Internet interventions for depression: new developments

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A wide range of Internet interventions, mostly grounded in methods of cognitive behavioral therapy, have been developed and tested for several mental disorders. The evidence to date shows that these interventions are effective in reducing symptoms of depression. Metaanalyses report small-to-medium effect sizes when Internet interventions are delivered as stand-alone self-help interventions (d=0.25-0.36), and medium-to-large effect sizes when delivered as therapist-guided interventions (d=0.58-0.78), both compared with usual care. Only a minority of people suffering from depression receive adequate treatment, and Internet interventions might help bridge the large treatment gap. This review summarizes the current body of evidence and highlights pros and cons of Internet interventions. It also outlines how they could be implemented in mental health care systems and points out unresolved questions, as well as future directions, in this research field.

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Availability of depression treatment

A diverse array of therapies, particularly cognitive behavioral therapy (CBT) and interpersonal therapy, have been established as effective for the treatment of depression.[1,2] Still, only about 54% of those with depressive disorders receive treatment for their condition.[3] Reasons for this treatment gap include, on the one hand, deficits in the health care system and, on the other hand, a reluctance to seek treatment on the part of those affected.

One shortcoming in the German health care system is failure to detect clinically relevant depression in primary care.[4] Another is the limited availability of outpatient professionals, especially in rural or remote areas.[5] Even in many industrialized countries, people with symptoms of depression have to wait long periods until treatment is available, for example, this wait period is about 3 to 4 months in Germany.[6]

Untreated depression can have severe consequences consisting of reduced quality of life, impairment in so-

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Selected abbreviations and acronyms

APOI	*Attitudes toward Psychological Online Interventions (Questionnaire)*
CBT	*cognitive behavioral therapy*
EVIDENT	*Effectiveness of Internet-based Depression Treatment*
iCBT	*Internet-based CBT*
RCT	*randomized controlled trial*
REEACT	*Randomized Evaluation of the Effectiveness and Acceptability of Computerized Therapy*

cial relationships or work functioning, and suicide in the worst case, as well as direct and indirect economic costs for society.[7] Even if depressed patients do get to see a therapist, there is a high probability that they do not receive evidence-based treatment.[8] Particularly in highly standardized treatments, such as CBT, clinicians often deviate markedly from the treatment manual.[9] In some cases, this may even worsen depression symptoms.[10]

Reluctance to seek available treatment options on the part of those affected by depression also contributes to the treatment gap. This reluctance is illustrated by the fact that about 8 years pass between the onset of a depressive disorder and actual treatment seeking.[11] Reasons for the reluctance to seek treatment include difficulties in attending therapy during usual business hours and financial constraints,[12] lack of motivation and negative attitudes toward psychotherapy,[13] fear of stigmatization,[12-14] and the anticipated waiting period for a psychotherapy.[15]

Internet interventions for depression

Novel modes of delivering psychotherapeutic interventions are required in order to narrow the treatment gap in depression as well as other mental disorders,[16] and self-help interventions are regarded as a promising option to augment health care systems in treatment of depression.[17] Self-help interventions, when highly structured and standardized, can be successfully delivered via the Internet. Internet interventions mostly comprise several modules containing information and exercises that are based on methods derived from CBT[18] and are therefore called Internet-based CBT (iCBT). However, there are also emerging efforts to establish Internet interventions for depression that are based on a psychodynamic understanding of mental illness.[19]

Some of the programs present mostly text-based, psychoeducational information in a sequential order, whereas other interventions are more sophisticated and include simulated dialogues with content tailored to a user's response (eg, Deprexis[20,21]). Whereas some of the available programs can be used without registration—such as MoodGym, probably the most widely disseminated Internet intervention for depression in the world[22]—other programs require registration or involve careful pre-assessments.

Internet interventions are often offered without therapist guidance (unguided interventions) but can be combined with minimal, though regular, therapist contact (therapist-guided interventions).[23] Therapist guidance can take different forms and may vary in terms of the amount of time devoted to the individual client.[24] Most studies involve rather low-intensity guidance with approximately 10 minutes of time spent by a clinician per client per week.[25] Guidance often consists of weekly scheduled written feedback by a therapist and the possibility for clients to pose questions. The main purpose of therapist guidance is to recognize and reinforce the participants' work with the self-help material.

Advantages and challenges

One reason why research on Internet interventions evolves at a rapid rate[26] is the fact that such programs have a number of advantages, including (i) low-threshold accessibility[27]; (ii) flexible usage independent of time and place[27]; (iii) usage at a self-determined pace, which is thought to enhance self-efficacy[28]; (iv) a high level of anonymity and privacy that is attractive for individuals with fear of stigmatization[29]; (v) standardized contents, making achievements independently of therapist skills[23]; (vi) easy translatability and cultural adaptability[30]; and (vii) low delivery costs even in large populations.[31]

Yet, a few challenges have to be kept in mind, including: (i) the possibility of technological issues, such as problems with downloads or weak Internet connections[23]; (ii) the need for a high degree of transparency concerning data security[32]; (iii) nonsuitability in case of crises, such as suicidality[33]; and (iv) a lack of personal contact, which eliminates the positive impact of a therapeutic relationship or might allow substantial comprehension mistakes due to a reduction in available communication channels.[34] In conclusion, the challenges

and advantages of Internet interventions are manifold, and strongly depend on the way such interventions are implemented.

Implementation opportunities

Internet interventions could be implemented in existing health care systems in diverse ways: (i) as a way to bridge the treatment gap during long wait periods until a face-to-face treatment is offered[35]; (ii) as stepped-care models in which patients are treated with the most adequate treatment of lowest intensity while continuously monitoring treatment progress and adjusting treatment level gradually whenever it is indicated[36]; (iii) as a preventive measure for individuals at high risk for depression[37]; (iv) as a relapse prevention measure for individuals with residual symptoms after depressive episodes[38,39]; and (v) as an integral part of face-to-face therapy, in what is called *blended treatment.*[18,40]

Efficacy in clinical trials

In recent years, the number of randomized controlled trials (RCTs) evaluating Internet interventions has grown rapidly. To date, several meta-analyses have unanimously confirmed the efficacy of Internet interventions for individuals with symptoms of depression. One meta-analysis of seven trials concluded that unguided Internet interventions for depression yield a small-to-medium effect size (d=0.28) compared with waitlist controls.[41] The same meta-analysis found that effects are mostly maintained over 4- to 12–month follow-up assessments (d=0.23), which was confirmed by a systematic review of 25 RCTs.[42]

Another meta-analysis found that therapist-guided Internet interventions reach a significantly greater symptom reduction (d=0.61) than unguided Internet interventions (d=0.25).[43] According to the authors, those superior effects might be due to better motivation, and thus, compliance under guided conditions. Authors of a more recent review and meta-analysis based on 19 RCTs also found a superior efficacy of therapist-guided (therapist support, d=0.78; administrative support, d=0.58) versus unguided Internet interventions (d=0.36) for depression, which they ascribe to better retention rates.[44] Thus, unguided Internet interventions seem to result in more modest outcomes and higher dropout rates than guided interventions. Furthermore, therapist-guided Internet interventions were found to yield comparable effects to those of face-to-face interventions for depression.[45-47]

Interestingly, one trial revealed that guidance from a technician (who was not permitted to provide clinical advice) was as effective as guidance from a clinician,[48] which leads to the conclusion that the crucial aspect of guidance in Internet interventions might be enhanced motivation rather than therapeutic assistance. Therefore, there is a need for future research on the incremental cost-effectiveness ratio of guided and unguided interventions.[49]

The aim of the REEACT trial (Randomized Evaluation of the Effectiveness and Acceptability of Computerized Therapy) was to examine if therapist-guided Internet interventions yield a substantially greater reduction in depression symptoms than usual general practitioner care.[50] The authors reported that there was no significant improvement in one condition over the other and concluded that guided Internet interventions are not superior to usual care. However, this interpretation was strongly criticized for the following reasons: (i) adherence in the Internet intervention group was low—the median number of completed sessions was two out of a possible eight and the dropout rate was 24%; (ii) general practitioner care was unusually effective; (iii) there was an overlap between the conditions in so far as 19% of the general-practitioner–care group used Internet interventions during the trial; (iv) the nature of the support provided in the trial would not likely meet current standards for guidance in this research field; and (v) the technology of the examined iCBT programs lag behind today's standards.[51]

Considering the evidence so far, it should be noted that many trials used Internet interventions as add-on treatments to the extent that they did not interfere with basic treatments, such as psychotherapy and medication. Because participants mostly received usual care in both the intervention and the control groups, effects of low-cost unguided interventions should not be weighed simply against established effects of traditional psychotherapy or antidepressants. Furthermore, studies on therapist-guided Internet interventions often included more complex diagnostic assessments (eg, made via telephone or even face to face instead of online self-reports), which might lead to a higher degree of internal validity in trials. Beyond that, trials with no therapist contact at all yield lower effects in general, which indicates that efficacy de-

pends on various factors, such as specific conditions of delivery.[42] For instance, one trial investigating therapist-guided versus unguided use of the Deprexis program in participants with a diagnosed depression found only minor differences between those two conditions and large effects compared with a waitlist control group.[52] This tentatively suggests that unguided Internet interventions can be as effective as therapist-guided Internet interventions under specific conditions.[52,53] Therefore, to avoid comparing apples and oranges, a consistent terminology, as well as clear differentiation of content-related and methodological differences, is mandatory in future research on Internet interventions. Finally, results of trials in which randomization is affected due to low adherence need sophisticated interpretation in order to avoid attrition-biased results.

Effectiveness and cost effectiveness in routine settings

Despite profound evidence for the efficacy of Internet interventions, it is yet to be shown that results can be transferred into routine clinical practice. So far, there are few studies that aimed to explore the effectiveness of Internet interventions in traditional health care settings, for example, when applied in primary care. One effectiveness study in 299 participants examined whether an Internet intervention for depression prescribed by primary care clinicians reduces suicidality.[54] After using the iCBT program, suicidal ideation dropped from 54% to 39%. Another uncontrolled study examined the effects of a therapist-guided Internet intervention on 413 participants with depression in the setting of a Dutch online mental health clinic; the post-treatment assessment found a reduction in symptoms (d=1.9), which was maintained at follow-up assessment 1 year later.[55] Beyond replicating this large within-subject effect with regards to the reduction in depressive symptoms with iCBT prescribed by primary care practitioners, results from an Australian effectiveness study in 359 participants suggested increased effects in individuals with severe depression.[56] Moreover, a recent study in 1203 depressed subjects in an outpatient psychiatric clinic showed a significant and stable reduction in suicidality (d=0.58) and insomnia (d=0.69) in a therapist-guided Internet intervention.[57]

In spite of these promising indications for the effectiveness of such interventions in primary and psychiatric care, a naturalistic study on a *blended treatment*—ie, face-to-face psychotherapy combined with Internet interventions—suggests that this implementation mode results in similar effects as face-to-face therapy, but does not lead to benefits in terms of cost effectiveness.[58] However, one recent trial that investigated whether behavioral activation treatment for depression can work if a smartphone app devoted to behavioral activation is combined with four face-to-face sessions showed that a four-session *blended treatment* can yield similar effects to a ten-session face-to-face treatment.[59] In conclusion, Internet interventions are effective when implemented in routine settings. Nevertheless, more research on the cost effectiveness of blended formats is needed.[60]

Efficacy in individuals with subclinical depression

Research on Internet interventions for subclinical depression is still scarce. The aim of one recent randomized controlled trial was to evaluate the efficacy of the therapist-guided program GET.ON Mood Enhancer, which is primarily based on behavioral activation and problem solving, in 406 individuals with subthreshold depressive symptoms who were recruited from the general population via a health insurance company.[61] Participants in the intervention group showed a significantly greater symptom reduction than the active control group (psychoeducation) with a moderate between-group effect size (d=0.69); the effect was reduced (d=0.28) at 6 months but still significant.

Another recent trial tested a therapist-guided intervention for depression against an active control group (physical exercise) as well as a waitlist control group in 946 patients with mild-to-moderate symptoms of depression.[62] Participants in both active groups reported significantly larger improvements in mild-to-moderate depressive symptoms than those in the waitlist group, whereas the treatment effect from exercise and the Internet intervention was approximately equal (waitlist vs iCBT between-groups effect; d=0.32).

Results of another large randomized controlled multicenter trial that aimed to examine the efficacy of Deprexis in a therapist-guided version, as well as in an unguided version, against usual care in a total of 1000 individuals with mild-to-moderate symptoms of depression (including subclinical as well as clinical depression) are currently in preparation.[63] Special characteristics of

this trial, named EVIDENT (Effectiveness of Internet-based Depression Treatment), include mid-term (6-month) and long-term (12-month) follow-ups as well as recruitment via various avenues (including in- and outpatient medical and psychological clinics, online forums, health insurance companies, and the media).

Efficacy in secondary depression

A growing research field is the administration of Internet interventions for individuals with comorbid depressive symptoms, for example in patients with neurological or somatic disorders. This research is groundbreaking because comorbid depressive symptoms often remain untreated as clinicians often fail to notice them. One recent trial investigated the efficacy of an unguided Internet intervention in patients with epilepsy, a neurological disorder that is often accompanied by comorbid depression.[64] A total of 78 patients received either unguided access to the intervention or usual care. Importantly, program contents were not tailored to the special problems and disabilities of those afflicted with epilepsy. In comparison with the control group, program users experienced a significant decline in depression symptoms with a small-to-medium effect size (d=0.29), and a significant improvement in fatigue with a medium effect size (d=0.32).

An analogous trial involved 71 patients with multiple sclerosis—an inflammatory, demyelinating neurodegenerative disease of the central nervous system that involves motor dysfunction and sensory impairments, as well as neuropsychiatric symptoms such as cognitive impairment, fatigue, and depressive symptoms.[65] In this trial, program users experienced a significant decline in depressive symptoms and motor fatigue with medium effect sizes (d=0.53 and d=0.46, respectively), compared with the control group. These results lead to the conclusion that Internet interventions could be suitable for patients with neurological disorders who are often unable to regularly attend face-to-face therapy because of reduced mobility.

Another clinical trial, GET.ON M.E.D. (GET.ON Mood Enhancer Diabetes), examined the efficacy of a therapist-guided Internet intervention for patients with diabetes and comorbid depression symptoms in a total of 260 participants.[66] They showed a significant amelioration of depressive symptoms with a large within-group effect size of d=1.06 (reducing to d=0.91 at 6-month follow-up), and a reduction in diabetes-specific emotional distress with a moderate effect size of d=0.68 (d=0.42 at 6-month follow-up).

Another RCT examined whether the unguided Internet intervention for depression, HelpID, which was not tailored to the specific problems of individuals with psychosis, could ameliorate depressive symptoms in individuals with schizophrenia.[67] A total of 58 participants received either 3 months of unguided access to the intervention or usual care. At post-treatment assessment, program users experienced a significant decline in depressive symptoms with a medium-to-large effect size compared with the waitlist control group. Feedback by the participants on the intervention was predominantly positive. Whether the effects are persistent over time still needs to be verified.

Future directions in research

Currently, the evidence for the efficacy of Internet interventions in individuals with depression as primary condition is well grounded. Firstly, results regarding effectiveness in routine care and efficacy for individuals with somatic or neurologic disorders and comorbid symptoms of depression are promising, but still need further replication. Furthermore, research on Internet interventions for comorbid depression could be expanded to a broader range of disorders with high depression rates, such as cardiac insufficiency.[68] In this context, it would be interesting to investigate whether tailoring program contents to crucial topics of the primary disorder enhances efficacy of one program in comparison with another program with standardized depression content.[69] Apart from that, studies often exclude individuals whose depression might be secondary to or part of schizophrenia, bipolar disorder, or substance use and dependence; thus, there is little data on whether these populations benefit from Internet interventions as well,[35] except for one recent trial in a psychotic sample, which is described above.[67]

Secondly, predictors of treatment outcome and the mechanisms of change that are involved in generating good outcomes in trials on Internet interventions for depression need to be investigated. To date, several studies have produced heterogeneous results on positive outcome predictors which include having monophasic,[70] severe,[71,72] or mild depression,[73] being widowed or single,[71] having a high education level,[72] and being

female.[74] Thus, far more studies examining moderators are needed in order to elucidate for which special populations Internet interventions are most effective. In addition, studies examining treatment mediators of treatment effects in trials on Internet interventions for depression are needed. Although the majority of studies have focused on iCBT, the available programs differ in content.[35] Some of them, for example, Deprexis, integrate cognitive behavioral content with elements from other treatment approaches.[20,21] Dismantling studies are needed to provide insight into core "effective ingredients" of such interventions and would have theoretical and clinical implications as they bring to light processes that may be causally related to the improvements observed in efficacy trials. Furthermore, it is of increasing interest to identify unique characteristics of the therapeutic alliance in therapist-guided interventions.[75]

Another important question is whether different recruitment sources produce different clinical and demographic profiles among participants. A recent study revealed that recruitment sources necessitating more active treatment-seeking behaviors (eg, postings on mental health Web sites) result in samples with more severe depression than recruitment sources that require less active treatment-seeking behaviors (eg, referral by peers[76]). If replicated, these findings may have important implications for the recruitment strategies of future projects on Internet interventions.

A further topic is related to the fact that many trials on unguided Internet interventions have had problems with nonadherence. Future research needs to examine reasons for this and to come up with strategies to decrease attrition rates, because adherence is a determinant of effectiveness in Internet interventions.[77] One recent meta-analysis across ten RCTs of unguided Internet interventions indicated that male gender, lower educational level, and comorbid anxiety symptoms significantly increased the risk of dropping out, whereas for older participants, the risk of dropping out significantly decreased.[78] Research suggest that adherence in participants using unguided Internet interventions can be significantly enhanced by integrating automated forms of support, such as regular reminders via email,[79] or by giving a choice of courses and timing.[77]

Another factor that awaits further investigation is the nature and scope of adverse events in Internet interventions.[80] Not all participants benefit from such interventions, and it is possible that some may experience negative effects. One recent qualitative content analysis of patients' experiences with Internet interventions revealed two broad categories and four subcategories of adverse events. The broad categories were: (i) patient-related negative effects; and (ii) treatment-related negative effects.[81] Patient-related negative effects consisted of deterioration of the targeted condition and the occurrence of novel symptoms, whereas treatment-related negative effects primarily encompassed difficulties with the implementation of assignments and aspects of the treatment format that were perceived as negative, for example, the pressure to complete treatment on time. Hence, regular assessment of negative events is important to prevent adverse events and to optimize existing Internet interventions, for example, by increasing the flexibility of treatment schedules.[81] This might also diminish the usually high dropout rates among participants undergoing interventions delivered via the Internet, as mentioned above. In the context of adverse events, it is also important to protect individuals with depression from programs of poor quality. Because not all Internet interventions are evidence-based, health care providers and individuals affected with depression need to be able to easily identify which interventions have shown effectiveness in research and to evaluate different programs in terms of data security and other issues. We suggest establishing some form of certification for Internet interventions that could be issued by national psychological and psychiatric associations.

Furthermore, it is hoped that availability of Internet interventions as a treatment method can motivate individuals who reject face-to-face treatments to seek professional help in the future. It is unclear whether this aim has been met or whether individuals that subjectively do not experience sufficient success are perhaps even less inclined to seek a therapist. Findings of one trial suggest that using Deprexis has neither positive nor negative influences on attitudes toward psychotherapy in individuals with symptoms of depression.[13] Whether this result also holds for other programs still needs to be verified.

Finally, studies that aim to provide insight into factors that promote or hinder the uptake and implementation of evidence-based Internet interventions in mental health care practice are needed,[82] because the use of Internet interventions in routine practice is yet limited. The ongoing "Mastermind project" attempts to bridge the gap between routine practice and effectiveness re-

search by evaluating the implementation of evidence-based Internet interventions for depressive disorders in mental health care settings in Europe. In view of slow dissemination, which could be associated with a low acceptability of Internet interventions, the aim of a recent study was to examine the dimensionality of user-relevant attitudes toward Internet interventions, as they likely influence the extent to which people with symptoms of depression engage with or benefit from such treatments.[83] Factor analyses of a newly devised measure called the "Attitudes towards Psychological Online Interventions Questionnaire" (APOI) revealed the following dimensions: Skepticism and Perception of Risks, Confidence in Effectiveness, Technologization Threat, and Anonymity Benefits.[83] Future studies should also examine attitudes in health care professionals, because some of them criticize Internet interventions in public, which might in turn influence the acceptability in individuals affected with depression and, therefore, dissemination of such novel treatment modes. To this end, efforts to provide evidence-based information on Internet interventions to health care providers might facilitate acceptability in general.[84]

Conclusion

Major depressive episodes, comorbid depression, and subclinical depressive symptoms reduce the quality of life in those affected and cause high costs for society. In view of the large treatment gap, there is a need for interventions to complement mental health care services at a low threshold. There is strong evidence that Internet interventions for depression are efficacious, with effects being stronger for therapist-guided than unguided interventions. Furthermore, there is some evidence that Internet interventions are effective in routine care settings, for example, when applied in primary care. Despite the effects of therapist-guided Internet interventions having been shown to be similar to those of ordinary face-to-face therapy, more studies, including noninferiority trials, are needed to arrive at solid conclusions. The challenges and advantages of Internet interventions are manifold, and strongly depend on how they will be implemented in existing health care. As health care systems differ largely across countries, there might be many possible ways of doing this rather than one standard method.

Additional research topics that should be addressed in the future relate to: (i) establishing the efficacy of Internet interventions for disorders with frequent comorbid depression; (ii) moderators and mediators of treatment effects in Internet interventions; (iii) effects of recruitment sources on outcomes; (iv) understanding reasons for nonadherence in Internet interventions; (v) the nature and scope of negative effects in Internet interventions; and (vi) factors that may influence dissemination of Internet interventions, such as cost effectiveness and attitudes toward such interventions in individuals with depression, as well as health care professionals. Finally, we hope that future research on these topics brings new evidence to light and supports implementation and upscaling of Internet interventions in a way that first and foremost fits the user's needs. ❑

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Intervenciones por internet para la depresión: nuevos desarrollos

Se ha desarrollado y probado una amplia gama de intervenciones por internet para diversos trastornos mentales y la mayor parte está basada en métodos de terapia cognitivo conductual. A la fecha la evidencia muestra que estas intervenciones son efectivas para reducir síntomas depresivos. Estudios de meta-análisis dan cuenta de efectos de pequeña a mediana cuantía cuando las intervenciones por internet son proporcionadas como intervenciones de auto-ayuda de forma autónoma (d=0,25-0,36), y efectos de mediana a gran cuantía cuando son proporcionadas como intervenciones guiadas por terapeutas (d=0,58-0,78), en ambos casos en comparación con el tratamiento habitual. Sólo una minoría de las personas que sufre una depresión recibe un tratamiento adecuado y las intervenciones por internet podrían ayudar a reducir la gran brecha terapéutica. En este campo de investigación la presente revisión resume el cuerpo actual de evidencia de las intervenciones por internet y destaca los pros y contras de ellas. También bosqueja cómo podrían ser implementadas estas intervenciones en los sistemas de atención de salud y señala tanto preguntas sin resolver como futuras orientaciones.

Nouvelles évolutions concernant l'utilisation des procédures Internet dans la dépression

Un large éventail de procédures Internet, dont la plupart sont fondées sur des méthodes de thérapie cognitivo-comportementale, ont été développées et testées pour plusieurs troubles mentaux. À ce jour, les données montrent que ces programmes sont efficaces pour réduire les symptômes dépressifs. Des métaanalyses rapportent que, comparées à un traitement classique, les procédures Internet délivrées en tant que programmes indépendants d'auto-assistance ont un effet de faible ampleur à moyenne ampleur (d = 0,25-0,36) et un effet de moyenne ampleur à forte ampleur lorsqu'il s'agit de programmes menés par un thérapeute (d = 0,58-0,78). Seule une minorité de personnes souffrant de dépression sont correctement traitées, et les procédures Internet peuvent aider à combler l'écart important (d'observance) du traitement. Cet article résume l'état actuel des connaissances et souligne les avantages et les inconvénients des procédures utilisant l'Internet. Il décrit aussi la façon dont elles pourraient être mises en œuvre dans les systèmes de santé mentale et indique les questions non résolues, ainsi que les axes de recherche à venir dans ce domaine.

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