



PSYCHOLOGICAL TREATMENTS FOR DEPRESSION DELIVERED VIA THE INTERNET AND SUPPORTED BY A CLINICIAN: AN UPDATE

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Abstract: Guided internet-delivered cognitive behaviour therapy (ICBT) has been tested in many trials since the early studies dating back to the late 1990's. The aim of this review was to investigate the most recent literature on guided ICBT for depression. We identified 11 controlled studies published between January 2013 and September 2014. Overall, large treatment effects were observed with a few exceptions. A majority (7 studies) provided some information regarding unwanted effects such as deterioration. Three studies directly compared guided ICBT against face-to-face CBT. We added an earlier study and calculated meta-analytic summary statistics for the four studies involving a total of 336 participants. The average effect size difference was Hedges $g = 0.12$ (95% CI: -0.08~0.32) in the direction of favouring guided ICBT, but with no practical importance. We conclude that guided ICBT is a promising treatment for depression and mood disorders and that the research is rapidly expanding.

Keywords: Internet; guided self-help; mood disorders, face-to-face treatment.

Tratamientos psicológicos para la depresión aplicados a través de Internet y con el apoyo de un clínico: Una actualización

Resumen: La terapia cognitivo-conductual aplicada vía internet (TCCI) ha sido puesta a prueba en muchos ensayos desde los primeros estudios en 1990. El objetivo de esta revisión fue investigar la literatura más reciente sobre la TCCI para la depresión. Se identificaron 11 estudios controlados publicados entre enero 2013 y septiembre 2014. Se observaron grandes efectos del tratamiento, con pocas excepciones. La mayoría (7 estudios) proporcionó información sobre los efectos no deseados, como el deterioro. Tres estudios compararon directamente la TCCI con TCC cara-a-cara. Se añadió un estudio anterior y se calcularon estadísticas de resumen meta-analíticas para los cuatro estudios incluyendo un total de 336 participantes. La diferencia promedia de tamaño del efecto fue Hedges $g = 0.12$ (95% CI: -0.08~0.32) en favor de la TCCI. Se concluye que la TCCI es un tratamiento prometedor para la depresión y los trastornos del estado de ánimo y que la investigación se está expandiendo rápidamente.

Palabras clave: Internet; auto-ayuda guiada; trastornos del estado de ánimo, tratamiento cara a cara.

INTRODUCTION

The Internet has become an integral part of our lives and with a few exceptions a majority

of the population in the industrialized countries use the Internet daily to communicate and share information (www.internetworldstats.com). Clinical psychology has been much influenced by this development, as clients seek information on the Internet, receive support via social media, and clinicians themselves use the Internet to search for information and increasingly to communicate with clients and colleagues (Andersson, 2014). Internet-delivered

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assessment and treatment is preceded by computerized assessment and treatment, for example computerized cognitive behaviour therapy (Kaltenthaler et al., 2006) (CCBT). This is a therapy format that has many similarities with internet-based psychological treatments but also differences such as the lack of online contact with a therapist from a distance and the need to have the CCBT program installed on a computer. It is often the case that CCBT and internet interventions are reviewed together (Marks, Cavanagh, & Gega, 2007), which arguably is not correct given their differences. Another important area of research is virtual reality treatments that are distinctly different as well (Powers & Emmelkamp, 2008), but given technological developments might become integrated with Internet-delivered psychological treatments. We will not cover CCBT in general or virtual reality treatments in this review. Neither will we cover the large literature on automated and unguided Internet treatments (Andersson, 2014). There are several advantages with unguided automated treatments, such as scalability, but the verdict is still out with regards to their effects and dropout rates, as most reviews indicate that dropout is larger and effects smaller with unguided as compared to therapist-guided treatments (Baumeister, Reichler, Munzinger, & Lin, In press).

The term guided Internet-delivered psychological treatments needs to be explained. Usually, it concerns mainly self-guided treatments with text, pictures, audio files, and sometimes streamed videos (Andersson, 2014) - all being delivered online using a secure platform. Such treatments can sometimes be delivered without any clinician contact, and for example having automated reminders, but when a clinician is involved a secure communication platform is also needed (Andersson et al., 2008). Thus therapist-guided Internet treatment is a form of blended treatment as it is different from both self-guided and regular face-to-face psychotherapies (Andersson, 2009).

There are numerous randomized controlled trials on Internet treatments in general and many on guided Internet treatments (Hedman, Ljótsson, & Lindfors, 2012), most being based on cognitive behaviour therapy (often referred

to as Internet-based cognitive behaviour therapy: ICBT). In this paper we will focus on mood disorders and depressive symptoms given that this is a costly and highly prevalent problem across the world (Wittchen et al., 2014). There are several reviews on the treatment of major depression using the Internet (Johansson & Andersson, 2012; Richards & Richardson, 2012), and also reviews including other conditions (Arnberg, Linton, Hultcrantz, Heintz, & Jonsson, 2014), and for this reason we focus this paper on recent literature on the treatment of depression and depressive symptoms as a way to highlight the progress in a rapidly expanding field. The aim of this paper was thus to review the most recent literature on guided Internet treatments for mood disorders and depressive symptoms from 2013 and onwards, with a focus on randomized controlled trials and if available references to previous reviews. We also investigated to what extent negative effects are mentioned in the current literature (Rozenental et al., 2014). Finally, we calculated meta-analytic statistics for the direct comparison studies in which guided ICBT and face-to-face CBT had been directly compared.

Literature search

Internet-based psychological treatments have been developed for a range of common psychiatric conditions (Andersson, Carlbring, Ljótsson, & Hedman, 2013), and in this paper we cover depression in adults. We searched the literature (Scopus, Medline, Web of Science), contents in established journals in the field (e.g., JMIR, Internet Interventions) and located studies published between January 2013 and September 2014. We did not include in press (early view) studies and also excluded non-randomized studies, studies on attention bias modification, studies in which no therapist guidance was provided, and studies in which the treatment provided was not psychological in its main content (e.g., physical activity for depression). We also excluded studies dealing with clearly non-clinical conditions. This resulted in 11 randomized trials of which three trials compared ICBT against face-to-face treatment.

Review of the recent studies (published January 2013 to September 2014)

Several studies have been conducted on guided Internet-delivered treatments for depression (Johansson & Andersson, 2012), and in the review period here we located as many as 11 randomized controlled trials.

From our own group, Carlbring et al. (2013) investigated the effects of a treatment based on behavioural activation with the addition of components from acceptance and commitment therapy in a sample of 80 adults diagnosed with depression and recruited from the general public (Carlbring et al., 2013). Following 8 weeks of treatment there were large between-group effects on the main outcome measure Beck Depression Inventory II ($d = 0.98$), when compared against a waitlist control group. There was a low dropout rate with only two persons not completing the post treatment assessment (in the control group). Results were maintained at 3-month follow-up. There was no deterioration as assessed by the BDI-II.

In another study from our group we compared guided ICBT against face-to-face group treatment in a sample of 69 persons diagnosed with depression and recruited from the general public. In addition, to post treatment data we also included follow-up data at 1 year and 3 years after treatment with randomization maintained (Andersson, Hesser, et al., 2013). The treatments lasted for 8 weeks and were similar in contents. Dropout rates varied during the course of the trial, but was generally low with as many as 62 completing the 3 year follow-up (90 %). There were large within-group effects for both treatments (Cohen's d 's above 1.0) and non-inferiority analyses could confirm non-inferiority of guided ICBT. Indeed, there was even a tendency for the guided ICBT group to be superior to the group-based CBT condition at 3-year follow-up. No participant in either group had deteriorated at post-treatment as assessed by a clinical interview. However it is important to note that some participants had received additional therapy at the time of the 3-year follow-up (19 psychological treatment and 13 change of medication).

A second study compared guided ICBT for depression against face-to-face treatment, with the difference being that it was individual treatment and not group treatment (Wagner, Horn, & Maercker, 2014). They included 62 participants in the study and while there was no structured diagnostic interview it is likely that a majority were depressed. The treatments lasted for 8 weeks and there was a 3-months follow-up. There was a somewhat larger dropout from the ICBT group (7 vs. 2 in the face-to-face group), and in particular at 3-months follow-up only 37/62 completed outcome measures. Both groups displayed large within-group effects ($d = 1.27$ and 1.37 at post treatment for ICBT and face-to-face treatments respectively). However, at 3-months follow-up there was a clear tendency for the ICBT group to fare better with a between-group effect of $d = 0.61$ in favour of ICBT. This was explained by a significant worsening on BDI-II scores in the face-to-face group. While the authors reported the deterioration in the face-to-face group no proportions of deterioration were presented for the ICBT group.

A third recent study compared ICBT against face-to-face treatment, but with both interventions being based on a form of CBT called Acceptance and Commitment Therapy (ACT) (Lappalainen et al., 2014). As with the Wagner et al. trial not all participants were diagnosed with depression. The Internet treatment (called iACT) and the individual face-to-face treatments lasted for 6 weeks. The iACT involved two visits at the clinic. Participants were recruited from the general public via advertisements, and in total 38 persons were randomized to either condition. There were almost no dropout with all but one participating in the post-treatment and follow-up assessments, the last one being at 18 months posttreatment. Results on the BDI-II showed large within-group effects, including large pre-to follow-up effects (Hedge's $g = 1.59$ for the iACT group and 1.37 for the ACT group). There were also indications that the Internet condition fared better than the face-to-face treatment at 6-month follow-up with a between group effect on the BDI-II of $g = 0.76$. Deterioration was reported but no participant deteriorated during the trial.

One treatment that has been tested in many studies is the MoodGYM program from Australia (Christensen, Griffiths, & Jorm, 2004). Most studies on MoodGYM have not involved therapist guidance, but a study from Norway using a translated version of the program tested the effects of MoodGYM with face-to-face therapist support in a controlled trial involving 106 participants with depression or depressive symptoms recruited from primary care (Høifødt et al., 2013). Treatment lasted for 6 weeks and was compared against a waiting list condition. A majority completed the posttreatment measures (71% in the intervention group and 87% in the waitlist group). The between-group effect size was $d = 0.65$ on the BDI-II at posttreatment. A 6-months follow-up showed moderate to large within-group effects as compared to the pretreatment values. Deterioration was reported and in the full sample one participant in the intervention group and three in the control group deteriorated.

Over the years, the role of guidance in ICBT has been discussed and in the field of depression most studies have indicated that support results in larger effects and better adherence (Andersson & Cuijpers, 2009). However, this conclusion is based on few direct comparisons. In a trial by Mohr et al. (2013) the effects of guided versus unguided ICBT for depression was compared against a waitlist control group in a sample of 101 persons with major depression (Mohr et al., 2013). The manualized telephone coaching involved weekly brief telephone calls (10-15 min) and the treatments lasted for 12 weeks. Adherence was better in the guided condition (greater number of login days), but there was no difference in depression outcomes. While the active treatments resulted in better outcomes than the waitlist control condition, the trial is hard to interpret due to lack of control group data at 12 weeks. Moreover, in spite of the telephone support the lost to follow-up rates were 29% in the coach group versus 17.1% in the self-directed group. Adverse events were monitored and there were none during the trial.

Symptoms of depression were treated in a study on employees ($N = 231$) who were randomized to either guided ICBT or to treatment as

usual (Geraedts, Kleiboer, Wiezer, van Mechelen, & Cuijpers, 2014). Only a minority were diagnosed with a current major depression (25%). There was some attrition in this study at posttreatment (26%), which was handled with imputation. Following six weekly treatment sessions results showed a small effect compared to the treatment as usual group ($d = 0.16$), which was explained by a large improvement in the control group (the treatment group had a within-group effect of $d = 1.03$ and the control group $d = 0.98$). Deterioration or adverse events were not reported.

In a study from our group we tested if a smartphone application based on behavioural activation was more effective than a smartphone application based on mindfulness, with both treatments being supplemented with support and information online (Ly et al., 2014). The study included 81 participants diagnosed with major depressive disorder who were randomized to either the behavioural activation treatment or to the mindfulness treatment. There were 9 participants who did not complete the post-treatment assessment. The results on the BDI-II showed a small between group effect at posttreatment ($d = 0.25$ in favour of the behavioural activation), but both groups improved substantially (within-group effect sizes 1.83 and 1.21 for the behavioural activation and mindfulness treatments respectively). Follow-up results at 6 months showed that treatment effects remained. Deterioration or adverse events were not reported.

Postpartum depression is a fairly common and debilitating problem for which there is evidence that psychological treatments can obtain positive effects (Cuijpers, Brännmark, & van Straten, 2008). In a controlled trial with 83 women the effects of a program called Netmums was tested against treatment as usual (O'Mahen et al., 2014). The program was supported by weekly phone calls. Depressive symptoms were measured at baseline, 17 weeks post-treatment and at 6 months follow-up. There was a low dropout rate, with 3 dropouts in the treatment condition at posttreatment and 8 in the control group. Results showed a large between group effect ($d = 0.87$) at posttreatment and at 6 months follow-up ($d = 0.78$). Negative outcomes in terms of adverse events or deterioration were not reported.

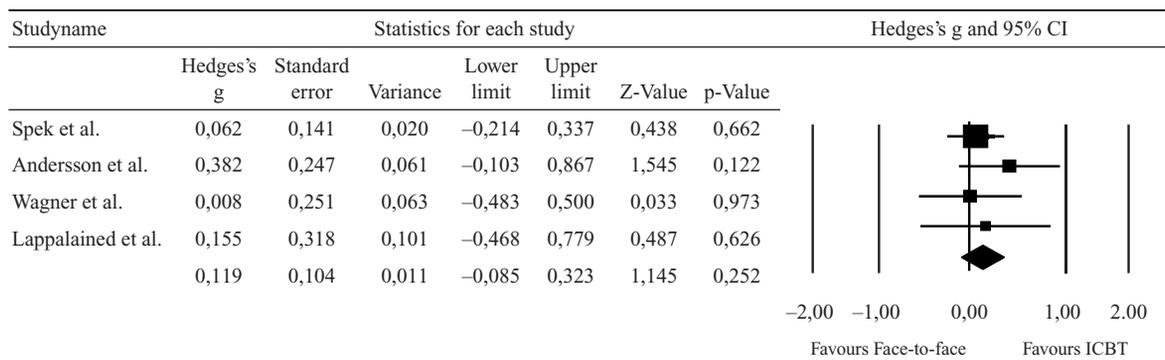
In this review we only focused on depression, but there are a large number of studies on guided ICBT for somatic problems (Andersson, 2014). In a trial by Glozier et al. (2013) persons with high cardiovascular disease risk and mild to moderate depression were recruited ($N = 562$). This study involved telephone reminders and also minor email contact and could in that respect be regarded as supported by a clinician even if the program e-couch was not guided in terms of content. Participants were randomized to either immediate treatment or to attention control group (called Healthwatch). Outcomes were assessed at baseline and at 12 weeks. While there was some missing data a majority of the control group (97%) and treatment group (76%) completed post intervention depression measures. While both groups improved there was a small effect in favour of the ICBT group. Adverse events were monitored and reported in the domain of risk of deliberate self-harm.

Most studies on ICBT for depression has been on mild to moderate depression or depressive symptoms, and in one case relapse prevention for persons with residual symptoms (Höglund et al., 2011). Much less has been done on other mood disorders such as bipolar disorder. In a controlled study 122 persons with diagnosed bipolar disorder I (70%) and II (25%) were randomly allocated to guided ICBT or to a control group (Todd, Jones, Hart, & Lobban, 2014). There were relatively few dropouts with 88% of participants in the intervention group

and 92% of participants in waiting list group remaining in the trial. Participants were given access to the program for a period of 6 months, and outcomes were assessed at 3 months and 6 months post randomization. Results for quality of life and symptom measures at 6 months showed small to moderate effect sizes ($d = 0.40$ to 0.70). Negative effects were not reported.

As effective as face-to-face CBT?

As two more studies directly comparing guided ICBT and face-to-face CBT have been added since the publication of a recent meta-analysis (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014), we decided to calculate meta-analytic statistics for the three studies included in this review and adding an earlier study (Spek et al., 2007). We used the program Comprehensive Meta-Analysis (version 2.2.021; CMA) to calculate pooled mean effect sizes. A forest plot for the four studies are presented in Figure 1. In total there were 183 participants who had been randomized to guided ICBT (in one case iACT) and 153 who were randomized to face-to-face CBT (in two studies group treatment). All studies used the Beck Depression Inventory II which we used when calculating effect sizes. The overall random effects effect size was Hedge's $g = 0.12$ (95% CI: $-0.08 \sim 0.32$) in the direction of favouring guided ICBT and with no signs of heterogeneity ($I^2 = 00\%$). Duvall and Tweedie's trim and



Meta Analysis

Figure 1. Meta-analysis. Forest plot of studies comparing guided internet-delivered CBT against face-to-face treatment for adult depression.

fill procedure and Egger's test also did not suggest publication bias (as implemented in CMA). Thus on the basis of the four controlled studies guided ICBT and face-to-face CBT appears to be as effective.

DISCUSSION

Based on the available evidence, partly reviewed in this paper, the following conclusions can be drawn. First, guided ICBT for depression has good support in the recent trials reviewed here, and we see no signs indicating that the effect found in the earlier trials has been overestimated. We located 11 studies, but there were more studies in which no guidance was provided that we did not include in this review. While we focused on depression and mood disorders the review period and our searches also revealed that many controlled trials had been published on anxiety disorders and somatic disorders. There is also an interesting trend to do studies on other treatments than CBT. For example, in our group we have conducted studies on both physical activity (Ström et al., 2013) and psychodynamic Internet therapy (Johansson et al., 2012). Another strong trend is to develop and test transdiagnostic and tailored interventions (Andersson & Titov, 2014). As we focused on controlled trials we did not include recent large studies showing that ICBT works in representative clinical settings (so called effectiveness studies), with studies from both Sweden (Hedman et al., 2014) and Australia (Williams & Andrews, 2013); for review see (Andersson & Hedman, 2013).

Seven trials provided data or information regarding deterioration and/or other unwanted effects. This is promising given the importance of reporting negative as well as positive effects of interventions and in light of a recent observation that reporting negative effects is a characteristic of high quality trials (Jonsson, Alaie, Parling, & Arnberg, 2014). There is an increased interest in reporting negative effects of ICBT, even if most studies and indeed the findings in the papers reviewed here do not suggest that adverse events and/or deterioration is common (Boettcher, Rozenal, Andersson, & Carlbring, 2014).

In a previous meta-analysis covering a broad range of clinical conditions it was found that guided ICBT and face-to-face treatments tended to be as effective (Andersson et al., 2014). Here we only covered depression and found a similar outcome, with two additional studies being included. The focus of this paper was on guided ICBT. However, an important question is who provides the support. There are some studies indicating that support can be provided mainly from a technical and administrative point of view with little need for psychotherapeutic expertise (Titov et al., 2010). On the other hand it may also be the case that some patients do not need any support at all (Titov et al., 2013). Future research needs to provide more information on who needs more versus less support as it is a fact that a significant minority of patients probably manage without any support, in particular if there is a clear deadline for completion (Nordin, Carlbring, Cuijpers, & Andersson, 2010) and automatic reminders (Titov et al., 2013).

Guided ICBT can be regarded as a form of blended treatment and in one of the studies reviewed in this paper telephone contact with participants was scheduled (Mohr et al., 2013), which is a procedure that has been tested previously (Andersson, Lundström, & Ström, 2003; Lindner et al., *In press*). It is somewhat unclear how much scheduled phone calls add to effects and adherence in ICBT, but from a clinical point of view treatments that blend information technology and face-to-face contacts are likely to become more common in clinical practice (Månsson, Ruiz, Gervind, Dahlin, & Andersson, 2013), for example for older persons (Botella et al., 2009).

This review paper has limitations. First, given the rapid expansion of Internet-delivered treatments and blurred distinctions between different forms of Internet treatment (including a non-coherent terminology) it is possible that we missed studies in our searches. Second, we did not include in press papers or unpublished papers. In particular in the latter case this can be motivated by the fact that studies may differ before and after a review process. In the former case it is also sometimes unclear if a paper has been proof-

read or not and we decided to focus on studies that had reached the final stage of being published. Third, comorbidity is a rule rather than an exception in studies on depression and depressive symptoms, and hence studies on transdiagnostic and tailored approaches probably capture a more clinically representative group of participants.

We conclude that guided ICBT for depression has several potentials for dissemination across the world with a rapid increase of new studies each year. It is more common to report side effects and overall studies are now becoming larger and less underpowered. Future research is needed to distinguish between different approaches and programs for depression as there appears to be some differences between research groups in terms of how large effects are obtained.

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