

Promises and risks of web-based interventions in the treatment of depression

Ulrich Hegerl, MD, PhD; Caroline Oehler, MS

Major depression (MD) is a highly prevalent and severe disorder with many patients having no access to efficient treatments such as pharmacological and psychotherapy. Web-based interventions promise to be a method to provide resource-efficient and widespread access to psychotherapeutic support. Meta-analyses summarizing studies that use face-to-face psychotherapy as a comparator provide evidence for equivalent antidepressant efficacy. Web-based interventions seem to be particularly efficacious when they are accompanied by some form of professional guidance. However, they are also associated with a variety of possible risks (eg, suicidal crises can be overlooked) and unwanted effects (eg, increase in rumination and somatization due to self-monitoring) that are so far under-studied. Although some naturalistic studies yield smaller effect sizes than randomized controlled trials (RCTs), well-designed interventions with adequate guidance have been shown to be successfully integrable into routine care.

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Web-based interventions for depression

Major depression (MD) is a highly prevalent, severe, and often life-threatening disorder. Efficient treatments are available, pharmacological and psychotherapy being the most relevant ones. However, even in countries with well-developed health care systems, only a minority of patients receive treatment in line with recommendations provided by evidence-based treatment guidelines. This constellation results in room for improvement, which seems to be greater in depression than in any other disorder. One of the many reasons contributing to these therapeutic deficits is the difficulty of gaining access to specialized care,¹ in particular psychotherapy. Even in countries with a comparably high density of psychiatrists and psychotherapists such as Germany, patients have to wait for months until a

specific psychotherapy can be started.² This treatment gap is even greater in older people, who are only rarely offered psychotherapy. Other reasons for the insufficient treatment can be a lack of knowledge about mental health disorders and available treatment options, difficulties accessing care due to geographical reasons or due to a shortage of care providers or fear of stigmatization and shame.³ Against this background web-based interventions are beginning to play an increasingly important role in the management and treatment of MD. The approach promises access to psychotherapeutic support for a variety of patients in a way that requires less time from the therapist. In addition, such web-based interventions are accessible from almost everywhere and can be used discretely without the fear of being stigmatized. Also, treatment fidelity is very high, as the program delivers the intended content in exactly the same way to every user.

Author affiliations: German Depression Foundation, Leipzig (Caroline Oehler); President of European Alliance Against Depression, Senckenberg Distinguished Professorship, Department of Psychiatry, Psychosomatics and Psychotherapy, Goethe-Universität Frankfurt, Germany (Ulrich Hegerl). **Address for correspondence:** Ulrich Hegerl, Prof Dr, President of European Alliance Against Depression, Senckenberg Distinguished Professorship, Department of Psychiatry, Psychosomatics and Psychotherapy, Goethe-Universität Frankfurt, Heinrich-Hoffmann-Str. 10, 60528 Frankfurt a.M., Germany (email: ulrich.hegerl@deutsche-depressionshilfe.de)

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Today, a large number of digital interventions is available in English and many other languages. Most of the interventions are based on the principles of cognitive behavioral therapy (CBT), but elements of other psychotherapeutic approaches—such as mindfulness-based interventions—have also been developed, and some have transferred psychodynamic techniques to the internet.⁴⁻⁶ A typical web-based intervention consists of 5 to 15 modules, each targeting a specific topic, and incorporates psychoeducational material as well as interactive elements or tasks.⁷ The core principle of CBT-based interventions is to teach patients how both behavior and cognition interact with emotions and how to actively use this interaction to feel better. Through activity monitoring and the conscious planning of positive activities supported through web-based templates, the “downward spiral” (a picture for depression often used in CBT) is broken. On the cognitive level, web-based interventions typically teach patients about negative automated thinking and introduce strategies on how to challenge such thoughts. Repeated practice is necessary for patients to change long-learned habits and to profit from CBT techniques. Therefore, many web-based interventions incorporate reminders in order to facilitate the transfer into everyday life. Although most interventions heavily rely on written content, other elements like audio or video and animations are increasingly being used. To illustrate what the content and structure of such an intervention could look like, the workshops of the iFightDepression tool are described in *Table 1*. This tool, offered by the European Alliance against Depression (www.eaad.net), is an example of a noncommercial web-based intervention available in 12 different languages, including an Arabic version.

Web-based interventions can be divided into those that are offered with some form of professional guidance and those that are completely self-guided. In the outpatient setting, guidance can, for example, be provided by general practitioners (GPs), psychiatrists, psychotherapists, or assistants specialized in providing support for online interventions. The guiding health care professional introduces the patient to the intervention, offers assistance at follow-up appoint-

ments, and asks about the patient’s experiences in working with the intervention. In order to be able to provide high-quality guidance, guides have to be familiar with the interventions themselves. For the iFightDepression tool, an e-learning platform is offered, which allows the guides to get acquainted with the iFightDepression tool. Other

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web-based interventions are accompanied by guidance without face-to-face appointments via asynchronous communication methods (eg, email or text messages) or synchronous communication methods (eg, using the telephone). For web-based elements that are interwoven with regular face-to-face treatment, the term “blended therapy” was coined. Web-based interventions can also be differentiated based on their position in the whole therapeutic concept. Some are conceived as alternatives to regular treatment with antidepressants and face-to-face psychotherapy and as first options in a stepped-care approach, others (eg, the iFightDepression tool) are seen as self-management tools and meant to be used as an addition to regular treatment. Unguided intervention should be considered with a critical eye, as it is a problematic message that people affected by a serious condition such as depression can treat themselves on the internet. There is the risk that such tools are used by patients as an alternative to professional guideline-oriented treatment. In addition, evidence for the efficacy of unguided interventions is questionable (see below). Therefore, guided interventions should be preferred.

Whereas the typical intervention that is currently being researched is accessible online using the browser of a computer, tablet, or smartphone, a rising number of apps are published in both the Apple App Store and the Android Market (Google Play). In a systematic review conducted in 2015, 117 were identified that claimed to offer CBT or behavioral activation (BA) for people suffering from depression. Only 10.3% of these seemed to be consistent with evidence-based principles, and none offered efficacy or effectiveness studies. Safety or privacy policies were often missing.⁸ Another study, using more lenient search criteria, identified 1054 apps claiming to be helpful in dealing with depression in 2014.⁹ Since this field is developing partic-

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NAME OF WORKSHOP	COGNITIVE BEHAVIORAL THERAPY–BASED CONTENT
1) Thinking, feeling, and doing	Information about how thoughts, emotions, and behavior are interconnected. Objective: monitoring of daily activities and corresponding mood changes to identify ways to improve daily routines.
2) Sleep and depression	Introduction of sleep diary. Objective: explore possible connections between patients' bedtimes and changes in mood.
3) Planning and doing enjoyable things	Instruction to plan ahead and to integrate at least one positive activity into the daily routine. Objective: to restore or establish the balance between duties and leisure activities.
4) Getting things done	Training of problem-solving abilities. Objective: break down one task into small steps and plan ahead when and how to complete it.
5) Identifying negative thoughts	Introduction of the "ABC model" and automated negative thought patterns. Objective: identify one's own negative thoughts habits.
6) Changing negative thoughts	Generate alternative thoughts to the ones listed in workshop 5. Objective: change thought patterns to more helpful and realistic ones.

Table 1. Description of the six core workshops of the iFightDepression tool.

ularly rapidly, the current number will be several times higher. Smartphone applications offer many of the advantages of browser-based internet interventions and are even more accessible. Smartphones are among the most rapidly adopted innovations from recent years. They also have the advantage of being the main tool to access the internet in many developing countries,¹⁰ expanding the potential global impact of web-based interventions to alleviate the burden of MD. Furthermore, smartphone applications offer unique functionalities—eg, sending push notifications—and are often used as a planning device, which makes them ideal to support changes in habit. Considering these features, it is very likely that their importance in the implementation of web-based interventions will increase significantly.

Evidence for antidepressant efficacy

Up to now, more than 100 studies on the antidepressant efficacy of digital interventions have been published, most of them with positive results. A recent meta-analysis on 40 studies of CBT delivered through the internet

found an overall effect size of $g=0.502$ directly after the completion of the interventions.¹¹ However, when evaluating the evidence provided by this field of research, it is crucial to consider a fundamental methodological problem: it is difficult to “blind” the patient concerning the control condition in psychological interventions. As a consequence, participants randomized into the control condition might even experience nocebo effects (nocebo being the negative side of placebo, describing negative expectations that lead to negative effects) through their awareness of receiving the ineffectual condition. But even if an active control is provided, the patient might recognize that she is “only in the control group” and might react with frustration and disappointment. This effect was, for example, visible in a randomized controlled trial (RCT) on primary care patients with milder forms of depression.¹² In this trial, an active control condition, consisting of supervised self-help groups and psychoeducation, lead to an outcome that was significantly worse than pill-placebo. It has been convincingly shown that, more than the kind of intervention itself, the choice of the control condition determines the observed

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effect size.¹²⁻¹⁴ Taking these methodological considerations into account, it is apparently difficult to draw any conclusion from studies with a waiting list (WL) or treatment as usual controls (TAU) concerning antidepressant efficacy. Still, most of the evidence collected on web-based interventions for depression so far comes from such studies. Only eight of the 40 studies of the meta-analysis mentioned above did not rely on WL or TAU as control condition.

In that sense, the best evidence on the efficacy of web-based interventions for depression comes from noninferiority trials that use face-to-face psychotherapy as an active comparator. A first small meta-analysis of such trials (based on in total 429 patients from five studies) indicates that web-based interventions have efficacy that is similar to face-to-face interventions.¹⁵ All included trials compared web-based interventions (lasting 6 to 10 weeks) with some form of face-to-face intervention, two of them using group interventions as comparator. Overall, Andersson et al¹⁵ found a between-group effect size of Hedge's $g=0.12$ that numerically even favored the web-based interventions but did not differ statistically significantly from zero. It has to be noted that the face-to-face interventions were often matched in duration to the web-based intervention and are therefore comparable to them, but do not necessarily resemble a full psychotherapy as provided in routine care.

It is well established that interventions incorporating some kind of guidance by a health-care professional have significantly larger antidepressant effects than unguided intervention, with the greatest improvements found in trials using face-to-face guidance, followed by telephone guidance, and support using text only (email or messages within the intervention tool).¹¹

Thus far, most scientific evidence has been collected on browser-based interventions and, although the apparent validity of transferring the interventions from browser to application is very high, it is still worth looking at the evidence base. A review by Firth et al¹⁶ aggregated data from 18 RCTs on 22 smartphone apps for depression, mainly including patients suffering from mild to moderate depression. They found small to medium effect sizes when compared with active ($g=0.22$) and inactive ($g=0.56$) control conditions. In this meta-analysis, studies that used interventions that involved app usage as well as human support yielded smaller effect sizes. This contradicts the

result consistently found in other web-based interventions that human support or guidance boosts the antidepressant effects of the intervention. The authors of the meta-analysis hypothesize that this result is due to the fact that apps not relying on guidance have been designed more comprehensively and to be user-friendly. Therefore, the result might be an artifact of differences in usability and comprehensive design of the apps.

It is important to keep in mind that, although web-based interventions and face-to-face psychotherapy seem to have comparable antidepressant effects, this does not implicate that they have the same value for the patient. In face-to-face psychotherapy, the chance that suicidal and other critical developments are detected by the psychotherapist are higher than in e-mental health approaches, even when some kind of guidance is provided. There might be other more subtle positive effects associated with a direct interaction with the psychotherapist that are hard to quantify. Such effects are likely to depend on the skills and personality of the psychotherapist. On the other hand, receiving an intervention with only minimal personal contact also reduces the possibility of negative effects related to unfavorable personal interactions. In this context, it might be of some anecdotal interest to know that in 1898, Sigmund Freud had 50 documented patients in his private practice. Four committed suicide, two immediately after leaving the cabinet of Freud (personal communication by the Freud biographer Christfried Toegel).

Risks and negative effects

As is known for pharmaco- and psychotherapy as first-line treatment options for depression,¹⁷⁻²⁰ every active ingredient or intervention also has the potential to induce negative or unwanted effects. A thorough exploration of possible unwanted effects gives users and prescribers the opportunity to consider them in their choice of treatment. Web-based interventions are associated with a variety of risks and possible negative and unwanted effects. This topic is so far largely unstudied, but could, corresponding to the possible negative effects of psychotherapy,²¹ include the following aspects:

(i) The **interventions can be used in an incorrect manner**. For example, patients could perceive web-based intervention as an alternative treatment that replaces or delays guideline-oriented treatment. This could happen even though the

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intervention might have been designed only as an add-on to regular treatment. GPs or other health professionals could misdiagnose depression and offer an intervention designed for depression to patients with other disorders, eg, obsessive compulsive disorder (OCD) or schizoaffective disorders, where the intervention is unlikely to be helpful or might even be detrimental. Furthermore, most web-based interventions are designed for patients with milder forms of depression. If patients with severe or even delusional depression are confronted with a web-based intervention, negative reactions such as increases in despair and self-blaming could occur. On the other hand, due to the often highly structured form of web-based interventions, treatment fidelity is usually high, and the treatment is delivered in a much more standardized way, avoiding a risk present in traditional psychotherapy.

(ii) The intervention can be offered to the right patients, but **guidance is provided with insufficient intensity or quality**. As in any psychosocial intervention, the interpersonal relationship can be both a negative and positive factor. So far, this factor has not been sufficiently investigated.

(iii) Even when used in the correct manner, **symptom deterioration** can occur during the use of web-based interventions. Since it is hard to disentangle if deterioration is directly related to the web-based intervention or results from the random variance due to uncertainties in the assessment of depression and the independent fluctuations of depression severity, reliable deterioration rates are used as an approximation. Reliable deterioration is based on reliable change scores and gives an estimate of how many participants' symptoms deteriorated, corrected for the reliability of the measure used. This, however, still leaves open the question of causality and natural fluctuations in symptom severity. In an individual patient data meta-analysis, Ebert et al²² found a risk of 3.36% for reliable deterioration in the intervention group, compared with 7.5% in the control conditions. In this analysis, participants with a lower educational level who were randomized into the intervention group were found to have a comparable risk of experiencing a significant deterioration as participants in the control condition. Especially patients with a lower level of education seem to need more intensive support when working with a web-based intervention. As an amendment to these results, Karyotaki et al²³ analyzed the risk of reliable deterioration in self-guided interventions for depression. In 16 trials with altogether

3805 participants, they found that 5.6% of participants in the intervention groups and 9.1% in the control groups experienced reliable symptom deterioration without the characteristics of the participants predicting the risk of deterioration. So far, web-based interventions seem to be comparable to psychotherapy with respect to reliable deterioration. In a meta-analysis on 18 studies researching psychotherapy for depression, a median deterioration rate of 4% was found, with single rates as high as 10%.²⁴

(iv) The delivery format brings further specific risks that are not routinely measured in RCTs. Patients might feel stressed by the tight treatment schedule, become frustrated by technical problems, or feel uneasy because of the limited possibility to contact a health care professional.²⁵

(v) Still more difficult to measure are subtle changes and **unwanted effects** that might be caused by the regular use of web-based health interventions, electronic devices, and self-monitoring. In a study that added daily self-monitoring via a guided app to the medical treatment in a specialized clinic, patients in the intervention group who reported alleviated symptoms of depression at baseline tended to deteriorate further than the control group.²⁶ The authors hypothesize that especially for patients with a higher initial score of depression, the daily confrontation with self-ratings of depression might have accentuated the symptoms and possibly increased worrying. Regular use of monitoring apps might even induce obsessive self-monitoring or strengthen somatization tendencies through constant direction of attention toward one's symptoms.

(vi) A further risk associated with web-based intervention is that **the chance of detecting suicidal crises** is likely to be smaller than with traditional approaches because direct personal contact is reduced. Considering the so far limited evidence for the antidepressant effects of web-based interventions, more research on and sensible consideration of possible unwanted effects are needed.

Acceptance, adherence, and its predictors

The satisfaction in participants of trials on web-based treatments of depression has been stated to be high,²⁷ and convenience, low cost, privacy, and the ability to proceed at one's own pace have been named as advantages of web-based interventions.²⁸ In contrast with this, acceptance among the

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public seems to be limited. In a review on four studies, most participants reported lower intentions to use media-assisted treatment (via apps or webpages) than medication or face-to-face treatment.²⁹ Also, the perceived helpfulness was higher for the latter methods than for e-health interventions. A survey conducted among a wide group of European mental health stakeholders found the acceptance to be higher for blended treatments than for stand-alone solutions.³⁰ For Germany, the German Depression Foundation assessed opinions about web-based interventions in 2017, both in the general public (N=2009) and in a sample of people with lived experience (N=990). Whereas over half of the participants in both samples reported being critical of web-based interventions for data protection reasons, the proportion of people stating that these interventions might provide helpful support was much higher in the sample of people with lived experience (59.7% vs 39.5%). Also, almost half of the public sample felt that these interventions might be dangerous, whereas only 18% of the people with lived experience did so. It seems that patients themselves might be more ready than the general public to try out new interventions using the internet as an adjunct. Still, only around 20% in both groups said that web-based interventions might be an alternative to face-to-face psychotherapy.³¹

Another problem that has been described in several instances, especially for routine care, is the low level of adherence to web-based interventions, with meta-analysis reporting dropout rates as high as 74% for unsupported interventions.³² The most prominent example is a large pragmatic trial (N=691) conducted with depressed patients in primary care in the UK, in which two web-based interventions were compared with TAU by the GP.³³ The adherence in the British sample was very low: only around 80% of the participants started using the intervention. The most frequent number of sessions completed was one, with only around 17% of the participants completing the online interventions. Low adherence in turn limits the benefit each individual can draw from the intervention,³⁴ and it has been shown that completion rate influences the effect sizes one can expect to find in a study.¹¹

To fully utilize the potential of web-based interventions, it is therefore important to apply strategies that enhance user engagement and adherence. This could on the one hand be accomplished through changes in the way the intervention is delivered. Among others, adherence to web-based inter-

ventions is influenced by guidance, whereby this relationship partly explains the superior effects of guided versus unguided interventions. The optimal time that should be spent on guidance to maximize the interventions effect is still a matter of discussion.³⁵ Other successful strategies for improving adherence could include using persuasive system design elements³⁶ and adding choice, cost, and reminders to the intervention,³⁷ with reminders probably being the most potent feature to increase both adherence and effectiveness.³⁸

On the other hand, patient characteristics have been found to predict the adherence and success of web-based interventions. Another strategy to optimize usage could be to select patient groups that will probably adhere or provide additional guidance to groups that usually show lower adherence rates. Possible predictors can be sociodemographic variables such as age and gender, on the one hand, and beliefs and expectations on the other. In an individual patient data meta-analysis on self-guided interventions for depression, male gender, lower educational level, and being younger predicted higher chances of nonadherence.³⁹ Treatment credibility and a positive working alliance with the intervention have been associated with a reduced probability of dropout and higher probability of reliable symptom improvement,⁴⁰ and Mira et al⁴¹ found that higher initial expectations were related to greater improvements in all measures. The later result was confirmed in a systematic review.⁴²

Conclusion

Web-based interventions are developed and researched at an accelerating speed. But the often-postulated good evidence for the efficacy of web-based interventions for depression requires a critical review: most of the studies conducted so far have used WLs and TAU groups as control conditions, which might artificially enhance their effect sizes due to placebo effects in the control condition. RCTs comparing web-based interventions and face-to-face treatment in noninferiority designs have yielded the best evidence on efficacy available thus far. A first meta-analysis on this type of study found that web-based interventions had a similar antidepressant effect to face-to-face interventions if they are offered with professional guidance.

Fields for further research are potential negative and unwanted effects of web-based interventions. Whereas

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first studies have shown similar deterioration rates as seen in traditional psychotherapy, other possibilities such as the opportunity to detect suicidal crises have not been quantified so far and should be the focus of future research. One of the most relevant barriers to fully exploit the potential of web-based interventions in routine care is a low rate of adherence, especially if the interventions are provided as stand-alone offers without any support. But if they are designed incorporating persuasive elements, eg, frequent reminders as well as regular guidance, at best in a face-to-face setting, they can lead to a significant decrease in symptoms of depression, even in routine care.^{43,44}

Digital interventions can be considered to be a promising means to meet the increasing demand for psychotherapeutic interventions worldwide. Especially in the treatment of depression, a highly prevalent, severe, and at the same time undertreated disorder, they are likely to play an increasingly important role in the future. ■

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