*Systematic review of cognitive interventions specialized against generalized anxiety disorder*

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# Abstract

This paper is meant as a framework that presents the clinical and methodological considerations, theoretical factors and scientific background, regarding the systematic review presented in part 2. The systematic review examined the ability of the three GAD specialized treatments Intolerance of uncertainty, Metacognitive therapy and Interpersonal emotional processing therapy, to reduce GAD relation symptoms pathological worry and anxiety. The paper was constructed around different aspects and the foundation of the systematic review, and was therefore meant as an methodological and theoretical elaboration, evaluation and discussion, of the review, and not an independent entity in its own right.

This paper provided an elaboration of the systematic reviews theoretical and clinical background, as well as an evaluation of the systematic reviews methodology. The theoretical underpinnings of the systematic review was presented in the theory segment. This included the cognitive understanding of anxiety and GAD, as well as GADs diagnostic history and features. Afterwards, the method segments evaluated the principles behind constructing research designs that is congruent with scientific imperatives. The systematic reviews design was evaluated and discussed according to the before mentioned principles of prober research designs. The quality of the research design, both for the included studies and the review in general, manifested in high internal, external and construct validity, along with reductions of the change of bias and confounders. It was concluded that the methodological quality of the systematic review were high, and thereby adding credibility to its results. The design could however be improved with more representative populations segments, with more even sex-distribution and age-distribution, and clinical trials with implementation of all three measurements, would improve the research design.

It was considered how future studies should be designed, in order to further improve the methodological quality of the studies. Meta-analysis was decided to be the best choice, since it is the research design that is deemed highest in regard to evidential power. The meta-analysis should be designed so that each effect size would be calculated instead of extracted, to reduce possible confounders by ensuring that the effect sizes were calculated in the exact same way.





# *Part**1: Framework for the article*

# Introduction

This paper is meant as a framework that presents the clinical and methodological considerations, theoretical factors and scientific background, that constitutes the justification of the systematic review conducted in the article, that is presented in part 2. The systematic review evaluates the effectivity of three GAD specialized treatments, called Intolerance of uncertainty, Metacognitive therapy and Interpersonal emotion processing therapy, in reducing its core symptoms pathological worry, and state- and trait anxiety.

Generalized anxiety disorder (GAD) is one of the most widespread and deliberating anxiety disorders worldwide (Maier et al., 2000, p. 29), and a high percentage of the clients treated, does not experience significant reductions in symptoms related to GAD (Hazlett-Stevens, 2008, p. 13). CBT implemented against other anxiety disorders, are as a rule specialized to target features that are distinct to that specific disorder (Hofmann & Smits, 2008). The fact that CBT for other anxiety disorders are very effective (ibid., p. 6), will be used as a premise for the systematic review, to argument that the high treatment resistance in GAD, is due to the lack of customization against the specific features of GAD. In order to bring about increased specialization to CBT for GAD the systematic review will evaluate the effectivity of the three GAD specialized treatments, to provide a evidential foundation for their use. The evaluation of the effectivity of GAD specific treatments, and the answering of the hypothesizes regarding the subject, will be addressed in the systematic review in part 2.

This paper is constructed around different aspects and background, of the systematic review, and is therefore meant as an methodological and theoretical elaboration, evaluation and discussion, of the review, and not an independent entity in its own right, as it is based on the article in part 2. Firstly the theoretical underpinnings of the systematic review will be presented in the theory segment. This entails the cognitive understanding of anxiety and GAD, as well as GADs diagnostic history and features. Afterwards, the method segments follows, which evaluates the principles behind constructing research designs that is congruent with scientific imperatives. The systematic reviews own design will be evaluated and discussed according to the before mentioned principles of prober research designs. Lastly, a conclusion about the evaluation of the systematic reviews methodology will be presented, along with consideration for the design of further studies examining GAD specialized treatments.

# Theoretical background of the systematic review of cognitive interventions specialized against GAD

Due to the concise nature of the article format, which is used in part 2, some concepts are presented in a shallow fashion. The introduced concepts are presented in a way that presumes that the reader already has prior knowledge about the subject. This approach is appropriate, since it makes it a lot easier for the reader to overview an articles presented findings and points, without the possibility of being distracted by the presentation of rudimentary theories, that he or she has already read in other articles of the same type. There is however an inherent danger in this approach, due to the possible reductionistic attitude, one might adapt, if it is never fully explained to the reader, for instance what exactly anxiety is, and which processes it relies on in the cognitive paradigm. In the following section there will be presented the theoretical framework, about the cognitive understanding of anxiety and GAD, which could not be incorporated into the article in part 2.

### GAD – diagnostic history and considerations

GAD can be traces back to 1968, were the DSM-II diagnosis anxiety neurosis, a condition characterized by long periods with excessive anxiety without avoidance behavior (Clark & Beck, 2010, p. 390). There were no differentiation concerning if the anxiety were acute or chronic (ibid.). In 1980 GAD got specific characteristics in DSM-III, but the diagnosis could be applied if the requirements for other disorders weren’t fulfilled. As a consequence, GAD mostly served as a thrash-bin diagnosis, for patients with anxiety symptoms that were difficult to classify (ibid.). In DSM-III-R, GAD underwent in 1987 a substantial revision, were most of the exclusion criteria in regards to absence of other disorder were removed, the required length of the duration of the disorder were expanded to six months, and worry were now seen as a central component of the disorder (ibid.). It was now possible to diagnose GAD despite the presence of another disorder, as long as the anxiety and the worry, were not related to the comorbid disease (Clark & Beck, 2010, pp. 390-391). In 1994, DSM-IV provided GAD with a reduction in the number of required symptoms, from three out of 18, to three out of six (ibid., p. 391). In order to illustrate how GAD is manifesting, the contemporary criteria for the disorder are from DSM-V (APA, 2013, p. 222), are here presented:

*A) Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).*

*B) The individual finds it difficult to control the worry.
C) The anxiety and worry are associated with three (or more) of the following six symptoms: Restlessness or feeling keyed up or on edge, being easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension and sleep disturbance*

*D) The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.*

*E) The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism).*

*F) The disturbance is not better explained by another mental disorder*

In GADs contemporary iteration, the disorder has broken free of its role as trash-bin diagnoses for anxiety disorders, that couldn’t be placed in other categories, which can be said to improve the justification of the use of the GAD diagnose considerably, and make it more usable as well. The diagnoses is now based on the presence of a phenomenon, instead of the absence of other phenomenons, which indicates the adaption of a paradigm viewing GAD is a independent disorder with its own expression, instead of atypical variants of other anxiety disorder. The cementation of GAD as a independent disorder, is probably facilitating the development of distinct GAD specialized intervention types. It could be argued that a manifestation for that development, is that worry has been identified as the defining feature of GAD, instead of earlier iteration use of the diffuse unclassifiable anxiety as a defining characteristic. This is also indicating that acknowledgment of the disorders characteristics as independent, is facilitating better more specialized treatment.

GAD is an impairing disorder, which affects individual´s life domains such as economy, ability to work, psycho-social functioning, psychological wellbeing and health (Sandelin, Kowalski, Ahnemark, & Allgulander, 2013, p. 125). GAD is widespread, affecting 2,9% of the population in America (Kessler et al., 2005, p. 4) and 2% in Europe over a period of 12 months (Lieb, Becker, & Altamura, 2005, p. 450). GAD is globally putting strain on the capacity of health (Wittchen, 2002, p. 162) and economic sectors (ibid., p. 166) making it a disorder with considerable societal consequences. Without treatment GAD is usually chronic with few cases of remission (ibid., p. 162).

### Delimination of GAD

GAD and major depression symptoms has a great overlap, which often gives rise to misdiagnostication (Clark & Beck, 2010, p. 391). The disorder has a very high comorbidity (Kessler, Chiu, Demler, & Walters, 2005, p. 622), and are both largely dependent on a genetic disposition (Crowe, 2012, p. 117). Is has been discussed whether or not is an anxiety disorder at all, and if it would be more appropriate to place among the affective disorders , especially because of its likeness and high comorbidity with major depression and affective disorders in general (Brown, Campbell, Lehman, Grisham & Mancill, 2001, pp. 585, 597). It has on the other hand been argued that GAD is the “fundamental anxiety disorder”, qua its main component, worry, are present in almost all anxiety disorders (Clark & Beck, 2010, p. 440). A thirds standpoint argues that GAD shouldn’t be a distinctive diagnosis at all, since none of its symptoms are unique for the disorder (Rachman, 2004, p. 184), and that GAD without any comorbid disorders are very rare. In a study, 90% of the participants with GAD, had a comorbid disorder (Wittchen, 2002, p. 164).

Clark and Beck (2010, pp. 391-392) are addressing the standpoints in the debate about GAD, by pointing out that GAD might not be symptomatically unique, but the disorders intensity and relentlessness are a differentiating characteristics (ibid., p. 392). Clark and Beck also refers to the huge body of research that indicated that GAD are characterized by a automatic attention bias, that selectively focuses on the threats in situations that would otherwise appear neutral (ibid., pp. 392, 407), which differentiates it from major depression, and other anxiety disorders (ibid., pp. 391-392). GAD and major depression are thereby very much alike, but are separate phenomenons (ibid.).

It has also been suggested that GAD is a manifestation of anxiety symptoms, based on traits. The phenomenon *high trait anxiety*, is defined as relatively stabile individual differences in depositions towards percepting stimuli as threats (Spielberger, Gorsuch, & Lushene 1970, p. 39). This trait-based phenomenon are highly correlating with GAD, and has been used synonymously to such an extent, that it has been suggested that GAD is a manifestation of high trait anxiety (Rapee, 1991, p. 422). Another point of view in the debate concerning the nature and origin of GAD, has been claiming htat GAD I s personality disorder (Wittchen, 2002, p. 163). An indicator for this being true, is that GAD are influencing virtually the entire personality of the individual, and often has a very early onset, as well as it being chronic if treatment is not applied (Portman, 2009, p. 20). But the fact that GAD in spite of its high comorbidity can exist an generate symptoms without comorbid disorders (including no personality disorders), are according to Portman, proving that GAD is a independent Axis-1 disorder (ibid.). Now that the GAD diagnosis history and development has been described and evaluated, the cognitive understanding of anxiety will be presented, since it constitutes the foundation for CBT of GAD.

The systematic review in part two examines GAD defined in the diagnostic classification manual DNS-V and not ICD-10. DSM is the foundation for most of the clinical trials in pathological mental processes (Mezzich, 2002, p 72), and therefor seems as the most appropriate classification manual to use for the purpose of the systematic review. However if a population has been examined with both DSM-V and ICD-10, the two diagnostic systems almost always registers the same number of participants with GAD (Wittchen, 2002, p. 163). Based on this it can be argued that by using DSM-V, the systematic review will generate knowledge about the same group of individuals, as it would have, had it been primarily using ICD-10. Since GAD lastly were object to diagnostically changes in DSM-IV, there will mainly be included studies and literature form 1994 or later, since operating with two different diagnostic definitions of GAD could lead to doubt regarding if it’s the same phenomenon that is being examined.

## Cognitive understanding of anxiety disorders

### Anxiety Diatheses

The cognitive understanding of anxiety is based on the diathesis-stress model (Clark & Beck, 2010, p. 103). According to the theory, some individuals have a *diathesis* (vulnerability) that disposes them toward the development of a physical or psychological disorder, which can be initiated by a stressor, and result in the development of pathology (Monroe & Simons, 1991, p. 406). The diathesis can be congenital or acquired, and be biological or psychological based (Clark & Beck, 2010, p. 103). The concept of diatheses covers a myriad of possible factors, from genetic disposition, maladaptive cognitive patterns, neurological deficiencies, to an unsafe childhood environment that has intervened with the natural development of the individual (ibid.). The diatheses is however only the potential for developing a disorder, and wont necessary result in the onset of a disorder (ibid.). For that to happened, a sufficiently intense physiological or psychological strain called a *stressor* needs to interact with the diathesis (ibid., p. 102). Just like the diathesis, the stressor can be diverse in nature. It could for instance be a traumatic event, substance use, a period with a lot of strain, a maladaptive work environment, which interacts with the diathesis and results in the disorder (ibid.). A diathesis will not always result in a disorder, if the stressor abstains, or if the individual has a sufficient beneficial mediating factor, like a highly efficient coping style that can counteract the influence of the stressor (ibid.). Anxiety disorders develop when an individual with an diatheses towards anxiety, is exposed towards a sufficient stressor, and the interaction between the stressor and the diathesis results in a maladaptive cognitive information processing pattern (ibid., p. 42).

### The role of cognition in anxiety disorders

Cognitive structures called *schemata*, dictates how the individual tendency to process collected information is structured. Maladaptive schemata constitutes the central cognitive diathesis towards the development of anxiety, and is created through the interaction of experience and genes (Clark & Beck, 2010, p. 116). When anxiety schemata are activated, other more adaptive schemata that percepts information in a more neutral and nuanced fashion, are deactivated (ibid., p. 116). An anxious individual will as consequence always perceive a certain kind of situation or sensation as anxiety provoking, because the collected information has a tendency to be perceived as threatening, and the schemata that could argue against the interpretation are deactivated (ibid., pp. 55-56).

The information processing that is influenced by the diathese/schemata, are called *primary appraisal* (ibid., pp. 32-34). In relation to anxiety, primary appraisals is a process, were information and stimuli from the environment and from the individuals internal mental processes, are processed, and on the basis on the conclusion it is evaluated if the situation or thought is dangerous (ibid.). Immediately afterwards, a process called *secondary appraisal*, is used to evaluate which possibilities the individual has to handle the situation, and if the individuals capability for coping is sufficient (ibid.). On the basis of this two-parted information processing, a situations threat-level is determined (ibid., pp. 32-33).

I the situation is deemed sufficiently threatening, the appraisal processes will result in anxious cognition patterns, that influences emotion, physiological response and behavior, so that a fight or flight response is facilitated (ibid.). In a evolutionary perspective the anxiety program ability to mobilize resources quickly has been very useful in dangerous situations, but can be extremely deliberating if the program is initiated as a response to situations, emotions, thoughts or physiological processes that aren’t dangerous (ibid., p. 33). Unfortunately, this often occurs in modern society, were the object that imitates the anxiety often is ambient, and it is not always clear when the perceived danger has subsided (ibid.). Some of the maladaptive information processing that creates anxiety are conscious, deliberate and analyzing, such as for instance worry and rumination, while others are more subconscious, simple an automated, such as anxiety in response to loud noises (ibid., p. 34).

Cognitive processes can never be divided into a dichotomy of exclusively complex and slow, or simple and fast, but are always a mix, were there is more present of one or the other (ibid.). CBT aims to make the client conscious of the effect of her or his fast and simple information processing patterns, and to reconstruct conscious more complex processes as well, through cognitive and behavioral interventions, aimed at maladaptive schemata and cognitive structures, so that these no longer influences emotions, physiological response and behavior (ibid., p. 36). In other words, both simple and complex cognitive processes are targeted. CBT is based upon the cognitive understanding of anxiety, and is based around intervention aimed at the before mentioned reciprocal relationship between thoughts, emotions, physiological response and behavior (ibid., p. 31).

# Methodology of the systematic review of cognitive interventions specialized against GAD

In the following section a critical evaluation and discussion of the research design applied in the systematic review of MCT, IUT and IEPS effectivity, will be conducted.

## Scientific theoretical considerations for choosing the systematic review as method of research

An scientific theoretical argument for choosing the systematic review, as the preferred method of researching the effectivity of IUT, MCT and IEP, over using for instance a theoretical study, can be found in *logic positivism*, which is an anti-metaphysicial theory of science, which argues that collection and elaboration of empirical information, is the only certain source of knowledge (Hjørland, 2005, p. 137). Logic positivism holds that objects of research that isn’t directly connected to empirical information, should be transformed into to concepts that can be observed and measured (ibid.), A systematic review, does exactly that: Collect information from different studies, that has transformed unobservable abstract concepts into measurable and observable data.

R.N. Giere, (2008, p. 2) argues that empirical measurements is not enough to create knowledge, since data must always be included in a interpretation process, before scientific knowledge can be created. Analysis, interpretation and reconstruction of others researchers theory and method, is seen by Giere as an important source of knowledge, that can make the implicit features of a theory explicit (ibid., pp. 2-3). But a systematic review can also be said to include the interpretational dimension that Giere argues must be prior to all generation of scientific knowledge. The data presented in a systematic review is not just presented in raw format, without the active participation of the author, but is analyzed, interpreted and concluded upon. This choice of the systematic review as the method of research in this study can thereby be said to be in accordance with influential paradigms regarding theory of science. Another scientific theoretical consideration that must kept in mind, for a more complete understanding of the systematic review, is that the theoretical models that is being described and evaluated in this study, need to be understood as representations of a phenomenon, and not the phenomenon itself (ibid., p. 60).

## Hierachy of evidence

All clinical psychological practice conducted in Scandinavia are under the imperative of evidence based practice, which dictates that all interventions should be based on the best available evidential based research (Ethical principles for Nordic psychologists, 2010-2012). The Danish manifestation of the imperative (Dansk Psykolog forening, 2012) is based on a manifest by *American Psychological Association* (APA; 2005). Due to the nature of the imperative, research of the effectivity of clinical interventions, should be based on the methods with the most evidential power. Therefor this study sought to implement a type of research design, which reduced the change of *confounding variables*, that is an uncontrolled variables that obscures any effect sought (Collican, 2009, p. 79), and ensured high *validity*. Validity is the extent to which an effect is demonstrated in research is genuine, and not produced by misleading variables, or limiting to a specific context (ibid., p. 104). The systematic review will be evaluated on several validity parameters, for instance *construct validity*, which is the extend the operational measures of a constructs is matching the theoretical construct (ibid.), and *internal validity* that concerns if the measured effect in a experimental condition is real, and a product of a manipulated experimental variable (ibid.), as well as *external validity* which is the degree to which an effect can be generalized to other places and conditions (ibid., pp. 104-105).

The medicinal researcher D. P. Byar is often referred to, when categorization of the evidential power of studies is being discussed. Byar argues that clinical research can be categorized in a hierarchal nomenclature, arranged after the internal and external validity of the methodological design (Piantadosi, 2005, p. 135-136). This is often referred to as the evidence-based pyramid, hence its often illustrated by a pyramid. Byars categorization from weakest to strongest evidential power is as follows: Case studies, database analysis, observation studies, controlled clinical studies and replication of clinical studies. In the top of the pyramid, Systematic reviews and meta-analysis are placed (ibid.). The higher a research method is placed on the pyramid, the lower is the designs risk of cofounders and biases (ibid., p. 136). Case-studies are only able to indicate whether or not a given phenomenon might have clinical value, while systematic reviews and meta-analysis is able to give a independent evaluation of for instance, the effectivity of a given intervention method (ibid.). In regards to the imperative to evaluate treatment on the grounds evidence based research, the choice of using the systematic review as research design appears justified. This systematic review has sought to mainly include studies that would be placed in the upper half of the pyramid of evidence, and as a results quantitative studies constitutes the majority of studies being referred too.

## Adherence to research protocols

This systematic review has been conducted according to *the population, intervention, comparators and outcomes* review protocol (PICO; Schardt et al., 2007), in order to ensure adhering to the requirements of evidence based research. PICO is a recognized methodical protocol often used to formulate clinical research questions and facilitate literature search (ibid.). The populations examined were individuals diagnosed with GAD by either the researchers or another authority. The interventions evaluated were MCT, IUT and IEP. Control groups were participants with GAD allocated to a waitlist condition, and the examined outcome were the intensity of the GAD related symptoms, measured with PSWQ, STAI-T and BAI. The systematic review has also been adhering to another protocol, called the *Preferred reporting items for systematic reviews and meta-analyses* checklist (PRISMA; Moher, Liberati, Tetzlaff, & Altman, 2009) to ensure transparency and adherence to methodology that is fulfilling the standards of systematic reviews of evidence based research.

### Search strategy

The digital databased used in the systematic review were deliberately selected because of their characteristics. Psychinfo was chosen because of its expansive archive, and the fact that it is administered by the organization The American Psychology association[[1]](#footnote-1), which is providing treatment guidelines and defining diagnostic criteria in USA[[2]](#footnote-2) . In order to have equal access to relevant articles in both America and Europe, and thereby avoid a potential regional oriented publishing bias, EmBase was chosen because of it being a more European oriented pendant to Psychinfo. PubMed was chosen due to its focus on health and treatment, in order to archive an database which focused on treatment efficiency, but from another paradigm, that is less likely to be as psychological oriented as EMbase and PsycNet. Therefore PubMed might be less prone to bias, concerning the efficiency of psychological interventions. The systematic reviews design has thereby tried to reduce the risk of potential biases, caused by loyalty to geopolitical founded traditions, and biases implemented by loyalty to the efficiency of psychological therapeutically oriented methods. Those are factors that adds to the validity of the design of the systematic review, by reducing possible confounders and publications biases. The choice of taking national deviations in spelling into account, might have reduced the change of only including GAD articles from regions were GAD are spelled in the same way.

To ensure that the systematic search in the digital databases would find relevant material, a series of studies deemed relevant were identified prior to the study for comparison. This comparison list were composed by manual seeking for studies in reference indexes in articles and books about the subject, as well as in online publication lists of prominent researchers of IEP, MCT and IUT. The search in the digital databases found all of the studies on the manually composed item list, and can there for be considered to be effective at identifying relevant studies.

The comparison list composed by manual seeking for relevant studies in reference indexes in articles and books about the subject, as well as in online publication lists of prominent researchers of IEP, MCT and IUT, provided a way to evaluate the effectivity of the systematic search in the databases, in identifying relevant clinical trials. Since the systematic search managed to identify all the articles on the comparison list, this approach provided a measure of verification to the methodology of the systematic search.

The focus on not including articles form before 1994, were the GAD diagnoses were last updated, appears to have added to the internal validity of the study, since it increases the chance that the included articles define GAD in the same way, by ensuring a diagnostic homogenous inclusion criterion. A shot at ensuring homogeneity in the examined interventions methods as well, was tried to be reached by comparing the studies description of the intervention method, to the recommended method in IEP, MCT and IUT literature (Newman, Castonguay, Borkovec & Molnar, 2003; Wells, 2006; Robichaud & Dugas, 2006). The exclusion of GAD articles from before 1994, and the standardization of GAD interventions, increased construct validity for the study, by ensuring that the systematic review examined the concept is was supposed to examine (Coolican, 2009, p. 88). The criteria of only using peer-review articles, increased the probability that the included study were adhering to rigid research protocols, and conducted there research according to academic standards.

WAT is a influential and empirically supported model which theoretical components are used in several other explanatory models of GAD (Clark & Beck, p. 399, Hazlett-Stevens, 2008, p. 10). IEP is the latest incarnation of a treatment based on WAT, and it was therefore surprising that it wasn’t possible to locate more than two clinical intervention studies examining IEPs effectivity. Unfortunately, one of these studies did not presents its mean scores, but only effect sizes, and therefor did not meet the inclusion criteria of the systematic review, leaving only one IEP study up for evaluation.

### Measurements

The use of PSWQ, BAI, STAI-T, allowed the systematic review to measure how IUT, MCT and IEP affected the core symptoms of GAD, pathological worry and anxiety. All three measurements have been subject to evaluative studies and have found to have good psychometric abilities, in regards to examining respectively worry, state and trait anxiety (Fresco, Mennin, Heimberg & Turk, 2003; Beck, Epstein, Brown, & Steer, 1988, Fisher and Durham, 1999). Their ability to measure the symptoms correctly reflects the systematic reviews internal validity, by ensuring that the symptoms that are central for GAD, are measured with sufficient sensitivity and specificity. Unfortunately most studies seems to favor either BAI or STAI-T. In an ideal scenario the included studies had included both the anxiety measurements, which would have made analysis more transparent.

The creators of BAI argues that STAI (and thereby also its sub-scale STAI-T) was developed for use by non-clinical population, whereas BAI were constructed with psychiatric disorders in mind (Beck, Epstein, Brown & Steer, 1988, p. 896), and there for is better at measuring anxiety at clinical levels. They also criticize STAI for not being able to differentiate effectively between different types of anxiety, and depression and anxiety, and concludes that BAI should be used over STAI for clinical trials (ibid.). This ability to effectively measure clinical anxiety, and distinguish between anxiety and depression symptoms, is the main reason for choosing the BAI as measure, instead of just using the STAI-T. On the other hand, since BAI only measure symptoms over the last week, it cannot measure trait-anxiety, which must be over are prolonged period of time (Bernstein & Eveland, 1982). Therefor STAI-T is essential in providing information on IUT, MCT and IEPs ability to reduce longer term and stable types of anxiety, instead of only anxiety symptoms that have occurred doing the last week, and could be circumstantial.

All studies implemented PSWQ, as it was a requirement for their inclusion in the systematic review. It is however worth noting that PSWQ is not a diagnostic tool, but is designed for screening (Meyer, Miller, Metzger, Borkovec, 1990, p. 102). PSWQs high sensitivity makes it fit to fulfill its purpose in this study, of identifying changes in levels of pathological worry in large populations. PSWQ can there by access the probability of the illness being present, but would not be optimal for determining with complete certainty wherever or not GAD symptoms are completely removed.

Evelyn Behar et al. (2009, p. 1020) points out that most research in GAD is based on self-report measurements, that requires the participant to recollect emotional states, which entails a lot of uncertainty (ibid.). It could flowingly be argued that GAD research need more objective measurement criteria, like the addition of naturalistic observations combined with collection of the clients history, which could augment the BAI, STAI-I and PSWQ measurements.

### Application of therapy

The interventions were all required to accommodate the theoretical components from the theories they derive from, but they weren’t standardized. Most of them had similar number of session (12), and a similar time span (45-60min) and were individualized, but group therapy, and two hour session did occur. In that respect the administering of the interventions wasn’t as methodologically homogenous as would be ideal. Regardless, the interventions did adhere to using their respective therapeutic components, and therefore the interventions can be said to be applied methodological correct, but differentiated. Group IUT is apparently just as effective as individual IUT, but with more dropouts. Most of the interventions were about 12 session between 45-60min, which mirrors the standard number of sessions for CBT, and is thereby comparable to a plausible intervention scenario. All of the studies and interventions were cognitively oriented, which could have led to a bias in its own right by, for instance, researchers emphasizing finding that supports the cognitive theoretical framework, and downplaying findings that do not.

### Data extraction and results

Mean scores and standard deviations of PSWQ, BAI and STAI-T, in interventions, conditions, waitlist conditions and 6 and 12 months follow-ups were extracted, along with the effect sizes (Cohens d) for within-subject differences from pre to posttest.

The number of participants for each condition in the reviewed studies, were extracted. This information were important since, a high number of participants improves the external validity of a study, by making the findings more generalizable (Coolican, 2009, p. 97). In every study with a waitlist condition, the waitlist control groups were later added to the intervention condition groups. In the studies where this occurred, the data from the original intervention condition participants + the former waiting list condition participants were included in the systematic reviews result section instead of the original interventions groups scores, and compared to the waiting list scores. The combined groups, had more participants than the original smaller treatment groups, which as before mentioned, improves the external validity of a study, and thereby improving the generalizability of the systematic reviews results overall. The included studies generally had a decent number of participants. Ideally there would be more participants, which would have improved the external validity of the review, but with a mean of 32,9 participants, it is possible to generalize the findings to a certain degree, and claim that the systematic review has some evidential power, that can be used to evaluate the state of the art for GAD specialized treatment. Almost all of the included studies had either waitlist conditions that served as control groups, or follow-up conditions or both. These conditions adds to the internal validity of the included studies, since use of control groups insures that experiments designs follows the principle of cause and effect, and thereby adds to internal validity (Coolican, 2009, p. 86). The interventions ability to reduce the measurement mean scores, is isolated by comparing the intervention condition to a control condition, and thereby examining if the outcome of treatment condition would happened if the treatment wasn´t applied. The follow-up conditions further solidifies the causal relationship, by making it possible to see if the effect endures over time, and thereby improving the validity as well.

I addition to the relatively large number of participants, most of the studies were randomized, so that the participants were randomly allocated to their experimental condition. A lot of the studies included alternative comparative interventions with randomly allocation and/or blinded assessors, so in a lot of instances, the participants, and their assessors applying the measurements were not aware of which kind of therapy they were receiving. This is called double-blind, and adds greatly to the Internal validity of the studies. With this degree of randomization, confounders like *the allegiance effects* are combated. Allegiance effects might occur when researchers wittingly or unwittingly favor a condition to which they experience a degree of loyalty, such as a treatment they have taken part in developing (Dugas et al., p. 2010, p. 48). A full biographical review of the used assessors and therapists, were not possible to obtain, but most studies stressed that they had chosen experienced people for the tasks, indicating that the chance of inexperienced administration of therapy or assessments affecting the study, were minimized. There were no indications that the research were funded by partial agencies, even though it can not be excluded.

Extraction of the variables sex distribution and age means, gave insight into some patterns: For all studies, the mean age were higher or equal to 35 years. Since many instances of GAD has its onset in childhood phenomenon (Holmes, Donovan, Farrell & March, 2014, p. 122), it can be argued that the participants unfortunately might constitute an asymmetrical representation of the age distribution of GAD. It might however just be a product of, that younger individuals might not be aware of that their disorder can be diagnosed as GAD, and therefore might be less available for recruiting to clinical studies. In any case, further studies should focus on a more even age distribution in their recruiting process, or examining if the age has any effect on the course of the disorder at all. In regards to sex distribution, most of the studies had a major overweight in female participants. This doesn’t reflect that many of the studies need to optimize their recruiting processes, but is more likely a manifestation of the sex distribution of GAD, which is characterized by a overwhelmingly majority in women (Lieb, Becker & Altamura 2005, p. 446). Since most of individuals with GAD worldwide are women, it is relevant that this systematic review generates knowledge about the effectivity of the intervention for a groups whose is majorly constituted of women, but there is a need to examine if being male affects the effectivity of the interventions. Subsequently, it would be relevant to conduct further studies in which a higher percentage of participants are male, or in which only men are examined, in order to identify possible differences in how the sexes react to GAD treatment.

Drop-out rates were not so large that the studies described them as constituting a problem, but evidently it would strengthen the systematic review if the drop-out rates were minimal or non-existent. In general the studies were good at providing transparent data that were relevant for the evaluating the effectivity of the interventions. Most of the studies had in addition to the data from pretest to posttest, also a 6m follow-up condition, which adds to the internal validity of the systematic reviews, since it makes it possible to extract, present and evaluate data for follow-up effect, for almost all of the studies, and there by illustrating that the causal effect of the interventions, endures six months after the termination of treatment. Many of the studies used a 12 month follow-up condition, but not enough to present it in the analysis section tables. If all the studies had presented a 12 months follow-up condition, it could be evaluated if the effects of IUT, MCT and IEP are able to endure over time, adding considerably to the strength of this systematic reviews design.

Effect sizes were extracted for all studies that had presented effect sizes for pre-to post within-subject differences, for the targeted mean scores in the relevant intervention groups. Effect sizes that did not meet these comparability criteria were not extracted. The supplement of effect sized in addition to the presented mean scores of the measurements, strengthens the systematic reviews research design. An advantage of using effect sizes compared to using only measurement mean scores, is that effect sizes calculates the difference between two variables, in a way that is not affected by the number of participants (Cohen, 1992). Effect sizes measures the effect in itself, and thereby avoiding the possibility of for instance fluctuation in the measurement becoming statistically significant, because of a large number of participants (Coolican, 2009, p. 48) which unfortunately occurs in some null hypothesis testing, thereby making effect sizes an often superior alternative (ibid., pp. 341-342). That makes it possible to compare the effectivity of the interventions, despite of the differences in the studies design and number of participants (ibid.). Since the included studies had great variability in the number of participants, the strategy of extracting effect sizes is advantageous. It was chosen to extract within-subject differences, instead of between-subject differences, due to within-subject differences ability to dramatically reduce the chance of *unsystematic variance*, which is unknown factors that differs between conditions, which can influence the results (Field, 2009, pp. 16, 342).

## Analysis

The implementation of the effect sizes in the systematic review, made it possible to analyze results that were more tangible than raw reductions in mean scores. When comparing a pretest and a posttest mean score, the difference between them says something about the effectivity of the intervention, but the reduction has no inherent criteria for categorizing the level of efficiency of the reduction. The categorization thresholds of PSWQ, BAI and STAI-T provided some sort of referential frame, that made it possible to classify and estimate worry, and anxiety, which were relevant for this systematic review, as it gave an impression of the interventions ability to reduce symptoms, and heighten the quality of life for individuals with GAD. But the threshold categorization approach is however dependent on the starting point of the populations symptom level: If a given population had exceptionally high or low anxiety or worry levels to begin with, it heightened or lowered the probability for the symptom to cross the threshold into a lower category. In order words: The reduction in mean scores, and the thresholds categorization approach, provides the systematic review with valuable information, that can be analyzed, but there is a need for the addition of effect sizes, which provides a parameter that can be used to evaluate the effectivity of the treatment, without being directly dependent on the starting point of the severity of the symptoms.

In addition, Cohens d considers 0.2 to 0.3 a small effect, 0.5 a medium effect and 0.8 or higher, a large effect (Cohen, 1988) which provides a set of indicators that can be used to evaluate the effectivity of a given effect, in this case, IUT, MCT and IEPs ability to reduce the mean scores of the measurements from pretest to posttest. As strong evidential power as the extracted effect sizes have, more statistical analyses would be an improvement in the validity of the results. With each study calculating its own effect sizes, there is a lot of room for confounders. A meta-analysis that calculated the effect sizes from the raw data from the studies, would be able to more accurately compare the effectivity of evaluated information, with less chance for confounding variables.

## Further studies

No matter how high evidential power a research design wields, the author(s) is always an integrated part of the study, not being passive but instead interpreting the findings, and thereby becomes an active part of the study (Giere, 2008, pp. 2-3). Subsequently reviewers might be selective or weight certain studies over others, and can be influenced by their own theoretical alignments or fail to take into account some characteristics that could explain some oddities in the collected data (Coolican, 2009, p. 101). In short, even though systematic reviews are considered to be one of the research forms with most evidential power, there is still considerable possibility of confounders influencing the data. A *Meta-analysis* is the employment of a set of statistical techniques to evaluate and compare results from a large number of studies, based on similar hypothesis and theoretical constructs (ibid). The process often involves a systematic review. The studies are reviewed and sorted according to their suitability of the method and hypothesis in regards to answering the research question (ibid). Afterwards the results are extracted and become subject to statistical procedures, that optimizes the comparisons of effect sizes across studies, by taking into account various statistical features of the data from each study (ibid). The aim of the procedure is to increase validity and to sort out consistent from unreliable results from a myriad of findings about a research topic (ibid., p. 386). This seeks to collect refine and create knowledge and comparability in a area were data is characterized by subjectivity, and were it is not possible to implement the more standardized techniques of natural sciences (ibid. p. 101). Further studies of MCT, IUT and IEPs effectivity of reducing GAD core symptoms, should consider conducting a meta-analysis, which are considered the highest ranked methodology for clinical research in terms of validity (Piantadosi, 2005, p. 135-136).

It would also be relevant for further studies to balance the participants so that a more even sex and age distribution is reached. Separate studies that focus on which interventions are effective for children with GAD and secondary GAD (as opposed to primary non-comorbid GAD), and comorbid substance abuse should be a point of interest too, since it would add tremendously to the body of research concerning some of the most widespread version of GAD. Are more representative sex and age distribution would also add more population validity to further studies, making their findings more generalizable (Coolican, 2009, p. 102).

# Conclusion

The clinical and scientific background for the systematic review was presented, and elaborated, along with the theoretical frame work for cognitive treatment of GAD. Scientific theoretical justification of choosing the systematic review as a research method, over for instance a theoretical study, can be found in a ethical imperative of evidential based treatment for Nordic psychologists, that dictates that clinical treatment should be based on the best available research. Therefore the systematic review was chosen since it is one of the highest ranked research methods in the pyramid of evidence that evaluates evidential power of clinical trials. The systematic reviews adherence to the recognizes research protocols PICO and PRISMA, adds to the methodological strength of the research design.

The consideration and deliberate choice in using the digital databases EmBase, PubMed and PSycNet for the systematic literature search, reduced potential regional publications biases in Europe and USA, as well as biases concerning the effectivity of psychological interventions in general. The use of the manually compiled comparative list of literature, increased the literature search ability to identify relevant articles, and flowingly made it more probable that the systematic review evaluated most the relevant articles on the subject. The included studies were all published peer reviewed articles. That inclusion criteria added greatly to the probability that the scientific quality of the included studies had a sufficient level, since in order to be included, the articles have had to pass methodological rigid criteria applied by impartial evaluators, to obtain these labels.

The PSWQ, BAI and STAI-T measurements has all been testing for their psychometric abilities concerning their respective symptomatic objects, pathological worry, state anxiety and trait anxiety, which are all GAD core symptoms. Their ability to measure the symptoms correctly reflects the systematic reviews internal validity, by ensuring that the symptoms that are central for GAD, are measured properly.

A systematic reviews ability to evaluate the object of research is considerably improved if the included studies overall scientific quality is high. Subsequently a number of aspects that could be used to evaluated the standard of the included studies research design, were evaluated. The frequent use of randomly allocation, and double blinded assessors and participants, adds greatly to the internal validity of the studies, and there by the systematic review in general. The relatively high number of participants that entered and finished the study, adds to the external validity, making the findings more generalizable. Most studies stressed that they had chosen experienced people for the administration of the interventions, and in the role as assessors administering the measurements, thereby reducing the chance that inexperience could influence the application of measurements and therapy. There were no indications that the research were funded by partial agencies in any of the studies.

The systematic reviews analysis of the extracted data, consisted of evaluating reduction in measurement mean scores from pretest to posttest, and categorizing the scores by the use of threshold categorization, that indicated if GAD core symptoms appeared less severe after application of the interventions. Finally within-subject effect sizes were extracted, in order to give an referential frame for evaluating the effectivity of the interventions, and evaluate the difference in a way that were minimally affected by number of participants, and external confounders. There is room for improvement in the systematic reviews methodology. A larger number of participants, and a more differentiated population of participants, that better represents populations with GAD (e. g. more men, children and adults in their 20ies), and clinical trials with implementation of all three measurements, would improve the research design.

As strong as the extracted effect sizes are, more statistical analysis in the form of an meta-analysis would be an improvement, because of its higher evidential power, and the calculation of each effect size would reduce possible confounders by ensuring that the effect sizes were calculated in the exact same way. Despite that, the research design of the systematic review, can overall be concluded to have high internal, external and construal validity. All the way from the adherence to research protocols, over the choice of digital databases that avoids regional publication biases, down to the included studies choice of implementing double blinded allocation to research conditions, there is a lot of precautions for ensuring that its results a generalizable, that confounders are reduced and that the causal relationship of the examined intervention are isolated.

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# *Part**2: Article*

# Systematic review of cognitive interventions specialized against generalized anxiety disorder

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# Abstract

*Objective:* A new wave of cognitive behavioral therapy specialized against Generalized anxiety disorder (GAD) has emerged. Metacognitive therapy (MCT), intolerance of uncertainty therapy (IUT), and interpersonal emotions processing therapy (IEP), are all manifestations of this. To this date, no systematic review of the effectivity of these treatments has been conducted. *Method:* By conducting a systematic review, this study aimed to evaluate the effectivity of the interventions, by assessing their ability to affect the mean scores of measurements for pathological worry and state- and trait anxiety in a GAD population. Extraction of effect sizes (Cohen´s d) of the interventions in the studies was performed in order to evaluate the effectivity of the treatments. *Results:* The systematic review indicated that all three interventions were effective in reducing GAD core symptoms, and implement a uniform reduction in pathological worry and state- and trait anxiety. This reduction continued at 6 and 12 months follow-up. MCT was found to be the most effective. IEP was less effective than the other two interventions, and the systematic review consisted of only one study. *Conclusion:* All three GAD specific interventions proved effective at reducing GAD core symptoms, but with less robust findings for IEP. The general methodological quality of the included studies were found to be high. However, for the results to be validated, a meta-analysis were considered to be the best course for further research into GAD specific interventions.

**Keywords** Generalized anxiety disorder – Treatments – Worry – State anxiety – Trait anxiety

# Introduction

Theoretical models of *generalized anxiety disorder* (GAD), are beginning to take into account, the specific components of the disorder, and how to target them with specialized interventions (Waters & Craske, 2005, p. 85). *Cognitive behavioral therapy* (CBT) is the recommended therapy for GAD (Ballenger et al., 2001, p. 56), and has significant results regarding symptom reduction (ibid.). The reductions in symptom severity are, however considerable lower compared to the reductions CBT has shown to have against other anxiety disorders (Hazlett-Stevens, 2008, p. 13). The percentage of participants that experience improvement lies between 38-63%, which is considerably less than in the case of treatment of, for instance panic disorder which is at 80-85% (Waters & Craske, 2005, pp. 85-86). GAD is the anxiety disorder with the greatest treatment resistance (Hazlett-Stevens, 2008, p. 13), and the disorder CBT is least effective against (Brown, Barlow & Liebowitz, 1994, p. 1276). Still other treatment interventions are even less effective against GAD than CBT (Okholm, 2014, pp. 5-6). Hence, there is a need for CBT interventions for GAD to be improved, in order to bring down the high treatment resistance.

Preliminary studies of specialized versions of CBT for GAD are promising (Behar et al., 2009, pp. 1010-1021), and could be a way to improve treatment of the disorder. A systematic review has yet to be conducted in order to evaluate the effectiveness of these models and their interventions. *Metacognitive therapy* (MCT), *Intolerance of uncertainty therapy* (IUT) and *Interpersonal Emotional processing therapy* (IEP) are all part of a relatively new wave of GAD specific interventions, and are based on three of the most influential GAD specialized theoretical models (Clark & Beck, 2010, p. 399; Hazzlett-Stevens, 2008, pp. 8-11; Portman, 2009, pp. 31-38). Thereby, they can be argued to represent the state of the art with respect to specialized GAD treatment. To evaluate the status of CBT for GAD, this article will perform a systematic review of the efficiency of these interventions.

CBT for GAD is traditionally generic, which means that it i´s designed to treat anxiety in general, without considering the specific properties of the disorder (Waters & Craske, 2005, p. 85). This might be due to the fact, that GAD has only recently begun to be considered a separate disorder (Hazlett-Stevens, 2008, p. 2). The generic focus is a deviation from the norm of other contemporary CBT anxiety treatments, which is most commonly specialized to fit each disorder, because of the often larger effect-sizes compared to non-specialized CBT for anxiety (Hofmann & Smits, 2008). CBTs efficiency against virtually all other kinds of anxiety disorders is backed by meta-studies (ibid., p. 6). This indicates that the inability to treat GAD with CBT is due to the treatment failing to consider aspects of the disorder, that are specific to GAD, rather than due to the CBT anxiety treatment being flawed in general. This study will work from the premise that traditional CBT anxiety treatment for GAD needs to be replaced by the new theoretical GAD models interventions targeting the processes that are specific to GAD. Therefore it is necessary to assess the effectiveness of IUT, MCT and IEPs interventions, in order to validate the implementation of GAD specific treatment with the intention of decreasing the high treatment resistance.

Worry and anxiety are considered the core symptoms of GAD (Clark & Beck, 2010, p. 389). Even though theoretical models of GAD hold differing opinions about the finer points, there is a broad consensus, that pathological worry is the central maintaining component of GAD (Okholm, 2014, pp. 15-26) and is used by individuals with GAD, as a cognitive and emotional avoidance strategy (ibid.). Several studies indicate that manipulation of worry increases or decreases the severity of anxiety (Brown, Antony & Barlow, 1992, p. 33), and other GAD related symptoms (ibid.). Therefore measures of worry and anxiety are deemed as relevant variables that can be evaluated in order to assess the effectivity of IUT, IEP and MCT ability to reduce GAD symptoms. Anxiety is believed to consist of two components: A transitory emotional reaction called state anxiety and a relatively stable personality disposition called trait anxiety (Bernstein & Eveland,1982, p. 361). Therefore, both state and trait anxiety will be measured.

## Aim of study

This aim of this study is to evaluate the effectivity of the GAD specialized CBT interventions, by conducting a systematic review of clinical trials involving IUT, MCT and IEP. The interventions´ ability to reduce mean scores of measurements evaluating worry and anxiety symptoms, will be the basis for establishing their effectivity. Worry will be measured by *the Penn state worry questionnaire* (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990), and anxiety will be measured by *Becks anxiety inventory* (BAI; Beck, Epstein, Brown, & Steer 1988) and *the State-trait anxiety inventory, trait version* (STAI-T; Spielberger et al., 1983). BAI measures state-anxiety and STAI-T trait-anxiety. The mean scores will also be categorized pretest and posttest by the use of the measurements distinctive categorization thresholds. The thresholds place the mean score on a spectrum that ranges from “low” to “high” severity, and thereby makes´ it possible to evaluate if the core GAD symptoms (represented by the measurements´ mean scores), at posttest can be classified as less severe than at pretest. The mean scores will be extracted, evaluated and compared between the interventions, the effect sizes (Cohens d) for the within-subject differences of the pretest to posttest means will be extracted, evaluated and compared as well.

Preliminary trials of MCT and IUT (Behar et al., 2009, pp. 1015-1017) as well as IEP (Newman et al., 2008), indicates that the interventions are effective in diminishing GAD symptoms, and either maintain or increase the reduction over time. It is thereby hypothesized that the interventions will generate effects 0.80 or larger, which constitutes a large effect (Cohen, 1988), and that the effects will be maintained or increased when measured at follow-up assessments. The methodology of the study designs will be evaluated as well.

## Hypotheses

It is hypothesized that MCT, IUT and IEP will affect the intervention conditions by:

1. Reducing the PSQW, BAI and STAI-T mean scores from pretest to posttest, and maintaining or increasing the reduction during follow-up.
2. Reducing the mean score of PSQW, BAI and STAI-T to a less sever anxiety or worry category threshold at posttest and/or follow-up than at pretest.
3. Generating effect sizes (Cohens d) for within-subject differences at pretest to posttest that are ≥ 0.80, and there by indicating that the reduction of the mean scores constitutes a large effect.

It is also hypothesized that:

1. Control groups will maintain roughly the same mean scores from pretest to posttest.

# Theoretical models and interventions

### The worry and avoidance theory of GAD

*The worry and avoidance theory* *of GAD* (WAT;Borkovec, 1994) views pathological worry, differentiated from normal worry by its excess and intensity, as a cognitive avoidance strategy that maintains anxiety. Worry is seen as serving the function of keeping the individual from confrontation with emotional material. The avoidance of the confrontation with the emotional material inhibits emotional and somatic response, but also keep the individual from coping with the material, causing anxiety (Hazlett-Stevens, 2008, pp. 9-10). The emotional and somatic activation that is inhibited, is needed in order to extinguish the anxiety response (ibid., p. 12). By avoiding coping with the material, the cause for worry and anxiety keeps causing anxiety (ibid., pp. 9-10). The reason that individuals with GAD tend to find the handling of emotional material extremely unpleasant, is thought to be because of developmental attachment vulnerabilities relating to handling of emotions (ibid., p. 10). WATs theoretical components are supported in numerous studies (Borkovec, Alcaine, & Behar, 2004, Behar & Borkovec, 2005, Borkovec & Roemer, 1995, pp. 28-29).

*Interpersonal emotional processing therapy* (IEP; Borkovec, Newman, & Castonguay, 2003) is based on WAT, and is taking the theoretical components of developmental vulnerabilities role in GAD into account. This is sought achieved by enriching standard CBT for GAD with psychodynamic modules targeting the individual’s ability to adaptively process emotions and interpersonal problems (ibid., pp. 387-388).

### Wells: Metacognitive model of GAD

According to *The metacognitive model of GAD* (MCM; Wells, 1995), GAD is based on both Type 1 worry and type 2 worry. Type 1 worry, is worry combined with cognitive schemata containing attitudes about the usefulness of worry to deal with a threatening object, and is initiated by threatening events/sensations/thoughts, and often results in anxiety (Wells, 2005, p. 108). Type 2 worry is worry combined with schemata implementing the attitude that worrying is maladaptive, dangerous and should be avoided, which results in the individual worrying about his or her type 1 worry, and thereby creating more anxiety (Behar et al., 2009, p. 1016). Type 2 worry is initiated when type 1 worry has been activated for a while (ibid.).

Type 2 worry is trait based, and functions as diatheses for GAD (ibid.). The Type 2 worry about type 1 worry results in an increase of anxiety symptoms, which in turn is perceived as dangerous, and results in more type 1 and 2 worry in a maladaptive circle, and ineffective tries to suppress thoughts, emotions and behavior, which manifests in GAD symptoms (ibid.). The existence and function of type 1 and 2 worry is validated in studies of non-clinical populations (Wells, 2004; Davis & Valentiner, 2000, p. 522; Ruscio & Borkovec, 2004, pp. 1479-1482), but only in few studies of clinical populations (Behar et al., 2009, p. 1016).

Metacognitive therapy (MCT) is the intervention based on MCM. It intervenes against attitudes about worry, metaworry and avoidance strategies (Wells, 2006, p. 259). The client is first trained to objectively evaluate and nuance the type 1 and type 2 worry attitudes about the nature and function of worry (ibid.). Later, the client is taught more adaptive coping strategies when confronted with anxiety prompting objects, situations and thoughts. Case formulation, discussion of attitudes and reconstruction are the central therapeutic interventions in MCT (Behar, et al. 2009, p. 1016).

### Intolerance of uncertainty

*The Intolerance of uncertainty* model (IUM; Dugas et al., 1995) is centered around a cognitive construct called intolerance of uncertainty (IU), which derives from a series of negative attitudes about uncertainty and its implications (Robichaud, 2013, p. 59). It both disposes towards and maintain GAD (Dugas, Buhr, & Ladouceur, 2004). The cognitive diathesis IU can, when activated by the proper stressor, make the individual perceive uncertainty as stressing, unpleasant and inhibiting, and uncertain events as something negative that should be avoided (ibid.). Research indicates that IU is strongly correlated with pathological worry, and with GAD specifically (ibid.). Interventions against IU affects both pathological worry and GAD symptoms (ibid., pp. 60-61). IU is considered the source for the worry process, and contains three sub-constructs that also maintain worry and GAD. Studies indicate that individuals with GAD have heightened levels of IU and the three constructs, when compared to healthy controls (Buhr & Dugas, 2002, p. 942; Dugas, Gagnon, Ladouceur & Freeston, 1998, p. 222).

Therapy based on IUM is called Intolerance of uncertainty therapy (IUT), and is focused on training of acceptance of uncertainty and on development of tolerance of uncertainty (Robichaud & Dugas, 2006, p. 290). IUT is also centered upon registration of the reciprocal relationships of situations, cognitions, emotions and physiological response, reconstruction of attitudes about worry, training of better problem solving, and processing of core fears, which involves confrontation with the feared object (Behar et al., 2009, pp. 1015-1016).

# Method

## Search strategy

To retrieve relevant articles about clinical trials of MCT, IUT and IEP targeting GAD, and administering PSWQ, BDI and STAI-T measurements, a digital search using PubMed, PsychInfo and EMbase was conducted. The commonly used abbreviation “GAD”, and both “Generalized anxiety disorder” or “Generalised anxiety disorder or GAD” (UK and USA spelling forms respectively) were used as keywords, combined with distinctive keywords for each search. Distinctive keywords for search 1: “Intolerance of uncertainty”. Search 2: “Integrative therapy or Interpersonal emotional processing therapy or Emotion-focused interpersonal therapy”. Search 3: “Metacognitive model or Metacognitive therapy”. The PICOS review protocol was consulted during the design of this review. To fulfill inclusion criteria the study had to include a population with GAD, with stable medication doses during the study, in order to rule out changes in medications as an influence on the GAD symptoms. All studies except one excluded participants who suffered from comorbid disorders, but for the systematic review, GAD populations with or without comorbid disorders were accepted. All nationalities, age groups and sex-distributions were included. Articles from any geographical area were accepted as long as they were written in English. To avoid diagnostic confusion, no studies before 1994, the date GAD was last revised in DSM (Clark & Beck, 2010, p. 391), were included. Only published peer-reviewed articles were included.

Only studies that applied IUT, MCT or IEP, and used PSWQ, and BAI and STAI-T were included. In order to fulfill inclusion criteria, PSWQ had to be implemented, since pathological worry were deemed an quintessential variable to evaluate, in relation to GAD symptom reduction. The interventions were allowed to vary as long as they fulfilled the protocols and/or theoretical implications of said interventions. In order to assess this, the studies’ methodological description of their applied interventions, was compared with the recommended structure of therapy in IEP, MCT and IUT literature (Borkovec, Newman, & Castonguay, 2003; Wells, 2006; Robichaud & Dugas, 2006). Studies that examined other interventions in addition to IEP, IUT or MCT, or other disorders in addition to GAD, were accepted, but only variables deemed relevant for the systematic review were extracted. The studies’ design had to be quantitative-empirical and present mean scores or individual scores of the measures. To be included, the participants scores on the measures had to be assessed pretest and posttest. Control groups on waiting-list condition were included in several of the studies, and used for comparison with the intervention conditions’ effect on the mean scores. In some of the studies comparative treatments were being designated to serve as control groups, but since this systematic review, only extracted either MCT, IUT IEP or waitlist control group conditions, some of the studies have no available control group. All studies except one had 6 months follow-up conditions, but four studies lacked 12 month follow-up. The lack of control groups, and 6 and 12 month follow-ups as well as a control group (in one case), was not an exclusion criteria, since the reduction of the PSWQ, BAI and STAI-T measurements immediately before and after the intervention, was the priority.

It is however noted that the studies which implemented control groups, greatly reduced the change of *confounding variables*, which is uncontrolled variables that obscures any effect sought (Collican, 2009, p. 79), and thereby the control groups facilitated a higher level of *validity*, than the studies without a control group. Validity is the extent to which an effect is demonstrated in research to be genuine and not produced by misleading variables, or limiting to a specific context (Coolican, 2009, p. 104). Control groups specifically adds to the *internal validity* of the study, that concerns if the measured effect in a experimental condition is real, and a product of a manipulated experimental variable (ibid.). It does so by enabling comparison of the effect seen in the experimental condition, to a control condition, were the manipulated experimental variable is not applied (ibid., pp. 86-87). In this systematic review, the manipulated experimental variable is the application of the interventions, and the outcome that is being examined, is the interventions ability to reduce the measurement mean scores. Thereby the addition of control groups, greatly adds to the quality of the results from the studies that implement them in their designs.

Follow-up assessments makes it possible to see if the effect endures over time, and persists after termination improving *external validity* (Rothwell, 2006, p. 4). External validity is the degree to which an effect can be generalized to other places, peoples, and times (ibid., pp. 104-105). Ideally all the included studies would had implemented both control groups and follow-up assessments in their design, in order to greatly add to the internal and external validity. The fact that it is not the case, does not mean that nothing can be deducted or generalized from the findings of the studies that didn’t use a control group, or the study without a follow-up condition, but the studies that did use them has results with higher validity, and therefore a bigger chance that their results can be considered a real effect.

## Data extraction

The mean scores of the PSWQ, BAI and STAIT-T measures, from pretest to posttest, and during follow-up were extracted, along with the standard deviation of the scores. In one case it was necessary to calculate the standard deviation. The formula used can be found at the Appendix. The number of participants (n) in the study was written down. It was noted whether the study was a randomized control trial, with random allocation, and whether a double-blind procedure was followed, so that neither the participants nor the assessors applying the measurements, had knowledge as to which experimental condition the participants were allocated to. It was extracted how many participants that were allocated to each experimental condition, as well as pretest and posttest and 6 month follow-up (6m) and 12 month follow-up (12m). Drop-out rates for each condition were retrieved where possible. The specifics about the intervention, length and number of sessions were extracted. The age mean and the sex distribution ratio of the populations were extracted. In several studies, the waitlist control groups were added later to the intervention condition groups. In the studies where this occurred, the data from the bigger groups (the original intervention condition participants + the former waiting list condition participants) were included in the systematic reviews result section instead of the original interventions groups’ scores, and compared to the waiting list scores. The reason for that is that the combined groups have more participants than the original smaller treatment groups, and a higher amount of participants improves the external validity of a study, by making the findings more generalizable (Coolican, 2009, p. 97). By including bigger treatment condition groups, the generalizability of the systematic reviews results, and so the external validity, is improved overall. Another argument for using the combined groups instead of the originals, is that the follow-up studies are based on the scores from the combined groups.

The therapy being evaluated, is represented by the term intervention condition (IC), and is compared to the waitlist controls (WL). Effect sizes were extracted for all studies that had presented effect sizes regarding pre- to post- within-subject differences on the targeted mean scores in the relevant intervention groups. Effect sizes that did not meet these comparability criteria were not extracted. For Cohen's *d* an effect size of 0.2 to 0.3 is considered a small effect, 0.5 a medium effect and 0.8 or higher, a large effect (Cohen, 1988). The advantage of evaluating within-subject differences, rather than between-subject differences is that within-subject differences, has a dramatically reduced chance of unsystematic variance, which is unknown factors that differs between conditions, influencing the results (Field, 2009, pp. 16, 342).

## Measurements

The following measurements were used to evaluate the effectivity of the interventions.

### PSWQ

The Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, Borkovec, 1990) is a widely used 16-item self-report inventory that measures the excessiveness, severity and uncontrollable nature of worry. Respondents are instructed to indicate for each of the 16 items how applicable they are to them, using a 5-point Likert scale (ibid., p. 487-488). Total scores on the PSWQ range from 16 to 80, with higher scores representing a stronger tendency to worry (ibid., pp. 489, 494). The PSWQ has been shown to be a reliable instrument for assessing worry, and is sensitive to treatment effects (ibid., p. 494). It has a high validity, as well as high specificity and sensitivity in identifying individuals with GAD (Fresco, Mennin, Heimberg & Turk, 2003, pp. 289-290), which could make it a suitable instrument for identifying treatment effects in this study. PSWQ is considered the golden standard of measurements assessing worry (Kertz, Lee, & Björgvinsson, 2014, p. 1). Categorization thresholds are the following: Scores ranging from 16-39 =Low Worry, 40-59 = Moderate Worry, 60-80 = High Worry (Ramsay, & Rostain, 2014, p. 36).

### BAI

The Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988) is a self-report scale, which includes 21 items designed to assess anxiety symptoms over a 1-week period (ibid., p. 893). Each item is rated on a 4-point Likert scale ranging from 0 representing the answer “not at all” to 3 “Severly – I could barely stand it”, and the total BAI score ranges from 0 to 63 (ibid., p. 895). The scale has been shown to have good psychometric properties (ibid., p. 896). BAI is widely used to measure anxiety symptoms, especially somatic (Lam, Michalaak & Swinson, 2004, p. 68). The BAI mean scores can be categorized by the thresholds: 0-7 = minimal level of anxiety.8-15 = mild anxiety, 16-25 = moderate anxiety, 26-63 = severe anxiety (ibid.).

### STAI-T

State-Trait Anxiety Inventory, trait version (STAI-T; Spielberger et al., 1983), is a 20-item self-report questionnaire. Respondents are asked to rate how much they agree with each of the 20 statements on a 4-point Likert scale. Total scores range from 20 to 80, with higher scores reﬂecting stronger feelings of anxiety (ibid.). The STAI has two scales: One that measures state anxiety (STAI-S) and one that measures trait anxiety (STAI-T). The score is calculated independently for each scale by summing up the items from the relevant items (Lam, Michalaak & Swinson, 2004, p. 109). The STAI-T which is used in this study has good construct validity with respect to GAD (Fisher & Durham, 1999). It has been used in a lot of GAD research, because of its ability to measure clinically significant criteria, which can be used to evaluate if improvement and recovery is reached (ibid.). It has sound psychometric properties (Spielberger et al. 1983). Scores in the range of 20-39 indicate low anxiety, 40-59 = moderate anxiety, 60-80 = high anxiety (Lam, Michalak & Swinson, 2004, p. 109).

## Literature search

## Search 1: Intolerance of uncertainty

Searching in the digital databases resulted in 35 hits in Psychinfo, 31 in PubMED and 35 in EMBase. After the removal of duplicates, 59 studies remained. After the articles were screened according to the inclusion criteria, 53 studies were excluded, and six articles were assessed for eligibility. One study was excluded, on the grounds of not having any measurements in common with the rest of the studies. Finally five studies of IUT were included for qualitative synthesis, which is a synthesization of quantitative data (Barnett-Page & Thomas, 2009, p. 1) were study characteristics, quality and findings are reported, and similarities and differences are compared across studies (Ibid., p. 3). The studies chosen for qualitative synthesis were: Ladouceur et al. (2000), Dugas et al. (2003), Ladouceur, Léger, Dugas & Freeston (2004), Dugas, et al. (2010), Van der Heiden, Muris & Van der Molen (2012)[[3]](#footnote-3). The results from the literature search in the digital databases are presented in table 1.

 (see Table 1 in the appendix)

Ladouceur et al. (2000) tested the efficiency of IUT against GAD, on 26 GAD patients, 20 women and six men, with a mean age of 39.7. The participants received 16 one hour sessions (over 16 weeks), and PSWQ and BAI were administered. There were no drop-outs during the study. The patients were randomly allocated, so that 14 were added to the IC and 12 to the delayed waitlist condition (WL).The waitlist participants were later added to the IC, and the pre- and posttest scores of this combined group (26) was measured and compared to the WL. Seven participants were lost to follow-ups, and their measures replaced by their last available scores (endpoint scores).

Effect sizes (Cohens d) were extracted for the IUT condition, from pre- to posttest: PSWQ: d = 2.38, BAI: d = 0.87

Dugas et al. (2003) evaluated the efficiency of group based IUT, against GAD. 52 participants (m = 41.2 years, 37 females) received 14 two hour sessions, over 14 weeks, in groups of 4-6. Participants were randomly allocated to a IC (25) and a WL (27). PSWQ and BAI were applied. WL was later added to IC, while four participants dropped out. The scores of this group (48) are listed in thee summary table. Nine participants were lost to follow-up.

Effect sizes (Cohens d) were extracted for the IUT condition, from pre- to posttest: PSWQ: d = 1.62, BAI: d = 0.87

Ladouceur et al. (2004) examined the efficiency of IUT group interventions on GAD in older adults. 8 participants (m = 64,20 years, seven females) received 14 weekly sessions of CBT. There were no dropouts. PSWQ and BAI were applied. The mean of the measurement scores, and standard deviations were not presented in the article, and was therefore calculated manually using the formula presented the appendix.

The presented effect sizes did not meet the comparability criteria, and were therefore not extracted.

Dugas, et al. (2010) randomly allocated 65 participants (m = 38.5 years, 43 females) to three conditions: A group that received IUT (23), a group that received applied relaxation (22), and a WL (20). The IUT and applied relaxation condition received 12 weekly one hour sessions. Following the 12 week waiting period, participants of the WL were allocated to either the IUT (33) or applied relaxation (31). Those mean scores are presented here, and compared to the WL. PSWQ and STAI-T were applied. Two participants dropped out form IUT, five from applied relaxation, and one on WL. Their posttest scores were replaced by pretest scores.

The presented effect sizes did not meet the comparability criteria, and were therefore not extracted.

Van der Heiden et al. (2012) compared the efficiency of IUT, and MCT for GAD. 126 participants (m = 35.00 years, 92 females) with GAD were randomly allocated to MCT (54), IUT (52) or WL (20). Each participant in the intervention conditions received 14 weekly sessions of 45min. PSWQ and STAI-T were applied. 15 participant from WL condition (five had dropped out) was randomly allocated to the two treatment conditions, and after subtraction of dropouts, a total of 43 participants in IUT and 43 in MTM completed the study through both follow-ups. Only measures from participants that completed the follow-ups were available in the article. The measurements of the combined group and the diminished group are presented.

Effect sizes (Cohens d) were extracted for the IUT condition, from pre- to posttest: PSWQ: d = 1.43, STAI-T: d = 1.42

Effect sizes (Cohens d) were extracted for the MCT condition, from pre- to posttest: PSWQ: d = 2.39, STAI-T: d = 2.01

## Search 2: Interpersonal emotional processing therapy

Searching in the databases resulted in three hits in Psychinfo, eight in PubMED and eight in EMBase. After the removal of duplicates, 10 studies remained. After the articles were screened according to the inclusion criteria, seven studies were excluded, and three articles were assed for eligibility. Two studies were excluded, because one did not present any individual or mean scores of the measurements, and the other was a case study. One study was included for qualitative synthesis: Newman et al. (2011).

The results from the search in the digital databases are presented in table 2.

(see Table 2 in the appendix)

Newman et al. (2011) randomly allocated 83 participants (m = 37.00 years 63 females) with GAD to 14 weekly session of either 50min CBT+ 50min IEP (43) or 50min CBT + 50min supportive listening (40). Blind assessors applied the measurements of PSWQ and STAI-T. 13 people dropped out from pretest to posttest.

The presented effect sizes did not meet the comparability criteria, and were therefore not extracted.

## Search 3: Metacognitive therapy

Searching in the digital databases resulted in seven hits in Psychinfo, 16 in PubMED and 16 in EMBase. After the removal of duplicates, 23 studies remained. After the articles were screened according to the inclusion criteria, 17 studies were excluded, and six articles were assed for eligibility. The following two studies was excluded: One on the grounds of not basing the tested intervention on MCT, and another for not using the PSWQ as a measure. Four studies were included for qualitative synthesis: Wells et al. (2010), Van der Heiden et al. (2012), Van der Heiden, Melchior & de Stigter (2013), McEvoy, et al. (2014). The results from the search in the digital databases are presented in table 3.

(see Table 3 in the appendix)

Wells, et al. (2010) evaluated the effectivity of MCT against GAD, by comparing it to applied relaxation. The participants reviewed 8-12 sessions, 45-60min. The 20 participants (m = 49.05, 12 females) were randomly allocated to a MCT condition (10) and a AR condition (10). PSWQ, BAI, and STAI-T were applied.

Effect sizes (Cohens d) were extracted for the MCT condition, from pre- to posttest: PSWQ: d = 3.41, BAI: d = 1.38

Van der Heiden et al. (2012). For results, see the IUT result section.

In Van der Heiden et al. (2013), 33 participant (m = 31 years,, 24 females) with GAD were administered 12 weekly 90min session of MCT, to three groups of 10-14 participants. Nine participants dropped-out which left 24 participants to complete the treatment. PSQW and STAI-T were applied. 17 completed the follow-up.

Effect sizes (Cohens d) were extracted for the MCT condition, from pre- to posttest: PSWQ: d = 1.86, STAI-T: d = 1.23

McEvoy et al. (2014) tested the effectiveness of Brief group MCT against primary and non-primary GAD. 52 participants (m = 38, 31 females) were allocated in 11 groups, with three to seven in each group, in which they received six weekly two-hours sessions plus a follow-up, one month after the last session. The follow-up data was not taken into consideration, since one month was deemed ineffective to measure long term effects of the intervention. 46 participants completed the study. PSWQ and BAI were applied.

Effect sizes (Cohens d) were extracted for the MCT condition, from pre- to posttest: PSWQ: d = 1.82, BAI: d = 0.58

## Analysis

A summarization of the mean scores presented in the result section is displayed in table 4, 5 and 6 (see the appendix).

### Reduction of mean scores

As seen in Table 4, the IUT interventions result in a considerable and uniform reduction in the mean scores for PSWQ, BAI and STAI-T from pre- to posttest across all studies, and the reductions continue at 6m and 12m. The only exception is Ladecour et al. (2004) which experiences a slight increase in the PSWQ score at 12m, but is still below the pretest score. The WL remains stable from pre-to posttest. The MCT studies show the same uniform tendency with considerable reduction that is maintained at 6m. Wells et al. (2010) is the only one of the MCT studies that has a 12m follow-up, and here the reduction is maintained at 12m as well. The IEP study does show a reduction from pre- to posttest, which is maintained at 6m and 12m, but the reduction is considerable smaller than in almost all of the other studies, and that on all measurements.

### Mean score categorization thresholds

At pretest the PSWQ mean scores in all studies, regardless of the type of intervention, were in the 60-80 category, which signifies “high worry”. At posttest all the PSWQ mean scores were reduced to between 40-59, which qualifies as “moderate worry”, except for Wells et al. (2010) which was at 39, and there by qualifying for “low worry”. The reductions continued at 6m and 12m, but remained at the spectrum of moderate worry. The BAI mean scores were all between 16-25 at pretest, thereby qualifying for “moderate anxiety”, except Ladecour et al. (2000), which was between 8-15, and therefor labeled “mild anxiety”. At posttest all of the BAI measures reached well beyond the threshold for the “mild anxiety” category. The mean scores remained in the range of the category at 6, and 12m.

The STAI-T scores were almost all between the range of 40-59 at pretest, qualifying for “moderate anxiety”. The exceptions were Newman et al. (2011) whose pretest BAI mean score was almost a third of the others, and fulfilled the 20-39 criteria for “low anxiety”, and Van der Heiden (2013) which fell into the 60-80 range, hence qualifying for “high anxiety”. At posttest, there was a sizeable reduction, in all the studies, even though most means continued to remain in the moderate category. Van der Heiden et al. (2013) entered the moderate anxiety category at posttest, and Wells et al. (2010) reached the “low anxiety” threshold. At 6m the reductions had continued, and Van der Heiden et al. (2012) MCT study, also reached the criteria of “low anxiety”. At 12m there was a further reduction, but no changes in the category, leaving Dugas et al. (2010) still in the “moderate anxiety” category.

It can be concluded that IUT, MCT and IEP intervention, in all instances except three, reduced the PSWQ, BAI and STAI-T mean scores, to a less severe anxiety or worry category, from pretest to follow-up. The only exceptions were the two IUT studies Dugas et al. (2010) and Van der Heiden et al. IUT (2012) and the IEP study Newman et al. (2011), which experienced reduction in their STAI-T scores but didn’t change to a less severe anxiety category.

### Effect sizes

A summarization of the extracted effect sizes is presented in table 7. In order to make the effect sizes more comparable, only pre-to posttest within-subject differences has been included in the table.

(see Table 7 in the appendix)

The extracted effect sizes of IEP, MCT and IUTs reduction in the mean score of PSWQ were all ≥ 0.80, and can therefore be considered large effects, according to Cohens (1992) definition. The effect sizes were well beyond the required minimum of a large effect sizes. All were over 1.0 and three were over 2.0. The effect sizes for the reduction in the mean score of BAI, were all large effects, with the exception of McEvoy et al. (2014), which only constituted a medium effect. All the extracted effect sizes for the reduction of the STAI-T mean score from pretest to posttest, were large. In all three measurements the IUT and MCT interventions had very large effect sizes, far beyond .80, except for McEvoy et al. (2014) before mentioned BAI mean score. It was not possible to extract effect sizes from Newman et al. (2011), which was the only IEP study.

# Discussion

This systematic review identified and 9 clinical trials that evaluated the three GAD specialized CBT interventions MCT, IUT and IEPs effectivity at reducing the measurement mean scores of PSWQ, STAI-T and BAI. The results indicated that all three interventions were effective at reducing GAD core symptoms. The interventions were able to implement a uniform reduction in measurement mean scores, from pre- to posttest, and continue the reduction at 6 and 12 months’ follow-up. In almost all instances, the interventions were able to reduce the mean scores to levels that represented less severe state anxiety, trait anxiety and worry symptoms. When the effect sizes (Cohens d) for within-subject differences from pre- to posttest were extracted, all effect sizes except one were large (≥ 0.80). MCT and IUT were however more effective in reducing the mean scores than IEP. Four studies supported the effectivity of MCT, and five supported IUT, while IEP was only supported by one investigation. Especially MCT had large effect sizes, but also fever participants compared to the IUT studies. In sum, this systematic review indicates that all three GAD specialized CBT interventions targeting processes specific to GAD are effective in reducing pathological worry, as well as state and trait anxiety, which are the core symptoms of the otherwise treatment resistant disorder.

Hypothesis 1 investigated whether the GAD specialized interventions IUT, MCT and IEP were able to reduce the mean scores of PSWQ, BAI and STAI-T, form pre- to posttest, and to continue or increase the reduction at 6m and 12m. This hypothesis was supported by the uniform reduction of the measurements mean scores across all studies from pretest to posttest, and the almost uniform continued reduction at 6m and 12m. The IEP studies’ mean reduction were however considerably smaller than in the other interventions studies, on all measures. Hypothesis 2, which predicted that all measurement mean scores would be reduced to a less sever anxiety or worry category threshold at posttest and/or follow-up, was supported in regard to the PSWQ mean scores. Regardless of the type of intervention, all PSWQ score at pretest were in the range that signifies “high worry” and were reduced to “moderate worry” and in one instance “low worry” at posttest. The reduction continued at follow-up, but the scores remained at the same thresholds. The BAI scores were all reduced from “moderate anxiety” to “mild anxiety” from pretest to posttest, except in Ladecour et al. (2000), in which the BAI mean score were already fulfilling the criteria for “mild anxiety”. The hypothesis is therefore partially fulfilled for the BAI scores, since virtually the only obstruction of a uniform category change, was that the BAI mean score in Ladecour et al. (2000) was low to begin with. At follow-up there was no change in the category for the BAI mean scores. Across all studies there was a sizeable reduction in STAI-T scores, regardless of the type of intervention, even though most means continued to remain in the moderate category. Out of the six studies that used the STAI-T measurement, half changed to a less severe category: Van der Heiden et al. (2013), Wells et al. (2010) and Van der Heiden et al. (2012). As a consequence, Hypothesis 2 was only partly supported in regard to STAI-T.

It can be concluded that IUT, MCT and IEP intervention, in all instances except three, reduced the PSWQ, BAI and STAI-T mean scores, to a less severe anxiety or worry category, from pretest to follow-up. The only exceptions were Dugas et al. (2010), Van der Heiden IUT et al. (2012) and Newman et al. (2011) STAI-T scores, which were reduced but did not change to a less severe category. As a consequence, Hypothesis 2 was only partly supported, but the answering of Hypothesis 2 leaves a convincing indication of the effectivity of IUT, MCT and IEPS ability to reduce GAD symptoms to a less severe state. Hypothesis 3 postulated that the interventions would create effect sizes for within-subject differences that were ≥ 0.80. By reviewing the extracted effect sizes from the MCT, IUT and IEP studies, it was found that all the effect sizes, regardless of interventions’ type and measurement, were over 0.80 and thereby large effects, with the exception of McEvoy et als. (2014) BAI score. Hypothesis 3 was thereby only partially supported, even though the effect sizes were almost unambiguously over 0.80. This is another powerful indication that the three GAD specialized interventions are effective at treating GAD. The PSWQ effect sizes were larger for the MCT interventions, than for IUT and IEP. This indicates that MCT is the most effective of the three reviewed GAD specialized CBT interventions, while all three seems to be very effective in reducing GAD core symptoms. Hypothesis 4 was supported by the fact that the waitlist conditions remained stable form pre- to posttest. The stability of the WL conditions, emphasized the cause and effect relationship, by illustrating that the reduction of the mean scores was isolated to the intervention conditions, and would not have happened if the treatment were not applied.

Some of the included studies had very few participants, and therefore caution must be exercised in generalizing the findings of these studies. It is worth noting that the IUT studies had considerably more participants than the MCT and IEP studies, which increases the validity of their findings. The high number of studies and participants adds greatly to the external validity of the findings of the MCT and IUT studies compared to the one IEP study. The general quality of the included studies were high. Many used random allocation, and had blinded assessors, which lessens the risk for bias. Further, many used control-groups, which further improved the internal validity, and all except one study had follow-up assessments, which improved the external validity. The use of one of the highest rated research design on the evidential-based pyramid, further improves the design of the systematic review. As a consequence, this systematic review provides sound support for the implementation of MCT and IUT in treatment of GAD, while there is less robust findings of the effectivity of IEP.

MCT, IEP and IUT all have different approaches to GAD treatment, and differs in their theories concerning which processes that maintain GAD. One reading of the results could be that GAD can be maintained through several different mechanisms, since all of the interventions appears to be able to reduce GAD symptoms. It does however seem plausible that individuals differs in whether it is higher order cognition, metacognition or emotional based vulnerabilities which is the most influential. That conjecture is based on the fact that late-onset GAD widespread (Le Roux, Gatz, & Wetherell, 2005, p. 27), and it is unlikely that these individuals disorder evolves around a childhood that facilitated emotional vulnerabilities, if their problems first emerge in adulthood.

The systematic reviews synthesis of different studies results, generated evidence of the interventions effectivity, with higher validity than the studies could have done individually. The clinical implications of this systematic reviews findings, is the solidification of IUT, IEP and MCTs effectivity at treating GAD, which hopefully increases the change of the interventions being implemented in healthcare facilities and psychological clinics, in order to replace the less effective generic GAD treatment. This would mark a shift for GAD specialized treatments, in that it would constitute a movement from a phase characterized by development of theories and preliminary testing, to clinical implementation, and being the default treatments for GAD.

 As before mentioned the findings could indicate that all three theories theoretical models of the maintenance of GAD are true, and that clients with GAD could have differences in which process is the most influential. A clinical implementation of that finding would be to consider developing measurements to screen which processes that are the most influential in maintaining the patients disorder, and base the choice of therapy on the results. For instance the intolerance-of-uncertainty Scale (Freeston et al., 1994) or the metacognitions questionnaire (Cartwright-Hatton & Wells, 1997) which measures the strength of respectively metacognitions about worry and the intolerance of uncertainty construct. Measurements for interpersonal and emotional problems should be applied as well.

# Conclusion

This systematic review found that the GAD specialized interventions IUT, MCT and IEP were very effective at reducing the GAD core symptoms pathological worry, state and trait anxiety. MCT was found to be the most effective of the three reviewed GAD specialized CBT interventions, while all three seems to be very effective in reducing GAD core symptoms. The IEP study did produce less robust findings compared to the other two interventions. The general methodological quality of the included studies were high, which improves the evidential power of the systematic review.

The interventions were able to induce a uniform reduction of the measurement mean scores of PSWQ, BAI and STAI-T across all studies, from pre- to posttest, and to continue or increase the reduction at 6m and 12m. It can be concluded that IUT, MCT and IEP intervention, in all instances except three, reduced the PSWQ, BAI and STAI-T mean scores, to a less severe anxiety or worry category, from pretest to follow-up, which leaves a convincing indication of the interventions ability to reduce GAD symptoms to a less severe state. Extracted effect sizes for within-subject differences from pre – to posttest reductions in mean measurement scores, were almost unambiguously over 0.80. The extracted within-subject effect sizes were larger for the MCT interventions, than for IUT and IEP, but the MCT studies does not seem to have the same degree of external validity as the IUT studies. Waitlist conditions remained stable form pre- to posttest.

## Strengths and limitations

All of the studies included in the review, except McEvoy et al. (2014), examined primary GAD, with no comorbid diseases. The upside to this tendency in the studies, is that it brings more knowledge about GAD as an isolated disease, with fever confounders that could affect the results. GAD is however a highly comorbid condition (Wittchen, 2002, p. 164). Valuable information about GADs frequent coexistence and interaction with comorbid disorders might therefore be lost. Further, all included studies used participant that was at least 18 year old. As a consequence this review does not evaluate IUT, MCT and IEPs effectivity against GAD with onset in childhood, which is a frequently occurring phenomenon (Holmes, Donovan, Farrell & March, 2014, p. 122). Similarly, individuals with substance abuse were excluded, even though it is highly comorbid with GAD (Smith & Book, 2010, p. 44), and it could be valuable to observe how it interacts with GAD. In order to solidify the findings from this systematic review, a meta-analysis of the IUT, MCT and IEPs effectivity against GAD should be conducted. Meta-analysis is considered the highest ranked methodology for clinical research in terms of validity (Piantadosi, 2005, p. 135-136.). It would also be relevant for further studies to focus on interventions for children with GAD. Secondary GAD, and comorbid substance abuse should be a point of interest too.

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# C:\Users\-Jakob\AppData\Local\Microsoft\Windows\INetCache\Content.Word\samlet.jpgAppendix: Tables



## Appendix: Formulas

Formula for standard deviation:



X represents each value in the population, x is the mean value of the sample, Σ is the summation (or total), and n-1 is the number of values in the sample minus 1.

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1. http://www.apa.org/pubs/databases/psycinfo/ [↑](#footnote-ref-1)
2. http://www.apa.org/about/ [↑](#footnote-ref-2)
3. Van der Heiden, Muris & Van der Molen (2012) examines both IUT and MCT, and therefore appears in both literature search 1 and 2, but with different variables extracted in the summary tables. [↑](#footnote-ref-3)