

Internet-Based Psychotherapy for Adult Depression: What About the Mechanisms of Change?

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Introduction: Internet-based cognitive behavioral therapy for depression (iCBT) has been advanced as a valuable alternative treatment option, generating promising results. However, little is known about its underlying mechanisms of change. **Objective:** We aimed to provide an overview of the state of the art regarding the mechanisms of iCBT for adult depression, in the context of iCBT efficacy. **Method:** We conducted a systematic qualitative review of 37 randomized clinical trials, assessed the risk of bias in the included studies, and used a systematic evaluative framework to establish the scientific status of iCBT, based on evidence regarding clinical efficacy and mechanisms of change. **Results:** Findings indicated that iCBT mechanisms of change are clearly underinvestigated, although iCBT is relatively efficacious, at least in the short term. The quality of iCBT randomized clinical trials proved to be suboptimal. **Conclusions:** The iCBT theory should be clearly specified and adequately investigated to design and implement highly efficacious therapeutic packages. Without considering the iCBT mechanisms of change along with iCBT efficacy, the extent to which iCBT is an empirically validated treatment remains questionable. © 2016 Wiley Periodicals, Inc. *J. Clin. Psychol.* 00:1–60, 2016.

Keywords: Internet-based CBT; adult depression; efficacy; mechanisms of change

Despite being a highly researched topic, and in many cases a condition that responds well to treatment, depression is still highly prevalent, affecting 4.3% of the global population in 2010 (Vos et al., 2012), and expected to become the leading cause of disability by 2030 (World Health Organization, 2011). This paradox has been explained in terms of limited accessibility of the treatment due to costs, stigma, or secondary adverse effects (in case of medication), among others.

One of the best empirically supported treatment approaches to depression is cognitive behavioral therapy (CBT; see, e.g., Butler, Chapman, Forman, & Beck, 2006; Driessen & Hollon, 2010; Hofmann, Asnaani, Vonk, Sawyer, & Fang, 2012). However, the high level of demand, limited availability of therapists, stigma, and logistical costs restrict access to CBT. The problem of making CBT more broadly accessible geographically and financially while simultaneously maintaining its efficacy still awaits solutions. With the advancement of communication technologies (e.g., broadband) and Internet penetration (34.3% of global population and 73.8% of people from developed countries use the Internet on a daily basis; Miniwatts Marketing Group, 2011), computerized CBT appears to be an attractive solution to this problem. CBT is very suitable to adaptation to an online format because it is a structured, manualized approach emphasizing active patient involvement and proactive emotional management skills.

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Internet-Based Psychotherapy for Depression

Internet-based CBT (iCBT) has the potential of facilitating the access to classical evidence-based CBT protocols while decreasing logistical barriers, associated costs, and stigma (Anderson, Jacobs, & Rothbaum, 2004; Marks, Kenwright, McDonough, Whittaker, & Mataix-Cols, 2004; Marks et al., 2003; McCrone et al., 2004). Existing computerized CBT intervention¹ protocols for depression have been found to be efficacious (Foroushani, Schneider, & Assareh, 2011; Kaltenthaler, Parry, Beverley, & Ferriter, 2008; Proudfoot et al., 2004), yielding comparable results with classical CBT, in both adult and youth samples (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Richardson, Stallard, & Velleman, 2010). These results prompted organizations such as The National Institute for Health and Clinical Excellence (NICE) to recommend computerized CBT as a low-intensity psychosocial intervention for persistent subthreshold depressive symptoms or mild to moderate depression (NICE, 2009).

However, despite being seemingly efficacious and having some advantages over traditional face-to-face psychotherapy, computerized CBT for depression faces a number of problems of its own (for a recent review, see Eells, Barrett, Wright, & Thase, 2014). For example, although preliminary evidence suggested that computerized CBT may be as effective as comparable treatments delivered within the traditional therapeutic context (Newman, Szkodny, Llera, & Przeworski, 2011; Richards & Richardson, 2012), a recent meta-analysis (So et al., 2013) reported that the beneficial effects of computerized CBT on depression are rather short lived, do not have a positive effect on functioning, and come with high attrition rates (see also Christensen, Griffiths, & Farrer, 2009; Kaltenthaler et al., 2008).

So et al. 2013 concluded that “the clinical usefulness of current computerized CBT protocols for adult depression may need to be re-considered downwards in terms of practical implementation and methodological validity” (p. 1). This is in line with the conclusions of another meta-analysis (Richards & Richardson, 2012), which reported that more than half (up to 74%, with a mean of 57%) of the patients receiving computerized CBT treatment give it up prematurely and highlighted significant methodological weaknesses of computerized CBT studies (i.e., unreliable diagnostic methods, extensive reliance of self-report measures). In a similar vein, a recent review of computer-assisted CBT for depression concluded that “with concerns about the generalizability of the findings and reliability of the diagnosis, the conclusions that can be drawn from these studies are suspect” (Eells et al., 2014, p. 196), although the investigations conducted to date are considered promising.

To summarize, the existing reviews in the field of iCBT point to an unclear status, characterized by mixed results describing an efficacious treatment having the potential of overcoming previously identified barriers related to traditional CBT accessibility but suffering from at least two main problems: high attrition rate, which seriously limits the clinical utility of iCBT, and significant methodological shortcomings of iCBT studies, which limit confidence in their results.

However, the limitations of the previous reviews might have themselves contributed to this unclear status: So et al. (2013) reported poor long-term outcome of computerized CBT for depression, but in most of the studies included in their meta-analysis, participants in the control group received treatment from posttest to follow-up, making it difficult to interpret the lack of the differences between groups at follow-up (as treatment was compared with the same treatment at follow-up). Other reviews (e.g., Eells et al., 2014) based their analysis on a limited number of iCBT programs, thus sketching a picture that could be distorted. More importantly, the distinction between guided and unguided iCBT has not always been considered (e.g., So et al., 2013), despite the fact that it has been suggested to be a crucial factor that influences iCBT

¹Internet-based CBT is implicitly computerized CBT, but computerized CBT is not necessarily Internet-based CBT (i.e., it is not necessarily delivered through Internet). Throughout the manuscript, we used “computerized CBT” when we referred to CBT protocols that have not necessarily been tested out over the Internet, and “Internet-based CBT” when we referred to protocols that have been used over the Internet. When referring to reviews that synthesized the results of both computerized and Internet-delivered protocols, we preferred “computerized CBT.”

efficacy and treatment adherence (Richardson & Richardson, 2012; van Ballegooijen et al., 2014)

In addition, none of the existing quantitative and qualitative reviews of computerized CBT interventions for depression considered the iCBT's mechanisms of change. They all focused exclusively on data regarding the efficacy of computerized CBT package, but are silent about the mechanisms of change (i.e., psychological factors assumed to be targeted by the intervention and to mediate the change in symptoms) underpinning these intervention packages.

Why Considering iCBT Mechanisms of Change is Important

In the context of the high proliferation of computerized CBT-based interventions for depression (e.g., Good Days Ahead [Wright, Wright, & Beck, 2002], Beating the Blues [Proudfoot et al., 2003], MoodGYM [Christensen, Griffiths, & Jorm, 2004; Christensen, Griffiths, Korten, Brittliffe, & Groves, 2004], Color Your Life [de Graaf et al., 2009], and BluePages [Mackinnon, Griffiths, & Christensen, 2008]), underinvestigating their mechanisms of change is clearly a shortcoming that needs to be addressed, to not only improve treatment outcomes but also prevent detrimental effects. In addition, although iCBT intervention protocols are largely computerized versions of traditional face-to-face CBT protocols, the iCBT mechanisms of change may not overlap entirely with those found in traditional CBT. We briefly discuss each of these issues below.

Mechanisms of Change and iCBT Therapeutic Outcomes

Knowing the mechanisms of change in iCBT can increase our understanding of the etiological factors underpinning depression and lead to the development of better (computerized) interventions (see also David & Montgomery, 2011). When we understand the factors that account for therapeutic changes, we can potentially optimize the therapeutic change by designing better, stronger, different, or more strategies that help bring about the critical change process(es) (Kazdin, 2007).

Indeed, even if So et al.'s (2013) conclusion that iCBT is not efficacious in the long term is distorted by methodological weaknesses in many studies included in their analysis, one cannot entirely rule out the possibility that the lack of reliable long-term benefits of iCBT is due to the lack of reliable changes in the mechanisms underpinning the symptoms of depression. If this is the case, then future studies should strive to improve iCBT protocols so that the mechanisms of change are properly addressed, potentially leading to more stable positive outcomes. This would ensure the transition from a symptomatic improvement (i.e., "feeling better") to a genuine clinical gain (i.e., "getting better") and, presumably, a better long-term retention of clinical gains achieved after iCBT.

When the mechanisms of change remain unknown, it is hard to make the treatment transition from the experimental to the clinical arena (Kazdin, 2007). If we do not exactly know what is needed to make the treatment work or the critical components that should not be compromised or diluted to achieve change, then we might have a treatment that may work well in an experimental context (contrived setting) but one that does not always lead to benefits in ecological contexts—and we do not know why this happens.

Ignoring iCBT Mechanisms of Change Could Be Detrimental

As the iCBT intervention protocols for depression become more widely available and begin to be commercialized without strong scientific evidence supporting them, serious negative consequences may arise. Basically, at this point is not clear if iCBT produces genuine clinical gain or just symptomatic improvement. If the improvement is only symptomatic, then offering iCBT to a person in need may prevent him or her from obtaining adequate help, thus placing the person at risk for developing more severe symptoms in the future (see also David & Montgomery, 2011). This challenges, from a practical point of view, the use of iCBT as a standard treatment.

Moreover, if we do not know how or why an intervention works, then we cannot anticipate or counteract the eventual adverse effects. Intriguingly, most of the iCBT studies did not report on adverse effects, including major self-harm and suicide, occurring during or after the program. From an ethical point of view, this challenges the offering of iCBT as treatment; namely, it is unfair to commercialize a product that is likely to elicit clinical gain (at least to some extent) but of which we do not have data on potential adverse effects. Understanding the mechanisms of change allows us to identify those factors that might be particularly influential in treatment outcome (i.e., moderators) and conduct better selection of suitable patients (Kazdin, 2007).

The iCBT Mechanisms of Change Are Not Necessarily Identical to the Traditional CBT Mechanisms of Change

We posit that the main reason why iCBT studies focused extensively on testing the therapeutic package while ignoring mechanisms of change resides in the general assumption that the iCBT theory is identical with the traditional CBT theory. However, as argued below, this may not be the case.

The distinction between common factors and specific factors in psychotherapy, championed by Wampold (Wampold, 2001; Wampold, Minami, Baskin, & Tierney, 2002), is now widely recognized. Common factors (e.g., the therapeutic relationship, providing clinical rationale for disorders and treatments, outcome expectancies) are those that account for the greatest psychotherapeutic gain regardless of the specific psychotherapeutic approach. By contrast, specific factors refer to those targeted by a specific psychotherapeutic approach (e.g., specific cognitive factors underlying symptoms, like dysfunctional attitudes, negative automatic thoughts, or irrational beliefs), which can increase the psychotherapeutic gain above and beyond what is attributable to common factors.

Arguably, the specific factors supporting iCBT efficacy are largely the same as the specific factors within traditional CBT because the iCBT protocols are essentially computerized versions of classical CBT-based strategies and techniques. However, because the iCBT protocols are designed and implemented differently than the traditional CBT protocols, and because the treatment content in iCBT protocols can vary considerably, these specific factors can be influenced by the iCBT intervention to various degrees. Differences related to how iCBT and traditional CBT affect the working mechanisms and subsequently influence symptoms should be topics for further research.

As far as the iCBT common factors are concerned—those factors that are generally responsible for most of the therapeutic change—they might also differ significantly from the common factors in the traditional face-to-face CBT. First of all, the psychotherapeutic relationship in face-to-face CBT may be different from the psychotherapeutic relationship in iCBT. Sometimes the therapeutic relationship is totally nonexistent within iCBT because the therapist's level of involvement within iCBT interventions can vary from no therapist assistance (in the case of fully automated interventions), to minimal therapist contact (e.g., regular phone check-in), to involvement equivalent to that seen in classical individual face-to-face therapy (usually in therapy sessions delivered through audio or two-way video communication; Barak, Hen, Boniel-Nissim, & Shapira, 2008). Even in the case of extensive therapist contact (similar to face-to-face therapy), the psychotherapeutic relationship may present certain particularities because it is technologically mediated.

Similarly, the outcome expectancies can vary widely, depending on a variety of personal factors and features related to how the iCBT protocol is designed and implemented. Features related to how the iCBT protocol is designed and implemented could constitute a separate category of common factors shared by various Internet-based self-help instruments and/or intervention and prevention protocols (unlike traditional CBT).

How Mechanisms of Change Are Critical for Evidence-Based iCBT: The State of the Art

According to a recent evaluative framework of psychosocial interventions, proposed by David and Montgomery 2011, there are two factors that guide the analysis of evidence supporting

	Therapeutic package		
Theory	Well supported	Equivocal data	Strong contradictory evidence
Well supported	Category I	Category II	Category V
Equivocal data	Category III	Category IV	Category VI
Strong contradictory evidence	Category VII	Category VIII	Category IX

			
Core of scientifically oriented psychotherapies	Scientifically oriented psychotherapies	Pseudoscientifically oriented psychotherapies	Core of pseudoscientifically oriented psychotherapies

Figure 1. Psychotherapies classification framework.
 Note. Adapted from David and Montgomery 2011.

psychological treatments: the psychological theory concerning therapeutic change (i.e., mechanisms of change), which should be evaluated first and the therapeutic package (i.e., psychological treatment) derived from the theory about the mechanisms of change. Strong empirical evidence collected for each of these factors “can separate scientifically from pseudoscientifically oriented psychotherapies, with major theoretical (e.g., what to teach and research) and practical implications (e.g., what to recommend as good scientific practices)” (David & Montgomery, 2011, p. 5). Each of these factors can be analyzed at three levels: (a) empirically well supported, (b) equivocal and no clear data, and (c) strong contradictory evidence.

By combining factors and levels of analysis, nine categories of psychotherapies can be derived, ranging from well-supported (in terms of both theory and therapeutic package) psychotherapies to psychotherapies for which strong contradictory evidence exists (both in terms of theory and therapeutic package; for a graphical, intuitive representation of the different categories of psychotherapies, see Figure 1). Levels within each factor are established based on the following criteria:

- *Empirically well supported*: Congruent evidence from at least two rigorous studies, conducted by different investigators or investigating. For theory, evidence can come from experimental studies and/or clinical trials (i.e., theory can be tested both independently and concomitantly with the therapeutic package).
- *Equivocal or no clear data*: No available data, preliminary data (i.e., fewer than two independently, well-conducted studies), or mixed data (i.e., both supporting and contradictory evidence).
- *Strong contradictory evidence*: Invalidating evidence coming from at least two rigorous studies, conducted by different investigators or investigating teams.

A psychological intervention can show the following types of clinical efficacy: *absolute efficacy* (i.e., the therapeutic package is significantly better than a no treatment, waiting list control, and placebo condition); *relative efficacy* (i.e., the therapeutic package is equivalent to or better than another evidence-based psychological intervention); or *specific efficacy* (both the conditions for

absolute and relative efficacy are met; the theory of the therapeutic package is also empirically supported; see David & Montgomery, 2011; Wampold, 2001).

Based on this framework, we conducted a detailed qualitative analysis of evidence supporting iCBT to assess its scientific status (i.e., how well iCBT theory and therapeutic package are supported), with the aim of deriving informed recommendations for future research.

Methods

Literature Search

Potential relevant studies were identified through a search of the PsycINFO and MEDLINE databases from August 1 2014, to November, 1, 2015, using the following search terms and combinations: “depression,” “CCBT,” “computerized cognitive behavioral therapy,” “iCBT,” “computerized CBT,” “Internet delivered CBT,” “Internet based CBT,” “web based CBT,” “mobile based CBT,” and “web delivered CBT” (see Appendix for exact search strings). We also systematically searched the references from recent randomized clinical trials, meta-analyses, and reviews on the topic (Cuijpers, Donker, van Straten, Li, & Andersson, 2010; Johansson & Andersson, 2012; So et al., 2013; van Ballegooijen et al., 2014).

Selection of Studies

The following criteria were applied for inclusion in the qualitative review:

- The study was a randomized clinical trial.
- The study was designed specifically to assess the efficacy of iCBT for depression in adults and/or the mechanisms underlying iCBT for depression.
- The study was written in English and published in a peer-reviewed journal.

Quality Assessment

We assessed the quality of included studies using three criteria of the “risk of bias” assessment tool, which was developed by the Cochrane Collaboration (Higgins & Green, 2011). The tool assesses the following possible sources of bias in randomized clinical trials: (a) the adequate generation of allocation sequence; (b) the concealment of allocation to the different conditions; (c) the adequate blinding of participants, personnel, and outcome assessors; (d) the incomplete provision of outcome data; (e) the selective provision of outcome data; and (f) other sources of bias. In this study, we have considered only the first three criteria because we did not find any relevant and/or clear information in any of the studies that the other three criteria influenced the quality of the study.

Procedure

For every eligible study, we retained the following variables: study identification data (author, year of publication); sample size; the affiliation of the first three authors (and the affiliation of the corresponding author, if she or he was not among the first three); description of the study design (number of groups, type of control group); description of the psychological interventions; follow-up related information; information about variables that could act as mediators and moderators of the intervention; information about how the data analysis had been conducted (intent-to-treat vs. nonintent-to-treat approach); and principal findings (see Table 1). We also assessed the possible risk of bias in each study, based on the first three criteria of the Cochrane Collaboration’s tool (Higgins & Green, 2011).

The first and the second author screened the identified records. Two raters (i.e., the first author and the second author, both certified clinical psychologists) independently coded the variables retained for each study and agreed on 87% of the cases. Minor disagreements were solved through discussions.

Table 1
Characteristics of the Studies

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition					Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol	Face-to-face psychotherapy					
1	Andersson et al., 2005	117	Yes	No	No	E-mail assisted iCBT; five modules, 8 weeks (recommended); based on Beck's cognitive therapy and behavioral activation plus online discussion group	2	Yes-online discussing group	No	No	No	No	No	Therapist time per participant and number of modules completed were assessed (no moderation analysis)	Yes	The number of modules completed was weakly correlated with post-treatment BDI scores. Significant reduction of depressive symptoms in iCBT group compared to WL (large between-groups effect sizes); no significant differences between groups at follow-up (but the control group received the treatment by the time of follow-up); results were maintained at follow-up for the treatment group	

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Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WI	TAU	Other active intervention including an iCBT protocol						
2	Andersson, Hesser, Veilord et al., 2013	69	Yes	?	No	Tested iCBT protocol modules; introduction to CBT, behavioral activation, cognitive restructuring, sleep management, defining goals/values, and relapse prevention; weekly homework included, with personalized feedback	2	No	No	No	No	Face-to-face group-based CBT	Yes-1 year and 3 years	No	No	Yes	Significant reduction of depressive symptoms from pre- to posttest, with large effect sizes within groups; no significant differences between groups at postintervention; gains maintained at follow-up, with no significant differences between groups (large effect sizes within groups)

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Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition			Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU					
3	Arpin-Cribbie, Irvine, & Ritvo, 2012	77	Yes	Yes	?	An unguided iCBT 10-week program designed to specifically target perfectionism (based on rational emotive and behavioral therapy) and GSM intervention	3	No	Yes	No	No	No	Yes	The iCBT group was superior to WL in decreasing perfectionism, automatic thoughts, depression, and anxiety (large effect sizes); no difference between iCBT and GSM regarding distress outcomes; but the iCBT group did significantly better regarding perfectionism (medium effect sizes); changes in perfectionism correlated with changes in anxiety and depression	

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Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition			Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU						
4	Berger et al., 2011	76	Yes	Yes	?	Tested iCBT protocol: Deprexis: 10 text modules and a summary module broadly consistent with a cognitive behavioral model (see a more detailed description in Study 15) plus weekly e-mail contact with a therapist	3	No	Yes	No	Yes	Yes	Yes	Yes	The unguided and the guided self-help groups were significantly less depressed compared to WL (moderate and large effect sizes); no significant difference between the unguided and guided self-help group was found; no significant differences were found at follow-up between treatment groups (but participants in WL received treatment by the time of follow-up)	

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Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms: mediation analysis	Moderation analysis	ITT analysis	Results: effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol						
5	Clarke, Reid, Eubanks et al., 2002	299	Yes	Yes	?	Overcoming Depression over the InterNet: 4-week self-paced skills training program focusing on the acquisition and use of cognitive restructuring techniques; 7 chapters, no audio-video materials; no psychotherapist assistance; iCBT was administered plus TAU	2	No	No	Unguided online bibliotherapy with no interactive skills training plus TAU	No	Yes—8, 16, and 32 weeks	No	No	No	Yes	No differences between groups

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Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol					
6	Clarke, Eubanks, Reid et al. 2005	255	Yes	Yes	?	Overcoming Depression over the InterNet: 4-week self-paced skills training program focusing on the acquisition and use of cognitive restructuring techniques; no behavioral activation techniques; 7 chapters, no audio-video materials; no psychotherapist assistance; periodic mail postcard reminders to access the treatment; iCBT was administered plus TAU	3	No	No	Unguided online bibliotherapy with no interactive skills training plus TAU	Overcoming Depression over the InterNet: 4-week self-paced skills training program focusing on the acquisition and use of cognitive restructuring techniques; no behavioral activation; 7 chapters, no audio-video materials or psychotherapist assistance; periodic short phone calls to access the treatment; iCBT plus TAU	No	No	Yes	Greater reduction in depression within iCBT groups compared to TAU (small between-group effect sizes), with more pronounced effects evident among those who were more severely depressed at baseline; no differences between the two iCBT groups; results maintained at follow-up	

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol						
7	Clarke, Kelleher, Hornbrook et al., 2009	160	160	?	?	Self-guided interactive behavioral and cognitive program: about 9 sessions (mean number of sessions; approximately 5 weeks) addressing psychoeducation, mood monitoring, cognitive restructuring, and guided behavioral intervention; no therapist support but personalized automatic feedback	2	No	No	Unguided online bibliotherapy with no interactive skills training plus TAU	No	Yes-10, 16, and 32 weeks	No	No	Yes	Small between-group effect, favoring the iCBT group; results maintained at 32 weeks follow-up; all participants were free to access alternative pharmacotherapy and/or psychosocial services for depression during the study	

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Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition						Results: effect sizes between and within groups		
								Placebo	WL	TAU	Other active intervention including an iCBT protocol	Face-to-face psychotherapy	Follow-up data		Mechanisms; mediation analysis	Moderation analysis
8	Choi et al., 2012	63	Yes	Yes	No	Tested iCBT protocol: Brighten Your Mood: 8-week program (based on the Sadness program) comprising 6 lessons (see a more detailed description in Study 17) with telephone support	2	No	Yes	No	No	No	No	No	Yes	Significant reduction of depressive symptoms in the iCBT group (large effect sizes); significant differences between groups at post treatment (large effect sizes). Gains maintained at follow-up

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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Placebo	Control condition			Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
									Other active intervention including an iCBT protocol	Face-to-face psychotherapy	Follow-up data					
9	Christensen, Griffiths, & Jorm, 2004	525	?	?	?	MoodGym: 5 interactive modules made available sequentially weekly plus one summary module in the sixth week; weekly lay interviewer contact	3	Yes-weekly phone contact; predetermined lifestyle and environmental factors influencing depression	No	No	No	No	Negative automatic thoughts were measured (no mediation analysis)	No	Yes	Significant reductions in depressive symptoms (small within intervention groups effect sizes); no significant difference on depression between BluePages and MoodGYM and both did better than WL (small effect sizes); only MoodGYM significantly reduced the negative automatic thoughts compared to WL

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Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition						Mechanisms: mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL TAU	Other active intervention including an iCBT protocol	Face-to-face psychotherapy	Follow-up data					
10	Christensen, Griffiths, Mackinnon, & Brittiffe, 2006	2794	No	No	No	Tested 6 versions of a website, each consisting of different combinations of the modules included in the MoodGym program (version 6 included all the modules, and it's what we considered the tested iCBT protocol)	6	No	No	Yes-various combinations of the MoodGym program modules	No	No	No	No	Yes	Better results for groups that received extended CBT (i.e., completed MoodGym program); small effect sizes (ranging from 0.20 to 0.40)	

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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol						
11	de Graaf et al., 2009	303	?	?	?	Color Your Life program (based on The Coping with Depression course); nine, 30-minute weekly sessions implemented over 9 weeks; homework between sessions; no professional assistance	3	No	No	Yes-4 to 5 biweekly GP consultations; medication, if needed	Yes-TAU plus iCBT protocol	No	Yes-12 months	Dysfunctional attitudes were measured (no mediation analysis)	Not reported	Yes	Significant reduction of depressive symptoms in all groups (medium effect sizes within iCBT group), with no significant differences between groups and no differences regarding dysfunctional attitudes between groups; no follow-up data reported
	de Graaf et al., 2010	303	?	?	?	Color Your Life program (based on The Coping with Depression course); 9 weekly 30-minute sessions implemented over 9 weeks; homework between sessions; no professional assistance	3	No	No	Yes-4 to 5 biweekly GP consultations; medication, if needed	Yes-TAU plus iCBT protocol	No	Yes-12 months	Not reported	Predictors and moderators tested: demographic, clinical, cognitive, and long/short-term improvement variables; the presence of major depressive disorder was a significant predictor of reliable change in the iCBT group.	Yes	Significant reduction of depressive symptoms in all groups (medium effect sizes within iCBT group), with no significant differences between groups; no follow-up data reported

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Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol					
	de Graaf et al., 2011	303	?	?	?	Color Your Life program (based on The Coping with Depression course) nine 30-minute weekly sessions implemented over 9 weeks; homework between sessions; no professional assistance	3	No	No	Yes-4 to 5 biweekly GP consultations; medication, if needed	Yes-TAU plus iCBT	No	Yes-12 months	Not reported	Not reported	At 12 months, no statistically significant differences between the three group interventions were found for depression severity; reliable improvement, remission, and relapse

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Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition			Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Other active intervention including an iCBT protocol	TAU	WL						
12	Donker, Batterham et al., 2013	1843	?	?	?	MoodGym: four 20-40-minute modules over 4 weeks; identify and counteract dysfunctional thinking, behavioral activation, assertiveness, and self-esteem training; personal workbook including exercises and assessments; no therapist assistance	3	No	No	No	Fully self-guided Internet-delivered CBT e-coach: 4 modules over 4 weeks; grief, role disputes, role transition, and interpersonal deficits; personal workbook including exercises and assessments; no therapist assistance	Yes-6 months	Not reported	Yes- moderators tested were gender, age, educational level, marital status, baseline depression level, skills, and previous depression but no overall significant moderation effect was identified; however, older participants in the MoodGym/CBT e-coach condition had larger improvements in depression scores than those in the IPT condition, whereas younger participants in the IPT condition had larger improvements in depression scores than those in the MoodGym/CBT e-coach condition	Yes	Significant reduction of depressive symptoms from baseline to posttest, with medium to large effects within groups; no significant differences between groups; gains maintained at follow-up.

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups	
								Placebo	WL	TAU	Other active intervention including an iCBT protocol						Face-to-face psychotherapy
Donker, Bennet et al., 2013		1843	Yes	?	?	MoodGym; four 20-40-minute modules over 4 weeks; identify and counteract dysfunctional thinking, behavioral activation, assertiveness, and self-esteem training; personal workbook including exercises and assessments; no therapist assistance	3	No	No	No	Internet-delivered IPT e-couch: 4 modules over 4 weeks; introduction to CBT, identify negative thoughts, and behavioral activation; personal workbook including exercises and assessments; no therapist assistance	Fully self-guided Internet-delivered CBT e-couch: 4 modules over 4 weeks; grief, role disputes, and inter-personal deficits; personal workbook including exercises and assessments; no therapist assistance	Yes-6 months	Dys-functional attitudes were measured (no mediation analysis); lower dysfunctional attitudes predicted better outcome regardless of the intervention type	Not reported	Yes	Significant reduction of depressive symptoms from baseline to posttest, with medium to large effects within groups; no significant differences between groups; gains maintained at follow-up (large effect sizes); differences on dysfunctional attitudes not reported

(Continued)

Table 1
Continued

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol						
13	Farrer, Christensen, Griffiths, & Mackin-Non, 2011	155	Yes	?	No	BluePages and MoodGym: 6 modules; 6 weeks; psychoeducation, thoughts and feelings, cognitive restructuring, behavioral activation, relaxation, and problem solving; no therapist assistance	4	Yes	No	Yes	No	Yes	No	No	No	Yes	Significant reduction of depressive symptoms within iCBT groups (with or without therapeutic support); significant differences between iCBT groups (any of them) and WL placebo groups (medium to large effect sizes, respectively), at both posttest and at follow-up

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition					Face-to-face psychotherapy	Follow-up data	Mechanisms: mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol	Yes-6 months						
14	Hoifodt et al., 2013	106	No	No	No	MoodGym: 5 weekly modules; thoughts and feelings, cognitive restructuring, behavioral activation, relaxation, and problem solving plus 15–30-minute weekly face-to-face support from a therapist and between-session tailored e-mails	2	No	Yes	No	No	No	Yes-6 months	No	No	Yes	Significant reduction of depressive symptoms within iCBT group and significant differences between groups (medium effect sizes); no significant differences between groups at follow-up (but participants randomized to WL received iCBT intervention in the meantime); improvements in the iCBT group were maintained at follow-up	

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
							Placebo	WL	TAU	Other active intervention including an iCBT protocol						
15	Johansson, Sjoberg, Sjogren et al., 2012	121	?	?	?	3	Yes—10 weeks; moderated discussion online group	No	No	No	Yes—6 months	No	No	No	Significant improvements in both treatment groups from pre- to post-treatment; results maintained at 6-month follow-up (large effect sizes); no significant differences between treatment conditions for participants with lower scores of depression at baseline and no significant differences were evident when treatment groups were compared to placebo; the tailored treatment was more effective than the standard one among participants with higher levels of depression of baseline (medium effect sizes)	

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
							Placebo	WL	TAU	Other active intervention including an iCBT protocol						
16	Kessler, Lewis, Kaur et al., 2009	297	Yes	Yes	Yes	2	No	No	Yes-usual care provided by GP	No	Yes-4 and 8 months	No	No	Yes	iCBT was superior to TAU in terms of reducing depressive symptoms and the effects were maintained to follow-up (medium between-group effect sizes)	
	Button, Wiles, Lewis, Peters & Kessler, 2012	297	Yes	Yes	Yes	2	No	No	Yes-usual care provided by GP	No	Yes-4 and 8 months	No	Yes-pretreatment severity; marital status, education, history of depression, and recent adverse life stressors were assessed; pretreatment severity and marital status significantly moderated treatment response, with more severe patients and those leaving without a spouse benefiting most from the intervention	Yes	iCBT was superior to TAU in terms of reducing depressive symptoms and the effects were maintained at follow-up (medium between-group effect sizes)	

(Continued)

Table 1
Continued

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition					ITT analysis	Results; effect sizes between and within groups	
								Placebo	WL	TAU	Other active intervention including an iCBT protocol	Face-to-face psychotherapy			Follow-up data
17	Kivi, Erikson, Hange et al., 2014	92	Yes	Yes	?	Depression Helper: 8 to 12 weeks, 7 modules based on behavioral activation and acceptance and committing therapy including interactive elements online, a workbook, and a CD with mindfulness and acceptance exercises; therapist contact included weekly e-mail contact plus 3 predetermined phone calls; further therapist support was available on request	2	No	No	Yes-GP consultations, antidepressants, WL, psychotherapy, or any combination of these	No	No	No	No	No differences between groups (large effect sizes in both TAU and iCBT groups)

(Continued)

Table 1
Continued

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Placebo	WL	TAU	Control condition			Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
											Other active intervention including an iCBT protocol	Yes	No						
18	Meyer et al., 2009	396	Yes	?	?	Depress: 9 weeks, ten 10-60-minute modules broadly consistent with but not limited to CBT (behavioral activation; cognitive modification; mindfulness and acceptance; interpersonal skills; relaxation, physical exercise, and lifestyle modification; problem solving, childhood experiences and early schemas; positive psychology intervention; dream work; emotion-focused intervention; psychoeducation) framed by one introductory and one summary module; unguided	2	No	Yes—participants in WL accessed standard care services in the meantime	?		No	Yes—6 months	No	Number of sessions completed, program acceptability, and subjective benefit were assessed; number of completed sessions correlated positively and significantly with study compliance and with the treatment effect size (no moderation analysis)	Yes	Significant reductions of depressive symptoms in iCBT group compared to the WL group (small between-group effect sizes, using ITT; moderate between-group effect sizes, without ITT; improvements maintained at follow-up within the iCBT group; no difference between groups at follow-up (but the WL group received the treatment by the time of follow-up)		

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol						
19	Moritz, Schilling, Hauschildt, Schröder, & Teszl, 2012	210	?	?	?	Deprexix; 8 weeks, 10 modules (see description above), framed by one introductory and one summary module; probably unguided	2	No	Yes—participants in WL accessed standard care services in the meantime	No	No	Dysfunctional attitudes measured (no mediation analysis)	Symptoms—severity—participants with mild depression benefited least and those with moderate depression benefited most from iCBT, while those with severe depression in the WL group benefited most from accessing TAU	Yes	Significant reductions of depressive symptoms in iCBT group compared to WL (small between-group effect sizes)		
20	Perini, Titov & Andrews, 2009	48	Yes	?	?	The Sadness Program comprises four components: six 8-week online lessons; homework assignments; participation in an online discussion forum; and regular e-mail contact with a mental health clinician; guided iCBT intervention	2	No	Yes	No	No	No	Yes—satisfaction with treatment and therapist time per participant were assessed (no moderation analysis)	Yes	The treatment group had significantly lower posttreatment depression scores than WL; large within-group effect sizes and moderate between-group effect sizes were found at posttreatment		

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol					
21	Newby, Williams, & Andrews, 2014	109	Yes	Yes	?	The Get Happy Program (based on The Sadness Program); six 8-week lessons using a comic book and assignments between lessons; limited psychotherapist support	2	No	Yes	No	No	Yes-3 months (for iCBT group only)	Yes-repetitive negative thinking and positive beliefs about rumination; positive beliefs about rumination mediated the intervention effect on depressive symptoms	No	Yes	Significant improvement in the iCBT group (large effect sizes) and significant differences between iCBT and WL groups (medium effect sizes); gains maintained at follow-up; reduction in repetitive negative thinking mediated the intervention effect on depressive symptoms

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition						Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol	Face-to-face psychotherapy	Yes-6 and 12 months					
22	Phillips, Schneider, Molosankwe et al., 2014	637	Yes	Yes	No	MoodGYM: five 1-hour modules addressing thoughts and feelings, cognitive restructuring, behavioral activation, relaxation, and problem solving; no therapist support	2	Yes-5 websites with general information about mental health	No	No	No	No	No	No	No	Yes	Similar improvement rates were found in the two groups, with no significant difference between groups; improvements were maintained at follow-up	
23	Pittaway, Cuppit, Palmer et al., 2009	100	No	No	No	Bearing the Blues (Ultras; http://www.ultras.com): eight 50-minute weekly therapy sessions; homework between sessions with limited professional support, on request	3	Yes-Living Life to the Full, a self-help CBT-based website	No	No	No	No	Yes-self-help CBT-based workbooks addressing depression, low mood, and anxiety	Yes-12 months	No	No	No	Significant reduction of symptoms within groups (large effect sizes), with no significant differences between groups; results maintained at follow-up

(Continued)

Table 1
Continued

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol					
24	Proudfoot, Ryden, Everitt et al., 2004	274	?	?	?	Beating the Blues (Ultrasis; http://www.ultrasis.com); eight 50-minute weekly therapy sessions; homework between sessions with limited professional support	2	No	No	Yes—standard care provided by GP and any other therapeutic intervention accessed in the community (professionals or not)	No	No	No	Yes	Significant improvement in both groups, with greater improvements in the iCBT group; the same pattern of results was evident at both post-intervention and follow-up	

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization?	Allocation concealment?	Blinding	Tested iCBT protocol	No. of groups	Control condition				Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol					
25	Radhu, Daskalakis, Arpin-Cribbie et al., 2012	47	?	?	No	A iCBT program aimed to reduce perfectionism and related effects on mood; 13 modules addressing cognitive restructuring, managing anxiety and negative moods, and relaxation; probably unguided	2	No	Yes	No	No	No	No	No	No	Active treatment condition was superior to WL in decreasing perfectionism, automatic negative thoughts, and depression (small to medium between-group effect sizes); changes in perfectionism and automatic negative thoughts correlated with changes in depression

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Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol					
26	Ruwaard, Schreken, Schrijver et al., 2009	54	Yes	?	No	A web-based program with therapist support; about ten 2-4-hour weekly sessions (including homework); based on cognitive therapy and behavioral activation principles; interactive workbook and personalized feedback from a therapist	2	No	Yes	No	No	No	No	No	Yes	Active treatment condition was superior to WL (moderate to large between-group effect sizes); gains were maintained at follow-up

(Continued)

Table 1
Continued

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition			Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU					
27	Spek, Cuijpers, Nyklicek et al. 2008	301	Yes	?	?	Eight modules based on Coping with Depression Course: 8 weeks (one session per week); text, exercises, videos, and figures; no professional support during the intervention	3	No	Yes	No	Yes	No	Yes	Significant improvements within groups (medium to large effect sizes) from pre- to follow-up measurement; better results obtained by participants in both iCBT and CBT groups compared to WL (no differences between iCBT and CBT); same pattern of results maintained at follow-up	

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition			Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU					
	Spek, Nyklicek, Smitis et al., 2007	301	Yes	?	?	Eight modules based on Coping with Depression Course; 8 weeks (one session per week), text, exercises, videos, and figures; no professional support during the intervention	3	No	Yes	No	No	No	No	Yes	Significant improvements within groups (medium to large effect sizes). Better results obtained by participants in both iCBT and CBT groups, compared to WL (No differences between iCBT and CBT)

(Continued)

Table 1
Continued

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol						
28	Tilov et al., 2010	141	Yes	No	No	Tested iCBT protocol: Sadness Program, technician assisted; same program as the clinician assisted group but without access to the forum; the technician was not allowed to provide clinical advice.	3	No	Yes	No	Sadness Program, clinician-assisted; four components with six online lessons (delivered within 8 weeks); homework assignments; participation in an online discussion forum; and regular forum, e-mail or telephone contact with a mental health clinician	No	Yes-4 months (no data for WL were available)	No	Yes	No difference was found at posttreatment on depression ratings between treatment groups, but significant differences between the treatment groups and WL were observed (large effect sizes); at follow-up, significant differences were found between the clinician-assisted and technician-assisted groups on the PHQ-9 in favor of the technician-assisted group (small effect sizes); no difference between groups on the BDI-II	

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Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition			Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU					
29	Titov, Dear, Johnston et al., 2013	257	Yes	No	?	The new Wellbeing Program with automated e-mails (TEG): 5 online lessons (8 weeks); psychoeducation about anxiety and depression, strategies for developing realistic cognitions, physical de-arousal, reengaging in reinforcing activities, avoidance and safety behaviors, and principles of graded exposure and relapse prevention	3	No	Yes	No	The new Wellbeing Program without automated e-mails (TG): 5 online lessons (8 weeks); psychoeducation about anxiety and depression, strategies for developing realistic cognitions, physical de-arousal, reengaging in reinforcing activities, avoidance and safety behaviors, and principles of graded exposure and relapse prevention	Yes—treatment satisfaction and number of lessons completed; no moderation analysis. Titov et al. (2013) concluded that "the inclusion of automated e-mails facilitated adherence and completion" and the TEG group had a significant higher rate of completion; higher levels of depressive symptoms in pretest were associated with not completing the follow-up assessment	No	Significant differences in depression ratings found between TEG and WL and between TG and WL at posttreatment (moderate effect sizes); no significant difference between treatment groups at posttreatment or 3-month follow-up.	

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition						Results: effect sizes between and within groups	
								Placebo	WL	TAU	Other active intervention including an iCBT protocol	Face-to-face psychotherapy	Follow-up data		Mechanisms; mediation analysis
30	Titov, Dear, Schweinke et al., 2011	77	Yes	?	No	The Wellbeing Program: 8 lessons implemented over 10 weeks; transdiagnostic intervention program targeting depression and anxiety and including CBT-based psychoeducation and a forum discussion; moderate support-by e-mail contact or phone-provided by a clinical psychologist; homework assignments	2	No	Yes	No	No	No	No	Yes	The active group was superior to WL in terms of reducing symptoms (moderate to large within-group effect sizes and moderate between-group effect sizes), gains were maintained at 3-month follow-up

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol						
31	Twomey, O'Reilly, Byrne et al., 2014	149	Yes	Yes	No	MoodGym: five 20-40-minute sessions of each; automated; weekly e-mails; no therapist support	2	No	Yes	No	No	No	Yes-12 weeks	No	No	No	MoodGYM was more effective than WL in reducing general distress but not depression (small to medium within-group effect sizes; small between-group effect sizes); very high rate of dropout

(Continued)

Table 1
Continued

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition					Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol	Face-to-face psychotherapy					
32	van Bastelaar, Pouwer, Cuijpers et al., 2011	255	?	?	No	An adaptation of Color Your Life program for adults with diabetes and comorbid depression; 12 weeks, 8 consecutive lessons; personalized feedback on homework assignments	2	No	Yes	No	No	Yes-1 month	No	No	Yes	iCBT was superior to WL in terms of reducing depressive symptoms (small effect sizes at posttreatment and medium to large effect sizes at 1-month follow-up)	
	van Bastelaar et al., 2012	255	?	?	No	An adaptation of Color Your Life program for adults with diabetes and comorbid depression; 12 weeks, 8 consecutive lessons; personalized feedback on homework assignments	2	No	Yes	No	No	Yes-1 month	No	Yes-presence of major depression disorder, anxiety disorder, and diabetes-specific emotional distress; no significant moderation effect	Yes	iCBT was superior to WL in terms of reducing depressive symptoms (small effect sizes at posttreatment and medium to large effect sizes at 1-month follow-up)	

(Continued)

Table 1
Continued

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol						
33	van Straten, Cuijpers, & Smit, 2008	213	Yes	?	No	A web-based problem-solving protocol; 4 weeks, 4 modules; identify personal goals and purposes; classify problems (unimportant, can be solved, cannot be solved); use problem-solving steps to get to a solution and implement it; support (including feedback) from a psychology student in implementing the intervention	2	No	Yes	No	No	No	No	No	No	No	iCBT was superior to WL in reducing depressive and anxious symptoms (moderate effect sizes)

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Table 1
Continued

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol						
34	Vermark et al., 2010	88	Yes	?	Yes	Tested iCBT: 8 weeks, 7 text modules; Guided iCBT: 8 weeks, introduction to CBT, behavioral activation, cognitive restructuring, sleep management, defining goals/values, and relapse prevention; weekly homework included, with personalized feedback	3	No	Yes	No	E-mail therapy; 8 weeks; CBT for depression; personalized treatment	No	Yes-6 months	No	No	Yes	Significant reduction of depression within CBT groups (i.e., active intervention and iCBT; large effect sizes); gains were maintained at follow-up; no significant differences between active intervention and iCBT groups, but significant differences between any of the interventions groups and WL (moderate to large effect sizes)

(Continued)

Table 1
Continued

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	No. of groups	Control condition						Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
							Placebo	WL	TAU	Other active intervention including an iCBT protocol	Face-to-face psychotherapy	Follow-up data				
	Andersson et al., 2012	49	Yes	?	Interview assessors were blinded	3	No	Yes	No	E-mail therapy: 8 weeks; CBT for depression; personalized treatment	No	No	Therapeutic alliance was assessed (no mediation analysis)	No	Yes	Alliance ratings were high regardless of the experimental condition; correlations between working alliance and residualized change scores were small and non-significant
	Andersson, Hesser, Hummerdal, Bergman-Nordgren, & Carlbring, 2013	51	Yes	?	Interview assessors were blinded	3	No	Yes	No	E-mail therapy: 8 weeks; CBT for depression; personalized treatment	No	Yes-42 months	No	No	Yes	No differences were found between the treatment conditions at follow-up; however, participants sought and received additional treatments in the meantime

(Continued)

Table 1
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Study No.	35	Study ID	Wagner, Horn, & Maercker, 2014	N	62	Adequate randomization	Yes	Allocation concealment	?	Blinding	No	Tested (CBT protocol writing)	Therapist supported (in writing)	No. of groups	2	Placebo	No	WL TAU	No	Other active intervention including an iCBT protocol	No	Face-to-face psychotherapy	Face-to-face CBT: 8-week weekly sessions; 7 treatment modules addressing introduction, behavioral analysis, planning of activities, daily structure, life review, cognitive restructuring, social competence, and relapse prevention	Follow-up data	Yes-3 months	Mechanisms; mediation analysis	Automatic negative thoughts and helplessness were measured (no mediation analysis)	Moderation analysis	Satisfaction with treatment and psychotherapy utilization (duration and quality of contact with therapist; no moderation analysis)	ITT analysis	Yes	Results; effect sizes between and within groups	Significant reduction of depressive symptoms in both groups (large effect sizes), with no significant differences between intervention groups at posttest; follow-up better for the iCBT group
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Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition						Results; effect sizes between and within groups			
								Placebo	WL	TAU	Other active intervention including an iCBT protocol	Face-to-face psychotherapy	Follow-up data		Mechanisms; mediation analysis	Moderation analysis	ITT analysis
						Tested iCBT protocol Internet-based CBT intervention: 8 weeks, 7 treatment modules; introduction, behavioral analysis, planning of activities, daily structure, life review, cognitive restructuring, social competence, relapse prevention; weekly sessions; personalized feedback on homework assignments											

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol					
36	Warmerdam, Straten, Twisk, Ripper, & Cuijpers, 2008	263	Yes	No	No	Eight modules based on Coping with Depression course: 8 weeks (one session per week), text, exercises, videos, and figures; extensive support received from a therapist by e-mail, including personalized feedback on homework assignments	3	No	Yes	No	No	No	No	No	Yes	Both active treatments were effective in reducing depressive symptoms (relative to WL); similar effect sizes and results maintained at follow-up

(Continued)

Table 1
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Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	No. of groups	Control condition			Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
							Placebo	WL	TAU					
	Warmerdam, Straten, Jongma, Twisk, & Cuijpers, 2010	263	Yes	No	No	3	No	Yes	No	Yes-3 months	Yes-	No	Yes	Both active treatments were effective in reducing symptoms, dysfunctional attitudes, worry, and negative problem orientation, and perceived control mediated the change in symptoms in both active treatment groups
							Other active intervention including an iCBT protocol solving protocol (computerized version): 5 lessons, 5 weeks; built-in feedback system; no audio-visual aids; extensive support received from a therapist by e-mail (including feedback on assignments)	Depression course: 8 weeks (one session per week), text, exercises, videos, and figures; extensive support received from a therapist by e-mail, including personalized feedback on homework assignments						WL (with no differences between the active conditions and between within-group and medium and medium effect sizes between groups when compared to WL); gains maintained at follow-up

(Continued)

Table 1
Continued

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Face-to-face psychotherapy	Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol						
	Warmerdam, Straten, Twisk, & Cuijpers, 2013	263	Yes	No	No	Eight modules based on Coping with Depression course: 8 weeks (one session per week), text, exercises, videos, and figures; extensive support received from a therapist by e-mail, including personalized feedback on homework assignments	3	No	Yes	No	Problem-solving protocol (computerized version); 5 lessons, 5 weeks; built-in feedback system; no audio-visual aids; extensive support received from a therapist by e-mail (including feedback on assignments)	No	Yes-9 months (but follow-up data for WL were not available)	No	Yes-the severity of symptoms at baseline, educational level, avoidance, problem-solving style, and dysfunctional attitudes; higher baseline depressive symptoms and higher education predicted improvement in both active treatment groups	Yes	Significant improvements within active groups (large effect sizes; symptoms and dysfunctional attitudes); no significant differences between groups

(Continued)

Table 1
Continued

Study No.	Study ID	N	Adequate randomization	Allocation concealment	Blinding	Tested iCBT protocol	No. of groups	Control condition				Follow-up data	Mechanisms; mediation analysis	Moderation analysis	ITT analysis	Results; effect sizes between and within groups
								Placebo	WL	TAU	Other active intervention including an iCBT protocol					
37	Watts, Mackenzie, Thomas et al., 2013	35	Yes	Yes	No	The Get Happy Program (based on The Sadness Program): 6 weekly lessons (conducted over a 8 weeks period) using a comic book and assignments between lessons; limited psychotherapist support; mobile version	2	No	No	No	Get Happy Program (based on The Sadness Program): 6 weekly lessons (conducted over an 8-week period) using a comic book and assignments between lessons; limited psychotherapist support; computer version	No	No	No	Significant improvements within groups (large effect sizes); no differences between groups at posttest or 3-month follow-up; no results reported on treatment credibility and expectancies for improvement	

Note. WL = waitlist control group; ITT = intent to treat; TAU = treatment as usual; iCBT = Internet-based cognitive behavioral therapy; GSM = general stress management; IPT = interpersonal therapy; BDI = Beck Depression Inventory. Shaded squares mark the fact that Donker et al. 2013 did not include a face-to-face psychotherapy comparison condition, but rather two active conditions, each involving a form of iCBT.

Results

Study Selection

After duplicates were removed, the initial search resulted in the identification of 1,275 records, which were screened based on title and abstract. We retained a total of 67 full-text articles to be assessed for eligibility.

Three studies were excluded from the final study sample because they were not randomized clinical trials (Gega, Smith, & Reynolds, 2013; Johansson, Nyblom, Carlbring, Cuijpers, & Andersson, 2013; Sharry, Davidson, McLoughlin, & Doherty, 2013). Another four studies were excluded because they included iCBT protocols for depression in young adults and/or adolescents younger than 18 years old (Abeles et al., 2009; Calear, Christensen, Mackinnon, Griffiths, & O'Kearney, 2009; Fleming, Dixon, Frampton, & Merry, 2012; Lillevoll, Vangberg, Griffiths, Waterloo, & Eisemann, 2014).

Five studies were excluded because the interventions they tested contained specific psychotherapy protocols for other psychological disorders (e.g., anorexia nervosa [Grover et al., 2011], social anxiety [Bowler et al., 2012], insomnia [Thorndike et al., 2013] or other mixed psychological problems such as depression and substance abuse [Kay-Lambkin, Baker, Lewin, & Carr, 2009], and depression and parenting behavior [Sheeber et al., 2012]).

Two articles reporting data from the same study were excluded because they included data on outcomes outside of our research interest (Christensen et al., 2013; Farrer, Christensen, Griffiths, & Mackinnon, 2012), and one study was excluded because it was a pilot study and did not report on depression outcomes (Cooper et al., 2011). Another two articles, based on the same study, were excluded because they employed a relapse prevention protocol for depression (Hollandare et al., 2011; Hollandare et al., 2013). Three articles (reporting on two studies) were excluded because they included participants with subthreshold depression (Imamura et al., 2014; Morgan, Jorm, & Mackinnon, 2012; Morgan, Mackinnon, & Jorm, 2013).

In the end, we selected 47 articles that reported on 37 studies investigating the efficacy of iCBT protocols for depression in adult populations. The discrepancy between the total number of articles and the total number of studies was given by the fact that there were seven studies for which multiple papers were published (up to three papers per study; see Table 1). Because this resulted in a total of 17 (45.94%) of the articles reporting findings from studies for which more than one paper has been published, in our analyses we considered studies, not articles (see Figure 2). We chose to do that to avoid overrepresentation of some studies and data overlapping.

Study Characteristics

A research group based in Australia published 12 of the studies. Two other research groups, one from Sweden (six studies) and the other one from Netherlands (six studies), published another considerable part of the available studies. The remaining studies were published by research teams from Germany and Switzerland (three studies), United States (three studies), United Kingdom (three studies), Canada (two studies), Ireland (one study), Norway, and Australia (one study).

In terms of iCBT protocol, most studies (68%) tested various protocols derived from CBT principles (without coining a name for them; 10 studies); the MoodGym program (seven studies); or variations of the Sadness program (five studies). The iCBT protocols included from 4 to 13 intervention modules or sessions, with most of the studies (73 %) using protocols of four to eight modules. Most iCBT protocols were clinician assisted (to various degrees; 16 studies), one was technician-assisted, three were phone-assisted (one by a lay interviewer), and the remaining 17 were unassisted.

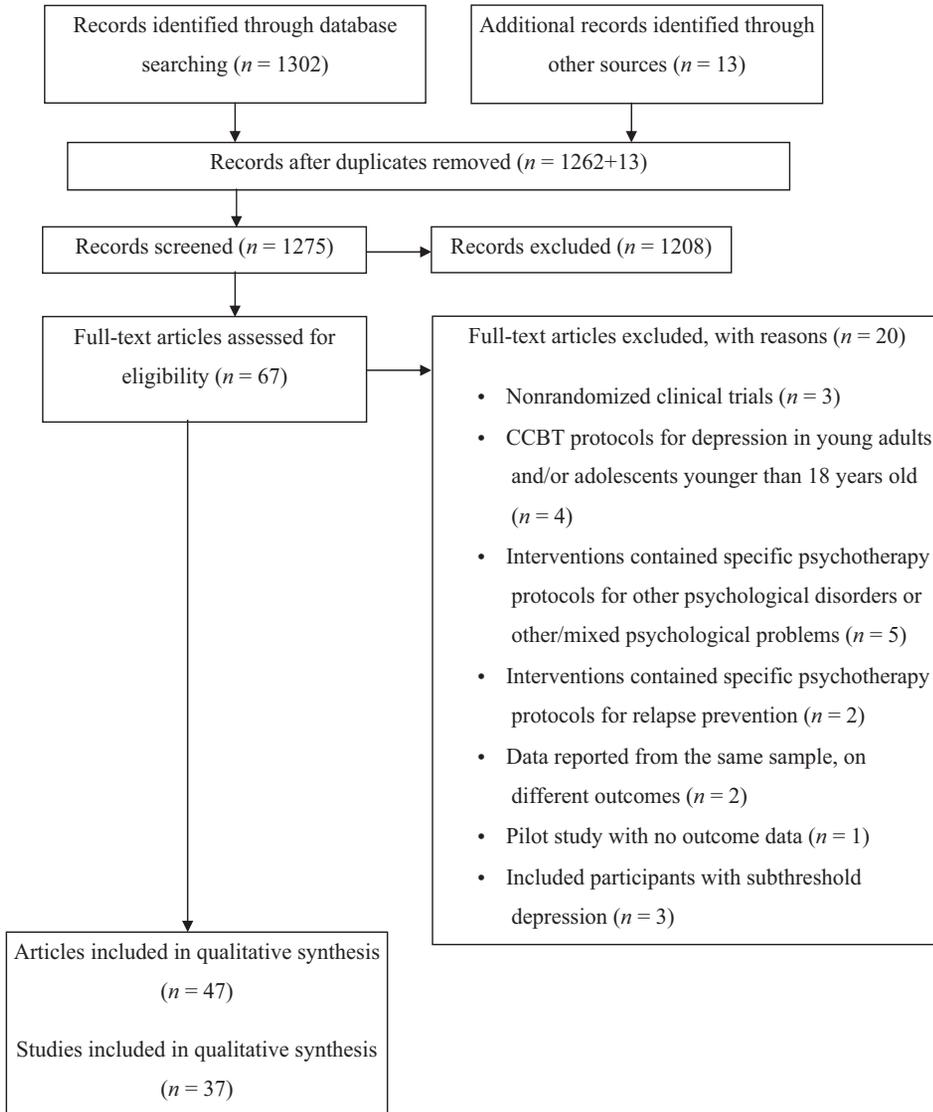


Figure 2. PRISMA flow chart.

iCBT Efficacy

In terms of efficacy, results consistently showed iCBT was superior to waitlist (WL) control: 20 studies² included a WL control condition and all of them reported that iCBT was superior to WL in terms of reducing symptoms, with moderate to large effect sizes (as reported in the original papers). Six studies compared iCBT to a placebo intervention, but only two of them reported iCBT was better than placebo. Placebo referred to regular phone calls to discuss lifestyle and environmental factors related to depression or less structured online activities related to decreasing depression (i.e., online bibliotherapy, online discussion groups). Seven studies investigated iCBT against treatment-as-usual (TAU; usual general practitioner consultations,

²In two studies (Hoifodt et al., 2013; Meyer et al., 2009), WL participants were free to access TAU if they wanted.

medication, if needed, and WL plus access to other community or psychotherapy services; see Table 1).

Three of them reported iCBT was as effective as TAU, while the other four reported iCBT was somewhat superior to TAU. However, in three of these studies (Clarke et al., 2002, 2005, 2009), participants from the iCBT group also were free to access TAU. Two other studies that used WL as control condition allowed WL participants to freely access TAU if they wanted (Hoifodt et al., 2013; Meyer et al., 2009), and both of these studies reported iCBT was superior to WL. Thirteen studies compared iCBT to other active interventions, including an iCBT protocol. The other active interventions including an iCBT protocol differed from the tested iCBT protocol on features like therapist support, content or content elaboration, degree of treatment (and/or feedback) personalization, mode of delivery, or the fact that it included also TAU.

Overall, studies showed iCBT was equally efficacious with other active interventions including an iCBT component. However, Christensen, Griffiths, Mackinnon, and Brittliffe 2006 reported that the complete MoodGym program was better than various combinations of its modules. Johansson et al. 2012 reported that more severely depressed patients benefited most from the tailored iCBT protocol compared to the untailored one. Four studies compared iCBT to face-to-face group CBT and reported iCBT was equally efficacious.

The therapeutic gains yielded by iCBT were generally maintained at follow-up. Follow-up intervals varied from 1 to 42 months (see Table 1). However, in most cases, follow-up data were collected only from the iCBT group and/or participants enrolled in the study were free to access other treatments from posttest to follow-up, which makes it difficult to interpret the follow-up data.

iCBT Mechanisms of Change

Evidence regarding the presumed mechanisms of change supporting the iCBT for depression proved to be scarce. Of the 37 studies reported, 10 considered specific cognitive factors assumed to act as mechanisms of depression (e.g., dysfunctional attitudes, negative automatic thoughts). Only two conducted mediation analyses, reporting that positive beliefs about rumination (Newby, Williams, & Andrews, 2014), dysfunctional attitudes, worry, negative problem orientation, and perceived control (Warmerdam, van Straten, Jongsma, Twisk, & Cuijpers, 2010) mediated the iCBT effect on depressive symptoms. Three studies considered factors that could act as general mechanisms of change (e.g., therapeutic alliance [Andersson et al., 2012] and treatment credibility and expectancies for improvement [Arpin-Cribbie, Irvine, & Ritvo, 2012; Watts et al., 2013]), but none of them conducted mediation or moderation analyses.

Thirteen studies considered other individual- and treatment-related variables that could have influenced the outcome of the treatment (e.g., symptoms severity at baseline, educational level, employment status, satisfaction with treatment, therapist contact). Six of them conducted moderation analysis and reported that symptoms severity at baseline, marital status, educational level, and parental psychiatric history moderated the iCBT effect on depressive symptoms (see Table 1).

Risk of Bias

Of the 37 studies reported, 32 reported adequate randomization, 12 reported allocation concealment, and only three reported adequate blinding of the assessors. Overall, only one study (Kessler et al., 2009) met all three criteria we considered here (adequate generation of the random sequence, allocation concealment, and adequate blinding of the assessors; see Table 1).

Putting it All Together: The Scientific Status of CBT

We used the criteria developed by David and Montgomery (2011) to assess the scientific status of iCBT as an evidence-based psychological treatment. Each of these criteria is reviewed below.

The treatment theory has been empirically supported in at least two rigorous studies, conducted by two different investigators or investigating teams, and tested both independently of its

therapeutic package, in two experimental studies, and in two complex clinical trials. According to our analysis of the available data, the iCBT treatment theory is clearly underinvestigated.

Moreover, the available attempts to investigate it are somewhat unstructured and theoretically uninformed. There are only two studies that conducted mediation analysis, both of which were conducted in the context of testing an iCBT protocol's efficacy but neither of which considered all the theoretically specified mechanisms of change (i.e., dysfunctional attitudes, negative automatic thoughts, therapeutic alliance, and treatment expectancies). Rather, Newby et al. (2014) focused on the repetitive negative thinking and positive beliefs about rumination, while Warmerdam et al. (2010) considered a mixture of factors, including dysfunctional attitudes, worry, negative problem orientation, and perceived control. Both studies found the above-mentioned factors as mediating the change in depressive symptoms³. Because of the scarcity of the available data coupled with the poor theoretical articulation of the factors tested as mechanisms of change, it is practically impossible to identify, at this moment, the essential factors that should be targeted by iCBT protocols for depression.

The treatment absolute efficacy shows that it is better than a WL control condition. Based on our analysis, this criterion is met. However, it should be noted that the diversity of the iCBT programs tested in different studies is quite large, making it difficult to say exactly what the treatment is.

The treatment relative efficacy shows that it is better than another evidence-based psychological intervention and that both are better than control conditions, in the form of WL. Based on our analysis, iCBT seems to be equally effective in reducing depressive symptoms as other (evidence-based) psychological interventions, and both iCBT and other (evidence-based) psychological interventions are better than WL.

The treatment specific efficacy shows that it is significantly better than other active and standard therapies and the underlying theory is based on analyses of mediation and/or moderation. According to our analysis, iCBT is equally effective compared to other active and standard therapies. Furthermore, mediation and moderation analyses are rather scarce and inconclusive. Notably, few studies (6 out of 37) investigated iCBT against placebo, reporting mixed results regarding iCBT superiority to placebo.

Therefore, iCBT for depression seems to have only preliminary support (at most) in terms of mechanisms of change, while data supporting the therapeutic package can be described, in our view, as equivocal. Our view is based on the following reasons. (a) iCBT appears to yield significant clinical benefits compared with WL control, but studies comparing iCBT with a placebo, active intervention, or other evidence-based intervention are rather few. In addition, the essential components of an iCBT protocol (i.e., there is a large diversity of iCBT protocols, in terms of contents, therapist support, duration) are unclear. (b) The quality of the available studies is clearly suboptimal. (c) The extent to which iCBT yields durable effects is unclear, mostly because of significant limitations of the research work conducted up to present.

Based on our analysis, iCBT currently falls in category four, according to David and Montgomery's (2011) framework classification of psychotherapies. This means that although scientifically oriented, iCBT should strive for better, more extensive empirical support for *both* mechanisms of change and the efficacy of the therapeutic package.

Discussion

Directions for Future Research: How Considering iCBT Mechanisms of Change Could Improve iCBT Protocols

Investigating iCBT mechanisms of change is essential in promoting scientifically based growth in the field. To date, the lack of research on the underlying mechanisms of change represents

³Except for repetitive negative thinking, which was found to mediate change in anxious symptoms only (Newby et al., 2014).

a significant weakness of the current iCBT protocols for depression. Most of the iCBT interventions for depression are exclusively designed based on classical CBT protocols and tested in terms of their efficacy in decreasing symptoms. However, as argued before, iCBT can differ significantly from traditional CBT. We pose that taking into account these differences regarding how the intervention works has the potential of increasing the iCBT's clinical value. For example, a significant problem with unguided iCBT is the very high attrition rate, which contributes to the problem of undertreating depression, although the treatment works and is widely available. A careful consideration of the iCBT common factors may help address this problem. Consider the *therapeutic relationship*, for example. A relatively recent review of 22 studies investigating iCBT for depression (Johansson & Andersson, 2012) reported a strong relationship between the therapeutic contact and support and the outcome measures, with iCBT interventions ensuring more therapeutic contact as being more efficacious in decreasing depressive symptoms.

Moreover, a recent meta-analysis (van Ballegooijen et al., 2014) that compared the adherence rate of guided Internet-based CBT to face-to-face psychotherapy did not find any differences between the two treatment delivery formats. Thus, optimizing the degree of the therapeutic contact during the implementation of iCBT protocols could enhance the iCBT efficacy and decrease the attrition rate (i.e., the more therapeutic contact, the better adherence to treatment and the more clinical gain). In addition, exploring how the therapeutic contact *before* and/or *after* the iCBT intervention influences the outcome might prove worthwhile.

Additionally, it is possible that the therapeutic contact might be technologically “modeled.” For example, a critical aspect may involve offering dynamic feedback, leading to the possibility that although there is no “human therapist” assisting the patient through the iCBT protocol (and thus no relationship to a human therapist), there could still be a kind of “therapeutic relationship” to the self-help intervention. However, the differences and commonalities between the therapeutic relationship within face-to-face psychotherapy and iCBT, respectively, are not yet sufficiently studied. Thus, how such a “modeling” differs from real therapeutic contact and how it might influence the outcome remain topics for future research that could contribute to the improvement of iCBT protocols for depression. For example, it is possible that the correlation with therapeutic success might be different in iCBT compared to face-to-face psychotherapy.

Speaking further of common factors shared by various Internet-based self-help instruments and/or intervention/prevention protocols, it may be that the *level of engagement with the intervention protocol*, the *attractiveness*, and *user-friendly features* of the protocols might also influence the adherence to treatment and thus treatment efficacy. Future studies should investigate these aspects. In addition, technical aspects like establishing strict deadlines and sending (automatic) reminders might constitute common factors that may influence iCBT efficacy. Similarly, different particularities of the patients (e.g., severity of symptoms, educational level) could interact with particularities of the protocol and moderate the efficacy of the intervention. When tested in moderation analysis, such factors could inform our selection of patients that would benefit most from iCBT.

Furthermore, the extent to which iCBT reliably modifies the cognitive factors underlying symptoms should be clearly established. To date, few attempts of investigating the mediators of iCBT effects on symptoms have been made. Even in the studies that did perform mediation analyses (Newby et al., 2014; Warmerdam et al., 2010), the requirements for establishing mediators (see Kazdin, 2007) were not fully met. Researchers should aim to meet these requirements while using theory as a guide in selecting mediators and/or moderators. Importantly, mediation and moderator analyses have not been coupled until now—i.e., we do not know if the mechanisms are the same or not in different categories of the relationships between independent and dependent variables (e.g., high symptomatic patients versus low symptomatic ones).

Depending on the results of such studies, designed to clarify mediators and moderators, the content of iCBT intervention protocols can be adjusted in terms of strategies and techniques aimed to modify these factors as well as customization and treatment flexibility. For example, a meta-analysis of computerized CBT (Andersson & Cuijpers, 2009) reported that tailored treatment was superior to nontailored treatment for patients with more severe forms of depression.

Limitations

First of all, this is a qualitative approach. A quantitative approach would be more informative because we could investigate aspects that are more specific and derive conclusions that are more data-based. However, there are few studies that investigated mechanisms of change, and most of them are of low quality. Moreover, the available studies are heterogeneous in terms of the iCBT protocols they tested. Therefore, synthesizing quantitative data from them would not make so much sense.

Second, we included only randomized clinical trials. This approach allowed us to localize the best sources of evidence for assessing the efficacy of iCBT for adult depression. However, we might have missed some studies that used moderation or mediation analyses to specifically investigate the iCBT mechanisms of change because moderation and mediation did not require necessarily a control group. Yet if moderation and mediation are conducted on a nonrandomized treatment group, then they may lead to biased results (e.g., patients who volunteer to participate in a study testing an iCBT protocol for depression can be more motivated or can have higher positive expectations for change). This is why we chose to include only randomized clinical trials.

Conclusions

This is the first systematic review aiming to examine the overall scientific status of iCBT for depression on the basis of David and Montgomery's 2011 evaluative framework of psychological interventions, which takes into account both the efficacy of the treatment package and the scientific support for the theoretical mechanisms of change underlying the treatment. Based on our review, we have some reasons to assert that iCBT works for adult depression (i.e., is responsible for change). However, before definitive conclusions can be drawn, we need well-designed and adequately implemented controlled trials that compare iCBT to placebo interventions. Notably, we have little knowledge of why or how iCBT works. The theory should be clearly specified and adequately investigated to design and implement highly efficacious therapeutic packages. We believe that considering the mechanisms of change in the field of iCBT may dramatically improve our current iCBT understanding, from both a scientific and a clinical perspective. Without considering the iCBT mechanisms of change along with iCBT efficacy, the extent to which iCBT is an empirically validated treatment remains questionable.

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Note: References marked with an asterisk denote articles included in the qualitative review.

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Appendix

MEDLINE and PsycINFO Search

#	Search string
1	(Depression) AND
2	(Computerized Cognitive Behavioral Therapy OR Computerized CBT OR Internet Delivered CBT OR iCBT OR Internet Based CBT OR Web Based CBT OR Mobile Based CBT OR Web Delivered CBT)
3	1 AND 2

Note. All searches were conducted up to November 1, 2015.