

INTERNET-DELIVERED TREATMENTS FOR GENERALIZED ANXIETY DISORDER

EFFECTIVENESS, COST-EFFECTIVENESS
AND THERAPIST FACTORS

BJÖRN PAXLING



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2011 by Björn Paxling, Malmö, Sweden

ISBN 978-91-633-9490-4

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The studies comprising this doctoral thesis was conducted with
a generous grant from the Swedish council for working and life
research

Cover illustration Pär Axell (inspired by Edvard Munchs *Skrik*)

Copy editing Christine Carter

Printing Holmbergs i Malmö AB

Art director StaffanLager.se

VRIJE UNIVERSITEIT

Internet delivered treatments for Generalized Anxiety Disorder
Effectiveness, cost-effectiveness and therapist factors

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. L.M. Bouter,
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de faculteit der Psychologie en Pedagogiek
op dinsdag 8 november 2011 om 15.45 uur
in de aula van de universiteit,
De Boelelaan 1105

door

Björn Paxling

geboren te Malmö, Zweden

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CONTENTS

CHAPTER 1	9
<i>General introduction</i>	
CHAPTER 2	23
<i>Guided Internet-delivered cognitive behaviour therapy for generalized anxiety disorder: A randomised controlled trial</i>	
CHAPTER 3	43
<i>Internet-delivered guided self-help for generalized anxiety disorder: Cost-effectiveness analysis of a randomised trial</i>	
CHAPTER 4	59
<i>Psychodynamic vs. cognitive behavioural internet-delivered guided self-help for generalized anxiety disorder: A randomised controlled trial</i>	
CHAPTER 5	83
<i>Therapist behaviour in Internet-delivered cognitive behaviour therapy: Analyses of e-mail correspondence in the treatment of generalized anxiety disorder</i>	
CHAPTER 6	95
<i>Internet-delivered treatments with or without therapist input: Does the therapist factor have implications for effectiveness and costs?</i>	
CHAPTER 7	107
<i>General discussion</i>	
SUMMARY	119
SAMENVATTING	123
REFERENCES	127
ABOUT THE AUTHOR	145
ACKNOWLEDGEMENTS	149

CHAPTER 1

General introduction

Generalized anxiety disorder

Generalized anxiety disorder (GAD) is an anxiety disorder characterized by excessive worrying over a number of different aspects of the patient's life. Worrying can be defined as cognitive anticipation of a threat, and the experience of worrying can be described as having mild anxiety. A diagnosis of GAD, according to the DSM-IV (American Psychiatric Association, 2000), requires that the worry is present more days than not for the last six months, the worry is hard to control, and at least three of the following six symptoms are present: (1) restlessness or feeling wound-up or tense (2) being easily fatigued, (3) difficulty concentrating or mind going blank, (4) irritability, (5) muscle tension, and/or (6) sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep). In addition, the worry content should not be limited to symptoms from another axis-1 disorder, the worry must cause clinically significant suffering, and the worry cannot be directly caused by the use of substances such as drugs or medicine, nor by a somatic disorder such as hyperthyroidisms, nor be present only when the subject is depressed or during a psychosis. The criteria for GAD differ somewhat in the International Classification of Diseases (World Health Organization, 1992), which excludes patients with comorbid conditions and requires autonomic arousal symptoms but does not require the worry to be excessive or cause clinically significant suffering (Slade & Andrews, 2001).

Compared to other psychiatric disorders, GAD is a relatively new diagnosis which was not formulated in the DSM as a separate disorder until 1980 (American Psychiatric Association, 1980). Its relatively recent formulation as a separate diagnosis may be an underlying factor to GAD's being understudied compared to other anxiety disorders (Dugas, Anderson, Deschenes, & Donegan, 2010). A mere 8% of all publications on anxiety are focused on GAD, and these publications focus on treatment more often than on process and descriptive issues, all of which might indicate that we understand GAD to a lesser degree than other anxiety disorders (Dugas, et al., 2010).

People with GAD suffer a considerably higher risk of having a depressive episode – men more so than women (Hettema, Kuhn, Prescott, & Kendler, 2006). Research has also shown that when a previously recovered patient's experience of social relationships deteriorates, there is increased risk that he or she will again suffer from GAD (Rodriguez, Bruce, Pagano, & Kellerb, 2005). It has been suggested (Brown, Barlow, & Liebowitz, 1994) that GAD is a “basic” anxiety disorder from which many other anxiety and mood disorders stem.

Worry content in GAD

Worrying is an internal cognitive process which is more likely to take place as thought, as a verbal process, rather than as internal images. This holds true for the GAD population as well as the non-GAD population, but in a relaxed state, the non-GAD population is almost four times as likely to think in images as opposed to verbal thoughts, whereas the GAD-population is about as likely to think in images as in verbal thoughts while relaxed. People diagnosed with GAD are more likely in general to think or talk to themselves (Borkovec & Inz, 1990). The worry content for people diagnosed with GAD is most often focused on their family and social interactions (Sanderson & Barlow, 1990), but the kind of worry that best separates a GAD population concerns various and smaller issues (Roemer, Molina, & Borkovec, 1997). Compared to panic disorder, people with GAD are not as worried about death or loss of self-control, but they are worried to a higher degree about inability to cope with situations, miscellaneous worry topics and injury to self and others (Breitholtz, Westling, & Öst, 1998). The content of the worry changes rapidly in GAD. A study following 27 GAD patients over a 1 year period (Constans, Barbee, Townsend, & Leffler, 2002) found that the patients initially reported an average of 3.67 worry topics, and at the end of the period, 24 of the 27 reported at least one new worry topic ($M=2.56$).

Understanding GAD

In order to explain the underlying mechanisms of GAD, several different theories have been proposed and tested. It has been suggested that GAD can function as avoidance of distressing emotions and thoughts (Borkovec, Alcaine, & Behar, 2004). From the patients' point of view, the worrying is seen as problem solving in order to prepare for perceived threats. However, the worrying functions rather as avoidance of distressing stimuli, and the long-term effects are that the patient must resort to more and more "problem solving". A model proposed by Macleod and Rutherford (Macleod & Rutherford, 2004) is the biased information processing model in which patients diagnosed with GAD are said to have a cognitive bias towards negative information. According to this model the patients are more likely to notice threatening information in their surroundings and they then proceed to overestimate the level of threat from this information. The model that has the best diagnostic specificity for GAD as opposed to panic disorder with agoraphobia (Dugas, Marchand, & Ladouceur, 2005) is GAD as intolerance of uncertainty. Here, the worrying in GAD-patients is proposed to be easily activated in situations in which the patients have little control and experience uncertainty concerning the outcome of the situation; since GAD-patients have a lower tolerance of uncertainty, this cognitive activation becomes common practice. GAD has

also been suggested to be the worry about worry, i.e., metacognitive beliefs (Wells, 2004). The “thinking about thinking” in GAD can be focused on the negative aspects of worry (worrying about not being able to stop worrying), which makes worrying more painful, or it may involve positive thoughts about worry (“If I worry about something, I’ll be prepared when it happens” or “The worry motivates me to get things done”), which makes the worrying more frequent. Finally, the activity in the amygdala has been used to explain GAD (Sinha, Mohlman, & Gorman, 2004) in that heightened activity increases the reactivity for stimuli which, in turn, increases worrying. Indeed, the anticipatory amygdala activity has been shown to be higher in a GAD population than in non-GAD controls (Nitschke et al., 2009).

Prevalence and comorbidity

A Swedish study on 10,000 twins in the twin-register indicated that the lifetime risk for developing GAD is 3.95% for women and 1.74% for men (Mackintosh, Gatz, Wetherell, & Pedersen, 2006). Another study on primary care patients in Sweden, Denmark, Norway and Finland found a prevalence of between 4.1 - 6.0% for women and 3.7 - 7.1% for men (Munk-Jørgensen et al., 2006). According to the World Health Organization, the global prevalence might be as high as 8% (Dugas & Robichaud, 2007). GAD is a disorder that usually lasts for a long period of time: A majority of those suffering from GAD report having had the condition for over 10 years, and a large proportion report having waited as long as 25 years before seeking treatment. GAD is a highly comorbid condition, with 90% of those diagnosed also suffering from another psychiatric condition some time during their lifespan; as many as 66% will have a current comorbid psychiatric condition (Kessler, Walters, & Wittchen, 2004). Among the most common comorbid conditions are social phobia (23-59%), dysthymia (50%) and depression (42%), but comorbid panic disorder (11-27%) and OCD (1-11%) are also relatively common. At least half of the people diagnosed with GAD have disturbed sleep (Monti & Monti, 2000). Comorbid somatic disorders are also highly prevalent, the most commonly reported of which are neurological, cardiovascular and endocrinal disorders, as well as chronic obstructive lung disease (Allgulander, 2010; Martens et al., 2010). Other somatic disorders/symptoms that are often present in patients with GAD are chronic pain (Beesdo et al., 2009), migraine, stuttering and irritable bowel syndrome (Allgulander, 2010).

Cost association with GAD

The societal economic burden of GAD is vast. From a direct medical perspective, patients suffering from GAD frequently utilize the health care system, not seldom reporting symptoms such as back/neck pain, insomnia, elevated stress levels and frequent infections, rather than seeking help for their worrying in itself. The long term costs associated with absenteeism and work cutback (defined as lesser efficiency at work due to feeling ill) in GAD are high. A Swedish study reported that the costs associated with psychiatric disorders in 2004 amounted to 3% of BNP (10,000 SEK, or about €1000, per inhabitant), and anxiety disorders stood for 14% of those costs (Andlin-Sobocki, Allgulander, Hillert, & Jönsson, 2007). All patients (n = 3,710) registered in the Swedish patient registry and the registry of medication during 2006 were followed for 13 months, and the healthcare costs per patient amounted to €835 for primary care, €9992 for in-clinic care and €599 for medication (Munk-Jørgensen, et al., 2006). In a Dutch population-based psychiatric cohort study covering 5,504 adults, the costs of nine common mental health disorders were calculated (Smit et al., 2006). The annual per capita excess costs associated with GAD was determined to be €917, and the direct medical costs amounted to no more than 1% of this. A review of cost-of-illness and cost-effectiveness in anxiety disorders (Konnopka, Leichsenring, Leibing, & König, 2009) concluded that GAD and panic disorder were the most costly anxiety disorders per identified case, although the reported direct excess costs varied greatly, from \$625 (Smit et al., 2006) to \$20,184 (Olfson & Gameroff, 2007). The cost-effectiveness of psychological and pharmacological interventions for GAD in Australia have been compared (Heuzenroeder et al., 2004), and the results were that CBT administered by a psychologist on a public salary was the most cost-effective treatment. When the CBT provided was not administered by a psychologist in jointly financed health care, the cost-effectiveness decreased and the pharmacological option Venlafaxin became as cost-effective as CBT.

TREATMENT OF GAD

Pharmacological treatments

GAD is commonly treated with medication, with tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors and selective serotonin reuptake inhibitors among the most commonly used (Rang, Dale, Ritter, & Moore, 2003; Schultz, Gotto, & Rapaport, 2005). These substances allow for an abundant presence of neurotransmitters in the central nervous system, facilitating positive fluctuations of mood. Anxiety alleviating medication such as benzodiazepines are also effective in the treatment of GAD, but the high risk for addiction should be taken into consideration.

The heightened activity of the amygdala observed in GAD patients is reduced by anxiety alleviating medication, and patients also report lower levels of anxiety symptoms (Nitschke, et al., 2009).

Psychological treatments

Although the differences in the effectiveness of pharmacological and psychological treatments are only minor, the attrition rates are lower for psychological treatments (Mitte, 2005). Cognitive behaviour therapy (CBT) is the treatment of choice for anxiety disorders (Barlow, Gorman, Shear, & Woods, 2000), and for GAD, individual CBT is the most studied treatment (Hunot, Churchill, Silva de Lima, & Teixeira, 2007). The most commonly utilized treatment model for GAD was created by Tom Borkovec and colleagues. Scheduled worry time (Borkovec & Costello, 1993; Borkovec, Wilkinson, Folsensbee, & Lerman, 1983) is an intervention in which the patient is suggested to postpone worry to a specific period each day, helping to increase discriminative control regarding stimuli that trigger worrying. The treatment also focuses on: working with the patient's thoughts using cognitive restructuring (Borkovec & Sharpless, 2004); obtaining new experiences with worry through worry exposure (Sanderson & Rygh, 2004); as well as practical problem solving, which helps patients to separate worry topics so they can do something practical about them and gives patients a concrete framework for acting accordingly (Zetterqvist, Maanmies, Ström, & Andersson, 2003). Since GAD has a tendency to have a negative impact on patients' social relationships, it has been suggested that treatment outcomes might improve by adding interventions focused on interpersonal problem solving to the treatment (Borkovec, Newman, Pincus, & Lytle, 2002), but so far there is no conclusive evidence suggesting that this intervention improves the effects of the treatment. Applied relaxation is a form of progressive relaxation technique which might be used as a treatment in itself or as a part of a larger treatment protocol (Öst, 1987). Applied relaxation has been found to be helpful in GAD (Borkovec, et al., 2002; Öst & Breitholtz, 2000). There is a scarcity of support for psychotherapy approaches other than CBT in the treatment of GAD (Schultz, et al., 2005). Psychodynamic treatments have been tested for GAD, both in terms of longer psychoanalytically-based treatments and shorter client-centred therapy (Sanderson & Rygh, 2004). An interpersonally oriented treatment manual (Luborsky, 1984) called supportive-expressive treatment has been rewritten to focus on GAD (Crits-Christoph, Connolly, Azarin, Crits-Christoph, & Shappel, 1996). The protocol involves 16 sessions and has been tested, and tests replicated, with satisfactory results (Crits-Christoph, Connolly, Narducci, Schamberger, & Gallop, 2005; Leichsenring et al., 2009). A specific working questionnaire, Core Conflictual

Relationship Theme, is used to map the core interpersonal conflicts of the patient; the treatment is then focused on how the patient might choose more constructive ways to interact with others.

Self-help and Internet-delivered treatment

Overall, previous studies on guided Internet-delivered CBT have often found improvements with this approach to be similar to those with face-to-face CBT (Andersson et al., 2006; Carlbring et al., 2005). Compared to other anxiety disorders, however, relatively few self-help trials have been conducted on GAD (Bowman, Scogin, Floyd, Patton, & Gist, 1997; Floyd et al., 2002). Early trials using computer-aided treatments include a study of a palmtop computer programme for treating GAD (Newman, Consoli, & Taylor, 1999) and a pilot study with three participants which indicated that Internet-based self-help without therapist support might be effective in reducing GAD symptoms (Draper, Rees, & Nathan, 2008). A more recent trial (Titov, Andrews, Robinson, et al., 2009) on Internet-delivered treatment has shown good effects in terms of large effect sizes (within-group Cohen's $d = 1.3$, between-group 1.1). In this trial, the treatment programme had a duration of six weeks and consisted of online lessons, contact with a clinical psychologist using e-mail and a moderated online discussion forum. Different ways of providing therapist support in the same treatment programme have also been tested for GAD (Robinson et al., 2010), and a trans-diagnostic Internet administered treatment programme has also shown to be effective for GAD as well as for other anxiety disorders (Titov, Andrews, Johnston, Robinson, & Spence, 2010). Another way to take comorbidity into account, besides developing trans-diagnostic treatments, is to tailor the treatment according to the individual problem areas and symptoms of the patient. This has been tested for patients with a variety of different anxiety problems, including GAD symptomatology (Carlbring et al., 2011).

More technologically advanced treatments have also been tested. In one study (Pallavicini, Algeri, Repetto, Gorini, & Riva, 2009), the treatment consisted of a biofeedback-enhanced virtual reality system with the option to use mobile phones. The study was conducted in an outpatient setting. No statistically significant results were found, however, possibly due to the study being underpowered ($n = 12$).

Internet-delivered therapy

Therapy delivered via the Internet is a treatment modality which has been gaining ground rapidly during the last 10 to 15 years. Although some modes of delivering therapeutic techniques are not easily translated to a digital format, such as confirming the patient with a warm empathic smile or giving reassurance with a slight nod, there are other ways to communicate these messages, and there is little doubt that the therapeutic process remains the same in psychotherapy delivered via the Internet (Anthony & Merz Nagel, 2010). In Sweden, two major institutions have performed literature reviews regarding Internet-delivered therapy for depression and anxiety disorders: the Swedish Council on Health Technology Assessment, in 2007 (Linton, 2007), and the the National Board of Health and Welfare, in 2010 (Socialstyrelsen, 2010). Both reached the conclusion that the treatment modality seems to work well and that further implementation is motivated.

History and exploration of the concepts

Internet-delivered therapy, as it is most commonly used in Sweden today, has many roots. As the patient and the therapist are not present in the same room at the same time, the psychotherapy is delivered by indirect means of communication. Indirect treatment contact has a long history in the psychotherapy literature. One prominent example is Sigmund Freud, who reportedly used letters to treat patients and to perform the analysis of the famous case “Little Hans” (Skinner & Zack, 2004). Besides letters, there are other ways of performing psychotherapy over long distances, such as using telephones or web-cams. When the telephone is used for psychotherapy, the patient and the therapist can be present at different locations, but they must synchronize their contact in order for this to work. Most of the Swedish Internet-delivered therapy programmes (Andersson et al., 2008), as with therapy through letters, utilize an asynchronous means of communication. This means that the therapist and the patient do not have to work on the therapy during overlapping time slots: they can both choose a time convenient to themselves, and the problem of one party being late to a session or not showing up at all is thus eradicated. The telephone does have its place in these programmes though: despite efforts (Carlbring et al., 2002), there are still no convincing ways to fully automate the diagnostic process over the Internet, so diagnosis is commonly confirmed through a structured clinical interview such as SCID-1 over the telephone. When patients show suicidal tendencies during Internet-delivered treatment, this is taken as a prompt to move from indirect means of contact to a direct form; the telephone is used to quickly reach the patient in order to perform an assessment of suicidal risk (Andersson, et al., 2008).

Patients living in rural areas, or those who are too anxious to leave their homes, have much to gain by receiving Internet-delivered therapy interventions (Newman, Erickson, Przeworski, & Dzus, 2003; Richards, Klein, & Carlbring, 2003). Since much less therapist time is needed for a complete treatment in Internet-delivered treatments than in traditional face-to-face treatments, each therapist is able to treat more patients. From a patient perspective, this may result in more available health-care and drastically shorter waiting times to begin treatment.

Self-help books for psychiatric disorders are generally popular, both among patients and therapists (Menchola, 2007). A vast majority of cognitive behavioural therapists in the UK, 89%, reportedly use self-help books in their work with patients (Keeley, Williams, & Shapiro, 2002). While self-help books can be an addition to conventional psychotherapy, they can also be offered as a treatment in themselves, as in bibliotherapy. A paper on the effectiveness of bibliotherapy was first published in the late 1930s (Menninger, 1937), and research on self-help increased in the 1970s (Gould & Clum, 1993). A review on bibliotherapy for panic disorder (Carlbring, Westling, & Andersson, 2000) suggests that the treatment can indeed be effective, with effect sizes ranging from medium to large. Merely buying a self-help book and working through it alone does not make for bibliotherapy. The book in question should be suggested by a clinician based on a thorough screening, and the results of working with the book are to be monitored (Marks, Cavanagh, & Gega, 2007). Before self-help books became the basis of many Internet intervention programmes, considerable efforts were made to create offline computer-aided psychotherapy programmes for mental health disorders. Although bibliotherapy has been shown to be as effective as computer-aided psychotherapy programmes (Ghosh, Marks, & Carr, 1988), there are advantages of using a computer platform, such as increased interactivity and more easily updated programmes, as well as the possibility that the patient might prefer one modality over another. Offline computer-aided psychotherapy used to sometimes be disseminated using CD-ROMs and specific rooms at psychiatric clinics where patients could access the programmes, often with help from a nurse who would assist when problems arose during the treatments.

The revolution in increased accessibility to evidence based treatments brought by Internet-delivered psychotherapy is the result of combining asynchronous distance therapy and computer-aided psychotherapy. The rapid growth of Internet interventions for mental health and behavioural health problems (Wantland, Portillo, Holzemer, Slaughter, & McGhee, 2004) has gone hand in hand with a dramatic increase in the

proportion of the population that has regular Internet access. In Sweden more than nine out of every ten citizens have regular Internet access (World Bank, 2011). At the same time, more and more municipalities offer online services with which citizens can log in to a system to see all of their scheduled appointments with health care professionals and check up on their prescriptions for medication. All of this makes Internet-delivered psychotherapy much more acceptable from a patient perspective. To facilitate collaboration among Internet intervention researchers and to guarantee continued high-quality research in the field, the International Society for Research on Internet Interventions (ISRII) has been formed (Ritterband, Andersson, Christensen, Carlbring, & Cuijpers, 2006), with an international conference held every 18 months.

Therapist factors in psychotherapy

Conventional face to face therapy is practically impossible to imagine without a therapist present, even though some might argue that this would constitute the ultimate tabula rasa. Studies have focused on what therapists should be doing and what they should not be doing to maximize the likelihood of a beneficial treatment outcome, and therapist factors are generally regarded as important (Beutler et al., 2004). In the field of Internet-delivered therapy, the role of the therapist is not as clear. Studies have primarily focused on whether having therapist support at all increases the effects of the programmes. So far the conclusion seems to be that by providing a therapist contact during the treatment period, drop-out levels decrease and effect sizes increase (Andersson & Cuijpers, 2009; Spek et al., 2007). To further increase the adherence and maximize effects of the treatments, several initiatives have been undertaken, such as adding the functionality of online communities/forums (Carlbring, et al., 2005; Richardson, Richards, & Barkham, 2010); adding telephone calls from the therapist, making the treatment multimodal (Carlbring et al., 2006); and increasing the frequency of e-mails from the therapist (Klein et al., 2009). The clinician working with discussion forums in Internet-delivered treatment trials is most often referred to as an administrator or a moderator, rather than as a group therapist, and this probably influences the way he or she behaves during the treatment. There is still little consensus regarding how to best utilize the therapist in Internet-delivered treatments, and even less is known about how the therapist should behave during treatment to maximize the likelihood of a positive outcome. An Australian research group has performed several studies in which the treatment programme is supported by either a clinician or a technician (Robinson, et al., 2010; Titov, Andrews, Davies, et al., 2010; Titov, Andrews, Johnston, et al., 2010; Titov, Andrews, Schwencke, et al., 2009). In these studies, a clinician is the equivalent of a therapist who might engage in active

treatment of the participants via the Internet even if the problem being addressed isn't exactly within the scope of the treatment programme. A technician, on the other hand, takes on the role of a coach or a counsellor who encourages patients to work through a treatment programme but does not engage actively in issues outside of the treatment programme in question.

The therapeutic alliance is a concept that refers to the therapeutic bond between patient and therapist as well as their joint focus and understanding of tasks and goals during the treatment contact (Bordin, 1979). Evidence shows that a good alliance can form between patient and therapist in Internet-delivered treatments (Knaevelsrud & Maercker, 2007). For all types of psychotherapy, reviews show that the therapeutic alliance has a robust but moderate effect on treatment outcome (Horvath & Symonds, 1991; Martin, Garske, & Davis, 2000). No research so far has shown that any specific individual therapist is associated with better treatment outcomes than any other therapist in Internet-delivered therapy. This has been tested both for depression (Almlöv, Carlbring, Berger, Cuijpers, & Andersson, 2009) and for anxiety disorders (Almlöv et al., 2011).

Aims and research questions

Given the high prevalence of GAD and the low occurrence of spontaneous recovery, the determination of better and/or more available treatment alternatives is well motivated. This thesis has three central aims: 1) to determine the effectiveness of Internet-delivered therapy for GAD, 2) to determine the health economic aspects of treating GAD over the Internet – more specifically, whether this kind of treatment is cost-effective, and 3) to analyse the role of therapist factors and behaviours in Internet-delivered therapy.

As a majority of the published treatment trials on online therapy have been based on CBT techniques, and because there is a lack of skilled CBT therapists, a trial was conducted comparing CBT and psychodynamic treatments, both over the Internet. The cost-effectiveness analysis and the analysis of therapist behaviours are performed on a first randomised controlled trial (RCT) in which online CBT is compared to a control condition. A literature review was performed in order to determine the role that the therapist variable has played in treatments of published trials.

Outline

In Chapter 2 the main findings from a research trial on Internet-delivered CBT for generalized anxiety disorder is presented. In Chapter 3 the cost-effectiveness analysis of the trial outlined in Chapter 2 is presented. The comparison between online CBT and online PDT is presented in Chapter 4. Chapters 5 and 6 address therapist variables in Internet-delivered therapy. More specifically, Chapter 5 examines and analyses the e-mails from the therapists in the first RCT, and Chapter 6 presents the conclusions of a literature review on therapist factors. Finally, Chapter 7 provides the conclusion of this thesis, including a general discussion of the results found, implications for clinical practice and recommendations for future research.

CHAPTER 2

*Guided Internet-delivered Cognitive
Behaviour Therapy for Generalized Anxiety Disorder.
A Randomised Controlled Trial*

Paxling, B., Almlöv, J., Dahlin, M., Carlbring, P., Breitholtz, E., Eriksson, T., & Andersson, G. (2011). Guided internet-delivered cognitive behavior therapy for generalized anxiety disorder: a randomized controlled trial. *Cognitive Behaviour Therapy*, 40(3), 159-73.

URL: <http://www.tandfonline.com/doi/abs/10.1080/16506073.2011.576699>

ABSTRACT

Generalized anxiety disorder (GAD) has been effectively treated with cognitive behavioural therapy (CBT) in face-to face settings. Internet-delivered CBT could be a way to increase the accessibility and affordability of CBT for people suffering from GAD. The aim of this study was to evaluate the effectiveness of guided Internet-delivered CBT for GAD in a controlled trial with a waiting-list control group. A total of 89 participants were included following online screening and a structured psychiatric telephone interview. Participants were randomised to either an 8 week treatment group (n = 44) or to a waiting list control group (n = 45). Treatment consisted of a self-help programme based on CBT principles and applied relaxation along with therapist guidance. The main outcome measure was the Penn State Worry Questionnaire. Ratings of clinical improvement and symptoms were included as well as secondary outcome measures dealing with anxiety, depression, and quality of life. In the treatment group 13.6% did not complete the post treatment measures. The treatment group showed significant improvement compared to the control group on all outcome measures. Large effect sizes (Cohen's $d > .8$) were found both within the treatment group and between the groups in favor of the treatment on all outcome measures except on a measure of quality of life. Results at 1- and 3-year follow-up indicated that treatment results improved or were maintained. We conclude that Internet-delivered CBT with therapist support can reduce symptoms and problems related to GAD.

INTRODUCTION

Generalized anxiety disorder (GAD) is a highly prevalent disorder characterized by excessive worry or anxiety about everyday events, whether they are internal, external, originating in the past, present and/or future (American Psychiatric Association, 2000). Since several situations and stimuli are capable of eliciting worry, GAD can become a crippling disorder, preventing the individual from taking part in and enjoying important areas of everyday life (Heimberg, Turk, & Mennin, 2004). It has been estimated that the life-time prevalence of GAD range between 1.3 – 5.9%, and a 12-month prevalence of 1.2 – 1.9 % has been found (Tyrer & Baldwin, 2006). While pharmacological treatment options exists (Tyrer & Baldwin, 2006), different psychological treatments have been tested, mainly in the form of individual face-to-face cognitive-behavioural therapy (CBT) (Hunot, et al., 2007). Although there are only minor differences in the effectiveness of pharmacological and psychological treatments, attrition rates are lower for psychological treatments (Mitte, 2005).

In spite of the promising effects of CBT for GAD, dissemination is hampered by the lack of trained CBT therapists. Internet-delivered guided self-help programmes have been developed as a way to increase access to CBT for anxiety and mood disorders (Andersson, 2009), with research to date providing promising outcomes (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Spek, et al., 2007). Internet treatments are often based on self-help manuals and studies suggest that guided self-help can help persons with anxiety disorders reduce their symptoms (Hirai & Clum, 2006; van Boeijen et al., 2005).

Few self-help trials have been done on GAD (Bowman, et al., 1997; Floyd, et al., 2002). A study of a palmtop computer programme for treating GAD was published as early as 1999 (Newman, et al., 1999), and another pilot study with three participants indicated that Internet-based self-help without therapist support might be effective in reducing GAD symptoms (Draper, et al., 2008). A recent randomised controlled trial on Internet treatment for GAD (Titov, Andrews, Robinson, et al., 2009) showed large within- and between group effect sizes (Cohen's $d = 1.3$ and 1.1 respectively), but did not include follow-up data. The treatment programme used in Titov's trial consisted of six online lessons with weekly homework assignments and continuous e-mail contact with a clinical psychologist, as well as a moderated online discussion forum. The same research group has also shown that effects are similar when support is given by a technician instead of a therapist (Robinson, et al., 2010), as well as proven that a transdiagnostic Internet-administered treatment can be effective for various anxiety disorders including GAD (Titov, Andrews, Johnston, et al., 2010).

Previous studies on guided Internet-delivered CBT have often found similar improvements as in face-to-face CBT (Andersson, et al., 2006; Carlbring, et al., 2005), but research on anxiety disorders has mainly dealt with panic disorder, social anxiety disorder and post-traumatic stress disorder . Internet treatment for GAD can involve many treatment ingredients. For example, applied relaxation has been found to be helpful in GAD (Borkovec, et al., 2002; Öst & Breitholtz, 2000). In addition, applied relaxation delivered via the Internet has been found to be effective in panic disorder (Carlbring, Ekselius, & Andersson, 2003) and social anxiety disorder (Furmark et al., 2009). Other CBT techniques that have been previously used over the Internet in treating GAD include cognitive interventions, exposure (Titov, Andrews, Johnston, et al., 2010), and problem solving (Robinson, et al., 2010).

The aim of this randomised controlled trial was to test if a guided Internet-delivered CBT programme could alleviate symptoms associated with GAD. As this was one of the first studies of an Internet-delivered CBT programme for GAD we decided to include a waiting-list control group. Patients in the wait-list group received the Internet treatment after the waiting period which lasted 8 weeks. A one-year and a three-year follow-up was included.

METHOD

Procedure

Participants were recruited from the general population by means of articles in newspapers and a webpage. A screening webpage was set up, and persons interested in the study were asked to complete four online self-report measures. Among these were the Penn State Worry Questionnaire (PSWQ; (Meyer, Miller, Metzger, & Borkovec, 1990a), which was the primary outcome measure in our trial. PSWQ has a test-retest reliability between .74 and .93 (2-10 weeks) and Cronbach's alpha between .86 and .93, a cut-off of 53 was used for inclusion (Fresco, Mennin, Heimberg, & Turk, 2003). We also included the Generalized Anxiety Disorder Questionnaire IV (GAD-Q IV) (Newman et al., 2002) measuring GAD symptoms. As cut-off for this instrument, a score of 5.7 or higher was used to indicate the presence of GAD. GAD-Q IV has excellent diagnostic specificity and sensitivity as well as good test-retest reliability and convergent and discriminant validity even across different racial groups (Robinson, Klenck, & Norton, 2010). The third measure was the Montgomery Åsberg Depression Rating Scale - Self rated (MADRS-S; (Svanborg & Åsberg, 2001) which was used to screen for severe depression and suicidal tendencies (which were exclusion criteria), using a cut-off score of 35. The test-retest reliability of MADRS-S is between .80

and .94, and Cronbach's alpha varies between .82 and .90 (Snaith, Harrop, Newby, & Teale, 1986). Fourth, the Alcohol Use Disorders Identification Test AUDIT; (Saunders, Aasland, Babor, de la Fuente, & Grant, 1993a) was used to screen for alcohol dependence, where a score of 19 or higher has been reported to indicate severe alcohol problems and was chosen as a cut-off in this study. Test-retest reliability of AUDIT is .97 and Cronbach's alpha between .62 and .95 (Bergman & Källmen, 2002). All measures were administered via the internet, which generally has proven to be acceptable in terms of psychometric properties (Carlbring, Brunt, et al., 2007).

Out of 266 applicants answering the screening questionnaires 158 (59.4%) met the initial inclusion criteria and were eligible for the diagnostic interview conducted via telephone by one of three psychology graduate students with two days specific training in diagnostic interviewing for the current trial. Research indicates that telephone-administered clinical interviews are comparable to face-to-face interviews (Rohde, Lewinsohn, & Seeley, 1997b). We used the Structured Clinical Interview for DSM-IV (SCID-I) to establish the diagnosis of GAD (First, Gibbon, Spitzer, & Williams, 1997). In addition to the GAD module we also included the mood disorder module of the SCID-I and screened for severe mental illness such as active psychosis. The reason not all possible comorbid conditions was assessed with the SCID-I was in order to minimize cost and time of the assessment. The diagnosis of GAD was later confirmed by a psychiatrist with training in diagnostic interviewing who also served as a consultant during the whole trial. To be included the participant had to fulfill the diagnostic criteria for primary GAD and be at least 18 years old. Participants also had to sign and send in informed consent via regular post. Participants on medication (e.g., antidepressants) had to be stabilized for at least one month and were asked to maintain a stable dose level during the study, and report if this criterion was violated. Use of anxiolytic medication was not an exclusion criterion, but patients were encouraged not to increase their use during the trial. The following exclusion criteria were used: persons with severe depression, suicidal intent, severe mental illness such as active psychosis, ongoing psychological treatment, alcohol abuse (as assessed by the AUDIT), and not being able to participate in the study for other reasons (e.g., giving birth mid trial). Patient flow is described in Figure 1.

In total, 117 applicants were interviewed and 89 were finally included to the study. The 177 applicants excluded from the study were each sent an e-mail stating the main reason for exclusion together with advice on health care contacts if needed. The participants included in the study were asked to complete four additional self-report measures. These were all secondary outcome measures and included the State-Trait

Anxiety Inventory (STAI state and trait versions, test-retest $r = .71$ and Cronbach's alpha = .86) (Spielberger, Gorsuch, & Lushene, 1970), the Beck Depression Inventory (BDI, test-retest $r = .86$, Cronbach's alpha = .86) (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), the Beck Anxiety Inventory (BAI, test-retest $r = .75$ and Cronbach's alpha = .92) (Beck, Epstein, Brown, & Steer, 1988), and the Quality of Life Inventory (QOLI, test-retest $r = .92$ and Cronbach's alpha = .81) (Frisch, Cornell, Villanueva, & Retzlaff, 1992).

The 89 participants were randomised to either a control ($n = 45$) or a treatment ($n = 44$) group by an independent person not involved in the study. A computer generated random list was obtained via www.random.org, which utilizes atmospheric noise to create random sequences of numbers. The protocol was approved by the local ethics committee.

Posttreatment measures were obtained from 38 out of 44 randomised participants in the treatment group (86%) and 44 out of 45 in the control group (98%). We conducted a telephone administered clinical interview after the treatment period. This included administration of the SCID-I GAD questions and an estimation of the degree of global improvement for each participant using an abbreviated version the Clinical Global Impression improvement (CGI-I) scale (Guy, 1976). In full form CGI is a three item interview list for assessing clinical improvement, for this study only one item was used, the Clinical Global Impression of improvement, which requires the clinician to assess how much the patient's illness has improved or worsened relative to a baseline state at the beginning of the intervention on a 7 point scale from 1 (very much improved) to 7 (very much worse) by asking specific questions about this where the participants exemplified changed that had occurred since baseline. The interviewers were blinded concerning participant status (e.g., treatment or control) since the posttreatment interviewers did not have access to information about the participants and started each interview by asking the participants not to say whether they were in the treatment or control condition. A one-year follow-up was conducted with all self-report inventories and a telephone interview. This only included participants in the treatment group. Since we had no control group by that time blinding was not possible. A three-year follow-up was also conducted, including both the treatment group and the control group, using both self-report inventories and telephone interview. Questions regarding change in medication and/or additional treatment seeking were asked at post-test and follow-up.

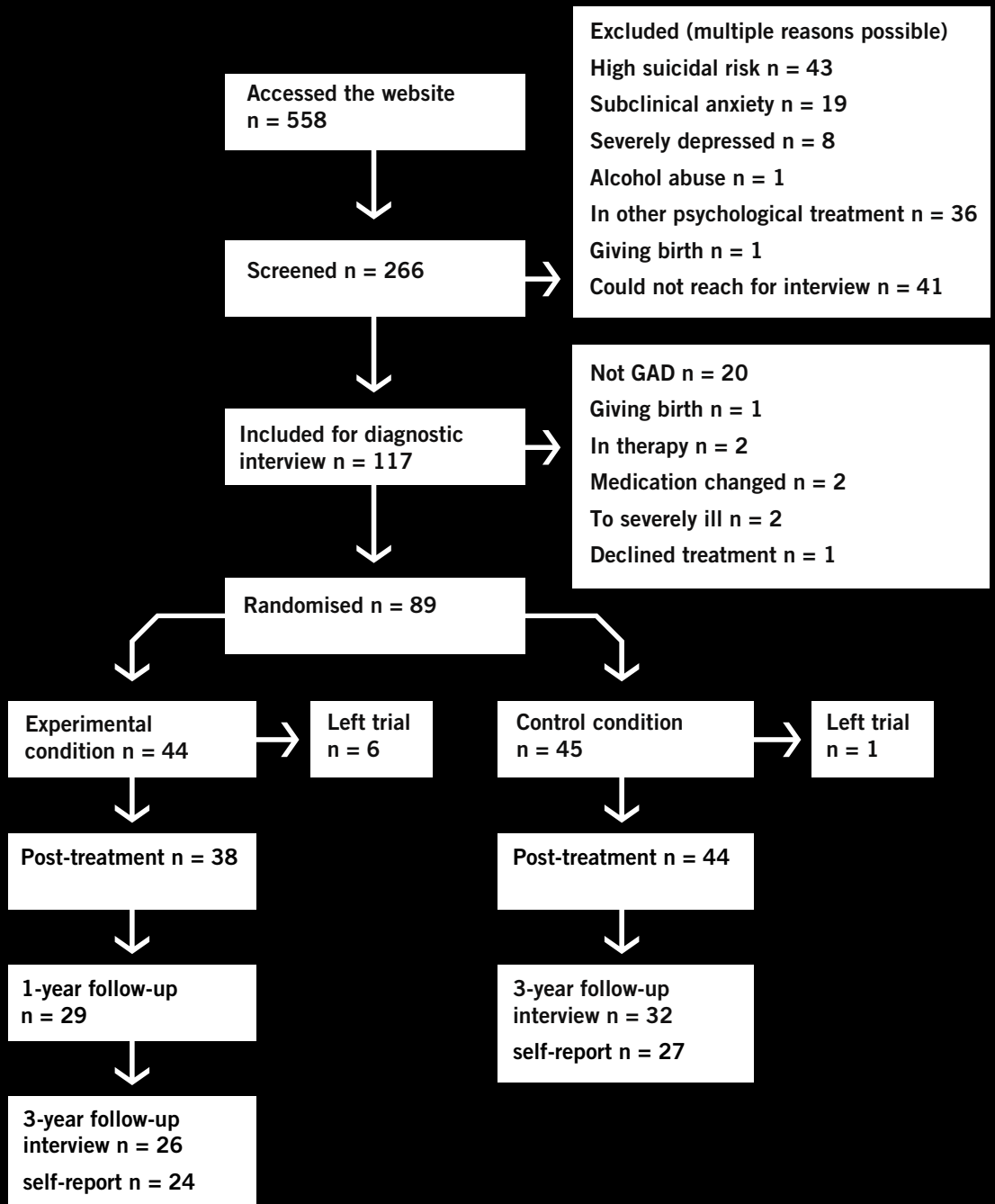


Figure 1. Flow chart of participants through the study.

Description of participants

The mean age of the included participants was 39.3 years (SD = 10.8), and the percentage of women was 79.8% (71/89). The treatment group consisted of 36 women and eight men aged between 18 to 66 years (M = 40.0, SD = 11.3). The control group consisted of 35 women and 10 men aged 21 to 62 years (M = 38.6, SD = 10.3). Comorbid depression was assessed and 22.5% (20/89) of the total sample were diagnosed with major depression and another 42.7% (38/89) had a history of one or more previous episodes of depression, but were not currently depressed. The mean duration of GAD was 20.0 years (SD=13.2). A total of 40.4% (36/89) had no current medication or history of medication (e.g., antidepressants), 37.1% (33/89) had ongoing stable medication, and 22.5% (20/89) had a history of previous medication for GAD. No significant differences were found between the treatment and control conditions on any of the variables at pretreatment, indicating that randomization had resulted in comparable groups.

Treatment

The treatment consisted of 8 text-based treatment modules delivered on a weekly basis for 8 weeks. Briefly, the treatment modules covered 1) Introduction to GAD and the treatment (psychoeducation), 2) Step 1 of applied relaxation (Öst, 1987), 3) Step 2 of applied relaxation, and worry time (Borkovec & Costello, 1993; Borkovec, et al., 1983), 4) Step 3 of applied relaxation, and cognitive restructuring (Borkovec & Sharpless, 2004), 5) Step 4 of applied relaxation, more on cognitive distancing, and problem solving (Zetterqvist, et al., 2003), 6) Step 5 of applied relaxation, and worry exposure (Sanderson & Rygh, 2004), 7) Step 6 of applied relaxation, interpersonal problem solving, and sleep management (Ström, Pettersson, & Andersson, 2004), and 8) Relapse prevention and maintenance of progress. In the different steps of applied relaxation, the participants first learn the relaxation technique in 15 minute session (step 1), and the duration of the relaxation is then shortened to 5-7 minutes (step 2), 2-3 minutes (step 3), 60-90 seconds (step 4) and finally to 20-30 seconds (step 5) before the relaxation becomes applied in everyday life (step 6). A CD with the instructions for applied relaxation audio recorded was sent to the participants, as well as a possibility to download digital audio files with the same content from the project website.

To access the treatment modules the participants had to logon to a secure website. The modules consisted mostly of text and images with a very basic layout thought to make the programme as easy to use as possible. All treatment modules were accompanied with home-work assignments that were sent in to therapists on a weekly basis. All

home-work assignments for one module had to be completed before that participant could start with the next one. We also provided a summary of the participants progress at the end of the programme and the participants made an agreement to continue practice for maintenance of treatment effects and provided a website where they could register how much they were using each technique taught in the treatment once a month for a maximum of six months.

Each participant was randomly assigned a therapist in their final year of psychologist training ($n = 3$) and supervision was provided by an experienced clinician specialized in GAD on a weekly basis. The therapists in this trial were also involved in writing the self-help treatment, and was given approximately one week of training in CBT-treatment for GAD by an experienced clinician specialized in GAD in order to maximize adherence to the treatment. The main focus for the therapists was to guide the participants through the self-help programme. The therapists gave verbal reports of the treatment to the supervisor, and also provided the supervisor with treatment e-mails upon request. Feedback from the therapist was provided on a weekly basis in association with the homework assignments, this feedback usually ranged between a half and three written pages. In addition occasional reminders were sent via e-mail. The communication took place over e-mail, the participants were encouraged to create an e-mail account with strong encryption, but could use their personal e-mail accounts if chosen. The therapist time devoted to each client ranged from 10-15 minutes per week, totaling 71 hours and 5 minutes for all patients in the trial, and $M = 97$ minutes ($SD = 52$; range 12-215) per patient. Each week the participants reported their progress with the possibility to include questions to the therapist. Feedback was given as soon as possible, most often within 24 hours. No contact took place between the therapists and participants except for e-mails and diagnostic interview. Participants who were assigned to the control group received the intervention when the treatment group had been treated for 8 weeks. Those who did not finish all treatment modules within the designated time period of 8 weeks were given the opportunity to continue working with the material themselves without the therapist support.

Statistical analyses

A power analysis indicated that 32 participants per condition were required to detect a difference in symptom reduction equivalent to a standard effect size of at least $d = .50$ in a two-sided test at $\alpha = .05$ and a power of $.80$ (Cohen, 1992). Thus the power was sufficient to detect even a moderate effect size. In order to account for dropouts without assuming that the first measurement was stable (e.g., the last observation carried forward assumption), we used a mixed effects models approach (Gueorguieva

& Krystal, 2004). Mixed effect models are able to accommodate missing data and integrate time-varying factors. It has been recommended to use mixed models analyses as a way to handle intention to treat data (Brown & Prescott, 1999). To compare the Internet treatment and control group according to the outcome measures at baseline and posttreatment an unstructured covariance pattern model was used. The restricted maximum likelihood (REML) model was used as estimation method. All analyses were performed in SPSS version 18.0 (SPSS, Inc., Chicago, IL).

Chi-square was used to test differences between the groups on categorical outcomes. To be defined as clinically significantly improved a participant had to fulfill the criterion for a reliable change and have a posttreatment score at least 2 standard deviations below the groups mean pretreatment score (Jacobson & Truax, 1991). In the intention to treat analyses of the categorical data we regarded dropouts as non-responders for the immediate treatment results but not for the long-term follow-ups. One-year follow-up data was available for the treatment group only, while three-year follow-up data covered both the treatment group and the control group. However, by that time the control group had received treatment. Effect sizes are presented as Cohen's *d* which is defined as the difference between the means of the two groups divided by the pooled standard deviation (Cohen, 1988).

RESULTS

Treatment completion

The mean number of treatment modules completed was 4.8 (SD = 2.1), and only 10.5% (4/38) completed all modules in time. However, the main reason for not completing the treatment in time was lack of time in relation to the wealth of text and assignments given. Moreover, participants were given full access to all modules after the treatment period, albeit without continuous therapist support. Three participants in the treatment group had not finished any modules at all at post-measurement, but posttreatment data were collected in keeping with the intention to treat procedure.

Main outcome

In Table 1 observed means and effect sizes are presented for each outcome measure. As evident from Table 2, which presents the immediate results of treatment versus no treatment control, there was a significant Time X group interaction for all measures (all *p*'s <0.01). Furthermore, the results were generally maintained at both the 1 year and the 3 year follow-up periods (see Table 1 and Table 3). Number of completed treatment modules was not correlated with outcome.

Table 1.

Observed means (SDs) at pretreatment, posttreatment, posttreatment for the control condition, 1-year follow-up, and 3-year follow-up. Also presented are the effect sizes

Assessment	Treatment		Control		Effect size
	M	SD	M	SD	Cohen's d
PSWQ					
Pretreatment	68.74	5.94	69.32	6.55	W: 1.08
Posttreatment	57.82	13.01	69.39	7.06	B: 1.11
Posttreatment 2	-	-	52.89	7.24	
1-year follow-up	53.00	12.05	-	-	W-FU: 1.66
3-year follow-up	51.33	16.59	53.38	13.69	
GAD-Q IV					
Pretreatment	10.08	2.42	10.34	2.13	W: 1.19
Posttreatment	6.45	3.59	9.89	2.77	B: 1.07
Posttreatment 2	-	-	7.25	3.26	
1-year follow-up	4.44	4.18	-	-	W-FU: 1.65
3-year follow-up	5.00	3.69	4.33	4.20	
STAI-S					
Pretreatment	57.24	10.45	58.07	10.24	W: 1.27
Posttreatment	43.82	10.65	57.61	9.73	B: 1.35
Posttreatment 2	-	-	41.89	4.83	
1-year follow-up	41.83	9.86	-	-	W-FU: 1.52
3-year follow-up	43.38	14.52	46.11	13.24	
STAI-T					
Pretreatment	58.84	6.45	61.57	6.51	W: 1.10
Posttreatment	50.21	9.01	60.61	7.02	B: 1.29
Posttreatment 2	-	-	44.79	3.87	
1-year follow-up	44.03	9.80	-	-	W-FU: 1.79
3-year follow-up	44.25	14.35	46.56	11.84	
BAI					
Pretreatment	20.61	10.64	20.98	9.66	W: .90
Posttreatment	12.37	7.43	19.20	8.56	B: .85
Posttreatment 2	-	-	12.29	7.97	
1-year follow-up	9.28	5.81	-	-	W-FU: 1.32
3-year follow-up	11.71	7.98	12.96	9.22	

<i>Assessment</i>	<i>Treatment</i>		<i>Control</i>		<i>Effect size</i>
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>Cohen's d</i>
<i>BDI</i>					
Pretreatment	17.66	9.81	16.93	7.91	W: .86
Posttreatment	10.08	7.75	16.70	7.60	B: .86
Posttreatment 2	-	-	9.79	7.19	
1-year follow-up	8.34	6.69	-	-	W-FU: 1.11
3-year follow-up	7.79	7.55	8.26	6.56	
<i>MARDS-S</i>					
Pretreatment	20.24	7.29	20.57	5.99	W: 1.21
Posttreatment	11.84	6.56	17.95	5.94	B: .98
Posttreatment 2	-	-	13.00	7.50	
1-year follow-up	10.03	7.06	-	-	W-FU: 1.42
3-year follow-up	9.38	7.44	10.00	6.67	
<i>QOLI</i>					
Pretreatment	0.38	1.55	0.24	1.74	W: 0.59
Posttreatment	1.34	1.72	0.44	1.79	B: 0.51
Posttreatment 2	-	-	1.26	1.95	
1-year follow-up	1.47	1.50	-	-	W-FU: 0.71
3-year follow-up	1.58	1.56	1.75	1.92	

Note: W= Cohen's *d* for the within group effect size for treatment group from pre- to posttreatment, B= Cohen's *d* for between group effect size at posttreatment, W-FU= Cohen's *d* for within treatment group effect size comparing pre measurement scores to 12 month follow up. At posttreatment only the treatment group had received treatment, at posttreatment 2 the control group had received the same treatment. PSWQ=Penn State Worry Questionnaire; GAD-Q IV= Generalized Anxiety Disorder Questionnaire IV; STAI-S=State-Trait Anxiety Inventory state; STAI-T=State-Trait Anxiety Inventory trait; BAI=Beck Anxiety Inventory; BDI= Beck Depression Inventory; MARDS-S=Montgomery Åsberg Depression Rating Scale - Self rated; QOLI= Quality of Life Inventory

Table 2.

Estimated means and standard errors (SEs) at pretreatment and posttreatment for treatment and control group respectively using mixed models.

Measure	Time	Treatment	Control	Interaction (F)
		Estimates M (SE)	Estimates M (SE)	
Penn State Worry Questionnaire				
	Pre	69.30 (0.94)	69.31 (0.93)	30.9***
	Post	58.26 (1.63)	69.38 (1.54)	
Generalized Anxiety Disorder Questionnaire-IV				
	Pre	10.13 (0.34)	10.34 (0.34)	22.9***
	Post	6.48 (0.51)	9.90 (0.48)	
State-Trait Anxiety Inventory (State)				
	Pre	56.61 (1.53)	58.11 (1.51)	29.4***
	Post	43.53 (1.62)	57.63 (1.52)	
State-Trait Anxiety Inventory (Trait)				
	Pre	58.84 (1.15)	60.62 (1.14)	30.7***
	Post	48.52 (1.45)	59.46 (1.38)	
Beck Anxiety Inventory				
	Pre	20.80 (1.55)	21.29 (1.53)	15.0***
	Post	12.47 (1.27)	19.37 (1.22)	
Beck Depression Inventory				
	Pre	18.34 (1.34)	17.04 (1.32)	28.3***
	Post	10.49 (1.2)	16.77 (1.15)	
Montgomery Åsberg Depression Rating Scale – self rated version				
	Pre	20.64 (0.98)	20.53 (0.97)	15.4***
	Post	11.99 (1.00)	17.94 (0.94)	
Quality of Life Inventory				
	Pre	0.41 (0.24)	0.22 (0.24)	9.0**
	Post	1.36 (0.27)	0.42 (0.26)	

Note: *** $p < .001$; ** $p < .01$

Table 3.

Means (SDs and SEs) at pretreatment, posttreatment, 1-year follow-up and 3-year follow-up with mixed models imputation. Pre n = 80, post n = 67, 1 year n = 29, 3 year n = 51.

Measure	Time	Mean Estimates	SD	SE	Time (F)	Significant Pairwise comparisons
PSWQ	Pre	69.30	6.19	0.66	55.5***	pre>post>fup1=fup3
	Post	55.96	12.67	1.33		
	Follow-up: 1 yr	52.28	17.07	1.81		
	Follow-up: 3 yrs	52.90	19.04	2.02		
GAD-Q-IV	Pre	10.24	2.26	0.24	55.6***	pre>post>fup1=fup3
	Post	6.78	3.93	0.42		
	Follow-up: 1 yr	4.83	6.29	0.67		
	Follow-up: 3 yrs	4.46	5.04	0.53		
STAI S	Pre	57.37	10.10	1.07	43.8***	pre>post=fup1=fup3
	Post	43.27	10.59	1.12		
	Follow-up: 1 yr	41.85	13.77	1.46		
	Follow-up: 3 yrs	44.80	18.09	1.92		
STAI T	Pre	59.74	7.66	0.81	51.8***	pre>post>fup1=fup3
	Post	47.23	9.93	1.05		
	Follow-up: 1 yr	42.83	14.36	1.52		
	Follow-up: 3 yrs	46.31	16.89	1.79		
BAI	Pre	21.05	10.24	1.09	43.0***	pre>post>fup1<fup3
	Post	12.66	9.17	0.97		
	Follow-up: 1 yr	9.42	7.85	0.83		
	Follow-up: 3 yrs	12.33	10.76	1.14		
MADRS-S	Pre	20.58	6.46	0.69	44.6***	pre>post=fup1=fup3
	Post	12.43	7.68	0.81		
	Follow-up: 1 yr	10.94	11.23	1.19		
	Follow-up: 3 yrs	10.33	8.91	0.94		

<i>Measure</i>	<i>Time</i>	<i>Mean Estimates</i>	<i>SD</i>	<i>SE</i>	<i>Time (F)</i>	<i>Significant Pairwise comparisons</i>
<i>BDI</i>	Pre	17.69	8.83	0.94	39.1***	pre>post=fup1=fup3
	Post	10.04	8.09	0.86		
	Follow-up: 1 yr	8.86	9.34	0.99		
	Follow-up: 3 yrs	8.85	8.80	0.93		
<i>QOLI</i>	Pre	0.31	1.61	0.17	13.3***	pre<post=fup1=fup3
	Post	1.27	1.85	0.20		
	Follow-up: 1 yr	1.37	2.33	0.25		
	Follow-up: 3 yrs	1.51	2.07	0.22		

Table 4.

Proportion of participants being clinically recovered, meaning that they had a reliable change and reached the 2 SD criterion of clinical significant improvement as defined by Jacobson and Truax (1991). Treatment group ($n = 38$; $n = 29$ at 1-year follow-up; $n = 21$ at 3-year follow-up) and control group ($n = 44$; $n = 29$ at 3-year follow-up).

	<i>Time</i>	<i>Treatment</i>	<i>Control</i>	$\chi^2(1)$
PSWQ	Posttreatment	42.0 % (16/38)	2.3 % (1/44)	19.69***
	1-year follow-up	48.3 % (14/29)	-	.
	3-year follow-up	57.1 % (12/21)	51.7 % (15/29)	
GAD-Q IV	Posttreatment	44.7 % (17/38)	6.8 % (3/44)	15.90***
	1-year follow-up	58.6 % (17/29)	-	
	3-year follow-up	66.7 % (14/21)	58.6 % (17/29)	
STAI-S	Posttreatment	21.1 % (8/38)	2.3 % (1/44)	7.40**
	1-year follow-up	34.5 % (10/29)	-	
	3-year follow-up	19.0 % (4/21)	44.8 % (13/29)	
STAI-T	Posttreatment	26.3 % (10/38)	2.3 % (0/44)	13.18 ***
	1-year follow-up	44.8 % (13/29)	-	
	3-year follow-up	33.3 % (7/21)	44.8 % (13/29)	
BAI	Posttreatment	10.5 % (4/38)	0.0 % (0/44)	4.28*
	1-year follow-up	17.2 % (5/29)	-	
	3-year follow-up	19.0 % (4/21)	17.2 % (5/29)	
BDI	Posttreatment	15.7 % (6/38)	0.0 % (0/44)	7.50**
	1-year follow-up	24.1 % (7/29)	-	.
	3-year follow-up	9.5 % (2/21)	13.8 % (4/29)	
MADRS-S	Posttreatment	39.5 % (9/38)	4.5 % (2/44)	6.43 *
	1-year follow-up	31.0 % (9/29)	-	
	3-year follow-up	23.8 % (5/21)	48.2 % (14/29)	
QOLI	Posttreatment	5.2 % (2/38)	0.0 % (0/44)	2.10
	1-year follow-up	6.9 % (2/29)	-	
	3-year follow-up	14.2 % (3/21)	17.2 % (5/29)	

* = $p < .05$; ** = $p < .01$; *** = $p < .001$

Note: The control group had received the same treatment as the treatment group at the 3-year follow-up. No data was collected for the control group at 1-year follow-up.

Clinically significant improvement

Table 4 presents an analysis of clinically significant improvement in terms of recovery, with the proportions of participants who displayed a reliable change and scored 2 SDs below the pretreatment group mean. On all measures except for the QOLI the treatment group had significantly more responders. On the main outcome measures PSWQ, 42% of the treated and 2.3% of the untreated participants fulfilled the criteria for Reliable Change Index and had decreased their ratings by 2 SD's. Considering dropouts as non-responders reduced the proportion of recovered participants on the PSWQ (36.4%), but the difference still remained statistically significant $\chi^2(1)=16.8$, $p<.001$. At the 1-year follow-up more participants had dropped out (23%), but for the ones who remained in the trial the proportion of recovery remained stable from posttreatment.

Discussion

The outcome of this study suggests that guided Internet-delivered CBT can be effective in the treatment of GAD, and typically participants in the treatment group improved whereas the controls did not. On the PSWQ the controlled between group effect size was large ($d = 1.11$), and in line with what Titov et al. (2009) found in their study ($d = 1.24$) where the treatment consisted of six online lessons based on CBT principles with weekly e-mail support from a clinical psychologist and contribute to a moderated online discussion forum over a 9 week period. Our study was larger and we also included a one and a three year follow-up, which suggested that effects were generally sustained. Results on secondary outcome measures also indicated improvements, even though the outcome on the QOLI was lower. This is in line with what has been found in previous Internet studies (Andersson, et al., 2006; P Carlbring, M Gunnarsdóttir, et al., 2007). The reason that the outcome on quality of life does is not as favorable as for anxiety and depression is probably that the treatment is directly focused on anxiety, meaning that any changes in quality of life are secondary effects. In addition to the continuous measures we also included a structured interview which showed that more than half of the treated participants had recovered. This corresponds with the clinical response rate found in a Cochrane review (Hunot, et al., 2007), in which 46% of participants in trials were found to respond to treatment. The Cochrane Collaboration is a group of over 27,000 volunteers in over 90 countries who review the effects of health care interventions tested in randomised controlled trials.

Treatment gains appear to have been maintained during the follow-up period when using a structured diagnostic assessment tool (i.e., SCID-I). One surprising feature, given the rate of improvement, was that few participants completed all modules. One reason could be that the treatment included too many treatment components such as applied relaxation, cognitive techniques (e.g., scheduled worry time) and exposure. Problems with non-completers are commonly reported in the Internet treatment literature (Eysenbach, 2005). Another possible explanation is that some of the participants made an improvement regarding their worry after the first few treatment modules and therefore were reluctant to finish the entire programme. The strict time frame of the trial might also have had an impact on the attrition. Indeed, a recent trial on CBT for GAD had a much longer treatment (30 weeks) and the effects were large (Leichsenring, et al., 2009). Moreover, following the work by Borkovec and coworkers one treatment module also included interpersonal problem solving (Borkovec, et al., 2002). The present design makes it impossible to differentiate effective components as techniques were presented in parallel (e.g., both worry time and applied relaxation). This is however not uncommon for CBT protocols. It may be that participants need different treatment components or that the applied relaxation would have been sufficient (Öst & Breitholtz, 2000). Unfortunately, because participants on the wait-list received treatment before the follow-up data were collected, there is no between-group comparison at follow-up. Hence, the robustness of the no-treatment control findings is unknown.

The dropout rate from the study was small (8%; 7/89) at posttreatment but substantially larger at one year follow-up (34%; 15/44). In the trial by Titov et al. (2009) the dropout rate was larger (19%; 9/48) at posttreatment but on the other hand more participants completed the whole programme. Since we did not include a face-to-face comparison it is not possible to claim that the results of either our study or the trial by Titov et al. show that guided Internet treatment is as effective as face-to-face treatment of GAD. However, previous randomised controlled trials on panic disorder suggest that the two treatment formats can both be effective (Carlbring, et al., 2005; Kiropoulos et al., 2008), and the effect sizes in our study and the trial by Titov et al. are in line or even better than the effect sizes reported in meta-analysis (Mitte, 2005). On the other hand, effectiveness trials are needed to determine if Internet treatment works under representative clinical conditions (Andersson, Carlbring, & Cuijpers, 2009).

There are limitations of this study, and we will comment on what we view as the most important issues. First, we only diagnosed GAD and depression and while GAD had to be the primary complaint, other comorbid conditions may have been present, in

particular since GAD is known to be comorbid with other anxiety disorders (Tyrer & Baldwin, 2006). Due to time constraints we did not include diagnosis of axis-II disorders. Second, we allowed participants with stabilized medication. Given the large uptake of antidepressants in this group the alternative would have been to exclude all these participants which would have decreased the external validity. On the other hand all participants had to fulfill the diagnostic criteria of GAD in spite of being on stable medication. We did control if use of medication influenced the outcome but no differences or interactions were detected. Third, we did not include an active control group or psychological placebo (Hofmann & Smits, 2008), and since it is known that waiting-list controls tend to inflate effect sizes our results may be an overestimation. Since GAD patients rarely remit without treatment, the use of a waitlist control group is a limitation of this trial. The clinical interview was conducted over telephone rather than face-to-face, which might have had an impact on the outcome. However, research indicates that telephone-administered clinical interviews are justified (Rohde, et al., 1997b). Finally, as the participants in the control condition were given the treatment, the 1 year follow-up interviews were not blinded, and this might have had impact on the results.

The clinical implications and potential cost savings of this study includes the possibility of overcoming distances to specialist clinics and thereby decrease the treatment-demand for treatment gap (Postel, de Haan, & De Jong, 2008). Data on cost-effectiveness of the treatment will be presented in a separate publication, but apart from initial costs of developing the treatment the lower cost of therapist time makes Internet treatment a promising complement. Moreover, computerized treatments are likely to be more prevalent in clinical settings not only as separate treatments but as integrated with regular services (Craske et al., 2009).

We conclude that guided Internet-delivered CBT may be effective for persons with GAD as a complement and sometimes alternative to other evidence-based treatment options. Future larger studies are needed to replicate this finding and treatment programme tested in this study should be updated to increase adherence. Moreover, a direct comparison with face-to-face CBT and active control groups, preferably in representative clinical settings, could further elucidate if Internet treatment of GAD is an effective treatment option.

CHAPTER 3

*Internet-delivered guided self-help for generalized anxiety disorder:
Cost-effectiveness analysis of a randomised trial*

Paxling, B., Smit, F., Almlöv, J., Dahlin, M., Andersson, E., Carlbring, P., Cuijpers, P., & Andersson, G. (submitted). Internet-delivered guided self-help for generalized anxiety disorder: Cost-effectiveness analysis of a randomised trial.

ABSTRACT

BACKGROUND: Generalized anxiety disorder (GAD) is a disorder that is both expensive and difficult to treat.

AIMS: To study the cost-effectiveness of an Internet-delivered CBT intervention for GAD.

METHOD: An economic evaluation was performed alongside a randomised controlled trial. Individuals diagnosed with GAD were randomised to an 8-week self-help programme with therapist support (n = 44) or to a control condition with unlimited access to care as usual (n = 45).

RESULTS: GAD-patients benefitted from Internet-delivered CBT, and 52.3% in the treatment condition no longer fulfilled the diagnostic criteria at post-treatment, compared to 15.6% in the control condition. This effect comes at a cost of £447 for each GAD remission.

CONCLUSION: This was the first study to demonstrate that Internet-delivered CBT was more effective than care as usual for a population with GAD. This outcome was produced at relatively low costs; therefore, this treatment is cost-effective.

BACKGROUND

Generalized anxiety disorder (GAD) is highly prevalent (Kessler et al., 2008), associated with poor health-related quality of life (Pollack et al., 2008; Smit et al., 2006), and known to have staggering economic ramifications (Smit et al., 2006). Compared to other anxiety disorders such as panic disorder and social phobia, GAD is understudied, poorly understood and relatively treatment resistant (Heimberg, Turk, & Mennin, 2004). A retrospective multivariate analysis performed in the US (Marciniak et al., 2005) indicated that GAD with comorbid depression is one of the most expensive psychiatric disorders to treat. According to Heuzenroeder et al. (2004), cognitive behavioural therapy (CBT) is the most effective and cost-effective intervention for generalized anxiety disorder, but it is not easily accessible for many people because there is a scarcity of CBT trained therapists. Delivering CBT over the Internet is a means of making it accessible to more people (Andersson, 2009; Griffiths, Lindenmeyer, Powell, Lowe, & Thorogood, 2006), while simultaneously cutting therapist time (Marks, Kenwright, McDonough, Whittaker, & Mataix-Cols, 2004).

METHODS

The treatment outcome and methodology of this trial have been described in Chapter 2. The aim of this article is to investigate the economic aspects of Internet-delivered CBT for GAD.

Ethics statement

The protocol was approved by the Linköping Regional Ethics Committee, and written informed consent was obtained from all study participants.

Sample

The trial was announced on a website where people wishing to participate in the study could register. Recruitment was conducted in a number of steps. First, participants entered their personal information and then filled in a brief battery of questionnaires administered via the Internet, consisting of Generalized Anxiety Disorder Questionnaire-IV (Newman et al., 2002), Penn State Worry Questionnaire (Meyer, Miller, Metzger, & Borkovec, 1990), Montgomery Åsberg Depression Rating Scale – Self rated (Svanborg & Asberg, 1994) and Alcohol Use Disorders Identification Test (Saunders, Aasland, Babor, de la Fuente, & Grant, 1993). The outcome measures have good psychometric properties, even when administered via the Internet (Carlbring et al., 2007; Thorndike et al., 2009). Those who fulfilled the inclusion criteria for these questionnaires were then submitted to a structured clinical interview (SCID-I) (First,

Gibbon, Spitzer, Williams, & Benjamin, 1999) via telephone and asked to send in a written informed consent to participate in the trial. An experienced psychiatrist with access to tape recordings of the SCID-interviews confirmed the diagnoses. To be included in the study, participants had to be: (a) 18 years of age or older, (b) diagnosed with GAD, (c) not severely depressed (a score of 35 or above on the MADRS-S), (d) have no current suicidal tendencies (scoring 4 or above on MADRS-S item nine), (e) not be in psychological treatment, and (f) not be heavily alcohol dependent (>19 on the Alcohol Use Disorders Identification Test). Use of pharmacological drugs was not among the exclusion criteria, but the participants had to be stabilized on the present dosage for at least three months leading up to participation. In addition, if on medication, the patients had to promise that they would keep the dosage at the same levels throughout the course of the study. A second set of questionnaires was administered online before the subjects entered the treatment.

The randomisation to the intervention (n = 44) and control condition (n = 45) was performed by an independent third party by concealed allocation, using a random number service on the internet (random.org). Post treatment assessment was administered using Internet questionnaires and clinical interviews via telephone (intervention n = 38, control n = 44). The interviewers performing the post treatment interviews were blind to whether the clients had been in treatment or control condition. For ethical reasons, those randomised to the control condition were given the same intervention as the experimental group after eight weeks.

A power analysis indicated that 45 participants per condition were required to detect a difference in recovery rate of 30% in a two-sided test at alpha = 0.05 and a power of 0.80.

Interventions

The experimental condition was an eight week Internet-delivered self-help programme with therapist support. The programme was divided into eight chapters building upon cognitive-behavioural principles. The programme consisted of psychoeducation, applied relaxation (an audio CD accompanies this part of the programme), problem solving, anxiety exposure, cognitive restructuring, worry-time, interpersonal intervention, interventions for sleep problems and a relapse prevention programme. Each chapter contained homework assignments.

The control condition participants were placed on a waiting list on the understanding that they would receive the intervention after eight weeks.

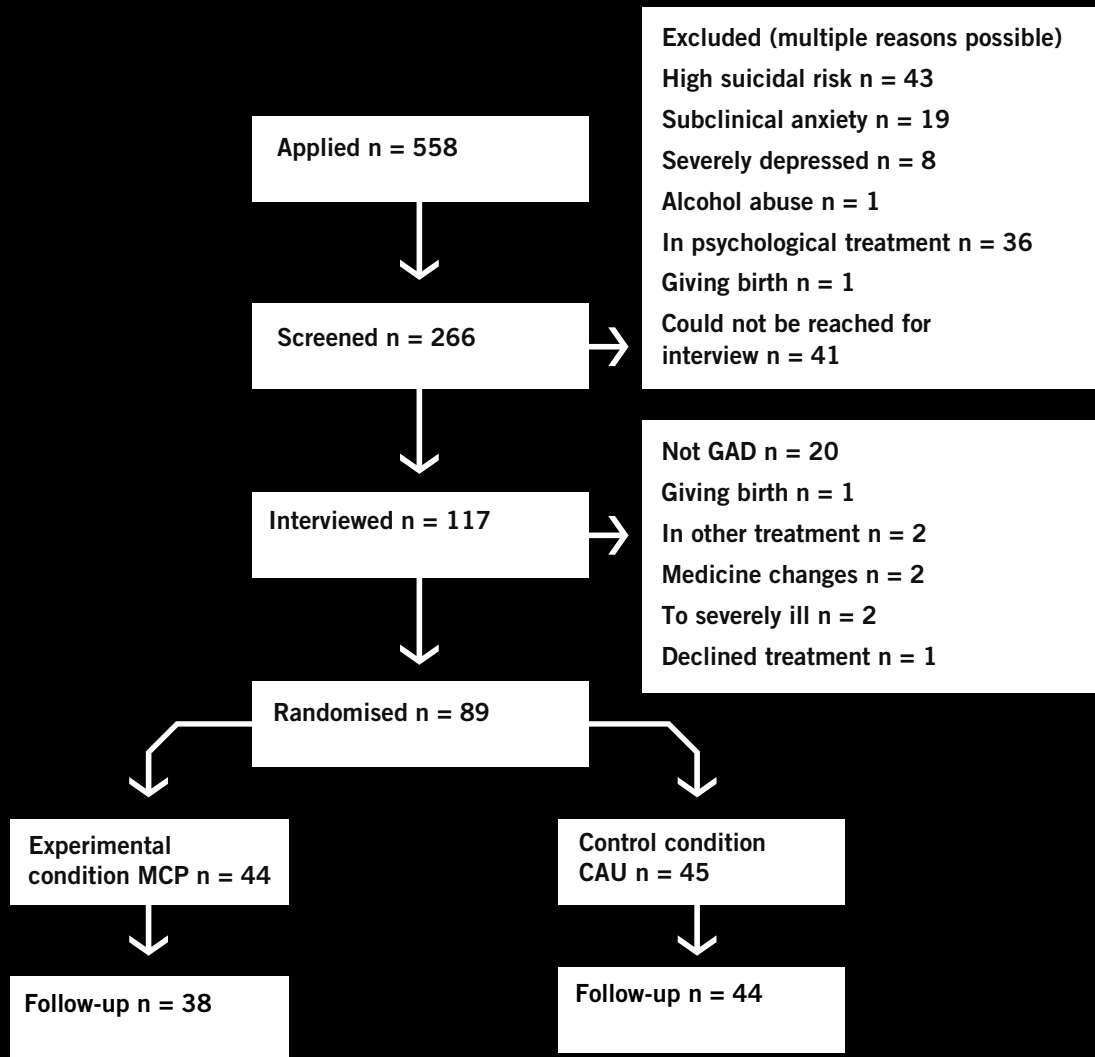


Figure 1. Patient flow

Clinical measures

In this study we report clinical outcome according to DSM-IV (American Psychiatric Association, 2000) diagnostic status of generalized anxiety disorder using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al., 1999) at post treatment. It entails a hierarchical system through which to conduct the interview and allows for both prerequisite and spontaneous questions to be asked during the assessment.

Table 1.
Costs by service type

	<i>Direct Medical</i> Costs (in 2006 UK £)	
<i>Health service type</i>	<i>Unit</i>	<i>Cost</i>
Medical doctor	Consult	117.49
Company doctor	Consult	110.49
Company counsellor	Contact	73.66
Counsellor	Contact	88.39
Psychotherapist	Contact	90.20
Regional addiction service	Contact	99.70
Psychiatrist at general hospital	Contact	168.53
Psychiatrist at psychiatric clinic	Contact	240.87
Private practice psychotherapist	Session	67.91
Physiotherapist	Contact	65.41
Home care	Hour	27.62
District nurse	Consult	31.10
Informal care (family, friends)	Hour	5.54

Measuring resource use

For this study we adopted a societal perspective, including the costs of all types of health services as well as costs associated with production losses. The time frame of this study is restricted to one year (2006); therefore, we did not correct for inflation and did not discount costs. For this article, all outcomes have been recalculated from Swedish crowns into pound sterling (GBP) using power purchasing parities (Organisation for Economic Co-operation and Development, 2006).

Information on the subjects' use of health services was obtained with the Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry (TIC-P) (Hakkaart-Van Roijen & Donker, 2002). With this questionnaire, patients register the number of visits to general practitioners (GPs), sessions with psychiatrists, hospital days, medication usage, and all other health care consumption. In addition, the number of work loss days (absenteeism from work) and the number of work cutback days (lesser efficiency at work due to feeling ill) were also measured with the TIC-P.

Direct medical costs

The intervention costs are costs associated with therapist support, screening interviews, computers, servers and Internet access. Therapist time was logged and multiplied by the full economic cost of a psychologist visit. The cost of developing the treatment programme has been excluded from the analysis because this is a onetime cost and has no monetary implication in future health care scenarios.

Direct medical costs are costs associated with both formal and informal health service providers (see Table 1). Medical services were calculated by multiplying the number of health service units (consultations, hospital days, etc.) by their standard full economic cost. To these we added the costs of medication, that is, the cost (Apoteket, 2006) per standard daily dose (Farmaceutiska Specialiteter i Sverige, 2006), plus 6% VAT, multiplied by the number of prescription days, plus the pharmacist's dispensing costs of £4.38 per prescription. The 6% VAT is included in our analysis because it is not deductible for private citizens in Sweden.

Direct non-medical costs arise when patients travel to health service providers and pay for parking. These 'out-of-pocket' costs were valued at £1.77 per km and £0.37 per hour of parking time. To this we added the costs of the patients' time spent in travel, waiting and treatment, at £5.54 per hour (see Table 1).

Indirect costs

Indirect non-medical costs arise when production losses occur due to illness. Three situations can be encountered here: First, people can be absent from paid work. To evaluate a lost working day we used the human capital approach which means that the monetary loss is based on the patient's gross earnings (Drummond, Sculpher, Torrance, O'Brien, & Stoddart, 2005).

Second, production losses also occur when people are less efficient at work due to illness. We estimated the number of work cutback days as the number of days actually worked when ill, multiplied by a self-reported inefficiency score, which ranges from 0.00 (as efficient as when in good health) to 1.00 (totally inefficient). Third, people may also be too ill to perform domestic tasks. These costs were evaluated at the free market price of domestic help at £5.54 per hour.

Statistical analysis

All statistical analyses were conducted using Stata/MP version 10.0 except for imputation with the Expectation Maximization algorithm, which was performed in SPSS (IBM) version 17.0. The analyses were conducted according to the intention to treat principle, and missing data at post treatment were imputed by last observation carried forward.

Analysis of clinical outcomes

Numbers needed to be treated (NNT) and incremental effects were calculated using the results from the diagnostic interview at post treatment.

Analysis of costs

The costs were computed by multiplication of the unit cost by the number of units (sessions, contacts, days of work lost etc.). This was done pre- and post-intervention. The differences were then computed between pre- and post-scores and compared between the two groups. Reported are the mean annual per capita costs of the intervention, plus the direct medical, direct non-medical and the indirect non-medical costs, including some of their major components (see Table 2). We compared the cost change distribution (pre- to post treatment) between intervention and control condition. The corresponding analyses were based on 5,000 bootstrap replications because cost data are non-normally distributed.

Analysis of cost-effectiveness

The incremental cost-effectiveness ratio is the ratio between the incremental costs and the incremental effects, which is calculated as $(C1 - C0)/(E1 - E0)$, where C is the average annual per capita cost change distribution and E is the percentage of people who were successfully recovered from generalized anxiety disorder at post-test in the experimental and control conditions (subscripted 1 and 0 respectively).

In the cost-effectiveness analysis, clinical outcomes (i.e., no longer fulfilling the diagnostic criteria for GAD) and costs in both arms were computed by means of non-parametric bootstrapping (5,000 times) with respect to both incremental costs and incremental health gains. The comparison of the simulated differences in costs and health effects is presented in a cost-effectiveness plane (see Figure 2), with differences in costs on the vertical axis and difference in health effects on the horizontal axis. Each dot represents a bootstrapped ratio between changes in costs and worry, so where a dot appears at the top left-hand quadrant in the plane, higher costs are paid for lower effectiveness; the intervention is then unacceptable from a cost-effectiveness perspective. If a dot appears in the lower right-hand quadrant, lower costs are associated with positive health effects; the intervention dominates and is acceptable. In the other two quadrants, higher (or lower) cost levels have to be weighed against greater (or lesser) effectiveness.

A second way of illustrating the cost-effectiveness results is the cost-effectiveness acceptability curve (Barrett & Byford, 2003). Such an acceptability curve represents the probability that the experimental condition is cost-effective relative to control condition, given varying thresholds for the willingness to pay for one successfully treated case (see Figure 3).

Sensitivity analyses

As cost data could be sensitive to outliers, we repeated the analysis excluding the top and bottom 5% of the observations. In order to test whether the imputation method (last observation carried forward) was to be regarded as a conservative estimate, we repeated all analyses imputing missing data with the Expectation Maximization (EM) algorithm in SPSS 17.0. A completers-only analysis was also performed.

RESULTS

Sample

The study had 89 participants aged 18 to 66 years (mean 39.3, SD = 10.8). The treatment group consisted of 36 females and eight males aged 18 to 66 (mean = 40.0, SD = 11.3). The control group consisted of 35 females and ten males aged 21 to 62

Table 2.

Annual per-capita change in costs (in UK £) by condition: means, standard deviation (SD) and differences (Diff.).

Costs	Experimental group (E)		Control group (C)		Difference (E – C)
	Mean	(SD)	Mean	(SD)	Diff.
Direct medical	-450	(2,496)	569	(3,623)	-1,019
Intervention	283	(139)	0	(0)	283
GP	-691	(2,516)	536	(3,604)	-1,227
Medication	-42	(123)	33	(213)	-75
Direct non-medical	1,051	(1,146)	-129	(679)	1,180
Indirect non-medical	-561	(7,870)	-561	(9,759)	0
Work loss	-1,925	(5,958)	-4,251	(8,281)	2,326
Work cutback	3,154	(6,860)	3,979	(7,683)	-825
Domestic	-339	(641)	-275	(456)	-64
Total	40	(8,856)	-121	(10,095)	161

(mean = 38.6, SD = 10.3). All the participants met the criteria for a GAD-diagnosis at baseline. Fifty-eight of the total 89 participants had comorbid depression. Twenty had a current episode of depression and 38 had a history of at least one previous episode of depression, but no current depression. No significant differences were found between the conditions on any variables at pre-testing, indicating that randomization had resulted in comparable groups and the baseline costs were distributed evenly across the trial arms.

Clinical outcomes

In the experimental group 23/44 patients (52.3%) recovered from GAD according to a diagnostic interview, compared to 7/45 (15.6%) in the control condition. The likelihood ratio of a favourable treatment response was $0.52/0.16 = 3.36$ (95% CI

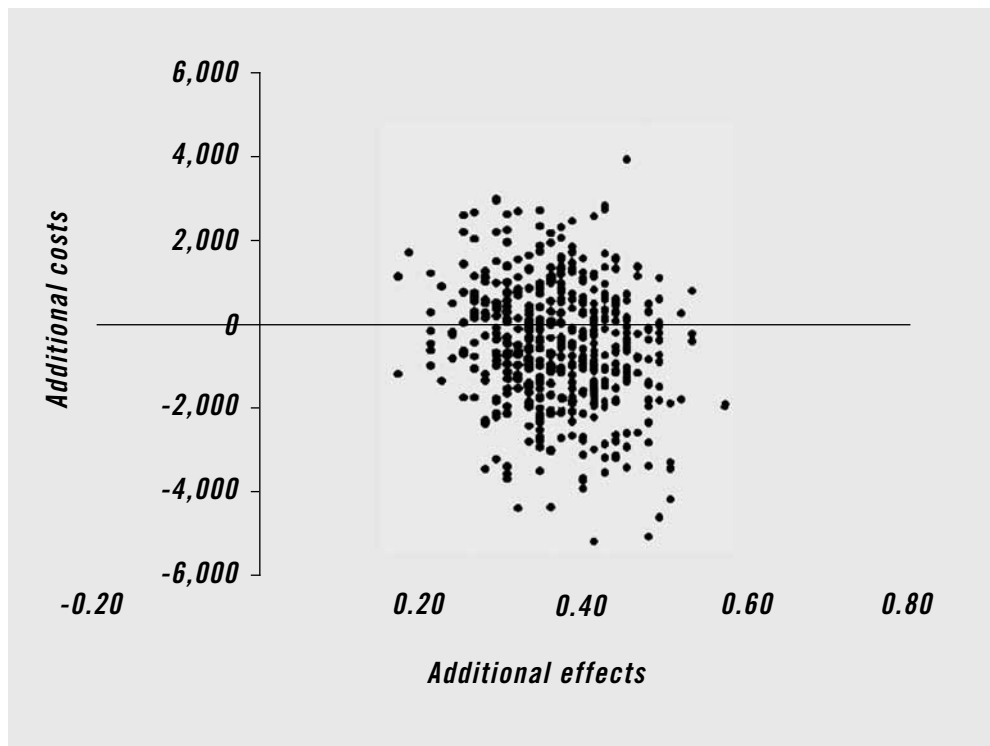


Figure 2. Cost-effectiveness plane: each dot ($n = 5000$) represents a bootstrapped C/E-ratio.

[1.61, 7.02]). The difference in the treatment response rate was therefore $52.3 - 15.6 = 36.7\%$ with a 95% confidence interval of 18.6 to 54.9%. The difference in treatment response between the conditions was statistically significant ($\chi^2 = 13.42$, $df = 1$, $p = 0.0002$). The NNT, numbers needed to be treated, was $1/0.367 = 2.7$ (95% CI [1.82, 5.39]), which means that three people need to receive the intervention rather than being placed on a wait list with unrestricted access to care-as-usual in order to obtain one recovered DSM-IV/SCID-I GAD patient.

Costs

Table 2 presents annual per-capita change in costs by condition. Several cost differences were negative, indicating cost reductions, or cost offsets. Direct medical costs were, on average, lowered by £450 per patient in the CBT condition, where reductions in GP visits (£691) were offset by the cost of the intervention (£283). The costs for GP visits increased in the control condition (£536). The participants in the CBT condition had lower costs due to absenteeism (£1,925) than the participants in the control condition (£4,251), but seemed to be more present at work when not feeling well, which accounts for increased work cutback costs (CBT = £3,154, control = £3,979).

Cost-effectiveness

The incremental cost-effectiveness ratio, $(C1 - C0)/(E1 - E0)$, is the difference of mean costs between the conditions divided by the difference in effect. Substitution yields $[40 - (-121)]/(0.52 - 0.16) = 447$, which means that the CBT condition produces one GAD remission to a price of £447. Figure 2 presents the cost-effectiveness plane for CBT vs. the control condition. On the y-axis are the incremental costs; on the x-axis, the incremental effects. Each dot ($n = 5,000$) represents a bootstrap replication of the incremental cost-effectiveness ratio; 47% of the dots are in the lower right-hand quadrant, indicating a 47% probability that Internet-delivered treatment produces cost savings alongside additional (superior) effects. The majority of the dots, 53%, are placed in the upper right corner, indicating that there is a 53% probability that Internet-delivered treatment produces better effects, but to additional costs.

Acceptability

Figure 3 presents the cost-effectiveness acceptability curve. The solid line curve intersects the y-axis at 0.47 where the willingness to pay is absent (equal to £0.00), indicating a 47% probability that Internet-delivered CBT is more cost-effective than the control condition. Generally, people are willing to pay for treating generalized anxiety disorder, and different ceilings are therefore presented on the x-axis. When

the willingness to pay is raised to £10,000 per treated case, the CBT intervention has a 91% probability of being cost-effective; this probability rises to 97% at £20,000.

Sensitivity analysis

When the analysis was repeated while excluding the top and bottom 5% of the sample with the lowest and highest costs, 60% of the dots fell in the upper right quadrant and 40% were located in the lower right hand quadrant. The analysis was also performed with completers-only (86% of dots in upper right quadrant, 14% in the lower right), and finally, with Expectation Maximization in SPSS, where 85% of the dots fall in the upper right quadrant and 15% in the lower right.

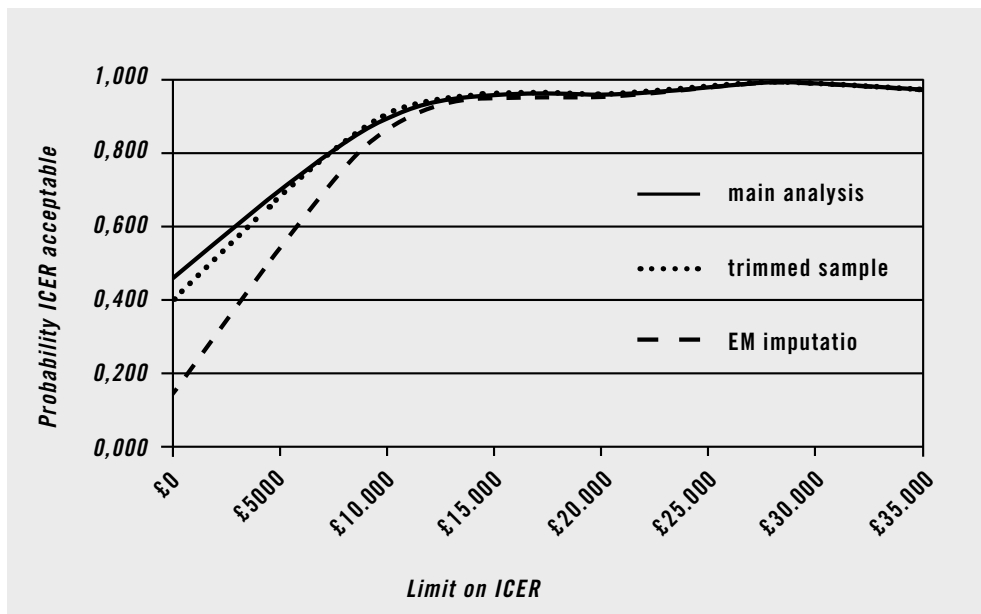


Figure 3. Cost-effectiveness acceptability curve: probability that the incremental cost-effectiveness ratio (ICER) is acceptable (y-axis) given varying thresholds for willingness to pay (x-axis) for total costs (solid line), for a trimmed sample with outliers removed (dotted line) and with estimation maximization imputation (dashed line), based on 5,000 bootstrap replications. The conclusion that the intervention is more cost-effective than the comparator condition is sensitive to the willingness to pay level across the £0 – 5,000 range.

DISCUSSION

Main findings

The data suggest that Internet-delivered CBT is more efficacious in providing diagnostic remission of GAD status with a likelihood ratio of 3.36 ($p = .0002$, 95% CI [1.61, 7.02]) and a NNT of 2.72 compared to the control condition. These results are produced at the relatively low cost of £447 for each GAD remission, according to the economic evaluation. When there is no willingness to pay for a remission of GAD diagnosis, the CBT intervention has a 47% probability of being cost-effective compared to the control condition with unrestricted access to care-as-usual. When the willingness to pay is raised to £5,000, the CBT intervention has a 71% probability of being the preferred option. The results came out to be robust in the sensitivity analyses. The clinical outcome in the present study is similar to that of Titov and colleagues (2009), where 63% of those treated with Internet administered CBT were defined as recovered at post-treatment assessment. In a recent randomised trial (Dugas et al., 2010), live CBT was compared with applied relaxation, and diagnostic remission at post-treatment was 70% for CBT and 55% for applied relaxation, though it should be noted that the way of defining remissions differs from the present study. Few cost-effectiveness evaluations have been performed on Internet-delivered CBT (Kaltenthaler et al., 2006), although some studies (McCrone et al., 2004; Warmerdam, van Straten, Jongasma, Twisk, & Cuijpers, 2010) indicate that Internet-delivered CBT can be cost-effective for anxiety and depression.

Limitations

We acknowledge the following limitations of this study. First, this trial has a short follow-up, and we are therefore unable to estimate the long term cost-effectiveness of the treatment. Second, the participants in the control condition did not get any credible placebo treatment and were instead told they would receive the real treatment after 8 weeks, which might have impacted the final result. On the other hand, this kind of control condition is common in randomised control trials (Carlbring et al., 2007; Ljotsson et al., 2007), and the patients in the control group also had unrestricted access to usual care. A third possible limitation to the study is the choice of using telephones for the structured clinical interview. The fact that the patients never met any of the therapists or researchers face to face makes it hard to tell how well the treatment might be implemented in regular health care, as patients there tend to meet their doctors or therapists face to face. The fact that the interviews were carried out over telephone should not, however, have impacted the results in any meaningful way (Rohde, Lewinsohn, & Seeley, 1997). Fourth, the trial was performed in Sweden, and

the generalizability of the results to other countries (and settings) can therefore be questioned. A fifth caveat is the attrition: 8% of the participants did not answer the post treatment questionnaires or were not subjected to a clinical interview. This was circumvented using last observation carried forward, and the results should therefore be regarded as a conservative estimate. In addition to last observation carried forward, other imputation techniques were used to gauge the robustness of the findings. The usage of a self-report questionnaire to collect economic data can be viewed as a limitation as compared to collecting data from national databases. However, Patel and colleagues (Patel et al., 2005) have compared different methods for collecting economic data and have found good agreement between self-report and case records. Finally, the relatively small sample size in this trial begs for replications with larger sample sizes.

The wider context

GAD is a condition that is difficult to treat and has a negative impact on life satisfaction. In the current trial, a new treatment modality, Internet-delivered CBT, has been tested with promising results. The presented treatment has proven to be relatively inexpensive and time-efficient; for a low cost, it can be offered to many patients in need of effective treatment. Although the patients in this study are absent from work to a high degree, the majority are still working, and this intervention makes it possible to undergo treatment without having to be absent from work. GAD is sometimes considered to be the “basic” or “underlying” anxiety disorder, and standard CBT has not yielded as good results for GAD as, say, for panic disorder or phobias. By providing a self-help CBT-treatment with clinician support, patients living in rural areas or who otherwise have difficulty visiting a psychiatric clinic regularly can now be given an effective treatment for a complex problem.

Directions for the future

Internet-delivered CBT could be a cost-effective treatment in alleviating GAD symptoms, but many questions remain unanswered. One recommendation for future research would be to conduct a similar research design but with a more active control condition, hence amplifying the placebo effect. Another recommendation would be to test the treatment in a psychiatric setting, giving a more realistic figure of this treatment’s cost-effectiveness. Larger sample sizes would make it possible to evaluate possible significant cost changes. Finally, longer follow-up times during which the control condition remains untreated would be beneficial. Provided replication studies show similar clinical outcomes to those of the present study, a nationwide implementation of the intervention is highly recommended.

CHAPTER 4

Internet-based psychodynamic vs. cognitive behavioural guided self-help for generalized anxiety disorder: A randomised controlled trial

Andersson, G., Paxling, B., Roch-Norlund, P., Östman, G., Norgren, A., Almlöv, J., Georén, L., Breitholtz, E., Dahlin, M., Cuijpers, P., Carlbring, P., & Silverberg, F. (submitted). Internet-based psychodynamic vs. cognitive behavioural guided self-help for generalized anxiety disorder: A randomised controlled trial.

ABSTRACT

BACKGROUND: Guided Internet-based cognitive behaviour therapy (CBT) has been tested in many trials and found to be effective in the treatment of anxiety and mood disorders. Generalized anxiety disorder (GAD) has also been treated with Internet-based CBT, but there are no randomised and controlled trials on guided Internet-based psychodynamic treatment (PDT). Since there is preliminary support for psychodynamic treatment for GAD, we decided to test whether a psychodynamically-informed self-help treatment could be effectively delivered via the Internet.

AIM: To investigate the effectiveness of guided Internet-based PDT for GAD and to compare with guided Internet-delivered CBT as well as a waiting-list control group.

METHOD: A randomised controlled superiority trial with individuals diagnosed with GAD comparing guided Internet-based CBT (n = 27) and PDT (n = 27) against a no treatment control group (n = 27). The primary outcome measure was the Penn State Worry Questionnaire.

RESULTS: Both Internet-based PDT and Internet-based CBT resulted in improvements with moderate to large within-group effect sizes at 3-month and 18-month follow-ups on the primary measure. The differences against the control group, although smaller, were still significant for both PDT and CBT when conforming to the criteria of clinically significant improvement. Both treatments performed equally, and there was a significant group by time interaction for reducing GAD symptoms, while on other secondary measures, the two treatment groups appeared better than the control group, though non-significantly.

CONCLUSIONS: Internet-based PDT and CBT both lead to symptom reduction in GAD, but more research is needed.

INTRODUCTION

Generalized anxiety disorder (GAD) is a common and persistent disorder characterized by intense and uncontrollable worry (American Psychiatric Association, 2000). Even if symptoms of worry in GAD can be situationally aggravated, such worry is not explained by reactions to recent stressful events. GAD is often comorbid with other anxiety and mood disorders and its life-time prevalence ranges between 4.3 to 5.9% (Tyrer & Baldwin, 2006). Different treatment options exist (Tyrer & Baldwin, 2006), and CBT is the psychological treatment approach that has received most empirical support in terms of number of trials conducted (Mitte, 2005). There are some indications that psychodynamic psychotherapy (PDT) can work well for patients with GAD (Crits-Christoph, et al., 1996; Leichsenring, et al., 2009). Recently, CBT has been transposed for delivery over the Internet (Andersson, 2009), and a few randomised controlled trials have investigated the effects of Internet-based CBT for GAD (See chapter 2; Robinson et al., 2010; Titov, Andrews, Robinson, et al., 2009). There are now numerous controlled trials on guided Internet-based CBT for anxiety disorders (Andrews, et al., 2010), but no prior studies on Internet-based PDT. The present study aimed to investigate the effects of a guided Internet-based PDT and CBT for GAD. We hypothesized that participants receiving Internet-based PDT, relative to those in a waiting-list control condition, would show a statistically significant reduction of worry and depressive symptoms and an improvement in quality of life. In addition, we added a comparison group which received Internet-based CBT. We expected similar outcomes for Internet-based PDT and CBT on measures of worry (Leichsenring, et al., 2009).

METHOD

Design

This was a superiority trial in which two active treatments were compared to a waiting-list group, with unrestricted randomisation in 1:1:1 ratio. The trial was conducted in Sweden.

Participants and recruitment

The study protocol was approved by the regional ethics committee. The participants were self-recruited using a website where they had previously registered as interested in participating in research on Internet-based treatment for GAD. The trial was also advertised in a major Swedish newspaper. The participants received an e-mail with

information about the treatment and screening procedures and they then entered their personal information, answered a battery of web-administered questionnaires for screening purposes, and finally signed and posted a letter of informed consent that was needed to enter the study. Those who fulfilled the initial inclusion criteria on the screening questionnaires were then interviewed via telephone using the Structured Clinical Interview for DSM-IV Axis I Disorders research version (SCID I-RV) (First et al., 1997). To be eligible for inclusion, potential participants had to meet the following criteria: (a) fulfil the diagnostic criteria for GAD according to DSM-IV, (b) be at least 18 years old, (c) have access to the internet, (d) have good knowledge of the Swedish language, (f) if taking prescribed medication for anxiety or depression, the duration had to be at least 12 weeks and the participant had to be on a stable dosage for at least 6 weeks leading up to participation and had to agree not to change medication and/or dosage during the trial, (g) not be in any other psychological treatment during the study period, and (h) not be severely depressed or suicidal as assessed by self-report and telephone interview. A psychiatrist served as consultant during the entire trial.

OUTCOME MEASURES

Primary outcome measure

The primary outcome measure in the trial was the Penn State Worry Questionnaire (PSWQ) (Meyer, et al., 1990a). The PSWQ has 16 items and is designed to capture the generality, excessiveness, and uncontrollability of pathological worry.

Secondary outcome measures

We additionally included the Generalized Anxiety Disorder Questionnaire IV (GAD-Q IV) (Newman et al., 2002) for measuring GAD symptoms. A third measure was the Montgomery Åsberg Depression Rating Scale - Self rated (MADRS-S) (Svanborg & Åsberg, 2001), which was used to screen for the exclusion criteria of severe depression and suicidal tendencies. The Quality of Life Inventory (QOLI) (Frisch et al., 1992) was used to measure life quality in 16 domains. The State-Trait Anxiety Inventory (STAI state and trait versions) (Spielberger et al., 1970), the Beck Depression Inventory (BDI-II) (Beck, Steer, & Brown, 1996), and the Beck Anxiety Inventory (BAI) (Beck et al., 1988) were used to measure depressed mood and anxiety symptoms. However, it should be noted that the three latter questionnaires were not administered in the 18-month follow-up.

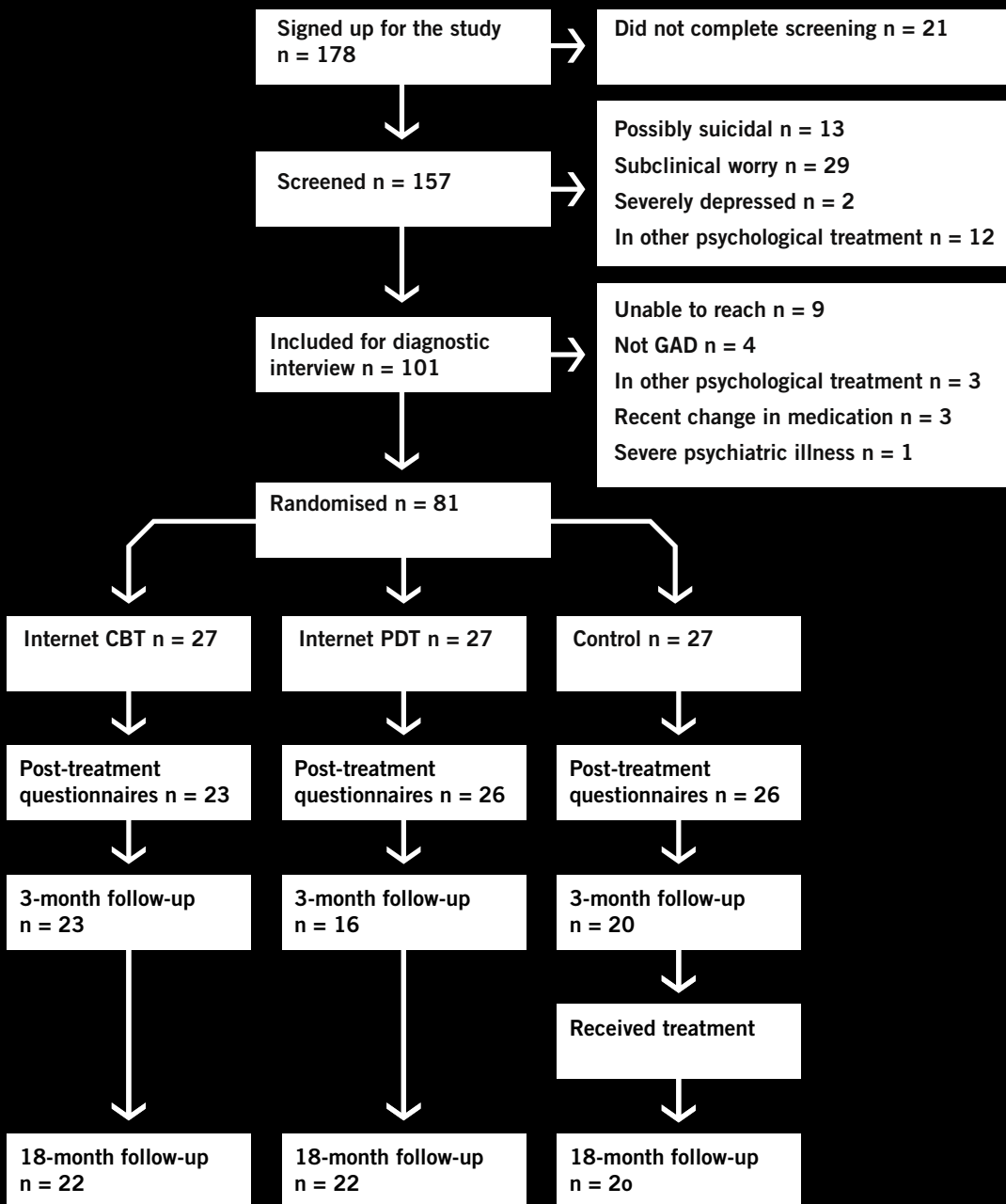


Figure 1. Flow chart of participants through the study.

Clinician administered measures

Psychiatric diagnoses were assessed using the Structured Clinical Interview for DSM Disorders (SCID I) (First et al., 1997)). Global functioning was measured by the Clinical Global Impressions (CGI) scale, a seven-item interview list for assessing clinical improvement (Guy, 1976).

PROCEDURE

Assessment points and randomisation

A telephone interview was conducted with each subject before and after the treatment, as well as at the 18-month follow-up, but not at the 3-month follow-up where only the self-report measures were used. The interview included the administration of the SCID-I (First et al., 1997). Those subjects assigned to the control group were told that they were being placed on a waiting list and that they would receive treatment after a 3-month waiting period. At post-treatment and follow-up, an estimation of the degree of global improvement for each participant was done using the CGI improvement scale (Guy, 1976). After the treatment period, the interviewers were blinded concerning participant status (i.e., as to which treatment group they had belonged).

Three months after the end of the initial treatment period, all self-report measures were administered again, and subsequently the control group received the CBT treatment. An 18-month follow-up was conducted with four self-report inventories, and a blinded telephone interview was conducted by a trained interviewer (who had not served as therapist nor previously worked in the project). Questions regarding change in medication and/or seeking of additional treatment were asked at post-test and at follow-up.

The randomisation procedure was managed by an external person who was not involved in the study. A true random number service (www.random.org) was used to ensure complete randomness. Randomisation was done after inclusion wherein participants were randomised to the three groups with no stratification.

INTERVENTIONS

Internet-based psychodynamic therapy

The Internet-based PDT used in this study was based on the method detailed in the book *Make the Leap* (Silverberg, 2005), which was translated into Swedish and

adapted to a format suitable for an Internet-delivered self-help programme. Make the Leap is a self-help book based on psychodynamic principles. The reader was guided through a programme called SUBGAP, which stands for (1) Seeing unconscious patterns that contribute to emotional difficulties, (2) Understanding these patterns, (3) Breaking such unhelpful patterns, and (4) Guarding Against Patterns and/or relapses in the future.

The treatment consisted of eight text-based treatment modules/chapters delivered on a weekly basis, wherein each module ended with a series of discussion themes about which the participants were encouraged to write and send such writings to the guiding therapist using a confidentiality-maintaining encrypted communication platform. The main focus for the therapists was to guide the participants through the self-help programme by giving feedback and encouragement in response to the weekly communications. No formal homework assignments were given. Supervision was provided by a certified training and supervising psychoanalyst from a post-degree psychoanalytic institute programme. Supervision was conducted via two-way videoconference over the Internet. In total, there were seven supervision sessions, each approximately 90 minutes in length. Treatment support for subjects in this arm of the study was provided by three therapists who were in their final year of a five-year clinical psychology programme and by one licensed psychologist. All had been trained in psychodynamic treatment, including supervised case experience conducting psychodynamic therapy.

The treatment modules varied in length between 11 and 17 pages each, with the entire treatment material consisting of 111 pages for the subjects to read. Briefly, the treatment modules covered: 1) introduction to the SUBGAP method; 2) systematic practice in discovering one's own unconscious patterns; 3) understanding patterns from an historical perspective of looking at one's life; 4) different methods that can be used to break the patterns that one discovers; 5) minimizing the risk of falling back into one's old and unproductive patterns; 6) applying the knowledge about patterns to solve working life dilemmas; 7) applying knowledge about patterns with a focus on improving personal relationships; and 8) the relationship between unconscious patterns and anxiety/worry (which was an additional module written specifically for this GAD research). The average therapist time devoted to each client during the entire treatment period was $M = 113$ minutes ($SD = 41$). Feedback was given as soon as possible, most often within 24 hours. Except for the weekly online treatment contacts and diagnostic procedures, no other contact took place between the therapists and participants.

Internet-based cognitive behavioural therapy

The Internet-based CBT employed in this study utilized the treatment protocol developed by Paxling et al. (Chapter 2 of the present work). The treatment consisted of eight text-based treatment modules delivered on a weekly basis for eight weeks. The treatment modules covered 1) introduction to GAD and the treatment (psychoeducation); 2) step one of applied relaxation (Öst, 1987); 3) step two of applied relaxation, and worry time; 4) step three of applied relaxation, and cognitive restructuring; 5) step four of applied relaxation, cognitive distancing, and problem solving; 6) step five of applied relaxation, and worry exposure; 7) step six of applied relaxation, interpersonal problem solving (Borkovec et al., 2002), and sleep management; and 8) relapse prevention and maintenance of progress. In the different steps of applied relaxation, participants first learn the relaxation technique in 15 minute sessions (step one), then the duration of the relaxation is progressively shortened to 5-7 minutes (step two), 2-3 minutes (step three), 60-90 seconds (step four), and finally to 20-30 seconds (step five) before the relaxation is applied in everyday life (step six). Audio files with instructions for applied relaxation were available as downloads on the project website. All treatment modules were accompanied by homework assignments that participants submitted to the therapists on a weekly basis. Homework assignments had to be completed before a particular participant could start with the next module. The main focus for the therapists was to guide the participants through the self-help programme.

In total, five therapists provided the treatment for this group. Two were licensed psychologists who had previous experience guiding Internet treatment for GAD, and three were psychology students in their final year. The therapists were supervised by a senior researcher and licensed CBT therapist. In total, four supervision sessions were given of approximately 90 minutes each. Feedback from the therapist was provided to the participants on a weekly basis in association with the homework assignments. In addition, occasional reminders were sent. The average therapist time devoted to each client during the overall treatment period was $M = 92$ minutes ($SD = 61$). Each week the participants sent in reports on their progress. Participants had the option to include in these reports questions directly addressed to the therapist. Feedback was given as soon as possible, most often within 24 hours. Except for the weekly online treatment contact and diagnostic procedures, no other contact took place between the therapists and participants.

Statistical analysis

Statistical analyses were conducted using the PASW version 18.0 (SPSS Inc., Chicago). In order to account for dropouts without assuming that the first measurement was stable (i.e., the last observation carried forward assumption), we used a mixed effects models approach with full information maximum likelihood estimation (Gueorguieva & Krystal, 2004). Mixed effects models are able to accommodate missing data and integrate time-varying factors. Mixed models analyses have been recommended as a way to handle intention-to-treat data (Brown & Prescott, 1999). We made the assumption that the missing data could be handled as missing at random. A first-order autoregressive covariance structure was used for the immediate effects, and an unstructured covariance matrix structure was employed for the long-term follow-up data.

Effect sizes are presented as Cohen's *d* (Cohen, 1988), defined as the difference between the means of the two groups divided by the pooled standard deviation. Within-group effect sizes are based on the pooled SDs; between-group effect sizes are based on the post-treatment means; and all effect sizes are based on collected completer's data (i.e., rather than any replacements).

Chi-square was used to test for differences between the groups on categorical outcomes. To be defined as clinically recovered, a participant had to fulfil the criterion for reliable change index (difference between baseline and post/follow-up measure divided by pooled standard deviation is larger than 1.96) and had to have a post-treatment score at least two standard deviations below the group mean at pre-treatment (Jacobson & Truax, 1991). In the intention-to-treat analyses of the categorical data, we regarded dropouts as non-responders.

We made a power calculation based on the comparison between the active treatments and the control group. The study was sufficiently powered ($\alpha = 0.05$) to yield 80% power to detect an effect size of $d = 0.80$. However, the comparison between the two active treatments was not sufficiently powered, given the large samples needed to test for non-inferiority (Piaggio, Elbourne, Altman, Pocock, & Evans, 2006).

Table 1.
Characteristics of the participants at pre-treatment

Variable		Internet-based CBT	Internet-based PDT	Control condition
		n = 27	n = 27	n = 27
Gender	Women	20	21	21
	Men	7	6	6
Age	Mean age (SD)	44.4 (12.8)	36.4 (9.7)	39.6 (13.7)
	Min-max	22-66	24-60	19-65
GAD	Mean duration, years (SD)	20.5 (11.6)	19.3 (12.3)	19.6 (16.5)
	Mean age at onset (SD)	23.8 (14.1)	17.2 (11.5)	20.0 (13.1)
Occupational status	Working	14	17	19
	Sick leave, part or full time	10	8	4
	Other	3	2	4
Education post upper secondary (e.g. university)		64.8%	59.1%	76.1%
Civil status	Married/relationship with children	13	12	12
	Married/relationship without children	5	5	3
	In relationship, living apart	2	1	1
	Single with children	3	2	1
	Single without children	2	5	6
	Widow/widower	1	1	1
	Living with parents	0	0	2
	Other	1	1	1
Psychotherapy	Previous	19	21	15
	Never	8	5	12
Medication for psychiatric illness	Ongoing	8	12	6
	Previous	13	8	11
	Never	6	6	10

Table 2.

Axis-1 comorbidity according to the DSM-IV for each group

Variable	Internet-based CBT	Internet-based PDT	Control condition
	n = 27	n = 27	n = 27
Social phobia	6 (22.2%)	7 (25.9%)	5 (18.5%)
Panic disorder	7 (25.9%)	3 (11.1%)	6 (22.2%)
OCD	0 (0.0%)	2 (7.4)	1 (3.7%)
Current depressive episode	10 (37.0%)	4 (14.8%)	5 (18.5%)
Previous depressive episode	16 (59.3%)	12 (44.4%)	12 (44.4%)
≥ 1 other axis-1 diagnosis	16 (59.3%)	13 (48.1%)	14 (51.9%)

Table 3.

Maintenance of effects using mixed models with “unstructured” as covariance.

Measure	Time		CBT		PDT		Time (p)	Interaction (p)	Pairwise comparison
Generalized Anxiety Disorder Questionnaire-IV									
	Pre	M (SD)	10.4	1.6	10.9	1.6	.000	.104	CBT=PDT
		SE		0.2		0.2			
	Post	M (SD)	8.6	4.4	8.3	4.2			CBT=PDT
		SE		0.6		0.6			
	3 mo	M (SD)	6.0	6.0	5.7	6.6			CBT=PDT
		SE		0.8		0.9			
	18 mo	M (SD)	5.8	1.9	5.2	1.9			CBT=PDT
		SE		0.3		0.3			
Penn State Worry Questionnaire									
	Pre	M (SD)	67.9	8.3	69.7	8.3	.000	.939	CBT=PDT
		SE		1.1		1.1			
	Post	M (SD)	60.8	13.2	61.9	12.6			CBT=PDT
		SE		1.8		1.7			

<i>Measure</i>	<i>Time</i>		<i>CBT</i>		<i>PDT</i>		<i>Time (p)</i>	<i>Interaction (p)</i>	<i>Pairwise comparison</i>
	3 mo	M (SD)	57.0	17.7	58.7	18.9			CBT=PDT
		SE		2.4		2.6			
	18 mo	M (SD)	51.0	17.5	53.8	17.3			CBT=PDT
		SE		2.4		2.4			
<i>Montgomery Åsberg Depression Rating Scale</i>									
	Pre	M (SD)	22.3	8.3	19.7	8.3	.000	.018	CBT=PDT
		SE		1.1		1.1			
	Post	M (SD)	13.5	12.1	16.0	11.5			CBT=PDT
		SE		1.6		1.6			
	3 mo	M (SD)	15.0	12.8	15.2	13.8			CBT=PDT
		SE		1.7		1.9			
	18 mo	M (SD)	9.9	13.7	16.0	13.6			CBT=PDT
		SE		1.9		1.8			
<i>Quality of Life Inventory</i>									
	Pre	M (SD)	0.6	2.3	0.8	2.3	.007	.328	CBT=PDT
		SE		0.3		0.3			
	Post	M (SD)	1.4	2.4	1.3	2.4			CBT=PDT
		SE		0.3		0.3			
	3 mo	M (SD)	0.9	2.7	1.7	3.1			CBT=PDT
		SE		0.4		0.4			
	18 mo	M (SD)	1.6	2.8	1.3	2.8			CBT=PDT
		SE		0.4		0.4			

RESULTS

Patient characteristics, attrition and adherence

Characteristics of the participants included are presented in Table 1. The three groups did not differ on any pre-treatment characteristic. In Table 2 we present data on comorbidity. Loss of data and participant flow are presented in Figure 1. The average number of completed modules in Internet-based PDT was 5.9 (SD = 2.2) and in Internet-based CBT, 5.1 (SD = 2.5).

Treatment effectiveness - primary outcome measure (PSWQ)

Observed means and Cohen's d within-group effect sizes are presented in Table 3. On the PSWQ there was a moderate-to-large between-group effect size between Internet-based PDT and the control condition at 3 months ($d = 0.64$; 95% CI [-0.05, 1.30]), and similarly for the Internet-based CBT versus control condition ($d = 0.76$; CI [0.10 – 1.33]). A post-hoc analysis showed that the difference between the two treatments was small and statistically insignificant ($d = 0.14$ CI [-0.50, 0.78]).

When conforming to the criteria of clinically significant improvement as defined by Jacobson and Truax (Jacobson & Truax, 1991) on the PSWQ, we find that the proportion of participants at 3 months who made a significant change was 8/27 (29.6%; 95% CI [11.2%, 48.0%]) for the PDT group, 12/27 (44.4%; 95% CI [24.4%, 64.5%]) for the CBT group, and 2/27 (7.4%; 95% CI [-0.3%, 17.9%]) for the control group. This difference was significant by means of chi-square $\chi(2) = 9.48, p = .009$. On this primary measure, the difference between PDT and control group was significant, $p = .04$, as was the difference between CBT and the control condition, $p = .002$. Post-hoc analyses indicated that the difference between the two treatments, PDT and CBT, was not significant, $p = .26$, all by chi-square.

Mixed models (AR1) analysis with estimated means accounting for missing data and SDs for 81 participants was conducted for the pre-, post- and 3-month data points. This analysis did not reveal a significant interaction ($p = .21$).

In a second post-hoc mixed models analysis, we included the 18-month follow-up data and excluded the control group data (Table 4, appendix). This revealed a significant effect of time ($p < .0001$), but no interaction effect ($p = .94$).

Treatment effectiveness – secondary outcome measures

Data from the secondary measures are provided in Table 4 (appendix to this chapter), including within-group effect sizes. Data were analysed in a similar manner as for the primary outcome measure.

For the GAD-Q IV, the effect size between Internet-based PDT and the control condition was large at 3 months ($d = 1.14$; CI [0.40, 1.82]), and similarly for the Internet-based CBT versus control condition ($d = 0.87$; CI [0.23, 1.48]) at 3 months. The difference between the two treatments was small ($d = -0.13$ CI [0.51, 0.77]). We found a significant interaction in the mixed models (AR1) analysis ($p = .003$), with pairwise comparisons showing that the two active treatments were superior to the waiting list group. For the 18-month follow-up data, there was a significant time effect ($p < .0001$), but no differences between Internet-based PDT and Internet-based CBT on this measure.

Data on self-reported MADRS-S showed large within-group effect sizes (Table 4). The between-group effect sizes showed a slight superiority at 3 months for Internet-based PDT versus the control condition ($d = 0.68$; CI [0.01, 1.34]), but no such between-group effect was seen for Internet-based CBT versus the control condition ($d = -0.18$; CI [-0.77, 0.43]). Internet-based PDT was not better than the CBT condition at 3 months ($d = -0.39$; CI [-0.22, 0.99]) according to post-hoc analysis. Mixed models (AR1) analysis did not show an interaction at 3 months. Post-hoc analysis indicates that for the 18-month data, where PDT and CBT were compared, we did find an interaction ($p = .02$), with pairwise contrasts showing a difference in favour of Internet-based CBT at 18-month follow-up.

As a measure of quality of life, we used the QOLI. Within-group effect sizes varied, and the between-group effect sizes were non-significantly in favour of Internet-based PDT at 3 months ($d = 0.51$, CI [-0.17, 1.16]) when compared with controls, and when compared with Internet-based CBT ($d = 0.16$, CI [0.03, 1.35]). CBT did not differ from the control condition at 3 months ($d = 0.15$). Mixed models showed no interaction at 3 months, and when we analysed the 18-month data, there were no interactions. There was, however, a within-group effect ($p = .007$).

Data for the STAI-S, STAI-T, BAI and BDI largely overlapped with the other measures (i.e., GAD-Q IV). Means and effect sizes including confidence intervals are presented in Table 4 (in the appendix). There was no statistical interaction on any of these measures.

Table 4.

Means, SDs and within-group effect sizes (Cohen's d) including confidence intervals for primary and secondary outcome measures at pre-, post-, 3- and 18-month follow-up.

	CBT		PDT		Control	
	n	M (SD)	n	M (SD)	n	M (SD)
<i>Penn State Worry Questionnaire (16-80)</i>						
Pre	27	67.89 (6.19)	27	69.74 (5.56)	27	68.52 (6.24)
Post	23	60.78 (9.83)	26	61.88 (7.73)	26	62.88 (9.39)
3-month	23	56.48 (12.17)	16	58.13 (10.83)	20	64.05 (7.81)
18-month n = 22	22	50.23 (11.82)	22	53.14 (10.89)	20	53.10 (10.70)
ES (pre-post, d, 95% CI)		.87 (CI: 0.25 – 1.46)		1.16 (CI: 0.56 – 1.73)		.72 (CI: 0.13 – 1.25)
ES (pre-3m)		1.18 (CI: 0.53 – 1.78)		1.35 (CI: 0.55 – 2.08)		.64 (CI: -0.01– 1.26)
ES (pre-18m)		1.88 (CI: 1.14 – 2.55)		1.92 (CI: 1.17 – 2.69)		1.76 (CI: 1.00 – 2.75)
<i>Generalized Anxiety Disorder Questionnaire IV (0-12)</i>						
Pre	27	10.44 (1.09)	27	10.95 (1.14)	27	10.82 (1.20)
Post	23	8.53 (2.37)	26	8.34 (3.31)	26	8.52 (3.70)
3-month	23	6.04 (4.12)	16	5.51 (3.70)	20	9.10 (2.66)
18-month	22	5.82 (1.19)	22	5.16 (1.19)	20	5.04 (1.35)
ES (pre-post)		1.04 (CI: 0.40 – 1.63)		1.05 (CI: 0.46 – 1.62)		0.84 (CI: 0.26 – 1.39)
ES (pre-3m)		1.46 (CI: 0.79 – 2.08)		1.99 (CI: 1.10 – 2.78)		.83 (CI: 0.17 – 1.46)
ES (pre-18m)		4.05 (CI: 2.96 – 5.00)		4.97 (CI: 3.70 – 6.06)		4.53 (CI: 3.28 – 5.59)
<i>Montgomery Åsberg Depression Rating Scale (0-54)</i>						
Pre	27	22.30 (6.52)	27	19.74 (5.11)	27	21.41 (5.99)
Post	23	12.87 (6.35)	26	16.12 (8.93)	26	17.15 (7.92)
3-month	23	14.91 (8.72)	16	11.69 (5.87)	20	16.35 (7.61)
18-month	22	9.32 (6.88)	22	15.36 (10.48)	20	11.65 (7.53)
ES (pre-post)		1.47 (CI: 0.79 – 2.09)		.50 (CI: -0.06 – 1.04)		0.61 (CI: 0.04 – 1.15)
ES (pre-3m)		0.96 (CI: 0.33 – 1.55)		1.46 (CI: 0.65 – 2.20)		0.74 (CI: 0.08 – 1.36)
ES (pre-18m)		1.94(CI: 1.19 – 2.61)		0.53 (CI: -0.08 – 1.12)		1.43 (CI: 0.71 – 2.10)

		<i>CBT</i>		<i>PDT</i>		<i>Control</i>
	n	M (SD)	n	M (SD)	n	M (SD)
<i>Quality of Life Inventory (-6 to 6)</i>						
Pre	27	0.57 (1.75)	27	0.80 (1.54)	27	0.67 (1.43)
Post	23	1.64 (1.50)	26	1.23 (1.65)	26	1.00 (1.56)
3-month	23	1.06 (2.01)	16	2.01 (1.35)	20	1.28 (1.50)
18-month	22	1.62 (2.00)	22	1.32 (1.59)	20	1.63 (1.32)
ES (pre-post)		-0.66 (CI: -1.25 – 0.05)		-0.27 (CI: -0.81 – 0.28)		-0.22 (CI: -0.76 – 0.33)
ES (pre-3m)		-0.26 (CI: -0.84 – 0.32)		-0.84 (CI: -1.54 – -0.09)		-0.42 (CI: -1.03 – 0.22)
ES (pre-18m)		-0.56 (CI: -1.14 – 0.05)		-0.33 (CI: -1.02 – 0.37)		-0.70 (CI: -1.32 – 0.05)
<i>State-Trait Anxiety Inventory –state (20-80)</i>						
Pre	27	63.11 (9.45)	27	59.59 (6.79)	27	61.63 (9.06)
Post	23	50.13 (11.36)	26	50.27 (9.52)	26	55.96 (12.00)
3-month	23	52.22 (13.43)	16	47.69 (11.66)	20	56.90 (9.41)
ES (pre-post)		1.24 (CI: 0.59 – 1.85)		1.13 (CI: 0.53 – 1.69)		0.53 (CI: -0.03 – 1.08)
ES (pre-3m)		0.95 (CI: 0.41 – 1.64)		1.25 (CI: 0.46 – 1.97)		0.51 (CI: -0.13 – 1.13)
<i>State-Trait Anxiety Inventory – trait (20-80)</i>						
Pre	27	58.74 (7.12)	27	59.96 (5.85)	27	59.89 (7.69)
Post	23	50.17 (8.34)	26	54.12 (8.07)	26	55.00 (8.90)
3-month	23	51.30 (11.82)	16	48.13 (9.54)	20	53.90 (8.66)
ES (pre-post)		1.10 (CI: 0.46 – 1.70)		0.83 (CI: 0.25 – 1.38)		0.59 (CI: 0.02 – 1.13)
ES (pre-3m)		0.76 (CI: 0.15 – 1.35)		1.49 (CI: 0.68 – 2.24)		0.73 (CI: 0.08 – 1.36)
<i>Beck Anxiety Inventory (0-63)</i>						
Pre	27	24.30 (9.10)	27	25.26 (8.59)	27	23.70 (10.61)
Post	23	15.09 (6.99)	26	15.88 (8.87)	26	19.52 (10.34)
3-month	23	16.65 (12.32)	16	13.13 (8.88)	20	19.30 (11.67)
ES (pre-post)		1.14 (CI: 0.49 – 1.74)		1.07 (CI: 0.48 – 1.64)		0.40 (CI: -0.16 – 0.94)
ES (pre-3m)		0.71 (CI: 0.10 – 1.29)		1.39 (CI: 0.59 – 2.12)		0.39 (CI: -0.24 – 1.01)

		<i>CBT</i>		<i>PDT</i>		<i>Control</i>
	n	M (SD)	n	M (SD)	n	M (SD)
<i>Beck Depression Inventory (0-63)</i>						
Pre	27	18.89 (8.59)	27	18.30 (6.67)	27	17.33 (7.18)
Post	23	9.35 (5.57)	26	11.72 (8.23)	26	13.60 (8.57)
3-month	23	12.26 (8.59)	16	7.69 (4.59)	20	14.10 (9.25)
ES (pre-post)		1.32 (CI: 0.66 –1.93)		0.88 (CI: 0.30 –1.43)		0.47 (CI: -0.09 –1.02)
ES (pre-3m)		0.77 (CI: 0.17 –1.36)		1.85 (CI: 0.98 –2.63)		0.39 (CI: -0.24 –1.01)

Note: By the time of the 18 month follow up, the control group had received the same treatment as the Internet-based CBT group.

Clinical global functioning

All available participants were assessed in a blinded interview at post-treatment and at 18-month follow-up. The distribution of the participants in terms of clinical global improvement from baseline was: Internet-based PDT group 4.5% and 4.5% very much improved, 36.4% and 45.5% much improved, 31.8% and 31.8% minimally improved, 22.7% and 13.6% showed no change, and 4.5% and 4.5% as minimally worse. For the Internet-based CBT group, 35% and 16.7% were very much improved for the post-treatment and 18-months, respectively. In the same group, 10% and 50% were rated as much improved, 35% and 16.7% as minimally improved, 10% and 12.5% showed no change, and 0% and 4.2% were minimally worse. For the control condition, which had received the Internet-based CBT treatment, the figures at 18 months were 0% and 14.3% very much improved, 0% and 42.9% much improved, 32.0% and 28.6% minimally improved, 48% and 9.5% showed no change, and finally, 8% and 4.8% were worse. Given the small number of subjects in each group, it was not regarded feasible to test for statistical significance.

Diagnostic status and clinically significant change on completers data

At post-treatment SCID-interviews, the percentage of participants who still fulfilled the GAD diagnosis was 55.6% for the Internet-based PDT group, 74.1% for the Internet-based CBT group, and 85.1% for the control condition [$\chi(2) = 6.5, p = .05$]. At 18-month follow-up, this had changed to 27.3%, 33.3%, and 38.1% for the Internet-based PDT, Internet-based CBT and control condition, respectively (by which time the controls had received their CBT treatment). Table 5 displays the proportion of participants reaching the criteria of being clinically recovered – where this means that they had a reliable change and reached the 2 SD criterion of clinically significant improvement as defined by Jacobson and Truax (Jacobson & Truax, 1991).

DISCUSSION

The present study is probably the first to demonstrate that a psychodynamically-informed guided self-help treatment can be delivered over the Internet and that it can be as effective as Internet-based CBT-informed guided self-help in the treatment of GAD. Both treatments demonstrated moderate to large within-group effect sizes on the primary outcome measure of worry, but were only marginally better than the waiting list group and did not prove to be more effective when intention-to-treat analyses were conducted (mixed models). The overall finding, however, was that the two active treatments were similar in terms of outcome on both primary and secondary

Table 5.

Proportion of participants clinically recovered, that is, having had a reliable change and having reached the 2 SD criterion of clinically significant improvement as defined by Jacobson and Truax (1991).

	ICBT	IPDT	Control
PSWQ			
Post-treatment	26.1 % (6/23)	15.4 % (4/26)	15.4 % (4/26)
3-month follow-up	52.2 % (12/23)	50.0 % (8/16)	10.0 % (2/20)
1-year follow-up GAD-Q IV	54.5 % (12/22)	68.2 % (15/22)	60.0 % (12/20)
Post-treatment	34.8 % (8/23)	34.6 % (9/26)	42.3 % (11/26)
3-month follow-up	47.8 % (11/23)	68.8 % (11/16)	25.0 % (5/20)
1-year follow-up MADRS-S	100.0 % (22/22)	95.5 % (21/22)	95.0 % (19/20)
Post-treatment	43.5 % (10/23)	11.5 % (3/26)	15.4 % (4/26)
3-month follow-up	30.4 % (7/23)	31.3 % (5/16)	30.0 % (6/20)
1-year follow-up QOLI	59.1 % (13/22)	27.3 % (6/22)	50.0 % (10/20)
Post-treatment	0.0 % (0/23)	0.0 % (0/26)	0.0 % (0/26)
3-month follow-up	0.0 % (0/23)	6.3 % (1/16)	0.0 % (0/20)
1-year follow-up	4.5 % (1/22)	4.5 % (1/22)	0.0 % (0/20)

Note: The control group had received the same treatment as the ICBT group at the 18 month follow-up.

outcomes. The sample was self-recruited and displayed substantial comorbidity, as is commonly seen in studies on GAD (Tyrer & Baldwin, 2006). While a substantial proportion improved and maintained the improvement at 18-month follow-up, there were other participants who remained symptomatic.

The CBT arm of the present study replicates previous guided Internet trials on GAD in which Internet-based CBT had been found to be effective (Draper et al., 2008; Paxling et al., 2011; Robinson et al., 2010; Titov, Andrews, Robinson, et al., 2009), with largely similar within-group effect sizes on the PSWQ. All previous trials have been based on CBT protocols, and therapists have most likely been less skilled (i.e., students) and less experienced than therapists in previous face-to-face trials on GAD (Borkovec et al., 2002), making comparisons to face-to-face GAD treatment studies

difficult at this point. To our knowledge, there are no direct comparisons between Internet-based CBT and face-to-face CBT for GAD, but previous studies on panic disorder (Bergström et al., 2010) and social anxiety disorder (Hedman et al., 2011) have yielded equivalent outcomes for the two treatment formats.

This is probably the first study to deliver a psychodynamically-informed treatment over the Internet, which makes comparison with previous PDT trials (Durham et al., 1994) difficult. However, there are a few PDT trials on GAD, and one recent controlled study directly compared PDT and CBT, showing large within-group effect sizes for both treatments (Leichsenring et al., 2009).

Although the SUBGAP treatment tested in our trial has much in common with the treatment tested in the Leichsenring et al. (2009) trial in terms of shared underlying psychodynamic principles, in the conduct of treatment there were clear differences due to the SUBGAP's self-administered guided internet delivery.

The treatment in the Leichsenring et al. study was based upon the Crits-Christoph et al. (Crits-Christoph, Connolly Gibbons, & Crits-Christoph, 2004) manual which was derived from Luborsky's Supportive-Expressive (S-E) short-term psychodynamic psychotherapy (Luborsky, 1984). Certainly, S-E treatment shares some similarities in underlying principles, most especially the shared emphasis on gaining insight into a psychodynamic understanding that helps facilitate change, as well as maintaining the psychodynamic principles that the patient's difficulties are perpetuated if such underlying dynamics remain hidden and, additionally, that the human mind, with its unconscious aspect, can keep these dynamics hidden unless a properly guided investigation is conducted. In carrying out the methods, however, these two treatments have significant differences. The SUBGAP method is self-administered by means of the subject reading the modules of educational material and augmented via coaching the subject through the text, while the S-E method, on the other hand, is exclusively therapist-driven. The S-E method is heavily dependent upon the therapist's in-session interpretations to the subject and is reliant on the transference relationship that happens in the therapy room as one focus for interpretation. By necessity, guided Internet-based treatment requires that the treatment is presented clearly in text, making the therapist less important – also attested to by small to non-existent therapist effects (Almlöv et al., 2011). In our trial, therapists were supervised by experienced clinicians, and some therapeutic alliance was formed, albeit at a distance, between therapist and client, which is in line with previous Internet trials (Knaevelsrud & Maercker,

2007). In addition, there was little overlap between the two treatments, as the PDT did not include homework assignments, relaxation, worry control or any typical CBT ingredients.

It may be an interesting aside to note for the purposes of future investigation that, in one regard, there may be some overlap between psychodynamic and CBT procedures in general. In the PDT treatment there was a focus on discovering unconscious patterns – on making the “unconscious conscious”, consistent with the cornerstones of psychodynamic theory – and, through such insight and through an understanding of a psychodynamic pattern’s connection to a person’s history (another way of discussing the “repetition compulsion”) and/or with his or her underlying emotions or motives, to initiate a change in such patterns. Similarly, in the CBT condition there was a focus on identifying and challenging habitual cycles of negative thought through the processes of cognitive restructuring and/or cognitive diffusion.

One could certainly say that the psychodynamic approach to recognising and working through unproductive patterns and the cognitive behavioural approach to restructuring negative thoughts could be seen as sharing some similarities that stem back to the crossroads at which CBT was conceived, and this similarity could be reflective of the psychodynamic approaches in which some of the fathers of CBT were trained. Nevertheless, regardless of such philosophically overarching issues, it is probably safest to regard our present study as a proof-of-concept trial and recommend that the SUBGAP treatment, which represents the first well-manualised and research-friendly form of psychodynamic self-guided treatment, be tested further given the fact that the literature on Internet-based psychological treatment is dominated by CBT approaches (Andersson, 2009).

This study has several limitations. First, although we did have a control group, it was not an active control group with a placebo condition (such as one that emulated the module model but did not deliver a treatment), the presence of which would have further enhanced the strength of the research design. Oddly, the waiting-list group did show some marginal improvements during the waiting period, which may be related to the extensive test procedures both in terms of online questionnaires and telephone interviews before and after the treatment period and non-specific helpful effects between interviewer and subject. In previous internet trials on GAD control groups, however, subjects have not improved at all during the waiting period (See chapter 2; Titov, Andrews, Robinson, et al., 2009). In addition, because we offered treatment to the waiting list control group after the waiting period, we had no control group at the 18-month follow-up.

Second, the dropout rate was substantial in the trial, and, in particular, the low response rate at 3-month follow-up for the PDT group limits the value of the findings. We re-analyzed all data using a mixed models approach in which all available data points were used, and those analyses showed clear within-group effects but no significant interactions on our primary measure. However, when a mixed models approach was applied to our secondary measures, there was a significant interaction for group by time that showed both treatments to be superior to the control group when looking at improvement over time in the symptoms of GAD, and there was no significant difference between the two treatments. Hence, with these mixed results, weak for our primary measure and within significance for a secondary measure, the intention-to-treat analyses could not make a strong statement about the superiority of the two active treatments over the control condition. While this finding seems to be in stark contrast to the within-group effect sizes for the observed means (a finding that largely replicates previous trials on Internet treatment for GAD), significance can certainly be found at the less stringent ($p < .05$) level of significance, supporting the effect of the active treatments over the control condition.

Third, the external validity of the findings remains as yet untested, as we recruited participants via newspaper advertisement rather than from a treatment clinic. There are prior studies showing that the effects of Internet-based CBT are generalizable to more customary clinical settings (Aydos, Titov, & Andrews, 2009; Bergström et al., 2009; Bergström et al., 2010), and although there is no reason to believe that PDT would be any less generalizable thereto, at the present time the question of such generalizability to regular clinical settings for Internet-based PDT remains to be tested in future studies. For example, as seen in Table 1, in the present study, a large proportion of the subjects had completed higher education following upper secondary school (i.e., after 18 or 19 years of age) and this may not hold true if conducted in a clinical setting. On the other hand, though not recruited from a clinical setting, the sample recruited in the present study was certainly characterized by a high level of comorbidity and showed scores on the symptom specific measures that did not indicate any lower level of distress than would be expected from a sample recruited in a clinical setting.

It is also interesting to note that, on the secondary measures designed to shed light on the change in GAD symptoms, there is a significant interaction between group condition and time – showing a clear benefit to both treatments over the waiting list condition and yielding no significant difference between the two treatments. While none of the other secondary outcome measures are significant, it is encouraging, in

terms of including PDT in future studies of Internet delivery, that the other secondary measures were all non-significantly in favour of Internet-based PDT when compared with Internet-based CBT and controls. Therefore, it is certainly recommended that PDT be included as a treatment condition in further studies into Internet-delivery of self-guided treatment and that such studies utilize a larger number of subjects and an active (placebo) control group. Additionally, it could be argued that change in GAD symptoms might be better considered, in future studies of Internet-delivered treatment of GAD, as a primary rather than secondary measure of treatment effects when studying GAD.

In conclusion, this study – possibly the first study of its kind for guided self-administered psychodynamic treatment – opens up treatment possibilities and accessibility by suggesting that psychodynamic treatment approaches may be transferred to the guided self-help format and delivered via the Internet. Given the expanding accessibility of the Internet across the world, and in light of the continuing popularity of psychodynamic treatment, our findings may expand the field of future possibilities for Internet-delivered treatment approaches beyond those that are CBT-based.

CHAPTER 5

*Therapist behaviours in Internet-delivered cognitive behaviour therapy:
Analyses of e-mail correspondence in the treatment of
generalized anxiety disorder*

Paxling, B., Lundgren, S., Norman, A., Almlöv, J., Carlbring, P., Cuijpers, P., & Andersson, G. (submitted). Therapist behaviours in Internet-delivered cognitive behaviour therapy: Analyses of e-mail correspondence in the treatment of generalized anxiety disorder.

ABSTRACT

BACKGROUND: Internet-delivered cognitive behaviour therapy (iCBT) has been found to be an effective way to disseminate psychological treatment, and support given by a therapist seems to be important in order to achieve good outcomes. Little is known about what the therapists actually do when they provide support in iCBT and whether their behaviour influences treatment outcome.

AIMS: This study addressed the content of therapist e-mails in guided iCBT for generalized anxiety disorder.

METHODS: We examined 490 e-mails from 3 therapists providing support to 44 patients who participated in a controlled trial on iCBT for generalized anxiety disorder.

RESULTS: Through content analysis of the written correspondence, eight distinguishable therapist behaviours were derived: deadline flexibility, task reinforcement, alliance bolstering, task prompting, psychoeducation, self disclosure, self-efficacy shaping, and empathetic utterances. We found that task reinforcement, task prompting, self-efficacy shaping and empathetic utterances correlated with module completion. Deadline flexibility was negatively associated with outcome and task reinforcement positively correlated with changes on the Penn State Worry Questionnaire.

CONCLUSIONS: Different types of therapist behaviours can be identified in iCBT, and though many of these behaviours are correlated to each other, different behaviours have an impact on change in symptoms and module completion.

INTRODUCTION

Therapist factors have been recognized in the literature as being important for the outcome of psychological treatments (Beutler et al., 2004). A commonly cited review estimated that therapeutic relationship and therapist factors explain almost as much as a third of the outcome in psychotherapy; according to the review, this is twice as much as can be explained by specific therapeutic technique (Lambert & Barley, 2002). There has been some controversy regarding how to define the therapist factor. It can refer to a broad spectrum of characteristics and/or behaviours such as, therapist demographics and characteristics (gender, religion, age, personality, maturity), meta-talk in session, therapeutic alliance in the form of the therapeutic bond, and the tasks and goals involved in psychotherapy (Bordin, 1979). Moreover, therapist factors may interact with treatment techniques, making it somewhat difficult to distinguish specific factors from therapist factors in psychotherapy research (Baldwin et al., 2011). In particular, this may be the case in cognitive behaviour therapy (CBT), where it is common to discuss the role of competence and adherence (Trepka, Rees, Shapiro, Hardy, & Barkham, 2004; Waller, 2009) but less common to discuss non-specific factors. According to one estimate, about 5% of the outcome variability in clinical trials of psychotherapy can be attributed to the therapist factor (Wampold & Brown, 2005). Although some controversy exists concerning the importance of therapist factors, a growing amount of evidence can be found in support of this notion (Wampold, 2001).

Internet-delivered CBT (iCBT) has been found to be an effective treatment for a range of psychiatric conditions and health problems such as major depression, social phobia, panic disorder, tinnitus and insomnia (Andersson, 2009; Andrews et al., 2010; Barak, Hen, Boniel-Nissim, & Shapira, 2008). Not all Internet-delivered interventions are therapist-assisted, and the type of therapist input in iCBT varies greatly, from a very minimal approach in which the patient contacts the therapist when needed, to more extensive contacts over chat, telephone and/or e-mail (Barak, Klein, & Proudfoot, 2009). The importance of having contact with a therapist during an Internet-delivered treatment has been shown in meta-analyses (Andersson & Cuijpers, 2009; Spek et al., 2007), though in a recent controlled study on iCBT for social phobia, the group that did not have any therapist contact during the treatment phase did as well as the two guided treatment groups (Berger et al., 2011). This was also found in a previous controlled trial on social phobia (Furmark et al., 2009); however, these trials included contact with study coordinators, and in iCBT studies in which no contact at all is included, dropout rates tend to be large (Christensen, Griffiths, Groves, & Korten, 2006; Folvolden, Denisoff, Selby, Bagby, & Rudy, 2005). The frequency of the therapist contact has also been studied, and results so far show that

a higher frequency of contact has a positive effect on treatment outcome (see Chapter 6). Another issue concerns treatment completion, which is often much lower than intended in the treatment protocol. For example, by adding weekly telephone calls, adherence and module completion increased in a study in panic disorder (Carlbring et al., 2006), but in a controlled trial on iCBT for headache, telephone calls did not make a difference (Andersson, Lundström, & Ström, 2003). Furthermore, it is as yet unclear if the therapist in iCBT actually needs to be a trained therapist, as a group of patients with generalized anxiety disorder (GAD) who received technician-assisted iCBT had an outcome as good as those who received support from a clinician (Robinson, et al., 2010). This has also been shown for depressed patients (Titov, Andrews, Davies, et al., 2010) and social phobia (Titov, Andrews, Schwencke, et al., 2009). Research shows that therapist-patient alliance appears to form in online settings (Knaevelsrud & Maercker, 2007). A trial on depression showed that it did not seem to matter which therapist provided the treatment, as no differences in clinical outcome could be found between patients that received treatment from specific therapists (Almlöv et al., 2009), and this finding was replicated in a study on therapist effects in iCBT for anxiety disorders (Almlöv et al., 2011). Even if it makes less difference who guides iCBT, it may still be important what the therapist actually does. Despite a growing interest in therapist factors in iCBT, little is known about specific therapist behaviours and whether they have an impact on the treatment outcome. In fact, therapist input has mostly been described in terms of minutes devoted to each client (Marks, et al., 2007), and little attention has been paid to the actual content. In this study we investigated the actual content of the therapist contact in iCBT for GAD. The aims of this exploratory study were thus to identify therapist behaviours as conceptualised via quantitative text analyses and to investigate whether therapist behaviours in iCBT are interrelated to one another and/or related with adherence to the programme and/or outcome.

METHOD

Participants and treatment content

The sample of therapist behaviours was derived from the correspondence provided by three therapists delivering iCBT to 44 participants diagnosed with GAD in a randomised controlled trial (Chapter 2). Therapists were all males in their 30s who were in their last term of the clinical psychology programme (five year M.Sc. level). Demographics of patients treated by the three therapists are presented in Table 1.

The treatment consisted of eight online text modules that communicated CBT strategies to the participants in order to reduce their problems with excessive worrying (Chapter

2). The modules were intended to be completed on a weekly basis by the participants and included applied relaxation, worry exposure, problem solving, cognitive restructuring and other common treatment ingredients in the treatment of GAD (Sanderson & Rygh, 2004). Each module contained homework assignments, and at the end of each week the patient sent an e-mail to the therapist containing answers to questions about their progress in the programme and registration forms detailing their work in the programme, as well as any of their own questions to their therapists on potential problems that had occurred during the week. The therapists sent back an e-mail with

Table 1.

Demographic data for participants treated by the three therapists.

	<i>Therapist 1</i>	<i>Therapist 2</i>	<i>Therapist 3</i>
<i>n</i>	15	15	14
<i>Female gender</i>	87%	80%	79%
<i>Age (SD)</i>	40.9 (10.1)	41.3 (13.0)	37.7 (10.9)
<i>Duration of anxiety (SD)</i>	24.5 (15.2)	18.9 (12.5)	16.5 (10.7)

feedback on the homework and answers to questions and topics that the patient had written about. Sometimes communications also took place more often than once a week, at the participant’s own initiative. The therapists were given weekly clinical supervision by an experienced psychotherapist with previous experience in treatment of and research on generalized anxiety disorder. No specific therapist manual was used by the therapists, and their instruction was to foster adherence to the programme as much as possible, answer questions about the programme, and give recommendations on how the patients might use the taught techniques to their full advantage. For more details regarding the treatment trial, see Chapter 2. The protocol was approved by the local ethics committee.

Coding of therapist behaviour

Therapist e-mails to the patients were first analysed via a preliminary content analysis (Sittig, 2003). Initially, four e-mails were studied and five independent factors were derived from this small sample. Three additional coding entities were extrapolated after subsequent coding of another five e-mails. The total sample of e-mails exchanged

between therapist and patients was more than 1000, but e-mails from patients to therapists were not examined in this study, hence it is not possible to make any inferences about the immediate function of the therapist e-mails. The main reasons for not including patient behaviour were that we did not aim to analyse the interaction between therapist and patients and that we regarded patient behaviour as a separate question with large heterogeneity (some patients wrote long e-mails and some very short). The coding procedure resulted in eight coding categories which could be quantified in 490 e-mails written from therapists to patient. This study examined the topography of the therapists e-mail correspondence in order to explore if any patterns of therapist behaviour were stable and linked to others therapist behaviour patterns visible in the material. When all e-mails had been coded for the eight specified behaviour types, a frequency matrix was constructed. E-mails containing of more than one behaviour from the same category were represented twice or more in the data set if and only if the behaviours occurred in separate paragraphs. If behaviour entities were considered as repeated statements, they were conjoined into one unit of therapist behaviour. Behaviours were rated on a dichotomous scale on which a behaviour was either present (1) or not present (0).

Interrater reliability of the codings was tested by randomly selecting e-mails for 10 patients for whom all data were coded by two independent raters. The interrater reliability based on the coding instructions (see Table 1 for description) was very high, often reaching perfect agreement ($r = .99$). The only exception for which we did not find a significant correlation between the raters was for the variable psychoeducation ($r = .61$, $p = .06$).

Statistical analyses

Correlations between frequencies of the derived categories were computed via Spearman's rho in order to better understand the dispersion of the data set and to safeguard against any violations of statistical assumptions. The relationship between therapist behaviours and treatment outcome was measured by Penn State Worry Questionnaire (PSWQ) (Meyer et al., 1990).

RESULTS

Categories, reliability and intercorrelations

The eight therapist behaviours that were coded in the therapist e-mails were Deadline Flexibility, Task Reinforcement, Alliance Bolstering, Task Prompting, Psychoeducation, Self-disclosure, Self-efficacy Shaping and Empathetic Utterance. These behaviours are outlined and defined in Table 2. The total frequency of behaviours coded was 1595. The most common was task reinforcement with 640 markings (40%). Then followed self-efficacy shaping with 541 markings (34%), task reinforcement with 191 markings (12%), alliance bolstering with 93 markings (5%), psychoeducation with 48 markings (3%), empathetic utterance with 53 markings (3%), deadline flexibility with 25 markings (2%), and self-disclosure with 4 markings (0.2%).

Correlational analyses between the observed therapist behaviours show that deadline flexibility did not correlate with the other examined therapist behaviours. Behaviours categorized as empathetic utterances correlated weakly with self-efficacy shaping ($r = .33$). The behaviours task reinforcement, alliance bolstering, psychoeducation, self-disclosure and self-efficacy shaping were pairwise moderately correlated with each other ($r = .37$ to $.77$). Task prompting was correlated to task reinforcement, alliance bolstering, self-disclosure and self-efficacy shaping ($r = .37$ to $.70$) but not to the other behaviours. Correlations are presented in Table 3.

Table 2.

List of content analysis derived therapist behaviours in the study.

<i>Behaviour</i>	<i>Specification of behaviour</i>	<i>Examples</i>
<i>Deadline flexibility</i>	Behaviours that pertain to lenience from the therapist concerning deadlines for homework submissions and allowance of extra time to work with a given module.	You'll get another couple of days to finish the task You can wait with this week's task and continue with the one you're working on
<i>Task reinforcement</i>	Behaviours aimed at reinforcing assignments already completed by the participant.	Well done! You've described your worry thoughts in a good way
<i>Alliance bolstering</i>	Non-treatment specific writings that pertain to interest in the participant's life situation and care for his or her situation.	How nice that you've had a good week That must have been tough on you
<i>Task prompting</i>	Behaviours prompting the participant to work with a given homework assignment and explicit interest in future results of the participant's progress.	I'm looking forward to hearing from you during the work with the coming modules Good luck with the next task
<i>Psychoeducation</i>	Information about psychological processes, goals of the treatment and explanation of purpose and meaning of the work involved in the treatment	Worrying is part of generalized anxiety disorder
<i>Self-disclosure</i>	Therapist behaviours that describe circumstances in the therapist's own life situation that are similar or relevant to the patients situation.	I've also had trouble sleeping
<i>Self-efficacy shaping</i>	Behaviours that prompt and reinforce the participant to spontaneously engage in the health promoting behaviours they have learnt through the treatment.	The more you practice this, the more often you'll be able to notice the thoughts
<i>Empathetic utterance</i>	Writings that attempt to convey understanding and empathy for the participant's suffering, frustration or general life situation.	I understand that you I can see why you

Table 3.

Correlations (Spearman's r) between therapist online behaviours and mean number per patient (including SD).

Variables	2	3	4	5	6	7	8	M (SD)
1. Deadline flexibility	-.05	.11	.03	.08	-.15	-.03	-.02	0.6 (0.66)
2. Task reinforcement		.44**	.70**	.40**	.39*	.77**	.26	14.5 (9.5)
3. Alliance bolstering			.46**	.27	.31*	.43**	.28	2.1 (1.8)
4. Task prompting				.22	.37*	.53**	.27	4.3 (2.5)
5. Psychoeducation					.43**	.54**	.32*	1.1 (1.4)
6. Self-disclosure						.44**	.09	.09 (.29)
7. Self-efficacy shaping							.33*	12.3 (8.4)
8. Empathetic utterance								1.2 (1.5)

* = $p < 0.05$, ** = $p < 0.01$

Table 4.

Correlations (Spearman's r) between therapist behaviours and module completion and change scores on PSWQ.

Behaviours	Change scores PSWQ Spearman	Module completion Spearman
1. Deadline flexibility	-.37*	-.21
2. Task reinforcement	.41**	.70**
3. Alliance bolstering	.06	.28
4. Task prompting	.28	.42*
5. Psychoeducation	.01	.34
6. Self-disclosure	.05	.26
7. Self-efficacy shaping	.15	.64**
8. Empathetic utterance	-.06	.49**

* = $p < 0.05$, ** = $p < 0.01$

Therapist online behaviour and outcome

Correlations between module completion and therapist behaviours are presented in Table 4. Statistically significant correlations were found between module completion and task reinforcement, alliance bolstering, task prompting, self-efficacy shaping, and empathetic utterance. There was a significant negative relationship between module completion and deadline flexibility.

Two therapist behaviours were significantly associated with treatment outcome as measured by change scores on PSWQ: deadline flexibility ($r = -.37$), and task reinforcement ($r = .41$). Correlations for all factors are presented in Table 4.

DISCUSSION

In this study we coded e-mails sent from therapists in guided iCBT for GAD. A majority of the e-mails concerned task reinforcement and self-efficacy shaping, which basically can be regarded as positive reinforcement for progress and independence in relation to the treatment content and application of the treatment ingredients in real life. The results suggest that different types of therapist behaviours can be identified in iCBT and that many of these behaviours are significantly correlated to each other. Different types of therapist behaviours also had an impact on module completion. Perhaps most interesting is the observation that deadline flexibility had a negative influence on treatment outcome, which implies that we have identified a factor that is detrimental to outcome (Barlow, 2010). On the other hand, task reinforcement correlated with a positive outcome, and in relation to the psychotherapy literature in general, the correlations observed were not small ($r = -.37$ and $r = .41$). For example, the association between homework adherence and outcome (Kazantzis, Deane, & Ronan, 2000) and between the therapeutic alliance and outcome (Martin et al., 2000) are in the same region, and interestingly, therapist adherence and competence were recently found to correlate weakly with outcome (Webb, DeRubeis, & Barber, 2010).

The results of this study indicate that distinct therapist behaviours do exist in online therapy. These behaviours are sometimes correlated, but not to the extent that they are inseparable units but rather as an array of responses and antecedents directed at the patient. Bolstering the therapeutic alliance was significantly correlated to every other therapist behaviour except deadline flexibility, which suggests that focusing on the therapeutic alliance was one of the more commonly used therapist behaviours in the study. This is in line with a few studies in which therapeutic alliance has been studied

in iCBT (D'Arcy, Reynolds, Stiles, & Grohol, 2006; Knaevelsrud & Maercker, 2006). It appears in this study that flexibility in terms of lenience regarding deadlines could be associated with poor completion rates of the assigned text units as well as poorer treatment outcome. This type of therapist behaviour might, however, be an inevitable result of situations in which the patient simply does not adhere to the treatment protocol. Other behaviours that are directed at the practical aspects of working through an internet-delivered CBT programme are positively correlated with completion of the programme, but task reinforcement was the only identified therapist behaviour that had a significant impact on treatment outcome as measured by the PSWQ. Since the therapists' main focus was to guide the patients through a highly structured self-help programme, it is complicated to compare these results with traditional face-to-face CBT or Internet-delivered treatments that only consist of correspondence between therapist and patient, or even real-time online conversations (Kessler et al., 2009). In a previous controlled trial on major depression, one of the treatment arms consisted only of e-mail correspondence between therapist and patient (Vernmark et al., 2010). It is possible that a different set of therapist behaviours would be identified from that material and that these behaviours would have had an even stronger impact on the treatment outcome. On the other hand, many Internet-delivered treatments (Carlbring, Gunnarsdóttir, et al., 2007; Hirai & Clum, 2005; Titov, Andrews, Johnston, et al., 2010) consist of a self-help programme which the patient is guided through. There is, however, one programme called Interapy in which much text is produced by both the patient and the therapist (Lange et al., 2003), and it would be interesting to investigate therapist correspondence in that treatment format which involves more therapist time than in the present study.

The role and function of the therapist in iCBT is not clearly defined within the field, perhaps due to treatment programmes being very different from one another. In one trial (Titov, Andrews, Davies, et al., 2010), patients were guided through the treatment by either a clinician or a technician, and it is possible that the support given by the clinician consists of a different set of therapist behaviours compared to the support given by the technician, even though no significant differences was found between the outcome for the different kinds of support provided. In an on-going controlled trial, the study protocol of which has been published (Donker et al., 2009), patients are randomised to one of five conditions: (1) problem solving through the internet without a coach; (2) the same as the first, but with coach help on demand, by e-mail; (3) the same as the first, but with weekly scheduled contacts initiated by a coach; (4) no web-based intervention, but weekly scheduled contacts initiated by a coach; (5)

information only (through the internet). When this trial is finished and published in full, we will have further insight into the effects of different ways of providing support in iCBT.

The study has several limitations, which will now be addressed in turn. First, the therapist e-mails were analysed out of context, as the behaviour of the participants was not analysed. It is thus possible that the identified therapist behaviours are merely responses to the content of the patient e-mails. However, since all the patients underwent the same highly structured treatment programme, it is highly probable that their weekly reports had considerable overlap in terms of content, and that the therapist behaviours were not only responses to the patients e-mails. Second, since all the patients shared the same diagnosis, GAD, it is possible that the therapist behaviours identified are specific for the treatment of worry and anxiety and that the therapists would have behaved differently in the treatment of another condition (e.g., depression). Third, the therapists studied in this trial were also involved in the treatment study including development of the self-help programme, and it is possible that therapists with no prior knowledge of the self-help programme would act differently when guiding patients through the treatment. Fourth, the content analysed in this trial came from only three therapists, and it is not known whether these therapists' behaviour in the trial can be generalized.

To our knowledge, this is the first study in which the actual content of therapist e-mails in iCBT has been analysed and correlated with adherence and treatment outcome. A larger sample size would be of great interest in future research, both in terms of therapists and patients. Since all therapists were in their final year of the same educational programme to become psychologists, and all patients had the same illness, GAD, future research in which different kinds of therapists/coaches and different kinds of psychological illnesses are included would be of great interest. In this study the e-mail support was given in addition to a highly structured self-help programme, but very little is known about the impact of e-mail support given in addition to traditional face-to-face therapy. Perhaps a relatively small investment in giving extra support in terms of task reinforcement and self-efficacy shaping –delivered via e-mail, for example – as an addition to face-to-face therapy would have an impact on adherence.

CHAPTER 6

Internet-delivered treatments with or without therapist input: Does the therapist factor have implications for effectiveness and costs?

Palmqvist, B.*, Carlbring, P., & Andersson, G. (2007). Internet-delivered treatments with or without therapist input: does the therapist factor have implications for efficacy and cost? *Expert Review of Pharmacoeconomics & Outcomes Research*, 7, 291-297.

URL: <http://www.expert-reviews.com/doi/abs/10.1586/14737167.7.3.291>

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SUMMARY

Psychiatric problems such as mood and anxiety disorders are highly prevalent, and are associated with high societal costs and individual suffering. Evidence-based psychological treatments obtain good results, but are not available to the needed extent due to lack of practitioners with adequate training. One way to solve this problem is to provide minimal contact self-help treatments, for example with the assistance of computers. Recently, Internet-delivered cognitive behavioural treatment has been tested in a series of controlled trials. However, the interventions come in many forms with different levels and kinds of therapist input, which have implications for the costs of the treatments, and possibly their effectiveness. In this review we found evidence for a strong correlation between therapist input and outcome. While emerging evidence attest to the effectiveness of Internet-delivered treatment when at least minimal therapist guidance is provided, most studies in the field have not included a formal evaluation of cost-effectiveness. Future research needs are discussed.

INTRODUCTION

Mood and anxiety disorders are common conditions associated with much distress (The WHO World Mental Health Survey Consortium, 2004). Furthermore, these disorders are known to cost society a great deal of resources, for example in terms of health care consumption and work absenteeism (F Smit, et al., 2006). Therefore, effective and inexpensive treatments should be made readily available. Numerous trials and meta-analyses have found cognitive-behavioural therapy (CBT) to be a highly effective form of therapy (Andersson, Asmundson, et al., 2005; Butler, Chapman, Forman, & Beck, 2006; Hollon, Stewart, & Strunk, 2006). CBT is an integrative therapy form and combines techniques and concepts from both cognitive and behaviour therapies. In CBT, behaviours and thoughts are addressed in a systematic way by using techniques such as graded exposure, behavioural experiments, challenging negative automatic thoughts and relaxation.

Despite the promising results of CBT for common mental disorders, many individuals with psychiatric disorders never receive this treatment (Przeworski & Newman, 2006). Limited accessibility is one reason why many individuals go untreated, and the use of computers to deliver CBT could be one way to handle this problem. Computerized CBT, or CCBT, comes in many forms, such as virtual reality therapy (Klinger et al., 2005), use of palmtop- or clinic based desktop computers (Marks et al., 2003), or administered via the Internet (Richards, et al., 2003). CCBT delivered via the Internet has been found to be an effective form of treatment for various psychiatric conditions (Griffiths & Christensen, 2006). However, a recent meta-analysis revealed better effects for trials on the anxiety disorders compared to studies targeting depression (Spek, et al., 2007).

Internet administered therapy presents many advantages over face to face therapy. It is convenient for the clients and can be accessed practically anonymously (Griffiths & Christensen, 2006). For clients not able to travel to a clinic, either because of severe phobias or due to geographical circumstances, it can be a feasible alternative to regular therapy (Kenwright, Marks, Gega, & Mataix-Coles, 2004). It has also been shown that the delegation of routine therapy aspects to a computer can reduce therapist time while maintaining treatment effects (Marks, Kenwright, McDonough, Whittaker, & Mataix-Cols, 2004). It is also possible that computer or Internet administered treatments reach different clients than traditional therapy, but this has not been researched enough to be regarded as an established fact.

Therapist input in computerized and Internet-delivered treatments

CCBT administered over the Internet comes in a wide variety of forms. On the one hand there are highly interactive and graphic multimedia presentations (see Christensen, Griffiths, & Jorm, 2004) for an example), in which the client is guided through the treatment. On the other hand there are treatments built mostly on self-help books with few illustrative graphical figures (such as Carlbring, et al., 2005) and (Andersson, Bergström, et al., 2005). This form of CCBT could be described as bibliotherapy administered over the Internet. The use of the Internet to administer therapy in regular clinical settings is probably still not very common.

Given its recency both in research and in clinic, there is no golden standard as to how Internet-delivered CBT should be delivered. Amount of therapist contact, either live, over the telephone or via e-mail, is one variable for which there has been a large variation in different Internet treatment trials. Some programmes rely almost exclusively on computerized interaction between the client and the Internet treatment programme (Christensen, et al., 2004; Clarke et al., 2002). These programmes do not require any further resources in terms of therapists' time once the programme has been written and the clients are screened and assigned to the programme. One major benefit with programmes of this kind is that there is virtually no limit as to how many clients can enter the programme, since additional clients will not imply additional therapist time. Indeed, there is at least one programme for depressive symptoms (<http://moodgym.anu.edu.au/>), where the application is entirely open and free after registration. A possible risk with the "open access" approach is that clients who are not motivated enough or too depressed to manage a self-help programme (e.g., become worse after screening) will not benefit from the programme. In a 'worst case scenario' these clients could conclude that "therapy doesn't work", thus not seek other any further treatment and even worsen. On the other hand, getting in touch with the principles of psychological treatment could instead lead to an increase in help seeking (Christensen, Leach, Barney, Mackinnon, & Griffiths, 2006), regardless of outcome of the CCBT. Given this scenario, access to Internet treatment could lead to an increase in health care utilization and not a decrease. This same concern applies to the popular notion of stepped care, which might begin with a small scale, cost-effective "minor intervention", since knowing that "there is something better than this" (e.g., live psychotherapy) might compromise the low cost early stage treatment. This is definitely an area in need of further research.

There are programmes with direct contact with clients that require more time from a therapists/administrator [e.g., (Andersson, Bergström, et al., 2005; Richards, et al., 2003)]. However, this contact is usually limited to reminding the client to continue working on the programme, or to provide information on how to use the programme. This kind of interaction, often called minimal therapist contact, can take form of brief phone calls, using postcards, SMS (short message service) or via e-mail. Contact of this kind could possibly increase the motivation of the clients, while not requiring a great deal of time or effort from the clinician. In one study, a self-help programme with the addition of reminders by either phone calls or postcards performed by staff which had not been therapy trained, resulted in significant improvements (Clarke et al., 2005), while the same programme without these additional features was ineffective (Clarke, et al., 2002). The downside of this approach is that it is not possible to treat as many clients as in a programme requiring no or very little therapist input. Moreover, minimal therapist input could also be inferior to live treatment and less effective for clients with more severe problems.

The most time consuming kind of interaction is when the therapist takes an active role in the treatment and provide continuous support during a self-help treatment. In this approach to guided self-help the treatment becomes more individualized in such a manner that both those with low motivation and those more severe problems could have their needs met. A recent meta-analysis concluded that programmes with therapist assistance had larger effect sizes and no heterogeneity as compared to programmes without therapist assistance (Spek, et al., 2007). More research is needed to ascertain the precise effects of the therapist variable on treatment outcome, more specifically if there is a breaking point where additional therapist time yields relatively little additional effects. Adding to this is the complexity of different needs for different diagnoses. For example, a panic disorder client might need less therapist input than a client with major depression. Another unanswered question is the extent to which education or experience of the therapists matter.

While most of the studies in the field have included minimal therapist contact, there are studies in which more therapist contact has been included. For example, in one trial the therapist was the sole provider of treatment in one arm of a RCT, and there were no modules or self-help text prepared in advance for this group (Patten, 2003). This kind of approach to Internet treatment is sometimes referred to as e-mail therapy. While this approach is understudied in research, it is a rather common way of administering treatment via the Internet by private practitioners. The approach is interesting as it

is probably the approach that most closely resembles traditional therapy and it does not require the creation of a sophisticated programme/text beforehand. In Table 1 a selection of trials are presented along with the form of therapist input, the reported therapist time (if available) and effect sizes. The cited studies have been selected by searching relevant databases (PubMed and PsycINFO), as well as searching references from meta-analyses and systematic reviews. Effect sizes have, when possible, been compared with available meta-analyses and systematic reviews (Spek, et al., 2007). As shown in the table the between group effect sizes vary between studies. Assuming that two trials on depression involved no therapist contact (Christensen, Griffiths, Mackinnon, & Brittliffe, 2006; Clarke, et al., 2002), a Spearman correlation of $\rho=.75$, $p<.005$ is obtained between amount of contact spent with clients and the effect size. A scatter plot of the association is presented in Figure 1. The correlation is in line with the already mentioned recent meta-analysis by Spek et al. who found that interventions with therapist support had a large mean effect size, whereas interventions without therapist support had lower effect sizes. It is recommended that future trials on Internet-delivered CCBT report the amount of time spent with clients in greater detail as the findings reported here and in the meta-analysis by Spek et al. could be imprecise and must be regarded with caution. Another caveat is that studies differ regarding the ways outcome has been analysed, as not all studies have endorsed an intention-to-treat principle.

Cost-effectiveness of computerized and Internet-delivered treatments

Cost-effectiveness is often reported in terms of the incremental cost per additional Quality-Adjusted Life-Years (QALYs), or as the probability that an incremental unit on a certain measure (such as scores on the Beck Depression Inventory) costs below a given sum. QALYs are calculated from scores on questionnaire called EuroQoL (Rabin & de Charro, 2001), which is easy to administer when measuring health related problems (Kind, Hardman, & Leese, 2005). The EuroQoL comprises five questions on mobility, self care, pain, usual activities, and psychological status with three possible answers for each item (1=no problem, 2=moderate problem, 3=severe problem).

Little is known regarding the cost-effectiveness of CCBT, and even less regarding purely Internet-delivered CBT programmes. A recent systematic review (Kaltenthaler, et al., 2006) concluded that there was only one published cost-effectiveness study for CCBT (McCrone, et al., 2004), which was conducted alongside a RCT for depression and anxiety (Proudfoot et al., 2004). This programme, Beating the Blues, lead to greater improvements compared to treatment as usual on all outcome measures

(Beck Depression Inventory, Beck Anxiety Inventory and the Work and Social Adjustment scale). The authors of the cost-effectiveness study (McCrone, et al., 2004) concluded that CCBT had a high probability of being cost-effective, even if a modest value was placed on unit improvements in depression. It should be noted though that this programme was not administered over the Internet, but on a computer in a clinic which the clients had to visit. The cost of the CCBT treatment was about 10% more costly than treatment as usual as measured by a mean service cost for delivery. However, total cost including loss of employment was 40% lower for the CCBT group. In their cost-effectiveness analysis, the authors concluded that when a 1-unit improvement on the Beck Depression Inventory was valued at £40, there was an 81% chance that CCBT would be cost-effective. The calculated cost per QALY was £1250. In the systematic review by Kaltenthaler and colleagues (Kaltenthaler, et al., 2006), cost-effectiveness analyses were calculated for several other programmes after enquiring for additional data. Their results, however promising, are associated with several uncertainties, such as no knowledge about long term outcome and small sample sizes in some of the studies. The largest cost of the programme in the only published study on cost-effectiveness (McCrone, et al., 2004) was the license fee to the owners of the programme. Other costs associated with CCBT in general practice are the hardware/computer costs, the costs of screening for suitable clients, and the cost for clinical support where applicable. The cost of the clinical support will vary greatly according to the profession of the supporting staff (e.g., a licensed psychologist will cost more than a nurse, who in turn costs more than a psychology student). Given the availability of CBT principles in published self-help books and the accelerating computer literacy among staff and the general public it is possible that in the future health care companies and institutions might prefer to develop their own CCBT or Internet-delivered programmes, thus ridding themselves of the license cost in the long run. However, the costs of providing clinical support will continue to play a role in future applications. This will make the intervention cost in CCBT higher. In conclusion, at the present stage it is premature to draw any firm conclusions regarding the cost-effectiveness of Internet-delivered CCBT.

Expert commentary & five-year view

Evidence is now emerging that CCBT, in its most recent development delivered via the Internet, is effective in the treatment of psychiatric conditions of mild to moderate severity (Spek, et al., 2007). In another related literature not reviewed here, similar findings have been observed in the treatment of somatic conditions such as tinnitus (Andersson, Strömngren, Ström, & Lyttkens, 2002), chronic pain (Buhrman, Fältenhag,

Ström, & Andersson, 2004), headache (Ström, Pettersson, & Andersson, 2000), child encopresis (Ritterband et al., 2003), insomnia (Ström, et al., 2004) and obesity (Tate, Wing, & Winett, 2001), to give a few examples. However, as is the case for the treatment of mental disorders cost-effectiveness issues have been sparsely investigated in these trials. It is interesting to speculate what the future may hold for computer applications in health care settings. We believe that combined treatments will be more common in the future, where live therapy is combined with CCBT-elements or Internet-delivered interventions, in particular as the Internet is now widely available for both patients and clinicians. For example, it is known that a vast majority of CBT practitioners use and recommend self-help material (Keeley, et al., 2002), but to a far lesser extent endorse CCBT (Whitfield & Williams, 2004). In particular for more severe conditions, combined treatments could potentially lead to better management strategies, but we are not aware of any published trial that has tested the actual combination of live and CCBT therapy, with the exception of a few live exposure sessions in trials of

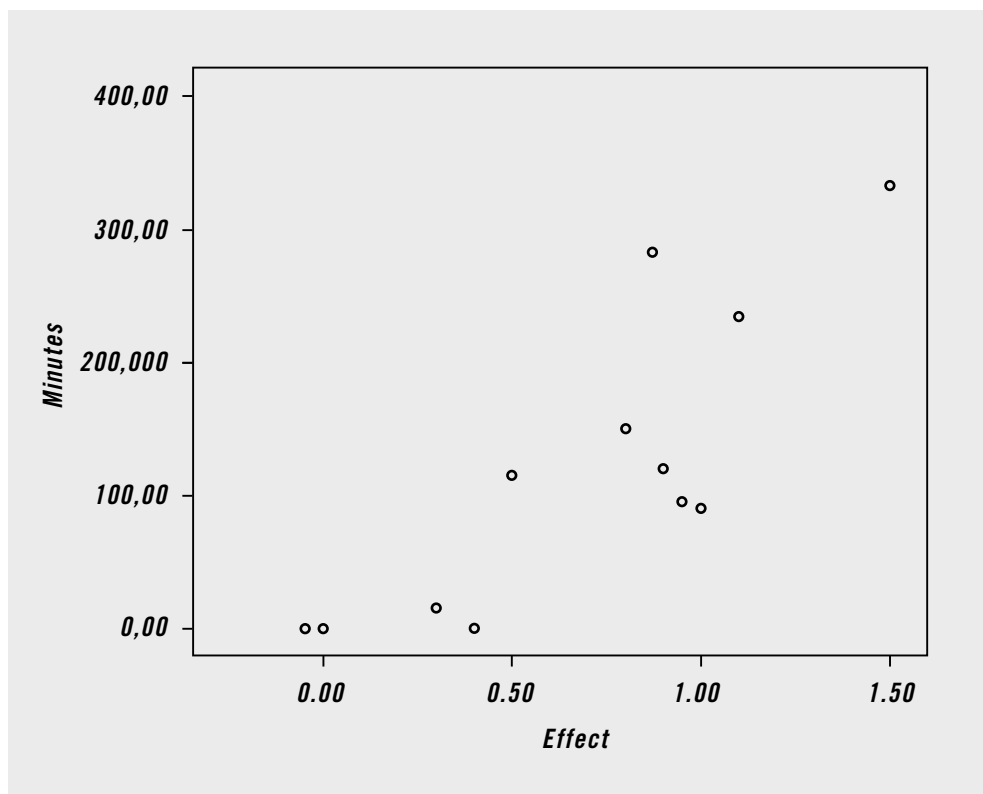


Figure 1. Association between therapist time in minutes per client and effect size (Cohen's d)

Internet treatment of social phobia (Andersson, et al., 2006). Perhaps even more urgent would be to test the possible added value of combining CCBT with prescribed psychopharmacological drugs, such as SSRIs. To our knowledge, with a few possible exceptions [e.g., (Robertson, Smith, Castle, & Tannenbaum, 2006)], this has not yet been investigated in the field of psychiatric disorders. Other interesting challenges can be identified. For example, low cost Internet interventions, with minimal but significant therapist input, could be used to prevent relapse. So far, this has mostly been tested using more traditional face to face format of psychotherapy (Paykel, 2007), but there are examples of bibliotherapy as a preventive treatment for panic disorder (Wright, Clum, Roodman, & Febbraro, 2000).

In this review we did not focus on the comparative effects of live versus Internet treatment (or CCBT). Direct comparisons in RCTs are needed here, but the few trials available suggest that Internet-delivered CCBT can obtain similar results as live treatment [e.g., (Carlbring, et al., 2005)]. Therapist input is a crucial question for future applications and dissemination of Internet-delivered CCBT. Obviously, there is a possibility that for example e-mail interaction with clients equals the amount of contact in live treatment and might even supersede the amount of contact spent per individual client in group treatments. For example, the research conducted in Holland on symptoms of PTSD with a method called Interapy (Lange, van de Ven, & Schrieken, 2003) involves substantially more therapist time than the approaches reviewed in this paper. Another potential future application of CCBT involves tailoring treatment according to the clients' presenting complaints and not necessarily the diagnosis. In most CCBT applications treatment consists of modules that are modeled according how manualized live psychotherapy usually is presented. For example, the sequence of modules for a client with a diagnosis of panic disorder will involve a set of modules that are similar for all clients who go through the programme with that particular diagnosis. However, as comorbidity is a rule rather than an exception, a client in a real life clinical setting is likely to have symptoms of both mood and perhaps several anxiety disorders, and might also suffer from insomnia. This observation has motivated us to tailor Internet treatment according to each individual client's needs. A client might then be "prescribed" three modules for social phobia, one for relaxation and two for behavioural activation as a way to deal with depressive mood. A randomised trial testing this way of delivering Internet treatment is currently under way.

Almost without an exception, most trials on CCBT including the recent Internet trials have been conducted following treatment protocols derived from CBT live treatment and self-help books. The dominance of CBT is understandable given the

strong evidence base underpinning this treatment approach. Even applied relaxation, which has been used as a control treatment (Carlbring, et al., 2003), is a CBT form of treatment (Öst, 1987). However, the relative ease of conducting Internet trials makes comparative studies of alternative treatment approaches (for example to the extent this is possible interpersonal and psychodynamic therapy), and their effects in relation to CBT possible to conduct. Dismantling studies of Internet treatments, where larger intervention programmes are “taken apart” to be presented to the client in smaller parts to be able to ascertain which part of the programme that yields effects, are beginning to appear and this is another likely future development (Christensen, Griffiths, Mackinnon, et al., 2006).

Finally, with the advent of CCBT and the spread of the Internet, we have in front of us a possibility to make psychological treatment available for a wider group of people, including the third world and people who live outside of the specialist centers in larger cities. We predict that there will be a steadily growing demand for cost-effectiveness analyses on psychological therapies in general and this will include costs and benefits of CCBT in relation to other more therapist demanding psychological treatments. While this review was unable to come up with any firm conclusions regarding cost-effectiveness of internet-delivered CCBT approaches, we believe that this will be an important challenge to investigate in research in the upcoming years.

Table 1. Overview of RCTs using Internet-delivered CCBT for the treatment of various mental disorders

<i>Study</i>	<i>Year</i>	<i>Country</i>	<i>Main diagnosis</i>	<i>Assessment format</i>	<i>Contact during treatment</i>	<i>Number of treatment modules</i>	<i>N</i>	<i>Missing at F-U</i>	<i>Main outcome</i>	<i>Time spent per client (min)</i>	<i>Effect size (Cohen's d between group)</i>
<i>Carbring et al.</i>	2001	Sweden	Panic Disorder	Internet	E-mail	6	31	16%	Treat > WL	90	1.0
<i>Carbring et al.</i>	2005	Sweden	Panic Disorder	Internet	E-mail	10	49	12%	CCBT = TCBT	150	0.8
<i>Carbring et al.</i>	2006	Sweden	Panic Disorder	Internet	E-mail + Telephone	10	60	5%	Treat > WL	234	1.1
<i>Klein et al.</i>	2001	Australia	Panic Disorder	Internet	None	2	22	0%	Treat > WL	None	0.4
<i>Klein et al.</i>	2006	Australia	Panic Disorder	Internet	E-mail	6	45	7%	CCBT > TCBT, WL	333	1.5
<i>Andersson et al.</i>	2006	Sweden	Social phobia	Internet + Live exposure	E-mail + Live	9	64	3%	Treat > WL	283	0.87
<i>Carbring et al.</i>	2007	Sweden	Social phobia	Internet	Telephone	9	57	2%	Treat > WL	95	0.95
<i>Hirai et al.</i>	2005	USA	Traumatic event related consequences	Internet	E-mail	n/a	27	0%	Treat > WL	n/a	0.8
<i>Schneider et al.</i>	2005	United Kingdom	Phobia and panic	Postal questionnaire + interview	Telephone or e-mail	9	68	29%	Treat > Treat without exposure	115	0.5
<i>Andersson et al.</i>	2005	Sweden	Depression	Internet	E-mail	5	117	27%	Treat > WL	120	0.9
<i>Christensen et al.</i>	2004	Australia	Depression	Internet	Telephone	5	525	17%	CCBT > Information > WL	n/a	0.4
<i>Clarke et al.</i>	2002	USA	Depression	Internet	No	7	299	26%	Treat = Control	None	-0.05
<i>Clarke et al.</i>	2005	USA	Depression	Internet	Telephone or postcard	7	255	36%	Treat > TAU	<15	0.3 postcard 0.2 phone
<i>Christensen et al.</i>	2006	Australia	Depression	Internet	No	1-5	2794	74%	No control group. Six versions of treatment	None	0.4
<i>Patten et al.</i>	2003	Canada	Depression	Internet	No	4	786	3%	Treat = General info	None	0.0

CHAPTER 7

General discussion

The main goals of this thesis were to test whether psychological interventions delivered over the Internet could be efficacious and cost-effective in the treatment of generalized anxiety disorder, and to examine the impact of therapist factors in Internet-delivered therapy. In this section, the main findings of the studies are discussed and compared with previous research in the area; clinical implications of the research are highlighted; and limitations of the studies are brought up. The section concludes with recommendations for future research. The first RCT conducted, in which Internet-delivered CBT was compared to a wait-list control group, will henceforth be called “the first trial”, and the second trial, in which Internet-delivered CBT and PDT were tested against a control condition, will be called “the second trial”.

MAIN FINDINGS AND PREVIOUS RESEARCH

Direct effects on primary outcomes and clinical recovery

The outcome of the two randomised controlled trials in this thesis suggests that Internet-delivered CBT as well as Internet-delivered PDT can be efficacious in the treatment of GAD compared to a wait-list control group. The effects of the CBT treatment were shown to be maintained at a three year follow-up, indicating that treatment gains are stable over time; this also holds true for the PDT treatment 18 months after the treatment is finished. There were favourable findings on long-term follow-up, evident in both self-report questionnaires and in diagnostic interviews using a structured clinical assessment. For unknown reasons, the participants in the wait-listed control group in the second RCT experienced spontaneous improvements to a much larger degree than in the first trial. Comorbidity was assessed in greater detail in the second trial, but prevalence of major depressive disorder was controlled for in both trials and does not seem to differ between the two trials (22.5% in the first trial and 23.5% in the second). Neither do levels of anxiety as measured by PSWQ differ between the trials (first trial PSWQ M = 69.3 and second trial PSWQ M=68.7). One possible explanation for the spontaneous improvements in the control condition in the second trial is that the treatment they were to receive after the wait-list period was not novel, as it had been successfully tested before. The participants in the control condition were informed that the CBT treatment had been previously tested in a randomised controlled trial, and it is quite possible that the knowledge that they would receive a potent treatment later on had an impact on their well-being. When intention-to-treat analyses (mixed models) were conducted in the second trial, neither of the two treatments were more effective than the control condition at post-test, but during the three months following treatment, the participants in both treatment groups continued to improve, whereas the participants in the control condition experienced elevated anxiety.

On the primary outcome measure, the between-group effect size was large ($d = 1.11$) in the first trial, but in the second trial, between-group effect sizes for the two treatment groups was only moderate when compared to the control condition (CBT $d = 0.76$, PDT $d = 0.64$) at three month follow-up. Other trials on Internet-delivered CBT treatments for GAD (Titov et al., 2009; Robinson et al., 2010; Draper, Rees, & Nathan, 2008) have resulted in similar within-group effect sizes on the PSWQ. No other trials have been found in which PDT is delivered over the Internet for GAD, but in comparison with the Leichsenring (2009) trial on live short-term psychodynamic psychotherapy as well as live cognitive behaviour therapy for GAD, similar within-group effect sizes are produced in both our Internet-delivered treatments.

In terms of clinical recovery, the CBT treatment in the first RCT led to 42.0% of the participants in the treatment group being clinically recovered as defined by Jacobson and Truax (1991) on the primary outcome measure (PSWQ) directly after the treatment; 48.3% were clinically recovered at 1-year follow-up, and at 3-year follow-up, this figure had risen to 57.1%. In the second trial the level of clinical recovery for the CBT treatment was 26.1%, 52.2% and 54.5% at post-treatment, 3-month follow-up and 18-month follow up, respectively; this can be compared to the PDT treatment, which led to 15.4%, 50.0% and 68.2% recovery levels. Compared to other trials on psychotherapy (Leichsenring et al., 2009; Öst & Breitholtz, 2000) for GAD, these recovery levels are rather decent; when compared to the clinical recovery made by patients with other anxiety disorders such as panic disorder and social phobia after undergoing Internet-delivered treatments (Berger, Hohl, & Caspar, 2009; Bergström et al., 2008; Titov, Andrews, Choi, Schwencke, & Mahoney, 2008), however, the results of these two GAD trials leave much room for improvement.

Our review of Internet-delivered treatments with or without therapist input suggests that guidance is needed for the treatments to be effective. There are a few examples of studies where sufficient treatment gains were reached without therapist input (Berger et al., 2011; Furmark et al., 2009), but so far meta-analyses in the field conclude that clinical guidance leads to a better treatment outcome (Andersson & Cuijpers, 2009; Spek et al., 2007). In our analysis of e-mail correspondence from the first trial, we examined what the therapists were actually doing when providing guidance in our self-help treatments. We found that the three therapists in this trial developed unique styles of communicating with their patients, though this did not seem to have any impact on treatment outcome. Despite their different personal communication styles as therapists, there were also similarities found between the therapists' communications. More

specifically, most of the e-mails to the patients included positive feedback concerning their progress in the treatment as well as help on how to apply techniques taught in the treatment to the patients' lives. More frequent expressions of flexibility regarding the meeting of deadlines agreed upon in the treatment programme correlated with a worse treatment outcome, but the study design does not permit any inference concerning whether this finding is best explained by characteristics of the patient (i.e., their having stressful life circumstances and therefore repeatedly asking for lenience on deadlines) or of the therapist (failing to be strict and set clear goals/borders in the treatment contact).

Regarding health economy, the cost-effectiveness analysis of the CBT treatment in the first trial resulted in an additional societal cost of £447 for each diagnostic remission, which should be regarded as a relatively low sum. Different levels of willingness to pay for a remission from GAD from a societal perspective produces different likelihoods that the treatment will be cost-effective compared to treatment-as-usual (TAU): when the willingness to pay is zero, there is a 47% probability that the treatment is cost-effective compared to TAU; when the willingness to pay is raised to £5,000 the probability of the treatment being cost-effective rises to 71%. A comprehensive review (Kaltenthaler et al., 2006) concluded that there is a shortage of cost-effectiveness evaluations on CBT-trials administered over the Internet, making comparison of these results to other studies problematic.

Module completion

In both RCTs, there were favourable treatment outcomes despite the fact that few participants completed all of the treatment modules during the assigned time. In the first trial, a mere 10.5% had finished all eight modules during the treatment period, and while this figure increased in the second trial (CBT = 22.2 %, PDT = 37.0 %), still far less than half of the participants finished all of the intended steps in the given timeframe. One might argue that patients today demand more from their guided self-help treatments and that a higher degree of interactivity is required to maintain patients' motivation during the treatment. While this may be true, it does little to explain why the adherence increased from the first to the second trial, especially since the second trial was conducted a few years after the first one and people using the Internet would be expected to gradually demand more and more interactivity from their Internet-delivered treatments, not less. Both the CBT and PDT treatment are mainly text-based and are presented in a strictly linear format.

When a group of participants with different comorbid anxiety disorders were presented with a self-help treatment tailored to their specific problem areas in another study (Carlbring et al., 2011), the percentage of participants that finished all the designated modules increased to 59%. With this tailored approach, the treatment length varied between six and ten weeks, and certain components from the CBT treatment used in the two RCTs presented in this thesis were also used in the tailored study. Internet-delivered treatments generally have a high degree of participants not finishing the entire treatment (Eysenbach, 2005), and our results indicate that perhaps it is not necessary to finish the entire treatment programme in order to achieve significant clinical improvements. The participants in our two trials were given the remaining treatment modules to work with on their own after the designated time period had ended, and it is possible that this explains why so many showed a positive treatment outcome despite not having finished the entire treatment programme.

Clinical implications

There are several clinical implications of the trials performed in this thesis. In a broader perspective, the increase in efficacy trials on Internet-delivered treatments for anxiety and mood disorders in the last couple of years has led to a wider implementation of these treatments in routine care in Sweden. In Stockholm, the unit Internetpsykiatri [Internet Psychiatry] has administered treatment to well over a thousand patients since the start 2007, and the group has produced several effectiveness trials (Bergström et al., 2010; Hedman et al., 2011, Bergström et al., 2009) proving that the treatment format is indeed suited for wider dissemination. From the perspective of the health-care units, providing Internet-delivered therapy as an alternative to their patients makes it highly probable that the same number of clinicians can treat a larger number of patients, leading to better productivity and possibly shorter waitlists. From the patients' point of view, treatment administered via the Internet can lead to better access to evidence-based health care, and for those living far from their closest specialist clinic, an Internet-delivered therapy could be a convenient treatment alternative. A majority of the patients in our trials were working or studying despite their anxiety, and for these individuals the convenience of being able to decide for themselves when to work on the treatment probably led to fewer hours away from work/school compared to face-to-face treatment.

GAD is known to be a disorder that has a negative impact on quality of life. Compared to other anxiety disorders, it is understudied and relatively treatment resistant. For these reasons, it is imperative that better treatments for GAD are developed, and the

knowledge gained from the RCTs in this thesis might help further this work. The treatments in our trials were administered at a low cost, as the therapist time spent on each patient was low: In the first trial the therapists spent an average of 97 minutes per patient (SD = 52); in the second trial, the therapists in the CBT treatment spent 113 minutes on average per patient (SD = 41); and in the PDT group, the average time spent was 92 minutes (SD = 61). A face-to-face CBT treatment for GAD typically lasts 10 to 15 sessions, which translates to between 450 and 675 minutes. Since our treatments have the potential to save so much time, they could be implemented and offered to many patients, and for those patients who do not experience a positive clinical outcome, there would still be time/resources left to provide them with further treatment of other varieties.

A majority of the published trials on Internet-delivered therapy has focused on CBT treatments. While this is quite understandable, given that CBT has the strongest evidence base for common mental health disorders, there is a risk that clinicians from other therapeutic disciplines might associate Internet treatment with CBT to such a degree that they conclude it is irrelevant to them and their work. By proving that an Internet-based PDT treatment can produce results similar to online CBT, it is our goal to stimulate psychodynamically oriented clinicians' interest in online guided self-help treatments, and we hope that we might see in the future a wider diversity in the treatment programmes studied. To our knowledge, this was the first time a guided self-help treatment based on psychodynamic principles was administered via the Internet, and a second aim of our study is to facilitate better understanding between clinicians and researchers in the CBT and PDT field.

In our study on therapist behaviours in online guided self-help treatments, we found that despite the fact that all therapists had unique styles of communicating with their patients, none of the therapists had significantly better or worse clinical outcomes in their treatments than the others. Our results seem to suggest that there is not a narrow set of rules that must be obeyed in order to produce favourable outcomes in Internet treatment, but rather, that it is perfectly acceptable to develop one's own therapeutic style in terms of how one communicates with the patient.

The most concrete clinical implication of this thesis is the implementation of the online CBT treatment in routine care in the south of Sweden. In 2009 a pilot study was performed in which the effectiveness and the cost-effectiveness of the treatment protocol developed for our first trial was tested with patients already present in the adult psychiatry system (Paxling, unpublished data). The study took the form of an

RCT, and results similar to the two RCTs in this thesis were found, resulting in the treatment being made available to everyone with GAD in Sweden's third largest city, Malmö.

Main limitations

Several important limitations of the studies presented in this thesis should be kept in mind when interpreting the results. First, we did not screen for personality disorders or ongoing psychosis in a structured way, so even though severe mental illness such as psychosis was an exclusion criteria in our trials, it is possible that some participants in our trials had undiagnosed personality disorders. If this were the case, it would probably strengthen the external validity because of the high level of comorbidity between GAD and personality disorders, but because this was not assessed in our trials there is no way to know for sure. Second, we allowed our participants to be on medication for psychiatric disorders under the condition that they were stable on their present medications and did not alter their dosages during the course of the treatment. This probably strengthened the external validity as well, since many patients diagnosed with GAD are also under medical treatment, but we had no way of controlling for this except by asking the participants themselves to promise that they would not alter the dosage during the treatment period. The participants were informed that if they did change medication type and/or dosage, they would still be allowed to finish the Internet-based treatment, but the results on their questionnaires would not be included in our analyses. By so doing, we hoped that the participants would truthfully report any changes in medication, as doing so would not have any negative consequences for them, but our means for controlling this was very limited. Third, all participants in our RCTs were self-recruited from a portal site on the web and from newspaper advertisements, which might have led to a study sample which is not representative of the whole GAD population. By comparing our participants' levels of distress as measured by several different self-report questionnaires, as well as controlling for comorbid conditions in our second trial with the structured clinical interview, we could conclude that the participants in our study seem to be representative of the larger GAD population. As the CBT protocol used in both our trials has since been tested in a clinical psychiatric hospital setting, more information is now available on the generalizability of the first two RCTs; however, the results from this effectiveness trial are not covered by the scope of this thesis. Fourth, there are at least two limitations regarding the control condition in our trials. The participants randomised to the control condition were informed that they would have to wait for the treatment and that they would receive the usual unrestricted access to health care during this waiting period. By not having

an active control condition, the results from both these trials may possibly be a bit exaggerated in terms of between-group effect sizes. By administering the treatment to the participants in the control condition (immediately after the first treatment group finished their treatment in the first trial and after a three month waiting period in the second) the possibilities to draw conclusions from the long term follow-ups are severely limited because the trials were, in fact, no longer randomised and controlled at these points in time. As a justification of our study design, it could be argued that the participants in the control condition would probably have sought other treatment had they been told that they would not receive active treatment from our group for 18 or 36 months, but this cannot be known for sure. The chosen design specifically impacts the quality of the cost-effectiveness analysis, since data on differences in costs between at least two groups has to be present in order to perform this kind of analysis. In the questionnaire we used to collect information on health care consumption and other costs, TIC-P, the participants are asked about their usage of different care providers (among many things) during the last month. Since the questionnaire was administered immediately following treatment, the period covered would have overlapped the treatment period, meaning that the treatment was not given optimal time to have effect before the covered period started. The implication of this is that all cost offsets will not be included since they are likely to occur later, probably rendering a rather conservative estimate of the ICER. Fifth, the studied samples were relatively small, and even though they were big enough to find statistically significant outcomes, a larger sample might have improved the possibility that the study population was representative of the larger GAD population. In the study on therapist behaviours, the sample of therapists studied was especially small, $n = 3$, indicating that the results should be interpreted as how therapists might behave in Internet-delivered interventions, and not as how therapists behave in general in these kinds of treatments. Sixth, one might call into question whether the treatments administered online are at all comparable to their face-to-face administered counterparts, especially when it comes to Internet-delivered PDT: Whether the treatment in our second study ought to be considered PDT delivered online or not is open to interpretation. By collaborating with a licensed psychoanalyst and using his self-help book in the treatment, we have taken steps to make the PDT treatment as credible as possible. It is known that a therapeutic alliance does seem to form in Internet-delivered therapies, as discussed in the introduction, but to our knowledge, the concepts of transference and countertransference have not been studied in the Internet context, and this may have bearing on the credibility of our PDT intervention.

Future research and recommendations

There are many future challenges in the research field of Internet-delivered treatments, both specifically for GAD and with regard to the method in general. Some suggestions for future research are presented in this paragraph. After having performed a large number of efficacy trials, it is our recommendation that more focus should go towards implementing Internet-delivered treatments in routine care. While the treatment programmes are thoroughly tested, one should expect other challenges stemming from adapting the treatments into current health care processes in psychiatry as well as primary care centres. Since most Internet-delivered self-help programmes are diagnosis specific, special care has to be taken to ensure that the patients referred to these interventions indeed fulfil the criteria for the specific diagnosis. Implementing these treatments in routine care probably leads to situations in which the programmes need to be adapted to the specific context in which they are given, and in the same way, the addition of these treatments would very likely lead to changes in the health care processes in existing units. Research focusing on issues raised by implementation processes would be a great addition to the literature, as well as valuable information in future implementations. While in the process of implementing these treatments, many new research opportunities appear. Larger studies, preferably multi-site studies, with more participants would be of great interest, since many factors would be harder to control, which in turn might help highlight aspects of the treatments that need improvement. A larger sample of patients as well as therapists would also be beneficial in the future study of therapist behaviours over the Internet, ideally in relation to patient behaviours in order to examine the interplay in the communication and its possible effect on treatment outcome. In this context it would also be easier to conduct RCTs in which Internet-delivered therapy is compared to face-to-face treatment. In some trials (Aydos et al., 2009; Bergström et al., 2010) Internet-delivered treatments have already been compared to live group therapy, but research comparing individual treatment live vs. online is still lacking.

Internet-delivered treatments have been proven to present a serious alternative to traditional therapy, and for this reason they will make a good addition to the current psychiatric services. However, still little is known about how the addition of Internet-based interventions to traditional live face-to-face therapy might affect outcomes. Technology could play many roles in the work with common mental disorders, from smaller issues such as reminding patients about scheduled appointments to bigger undertakings in which the patient fills in online questionnaires about their status on a regular basis or registers their experience of practice given as homework assignments

or perhaps even undergoes an Internet-based treatment at the same time as meeting a therapist face-to-face. In dialectical behaviour therapy (Linehan et al., 1999), the patient undergoes a combination of individual and group therapy, and for this kind of combination treatment it might also be a good idea to include Internet-delivered interventions. The possibility of preventing relapses of mental disorders has already been shown (Holländare et al., 2011), but perhaps an Internet intervention could also be used to prepare patients for live treatment with a therapist?

A relatively large percentage of the participants in our trials do not finish all treatment modules within the intended period of time. Another study (Carlbring, et al., 2011) in which the self-help treatment is tailored to each individual in a highly comorbid sample of patients suffering from anxiety disorder yielded a higher level of follow-through. Future research could focus on the possibility of tailoring the self-help treatment for GAD to a higher degree; perhaps the applied relaxation could be omitted for those patients who have already tried different relaxation techniques extensively.

CONCLUSIONS

Internet-delivered therapy based on either CBT or PDT principles can lead to a positive outcome in the treatment of GAD. Results from both treatments seem to be maintained up to 18 months follow-up, and for the CBT treatment the treatment effects have proven to be maintained three years after the completion of treatment. The CBT treatment was shown to be cost-effective compared to treatment as usual, and societal monetary gains can be expected from the treatment, as work absenteeism and work cutback decreased following the treatment. There were, however, several patients that did not seem to benefit from the CBT or the PDT treatments. This warrants further development of treatment programmes for GAD as well as a closer examination of why these persons do not get better. Since these treatment programmes have fairly good outcomes and make treatment more easily available to the general public, implementation in the health care system is a good idea, but the programmes should be developed further in parallel to this. Our literature overview suggests that therapist contact leads to greater treatment outcome, but our analysis of therapist correspondence with patients did not lead to any concrete guidelines on how to behave to maximize treatment benefits.

SUMMARY

SUMMARY

CHAPTER 1 provides the general introduction to the contents of this thesis. In summary, this chapter states that GAD is a mental disorder characterized by excessive worrying about a number of different topics which also tend to change over time. GAD is associated with negative impact on quality of life and is a highly prevalent and comorbid condition, with many patients also suffering from other anxiety disorders, depression and somatic disorders. Several models for explaining GAD are presented, where one such explanation is that GAD is driven by an intolerance of uncertainty. The psychological treatment of choice for GAD is CBT, and Internet-delivered therapy is an initiative to make CBT available to more patients who might benefit from treatment. Internet-delivered therapy has its roots in distance treatments using the telephone or letters and in bibliotherapy, in which patients work with self-help books focusing on their disorder. Treatment outcome in online therapy seems to be partly moderated by the therapist factor; the programmes that offer clinical guidance by a therapist have better outcomes than the programmes that are unguided, but it remains unclear how the guidance should be given in order to maximize the benefits.

CHAPTER 2 describes the study on Internet-delivered CBT for GAD. The study is a randomised controlled trial in which active treatment is compared to a wait-list control group. A total of 89 patients were randomised to one of the conditions. The CBT treatment consists of an 8-week self-help programme divided into eight modules, and each week the participants received feedback and support from an online therapist. The main outcome measure was the Penn State Worry Questionnaire, and large effect sizes were found both within the treatment group and between the conditions in favour of the CBT treatment on all outcome measures except for quality of life. The treatment gains were maintained at 1- and 3-year follow-up.

CHAPTER 3 reports an economic evaluation in which the cost-effectiveness of the Internet-delivered CBT treatment was evaluated. A self-report questionnaire, TIC-P, was used to gather information on economic factors such as health care and medication consumption, work absenteeism, work cutback and domestic cutback. In the treatment group, 52.3% did not fulfil the diagnostic criteria for GAD after the treatment, compared to 15.6% in the control condition. This effect comes at the relatively low cost of £447 for each remission. When there is no societal willingness to pay for a GAD remission, the treatment has a 47% chance of being cost-effective compared to the control condition. When society is prepared to pay £5,000 for a remission, the treatment instead has a 71% probability of being more acceptable than the control condition from a societal perspective.

CHAPTER 4 describes a study in which psychodynamic therapy was administered online and compared to Internet-delivered CBT as well as a wait-list control group. The trial had three arms with 27 participants in each. The Internet-delivered PDT programme was based on the self-help book *Make the Leap*, written by psychoanalyst Farrel Silverberg. The treatment outcome showed moderate to large within-group effect sizes for both the PDT and CBT treatments at 3- and 18-months follow-up on the primary outcome measure, the Penn State Worry Questionnaire. Our findings suggested that Internet-delivered PDT seems to work as well as CBT in the treatment of GAD.

CHAPTER 5 presents the results of an analysis of therapists' e-mails to patients in our first trial of Internet-delivered CBT for GAD (which was described in Chapter 2). Examined were 490 e-mails from three therapists, and through content analysis, eight distinguishable therapist behaviours were found. The therapists in this trial used, to a greater or lesser extent: deadline flexibility, task reinforcement, alliance bolstering, task prompting, psychoeducation, self-disclosure, self-efficacy shaping, and empathetic utterances. Many of these therapist behaviours correlated positively with each other, and several correlated with module completion, but only two correlated with treatment outcome: deadline flexibility was negatively associated with outcome, and task reinforcement positively correlated with changes on the primary outcome measure. Although the therapists in this study behaved in different ways compared to one another, no single therapist style was superior to any other.

CHAPTER 6 outlines different ways that therapists are utilized in online treatment programmes as found in a literature review. Implications of the costs of administering treatments when these are guided by a therapist are discussed since there are also programmes that are fully automated and do not require therapist guidance. In the review a strong correlation was found between therapist input and treatment outcome.

CHAPTER 7 provides the general discussion of this thesis. The main results from our studies are discussed in light of previous findings. Main limitations are presented, clinical implications are discussed, and recommendations for future research are given.

SAMENVATTING

SAMENVATTING

HOOFDSTUK 1 is de algemene inleiding voor de inhoud van dit proefschrift. Samengevat beschrijft dit hoofdstuk dat GAS een psychische stoornis is die gekarakteriseerd wordt door het zich buitensporig zorgen maken over verschillende, door de tijd heen veranderende zaken. GAS wordt geassocieerd met een negatieve invloed op de kwaliteit van leven en is een zeer prevalentie aandoening die gepaard gaat met veel comorbiditeit, waarbij veel patiënten ook lijden aan andere angststoornissen, depressie en somatische aandoeningen. Diverse modellen voor GAS worden besproken, waarbij een van de verklaringen is dat GAS gedreven wordt door een intolerantie voor onzekerheid. De psychologische voorkeursbehandeling voor GAS is CGT, en internetbehandeling is een initiatief om CGT beschikbaar te stellen aan meer patiënten die baat zouden kunnen hebben bij behandeling. Internetbehandelingen vinden hun oorsprong in behandelingen op afstand via de telefoon of brieven en in bibliotherapie, waar patiënten zelfhulpboeken voor hun aandoening doorwerken. De uitkomst van de internetbehandeling lijkt gedeeltelijk gemodereerd te worden door de aanwezigheid van een therapeut - de programma's die klinische begeleiding door een therapeut aanbieden hebben betere resultaten dan de onbegeleide programma's - maar het blijft onduidelijk op welke begeleiding gegeven moet worden om de voordelen te maximaliseren.

HOOFDSTUK 2 beschrijft het onderzoek naar CGT voor GAS via het internet. Het onderzoek is een gerandomiseerde trial waarin de interventie werd vergeleken met een wachtlijst controlegroep. In totaal werden 89 patiënten gerandomiseerd naar een van de twee condities. De CGT-behandeling bestond uit een zelfhulpprogramma van acht weken die opgedeeld was in acht modules, waarin de deelnemers iedere week feedback en ondersteuning ontvingen van een online therapeut. De primaire uitkomstmaat was de Penn State Worry Questionnaire en er werden grote effectgrootten gevonden - zowel binnen de interventiegroep en tussen beide groepen - ten voordele van CGT, op alle uitkomstmaten behalve kwaliteit van leven. De verbeteringen bleken behouden te zijn bij de opvolgmetingen na 1 en 3 jaar.

HOOFDSTUK 3 beschrijft een economische evaluatie waarin de kosteneffectiviteit van de CGT-therapie internet werd onderzocht. Een zelfrapportage-vragenlijst, TIC-P, werd gebruikt om informatie verzamelen over economische factoren zoals zorg- en medicijngebruik, werkverzuim en werk- en huishoudelijke beperkingen. In de interventiegroep voldeed na de behandeling 52,3% niet aan de diagnostische criteria voor GAS, vergeleken met 15,6% in de controlegroep. Dit effect werd bereikt voor de relatief lage kosten van €513 per remissie. Wanneer er geen maatschappelijke bereidheid is om te betalen voor een GAS-remissie dan heeft de behandeling 47% kans

om kosteneffectief te zijn ten opzichte van de controlegroep. Wanneer de maatschappij bereid is om €5737 te betalen voor een remissie dan heeft de behandeling uit maatschappelijk perspectief 71% kans om acceptabler te zijn dan de controlegroep.

HOOFDSTUK 4 beschrijft een onderzoek waarin psychodynamische therapie online werd uitgevoerd en vergeleken met zowel CGT via het internet als een wachtlijst controlegroep. Deze trial had drie condities, elk met 27 deelnemers. Het PDT-programma via internet was gebaseerd op het zelfhulpboek *Make the Leap*, geschreven voor psychoanalyticus Farrel Silverberg. De uitkomsten van de behandeling lieten gematigde tot grote tussen-groep effectgrootten zien op de primaire uitkomstmaat, de Penn State Worry Questionnaire, voor zowel de PDT als CGT-groep op de opvolgmeting na 3 en 18 maanden. Onze resultaten laten zien dat, via het internet, PDT even goed als CGT lijkt te werken voor de behandeling van GAS.

HOOFDSTUK 5 laat de resultaten zien van een analyse van e-mails van therapeuten aan patiënten in ons eerste onderzoek naar CGT voor GAS via het internet (zoals beschreven in hoofdstuk 2). Er werden 490 e-mails van drie therapeuten onderzocht, en door middel van inhoudsanalyse werden acht afzonderlijke therapeutengedragingen gevonden. De therapeuten in dit onderzoek gebruikten, in meer of mindere mate, deadline flexibility, task reinforcement, alliance bolstering, task prompting, psychoeducation, self-disclosure, self-efficacy shaping, en empathic utterances. Veel van deze gedragingen correleerden sterk met elkaar, een meerdere correleerden met het aantal afgeronde modules, maar slechts twee correleerden met behandeluitkomst: deadline flexibility was negatief gerelateerd aan uitkomst, en task reinforcement correleerde positief met veranderingen op de primaire uitkomstmaat. Hoewel de therapeuten in dit onderzoek zich verschillend gedroegen was geen enkele stijl van begeleiding beter dan een ander.

HOOFDSTUK 6 beschrijft een literatuuronderzoek waarin besproken wordt op welke verschillende manieren therapeuten worden ingezet bij online behandelingen. Implicaties van de kosten van het uitvoeren van door een therapeut begeleide behandelingen worden besproken, aangezien er ook programma's zijn die volledig geautomatiseerd zijn en geen begeleiding door een therapeut nodig hebben. In dit literatuuronderzoek werd een sterke correlatie gevonden tussen de inbreng van de therapeut en de uitkomst van de behandeling.

HOOFDSTUK 7 geeft de algemene discussie van dit proefschrift. De belangrijkste resultaten van onze onderzoeken worden besproken in het licht van eerdere bevindingen. De belangrijkste beperkingen worden gegeven, klinische implicaties worden besproken, en aanbevelingen voor toekomstig onderzoek worden gegeven.

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ABOUT THE AUTHOR

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Björn Paxling, born on the 14th of February 1980 in Malmö, Sweden, is a licensed clinical Psychologist and a Researcher who has taken a special interest in CBT, anxiety, health economics and Internet delivered therapy.

Since his graduation from Linköping University in 2007 Björn has been involved in various research projects including randomised controlled trials (with cost effectiveness analyses) of Internet-delivered CBT for erectile dysfunction, for generalised anxiety disorder and for psychological symptoms after breast cancer treatment with individualized/tailored treatments. Björn has also been involved in implementing Internet-delivered therapy in general psychiatric care in southern Sweden.

Björn is interested in open source treatments, and in 2010 he was involved in creating a self-help treatment for social phobia licensed under Creative Commons, making it available for other researchers and clinicians to use and/or rewrite. Alongside his research, Björn was employed part-time as a clinical psychologist, working with individual and group therapies for anxiety, depression, eating disorders and personality disorders.

In 2009 Björn was elected to join the board of the Swedish Association of Behaviour Therapy (SABT). During SABT's 40th anniversary conference in 2011, Björn was elected president of the association. He is also one of the founders of a Swedish research network for researchers focusing on Internet-delivered treatments, and has been involved in organizing the network's annual conferences. Björn currently resides in Malmö in southern Sweden with his wife, and is also a board member of the Swedish association of Vegan Runners.

ACKNOWLEDGEMENTS

ACKNOWLEDGEMENTS

The present body of work would not have been if not for the guidance, support and love I've had the pleasure to receive from a vast number of people. First and foremost I want to thank all those who has participated in our trials. You have shared you worry and taken a great leap of faith in trying out treatments administered in an unconventional way, and I truly believe that many others with generalized anxiety will be better off because of this!

As a PhD-student I have had the great privilege of having a team of international superstar-researchers as supervisors, and I sincerely hope that I will have the pleasure of collaborating with all of you again in the future! I am forever indebted to Gerhard Andersson, for believing in me and providing me with a research platform to test hypotheses from, for opening so many doors for me, and for giving me so many challenges from which I have grown! If it weren't for you Gerhard, I probably wouldn't have found my way into doing clinical research, and I would have missed out on some amazing years which comes to an end with the publication of this thesis. Pim Cuijpers, since I first met you at an ISRII-conference in Stockholm you have been one of my role models, both scientifically where your warmth and clarity in summarizing and explaining wide areas of research really has made an impact on me, and as a fellow human being who always seems to have time for a discussion despite your incredible work output. I am really grateful for being given the chance to work at your department! Everything I know about health economics, I have learned from Filip Smit. When I think back today, I find it amazing that you Filip devoted so much time and effort to guide me in this field of research even when I was still only a psychology major whom you'd only met once at a conference. Being around you is a humbling experience regardless if we are working on a scientific project together or discussing developmental issues in the third world over a beer, and I thank you for having helped me grow both as a researcher and as a person!

Back in 2005, me and two classmates at the psychologist programme in Linköping started discussing the possibility of conducting a larger project together for our master theses. This resulted in the first trial on Internet delivered CBT for GAD, and despite knowing how hard we worked and how stressed out we were from time to time, what I remember most clearly is us playing Worms together and having a laugh. Jonas Almlöv, I thank you for showing me the light in terms of behavioristic and scientific principles, for challenging my way of thinking and reasoning, and for simultaneously being a damn good friend! I admire your conviction in life even though it saddened me

that this conviction led you away from researching in the end. My close friend Mats Dahlin, you deserve my gratitude for so many reasons: you have always been generous in sharing your knowledge in the CBT-field, you are always there for me in times of need giving advice on how to tackle problems be they technical or social, and your commitment to being a good friend is fantastic. What do you say Mats, should we find a date and watch the Ping-Pong Club again from start to finish?

Conducting research is an activity best performed in teams, and I have had the privilege of working together with the best colleagues imaginable! Per Carlbring, you have been a driving force in practically all projects I've been working on, where your technological know-how combined with your scientific knowledge and rigour has paved the way for robust projects with excellent outcome. It is also inspiring to see someone so young become a professor, I think Umeå is lucky to have you! My first mentor in the field of GAD was Lisa Breitholtz who generously shared her knowledge and provided excellent clinical supervision! Besides all her expertise, Lisa also brought Sara Widén into the project which Sara made better in many ways. Thomas Eriksson, I thank you for good collaboration on our first trial where your knowledge as a psychiatrist helped a lot, and for making me more openminded towards coworking with doctors in helping those with mental problems! I thank also Lise Bergman Nordgren for helping our research group with looking further into the horizon and performing long-term follow-ups. To days date no less than four randomised controlled trials has been conducted in Sweden on Internet delivered treatments for GAD, and none of these trials would have been possible to perform without the help of psychology master students. I want to thank Emma Carlsson, Manja Enström, Linus Fhärm, Anna Johansson, Susanne Lundgren, Lena Jonsson, Anita Norman, Teresa Michel, Pie Roch-Norlund, Gunnar Östman, Anna Norgren, Lisa Georén, Johanna Mehra, Paul Howard, Patrik Fridlund and Sara Hillbom for your invaluable efforts in furthering our knowledge on the treatment of GAD! I have had the great honor of supervising many of your master theses besides working closely with you on these projects, and today I can say that this has been one of the most rewarding aspects of working as a researcher! It is with great pride that I write that the CBT-based Internet delivered treatment that was written for our first trial is implemented in routine psychiatric care in southern Sweden, mostly thanks to the the blessings from local Director Sven-Erik Andersson and the hard work of Olof Johansson, Project Leader!

Despite moving to Malmö shortly after I finished my Master studies and enrolling as a PhD-student at the VU in Amsterdam, Linköping University has always been my home

university which I have visited on countless occasions. Besides those already mentioned, many colleagues and friends have always greeted me with love and kindness on my visits where I especially want to thank Maria Jannert, Malin Gren Landell, Vendela Zetterqvist and Cornelia Weise for always making me feel welcome! Linda Snecker, thank you for all your efforts in making everything run smoothly and for going the extra mile helping me with everything I've had problems with! My gratitude also towards Alexander Alasjö for all the invaluable tech-help! At the department I have also had the pleasure of visiting my close friend and mentor in feminism and hbtq-related issues, Anna Malmquist, who I want to thank for making me feel good about who I am, and for always being there for me! Our research group has grown considerably the last few years, and I want to thank Hugo Hesser, Robert Johansson, Kristin Silfvernagel, Marie Blom, Nina Bendelin, Jesper Dagöö and Hoa Ly for enrichening this group, and I wish you the best of luck on your future research endeavors!

As a young researcher I did not know what to expect when I first visited VU and Trimbos Instituut back in 2007 in order to learn more about health economics. My expectations were high, yet there was no way I could have prepared for the extent of the hospitality and the loving kindness shown to me by those I am now happy to call colleagues and friends! Sherida Slijngaard, you are one of the nicest people I know, and you have helped me so much both in and out of the department by letting me stay at your place. Your hospitality is something out of the ordinary, just like your cooking, and I am happy to have you in my life! In terms of how much we've met, I have only known Tara Donker for a few weeks divided over conferences and my visits to Amsterdam, but nevertheless she is one of my closest friends today! Tara, I want to thank you for always being cheerful and smiling all the while being philosophical and insightful, you have opened up your home and let me into your life which I am truly grateful for! Annemieke van Straten, thank you so much for all the help in the final stages of working with this thesis! I would also like to thank Robin Kok for helping me with translating my summary of the thesis! Many other friends and colleagues has made my stay in Holland memorable and enjoyable, and I want to especially thank Bregje van Spikjer, Carmen Vos, Burçin Ünlü, Irene Riepma, Marianne Ouwehand, Heleen Ripper, Jorne Grolleman, Lisanne Warmerdam, Monique Jordan, Willemijn Hoek, Wike Seekles, Annemiek Huisman and Edith Van 't Hof for all the kindness!

While living in Malmö, working on projects based at Linköping University and being a Dutch PhD-student, I have for some strange reason often found myself working from Karolinska Institutet in Stockholm, more specifically at the Internet Psychiatry unit.

I want to thank Nils Lindefors and Christian Rück for inviting me here and allowing me to return and work from the unit on several occasions, always cheering me on in my research endeavors. If someone would ask me what I'm most proud of after my years as a PhD-student, I would answer witnessing and being a part of Erik Anderssons journey from a Master student to an excellent researcher. Erik, your dedication to your work makes the rest of us look lazy, and you have really helped me hang in there when my research hasn't gone so well, thank you for being who you are! Many are the people who have made me feel like a part of the team when I've visited the Internet Psychiatry unit which has made come back time and time again. Brjánn Ljóts-son, thanks for fighting the good fight, for serious hugs, and for showing us all how to balance the fine line between geniality and insanity! Erik Hedman, thanks for all your support in my health economics research and for furthering my understanding of my research by asking all the tough questions. Erik and Brjánn, you are truly the Chip 'n' Dale of Internet delivered therapy research, and I look forward to meeting you both again! For his groundbreaking work in the field, for all he has done for behavior therapy in Sweden, and for being a great role model in terms of leadership I extend my gratitude toward Viktor Kaldö. Kerstin Blom, thank you for all the christian side hugs! My gratitude also to Sara Rydh for a long and memorable walk and talk, to Evelyn Andersson for furthering my knowledge regarding the norwegian black metal scene and to Lisa Jansson for having enough faith in me to lend me her kick-bike!

During these last few years, I have had the great pleasure of being involved in three professional networks which has made my life better both work-wise and socially. I want to thank all my friends and colleagues, too many to mention by name, in the International Society for Research on Internet Interventions, in the Swedish Association of Behaviour Therapy and the Swedish IT Alumni, without you all my life would have been a lot less colorful!

Parallel to conducting research on Internet delivered therapy, I have also been working in more regular health care settings meeting patients in a more old school face-to-face manner. I want to acknowledge and thank my old colleagues from the psychiatry company Hjärnhälsan, for allowing me to combine Internet delivered treatments with regular psychiatric care, for being flexible in regards to my research, and for filling my workdays with smiles and laughter. Ulrika Ermedahl Bydairk, thank you for arranging a whole course with me on Internet delivered treatments in Lund, and thank you for always being there for me in times of need. My sincerest gratitudes to Johan Holmberg for all you have taught me, for always looking out for my best interests, and for show-

ing me that it's perfectly alright to be a little crazy yourself while working with mental illness. I would also like to thank all my new colleagues at the primary care company Hälsomedicinskt Center who have been supporting and cheering me on in the final stages of finishing up this thesis, I'm really glad to be a part of the team!

For always giving me a place to sleep (even when my planning has been bad and I call just one day ahead), for giving me perspective on my work, and for letting me share the love in your families, I want to thank Maria, Johan, Hanna and Anton Ymerstaf in Linköping, and Pelle, Sussi, Simon and Sebastian Axbom in Stockholm!

Mom, like I said when I was little, I thank you for *borning* me! Your help with proof reading treatment modules has been of great importance, and closely following your academic and professional career has taught me that anything and everything is possible if you set your mind to it! Also mom, seeing you beam with pride over my work is one of the most rewarding experiences during this whole undertaking! Dad, you have taught me to be a sensible man attuned to the emotions and needs of others which I am immensely grateful for! Gradually I'm realising how much I am like you, I might not have "landed" yet, but I take great pride in following in your footsteps and I continuously learn a lot from what you have told me about working with yourself. Sonja Axbom, you have taught me more about love than five years worth of psychologist education could, I thank you for your help during my first research project, and for teaching me so much by sharing your fascinating life! My sister Karin Palmqvist, thank you for all the smiles and insights, and for showing me how to overcome fear when doing something really important! Sister Karoline Palmqvist, thank you for being a role model in terms of working towards a long-term goal, your dedication has made a great impression on me, and thanks for feeding me together with Styvas Persson at the world's best restaurant, Kao's!

Linda, my Linda. We need not words.

