the link between neuroticism and worry. The variation in depressive symptoms was explained by both neuroticism and (low) extraversion, which was as predicted. Low extraversion was only found to exert a direct effect on depressive symptoms. The effect of neuroticism on depressive symptoms was found to be both direct and indirect. Particularly the vulnerability factors of negative metacognitions and intolerance of uncertainty were found to have a mediating effect, whereas positive metacognitions did not influence the relationship between neuroticism and depressive symptoms in patients with GAD. Figure 3.2 presents the hierarchical model in which the observed significant direct and indirect effects are shown.

3.4 | Discussion

Despite empirical support for the causal role of personality traits in the development of anxiety disorders (see Kotov et al., 2007), little is known about the precise mechanisms by which such traits influence specific disorders. The investigation of factors mediating the relations between personality traits and symptomatic manifestations of specific anxiety disorders advances our understanding of etiology, and may lead to the development of more effective treatments. In the present study, we tested a hierarchical model for GAD, which was based on a recently developed and tested model for various emotional disorders (Norton & Mehta, 2007; Norton et al., 2005; Sexton et al., 2003). In this model the two basic personality dimensions of neuroticism and extraversion served as higher-order vulnerability factors, whereas IU and metacognitive beliefs, two trait-like constructs that are hypothesized to contribute to GAD, acted as specific second-order vulnerability factors. At the symptom level worry featured as the specific manifestation of GAD. Moreover, we also examined the contribution of both the higher-order and second-order vulnerabilities to depressive symptoms in GAD patients, given the high comorbidity rate and the shared genetic and environmental risk factors between GAD and depression (Goldberg, 2008).

Overall, results of the multiple mediation analysis are generally consistent with the hypothesized theoretical model. As expected, the general vulnerability factor of neuroticism was significantly associated with symptoms of worry and depressive symptoms in these clinically referred GAD patients. Further, both negative metacognitions and, to a lesser extent,

IU were found to mediate the relationship between the higher-order factor of neuroticism and the symptom variables, and this was particularly true for worry. In contrast with the predictions, positive metacognitions did not have a mediating effect on the relationship between the higher-order factor of neuroticism and both symptom variables, although it should be noted that there are also earlier findings that have demonstrated that positive beliefs about worrying are not convincingly associated with symptom levels (Wells & Carter, 1999). Finally, as hypothesized, low extraversion was only found be associated with depressive symptoms in the present sample of patients with GAD. This relationship was direct in nature and not mediated by IU or metacognitive beliefs. All in all, these findings suggest that worrying and depressive symptoms are related but nevertheless distinct manifestations in patients with GAD, and that low extraversion may define the difference between them.

Results of the current study support a hierarchical model of GAD that serves as a descriptive framework for understanding this anxiety disorder, and may provide a basis for developing more specific treatments for GAD that not only target the main symptoms of this disorder, but also the specific processes that underlie them. As such, the model supports the appropriateness of two recently developed cognitive-behavioral treatments for GAD, based on the metacognitive (Wells, 1995) and the intolerance of uncertainty (Dugas & Ladouceur, 2000) accounts of this specific disorder. Preliminary results from research into the efficacy of these GAD-specific interventions have shown that recovery rates are higher than recovery rates obtained by other less targeted treatment approaches (Fisher, 2006). Interestingly, our data seem to suggest that it may be important to target both intolerance of uncertainty and negative metacognitions in the treatment of GAD.

Further, as most variables in the hierarchical model reflect transdiagnostic phenomena (Harvey, Watkins, Mansell, & Shafren, 2004), it might be worthwhile to examine specific second-order vulnerability factors also in the context of other emotional disorders. Increasing knowledge about common, underlying core psychopathological processes may be particularly helpful to better explain the high comorbidity rates between several emotional disorders (see Krueger, 1999; Watson, 2005). For instance, the fact that GAD is strongly linked to depression, both phenotypically and genotypically (e.g., Goldberg, 2008; Kendler, Prescott, Myers, & Neale, 2003; Mineka et al., 1998), might be well explained by the overlap in generalized and specific vulnerability factors that are linked to both types of disorder (Krueger, 1999; Watson, 2005).

Results of this study should be interpreted in the context of various limitations. To begin with, although hierarchical models of anxiety and depression implicate neuroticism as an underlying vulnerability factor (Clark & Watson, 1991; Mineka et al., 1998; Norton et al., 2005), the current study does not permit definitive conclusions regarding etiology of GAD because of the cross-sectional, correlational design of this investigation. A further shortcoming

pertains to the fact that the variables in our model were only assessed by one measure that was completed by one informant (i.e., GAD patients). To effectively deal with this critique, a multitrait-multimethod approach would be preferable (Kotov et al., 2007; Sexton et al., 2003; Starcevic & Berle, 2006). Furthermore, apart from the higher-order factors and two second-order factors of IU and metacognitions, there may still be other vulnerability factors involved in the etiology of GAD, a notion that is supported by the finding that the included variables only accounted for a limited proportion of the variance in worry scores. Finally, although the comorbidity rate among the sample of GAD patients used in this study (57.8%) is in keeping with that observed in other clinical studies (i.e., 45-98%; Holaway, Rodebaugh & Heimberg, 2006), the comorbidity rates with some of the disorders (e.g., depression, insomnia) seemed to be considerably lower than those found in large epidemiological studies (e.g., Carter, Wittchen, Pfister, & Kessler, 2001). Thus, it is not fully clear whether the participants in this study were 'typical' GAD patients, and to what extent the present findings can be generalized to other samples of patients with this anxiety disorder.

In sum, results of this study extend findings of Norton and Mehta (2007), Norton et al. (2005), and Sexton et al. (2003), by providing support for a hierarchical model of the vulnerability for GAD, in which neuroticism serves as a common higher-order vulnerability factor, IU and metacognitions act as more specific vulnerability variables, while extraversion only seems to be involved as a higher-order vulnerability factor in the comorbid depressive symptoms of patients suffering from this anxiety disorder.

Chapter 4

Factor structure of the Dutch version of the Penn State Worry Questionnaire

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Factor structure of the Dutch version of the Penn State Worry Questionnaire.

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Abstract

The Penn State Worry Questionnaire (PSWQ) is a 16-item self-report scale for measuring the excessiveness and uncontrollability of worry. The current study examined the factor structure of the PSWQ in (1) a large community sample (*N* = 455), and (2) a clinical sample of patients with generalized anxiety disorder (GAD; *N* = 102), the disorder for which worry is the key feature. Confirmatory factor analysis was employed to test three models: (1) a one-factor model in which all items loaded on one and the same dimension, (2) a two-factor model in which positively and negatively worded items loaded on two separate but correlated factors, and (3) a one-factor model, that included the reverse items as a method factor. In the community sample the one-factor/method factor model provided the best fit for the data.

This was also true in the clinical GAD sample, but only after error covariances between a number of items were allowed to correlate.

4.1 | Introduction

Worry can be defined as 'a chain of thoughts and images, negatively affect-laden and relatively uncontrollable; it represents an attempt to engage in mental problem-solving on an issue whose outcome is uncertain but contains the possibility of one or more negative outcomes' (Borkovec, Robinson, Pruzinsky, & DePree, 1983; p.10). Worrying is associated with various types of psychopathology. Excessive and uncontrollable worry is the most prominent feature of generalized anxiety disorder (GAD; American Psychiatric Association, 2000), but worrying also occurs in other anxiety disorders, depression, pain, sleeping disorders, and eating disorders (Harvey, Watkins, Mansell, & Shafran, 2004).

The Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990) is an instrument for measuring process characteristics of worry. Research has demonstrated that the PSWQ assesses a construct separate from anxiety and depression (Meyer et al., 1990), and is capable of discriminating GAD from other anxiety disorders (Brown, Anthony, & Barlow, 1992; Meyer et al., 1990). Furthermore, various studies in both clinical and community samples have reported that the psychometric qualities of the PSWQ are good. That is, the internal consistency and test-retest reliability are high, whereas the scale correlates in a meaningful way with other measures of worry and psychopathological symptoms (Startup & Erickson, 2006). For these reasons, the PSWQ has emerged as a widely used self-report measure of worry and GAD.

Although the PSWQ was originally developed as a unifactorial measure (Meyer et al., 1990), several investigators who performed an exploratory factor analysis (EFA) have noted

that a two-factor solution might provide a better fit (Brown et al., 1992; Stöber, 1995; Beck, Stanley, & Zebb, 1995; Van Rijsoort, Emmelkamp, & Vervaeke, 1999). In these studies the first factor consisted of the 11 positively worded items (e.g., 'When I'm under pressure, I worry a lot'), whereas the second factor was comprised of the 5 negatively worded items (e.g., 'When there is nothing more I can do about a concern, I don't worry about it anymore'). However, an important limitation of exploratory factor analytic studies of the PSWQ, is that an evaluation of competing explanations of the latent structure is precluded (see Brown, 2003). Therefore, Fresco, Heimberg, Mennin, and Turk (2002) compared the unifactorial solution of the PSWQ to the two-factor solution in a large sample of college students (N = 788) using confirmatory factor analysis. The two-factor model, which comprised the positively and negatively worded items factors, yielded a significantly better fit than the one-factor model. Fresco et al. (2002) concluded that the PSWQ measures two lower-order constructs, 'worry engagement' (defined by the 11 items phrased in the symptomatic direction) and 'absence of worry' (consisting of the five reverse-worded items). This conclusion has been questioned because Fresco et al. (2002) used CFA only as a method to statistically compare the fit of the one- and two-factor solutions, and based their conclusion solely on goodness of fit, without due consideration of the interpretability and acceptability of the two-factor solution (Brown, 2003). Although the two-factor solution provided a better fit to the data, obviously there is no apparent theoretical foundation for an 'absence of worry' dimension (Brown, 2003). As such, the question remained whether this second factor really has substantive meaning. One alternative explanation for the second factor which has not been considered by Fresco et al. (2002) is that the second factor might only be an artifact of a response style associated with the negative wording of the items, a so-called method factor (see Brown, 2003; Hazlett-Stevens, Ullman, & Craske, 2004; Marsh, 1996). In other words, factor analyses of measures with positively and negatively worded items sometimes show two factors, each of which contains items formulated in only one direction, in the absence of multiple constructs (see Marsh, 1996; Spector, Van Katwyk, Brannick, & Chen, 1997). Separate factors emerge because items group together statistically resulting from different patterns of responding to items rather than reflecting theoretically meaningful distinctions between qualitatively different constructs (Ullman, 2001).

To further address this issue within the context of the PSWQ, Brown (2003) evaluated the latent structure of this questionnaire in 1200 outpatients with anxiety and mood disorders. More precisely, Brown not only investigated the fit of the one-factor and two-factor solution of the PSWQ, but also tested an alternative one-factor model in which the reverse items were included as a measuring artifact (i.e., method factor). In line with the results obtained by Fresco et al. (2002), it was found that the two-factor model with separate components for 'worry engagement' and 'absence of worry' provided a better fit for the PSWQ data than the

one-factor model. However, Brown (2003) also demonstrated that the alternative one-factor model, which included the reverse items as a method factor, even yielded a significantly better fit. Brown (2003) concluded that the covariances among the 16 items of the PSWQ are best explained by a single underlying construct, like 'excessive/uncontrollable worry' as suggested in prior investigations (Meyer et al., 1990; Brown et al., 1992), and that the second factor ('absence of worry') that was found in several studies (e.g. Fresco et al., 2002) seems to be the result of method effects, due to the use of positively and negatively worded items.

In another study among college students, Hazlett-Stevens et al. (2004) also employed a confirmatory factor analytic approach to test the factor structure of the PSWQ. They compared the two-factor solution as proposed by Fresco et al. (2002) to a one-factor model in which reverse-scored items loaded on the method factor. The latter model was found to provide an equally good fit as compared to the two-factor solution, leading to the conclusion that the one-factor/method factor model is a reasonable competing alternative, which may even be preferable from a theoretical point of view.

Although the studies of Brown (2003) and Hazlett-Stevens et al. (2004) seem to indicate that the PSWQ actually measures a single-factor construct, both studies used rather specific samples consisting of patients suffering from various affective disorders and undergraduate students, respectively. As such the question remains to what extent this finding can be generalized to other populations. With this in mind, the purpose of the current study was to investigate the structure of the PSWQ in (1) a non-clinical sample recruited from the general population, and (2) a clinical sample of patients with GAD. The latter population had our special interest as worry is the key feature of this specific anxiety disorder. Following Brown (2003) and Hazlett-Stevens et al. (2004), confirmatory factor analysis was employed to test three models of the PSWQ: 1) a one-factor model in which all 16 items loaded on one and the same dimension (Figure 4.1A), 2) a two-factor model in which positively and negatively worded items loaded on two separate but correlated factors (Figure 4.1B), and 3) a one-factor model, which included the reverse items as a method factor (i.e., the one-factor/method factor model; Figure 4.1C).

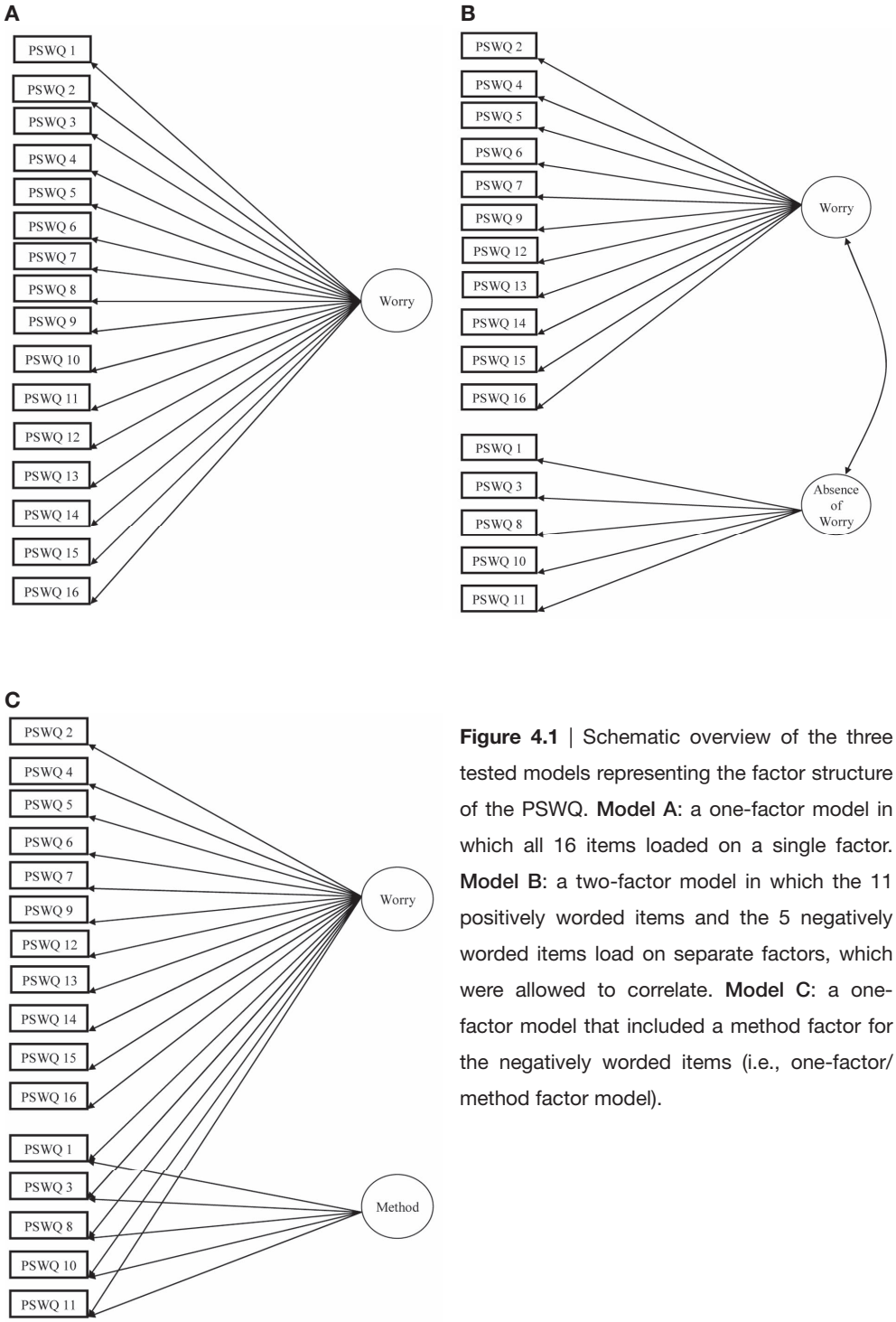

Figure 4.1 | Schematic overview of the three tested models representing the factor structure of the PSWQ. **Model A**: a one-factor model in which all 16 items loaded on a single factor. **Model B**: a two-factor model in which the 11 positively worded items and the 5 negatively worded items load on separate factors, which were allowed to correlate. **Model C**: a one-factor model that included a method factor for the negatively worded items (i.e., one-factor/method factor model).

4.2 | Method

4.2.1 | Participants and procedure

The community sample consisted of 455 participants who participated in a panel survey conducted by Flycatcher, a full-service online research company. The sample was stratified on gender, age, educational level and province, in order to be representative for the adult Dutch population on these characteristics (Centraal Bureau voor de Statistiek, 2009). The participants completed the PSWQ as part of a larger survey, in return for a small financial reward. The overall sample consisted of 455 participants, 232 men and 223 women, who had a mean age of 48.2 years (*SD* = 16.1; range 19-83 years). The sample breakdown of educational level was: 25.7% had a low level of education, 40.4% an average level of education, and 33.8% a high level of education.

The clinical sample consisted of 102 patients with a principal diagnosis of GAD. They completed the PSWQ as part of the standard assessment at PsyQ, a mental health care organization specialized in cognitive-behavior therapy. The medical ethics committee of the participating treatment center officially approved the study. The sample consisted of 26 men and 76 women. Their mean age was 34.2 years (*SD* = 10.5; range 19-66 years). The sample breakdown of educational level was: 18.3% had a low level of education, 41.5% an average level of education, and 40.2% a high level of education. The diagnosis of GAD was established by means of a structured, DSM-IV-based clinical interview (SCID-I; First, Spitzer, Gibbon, & Williams, 1994), which was administered by a trained psychologist. More than half of the participants (56.9%) met the criteria of one or more comorbid axis-I disorders, which is in keeping with the comorbidity rates as observed in other clinical studies (i.e., 45-98%; Holaway, Rodebaugh & Heimberg, 2006). The most common comorbid diagnoses were depressive disorder (21.6%), panic disorder (13.7%), social phobia (10.8%), somatoform disorder (9.8%), obsessive-compulsive disorder (5.8%), dysthymic disorder (3.9%), specific phobia (1.9%), and insomnia (2.9%). Patients were not screened for DSM-IV axis-II disorders.

4.2.2 | Questionnaire

The PSWQ (Meyer et al., 1990) consists of 16 items that have to be rated on a 5-point Likert scale, with 1 = *not at all typical of me* and 5 = *very typical of me*. Eleven items are positively worded (e.g., 'I worry all the time'), the remaining five items are negatively worded (e.g., 'I find it easy to dismiss worrisome thoughts'). A total score can be computed by summing across all items, after recoding the scores on the negatively worded items. As mentioned in the introduction, the PSWQ is a widely used measure of pathological worry with good psychometric qualities. Several studies demonstrated high internal consistency for the scale in clinical and non-clinical samples (Cronbach's alphas ranging between .88 and .95) and

good test-retest reliability (*r*s varying between .74 and .92 over intervals of 2 to 10 weeks; see Startup & Erickson, 2006). The Dutch version of the PSWQ also showed high internal consistency in clinical samples (Cronbach's alpha = .86; Kerkhof et al., 2000) and non-clinical samples (Cronbach's alphas ranging from .88 to .90; Van Rijsoort, Vervaeke, & Emmelkamp, 1997; Van Rijsoort et al., 1999).

4.2.3 | Data analysis

Confirmatory factor analysis (with a maximum likelihood estimation) was conducted using the software program of AMOS (Version 6.0; Arbuckle, 2005). As mentioned in the introduction, three models for the PSWQ were tested: (1) a one-factor model in which all 16 PSWQ items were indicators of a single latent factor; (2) a two-factor model with the 11 positively worded items as indicators of the first latent factor and the five negatively worded items as indicators of the second latent factor, in which both factors were allowed to correlate; and (3) a one-factor model that included a negative wording method factor (i.e., one-factor/method factor model), in which all 16 PSWQ items were indicators of a single factor of worry and the five negatively worded items as indicators of a latent method factor, which covers the systematic error variance among these items (see Brown, 2003; Hazlett-Stevens et al., 2004; see Figure 1). Goodness of fit was evaluated using the following indices: (a) chi square divided by degrees of freedom (χ^2/df; with large sample sizes as in the current study, this value should be 4.00 or smaller; the lower this value, the better the fit), (b) the Root Mean Square Residual (RMR; this value should be .08 or lower; the lower this value, the better the fit), (c) the Root Mean Square Error of Approximation (RMSEA; this value should be around .08 or lower; the lower the value, the better the fit), (d) the Comparative Fit Index (CFI; this value should be .90 or higher for a good fit; the higher this value, the better the fit), and (e) the Tucker-Lewis Index (TLI; this value should be .90 or higher for a good fit; the higher this value, the better the fit) (for a discussion of the cut-off values of the goodness of fit indices, see e.g., Gerbing & Anderson, 1993). Confirmatory factor analysis was carried out on the PSWQ data of the total sample, and males and females separately. As gender-specific analyses essentially revealed a similar pattern of findings, only the results for the total samples will be presented hereafter.

4.3 | Results

4.3.1 | General findings

Mean scores on the PSWQ were 43.9 (*SD* = 11.7; range 17-80) in the non-clinical community sample and 67.1 (*SD* = 8.8; range 37-80) in the sample of patients with GAD. Analyses of variance (with gender and age as covariates) demonstrated that GAD patients indeed

displayed higher scores on the PSWQ than participants from the community sample [$F(1,940) = 376.07$, $p < .001$, $p\eta^2 = .29$]. The PSWQ showed high internal consistency in both the community sample (Cronbach's alpha = .92) and the clinical sample of GAD patients (Cronbach's alpha = .83).

4.3.2 | Confirmatory factor analysis

Table 4.1 displays the goodness-of-fit statistics for the models that were tested. First, the one-factor solution was fit to the data of the community sample (N = 455). As shown in Table 4.1, the one-factor model did not provide an adequate fit (i.e., χ^2/df = 5.81, CFI = 0.88, TLI = 0.86, RMR = 0.08, and RMSEA = 0.10). The two-factor model and the one-factor/method factor model both yielded fairly good fits for the PSWQ data, as all fit indices can be qualified as satisfactory (see Table 4.1). Chi square difference tests revealed that both models provided a better fit than the one-factor model ($\Delta\chi^2$ values being 200.76, df = 1, $p < .001$ and 218.40, df = 5, $p < .001$, respectively). Further, although fit indices were highly comparable, an additional chi square difference test indicated that the one-factor/method factor model yielded a significantly better fit than the two-factor model ($\Delta\chi^2 = 17.64$, df = 4, $p < .001$).

Table 4.1 | Goodness-of-fit statistics for the one-factor, two-factor, and one-factor/method factor models of the PSWQ in a Dutch community sample and a sample of GAD patients.

	χ^2	χ^2/df	CFI	TLI	RMR	RMSEA
Community sample (N = 455)						
One factor	604.04	5.81	0.88	0.86	0.08	0.10
Two factors	403.28	3.92	0.93	0.91	0.06	0.08
One factor/method factor	385.64	3.90	0.93	0.91	0.05	0.08
Clinical GAD sample (N = 102)						
One factor	200.43	1.93	0.82	0.79	0.09	0.10
Two factors	199.52	1.94	0.82	0.79	0.11	0.10
One factor/method factor	186.20	1.88	0.84	0.80	0.09	0.09
One factor/method factor with $\theta_{4,16}$, $\theta_{9,16}$, $\theta_{7,8}$ free[a]	131.80	1.37	0.93	0.92	0.07	0.06

Note. **PSWQ** = Penn State Worry Questionnaire. **CFI** = Comparative Fit Index, **TLI** = Tucker-Lewis Index, **RMR** = Root Mean Square Residual, RMSEA = Root Mean Square Error of Approximation. [a] $\theta_{4,16}$, $\theta_{9,16}$, $\theta_{7,8}$ freely estimated in the one-factor/method factor model.

Table 4.2 | Standardized factor loadings for the one-factor, two-factor, and one-factor/method factor models of the PSWQ in a Dutch community sample (CS) and a sample of GAD patients.

	One-factor		Two-factor				One-factor/Method factor			
PSWQ items	I. Worry		I. Worry		II. Absence of worry		I. Worry		II. Method	
	CS	GAD	CS	GAD	CS	GAD	CS	GAD	CS	GAD
2	0.69	0.62	0.69	0.61			0.69	0.62		
4	0.82	0.82	0.83	0.82			0.83	0.82		
5	0.83	0.62	0.83	0.62			0.83	0.63		
6	0.78	0.61	0.78	0.62			0.78	0.61		
7	0.82	0.86	0.82	0.88			0.82	0.86		
9	0.62	0.52	0.62	0.53			0.62	0.52		
12	0.80	0.37	0.80	0.37			0.80	0.37		
13	0.78	0.74	0.78	0.74			0.78	0.74		
14	0.78	0.69	0.78	0.69			0.78	0.69		
15	0.83	0.72	0.83	0.71			0.83	0.72		
16	0.64	0.42	0.64	0.42			0.64	0.42		
1	0.14	0.02			0.33	0.17	0.12	0.02	0.37	0.19
3	0.31	0.04			0.58	0.39	0.28	0.04	0.56	0.38
8	0.48	0.38			0.66	0.17	0.46	0.38	0.45	-0.07
10	0.43	0.07			0.66	0.41	0.41	0.07	0.50	0.42
11	0.37	0.14			0.61	0.56	0.34	0.14	0.50	0.58

Note. **PSWQ** = Penn State Worry Questionnaire.

In the sample of clinically referred GAD patients initially none of the models provided a good fit for the data. More precisely, although the χ^2/df values for all the models were acceptable, all other indices did not indicate a good fit (i.e., RMR and RMSEA > .08, and CFI and TLI < .90). Again, chi square difference tests demonstrated that the one-factor/method-factor model provided a relatively better fit than the one-factor and the two-factor models ($\Delta\chi^2$ values being 14.23, df = 5, $p < .05$ and 13.32, df = 4, $p < .01$, respectively). Therefore, we localized and evaluated areas of strain within this particular model to specify correlated residuals that represent nonrandom measurement error (cf. Byrne, Shavelson, & Muthén, 1989; Floyd & Widaman, 1995; Gerbing & Anderson, 1984). Modification indices revealed the

existence of significant error covariances between items 4 and 16 ('Many situations make me worry' and 'I worry about projects until they are all done', which both seem to reflect the pervasiveness of worry), 9 and 16 ('As soon as I finish one task, I start to worry about everything else I have to do' and 'I worry about projects until they are all done', which pertain to task-related worry), and 7 and 8 ('I am always worrying about something' and 'I find it easy to dismiss worrisome thoughts' [reversed item], which have to do with the [lack of] control over worry). Accordingly, the one-factor/method factor model was refit to the data while freely estimating the error covariance between these item pairs. This procedure resulted in a clear improvement of the model fit and yielded satisfactory fit indices (i.e., χ^2/df = 1.37, CFI = 0.93, TLI = 0.92, RMR = 0.07, and RMSEA = 0.06).

Table 4.2 presents the standardized factor loadings for each PSWQ item as obtained with various models in the community sample and the sample of GAD patients. Inspection of these data confirms the notion that various hypothesized models fitted somewhat better in non-clinical participants than in GAD patients. In most cases items appeared to be more clear-cut indicators of latent factors in non-clinical participants than in GAD patients.

4.4 | Discussion

Factor analytic studies by Brown (2003) and Hazlett-Stevens et al. (2004) have indicated that the 16 items of the PSWQ represent a single underlying construct (i.e., 'excessive/uncontrollable worry'). These researchers demonstrated that the second factor, 'absence of worry', which has been reported by a number of other researchers (e.g., Beck et al., 1995; Fresco et al., 2002), is most likely to represent a statistical artifact, that is probably caused by a different response pattern to negatively worded items (i.e., method factor). Yet, the samples used in the studies by Brown (2003) and Hazlett-Stevens et al. (2004) were rather specific (i.e., patients with various affective disorders and undergraduate students, respectively). Therefore, it is still necessary to investigate the latent factor structure of the PSWQ in other relevant populations, especially because comparable research with other self-report questionnaires has demonstrated that the factor structure, and in particular the emergence of a method factor for negatively worded items, may vary from one to another population (Marsh, 1986, 1996). The key purpose of the present study was to replicate the findings of Brown (2003) and Hazlett-Stevens et al. (2004) in two different populations, a non-clinical community sample and a clinical GAD sample. The results in the community sample confirm the conclusion that the one-factor/method factor model provides a good competing alternative for the two-factor solution of the PSWQ reported in previous studies, which should be preferred because it is more acceptable from a theoretical point of view. Moreover,

the findings for the sample of patients with GAD also revealed that the one-factor/ method factor model yielded the most optimal fit, although it should be mentioned that acceptable fit indices were only found for this model after error covariances between a number of items were allowed to correlate.

The fact that we encountered more problems in finding an acceptable fit for the structure of the PSWQ in the clinical sample may be due to the fact that a number of the items in this scale were strongly endorsed by almost all of the GAD patients. The distribution of these items was extremely (negatively) skewed and had a high positive value of kurtosis, and this implies that the standard (i.e., maximum likelihood) estimation procedure as employed in the present study may have been less appropriate. To deal effectively with this problem, a weighted least squares estimation should be used, but this procedure can only be carried out with the software MPlus, which was not available to the researchers of the present study.

Strengths of this study are the large sample size for the community sample, and the adequate sample size for the sample of patients with GAD, the anxiety disorder for which worry is the main source of complaint. Another strength is that the SCID-I was administered to the clinical participants. However, limitations should also be pointed out, and these were particularly relevant for the clinical sample of GAD patients. Besides the already mentioned problem with the unequal distribution of some items within this sample, it also remains unclear to what extent the participants in the clinical sample were 'typical' GAD patients, and to what extent the present findings can be generalized to other samples of patients with this anxiety disorder. That is, the response rate of this sample was unknown and further it should be noted that the comorbidity rates with some of disorders (e.g., depression, insomnia) seemed to be somewhat lower than those found in large epidemiological studies (e.g., Carter, Wittchen, Pfister, & Kessler, 2001).

In sum, the present findings confirm previous research showing that the PSWQ measures worry along a single dimension (Brown, 2003; Hazlett-Stevens et al., 2004), and supports the continued use of the total scale as a diagnostic indicator of the excessiveness and uncontrollability of worry in both non-clinical populations and patient samples. Note that the single dimension conceptualization is nicely in keeping with current theories which view normal and pathological worry at the ends of one and the same continuum (Ruscio, Borkovec, & Ruscio, 2001). Further, this study provides an interesting example of how method variance associated with the way in which items are phrased can affect the factor structure of a self-report measure.

Chapter 5

Normative data for the Dutch version of the Penn State Worry Questionnaire

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Abstract

Worry is a common symptom in various psychiatric problems and the key symptom of generalized anxiety disorder (GAD). The Penn State Worry Questionnaire (PSWQ) is the most widely used self-report scale for measuring worry. The present study provides normative data for the Dutch version of the PSWQ for a large community sample and a clinically referred sample of patients with GAD. Norms are not only provided for the original 16-item version, but also for an abbreviated 11-item version, which only consists of the positively worded items and has been shown to be a promising alternative to the full-length version. The percentile scores obtained for the community sample and the clinical GAD sample did not show much overlap, and this appeared true for the full-length as well as the abbreviated version of the PSWQ. These normative data seem suitable for differentiating between normal and abnormal manifestations of worrying and for evaluating the efficacy of treatments for GAD.

5.1 | Introduction

Worry is a common symptom in various psychiatric problems, including anxiety, mood, and eating disorders (Harvey, Watkins, Mansell, & Shafran, 2004). In addition, excessive and uncontrollable worrying is viewed as the cardinal feature of generalized anxiety disorder (GAD; American Psychiatric Association, 2000). To assess the frequency, intensity, and uncontrollability of worry and to evaluate the efficacy of treatments for GAD, psychometrically sound assessment tools are strongly needed, as well as representative normative data for such measures. In the case of worry and GAD, the Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990) has emerged as the most widely used self-report measure, in both research and clinical practice.

The PSWQ was originally developed as a unifactorial measure, with 11 positively worded items (e.g., 'I worry about projects until they are all done') and five negatively worded items (e.g., 'I never worry about anything'). Factor analytic studies have indicated that a two-factor model (with the positively worded items loading on the first factor and the negatively worded items loading on the second factor) provided a better fit for the data than the hypothesised one-factor model (Brown, Antony, & Barlow, 1992; Stöber, 1995; Beck, Stanley, & Zebb, 1995; Van Rijsoort, Emmelkamp, & Vervaeke, 1999). However, more recent research has shown that the negatively worded items form a method factor that should be considered a statistical artifact and is not really meaningful (Brown, 2003; Hazlett-Stevens, Ullman, & Craske, 2004; Van der Heiden, Muris, Bos, & Van der Molen, 2010, see also Chapter 4). As such, it has been argued that the negatively worded items may undermine the psychometric

qualities of the PSWQ (Woods, 2006), and so it has been suggested to remove these items from the scale and to employ an abbreviated scale that only includes the positively worded items (Hazlett-Stevens et al., 2004; Fresco, Heimberg, Mennin, & Turk, 2002). There is indeed some evidence indicating that such a shortened version of the PSWQ is just as or even more reliable and valid than its full-length counterpart (Hazlett-Stevens et al., 2004; Fresco et al., 2002).

While many studies have investigated the reliability and validity of the PSWQ (see for a review: Startup & Erickson, 2006), research presenting normative data for this measure is sparse. So far, only one investigation has provided norms for the PSWQ in a community sample (Gillis, Haaga, & Ford, 1995). Further, normative data in clinical populations are limited to a handful of studies that reported cut-off scores that may be helpful for discriminating GAD patients from other patient groups (Behar, Alcaine, Zuellig, & Borkovec, 2003; Fresco, Mennin, Heimberg, & Turk, 2003). The present study was designed to provide normative data for the Dutch version of the PSWQ for a sample from the general population and a clinical sample of patients with GAD. Given its potential we also provided cut-off scores for the shortened 11-item version of the PSWQ, for which currently no normative data exist.

5.2 | Method

5.2.1 | Participants and procedure

In order to obtain a large and representative sample of the general population, we approached participants in three ways. First, the sample of 455 participants that is already described in Chapter 4 was included in this study. This sample was drawn from the Dutch population by Flycatcher, a full-service online research company. Effort was made to match this sample to the demographic profile of the adult Dutch population. Participants completed the PSWQ as part of a larger survey in return for a small financial reward. In addition, 340 participants filled in the PSWQ, after the questionnaire had been distributed by e-mail within the personal networks of the first author and several colleagues, friends, and family, and within the networks of some of the participants themselves (i.e., snowball sampling method). Examples of networks where the PSWQ was administered were sport clubs (e.g., soccer club), church communities, and companies (e.g., cleaning company). Finally, 47 participants were approached at two shopping malls in Rotterdam, the Netherlands, with the request to complete the PSWQ. Participants in the last two groups did not receive a reward for their participation. The overall sample consisted of 842 participants (379 men and 463 women; mean age = 43.6 years, *SD* = 15.8; range 16-84 years), none of whom were actually being

treated for a psychological disorder and thus were defined as 'non-clinical' (Kendall & Sheldrick, 2000; Sabshin, 1989).

Participants in the clinical sample of GAD patients completed the PSWQ as part of the standard assessment at PsyQ, a mental health care organisation specialised in cognitive-behavioral therapy. The diagnosis of GAD was established using the Structured Clinical Interview for DSM-IV (SCID I: First, Spitzer, Gibbon, & Williams, 1994), which was administered by a trained psychologist. In a second diagnostic interview, the diagnosis of GAD was confirmed by another experienced clinician. In total, 102 patients took part in this study (26 men and 76 women; mean age = 34.2 years, *SD* = 10.5, range 19-66 years).

5.2.2 | Questionnaire

As already described in the introduction, the PSWQ was designed to assess the intensity, excessiveness and uncontrollability of worry (Meyer et al., 1990). Respondents are instructed to indicate for each of the 16 items how applicable they are to them, using a five-point scale ranging from 'not at all typical of me' to 'very typical of me'. A total score is calculated by summing all items, after recoding the scores on the five negatively worded items. As such, scores range from 16 to 80, with higher scores representing a stronger tendency to worry. Psychometric properties of the original English version are good (Meyer et al., 1990), and this is also true for the Dutch version of the scale (Kerkhof, Hermans, Figee, Laeremans, Pieters, & Aardema, 2000; Van Rijsoort, Vervaeke, & Emmelkamp, 1997; Van Rijsoort et al., 1999). In the present study, Cronbach's alpha values for the full-length PSWQ were 0.92 in the community sample and 0.83 in the clinical sample of GAD patients. For the shortened version these values were 0.93 and 0.87, respectively.

5.3 | Results

The Statistical Package for the Social Sciences (SPSS) was used to compute mean scores, standard deviations, and percentile scores (i.e., cut-off scores for 10 equal groups) for the full-length PSWQ and the abbreviated 11-item PSWQ in both the community and the clinical GAD sample.

For the full-length version of the PSWQ, the range of total scores in the non-clinical sample was 17-80 (*M* = 42.4, *SD* = 11.8), for the abbreviated PSWQ the range was 11-55 (*M* = 25.9, *SD* = 9.4). Significant sex and age differences were found for both the full-length and the abbreviated version of the PSWQ. Participants younger than 45 years (PSWQ: *M* = 43.1 *SD* = 11.8; abbreviated PSWQ: *M* = 26.6, *SD* = 9.3) displayed significantly higher PSWQ scores than participants aged 45 and above (PSWQ: *M* = 41.4, *SD* = 11.6; abbreviated PSWQ:

M = 25.2, *SD* = 9.5) [*t*(840)'s being 2.08, $p < 0.05$ and 2.27, $p < 0.05$ respectively]. Further, women (PSWQ: *M* = 44.1, *SD* = 12.0; abbreviated PSWQ: *M* = 27.1, *SD* = 9.7) reported significantly higher levels of worry than men (PSWQ: *M* = 40.2, *SD* = 11.1; abbreviated PSWQ: *M* = 24.5, *SD* = 8.8) [*t*(840)'s being 4.89, $p < 0.01$ and 4.09, $p < 0.01$ respectively].

In the clinical sample of patients with GAD the range of total scores was 37-80 (*M* = 67.1, *SD* = 8.8) for the full-length PSWQ, and 17-55 (*M* = 44.9, *SD* = 7.8) for the abbreviated version. Here, no significant sex and age differences were found.

Percentile scores for the full-length PSWQ are presented for both the community and the clinical sample in Table 5.1. Age- and sex-specific norms for the community sample are displayed in Table 5.2. For the abbreviated PSWQ, these normative data are provided in Tables 5.3 and 5.4. It is noteworthy that for both versions of the PSWQ, there was hardly any overlap in the percentile scores for the community and clinical samples (see Tables 5.1 and 5.3). A score of 58 or 59 on the full-length version, and a score between 35 and 39 on the abbreviated scale appeared to differentiate between both samples, and thus seems to indicate the boundary between normal and pathological worrying.

Table 5.1 | Cut-off scores for 10 equal groups of the PSWQ in a community sample (*N* = 842) and a sample of clinically referred GAD patients (*N* = 102).

Community sample		GAD patients	
Percentiles	Cut-off scores	Percentiles	Cut-off scores
10	28		
20	32		
30	35		
40	38		
50	42		
60	45		
70	48		
80	52		
90	59	10	58
		20	60
		30	62
		40	66
		50	69
		60	71
		70	72
		80	75
		90	77

Table 5.2 | Cut-off scores for 10 equal groups of the PSWQ scores in various age and sex-based subgroups of the community sample.

	Women		Men	
Percentiles	< 45 (*N* = 275)	≥ 45 (*N* = 188)	< 45 (*N* = 184)	≥ 45 (*N* = 195)
10	29	27	28	28
20	34	32	32	30
30	37	36	34	33
40	41	40	36	36
50	44	43	39	39
60	48	46	42	42
70	51	48	45	45
80	56	52	49	48
90	61	60	56	54

Table 5.3 | Cut-off scores for 10 equal groups of the abbreviated PSWQ in a community sample (*N* = 842) and a sample of clinically referred GAD patients (*N* = 102).

Community sample		Clinically referred GAD patients	
Percentiles	Cut-off scores	Percentiles	Cut-off scores
10	14		
20	17		
30	20		
40	23		
50	25		
60	28		
70	31		
80	34	10	35
90	39	20	39
		30	42
		40	45
		50	46
		60	49
		70	50
		80	51
		90	53

Table 5.4 | Cut-off scores for 10 equal groups of the abbreviated PSWQ scores in various age and sex based subgroups of the community sample.

	Women		Men	
Percentiles	< 45 (*N* = 275)	≥ 45 (*N* = 188)	< 45 (*N* = 184)	≥ 45 (*N* = 195)
10	16	13	15	14
20	19	17	17	16
30	22	20	20	18
40	24	24	21	20
50	27	26	24	23
60	30	29	26	25
70	33	31	29	29
80	36	34	32	32
90	41	40	38	37

5.4 | Discussion

Statistical significance testing is traditionally the predominant way in research evaluating the efficacy and effectiveness of treatments for psychological disorders. While it is important to demonstrate that an intervention yields reductions in symptoms at a 'beyond chance' level, it is also essential to quantify the magnitude and meaningfulness of this improvement, which is generally referred to as 'clinical significance'. A statistically significant result could represent only modest benefits from therapy if the within-group variability is small or the sample size is large (Gillis et al., 1995). Therefore, methods have been developed for measuring the extent to which treatments produce clinically significant benefits. For example, Jacobson and Truax (1991) introduced the Reliable Change Index, which basically considers a patient to be 'recovered' when he/she displays improvement to a statistically reliable degree. Kendall and Grove (1988) proposed another possibility to compare data from treated individuals to normative data, typically collected from community samples. Such comparisons answer the question to what extent the treated individual, at post-treatment, is clinically equivalent to the normative group. Typically, these methods require normative data for outcome measures which possess good reliability and validity.

The present study provides such normative data for the PSWQ, the most widely employed self-report scale for measuring worry, the key feature of GAD. For this purpose, the PSWQ was administered in a large community sample as well as a clinically referred sample of patients

with GAD, for which currently no such normative data are available. Normative data were not only provided for the original 16-item version, but also for an abbreviated version from which the five negatively worded items have been removed. This shortened version of the PSWQ has been shown to be a promising alternative for the full-length version (Hazlett-Stevens et al., 2004; Fresco et al., 2002), and might overcome some of the problematic aspects of the use of reversed items. That is, negatively worded items can reduce the reliability and validity of a scale, and frequently form a separate method factor that has no substantive meaning (Woods, 2006), which was also shown to be the case with the PSWQ (Brown, 2003; Hazlett-Stevens et al., 2004; Van der Heiden et al., 2010; see also Chapter 4). Thus, for the assessment of treatment effects it seems most appropriate to employ the normative data of the abbreviated version of the PSWQ. Nevertheless, it is recommended to administer the full-length version, as the negatively worded items may be helpful to disrupt a potential response bias when completing the scale (Marsh, 1996).

Positive features of this study are the adequate sample size of the community sample and the use of a well-diagnosed clinical sample of adult patients with GAD, the disorder for which worry is the key symptom. Furthermore, this is the first study that provides cut-off scores for the PSWQ for a clinically referred sample of patients with GAD, and the first to provide normative data for the abbreviated version of the PSWQ for both a community sample and a sample of GAD patients. Besides these strengths, a number of limitations should also be mentioned. First, the community sample may not be fully representative for the demographic profile of the adult population. Second, with the exception of the Flycatcher subsample of the community sample, we do not know the response rate in the other subsamples, so in this respect the representativeness of these populations is questionable. Nevertheless, it should be noted that the current cut-off scores of the PSWQ compare really well with those obtained in previous research (Behar et al., 2003; Fresco et al., 2003; Gillis et al., 2005), and so it seems reasonable to conclude that the normative data as provided in the current study are suitable for identifying high worrying individuals and for interpreting treatment outcome results. Further, to assist clinicians in assessing treatment progress, on which they can base their decision to continue, adjust or terminate treatment, normgroups for both the full-length and the abbreviated PSWQ in the community sample are presented in Table 5.5.

Table 5.5 | Normgroups for the full-length and abbreviated PSWQ in a community sample (*N* = 842).

Normgroup	Total score full-length PSWQ	Total score abbreviated PSWQ
Very low	<29	<17
Low	29-38	18-23
Average	39-48	24-31
High	49-59	32-39
Very high	>59	>39

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Chapter 6

Generalized anxiety disorder: Recent developments in theory and treatment

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Abstract

GAD is responsive to treatment, particularly cognitive-behavioral therapy and pharmacotherapy. However, a reanalysis of data from eleven CBT outcome studies showed a recovery rate across all treatments of 40%, showing a need for more effective treatments. Progress might be made by basing treatment on a model of the mechanisms and factors underlying pathological worry, the hallmark of this disorder. In this chapter, two promising forms of cognitive-behavioral therapy that are based on specific theoretical models of GAD, metacognitive therapy (MCT) and intolerance-of-uncertainty-therapy (IUT), are described using case examples.

6.1 | Introduction

Cognitive-behavioral therapy (CBT) and psychopharmacological treatment are efficacious in the treatment of generalized anxiety disorder (GAD) (Hunot, Altamura, & Silva de Lima Teixeira, 2007; Mitte, 2005). However, as compared to other anxiety disorders, GAD appears only moderately responsive to traditional cognitive-behavioral therapy (Hunt, 2002; Wells & Butler, 1997). A review of the clinical significance of psychological treatments for GAD indicated that about 50% of the patients achieve recovery following treatment (Fisher & Durham, 1999). Further, it was shown that patients still worry (on average) 40% of the day after treatment has ended (Craske, 1999). A possible explanation for these relatively poor results might be that most treatments are not based on a specific theoretical model for GAD (Öst & Breitholtz, 2000; Wells, 1997). More precisely, the focus of treatment in traditional cognitive-behavioral therapy has been on challenging and restructuring the content of worry rather than targeting the basic mechanisms of GAD.

In the past 15 years, the theoretical conceptualization of GAD has undergone considerable scrutiny and refinement. Contemporary models of this disorder emphasize the avoidance of internal affective experiences, with some of them assuming a special role for aberrant cognitive processes (Behar, Dobrow DiMarco, Hekler, Mohlman, & Stapes, 2009). Two prominent examples are the metacognitive model (Wells, 1995) and the intolerance-of-uncertainty model (Dugas & Ladouceur, 1998). The specific cognitive-behavioral treatment programs that are based on these models, aim to correct the presumed distorted cognitive processes underlying the disorder, instead of the worrying itself. So far, the results of a limited number of studies on the efficacy of both treatment programs have been promising (Dugas et al., 2003; Ladouceur et al., 2000; Wells & King, 2006; Wells et al., 2010). This chapter

describes both of these theoretical models and treatments using case examples. Session-by-session treatment outlines are provided in Appendix 1.

6.2 | The metacognitive model

6.2.1 | Theory

Central to the metacognitive model (Wells, 1995; 1997) is the difference between the content of worrying and patients' beliefs about worrying, the so-called metacognitions (e.g., 'I have to worry to stay in control'). As the content of GAD worrying cannot be differentiated from 'normal' worrying, Wells assumed that it was not the content (referred to as 'type-I worrying') that is causing the disorder, but the patients' own perceptions of their worrying (referred to as metacognitions or beliefs about worrying).

According to the metacognitive model, worrying is initially used as a coping strategy for real or imagined problems, based on positive beliefs one holds about worrying (e.g., 'worrying helps me to be prepared to deal with problems'). These so-called positive metacognitions are learned by modelling and reinforcement (see also Borkovec, Hazlett-Stevens, & Diaz, 1999). For example, if a feared event does not occur, patients may attribute this to the act of worrying about it, which may lead to the development of beliefs such as 'worrying helps me prevent negative events' or 'worrying makes me well prepared'. As a result of such positive beliefs, worrying will be used as a coping or safety strategy more often. In the short term this leads to the assumed positive results: feared events do not take place and feelings of anxiety and fear decrease. In the long run, however, worrying continues to occur and is even strengthened. In addition, worrying can result in a greater sensitivity to 'danger related' information. This means that people start to interpret more and more neutral situations as dangerous, and focus on the negative aspects of a situation. Furthermore, constant worrying results in thinking of more and more possible negative outcomes, each of which may lead to more worrying.

Jerry, the worrying bank employee

Jerry is a 38-year-old bank employee, whose company doctor has referred him because of frequent short sick breaks related to anxiety (headache, irritability, restlessness, agitation), worrying and fatigue. This pattern originated after a reorganisation within the company a year and a half earlier, which caused Jerry to lose his job as a manager. In the assessment phase, Jerry reports a long history of anxiety and worrying. He describes himself as a worrier, 'just like his mother'. For as long as he can remember, he has had the tendency to see the negative side of everything and to worry about all sorts of things. After further questioning, it appears

that his mother has acted as a role model to him. Her motto was: 'as long as you think things through, you will not get caught in a sticky situation'.

As patients use the (in their opinion) successful coping strategy longer and more frequently over time, at some point worrying can become the focus of negative appraisal, resulting in the formation of negative metacognitions (such as 'worrying is harmful'). This may result from worrying to such an extent that it has become an increasingly disruptive influence in one's life. New information can also lead to the development of a negative belief about worrying. For example, if a role model who worried a lot gets a heart attack or becomes depressed, or if patients themselves start to get more complaints related to worrying (e.g., headaches). Finally, general opinions in society (which Wells refers to as 'general folklore') about the dangers of stress and worrying can contribute to the development and maintenance of negative metacognitions.

Jerry's worrying has worsened within the last two years as a result of several stressful events. Firstly, his wife's health problems. She is overstressed and is suffering from a stomach ulcer. Secondly, Jerry thinks his 7-year-old daughter is developing too slowly. The previously mentioned reorganisation and degradation at work and the decline of share prices are also causing a lot of worrying. Finally, he worries about his own anxiety complaints, which are caused by his own worrying. Jerry is constantly thinking up disaster scenarios. For example, he is worried that his daughter will not be able to keep up in school, which would mean she will not be able to get a job later on and will be alone forever. That would cause her to have psychological issues and could lead her to become suicidal. When Jerry worries about his work degradation, he thinks he is being judged on his faults, which would cause him to get fired. This would lead to financial problems, meaning he would have to sell his house and his car. Consequently, his family would leave him. According to Jerry, he worries constantly. When he has worn out one subject, the next one is just around the corner. Worrying is affecting his ability to sleep. He is gradually becoming more tired and the anxiety is leading to physical complaints. He cannot stop the thought process. This leads him to worry about the consequences of this constant worrying for his health and his family, and his life in general. He is particularly worried about becoming depressed from all the worrying, which he thinks would cause his family to abandon him. Jerry compares this to what happened to his mother. She became depressed and Jerry feels this was the cause of his parents' divorce (Jerry had been out of the house for ten years by then).

Once activated, negative metacognitions lead to 'worrying about worrying', in the meta-cognitive model referred to as 'type-II worrying' or 'meta-worrying', resulting in or exacerbating

feelings of anxiety and fear. These emotional responses that accompany the worrying can be interpreted as a confirmation of the negative metacognitions, which ultimately increase the negative feelings. In an attempt to stop this self-amplifying process, patients try to prevent the worrying itself, or to reduce the negative consequences, by several behavioral responses and thought control attempts.

The 'behavioral responses' can be divided into multiple categories. First, attempts to avoid things or events that can lead to worrying, e.g., avoiding information from the media about diseases or burglaries in the neighborhood. Attempts to avoid the worrying itself form the second type of behavioral strategies. For instance, by constantly staying active patients try to distract themselves from worrying. Another behavioral strategy is reassurance seeking. If, for instance, a patient is worried her daughter may have been involved in an accident on her way to school, a call to her school can give relief, when it appears that nothing has happened. Another example of reassurance seeking is asking an important figure, for instance the partner or family doctor, whether it is possible to lose your mind from too much worrying.

The use of 'thought control' (or: cognitive attempts to control worrying) in GAD also manifests in different ways. First, there are attempts to suppress worrying that is thought to be threatening. However, this often increases worrying. For example, in the 'white bear' experiment participants who had been instructed not to think about a white bear, reported to have thought about a white bear a lot more than participants who were allowed to think about a white bear (Wegner, 1989). The increase in worrying in reaction to the attempts to suppress thoughts, results in the development of new or the reinforcement of existing negative beliefs about worrying (e.g., 'worrying is uncontrollable'). Second, worrying is used as a cognitive strategy to avoid more threatening or aversive images (Borkovec & Inz, 1990). This strategy will be explained in more detail later on in this chapter.

Jerry reports several worry behaviors. He calls home multiple times a day to see if his wife is doing all right (even though she is doing a lot better now), he tutors his daughter and tries to avoid tasks and situations in which he could be judged. To decrease the chance of errors, he thoroughly plans his activities. He also leaves the house as little as possible, for fear of burglars. This is because of recent reports in the media about burglaries in his neighborhood. He tries to avoid media reports about diseases. Such reports usually lead him to believe he will get the diseases in question. Furthermore, he tries to stop worrying by either finding distractions (crossword puzzles, watching television) or thinking positive. This is to no avail.

Each of these strategies contributes to the maintenance of the negative metacognitions, because they are keeping conflicting information away from the individual (e.g., that worrying

does not make you 'lose your mind'). The metacognitive model of GAD (Wells, 1997) is shown in Figure 6.1.

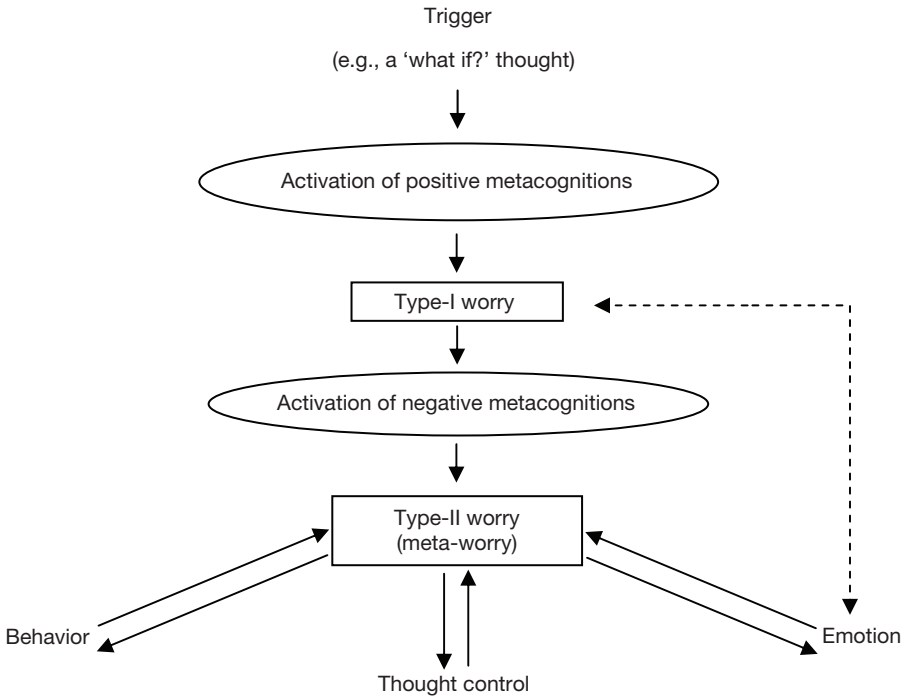

Figure 6.1 | The metacognitive model of generalized anxiety disorder (GAD) (Wells, 1997).

Several studies have provided support for the metacognitive model (see Wells, 2009, for an extensive overview of these studies). First, both positive and negative beliefs about worrying have been found to correlate with a tendency towards pathological worrying (Cartwright-Hatton & Wells, 1997). Further, GAD patients have higher scores judging the positive reasons for worrying than non-anxious people (Borkovec & Roemer, 1995), and they report significantly more negative ideas about worrying compared with patients who have a panic disorder or social phobia, and with a non-clinical control group (Wells & Carter, 2001). Finally, type-II worrying has been found to be a better predictor for pathological worrying than type-I worrying (Wells & Carter, 1999), whereas negative metacognitions have been found to predict GAD (Nassif, 1999).

6.2.2 | Treatment

The implication of the metacognitive model is that the modification of metacognitions is essential to the success of treatment. Different from other GAD treatment programs, metacognitive therapy (MCT) is not aimed at the content of worrying (type-I worrying) and does not teach ways to control worrying. Apart from standard cognitive interventions (see e.g., Beck, 1999; Ten Broeke, Van der Heiden, Meijer, & Hamelink, 2008), in MCT several interventions that were specifically designed for examining metacognitions are used (Wells, 1997, 2009).

MCT consists of four phases. Central to the first phase are case conceptualisation and socialization to the model (Phase I). In the next phase negative beliefs about worrying are examined, first the patients' beliefs about the uncontrollability of worrying and next their beliefs about the dangerous consequences of worrying (Phase II). In the third phase positive metacognitions are examined (Phase III), and in the fourth and final phase alternative coping strategies to judge danger and handle imagined threats are explored and practiced (Phase IV).

6.2.3 | Phase I: Case conceptualisation and socialisation to the model

Several techniques are available for eliciting information for case conceptualisation. A first option is to ask patients for their appraisals of the consequences of worrying, for the worst that could happen, and for the reasons they cannot stop the worrying. Also, patients can be asked to list both the advantages and disadvantages, as a means of eliciting beliefs about worrying. A third strategy is to draw up an experiment, in which patients are asked to concentrate on their worrying. As a result, negative metacognitions will be activated. Asking patients for the reasons of their control strategies will also uncover (negative) beliefs about worrying. Finally, the Meta-Cognitions Questionnaire (MCQ) (Cartwright-Hatton and Wells, 1997), a self-report questionnaire aimed at measuring inter-individual differences regarding positive and negative ideas about worrying and intrusive thoughts, can also be helpful in eliciting beliefs about worrying.

Identifying negative metacognitions is relatively easy for Jerry. When asked for the supposed consequences of his constant worrying, Jerry expresses his fear of becoming depressed (negative metacognition 1). According to him, the worst thing that can happen is being abandoned by his family (negative metacognition 2). In response to the question why he does not stop worrying if he sees it as threatening, Jerry says that he is no longer able to control the worrying (negative metacognition 3).When asked if worrying has been advantageous to him at any point, Jerry says that, for years, worrying caused him to think that he was at least prepared for the worst (positive metacognition 1). Jerry also thought that by thinking

about possible problems, he could still jump into action to prevent such problems (positive metacognition 2). Figure 6.2 shows Jerry's beliefs about worrying within the metacognitive model.

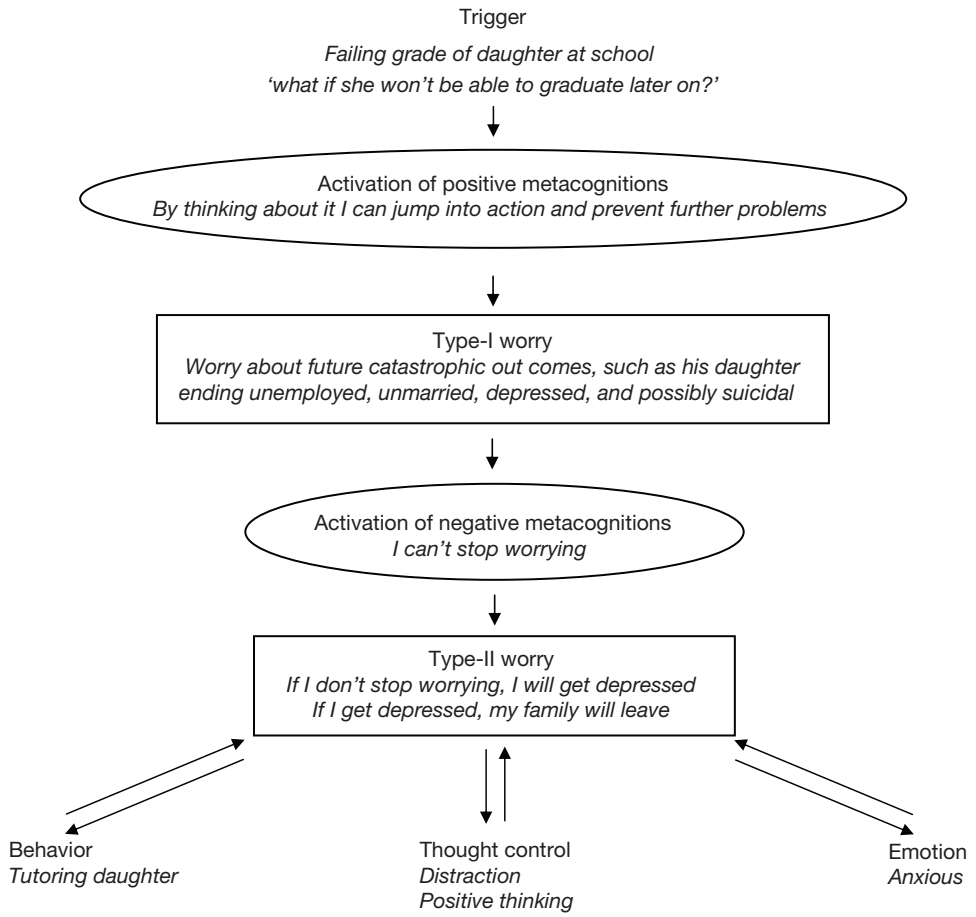

Figure 6.2 | Metacognitive case conceptualisation of Jerry.

6.2.4 | Phase II: Examining negative metacognitions

In MCT, negative metacognitions about the uncontrollability of worrying are targeted first, and then beliefs about the danger of worrying (Wells, 1995; 1997). To challenge these beliefs clinicians can use a range of verbal reattribution techniques and behavioral experiments. An example of a GAD-specific verbal technique is asking patients for experiences in which they could divert their attention away from the worrying, and for the meaning of such

experiences for their beliefs about the uncontrollability of the worrying. Another verbal strategy is the dissonance technique, in which cognitive dissonance is heightened by means of guided questioning. It is pointed out to patients that they hold both positive and negative metacognitions; they are then asked to explain how something can be positive and negative at the same time. Examples of behavioral experiments for examining negative beliefs about worrying in MCT for GAD are: 1) postponed-worry experiment, in which worrying is postponed to an established worry period once patients catch themselves worrying, to test whether worrying is (un)controllable, 2) paradoxical experiments, in which patients attempt to 'lose control' over worrying at specified worry periods, thereby establishing that loss of control is not possible, or 3) pushing-worry-limits experiments, in which patients are asked to worry 'worse' during spontaneous worry periods to test out feared consequences of worrying.

Jerry's belief about the uncontrollability of worrying is examined mainly using behavioral experiments. Postponing worrying to planned worry periods gives Jerry a 'sense of control'. He is less tense and even has a positive feeling about it. As a result, his estimation of the chance to become depressed by his worrying slightly decreases. Consequently, when he tries to lose control during the planned worry periods, he is unable to do so. In fact, after a while, the worrying starts to decrease. Based on these positive experiences, Jerry is asked to stop his thought control strategies, to find out if the worrying will decrease accordingly. As this turns out to be the case, as a next step Jerry is asked to exaggerate his worries during problematic worry episodes, by engaging in heightened catastrophising, deliberately having crazy thoughts, or trying to lose mental control. These pushing-worry-limits experiments have paradoxical effects; his worrying decreases when Jerry tries to make it worse (instead of suppressing it). As a result of these interventions, Jerry's belief about the uncontrollability of worrying changes for the better, and his fear and worrying decrease all on their own. After examining the uncontrollability beliefs, Jerry's negative beliefs about the dangerous consequences of worrying were challenged. First, the evidence supporting his belief 'worrying will make me depressed and cause my family to abandon me' was questioned. As only evidence, Jerry presents his parents' divorce, which in his opinion was due to his mother becoming depressed from her excessive worrying. As counterevidence Jerry notes that his wife has repeatedly told him that she will not leave him and that she loves him, that his physician and his clinician have explained to him that worrying is very common and does not automatically lead to depression, and that a friend of his has been depressed without his family abandoning him. Another argument against his belief is that he has been worrying all his life, but has never become depressed. After reviewing all the evidence, Jerry rates the chance of him becoming depressed from worrying lower than before. The chance of being abandoned by his family if he would become depressed, has now become almost zero.

Despite this decreased credibility of the negative metacognitions, Jerry still states that he does not exclude the fact that he might get 'something' from all his worrying, and therefore he would still like to get rid of it.

6.2.5 | Phase III: Examining positive beliefs about worrying

In order to prevent worrying from remaining a coping strategy in the future, and (thus) to prevent the recurrence of GAD, positive metacognitions have to be modified as well. Again, both verbal reattribution techniques and behavioral experiments offer effective means of modifying such beliefs. For example, patients can be asked whether they remember situations when worry was not used but events turned out positively. If so, the implication of these experiences for the usefulness of worry is being discussed. Further, mismatch-strategies can be used, in which the content of anticipatory worry is contrasted with the actual events. By doing so, the accuracy of the assumption that worrying leads to accurate predictions is questioned. The results of the mismatch-strategies are discussed with respect to the credibility of the beliefs about the value of worrying. In the retrospective variant, patients are asked to describe a recent worry period in detail, including thoughts and images of negative outcomes, and then to compare the worry scenario with the actual outcome. The prospective variant requires entering worried-about situations, and then to contrast the content of the anticipatory worry with the actual events encountered. Examples of behavioral experiments to test positive metacognitions are worry-abandonment experiments, in which patients give up worrying in order to test if negative consequences actually occur, and worry-enhancement experiments, in which patients increase their worrying to determine to examine if achievements and functioning improve and/or positive events occur.

As a first step in challenging Jerry's positive beliefs about worrying, all evidence that supports or contradicts these metacognitions is elicited. Jerry reports several arguments that prove that he can jump into action and prevent possible problems. For instance, he thinks he has prevented a few failing grades by tutoring his daughter. On the other hand, worrying often leads to anxiety and meanwhile he is thinking of so many possible dangers, that he seems to be constantly working on coming up with solutions for them. In the end, he does not find solutions to a lot of them, while most of the imagined 'disasters' after all do not come true. Based on the elicited evidence Jerry comes up with an alternative cognition about the usefulness of worrying: 'Sometimes it helps to think about problems, but more often it works against me: it makes me anxious and I worry so much, and about so many things that I no longer find solutions to any of them. On top of that, most of my predictions do not come true, so worrying is not useful at all.' Jerry also remembers several situations that had a positive outcome, without him worrying about it beforehand. At first, Jerry can only come up

with older situations, because he has been worrying about almost everything lately. These memories do help him devalue his positive ideas about worrying. As worrying decreases over the course of the treatment, Jerry experiences more and more current situations that end well without any worrying.

6.2.6 | Phase IV: Modifying cognitive bias and strategy shifts

The fourth and final phase of MCT is focused on modifying cognitive biases and practicing alternative ways of processing information. Interventions are aimed at (1) decreasing hypervigilance for external (e.g., looking out for reports in the media on burglaries) or internal (e.g., focusing on physical complaints that prove that worrying does lead to certain complaints) threats, and (2) modifying the 'thinking strategy' of patients.

Standard cognitive therapy techniques aimed at processing information that is inconsistent with the content of worrying (type-I worrying), such as the Socratic dialogue, the pie-chart technique, a log of positive events and behavioral experiments (see e.g., Beck, 1999; Ten Broeke et al., 2008), can be used to decrease hypervigilance for external and internal threats. As a result, the credibility of the initial worries will diminish and more credible alternative thoughts can be formulated, which will result in a change in negative feelings.

Jerry pays attention to every mistake of his daughter, which proves to him that she really is falling behind in her development. In an attempt to learn to (also) pay attention to the positive sides of his daughter, Jerry is asked to keep a log of positive events. He is also tasked with a mini-survey (in which he interviews both her teacher and a few parents of classmates), and some research on child development. These interventions change his perspective; his daughter may not be a genius, but she does not lag behind in her development. She is viewed as a sweet and fun child by others, something that Jerry now admits is equally important, and reduces his fear that she will end up alone. Concerning his fear of burglars, Jerry is instructed to stop looking for information about burglaries in the neighborhood. As a result, his fear subsides over time, allowing him the courage to gradually go out more.

As worrying is longstanding used as a coping strategy some patients have only limited experience of contemplating uncertain and mildly stressful events in a positive way. In MCT, three strategy-shifting techniques are available. First, patients can be taught to examine new endings for old worries, by generating positive outcomes in brainstorm sessions. Second, instead of controlling their worries, patients practice the passive 'letting go of thoughts', to increase awareness of worrying without doing anything with it. A third and final strategy shift is the use of exposure and response prevention exercises to abandon avoidance and safety behavior, such as no longer calling to check if a significant other has arrived safely at work or

school, no longer asking for reassurance, or consciously looking up information that would have been avoided previously.

Jerry is taught to examine and note alternative outcomes to possible problem situations at set times. For example, he imagines that the decreasing share prices will eventually improve as they always do, that he can wait to sell his shares until the stock market improves, and that he will not lose too much money if he unfortunately would have to sell at a lower price. As a result, he is less afraid to go bankrupt, feels more at ease and decides to stop trading stocks in the future. Regarding his daughter, Jerry keeps up his earlier attempts to keep his disaster scenario in perspective; even though she may not be a genius, she will still be able to find a job, she will be valued by others for different qualities, and her ability to find a partner does not depend on her performance in school or work. He starts to look at her differently and to appreciate her more. He stops tutoring her, which does not impact her performance negatively. Jerry also stops avoiding reports on diseases. If exposure to such reports result in worrying, he is able to address it successfully in brainstorm sessions, in which he thinks up alternative outcomes.

6.3 | The intolerance-of-uncertainty model

6.3.1 | Theory

An alternative account is the intolerance-of-uncertainty model of GAD, in which intolerance-of-uncertainty (IU) is the cornerstone (Dugas, Gagnon, Ladouceur, & Freeston, 1998). IU refers to the tendency to react negatively to uncertain and ambiguous events, independent of their probability of occurrence and their associated consequences. As everyday life is full of uncertain and ambiguous situations, people who are intolerant of uncertainty may experience many worries and negative emotions, such as fear and sadness (Dugas, Freeston, Blais, & Ladouceur, 1994; Macleod & Mathews, 1988). IU is thought to be the result of (1) a lower threshold for perceiving ambiguity, (2) stronger reactions in ambiguous situations (more uncertainty and fear, and more worrying, compared to people who are low in IU), and (3) anticipating feared future consequences of uncertainty (Krohne, 1993).

Diane, the worrying mother-to-be with the alleged unfaithful partner

Diane, a 34-year-old lawyer, is referred by her family doctor because of strong feelings of agitation and fatigue. The feelings of agitation have been present for as long as she can remember, both physically (not being able to sit still) and mentally (constant worrying). The agitation regularly results in panic attacks, which she interprets as an anxiety complaint.

The feelings of panic decrease when she calls an acquaintance or writes in her diary. She describes herself as a worrier, who always has a negative outlook on things. An important theme of Diane's worries is the relationship with her partner; they argue a lot, and there is little positive communication to make up for it. She worries about her partner's possible betrayal, although she does not have any evidence. She also worries a lot about the relationship with her mother, her work (possible mistakes) and her capabilities, her health, and having children. She ponders whether she is healthy and strong enough to be a mother, and how having children would impact her life. As she cannot find answers to the questions she has in her worries, she feels very insecure and tense. In an attempt to get reassurance and feel more certain, she repeatedly asks family and close friends if they think she would be a good mother, or if they can give her advice about having children. Other strategies to feel more certain are checking on her partner by calling him at work when he needs to work late, and checking his clothes for traces of perfume or lipstick Diane also seeks reassurance by visiting her family doctor whenever she feels something 'strange'. At work, she tries to reduce her insecurity by asking her boss for his opinion about her, asking her colleagues to check her work for mistakes, and by working long hours (10 to 11 hours a day). She also carries out her work very precisely to minimize the risk of making mistakes. In the meantime, she has been trying to avoid worrying by constantly remaining active, even outside of work. At first, this was a reasonably effective strategy, but lately it has been wearing her out.

IU exacerbates initial 'what-if?' thinking, which triggers repetitive questioning in the absence of real problems, thereby increasing worry and hindering problem solving and decision making (Dugas et al., 1998; Freeston, Rheaume, Letarte, Dugas, & Ladouceur, 1994). In response to ambiguous situations patients with GAD are prone to display chronic worry, based on beliefs that worry will either help them to cope more effectively with such events, or to prevent feared events from happening (Borkovec & Roemer, 1995; Davey, Tallis, & Capuzzo, 1996). These positive beliefs about worrying form the second variable in the IU model.

Diane reports that she has often worried, because she did not know another way to deal with stressful events (a positive metacognition). She had hoped worrying would lead to a solution (another positive metacognition). When asked, she says that this did not happen most of the time; worrying mostly led to 'thinking in circles'. Despite the fact that worrying did not lead to finding solutions, Diane still thinks that worrying at least helps her prepare for the worst. According to Diane, this means that when the worst actually does happen, she will not be overly disappointed (a third and final positive metacognition). Despite these advantages, Diane also thinks that worrying will make her a negative person, and that if she will continue

worrying as much as she already does, it finally will be all she does. Therefore, she wants to stop worrying.

Problem orientation is defined as the ideas someone holds about problems (e.g., problem perception, problem attribution and problem estimation), and about their ability to solve problems autonomously (Maguth, Nezu, D'Zurilla, & Friedman, 1996). A negative problem orientation is the third variable in the model, and refers to the tendency to view ambiguous situations as problematic and problems as threatening, to have little confidence in one's own problem-solving abilities, and to be pessimistic about problem-solving outcomes (Davey, Hamptom, Farrell, & Davidson, 1992; Ladouceur, Blais, Freeston, & Dugas, 1998). As it has been shown that patients with GAD are able to come up with solutions (Davey et al., 1992; Ladouceur et al., 1998), it seems that they do not lack problem-solving skills but rather have trouble applying these solving skills due to the ambiguous or uncertain elements of a problem situation and the problem-solving process. In an attempt to deal with the uncertainty surrounding both the problem and the problem-solving process, patients with GAD think excessively about a lot of relatively unimportant details of the worrisome situation. Unfortunately, this thinking about details disrupts the problem-solving process, and results in an extended length of time needed for decision-making in ambiguous situations (Dugas & Ladouceur, 2000; Ladouceur, Talbot, & Dugas, 1997).

A negative problem orientation already comes up in Diane's positive beliefs about worrying; she feels she has no other option than to worry when faced with problems, and she hopes this will lead to a solution, although she reports that she does not come up with concrete solutions. For example, she tries to deal with her insecurity about her performance at work by working long hours, trying to be meticulous, and asking her colleagues for reassurance. This strategy is ineffective, as becomes clear from the fact that Diane, as soon as she is at home, starts to worry about her performance, going through the day step by step. She usually finds something she did not do perfectly, which makes her worry more. In the end, she is afraid to be 'discredited', which means she will be fired. To get some certainty concerning her worries about her partner ending the relationship, she checks on her partner all the time. However, when he notices this, he gets angry, which Diane in turn sees as proof that he wants to end the relationship, which increases her worrying. It hardly ever happens that she discusses these problems calmly to come up with a solution.

The final process variable included in the IU model is cognitive avoidance. Worry is primarily a verbal-linguistic mental activity, which may serve to avoid fear-related mental imagery (Borkovec & Inz, 1990; Borkovec & Lyonsfields, 1993). Because the avoidance of

images appears to lead to an inhibition of peripheral somatic activity, it has been suggested that one of the functions of worry may be to avoid the evocation of threatening images, and its accompanying arousal (Borkovec & Hu, 1990; Borkovec, Lyonfields, Wiser, & Deihl, 1993). However, cognitive avoidance may promote the maintenance or even escalation of worry and anxiety, because it negatively reinforces worry and interferes with emotional processing (Butler, Wells, & Dewick, 1995; Wells & Papageorgiou, 1995).

When asked, Diane says that she mostly worries in sentences. Worrying initially leads to a 'sense of relief' (which is also apparent in her positive metacognitions), but it does not lead to solutions or a decrease in worrying. She usually does not see images when she worries, but when she does visualise feared negative events, such as her partner with another woman, she slightly panics. By carrying out the above-mentioned behaviors (in this example: calling up her partner at work to check on him), she tries to get reassurance, which causes her panic to subside a little bit. However, afterwards the worrying only continues.

Empirical support for the IU model has emerged from several studies (see Dugas & Robichaud for an extensive overview of these studies). First, IU has been found to be a strong predictor for the tendency to worry (Dugas, Ladouceur, & Freeston, 1995; Lachance, Dugas, & Ladouceur, 1995), as well as to be associated with worrying (Ladouceur et al., 2000). Based on their IU level, patients with GAD can be successfully distinguished from non-clinical average worriers (Dugas, Freeston, & Ladouceur, 1994), a normal population (Dugas et al., 1998), and other anxiety disorders like obsessive-compulsive disorder, panic disorder and social phobia (Ladouceur, Blais, Freeston, & Dugas, 1998). Second, levels of worry have been found to be strongly related to having a negative problem orientation, but not to knowledge of problem-solving skills (Dugas, Freeston, & Ladouceur, 1997; Dugas et al., 1998; Dugas, Letarte, Rhéaume, Freeston, & Ladouceur, 1995). Also, negative problem orientation was found to make a specific contribution to the prediction of worry (Robichaud & Dugas, 2005), and to be related to the severity of GAD symptoms (Dugas & Robichaud, 2007). In terms of comparisons between different clinical groups, patients with GAD have been found to have a more negative problem orientation than patients with various other anxiety disorders (Ladouceur et al., 1999), except those with panic disorder (Dugas, Marchand, & Ladouceur, 2005). Concerning the component of cognitive avoidance, it has been shown that fear- inducing images lead to an increase in peripheral somatic activity (e.g., cardiovascular activity; Vrana, Cuthbert, & Lang, 1986), whereas (the primarily verbal-linguistic) worrying leads to an inhibition of such aversive activity (Borkovec & Lyonfields, 1993; Lyonfields, Borkovec, & Thayer, 1995; Thayer, Friedman, & Borkovec, 1996). The cognitive avoidance hypothesis is further supported by self-report data showing that GAD patients think of worrying as a way

to 'distract themselves from more emotional subjects' (Borkovec & Roemer, 1995; Freeston, Rheaume, Letarte, Dugas, & Ladouceur, 1994). Fourth and finally, it has been shown that positive beliefs about worrying make a unique contribution to the explanation of how much people worry (Freeston, et al., 1994), and that patients with GAD reported stronger beliefs than non-clinical moderate worriers (Ladouceur, Blais, Freeston & Dugas, 1998). However, GAD patients have not been found to hold stronger beliefs about the usefulness of worry than patients with other anxiety disorders, suggesting that such beliefs are a characteristic of clinically anxious individuals rather than being a GAD-specific characteristic (Ladouceur et al., 1999; Dugas, Marchand et al., 2005).

The central component of the intolerance-of-uncertainty model, intolerance of uncertainty, appears to be a higher-order process that contributes to the other three model components, as empirical data have shown that the relationship between GAD and the other components in the model can be explained, at least partially, by the level of IU (see Dugas & Robichaud, 2007). However, IU not only influences the other model components, all components are thought to interact in complex ways, as is shown in Figure 6.3. Apparently, we are just beginning to understand the ways in which the model components interact (Dugas & Robichaud, 2007).

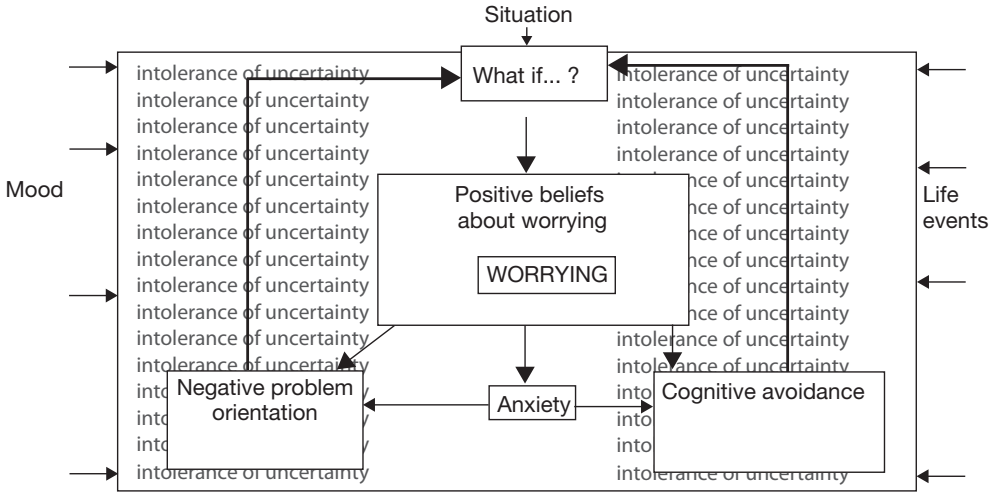

Figure 6.3 | The intolerance-of-uncertainty (IU) model (Dugas et al., 1998).

6.3.2 | Treatment

Following the IU model, treatment should focus on decreasing anxiety and the tendency to worry by promoting an increased tolerance of uncertainty. Intolerance-of-uncertainty therapy (IUT) consists of four phases. Following a brief explanation of the presumed role of IU in the etiology of worry and anxiety problems, IUT proceeds with worry awareness training, during which patients learn to make a distinction between worries that are amenable to problem solving and worries that are not. Once patients are able to properly discriminate between these two types of worry, the next treatment phase involves a problem-solving training for soluble worries, which consists of five steps: (1) problem definition, (2) goal formulation, (3) generation of alternative solutions, (4) decision making, and (5) solution implementation and verification (D'Zurila & Nezu, 1999). In the following phase of IUT, cognitive avoidance is addressed by means of worry exposure exercises. During these exercises, patients vividly experience and process their core fears by focusing on images of the most feared expectations of insoluble worries (Van der Heiden & Ten Broeke, 2009). In the final phase, positive beliefs about worry are directly modified by cognitive therapeutic interventions (e.g., questioning the evidence supporting these beliefs, worry experiments).

6.3.3 | Phase I: Worry awareness training

Worry awareness training involves the identification of worry themes and the classification of worries into one of two categories: (1) worries that are amenable to problem solving (or: worries about current problems), and (2) worries that are not amenable to problem solving (or: worries about hypothetical problems). A conflict with a colleague is an example of the first type of worries, worrying about the possibility of bankruptcy without any financial problems is an example of the second type (Dugas & Ladouceur, 2000). During this phase patients are instructed to stop four times a day what they are doing to take note of any worries they may be experiencing at that moment, and the type of worry. The worries are written down in a worry diary, in which the two types of worry are distinguished.

Diane registers her worries four times a day: after breakfast, lunch, and dinner, and at nine o'clock in the evening. These registrations reveal that she hardly worries after breakfast and lunch, probably because she is so intensely occupied with her work. But after work and in the evening, she worries a lot. After dinner she mainly worries about her workday (and possible mistakes at work), in the evening she worries mostly about her partner, but also about her mother, having children, and her health. Diane has no problem distinguishing between the two types of worrying. The worries she has about her relationship, her mother, and her work are classified as 'soluble', the worries about the alleged cheating, her health, and motherhood are not. Some of her worries about her work are also categorized as 'insoluble'.

6.3.4 | Phase II: Problem orientation training

In the second phase of IUT the interventions are aimed at worries about situations that are amenable to problem solving. Two discrete elements are involved in this treatment phase, namely improving problem orientation and applying problem-solving skills. The first refers to the way in which an individual views problems and problem solving, the second to the application of steps that need to be carried out in order to actually solve a problem. The process of constructive problem solving includes five steps (D'Zurilla & Goldfried, 1971; D'Zurilla & Nezu, 1999):

- Defining the problem;
- Formulating problem-solving goals;
- Generating alternative solutions;
- Choosing a solution; and
- Implementing the solution, and evaluating its effectiveness

The therapist helps patients to stay focused on the problem at hand, and to identify the most important elements of the problematic situation, instead of concentrating excessively on relatively unimportant details (step 1). Next, patients are taught to formulate clear and concretely defined goals, which are realistic and attainable. Depending on the problem, it might be helpful to be aware of the timeline for achievement of particular goals. As some goals may take longer to achieve than others, patients might develop both short and long-term goals, so as not to experience feelings of disappointment when the final goal is a long-term one. In steps 3, 4 and 5 patients actually practice problem-solving skills. A step-by-step problem-solving plan can be used for this, which consists of seven steps (see Van der Heiden, 2004). Table 6.1 presents Diane's step-by-step problem-solving plan, regarding her worries about her relationship with her partner. By applying these problem-solving skills, Diane learned to deal with her 'solvable' worries in a more concrete way, resulting in a decrease in worrying about such problems, and a heightened sense of control over these situations.

6.3.5 | Phase III: Worry exposure

In the third phase of IUT, cognitive avoidance is addressed by means of worry exposure exercises, during which patients imaginally expose themselves for at least 25 minutes to images of the most feared outcomes of worried about situations. Together with this exposure assignment, a response-prevention instruction is given. Patients are told that attempts to neutralise the image (e.g., by seeking distraction, or by thinking about/doing something else) are not allowed. After exposure to the most feared image, time is dedicated to thinking about alternative outcomes. This enables patients to realize that, even if the worst scenario materialises, they can appeal to some rescue and/or coping strategies. It is hypothesised

that patients learn to tolerate the previously avoided images and the unpleasant physiological reactions typically associated with that imagery, and to (more easily) develop a better balanced viewpoint about the worrisome event or situation (see Van der Heiden & Ten Broeke, 2009, for a detailed description of worry exposure).

Table 6.1 | Diane's step-by-step problem-solving plan.

1. **Description of the problem causing the worrying**

   Bad communication with David: when we talk to each other, it is mostly confrontational.

2. **Formulation of the goal, in concrete terms**

   I would like to be able to talk calmly to David again, about both day to day things and our relationship.

3. **Brainstorming about possible solutions**

   - Relationship counselling
   - Discussing better communication with David
   - Divorce
   - Asking friends or David's parents for advice
   - Asking my mother for advice

4. **Pros and cons, and expected result of each solution**

   – ***Relationship counseling***

pro:	*professional help*
	we do not have to face the problem alone
	an impartial opinion
con:	*I do not know if David wants to*
	it takes up a lot of time and we are both already quite busy
	what would other people think of us?
expected result:	*David does not want to participate and we will fight about it*

   – ***Talk to David myself***

pro:	*it costs less time*
	it would make us feel good to solve our problems ourselves
	we have to be able to do it ourselves
	David would not want to go to therapy anyway
con:	*it has not worked so far*
	it might cause even more conflict

expected result: *With the advice of my therapist I will be able to do this, and it will feel good to do it myself*

– ***Divorce***

pro: *we would not fight anymore*

we might find a more suitable partner

con: *we do want to continue together!!*

I cannot go on without David

we would have to sell our house

we would have to split our friends

I might never find another partner

expected result: *we would both feel bad*

– ***Asking friends or David's parents for advice***

pro: *they are familiar with us*

they are rational people

con: *we do not want to expose our problems*

what would they think of us?

expected result: *I would rather try something else first: this seems too embarrassing*

– ***Asking my mother for advice***

pro: *she has experience with this sort of problem*

con: *my mother and I cannot talk well either*

she will probably be negative about me and try to make me feel guilty

expected result: *negative feelings*

5. Pick the solution that you will apply (based on step 4)

I want to talk to David myself. I am going to plan a conversation with him and prepare for that in the therapy session. I will write down the points I want to discuss. I want to practice the conversation during therapy, so that I am well prepared.

6. Implementation of the chosen solution

On Tuesday June 7th, we will have a quiet evening together. That is when I will discuss the problem with David.

7. Evaluation: has the chosen solution served its purpose?

The conversation went well. I have handled the conversation well and I am glad to have brought up the problem myself. The result is quite satisfying. David also wants to communicate differently. We have agreed to sit at the table every day after dinner for at least fifteen minutes to discuss things. We have decided to discuss difficult subjects at calm moments from now on. If the tension rises, we will take a time out and come back to it the day after.

Diane describes the following worries regarding her possible future motherhood: 'If I have children they will probably have the same complaints as me. How can I be a good mother when I am constantly anxious and worried. They will be driven mad by me. I will constantly be worried something will happen to them and I might start checking them as well or accompany them everywhere. I will be so worried that it will wear me down and then I will not be able to take care of them at all. I am too much of a worrier to be a good mother.' When asked about how she pictures this, she describes an image of herself in bed, crying, causing her children to panic. The meaning of this image is that she will be a bad mother. By exposing herself to this fearful image frequently, her feelings of fear and anxiety subside slightly. After a while, Diane admits her fear is exaggerated. She still thinks her anxiety could be a problem, but she is also aware that she has many qualities of a good mother (among other things, she reports that she is kind and caring, is very keen on having children and gets along with children very well). Especially the latter makes her insecurity about her future motherhood less severe.

6.3.6 | Phase IV: Re-evaluation of positive beliefs about worrying

The last phase of IUT involves addressing positive beliefs about the usefulness of worry. These beliefs can be elicited in the same ways as already described for MCT (e.g., asking patients for positive appraisals of their worrying, listing the advantages of worrying, or discussing the items of the MCQ concerning positive beliefs). Another way to assist patients in identifying their positive beliefs about worrying, is to present the most common beliefs typically held by patients with GAD, and then ask patients to generate personal examples from their own worries. These beliefs typically fall into five categories (Dugas & Robichaud, 2007): (1) worrying helps to find solutions to problems, (2) worrying serves a motivating function that ensures things will get done, (3) worrying can protect a person from negative emotions, (4) worrying can prevent negative outcomes, and (5) worrying represents a positive personality trait. Once identified, the positive beliefs are challenged in a nonjudgmental manner with the primary goal to help patients to acknowledge that their beliefs are thoughts instead of facts. Standard cognitive therapy techniques are useful strategies for re-evaluating positive beliefs about worrying, such as questioning the evidence for the value of worrying in a Socratic way, completing worry thought records, and behavioral strategies, such as the lawyer-prosecutor role play. In this role play patients take the role of a lawyer who must convince the members of a jury that an identified worry is useful. For detailed descriptions and verbatim reports about these basic cognitive therapy techniques, see e.g. Beck (1999) and Ten Broeke et al. (2008).

At first, Diane's positive beliefs about worrying are examined using Socratic questioning, by questioning the evidence that supports the supposed usefulness of worrying, and next the

evidence that contradicts this belief. Diane eventually formulates the following alternative belief about worrying, which she sees as credible: 'I worry too long about a lot of things without coming up with a solution. Therefore, it is not a useful strategy. It would be better if I find solutions in a different way, such as the problem-solving strategy I learned in therapy.'

6.4 | Conclusion

In this chapter, two recently developed cognitive-behavioral treatments are described, which are based on GAD-specific theoretical models. The metacognitive model proposes that negative beliefs about worry (i.e., its uncontrollability and dangerousness), resulting in 'worry about worry', play a key role in the development and maintenance of GAD (Wells, 1995; 1997). As such, not the process of worry in itself, but rather these negative metacognitions (e.g., 'If I cannot stop my worrying, I will go crazy') are regarded as crucial for the development of GAD. Following the metacognitive model, the main focus of MCT is not worry itself, but rather the metacognitive factors that contribute to the development and persistence of GAD, including negative beliefs about the uncontrollability and dangerousness of worry, positive beliefs related to the patient's reliance on worry as a coping strategy, and ineffective attempts to avoid worry and to control thoughts. The intolerance-of-uncertainty model (Dugas et al., 1998) is based on the idea that patients with GAD become distressed and upset when confronted with uncertain or ambiguous situations, and experience persistent worry in response to such events, based on positive beliefs about the usefulness of worry. However, the excessive worrying hinders problem solving and decision making, and leads to cognitive strategies to avoid the evocation of threatening images, thereby further increasing worry and anxiety. Following the IU model, IUT focuses on decreasing anxiety and the tendency to worry by promoting an increased tolerance of uncertainty.

Empirical support has emerged for both these GAD models and the efficacy of both treatment packages (see Dugas & Robichaud, 2007, and Wells, 2009, for overviews of these studies). However, the number of studies providing support for the efficacy of both MCT and IUT is limited, and all these studies had more or less important methodological limitations, e.g. a relatively small sample size, and/or lack of a control group. Therefore, this evidence should be seen as only preliminary. Nevertheless, in a recent review Fisher (2006) noted that both of these GAD-specific interventions for GAD seem to produce clearly superior recovery rates as compared to more traditional cognitive-behavioral interventions.

Based on their promising potential for the treatment of GAD, we conducted a study to compare the effectiveness of metacognitive therapy (MCT) and intolerance-of-uncertainty therapy (IUT) in a large sample of clinically-referred patients with GAD. The study was

designed as a randomized controlled trial to allow to demonstrate the effectiveness of both treatments as compared to a delayed-treatment control condition, and to explore whether one type of cognitive treatment produced better results than the other. The results of this study are presented in Chapter 7.

Chapter 7

Randomized controlled trial of the effectiveness of metacognitive therapy and intolerance-of-uncertainty therapy for generalized anxiety disorder

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Randomized controlled trial of the effectiveness of metacognitive therapy and intolerance-of-uncertainty therapy for generalized anxiety disorder.

Abstract

Objective: Preliminary evidence indicates that metacognitive therapy (MCT) and intolerance-of-uncertainty therapy (IUT) are efficacious treatments for generalized anxiety disorder (GAD). This randomized controlled trial compared the effectiveness of MCT and IUT for GAD in an outpatient context.

Method: Adult patients diagnosed with GAD (*N* = 126, 73% female, mean age = 35 years) were randomly allocated to MCT, IUT, or a delayed treatment (DT) condition. Patients in the treatment conditions received up to 14 weekly sessions, patients in the DT condition received no treatment for 14 weeks. Assessments were conducted before treatment (pretreatment), after the last treatment session (posttreatment), and six months after treatment had ended (follow-up). Primary outcome measures were the Penn State Worry Questionnaire (PSWQ) and the trait version of the State-Trait Anxiety Inventory (STAI-T).

Results: At posttreatment and follow-up assessments, substantial improvements were observed in both treatment conditions across all outcome variables. Both MCT and IUT, but not DT, produced significant reductions in GAD-specific symptoms, with effect sizes on various outcome measures ranging between 0.94 and 2.39, and the vast majority of the patients (i.e., 91% in the MCT group, and 80% in the IUT group) no longer fulfilling the diagnostic criteria for GAD. There were no significant differences between the two active treatments, except for worrying at posttreatment. However, between-group effect sizes and the degree of clinically significant change on the outcome measures indicate that MCT produced somewhat better results.

Conclusions: Both therapies are effective for GAD, but MCT may be preferred.

7.1 | Introduction

Generalized anxiety disorder (GAD) is characterized by excessive anxiety and uncontrollable worry (APA, 2000). It is one of the most frequently occurring psychological disorders, leading to significant functional impairment (Lieb, Becker, & Altamura, 2005). Without treatment the prognosis is poor (Yonkers, Massion, Warshaw, & Keller, 1996). Recent comprehensive meta-analyses have shown cognitive-behavioral therapy (CBT) and psychopharmalogical treatment to be efficacious as compared to wait-list or treatment-as-usual control groups (Hunot, Churchill, & Silva de Lima Teixeira, 2007; Mitte, 2005). However, only about 50% of treatment completers achieve high end-state functioning (Hunot et al., 2007) or recovery (Fisher, 2006) following treatment, so more effective treatments for GAD are urgently needed. This need is further emphasized by studies showing that GAD is a strong predictor of later

secondary disorders such as major depressive disorder (MDD) (Kessler, 2002), and worsens the prognosis of chronic physical conditions (Ballenger et al., 2001).

A possible explanation for the relatively poor results might be that most treatments are not based on a specific theoretical model for GAD (Wells, 1995). In an attempt to improve the understanding and treatment of GAD, in the past 15 years several specific theoretical models for GAD have been developed (Behar, Dobrow DiMarco, Hekler, Mohlman, & Staples, 2009). These models emphasize the avoidance of internal affective experiences, with some of them assuming a special role for aberrant cognitive processes. One prominent example is the metacognitive model, which assumes that worry is non-pathological in nature and can best be viewed as an attempt to generate ways of coping for potentially threatening events, based on positive beliefs about the usefulness of worry (Wells, 1995). Instead of the process of worry in itself, negative beliefs about the uncontrollability and dangerousness of worry (e.g., 'If I cannot stop my worrying, I will go crazy') are regarded as crucial for the development of GAD. Once activated, such negative beliefs result in meta-worry, in which patients with GAD worry about the fact that they worry. As a result, patients with GAD experience an elevation in anxiety and worrisome thoughts, which ultimately leads to the use of counterproductive mental regulation (e.g., thought suppression) and avoidance strategies (e.g., reassurance seeking). Engagement in such strategies is unhelpful, or even reinforces the negative beliefs about worry, as it precludes the experience of discovering that worrying is controllable and not dangerous, diminishes patients' confidence in their ability to control worry, and leads to a further increase of anxiety (Wells, 2005).

An alternative account highlights the role of intolerance of uncertainty (IU) in the development and maintenance of GAD (Dugas, Gagnon, Ladouceur, & Freeston, 1998). Patients with GAD are highly intolerant of uncertainty, which refers to the tendency to react negatively to uncertain and ambiguous events, independent of their probability of occurrence and their associated consequences. According to the IU-model, patients with GAD are prone to display chronic worry in response to uncertain and ambiguous situations, based on beliefs that worry will either help them to cope more effectively with such events, or to prevent feared events from happening (Davey, Tallis, & Capuzzo, 1996; Dugas et al., 1998). This chronic worry and the accompanying anxiety lead to a negative problem orientation (the tendency to view problems as threatening and to have doubts about one's problem-solving abilities) (Ladouceur, Blais, Freeston, & Dugas, 1998) and cognitive avoidance (cognitive strategies to avoid the evocation of threatening images, and its accompanying arousal, e.g., distraction or thought suppression) (Borkovec & Hu, 1990), both of which may promote the maintenance or even escalation of worry and anxiety.

So far, a limited number of studies has provided support for the efficacy of the treatment programs that have been developed to correct these presumed distorted processes

underlying the disorder (Dugas, Ladouceur, Léger, Freeston, Langlois, Provencher, & Boisvert, 2003; Ladouceur, Dugas, Freeston, Léger, Gagnon, & Thibodeau, 2000; Wells & King, 2006; Wells, Welford, King, Wisely, & Mendel, 2010). However, this evidence is preliminary given the methodological shortcomings of these studies, such as the fairly small sample sizes and the lack of active control groups. Further, the extent to which the positive results from such studies generalize to practitioners who may serve a different patient population and have different supervision intensity remains to be investigated. For broad dissemination, treatment for GAD should be manualized, with minimal training and supervision demands (Bateman & Fonagy, 2009). A randomized design for assessing such a treatment must meet the following minimal criteria (Bateman & Fonagy, 2009): 1) a comparison group also receiving a manualized, structured treatment with equivalent supervision, 2) delivery of both by professionals trained to similar levels, 3) statistical power to detect relatively small differences, and 4) a representative sample of clinically referred patients with a confirmed diagnosis of GAD. The present trial was initiated to meet these criteria.

7.2 | Method

The present study was set-up as a randomized controlled trial to compare the effectiveness of metacognitive therapy (MCT) and intolerance-of-uncertainty therapy (IUT) in a large sample of clinically referred patients with GAD. To control for the nonspecific benefits of a structured treatment, patients in both active treatment groups received a protocol-driven treatment in an outpatient context. To control for time effects, a delayed treatment (DT) condition was included. Practitioners were equally experienced, and received equivalent training and supervision in the treatment they had to deliver.

7.2.1 | Design and procedure

Patients referred to PsyQ, a community mental health center in the Netherlands, received extensive information about the design and procedures of the study at the end of the clinical screening. Following informed consent, patients were randomly assigned to the MCT, IUT, or the DT condition by the principal investigator, using a simple randomization method (throwing a die, with 1 and 4 = MCT, 2 and 5 = IUT, and 3 and 6 = DT). Each treatment consisted of up to 14 weekly sessions of 45 minutes. Patients in the DT condition received no treatment for 14 weeks, after which they were rerandomized into one of the two treatment conditions (unless they did not longer meet the criteria for GAD). Patients were assessed at entry (pretreatment), after the last treatment session (posttreatment), and six months after

treatment had ended (follow-up). No additional treatment was provided after posttest. The medical ethics committee of the participating treatment center officially approved the study.

7.2.2 | Patients

Patients (*N* = 165) were recruited from consecutive referrals for anxiety disorder treatment from clinical services between February 2005 and November 2008. Diagnosis was established using the Dutch version of the Structured Clinical Interview for DSM-IV axis-I (SCID-I) (First, Spitzer, Gibbon, & Williams, 2001). Inclusion criteria were 1) primary diagnosis of GAD, and 2) age 18-65. To enhance the clinical representativeness of the sample, exclusion criteria were kept to a minimum. Patients were only excluded if they currently 1) met DSM-IV-TR criteria for severe major depressive disorder that required immediate treatment, psychotic disorder, or bipolar disorder, 2) had mental impairment or evidence of organic brain disorder, 3) had substance abuse requiring specialist treatment, or 4) had a change in medication type or dose in the six weeks before assessment or during treatment. The presence of other comorbid disorders or the continued use of psychopharmaca patients already used longer than six weeks before assessment were not exclusion criteria. Five of the 165 potentially eligible patients did not meet inclusion criteria, one had a psychotic disorder. Of the 159 patients enrolled, 33 refused randomization leaving 126 entering the two outpatient treatment programs (MCT: *N* = 54, IUT: *N* = 52) and the DT condition (*N* = 20). For ethical reasons, it was decided to close the DT condition ahead of schedule as a preliminary analysis indicated that the patients in the DT condition hardly improved. Of the 20 patients in the DT condition, one patient discontinued participation during the waiting period, two patients renounced treatment after the waiting period, one did no longer meet the criteria for GAD, and one preferred psychopharmacological treatment. As a result, 15 patients were randomly reallocated after the waiting period: 7 patients to MCT and 8 patients to IUT. Figure 7.1 summarizes the patient flow through the trial.

Almost one-third of the participants (62.6%) met the DSM-IV criteria for at least one comorbid axis-I diagnosis. The most common comorbid diagnoses were depressive disorder (23.0%), panic disorder (14.3%), social phobia (11.1%), somatoform disorder (8.7%), obsessive-compulsive disorder (4.8%), dysthymic disorder (3.2%), specific phobia (3.2%), and insomnia (2.4%).

7.2.3 | Measures

Treatment outcome was evaluated by means of the Dutch versions of standardized self-report scales for measuring the core symptoms of GAD, worry and anxiety (primary outcomes). In addition, questionnaires of general psychopathology and depression were administered to assess comorbid symptoms (secondary outcomes). A final outcome measure was the clinical

diagnosis as established using the SCID-I. To study changes in the cognitive processes as targeted by MCT and IUT, self-report inventories were also included to study changes in metacognitions and in IU.

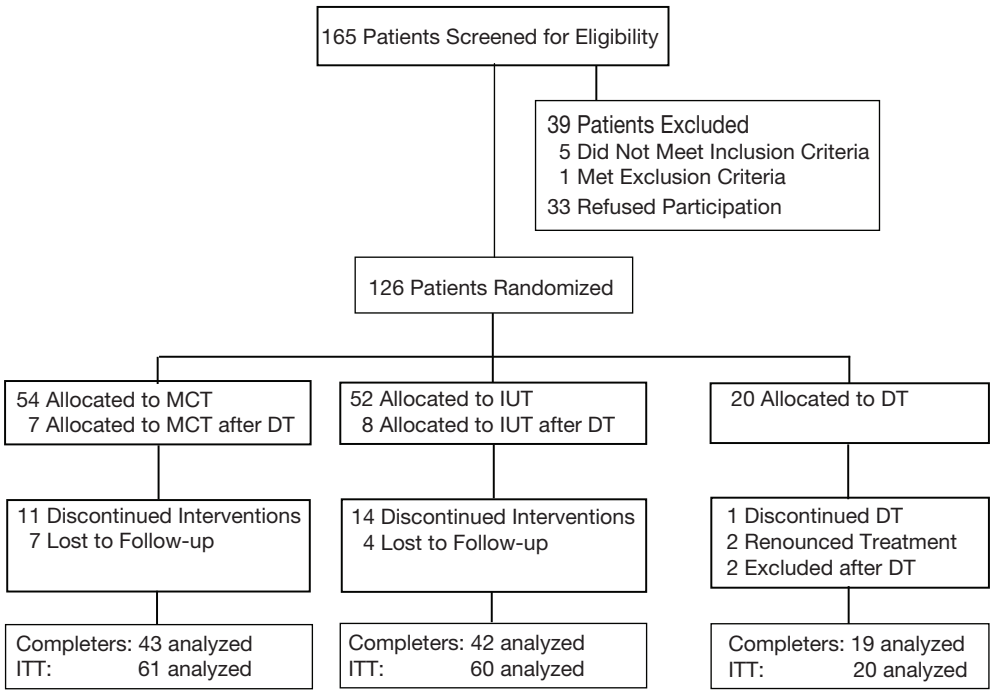

Figure 7.1 | Flowchart of participants through various stages of the clinical trial. **MCT** = metacognitive therapy; **IUT** = intolerance-of-uncertainty therapy; **DT** = delayed treatment; **ITT** = intent-to-treat sample.

7.2.3.1 | Outcome measures

Penn State Worry Questionnaire (PSWQ). The PSWQ (Meyer, Miller, Metzger, & Borkovec, 1990) is a widely used 16-item self-report inventory that measures the pervasiveness, excessiveness, and uncontrollable nature of worry. Total scores on the PSWQ range from 16 to 80. The PSWQ is a reliable and valid instrument for assessing worry (Meyer et al., 1990), and this is also true for the Dutch version of the scale (Van Rijsoort, Emmelkamp, & Vervaeke, 1999). In the present trial, Cronbach's α at pretreatment was .83.

State-Trait Anxiety Inventory, trait version (STAI-T). The STAI-T (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) was employed as an index of general anxiety. Total scores of this 20-item self-report questionnaire range from 20 tot 80. Both the original STAI-T (Spielberger et al., 1983) and the Dutch translation (Van der Ploeg, 2000) have sound psychometric properties. In the present trial, α = .89.

Symptom Checklist (SCL-90). General psychopathology was assessed with the SCL-90 (Derogatis, 1983), a 90-item self-report measure with total scores ranging from 90 to 450. The Dutch version has been shown to possess good psychometric qualities (Arrindell & Ettema, 1986). In the present trial, α = .88.

Beck Depression Inventory (BDI-II). Because depression is commonly associated with GAD, the BDI-II (Beck, Steer, & Brown, 1996) was used as a secondary outcome measure to assess symptoms of depression. The Dutch version of this 21-item self-report questionnaire, with total scores ranging from 21 to 63, has shown good internal consistency and reliability (Van der Does, 2002). In the present trial, α = .91.

Structured Clinical Interview for DSM-IV axis-I (SCID-I). The diagnostic criteria of GAD were checked at pretreatment, posttreatment and follow-up, using the Dutch version of the SCID-I (Van Groenestijn, Akkerhuis, Kupka, Schneider, & Nolen, 1996), which was administered by trained psychologists. The SCID-I is considered the gold standard in psychiatric diagnosis and has shown largely consistent diagnostic reliability across studies (Segal, Hersen, & Van Hasselt, 1994).

7.2.3.2 | Measures of treatment process

Meta Cognitions Questionnaire (MCQ). The MCQ (Cartwright-Hatton & Wells, 1997) is a 65-item self-report scale for assessing individual differences in positive beliefs about worry, negative beliefs about worry, beliefs about the need to control thoughts, metacognitive monitoring of thoughts, and judgment of cognitive effectiveness. In the present study, the MCQ was employed to assess negative beliefs about worry (MCQ-NEG) and positive beliefs about worry (MCQ-POS). The Dutch translation of the MCQ has been shown to possess good psychometric properties (Hermans, Crombez, Van Rijsoort & Laeremans, 2002). In the present trial, α =.89 for the MCQ-POS and .93 for the MCQ-NEG subscales.

Intolerance-of-Uncertainty Scale (IUS). The IUS (Freeston, Rheaume, Letarte, Dugas, & Ladouceur, 1994) contains 27 items to measure individual differences in reactions to ambiguous situations, implications of being uncertain, and attempts to control the future. Total scores range from 27 to 135. The Dutch version of the IUS has demonstrated adequate psychometric properties (De Bruin, Rassin, Van der Heiden, & Muris, 2006). In the present trial, α =.80.

7.2.4 | Interventions

Following the metacognitive model, the main focus of MCT is not worry itself, but rather the metacognitive factors that contribute to the development and persistence of GAD, including negative beliefs about the uncontrollability and dangerousness of worry, positive beliefs related to the patient's reliance on worry as a coping strategy, and ineffective attempts to avoid worry and to control thoughts. After providing the rationale of the model, MCT proceeds with the direct modification of metacognitions by means of verbal cognitive restructuring strategies (e.g., questioning the evidence supporting these beliefs, inducing cognitive dissonance by eliciting both positive and negative beliefs about worrying). In addition, patients are prompted to carry out behavioral experiments, such as postponed worry experiments in which patients postpone worrying until an established worry period to test whether worrying is controllable, and worry enhancement experiments in which patients increase worrying to determine if positive events occur. The modification of metacognitions follows a particular sequence: first negative beliefs about worrying are targeted since these are conceptualized as the vehicle behind the activation of meta-worry, and then positive beliefs concerning the usefulness of worrying are addressed. During the last stage of MCT, alternative strategies for processing threatening triggers are explored (e.g., letting go of thoughts instead of trying to deal with them).

Resulting from the IU-model, treatment of GAD should be aimed at helping patients develop the ability to tolerate, cope with, and even accept uncertainty in their everyday lives (Dugas & Robichaud, 2007). Following the rationale of the model, IUT proceeds with worry awareness training, during which patients learn to make a distinction between worries that are amenable to problem solving and worries that are not. Once they are able to properly discriminate between these two types of worry, patients are first taught to apply a problem-solving strategy to soluble worries, which consists of five steps: (1) problem definition, (2) goal formulation, (3) generation of alternative solutions, (4) decision making, and (5) solution implementation and verification (D'Zurilla & Nezu, 1999). In the next phase, patients are encouraged to expose themselves to images of the most feared expectations of insoluble worries by means of worry exposure (Van der Heiden & Ten Broeke, 2009) as a way to confront core fears and prevent cognitive avoidance. In the final phase, positive beliefs about worry are directly modified by cognitive therapeutic interventions (e.g., questioning the evidence supporting these beliefs, lawyer-prosecutor role play).

Both MCT and IUT were conducted within a structured framework following manuals based on publications of the researchers who developed these interventions (Dugas & Ladouceur, 2000; Wells, 1997), and are described in detail elsewhere (Van der Heiden, 2009a en b; see also Chapter 6). Overviews of both treatments are provided in Table 7.1. Session-by-session treatment outlines are described in Appendix 1.

Table 7.1 | Overview of metacognitive therapy (MCT) and intolerance-of-uncertainty therapy (IUT) for generalized anxiety disorder (GAD).

	MCT			IUT		
Module	Topic	Goals	No. of sessions	Topic	Goals	No. of sessions
1	Introduction	Engage patient in program Provide treatment overview	1	Introduction	Engage patient in program Provide treatment overview	1
2	Identifying metacognitions	Help patients to elicit metacognitions, e.g., by guided questioning.	2	Worry awareness training	Help patients to differentiate between worries that are amenable to problem-solving, and worries that are not	2
3	Examining negative metacognitions	Teach patients to challenge negative beliefs about the uncontrollability and danger of worrying, using verbal and behavioral interventions for cognitive restructuring	5	Problem orientation training	Gradually practice the five steps of problem solving training for worries that are amenable to problem solving	4
4	Examining positive metacognitions	Teach patients to challenge positive beliefs about worrying, using verbal and behavioral interventions for cognitive restructuring	2	Worry exposure	Help patients practice worry exposure-exercises for worries that are not amenable to problem solving	2
5	Modifying cognitive bias and strategy shifts	Help patients to give up residual avoidance and safety behavior using exposure with response prevention Teach patients alternative processing strategies	4	Re-evaluation of positive beliefs about worrying	Help patients to acknowledge that their beliefs are thoughts and not facts, using cognitive restructuring	5

Note. MCT = metacognitive therapy; IUT = intolerance-of-uncertainty therapy.

Table 7.2 | Characteristics of therapists.

Characteristic	MCT (*N* = 4)		IUT (*N* = 5)	
	Mean	Range	Mean	Range
Age in years	36	26-48	32	29-35
Years of clinical experience	5	0-7	6	4-7
Confidence in treatment*	6.5	5-8	7.4	7-8
No. of study patients	15.3	8-25	12.0	7-17

Note. **MCT** = metacognitive therapy; **IUT** = intolerance-of-uncertainty therapy.
*Prior to the study, therapists' confidence in the treatment they had to deliver was measured on a 10-point scale (with 10 reflecting maximal confidence).

7.2.5 | Therapists, training, and treatment integrity

The therapist teams consisted of four (MCT) and five (IUT) staff psychologists of the participating mental health care center. All of them were familiar with the provision of cognitive-behavioral treatment manuals, and all but one were certified cognitive-behavioral therapists. Information about therapists is given in Table 7.2. *T*-tests revealed no significant differences between the therapists in the two treatment conditions with regard to age [$t(7) < 1$], degree of clinical experience [$t(7) < 1$], degree of confidence in the treatment they had to deliver [$t(7) = 1.49$, $p = .18$], and number of patients treated [$t(7) < 1$].

The therapist training program for both MCT and IUT encompassed a one hour information meeting, and one hour supervision meetings in separate group sessions for MCT and IUT with the principal investigator. These meetings were held biweekly in the first year of the study, and on average once per two months after the first year. At these meetings all active cases and therapy notes were reviewed to ensure treatment quality and adherence to the treatment manuals. Adherence to the manuals was further evaluated by means of assessing a sample of 71 randomly selected recordings of treatment sessions against a session-by-session intervention checklist by trained clinical psychology students (at a master level), revealing that the therapists closely followed the treatment manuals (i.e., in only 3% of the sessions interventions were applied that were not described in the manual).

7.2.6 | Statistical analysis

Data were analyzed using SPSS for Windows 14. Adequacy of randomization was assessed by conducting between-group comparisons of baseline clinical and demographic variables by means of chi-square tests for dichotomous variables and one-way ANOVAs for continuous variables. Treatment outcome and effects on process measures were examined by repeated measures ANOVAs and *T*-tests for the continuous data, and chi square tests in case of dichotomous outcome indices. To gain further insight into the statistical significance of the

improvements achieved in the two treatment conditions, Cohen's *d* statistic (*M*1 – *M*2 / pooled *SD*; Cohen, 1992) was employed to calculate within-group effect sizes (ES) for changes on outcome measures and to evaluate between-group differences, with $d > 0.80$ indicating a large effect, *d* between 0.20 and 0.80 indicating a moderate effect, and *d* below 0.20 indicating a small effect. In addition to statistical significance tests, the clinical significance of treatment effects was examined on the PSWQ and STAI-T, the primary outcome measures, using the procedures outlined by Jacobson and Truax (1991). Patients are classified as recovered, if they 1) score within the normal range of a certain outcome measure after treatment (i.e., below a calculated cut-off point), and 2) display statistically reliable improvement on that measure (i.e., making a change larger than a calculated reliable change index [RCI]). Patients are classified as improved but not recovered if they meet only one criterion. Indices were calculated using normative data of the Dutch versions of the PSWQ (Van Rijsoort, Vervaeke, & Emmelkamp, 1997; RCI = 7, cut-off point ≤ 53), and the STAI-T (Van der Ploeg, 2000; RCI = 7, cut-off point ≤ 45). Further, diagnosis-free status was used as index of clinically significant change.

Analyses of treatment effects are presented for the patients who completed treatment. Analyses were repeated for the completers plus dropouts (i.e., intent-to-treat analysis), using the last-observation-carried-forward procedure. Due to occasional missing values, degrees of freedom may vary slightly across analyses.

7.3 | Results

7.3.1 | Descriptive and preliminary analyses

Demographic and clinical characteristics for the three groups are displayed in Table 7.3. Between-group comparisons revealed no differences on any of these variables (all *p*s >.05). About 70% of the subjects across the two active treatment conditions met our criteria for completion (receiving up to 14 treatment sessions, and meeting all assessment points). There was no significant difference in attrition rate [$\chi^2 < 1$] and number of sessions (MCT: $M = 12.30$, $SD = 2.98$, range 4–14; IUT: $M = 12.88$, $SD = 2.25$, range 6–14; $t(82) < 1$) for completers across the treatment groups. Table 7.4a shows scores on outcome and process measures throughout the trial for the completers group, Table 7.4b for the intent-to-treat sample. No significant pretreatment differences between conditions emerged for both outcome (*F*s ≤ 2.18, *p*s > .05) and process measures (*F*s ≤ 2.65, *p*s > .05). When repeating these analyses for the intent-to-treat sample, significant pretreatment differences between the three groups were found for the STAI-T [$F(2,124) = 3.46$, $p < .05$] and the MCQ-NEG [$F(2,135) = 4.32$, $p < .05$]. Post-hoc tests revealed that on both measures the MCT group displayed higher scores than the DT group. Most importantly, however, no differences were observed between the two active treatment conditions.

Table 7.3 | Demographic characteristics by treatment group.

Characteristic	All patients (*N* = 126)		MCT (*N* = 61)		IUT (*N* = 60)		DT (*N* = 20)	
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Age in years	35.0	10.8	33.9	10.6	35.3	10.9	39.6	11.5
	N	%	*N*	%	*N*	%	*N*	%
Female	92	73	45	74	42	70	18	90
Married/partnered	87	69	37	61	44	73	16	80
Living alone	39	31	24	39	16	27	4	20
Tertiary education	52	41	23	38	28	47	6	30
Current employment	103	82	51	84	50	83	16	80
Use of psychopharmaca	35	28	16	26	17	28	6	30
≥ 1 comorbid axis I disorder	79	63	35	57	34	57	15	75

Note. **MCT** = metacognitive therapy; **IUT** = intolerance-of-uncertainty therapy; **DT** = delayed treatment.

7.3.2 | Treatment outcome

A series of 3 (Treatment group: MCT vs. IUT vs. DT) x 2 (Time: pre vs. posttreatment) repeated measures ANOVAs revealed significant main effects of time (Fs ≥ 15.62, ps < .05) and interaction effects of group and time (Fs ≥ 77.48, ps < .05) for all treatment outcome measures, indicating that pretreatment to posttreatment improvements occurred, which were different among the groups. Similar results were found with the intent-to-treat analysis.

MCT and IUT were both associated with significant pretreatment to posttreatment reductions and large effect sizes in worrying [PSWQ; MCT: $F(1,42) = 132.72$, $p < .05$, ES = 2.39; IUT: $F(1,41) = 126.01$, $p < .05$, ES = 1.43], trait anxiety [STAI-T; MCT: $F(1,36) = 126.97$, $p < .05$, ES = 2.01; IUT: $F(1,33) = 64.69$, $p < .05$, ES = 1.42], general psychopathology [SCL-90; MCT: $F(1,42) = 89.42$, $p < .05$, ES = 1.53; IUT: $F(1,40) = 52.27$, $p < .05$, ES = .98] and depression [BDI-II; MCT: $F(1,42) = 132.04$, $p < .05$, ES = 1.66; IUT: $F(1,38) = 49.12$, $p < .05$, ES = 1.12], whereas no significant effects of time were found for the DT group [PSWQ, $F(1,18) < 1$, ES = .12; STAI-T, $F(1,17) = 2.94$, $p = .11$, ES = .23; SCL-90, $F(1,18) < 1$, ES = .01; BDI-II, $F(1,17) < 1$, ES = .14]. Largely comparable findings were obtained when analyzing the intent-to-treat sample. That is, in both treatment groups symptom levels were significantly reduced (all Fs 36.76, ps < .05), while no such positive change could be observed in the DT group (all Fs ≤ 2.92, ps > .05). However, in the intent-to-treat sample all within-group effect sizes for the outcome measures in the MCT condition were still large (ESs ≥ 1.15), but the effect sizes on some outcome indices (i.e., SCL-90, ES = .63, and BDI-II, ES = .73) in the IUT condition

were only indicating a medium treatment result. For the DT condition, all ESs were small and negligible again (Ess ≤ .22].

Post-hoc tests with a Bonferroni correction revealed that at posttreatment both MCT and IUT were significantly superior to DT on GAD symptoms and the index of general psychopathology (*F*s ≥ 5.52, *p*s < .05), whereas only MCT was superior to DT on the measure of depression [$F(1,61) = 6.75$, $p < .05$]. Further, the post-hoc tests indicated that MCT was significantly superior to IUT on the PSWQ [$F(1,84) = 16.31$, $p < .05$]. When performing the between-group comparisons for the intent-to-treat sample, differences among the three groups were less clear-cut. However, on the PSWQ the MCT and IUT groups displayed significantly lower symptom levels than the DT condition (*F*s ≥ 9.07, *p*s < .05), with again MCT showing better effects than IUT [$F(1,118) = 9.58$, $p < .05$].

A series of 2 (Treatment group: MCT vs. IUT) x 2 (Time: posttreatment vs. follow-up) repeated measures ANOVAs exploring changes in symptom levels from posttreatment to follow-up scores only yielded a significant interaction effect of group and time for the PSWQ [$F(1,81) = 3.98$, $p < .05$]. Closer examination of this effect revealed that the improvement in worrying during the follow-up period was larger in the IUT group than in the MCT group, indicating a 'catch-up' on this outcome measure for the former group. At the follow-up assessment itself, there were no significant differences between MCT and IUT on any of the outcome measures (*p*s ≥ .05). The intent-to-treat analysis yielded comparable results.

At follow-up, all within-group effect sizes for the outcome measures in the MCT condition were large (PSWQ, ES = 2.38; STAI-T, ES = 2.00; SCL-90, ES = 1.70; BDI-II, ES = 1.61), and this appeared to be true for both completers and the intent-to-treat sample. In the IUT condition, the within-group effect sizes for the completers sample were all large (PSWQ, ES = 1.60; STAI-T, ES = 1.56; SCL-90, ES = 1.27; BDI-II, ES = 1.27), but in the intent-to-treat sample the effect sizes on the SCL-90 (ES = .76) and BDI-II (ES = .78) were only indicating a medium treatment result.

Between-group effect sizes revealed superiority of MCT over IUT in both the completers and the intent-to-treat sample, substantiated by medium between-group effect sizes on all outcome measures at posttreatment (ESs ≥ .52) and follow-up (ESs ≥ .41), with even a large between-group effect size on the PSWQ at posttreatment (ES = .96) in the completers sample (see Tables 7.4a and b).

Table 7.4a | Mean scores (standard deviations) and between-group effect sizes on outcome measures and mean scores (standard deviations) on cognitive measures as obtained during the pretreatment, posttreatment and follow-up assessments for the completers sample*.

Measure and Time	MCT (*N* = 43)		IUT (*N* = 42)		DT (*N* = 19)		Between Group Effect Sizes		
	Mean	SD	Mean	SD	Mean	SD	MCT-IUT	MCT-DT	IUT-DT
Primary outcomes									
PSWQ									
Pretreatment	67.88	7.12	66.93	8.60	66.42	11.66			
Posttreatment	42.91_{a}	12.93	53.14_{a}	10.24	64.95_{a}	12.01	0.96	2.27	1.31
Follow-up	43.63	12.50	49.13	12.80			0.78		
STAI-T									
Pretreatment	59.28	7.97	57.53	10.57	53.61	11.83			
Posttreatment	40.17_{b}	10.81	42.82_{b}	10.14	50.84_{b}	12.20	0.59	1.78	1.19
Follow-up	39.81	11.22	40.83	10.83			0.44		
Secondary outcomes									
SCL-90									
Pretreatment	204.53	52.68	190.07	54.48	176.63	64.48			
Posttreatment	131.81_{b}	41.94	141.37_{b}	43.98	175.68_{b}	67.29	0.55	1.52	0.97
Follow-up	127.76	36.15	133.83	30.97			0.43		
BDI-II									
Pretreatment	24.19	10.42	21.29	12.50	17.22	14.52			
Posttreatment	7.84_{c}	9.23	9.03	9.13	15.32_{c}	12.85	0.55	1.52	0.98
Follow-up	8.36	9.21	8.49	8.37			0.41		

Measure and Time	MCT (*N* = 43)		IUT (*N* = 42)		DT (*N* = 19)		Between Group Effect Sizes		
	Mean	SD	Mean	SD	Mean	SD	MCT-IUT	MCT-DT	IUT-DT
Process measures									
IUS									
Pretreatment	82.30	21.08	78.69	20.44	75.32	22.97			
Posttreatment	55.84_{b}	18.22	60.98_{b}	18.31	75.21_{b}	26.55			
Follow-up	54.85	18.52	57.93	15.97					
MCQ-NEG									
Pretreatment	52.28	7.07	49.29	8.21	47.78	8.59			
Posttreatment	28.29_{a}	8.59	35.60_{a}	8.86	47.61_{a}	8.51			
Follow-up	29.29	10.18	33.24	9.43					
MCQ-POS									
Pretreatment	32.77	10.82	33.34	10.86	34.89	12.36			
Posttreatment	24.07_{b}	5.65	27.00_{b}	7.69	33.78_{b}	12.61			
Follow-up	24.39	6.12	26.18	7.96					

Note. **MCT** = metacognitive therapy; **IUT** = intolerance-of-uncertainty therapy; DT = delayed treatment.
*Subscripts indicate significant differences between conditions ($p < .05$): $_{a}$MCT > IUT >DT, $_{b}$MCT = IUT > DT, $_{c}$MCT > DT.

Table 7.4b | Mean scores (standard deviations) and between-group effect sizes on outcome measures and mean scores (standard deviations) on cognitive measures as obtained during the pretreatment, posttreatment and follow-up assessments for the intent-to-treat sample*.

Measure and Time	MCT (*N* = 61)		IUT (*N* =60)		DT (*N* = 20)		Between Group Effect Sizes		
	Mean	SD	Mean	SD	Mean	SD	MCT-IUT	MCT-DT	IUT-DT
Primary outcomes									
PSWQ									
Pretreatment	68.67	6.89	66.62	9.04	65.45	11.35			
Posttreatment	48.30$_a$	15.82	56.10$_a$	11.45	65.05$_a$	11.70	0.65	1.66	0.91
Follow-up	48.82	15.39	53.43	13.89			0.53		
STAI-T									
Pretreatment	60.67$_b$	8.31	57.64	9.99	54.26$_b$	11.85			
Posttreatment	43.93	13.34	47.13	12.25	51.60	12.35	0.57	1.32	0.75
Follow-up	43.46	13.57	45.54	13.12			0.48		
Secondary outcomes									
SCL-90									
Pretreatment	210.31	57.80	197.18	58.00	179.05	63.69			
Posttreatment	146.49	53.33	160.07	59.07	178.15	66.42	0.52	1.13	0.61
Follow-up	143.90	51.32	154.48	54.78			0.46		
BDI-II									
Pretreatment	25.20	11.01	21.82	12.19	18.26	14.82			
Posttreatment	10.92	11.28	13.16	11.64	16.40	13.41	0.57	1.16	0.59
Follow-up	11.34	11.19	12.64	11.32			0.47		

Measure and Time	MCT (*N* = 61)		IUT (*N* =60)		DT (*N* = 20)		Between Group Effect Sizes		
	Mean	SD	Mean	SD	Mean	SD	MCT-IUT	MCT-DT	IUT-DT
Process measures									
IUS									
Pretreatment	83.36	21.16	79.82	20.65	76.55	23.03			
Posttreatment	61.28_{b}	22.33	67.38	21.96	76.45_{b}	26.43			
Follow-up	60.78	22.78	65.50	21.47					
MCQ-NEG									
Pretreatment	52.78_{b}	7.23	49.42	8.04	47.79_{b}	8.35			
Posttreatment	32.93_{a}	12.65	39.62_{a}	11.14	47.63_{a}	8.27			
Follow-up	33.56	13.05	37.92	12.05					
MCQ-POS									
Pretreatment	32.72	11.13	33.16	10.39	34.95	12.03			
Posttreatment	24.47_{a}	6.22	28.29_{a}	8.44	33.89_{a}	12.27			
Follow-up	24.69_{c}	6.52	27.89_{c}	8.76					

Note. **MCT** = metacognitive therapy; **IUT** = intolerance-of-uncertainty therapy; **DT** = delayed treatment.
*Subscripts indicate significant differences between conditions ($p < .05$): $_{a}$MCT > IUT > DT, $_{b}$MCT > DT, $_{c}$MCT > IUT.

7.3.3 | Cognitive processes

Cognitive processes were investigated by examining changes in scores on the IUS, MCQ-NEG, and MCQ-POS. A series of 3 (Treatment group: MCT vs. IUT vs. DT) x 2 (Time: pre vs. posttreatment) repeated measures ANOVAs indicated significant main effects of time (*F*s ≥ 27.66, *p*s < .05) and interaction effects of group and time (*F*s ≥ 3.50, *p*s < .05) on all process measures, indicating differential pretreatment to posttreatment change across the three groups. MCT and IUT were both associated with significant changes in intolerance of uncertainty [IUS; MCT: $F(1,42) = 86.61$, $p < .05$; IUT: $F(1,41) = 40.90$, $p < .05$], negative beliefs about worrying [MCQ-NEG; MCT: $F(1,40) = 279.14$, $p < .05$; IUT: $F(1,38) = 109.61$, $p < .05$], and positive beliefs about worrying [MCQ-POS; MCT: $F(1,40) = 37.15$, $p < .05$; IUT: $F(1,38) = 10.74$, $p < .05$], while no such effects were observed for the DT group (all *F*s ≤ 1.73, *p*s > .21). Examination of the intent-to-treat sample revealed similar findings, indicating that both MCT and IUT, but not DT, produced a significant decline in intolerance of uncertainty, negative beliefs about worrying, and positive beliefs about worrying.

Post-hoc tests with a Bonferroni correction confirmed that at posttreatment both MCT and IUT yielded significantly better effects than DT on all process measures (*F*s ≥ 6.21, *p*s < .05), and revealed that MCT was superior to IUT on the measure of negative metacognitions [$F(1,79) = 13.78$, $p < .05$]. Similar tests for the intent-to-treat sample yielded a somewhat different pattern of results. MCT proved to be significantly superior to DT on all process measures (*F*s ≥ 3.52, *p*s <.05), and to IUT on both positive and negative beliefs about worrying (*F*s ≥ 7.61, *p*s < .05). IUT produced only better effects than DT on both metacognition indices (*F*s ≥ 4.92, *p*s < .05).

A series of 2 (Treatment group: MCT vs. IUT) x 2 (Time: posttreatment vs. follow-up) repeated measures ANOVAs to explore posttreatment effects neither revealed significant main effects of time nor for group-by-time interactions (all *F*s ≥ .05, *p*s ≥.05), indicating no further changes in cognitive processes during the follow-up period. Further, at this assessment point no significant differences on any of the process measures were observed between the treatment conditions. The examination of the intent-to-treat sample yielded similar results, with the exception of MCT being superior to IUT on the measure of positive beliefs about worrying [$F(1,109) = 4.81$, $p < .05$].

7.3.4 | Clinical significance

Table 7.5a and b present proportions of patients who achieved recovery or improvement on the main outcome measures at posttreatment and follow-up. Both treatments proved to be superior with regard to rate of recovery to the DT condition (all χ^2s ≥ 10.98, *p*s < .05), with MCT producing a better outcome than IUT on the PSWQ at posttreatment [$\chi^2(1) = 5.30$,

$p < .05$], but not at follow-up [$\chi^2(1) = 1.37$, $p = .34$]. The same pattern of results was found for the intent-to-treat sample.

Table 7.5a and b also show the percentages of patients with a diagnosis-free status. Significant differences were observed between the two treatment groups and the DT condition (χ^2s ≥ 29.92, $p < .05$), but not between MCT and IUT at posttreatment assessment [$\chi^2(1) = 1.79$, $p = .18$] and follow-up [$\chi^2(1) < 1$]. Similar results were found for the intent-to-treat sample.

Table 7.5a | Changes in clinical status from baseline to treatment termination to 6-month follow-up of patients who completed the study*.

Measure	Pre to posttreatment			Pretreatment to follow-up	
	MCT (*N* = 43)	IUT (*N* = 42)	DT (*N* = 19)	MCT (*N* = 43)	IUT (*N* = 42)
PSWQ					
Recovered	72_a	48_a	0_a	74	63
Improved	21	33	25	19	20
STAI-T					
Recovered	68_b	59_b	11_b	72	62
Improved	27	20	10	18	15
Diagnosis-free	91_b	80_b	5_b	93	90

Note. **MCT** = metacognitive therapy; **IUT** = intolerance-of-uncertainty therapy; **DT** = delayed treatment.
*Data are given as percentages of patients. Subscripts indicate significant differences between conditions ($p < .05$): $_a$MCT > IUT > DT, $_b$MCT = IUT > DT.

Table 7.5b | Changes in clinical status from baseline to treatment termination to 6-month follow-up for patients who entered treatment*.

Measure	Pre to posttreatment			Pretreatment to follow-up	
	MCT (*N* = 61)	IUT (*N* = 60)	DT (*N* = 20)	MCT (*N* = 61)	IUT (*N* = 60)
PSWQ					
Recovered	60_a	37_a	0_a	62	47
Improved	17	26	26	15	17
STAI-T					
Recovered	59_b	44_b	11_b	62	45
Improved	21	16	6	15	14
Diagnosis-free	64_b	57_b	5_b	66	63

Note. **MCT** = metacognitive therapy; **IUT** = intolerance-of-uncertainty therapy; **DT** = delayed treatment.
*Data are given as percentages of patients. Subscripts indicate significant differences between conditions ($p < .05$): $_a$MCT > IUT > DT, $_b$MCT = IUT > DT.

7.4 | Discussion

Results of this study indicate that both MCT and IUT are effective treatments for GAD. Both treatments produced significant pre to posttreatment decreases in both GAD symptoms and comorbid symptoms, with large within-group effect sizes and high proportions of clinically significant change, which were not observed in the DT condition. At posttreatment, only one significant difference was found, with MCT being superior as compared to IUT on the PSWQ.

As GAD is a chronic condition maybe the most important finding is that at follow-up the improvements were maintained. Even more, after IUT a further reduction in worry was observed, suggesting that it takes more time before the full effects of IUT on worry occur. However, at follow-up still a lower percentage of patients in the IUT-condition could be classified as recovered on the PSWQ than after MCT. The same was true for the STAI-T, although these differences were not statistically significant. In a similar vein, between-group effect sizes also indicated that MCT produced somewhat better results than IUT.

The different time course of change in worrying between treatments may be due to their different focus; MCT on direct reattribution of beliefs about worrying and IUT on increasing tolerance of uncertainty by teaching more adaptive ways to cope with uncertain situations and by reevaluation of the usefulness of worrying. As the main difference between the two treatments is the explicit targeting of negative beliefs about worrying, and MCT outperforms IUT in changing these beliefs, it can be argued that the correction of negative metacognitions is the specific vehicle that is responsible for the differential effects of MCT and IUT. However, as no formal mediation analysis has been carried out no definitive conclusions can be drawn yet. To address this issue future studies should use repeated measures of both the cognitive processes and symptom variables across the active treatment phases.

Interestingly, as therapists in the trial received only modest training in the treatment they had to deliver, the positive results of the current study suggest that reasonable outcomes are achievable within the framework of clinical practice without lengthy specialist training. As both treatments use common CBT interventions to address the specific cognitive mechanisms that are supposed to maintain the disorder, therapists may have to modify their practice rather than learn new techniques. However, it could also be argued that a more extensive training program would have resulted in even better treatment results. Besides these and other strengths of the study, such as the inclusion of both an active and a passive control condition and the careful checking of the treatment integrity, this study has a number of limitations. First, although the sample of GAD patients used in the study is comparatively large given the comparison of two active treatments, the study may be underpowered, and as such conclusions drawn from the data analyses could not be accurate in detecting subtle differences between the two cognitive-behavioral treatments that were compared in

this study. Second, it is not fully clear whether the participants were 'typical' GAD patients, as the comorbidity rates with some disorders (e.g., depression, insomnia) were lower than those found in epidemiological studies. Therefore, it remains to be seen to what extent the current results are generalizable to other samples of patients with GAD, although the common rate of comorbidity (63% of the patients met the criteria for at least one comorbid disorder) was in keeping with that observed in other clinical studies (Hollaway, Rodebaugh, & Heimberg, 2006). Third, the IUT-manual as used in the current study deviates in two ways from the treatment as described by the developers (Dugas & Ladouceur, 2000). Reevaluation of positive beliefs about worrying was the final component of IUT in this study, whereas in the original manual this element was introduced immediately after the worry awareness training. This modification was based on the notion of patients in a number of pilot cases that it was more logical to learn how to deal with the different types of worries immediately after the worry awareness training. However, it could be argued that IUT performed less well as a result of this reordering of interventions, although percentages of patients in the IUT condition that were 'recovered' at both posttreatment and follow-up are in keeping with those reported for IUT in a recent review of the clinical significance of psychological treatments for GAD (Fisher, 2006). Another alteration in the IUT-manual was that patients in the current trial used worry exposure to expose themselves to images of worries that are not amenable to problem solving (Van der Heiden & Ten Broeke, 2009), instead of regularly listening to the recording of descriptions of these images on a looped tape. Compared to imaginal exposure as used in the original manual, this so-called worry exposure holds an explicit component of cognitive restructuring, as patients are asked to think about alternative outcomes after exposure to the most feared image. Interestingly, worry exposure has recently been found to be efficacious as a stand-alone technique in the treatment of GAD (Hoyer, Beesdo, Gloster, Runge, Höfler, & Becker, 2009). It is also noteworthy that recently the developers of IUT altered their treatment program themselves, by adding a new module in which patients learn to recognize uncertainty-inducing situations and manifestations of IU, and to expose themselves to such situations and manifestations. The same is true for MCT, in which a form of mindfulness is recently added as an integral first step in the modification of beliefs about the uncontrollability of worrying (Wells, 2009). However, research is needed to find out whether these alterations improve the effectiveness of IUT and MCT. A fourth limitation of the current study is that the principal investigator executed the randomization procedure, and trained and supervised the therapists in both treatment conditions. In future studies therapists in distinct conditions should be trained and supervised by different trainers, preferably the developers of MCT and IUT. Fifth, we relied on single self-report measures for each symptom and process characteristic, whereas a multitrait-multimethod approach would have been preferable (Kotov, Watson, Robles, & Schmidt, 2007). Future

studies would benefit from including clinical ratings such as the Hamilton Anxiety Rating Scale (HAM-A; Hamilton, 1959). Sixth, the lack of an evidence-based approach for GAD as a control condition, limits the understanding of the unique or incremental benefits of MCT and IUT. To enhance this understanding, future studies should explore the effectiveness of those new approaches relative to CBT or pharmacotherapy. Seventh and finally, rates of discontinuation in the treatment groups were substantial (almost 30% in both conditions), although considerably lower than both the mean rate of dropouts in clinical settings of 47% found in a meta-analysis of 125 outpatient psychotherapy studies (Wierzbicki & Pekarik, 1993), and the dropout rate of 72% recently found in an outpatient effectiveness study for patients with GAD (Kehle, 2008). But even when dropouts were included in the analyses, results were relatively good in terms of percentage diagnosis-free (> 60% in both conditions) and recovery (MCT > 60%, IUT almost 50%).

Chapter 8

General discussion

8.1 | Introduction

This chapter reviews the main conclusions pertaining to the hypotheses that were tested in the studies described in the previous chapters. First, the main findings of each chapter are presented. Next, methodological issues and clinical implications of the findings are described. Finally, recommendations for future research are provided.

8.2 | Short summary of findings

Generalized anxiety disorder (GAD) is characterized by excessive anxiety and uncontrollable worry about a number of events or activities for at least six months (APA, 2000). GAD is a highly prevalent and chronic disorder, that is associated with both significant impairment in life satisfaction and well-being (APA, 2000; Ballenger et al., 2001; Lieb et al., 2005; Weisberg, 2009; Wittchen, Beesdo, & Kessler, 2002) and high rates of comorbidity with other psychiatric disorders and with general medical conditions. If left untreated, the prognosis of GAD is poor (Yonkers, Massion, Warshaw, & Keller, 1996; Yonkers, Dyck, Warshaw, & Keller, 2000), resulting in intensive use of healthcare facilities for a long period (e.g., Lieb et al., 2005).

In this thesis three problems concerning GAD were addressed. First, despite considerable changes in the diagnostic criteria in the successive editions of the DSM (APA, 1987, 1994, 2000), (a) the diagnostic reliability of the disorder is still relatively low (Brown, DiNardo, Lehman, & Campbell, 2001), (b) the diagnostic criteria continue to be debated (Weisberg, 2009), and (c) GAD is still poorly recognized in clinical practice (Beesdo et al., 2009). As a better recognition of GAD would allow for earlier treatment, in Chapter 2 guidelines for discriminating GAD from other disorders are provided. In Chapter 3, the results are presented of a study into a hierarchical model for the relationships between general (i.e., neuroticism and extraversion) and specific vulnerability factors (i.e., metacognitive beliefs about worrying and intolerance of uncertainty [IU]) and symptom manifestations of GAD (i.e., worry and depressive symptoms), in order to improve the understanding of the etiology of GAD, and thereby to better determine the nosology of GAD. This study yielded support for a hypothesized model in which the relationships between the general vulnerability factor of neuroticism and symptoms of worry and depression were mediated by the specific vulnerability factors of negative beliefs about worrying and IU. However, in contrast with the predictions, this relationship was not mediated by positive beliefs about worrying. Further, as hypothesized, no relationship was found between extraversion and worry, whereas the relationship between low extraversion and depressive symptoms was direct in nature and not mediated by the specific vulnerability factors. Altogether, the results of this study suggest that worrying and depressive symptoms

are related but distinct manifestations in patients with GAD, and that low extraversion may define the difference between these two symptom variables. Further, results support a hierarchical model of GAD which (1) helps to improve the understanding of this disorder, and (2) supports the appropriateness of the two treatments that are described in Chapter 6 and examined in Chapter 7. These treatments, metacognitive therapy (MCT; Wells, 1995) and intolerance-of-uncertainty therapy (IUT; Dugas & Ladouceur, 2000) are designed to not only target the main symptoms of the disorder, but also the metacognitive beliefs about worrying respectively IU, which have been found to mediate the relationship between neuroticism and worrying.

A second problem concerning GAD that is addressed in this thesis is the usefulness of the Penn State Worry Questionnaire (PSWQ: Meyer, Miller, Metzger, & Borkovec, 1990), the most frequently used measure to assess worrying in GAD as well as to monitor treatment effects. The factor structure of this 16-item self-report questionnaire remains unclear, and normative data for describing individual treatment effects in clinical practice are scarce. The study described in Chapter 4 examined the factor structure of the PSWQ by testing three models in both a large community sample and a clinical sample of patients with GAD: (1) a one-factor model in which all items loaded on one and the same dimension, (2) a two-factor model in which positively and negatively worded items loaded on two separate but correlated factors, and (3) a one-factor model, that included the reverse items as a method factor. Results of confirmatory factor analyses showed that in both samples the one-factor/method factor provided the best fit for the data, although in the clinical GAD sample this was only true after error covariances between a number of items were allowed to correlate. These findings confirm previous studies showing that the PSWQ measures worry along a single dimension (Brown, 2003; Hazlett-Stevens, Ullman, & Craske, 2004), and support the use of the total scale as an indicator of pathological worry. In Chapter 5 normative data for the Dutch version of the PSWQ are provided, which can be used to differentiate between normal and abnormal manifestations of worrying as well as for evaluating individual treatment effects in clinical practice and the effectiveness of treatments in effectiveness studies.

Although cognitive-behavioral therapy (CBT) has proven to be the best treatment for many anxiety disorders (Roth & Fonagy, 2005), its effectiveness in the treatment of GAD has only shown to be moderate. Therefore, this is the third and final problem that is addressed in this thesis. As the relatively poor results might be due to the lack of specific etiological models of GAD on which treatments were based, several theoretical conceptualizations of this disorder have been developed in the past 15 years (Behar et al., 2009). Two prominent examples are the metacognitive model (Wells, 1995), in which beliefs about worrying are central in the development and maintenance of worrying, and the intolerance-of-uncertainty model (Dugas, Gagnon, Ladouceur, & Freeston, 1998), which proposes that patients with

GAD experience persistent worry in response to uncertain or ambiguous situations which cannot be tolerated. In Chapter 6 both GAD-specific models, and the treatments which are based on them, are described and illustrated with case examples. Both MCT and IUT seem to be efficacious treatments for GAD. However, so far only a limited number of studies into the efficacy of these treatments have been carried out, all of which had more or less important methodological shortcomings (such as fairly small sample sizes, no active control groups, risk of 'researcher allegiance'). Further, the extent to which the positive results from such efficacy studies generalize to practitioners who may service a different patient population and have different supervision intensity remains to be investigated. In Chapter 7 the results are presented of a randomized, wait-list controlled trial, in which the effectiveness of both treatments was compared in a large sample of clinically referred patients with GAD. This study showed that both MCT and IUT are effective treatments for GAD, with MCT performing slightly better than IUT in reducing worrying. The results further suggest that the explicit targeting of negative beliefs about worrying, which is a cornerstone of MCT, might be crucial to diminish worrying in patients with GAD.

8.3 | Methodological issues

The studies presented in this thesis had some important limitations that should be considered. A common limitation is that it is not fully clear whether the participants of the clinical GAD sample in these studies were 'typical' GAD patients, as the comorbidity rates with some disorders (e.g., depression, insomnia) were lower than those found in epidemiological studies. Thus, although the common comorbidity rate was in keeping with that observed in other clinical studies (Holaway, Rodebaugh, & Heimberg, 2006), it remains to be seen to what extent the current results are generalizable to other samples of patients with GAD. A second general limitation was the reliance on self-report measures that were completed by one informant to assess GAD symptoms, vulnerability factors, and process characteristics. This approach does not allow to determine whether such measurements represent valid indicators of the target constructs.

The study in which we examined a hierarchical model for the relationships between general and specific vulnerability factors and symptom manifestations of GAD (Chapter 3) does not permit definitive conclusions regarding etiology, because of the cross-sectional, correlational design. Another consideration with regard to this study is that there may be other vulnerability factors involved in the etiology of GAD, than the two higher-order factors (neuroticism and extraversion) and two second-order factors (metacognitive beliefs about worrying and IU) that were included in this study. This notion is supported by the fact that

the included variables in our study only accounted for a limited proportion of the variance in worry scores.

A main problem of the study on the factor structure of the PSWQ (Chapter 4) was the unequal distribution of some item scores in the sample of clinically referred GAD patients, which may be responsible for the problems in finding an acceptable fit for the structure of this questionnaire. To deal effectively with this problem, a weighted least squares estimation may be a more appropriate method than the standard (i.e., maximum likelihood) estimation procedure as employed in our study. However, this procedure can only be carried out with the software MPlus, which was not available to us.

With respect to the study evaluating the effectiveness of MCT and IUT, the lack of a traditional evidence-based treatment approach (i.e., CBT) as a control condition limits the understanding of the unique or incremental benefits of both new treatments. Another concern is the substantial rate of discontinuation in both treatment groups (almost 30%), although these rates are considerably lower than the general rate of dropouts as documented in clinical settings (47%) which was reported in a meta-analysis of 125 outpatient psychotherapy studies (Wierzbicki & Pekarik, 1993).

8.4 | Conclusions and clinical implications

The diagnosis of GAD is frequently missed in clinical practice, and as a result quite a number of patients do not receive (adequate) treatment. To improve the recognition of GAD, and to enhance the distinction from other clinical disorders in clinical practice, we provided diagnostic guidelines which are based on theoretical considerations and clinical experience. As there currently is no scientific evidence that these guidelines improve the specificity, validity and reliability of the diagnosis of GAD, they only should be used in addition to structured clinical interviews to arrive at a diagnosis. For this purpose, the PSWQ can also be used in addition to such interviews. This measure of pathological worry is also recommended for both monitoring individual treatment effects and examining the effectiveness of interventions. As our study on the factor structure confirmed that this self-report questionnaire measures worry along a single dimension, it is recommended to use the total score of the scale to assess the excessiveness and uncontrollability of worry. The normative data of the PSWQ can assist clinicians in evaluating treatment progress, on which they can base their decision to continue, adjust or terminate treatment.

We found negative beliefs about worrying and IU, but not positive beliefs about worrying, to mediate the relationship between the general vulnerability factor of neuroticism, and the symptom variables of worrying and depressive symptoms in patients with GAD. These

findings suggest that specific treatments for GAD should not only target the main symptoms of the disorder, but also the specific processes that underlie them. As such, the examined hierarchical model of GAD supports the appropriateness of the two treatments, MCT and IUT, that we evaluated in our effectiveness study. These treatments both target one of the specific vulnerability factors that we found to play a mediating role in the hypothesized hierarchical model. MCT targets negative metacognitions, while IUT targets IU. Results of the randomized controlled trial into the effectiveness of these treatments, showed that both MCT and IUT are effective treatments for reducing symptoms of GAD, with MCT producing somewhat better results than IUT in reducing worrying, the key feature of GAD. Further, results of this study suggest that the explicit targeting of beliefs about the uncontrollability and dangerousness of worrying might be crucial in reducing worrying in patients with GAD. Interestingly, percentages of patients in the current study that were 'recovered' are in keeping with those reported for MCT and IUT in a recent review of the clinical significance of 11 psychological treatments for GAD (Fisher, 2006). Moreover, Fisher noted that of the 9 active treatments (other than MCT and IUT) only two achieved a recovery rate of at least 50% on the PSWQ. For the STAI-T, of the 25 active treatments (other than MCT and IUT) only four achieved a recovery rate of at least 50%. As such, the recovery rates of 72% on the PSWQ and 68% on the STAI-T as obtained for MCT in the present study seem to outperform all treatments for GAD as included in Fisher's review.

8.5 | Recommendations

It is important to mention again that the diagnostic guidelines provided in Chapter 2 are mainly based on theoretical considerations and clinical experience. Although they might well contribute to the successful identification of GAD, this remains to be investigated. Such an examination of the guidelines should be carried out prior to the publication of the DSM-V, the release of which is expected in 2013, in order to determine whether they should be adapted into, instead of only supplementing, future versions of structured diagnostic interviews, such as the SCID-I. The same is true for the diagnostic criteria of GAD as presented in the DSM-IV-TR (APA, 2000), which are still surrounded by several controversies regarding validity. Further research is needed to obtain more clarity about these controversies, as well as about whether suggestions to solve them will mprove the specificity, validity, and reliability of the diagnosis.

As to the etiology of GAD, our study into the hierarchical relationships between the higher-order factors of neuroticism and extraversion and the symptom manifestations of worry and depression, revealed that negative metacognitions and IU may play a mediating role between neuroticism and both symptom variables. However, although the results add to a greater

understanding of the mechanisms or pathways by which neuroticism exerts influence on GAD symptoms, it remains to be seen whether the relationships are indeed causal. Longitudinal studies would permit conclusions about the direction of the associations. Such studies should also include other vulnerability factors that may be involved in the etiology of GAD, as negative metacognitions and IU only accounted for a limited proportion of the variance in worry scores. A final recommendation pertaining to studies into the hierarchical structure of GAD is to include multiple markers of each construct within the hierarchical models. The use of more than one measure for each construct, preferably completed by more than one informant (e.g., a self-report measure and a clinical rating scale completed by an independent assessor) allows to examine the distinctiveness of the constructs by comparing discriminant and convergent correlations.

The study into the effectiveness of two relatively new specific treatments for GAD, MCT and IUT, indicates that both have the potential to be more effective than the current 'gold standard' treatments for GAD, i.e., CBT and pharmacotherapy. However, more research by other research groups is needed to permit definitive conclusions on this issue. Such randomized controlled trials should directly compare MCT or IUT with these 'gold standard' treatments in order to explore whether they produce better results. Further, as the results of our study suggest that the explicit targeting of negative metacognitions may be crucial to diminish worrying, we recommend to further examine the mediating role of processes underlying the development and maintenance of GAD, such as metacognitions and IU, by using a study design with repeated measures of both hypothesized mediators and symptom variables across the active treatment phase. Recently, we started such a study to examine whether changes in metacognitions during MCT occur before, and become a predictor of, changes in worrying.

A further recommendation is to study the long-term effects of MCT and IUT, beyond the 6-months follow-up period as used in our trial. In spite of the finding that patients did not seem to relapse at follow-up, which was one of the most important findings of our study, it would be of particular interest to examine whether treatment gains are maintained over follow-up intervals that extend to 24-months and beyond. One study that did examine follow-up beyond a two-year period revealed that two to 14 years after a brief CBT intervention 34% of patients met the criteria for GAD, whereas 52% fulfilled the criteria for a co-occuring psychiatric disorder (Durham et al., 2005). Another investigation focusing on the long-term (8-14 years) outcomes of two CBT-trials for GAD (Durham et al., 2003) demonstrated that 37 to 70% of the patients did no longer meet criteria for any psychiatric disorder. In continuation of the reported trial, we currently examine the long-term effects of MCT and IUT, 30 months after the interventions had ended.

A final recommendation for future research pertains to the problem of attrition. In our trial 30% of patients in both MCT and IUT discontinued participation in the study. As high dropout rates are a common problem in clinical settings (see, for instance, Wierzbicki & Pekarik, 1993; Kehle, 2008), future studies should examine (1) factors that predict attrition from treatment, (2) differences between treatment completers and non-completers in terms of socio-demographic or symptom patterns, and (3) the effectiveness of interventions that aim to decrease dropout (or to improve treatment adherence).

Chapter 9

9.1 | References

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9.2 | Appendix 1

Session-by-session description of metacognitive therapy (MCT) and intolerance-of-uncertainty therapy (IUT).

Metacognitive therapy (MCT)	*Intolerance-of-uncertainty therapy (IUT)*
Session 1: *Assessment and treatment rationale* – Review a recent worry episode using the metacognitive model – Demonstrate the counterproductivity of (a) worrying as a coping strategy, and (b) thought suppression – Provide the rationale of MCT – Homework: worry registration	**Session 1:** *Assessment and treatment rationale* – Review a recent worry episode using the Intolerance-of-Uncertainty model – Provide the rationale of IUT – Homework: (a) worry registration, (b) worry diary (monitoring worry themes 4 times a day)
Session 2 and 3: *Identifying metacognitions* – Check homework. Fit result to the metacognitive model – Elicit metacognitions (e.g., by guided questioning, listing the advantages and disadvantages of worrying). – Homework: (a) worry registration, (b) identify metacognitions using Worry Thoughts Records (WTR)	**Session 2-3:** *Worry awareness training* – Check homework. Fit result to the Intolerance of uncertainty model – Discuss the difference between worries that are amenable to problem-solving, and worries that are not – Homework: (a) worry registration, (b) worry diary, including categorizing worries as (not) amenable to problem-solving
Session 4-8: *Examining negative metacognitions* – Check homework – Elicit and challenge negative beliefs about the uncontrollability (session 4-6) and danger (session 7-8) of worrying, using (a) verbal strategies, such as questioning the evidence, questioning the causal mechanism by which worry could lead to a catastrophe, and inducing cognitive dissonance by eliciting co-existing positive and negative beliefs about worrying (b) behavioral experiments, such as postponed worry experiments, and paradoxical experiments (e.g., trying to lose control over worrying, exaggerating worries during problematic worry episodes)	**Session 4-7:** *Problem orientation training for worries that are amenable to problem solving* – Check homework – Gradually practice the five steps of problem solving training: (a) problem definition, (b) goal formulation, (c) generation of alternative solutions, (d) decision making, and (e) solution implementation and verification – Homework: (a) worry registration, (b) worry diary, (c) carry out problem solving training

Metacognitive therapy (MCT)

- Homework: (a) worry registration, (b) complete WTRs, (c) behavioral experiments to test the uncontrollability of worrying, (d) behavioral experiments to test out feared consequences of worrying

Session 9-10: *Examining positive metacognitions*

- Check homework
- Continue challenging negative beliefs about worrying
- Elicit and challenge positive beliefs about worrying, using:
  (a) verbal strategies, such as questioning the evidence, generating examples of situations when worry was not used but events turned out positively, and mismatch strategies in which the content of anticipatory worry is contrasted with the actual events
  (b) behavioral experiments, such as worry abandonment experiments (giving-up worrying to test if negative consequences occur), and worry enhancement experiments (increasing worrying to determine if positive events occur)
- Homework: (a) worry registration, (b) complete WTRs, (c) behavioral experiments to test predictions about the value of worrying

Session 11-14: *Modifying cognitive bias and strategy shifts*

- Check homework
- Work on residual negative and positive beliefs about worrying
- Explore the nature of residual avoidance and safety behaviour and introduce exposure with response prevention
- Training in alternative processing strategies, such as 'letting go of worries' instead of controlling them, and examining positive outcomes in association with initial worries
- Develop therapy blueprint
- Homework: (a) worry registration, (b) exposure and response prevention, (c) cognitive interventions for type 1 worries, (d) strategy shifts

Intolerance-of-uncertainty therapy (IUT)

Session 8-9: *Worry exposure for worries that are not amenable to problem solving*

- Check homework
- Continue problem solving training for worries that are amenable to problem solving
- Introduce and practice worry exposure during the session
- Homework: (a) worry registration, b) worry diary, (c) continue problem solving training, (d) worry exposure exercises

Session 10-14: *Re-evaluation of positive beliefs about worrying*

- Check homework
- Continue problem solving training and worry exposure
- Elicit and challenge positive beliefs about worrying with the primary goal to help patients to acknowledge that their beliefs are thoughts and not facts, using:
  (a) verbal strategies, such as questioning the evidence for the value of worrying
  (b) behavioral strategies, such as lawyer-prosecutor role play
- Complete Worry Thoughts Record (WTR) for examining the value of worrying
- Develop therapy blueprint
- Homework: (a) worry registration, (b) worry diary, including categorizing worries as (not) amenable to problem-solving, (c) continue problem solving plans, and worry exposure exercises, (d) Complete WTRs, (e) reattribution of predictions about the value of worrying

9.3 | Summary

Generalized anxiety disorder (GAD) is characterized by excessive anxiety and uncontrollable worry about a number of events or activities for at least six months (APA, 2000). GAD is a highly prevalent and chronic disorder that is associated with both significant impairment in life satisfaction and well-being (APA, 2000; Ballenger et al., 2001; Lieb et al., 2005; Weisberg, 2009; Wittchen, Beesdo, & Kessler, 2002). GAD has high rates of comorbidity with other psychiatric disorders and with general medical conditions (Nutt, Argyropoulos, Hood, & Potokar, 2006). If left untreated, the prognosis of GAD is poor (Yonkers, Massion, Warshaw, & Keller, 1996; Yonkers, Dyck, Warshaw, & Keller, 2000), resulting in intensive use of health care facilities for a long period (e.g., Lieb et al., 2005). Therefore, effective treatments for GAD are needed, but so far GAD appears only moderately responsive to traditional cognitive-behavioral therapy, which is the psychological intervention of first choice for anxiety disorders (Roth & Fonagy, 2005). After a historical overview of the modifications of the diagnostic criteria of GAD since the introduction in the DSM-III (APA, 1980), **Chapter 1** provides a description of the problems pertaining to (1) the diagnosis and etiology, (2) the measurement of worrying, which is considered as the hallmark of GAD, and (3) the treatment of GAD.

Chapter 2 addresses the clinical presentation of GAD and provides guidelines for improving the recognition of GAD, and for effectively distinguishing GAD from other psychiatric disorders, based on theoretical considerations and clinical experience. Debate relating to the validity of the definition of GAD is summarized, and suggestions are made for improving the criteria for GAD, which may guide future versions of classification systems such as the DSM.

In **Chapter 3** the results are presented of a study examining a hierarchical model for the relationships between general and specific vulnerability factors and symptom manifestations of GAD. More specifically, the relationships between the general higher-order vulnerability factors of neuroticism and extraversion, the specific second-order vulnerability factors of intolerance of uncertainty (IU) and metacognitive beliefs about worrying, and symptoms of generalized anxiety (i.e., worry) and depression were investigated in a sample of clinically referred patients with GAD (N = 137). A *bootstrapping analysis* yielded support for a model in which the relation between the general vulnerability factor of neuroticism and symptoms of GAD were mediated by the specific vulnerability factors of intolerance of uncertainty and negative metacognitions, but not by positive beliefs of patients about worrying. These results suggest that treatments should target not only symptoms of generalized anxiety, but also underlying processes of the disorder, such as IU and negative beliefs about worrying. As such, the findings of this study support the appropriateness of treatments that make

an attempt to alter these processes. These treatments, metacognitive therapy (MCT) and intolerance-of-uncertainty therapy (IUT), are described in Chapter 6, the results of a study evaluating their effectiveness are presented in Chapter 7.

In **Chapter 4** the factor structure of the Penn State Worry Questionnaire (PSWQ), a 16-item self-report scale for measuring the excessiveness and uncontrollability of worry, is examined in (1) a large community sample (*N* = 455), and (2) a clinical sample of patients with generalized anxiety disorder (GAD; *N* = 102). Confirmatory factor analysis was employed to test three models: (1) a one-factor model in which all items loaded on one and the same dimension, (2) a two-factor model in which positively and negatively worded items loaded on two separate but correlated factors, and (3) a one-factor model, that included the reverse items as a method factor. In the community sample the one-factor/method factor model provided the best fit for the data. This was also true in the clinical GAD sample. The results of this study confirm previous findings showing that the PSWQ measures worry along a single dimension (Brown, 2003; Hazlett-Stevens, Ullman, & Craske, 2004), and support the use of the total scale as an indicator of pathological worry in both scientific research and clinical practice.

In **Chapter 5** normative data for the Dutch version of the PSWQ are provided for a large community sample (*N* = 842) and a clinically referred sample of patients with GAD (*N* = 102). Norms are not only provided for the original 16-item version, but also for an abbreviated 11-item version, which only consists of the positively worded items and has been shown to be a promising alternative to the full-length version. The percentile scores obtained for the community sample and the clinical GAD sample did not show much overlap, and this appeared true for the full-length as well as the abbreviated version of the PSWQ. These normative data seem suitable for differentiating between normal and abnormal manifestations of worrying and for evaluating the efficacy of treatments for GAD**.**

In **Chapter 6** two relatively recently developed specific theoretical models for GAD are described, the metacognitive model and the intolerance-of-uncertainty model. The metacognitive model proposes that negative beliefs about worry, resulting in 'worry about worry', play a key role in the development and maintenance of GAD (Wells, 1995), whereas the intolerance-of-uncertainty model (Dugas & Ladouceur, 2000) is based on the idea that patients with GAD become distressed and upset when confronted with uncertain or ambiguous situations, and experience persistent worry in response to such events. Empirical support has emerged for both of these GAD models, as well as for the specific treatment programs (i.e., MCT and IUT) that have been developed on the basis of these disorder-specific conceptualizations of GAD. Both treatments are outlined and illustrated with case examples.

As the empirical support for both MCT and IUT is only preliminary given the fairly limited number of efficacy studies and the methodological shortcomings of this research, in **Chapter 7** the results are presented of a randomized, delayed treatment (DT) controlled trial comparing the effectiveness of metacognitive therapy (MCT) and intolerance-of-uncertainty therapy (IUT) for GAD in an outpatient context (*N* = 126). The outcome variables were worrying, trait anxiety, general psychopathology, and depressive symptoms. At posttreatment and 6-month follow-up assessments, substantial improvements were observed in both treatment conditions across all outcome variables. Both MCT and IUT, but not DT, produced significant reductions in GAD-specific symptoms, with effect sizes (ESs) on various outcome measures ranging between 0.94 and 2.39, and the vast majority of the patients (i.e., 91% in the MCT group, and 80% in the IUT group) no longer fulfilling the diagnostic criteria for GAD. There were no significant differences between the two active treatments, except for worrying at posttreatment. However, between-group ESs and the degree of clinically significant change on the outcome measures indicated that MCT produced somewhat better results.

In the final **Chapter 8** the main conclusions from the previous chapters are summarized. In addition, various methodological issues are considered, and clinical implications of the findings are discussed. The chapter ends with recommendations for future research.

9.4 | Samenvatting (Summary in Dutch)

De gegeneraliseerde angststoornis (GAS) wordt gekenmerkt door buitensporige angst en onbeheersbaar piekeren over verschillende gebeurtenissen of activiteiten, gedurende tenminste een half jaar (APA, 2000). GAS is een veel voorkomende, chronische stoornis, die leidt tot een duidelijke afname van tevredenheid en welzijn (APA, 2000; Ballenger et al., 2001; Lieb et al., 2005; Weisberg, 2009; Wittchen, Beesdo, & Kessler, 2002). Bovendien heeft GAS een hoge comorbiditeit met andere psychiatrische stoornissen en algemene medische aandoeningen (Nutt, Argyropoulos, Hood, & Potokar, 2006). Zonder adequate behandeling is de prognose slecht (Yonkers, Massion, Warshaw, & Keller, 1996; Yonkers, Dyck, Warshaw, & Keller, 2000)2000), wat vaak leidt tot langdurig en intensief gebruik van verschillende vormen van niet-specifieke zorg (zie Lieb et al., 2005). Effectieve behandeling van GAS is dan ook van groot belang. Echter, ook cognitieve gedragstherapie, de behandeling die bij de meeste angststoornissen de beste effecten heeft (Roth & Fonagy, 2005), sorteert slechts een matig effect. Na een historisch overzicht van de veranderingen in de diagnostische criteria voor GAS sinds de introductie van de stoornis in de DSM-III (APA, 1980), worden in **Hoofdstuk 1** de problemen met betrekking tot (1) de diagnose en etiologie van GAS, (2) het meten van piekeren, dat algemeen beschouwd wordt als het kernsymptoom van GAS, en (3) de behandeling van GAS besproken. Deze drie onderwerpen staan centraal in dit proefschrift.

Hoofdstuk 2 behandelt het klinisch beeld van GAS en verstrekt richtlijnen om de herkenning en differentiaaldiagnostiek van de GAS in de klinische praktijk te verbeteren. Deze richtlijnen zijn gebaseerd op theoretische overwegingen en klinische ervaringen. Ook worden controverses rondom de validiteit van de diagnostische criteria besproken, gevolgd door suggesties om deze criteria aan te scherpen in toekomstige edities van classificatiesystemen als de DSM.

In **Hoofdstuk 3** worden de resultaten gepresenteerd van een studie waarin een hiërarchisch model voor GAS werd onderzocht in een klinische populatie van patiënten met deze angststoornis (N = 137). Onderzocht werden de relaties tussen de hogere-orde kwetsbaarheidsfactoren neuroticisme en extraversie, de specifieke tweede-orde kwetsbaarheidsfactoren metacognitieve opvattingen over piekeren en intolerantie voor onzekerheid (IU), en de symptoomvariabelen piekeren en depressieve klachten. Uit een *bootstrapping* analyse kwam naar voren dat twee specifieke kwetsbaarheidsfactoren, negatieve opvattingen over piekeren en IU, een mediërende rol speelden bij de relatie tussen de algemene kwetsbaarheidsfactor neuroticisme en de symptomen van de GAS. Tegen de verwachting in bleken positieve opvattingen over piekeren hierbij geen mediërende factor te zijn. De klinische implicatie van deze resultaten is dat behandelingen voor GAS niet louter

gericht zouden moeten zijn op de symptomen zelf, maar ook op factoren die bijdragen aan de ontwikkeling en instandhouding van de stoornis, zoals IU en negatieve opvattingen van de patiënt over piekeren. De bevindingen van deze studie vormen daarmee ondersteuning voor de twee behandelmethoden voor GAS die in dit proefschrift op hun effectiviteit zijn onderzocht. Deze behandelingen, metacognitieve therapie (MCT) en intolerantie-voor-onzekerheid therapie (IUT), worden in Hoofdstuk 6 beschreven. De uitkomsten van de effectstudie worden in Hoofdstuk 7 gepresenteerd.

In **Hoofdstuk 4** wordt de factorstructuur van de Penn State Worry Questionnaire (PSWQ), een vragenlijst van 16 items om overmatig en onbeheersbaar piekeren te meten, onderzocht binnen een grote algemene populatie (*N* = 455), en een klinische populatie van patiënten met GAS (*N* = 102). Met behulp van een confirmatieve factoranalyse werden drie modellen onderzocht: (1) een één-factor model waarin alle items op één en dezelfde factor laadden, (2) een twee-factoren model waarin de positief en negatief geformuleerde items op twee verschillende, maar samenhangende factoren laadden, en (3) een één-factor model, waarin de negatief geformuleerde items als zogenaamde *method factor* opgenomen waren. In zowel de algemene populatie als in de groep patiënten met GAS gaf het één-factor/*method factor* model de beste fit voor de data. De resultaten van deze studie bevestigen bevindingen uit eerder onderzoek naar de factorstructuur van de PSWQ, waaruit naar voren kwam dat deze vragenlijst piekeren als een eendimensionaal begrip meet (Brown, 2003; Hazlett-Stevens, Ullman, & Craske, 2004). De implicatie hiervan voor zowel de klinische praktijk als wetenschappelijk onderzoek is dat de totale score van de PSWQ gebruikt dient te worden om pathologisch piekeren te meten.

In **Hoofdstuk 5** worden normgegevens voor de PSWQ verstrekt voor zowel een grote algemene populatie (*N* = 842) als een klinische populatie van patiënten met GAS (*N* = 102). Naast normscores voor de originele, 16-item versie, worden ook gegevens verstrekt voor een verkorte versie, bestaande uit alleen de 11 positief geformuleerde items van de PSWQ. Voor beide versies kwam naar voren dat de percentielscores van de beide populaties weinig overlap vertonen. De normscores lijken ten eerste bruikbaar om onderscheid te maken tussen normale en abnormale vormen van piekeren, en ten tweede om de effecten van behandelingen in kaart te brengen.

In **Hoofdstuk 6** worden twee relatief recent ontwikkelde specifieke theoretische modellen voor GAS beschreven. Ten eerste het metacognitieve model (Wells, 1995) en ten tweede het intolerantie-voor-onzekerheid (IU-)model (Dugas & Ladouceur, 2000). Binnen het metacognitieve model worden negatieve opvattingen van de patiënt over piekeren, die leiden tot ‘gepieker over het piekeren’, gezien als cruciaal voor de ontwikkeling en de instandhouding van GAS. Het intolerantie-voor-onzekerheid model gaat er daarentegen van uit dat patiënten met GAS onzekere of ambigue situaties niet kunnen verdragen, en op

zulke situaties reageren met gepieker in een poging deze het hoofd te bieden. Voor beide conceptualisaties van GAS bestaat inmiddels empirische ondersteuning. Hetzelfde geldt voor de beide behandelingen (MCT en IUT) die op basis van deze stoornis-specifieke modellen ontwikkeld zijn. Beide behandelingen worden in dit hoofdstuk beschreven, en geïllustreerd met behulp van casusbeschrijvingen.

Vanwege het beperkte aantal studies naar de effecten van beide behandelmethoden, en de methodologische beperkingen van deze studies, is meer en gedegen onderzoek nodig alvorens duidelijke conclusies getrokken kunnen worden met betrekking tot de effectiviteit van MCT en IUT. In **Hoofdstuk 7** worden de resultaten gepresenteerd van een groot gerandomiseerd, gecontroleerd onderzoek in een ambulante setting onder 126 patiënten met de diagnose GAS. In dit onderzoek werd de effectiviteit van beide behandelingen met elkaar vergeleken, alsmede met een wachtlijstgroep (die na de wachttijd alsnog één van de twee behandelingen aangeboden kreeg). Zowel na afloop van de behandeling als een half jaar daarna waren patiënten in beide behandelcondities aanzienlijk verbeterd op alle uitkomstmaten, te weten piekeren, angst, algemene psychische klachten, en depressieve klachten. In tegenstelling tot de wachtlijstconditie, leidde zowel MCT als IUT tot significante afnames van piekeren en angst (de kernsymptomen van de GAS), met *effect sizes* (ESs) variërend van 0.94 and 2.39 op de verschillende uitkomstmaten, terwijl de ruime meerderheid van de patiënten (91% in de MCT conditie, en 80% in de IUT conditie) niet langer aan de diagnostische criteria voor GAS voldeed. Behalve voor piekeren bij de meting direct na afloop van de behandeling, werden geen significante verschillen tussen beide behandelmethoden gevonden. Toch duiden de *between-group ESs* en de verschillen tussen MCT en IUT in de mate van klinisch relevante verbetering er op dat MCT iets betere resultaten geeft.

In het afsluitende **Hoofdstuk 8** worden de belangrijkste bevindingen uit de voorgaande hoofdstukken samengevat. Vervolgens worden verschillende methodologische kwesties van de verschillende onderzoeken aan de orde gesteld, en worden de klinische implicaties van de onderzoeksresultaten besproken. Afgesloten wordt met aanbevelingen voor toekomstig onderzoek.

9.5 | Dankwoord (Ackowledgements in Dutch)

Met het afronden van dit proefschrift wordt een mooie tijd afgesloten (en kunnen er weer andere mooie tijden komen!). En dat het een mooie tijd was, mag bijna een wonder heten, gezien alle waarschuwingen die ik voorafgaand aan, maar ook tijdens, het traject kreeg. Het zou ten koste van je privéleven, je gezin en je relatie gaan, en eigenlijk had je nergens anders meer tijd voor, zo hoorde ik menigmaal. Dat is allemaal nogal meegevallen, dus aankomende promovendi die dit lezen kan ik van harte geruststellen. Zeker in de tijd dat de behandelingen liepen had ik het eigenlijk vrij rustig. Dat is overigens wel te danken aan verschillende personen. Hen wil ik dus als eerste bedanken. Om te beginnen Gerda Methorst, die als een rode draad door mijn carrière loopt, en mij als directeur van Ensis de gelegenheid gaf een aanzienlijk deel van het onderzoekswerk in werktijd te doen. Maar zeker ook de verschillende stagiaires die mij hielpen met (of moet ik zeggen: ontlastten van) het 'vuile werk': het verzamelen en in SPSS verwerken van de data, en het afluisteren van de cassettebandjes van therapiesessies om na te gaan of de behandelaars zich wel aan het protocol hielden. In de hoop niemand te vergeten noem ik: Ellen Beelen, Joey Frankhuijzen, Wim Labree, Martijn Oostra, Natascha van der Steen, Abigail Struik en Noortje van Wijk. Maar vooral Andrea Rau, Yvonne van der Straaten (na haar stage ook een periode als assistent-onderzoeker) en Kim Melchior, die alle drie een zeer belangrijke bijdrage hebben geleverd aan het opzetten en up-to-date houden van het SPSS-bestand en het Excell-bestand, waardoor metingen op tijd plaats konden vinden. En niet in de minste plaats door de behandelaars, die zoals ook blijkt uit de resultaten, een dusdanige topprestatie leverden dat ik me kon beperken tot het verzamelen van data: Marthe de Bel, Madeleine Bowen, Petra Frets, Marjolijn Heskes, Monique Janssen, Maria Poppe, Karin Smeenk, Ella de Stigter en Erik Stolk. En natuurlijk vooral ook alle patiënten die bereid waren mee te werken aan het onderzoek. Zonder hen was dit proefschrift er zeker niet geweest. Ik ben hen dan ook zeer erkentelijk de stap te wagen om een nog experimentele behandeling te ondergaan, met ook nog eens het risico eerst in een wachtlijstgroep ingeloot te worden, en dan als klap op de vuurpijl op drie momenten negen vragenlijsten te moeten invullen! Voorwaar geen makkelijke stap, zeker niet voor mensen die toch al gekweld worden door zorgen over allerlei rampscenario's.

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9.7 | Curriculum Vitae

Colin van der Heiden werd geboren op 10 april 1967 in Schiedam. In 1986 behaalde hij zijn VWO diploma aan de S.G. Spieringshoek in Schiedam. Hierna studeerde hij eerst een jaar economie aan de Erasmus Universiteit in Rotterdam en vervulde daarna zijn militaire dienstplicht. In 1988 startte hij met de studie psychologie aan de Rijksuniversiteit in Leiden, waar hij in 1993 afstudeerde in de richting klinische- en gezondheidspsychologie. Na afronding van deze studie volgde een postdoctorale stage op de polikliniek en de kliniek van Psychiatrisch Centrum Joris in Schiedam. De stageplek werd al snel omgezet in een tijdelijke aanstelling. In deze periode werd een start gemaakt met de opleiding tot gedragstherapeut. In 1997 stapte hij over naar de HSK Groep, waar hij achtereenvolgens als behandelaar, waarnemend vestigingsmanager, vestigingsmanager en staffunctionaris zorg werkzaam was, en bovendien docent in de opleiding tot gedragstherapeut werd. In deze periode rondde hij de opleiding tot gedragstherapeut af (2000), en behaalde hij de BIG-registraties gezondheidszorgpsycholoog en psychotherapeut. Ook schreef hij (in 1999) zijn eerste wetenschappelijke publicatie. In 2001 trad hij in dienst van de GGZ Groep Europoort in Rotterdam, waar hij Ensis oprichtte, een instelling voor kortdurende behandeling van milde psychische klachten. Tot 2004 was hij directeur van deze instelling. Tevens bleef hij als behandelaar en docent gedragstherapie werkzaam. In deze periode ontstond de belangstelling voor wetenschappelijk onderzoek en werd de basis gelegd voor het huidige proefschrift. Medio 2004 legde hij zijn functie als directeur van Ensis neer, om zijn taken van behandelaar, onderzoeker en opleider weer op te pakken. Vanaf 2004 werd gestart met het onderzoek waarvan in dit proefschrift verslag wordt gedaan. In 2005 werd hij erkend supervisor van de Vereniging voor Cognitieve therapie en Gedragstherapie, en nam hij de taak van hoofdopleider cognitieve gedragstherapie van Ensis op zich. Medio 2007 werd hij benoemd tot hoofd wetenschappelijk onderzoek van PsyQ Rijnmond, een instelling die opgericht werd in het kader van de fusie tussen de GGZ Groep Europoort, de Bavo RNO Groep en de Parnassia Groep. In 2008 en 2009 was hij op detacheringsbasis half-time werkzaam als universitair docent aan het Instituut voor Psychologie van de Faculteit der Sociale Wetenschappen van de Erasmus Universiteit Rotterdam. Sinds 1 januari 2010 richt hij zich weer volledig op zijn taken als behandelaar, hoofdopleider cognitieve gedragstherapie en hoofd wetenschappelijk onderzoek van PsyQ Rijnmond.