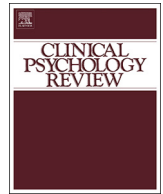




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## Review

## Do guided internet-based interventions result in clinically relevant changes for patients with depression? An individual participant data meta-analysis

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## HIGHLIGHTS

- Little is known about clinically relevant changes in guided Internet-based interventions.
- Guided Internet-based interventions result in significantly higher remission and response compared to controls
- Severity of depression, age and ethnicity significantly moderate treatment outcome.

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## ABSTRACT

Little is known about clinically relevant changes in guided Internet-based interventions for depression. Moreover, methodological and power limitations preclude the identification of patients' groups that may benefit more from these interventions. This study aimed to investigate response rates, remission rates, and their moderators in randomized controlled trials (RCTs) comparing the effect of guided Internet-based interventions for adult depression to control groups using an individual patient data meta-analysis approach. Literature searches in PubMed, Embase, PsycINFO and Cochrane Library resulted in 13,384 abstracts from database inception to January 1, 2016. Twenty-four RCTs (4889 participants) comparing a guided Internet-based intervention with a control group contributed data to the analysis. Missing data were multiply imputed. To examine treatment outcome on response and remission, mixed-effects models with participants nested within studies were used. Response and remission rates were calculated using the Reliable Change Index. The intervention group obtained significantly higher response rates (OR = 2.49, 95% CI 2.17–2.85) and remission rates compared to controls (OR = 2.41, 95% CI 2.07–2.79). The moderator analysis indicated that older participants (OR = 1.01) and native-born participants (1.66) were more likely to respond to treatment compared to younger participants and ethnic minorities respectively. Age (OR = 1.01) and ethnicity (1.73) also moderated the effects of treatment on remission. Moreover, adults with more severe depressive symptoms at baseline were more likely to remit after receiving internet-based treatment (OR = 1.19). Guided Internet-based interventions lead to substantial positive treatment effects on treatment response and remission at post-treatment. Thus, such interventions may complement existing services for depression and potentially reduce the gap between the need and provision of evidence-based treatments.

## 1. Introduction

Major Depressive Disorder (MDD) is highly prevalent (Alonso et al., 2004; Kessler, Chiu, Demler, & Walters, 2005; Waraich, Goldner, Somers, & Hsu, 2004) and associated with substantial impairment (Saarni et al., 2007; Üstün, Ayuso-Mateos, Chatterji, Mathers, & Murray, 2004) and economic costs (Berto, D'Ilario, Ruffo, Virgilio, & Rizzo, 2000; Greenberg & Birnbaum, 2005; Smit et al., 2006). Psychological treatments have been shown to be effective in the treatment of depression (Cuijpers et al., 2014; Cuijpers, van Straten, Andersson, & van Oppen, 2008a). However, the majority of depressed people remain untreated (Kohn, Saxena, Levav, & Saraceno, 2004; Wittchen et al., 2011). Epidemiological data from Europe have shown that only 14% and 38% of those who experience mood disorders receive psychotherapy and pharmacotherapy respectively (Alonso et al., 2004). These percentages are lower (7–21%) in low- and middle-income countries where mental health care facilities are scarce (Chisholm et al., 2016).

Using the Internet to provide guided interventions may help overcome some of the limitations of traditional treatment services (Andersson & Titov, 2014; Ebert et al., 2014a). A guided internet-based intervention is a psychotherapeutic intervention primarily based on self-help material delivered via the Internet with some form of minimal guidance related to the therapeutic content. This guidance is considered minimal if provided at low intervals through electronic means, such as emails, phones and e-chats (e.g., brief weekly emails after each online session). Such guided Internet-based interventions (a) provide high accessibility, (b) may attract people who do not use traditional mental health services, and (c) are easily scalable. A relatively recent meta-

analysis (MA) showed that guided Internet-based interventions for depression can have positive effects on depressive symptoms (Richards & Richardson, 2012). However, statistical comparisons based on group means provide limited information about clinical significance (Jacobson & Truax, 1991). Therefore, response and remission have been suggested as the outcome criteria of choice for depression treatment (Keller, 2003; Rush et al., 2006). Remission is generally considered a state in which symptoms of the illness are (nearly) absent (Rush et al., 2006). It is associated with better functioning (Hirschfeld et al., 2002; Riso et al., 1997), lower relapse rates, and improved long-term prognosis (Bech, Lönn, & Overø, 2010; Fava, Fabbri, & Sonino, 2002; Karp et al., 2004; Kennard et al., 2009; Ogrodniczuk, Piper, & Joyce, 2004; Taylor, Walters, Vittengl, Krebaum, & Jarrett, 2010). It is the accepted goal of treatment of acute depression (Anderson et al., 2008; Gelenberg et al., 2010; Lam et al., 2009; NICE, 2010; Thase & Ninan, 2001). However, while not all patients achieve remission (Cuijpers et al., 2014), some may still be classified as responders, i.e. achieve a clinically significant reduction in depressive symptoms (Frank et al., 1991).

Neither remission nor response has been addressed in any meta-analyses of guided Internet-based interventions for depression (Andersson & Cuijpers, 2009; Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014; Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Johansson & Andersson, 2012; Richards & Richardson, 2012). Inconsistencies in methodology for defining response and remission as well as missing reports of these outcomes in studies hinder their evaluation using conventional meta-analytic approaches. Another issue not yet addressed is the possibility that not all subgroups of patients benefit from this specific treatment delivery. For example, it may be argued

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