

## **Internet and mobile-based psychotherapy: applications, efficacy and potential for improving mental health care in Europe.**

A report of the EFPA e-health taskforce

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**Abstract**

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## Introduction

Mental health disorders (MHD) are highly prevalent, with estimated lifetime and 12 month- prevalence rates, ranging across countries between 18.1–36.1% and 9.8-19.1%, respectively (R. C. Kessler et al., 2009). MHD are one of the leading causes of disability (Whiteford et al., 2013) and associated with other impacts or associated conditions, such as: poorer quality of life of sufferers and their loved ones; an increased risk of developing chronic physical conditions and related mortality (Cuijpers & Smit, 2002; Saarni et al., 2007; Ustün, Ayuso-Mateos, Chatterji, Mathers, & Murray, 2004). The economic burden of these disorders is enormous, including substantial economic costs, reduced workforce participation, occupational impairment and lost productivity (Berto, D’Ilario, Ruffo, Di Virgilio, & Rizzo, 2000; Greenberg & Birnbaum, 2005; Smit et al., 2006).

In the past decades, a variety of interventions have been developed to treat mental health disorders for which efficacy has been demonstrated in a large number of randomized control trials (Cuijpers, van Straten, Andersson, & van Oppen, 2008; Hofmann & Smits, 2008). However, in most European countries, the majority of individuals suffering from a mental health disorder remain untreated (Mack et al., 2014; Wittchen et al., 2011). In fact, less than half of the individuals with a MHD are recognized and treated (Kohn, Saxena, Levav, & Saraceno, 2004) and treatment rates for children and adolescents are even more problematic (Essau, 2005; Zachrisson, Rödje, & Mykletun, 2006).

The reason for the seemingly low treatment rate appears not to be due only to structural supply shortfalls, such as long waiting times or lack of available therapy within a close distance, such as in rural areas. Recent studies suggest that a large number of those afflicted simply do not take available psychological and medical treatment into consideration, regardless of the accessibility (Andrade et al., 2014).

Many limitations of traditional psychotherapeutic interventions such as limited availability of evidence based interventions and clinicians could potentially be overcome by providing Internet- and mobile-based self-help interventions (IMIs). This relatively new medium for preventing and treating mental health disorders introduces a fresh array of possibilities, including the provision of evidence-based psychological interventions that are free from the restraints of travel and time and which allow reaching participants for whom traditional opportunities are not an option. Depending on the concept, such approaches can reduce costs of psychotherapy or on the other hand increase the efficacy by increasing the treatment intensity using digital technologies or by helping patients to integrate therapeutic strategies into daily life between sessions.

IMIs can therefore be a huge opportunity for the optimization of treatment across Europe. At the same time, the implementation of IMIs poses new questions regarding effectiveness, safety, as well as patients and professional preferences.

The following article will provide an introduction to the subject and narratively reviews the available evidence for the effectiveness of IMIs with regard to the prevention and treatment of MHD. Subsequently we will discuss potential limitations and risk involved with IMIs, briefly review the status of the implementation into routine health care across Europe and offer some suggestions regarding the direction of future research in this field.

### **Characterizing Internet and Mobile-based Interventions**

The possibilities to use IMIs for the prevention and treatment of MHD range from mobile-based apps for the monitoring of health behavior and stand-alone self-help interventions to supplemental elements integrated in conventional on-site psychological interventions (blended concepts). One common element of such interventions is that emotional, cognitive, and behavioral processes are modified and that their generalizations to users' daily lives are promoted using established psychotherapeutic techniques. IMIs can be categorized with regard to their use of technology, the extent of human support, the theoretical basis, and with respect to their areas of applications and indications (Figure 1).

#### *Technical Implementation*

For the implementation of IMIs, numerous technical possibilities are applicable. These range from 1) the provision of evidence-based strategies as interactive self-help lessons; 2) e-mail, chat, or video-based sessions (D. Kessler et al., 2009); 3) virtual reality for exposure interventions (Garcia-Palacios, Hoffman, Carlin, Furness, & Botella, 2002); 4) serious-games, in which psychological strategies are trained in the context of a computer game (Merry et al., 2012); 5) avatar led sessions (Savvides & Karekla, 2015); 6) the use of automated memory, feedback, and reinforcement interventions, for example through apps, e-mails, text messages, or short prompts, which support the participant in incorporating intervention content into everyday life; to 7) phone- and wearable-sensors as well as apps for monitoring symptoms, health behavior such as homework completion, which can be used to support the therapeutic process (Jiaxi Lin, Ebert, Lehr, Berking, & Baumeister, 2013).

#### *Theoretical Basis*

Due to their distinctive structured nature, standardization, and focus on the training of strategies and specific behavior, IMIs are particularly suited for techniques that target changes in thoughts and

behaviors. These include well-researched cognitive, behavioral, and interpersonal interventions. Although the majority of evaluated IMIs are built on standard Cognitive Behavioral Treatment (CBT) principles, there is also some promising evidence for the potential of other theoretical approaches, such as mindfulness-based methods, acceptance-and commitment therapy, or psychodynamic treatments (G. Andersson, Paxling, Roch-Norlund, et al., 2012; Donker et al., 2013; Johansson, Hesser, Ljótsson, Frederick, & Andersson, 2012; J. Lin et al., 2015; Mak, Chan, Cheung, Lin, & Ngai, 2015).

### *Human support*

As a basic principle, IMIs can be implemented with varying degrees of human support. The current most commonly used method is the so-called “guided self-help”, in which evidence-based content is usually provided as self-help material so that the participants can perform most tasks independently. An accompanying psychologist then provides regular feedback / guidance on the tasks, most often once a week. Fostering adherence to the content of the intervention is usually the main aim of human support, rather than the delivery of new therapeutic techniques that go beyond the content of the current lesson (Ebert, Lehr, Smit, et al., 2014; Zarski et al., 2016). More specifically, this includes clarifying content and tasks, facilitating comprehension, providing feedback on solved problems and progress, and encouraging participants to continue to work by themselves. In order to reach these purposes, communication can happen either synchronously (via text, audio or video) or asynchronously (for example by email); the latter is more commonly used, and normally takes from a few minutes to a few hours (1-4 hours) per participant and intervention. For the participant, the processing of self-help material, execution and repetition of exercises, as well as correspondence with a therapist can, however, be very intense and require a much greater time investment than that of the supporting therapist (Berger & Andersson, 2009). The combination of self-help material with therapist guidance via the technologies thereby could increase empowerment of the patients and the degree of self-directed coping while maximizing the efficiency of the accompanying therapist. Irrespective of location, asynchronous contact and time-independent communication result in increased flexibility and autonomy for both participants and therapist.

### *Areas of Application*

Applications of IMIs range from mental health promotion and mental disorder prevention to full treatment of mental disorders, as well as interventions to reduce relapse or recurrence and the management of chronic conditions. IMIs are considered a promising approach for increasing the accessibility of evidence-based psychotherapeutic techniques to people on a larger scale due to their low

threshold for accessibility, location and time independence, and anonymous usability (Buntrock et al., 2014). IMIs can be used in either as a stand-alone approach, as part of a stepped-care approach or as an integrated element of a psychotherapeutic intervention consisting of online and conventional on-site sessions (blended treatment).

As **stand-alone measures**, IMIs increase the reach of effective psychological interventions. Telehealth interventions (live therapy online) can transcend space. Stand Alone IMIs, however can transcend both space and time. For example, the temporal and spatial independence of IMIs facilitates access to evidence-based interventions for individuals with limited mobility or those living in areas with limited access to psychotherapy. Individuals who are not able to attend appointments during usual visiting hours and, therefore, are not able to attend other on-site face-to-face options, would then also be able to participate in interventions in the evenings or at the weekend at their own pace. Such approaches could also help those people who have difficulty expressing themselves or do not enjoy social or human contact (Lal & Adair, 2014). People who would have not sought to participate in a psychotherapeutic intervention due to other individual reasons, such as fear of stigma, could also have access to IMIs. Despite increasing social acceptance of psychotherapy, everything which might be associated with mental problems produce for some individuals still a sense of shame, which in itself creates a barrier to the actual use of a psychological intervention (Clement et al., 2015; Henderson, Evans-Lacko, & Thornicroft, 2013). Using technologies may reduce the sense of shame as well as increase acceptance and adherence to treatment.

In the combination of IMIs and personal face-to-face psychotherapy, the so-called **blended-concept**, IMIs take over areas that need not necessarily be mediated by a psychotherapist, allowing more time during the sessions for face-to-face psychological process work. Psychotherapists could for example delegate time-consuming routine aspects of the intervention, such as the delivery of psychoeducation to digital tools. In principle, IMIs could also be used to improve face-to-face interventions by providing exercises for the participant to work on in between the intervention sessions, thereby increasing intervention intensity. Another way in which IMIs could be used to improve the outcome of face-to-face interventions is by supporting the integration of behavior changes or training of techniques into routine life, thus extending the reach of the psychological intervention into the daily lives of participants. This can be achieved through methods such as smartphone-based behavioral diaries, sending of messages with ultra-short prompts aimed at training specific strategies in daily life, or smartphone-based coaches which lead patients through potential anxiety-provoking or other difficult situations. Just-in-time interventions using intelligent predictive algorithms based on smartphone based

user and sensor data such as movement, interaction frequencies, voice analytics etc. allow the prediction of symptom change and help patients to cope with symptoms in the moment or manage at risk situations (Luxton, 2016; Van Daele & Vanhoomissen, 2015). Furthermore, the objective of most psychological interventions is that participants actively try to integrate new behavior into their daily life and maintain these changes in the long term. IMIs emphasize the active role of the person concerned in this process, thus promoting a sense of empowerment through encouraging them to use their own resources to solve problems.

Blended concepts allow for example to provide psychological interventions in primary health care such as the GP setting and to foster systematic multi-professional care of patients in primary care by for example that psychologists support patients and GPs to deliver IMIs in primary health care. Another promising application might be the delivery of psychological IMIs in chronic somatic care (Ebert, Nobis, et al., 2016; Jiayi Lin et al., n.d.; Nobis et al., 2015).

Within **stepped-care approaches**, the degree of support participants receive are stepped up based on previous treatment intervention effects. For example, in depression unguided or guided self-help approaches can be offered as a first step, for example, to individuals in the prodromal disease stage (indicated prevention) in order to prevent the transition to the full blown disorder (Ebert, Buntrock, et al., 2016), or also in full syndromal cases as a first step in the chain of treatment. Further intensive therapeutic support, such as outpatient psychotherapy, could then be provided to patients not responding to the IMI's. Similarly, step-down interventions supplement more intensive therapeutic measures with lower intensity support. For example, IMI-relapse prevention and chronic care concepts could be offered to patients following an acute treatment in order to stabilize acute treatment effects and thereby prevent relapse and recurrence (Bockting et al., 2011; Ebert, Gollwitzer, et al., 2013; Ebert, Tarnowski, Gollwitzer, Sieland, & Berking, 2013; Golkaramnay, Bauer, Haug, Wolf, & Kordy, 2007; Kok, Bockting, Burger, Smit, & Riper, 2014).

## **Effectiveness**

### IMIs compared to untreated control groups

There are currently well over 100 randomized clinical studies of, which clearly indicates the huge potential of this approach for the prevention and treatment of mental and behavioral disorders. Especially well researched are Stand-Alone interventions, most of which are based on the concept of guided self-help.

The most well-established and frequently researched IMIs are programs for anxiety disorders and

depression. In comparison to non-treated control groups, high efficacy has been documented in a large number of studies (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010b; Ebert, Zarski, et al., 2015; Mayo-Wilson & Montgomery, 2013; Richards & Richardson, 2012a; Richards, Richardson, Timulak, & McElvaney, 2015). In one meta-analysis of IMIs based on 22 randomized-controlled trials (RCTs) used for depression and anxiety disorders, a standardized average effect size of 0.88 was shown (Andrews et al., 2010). Through meta-analysis based on RCTs, the applicability and efficacy of IMIs was further confirmed for other mental disorders, such as posttraumatic stress disorder, sleep disorders, eating disorders, pain disorders or substance abuse (Hedman et al., 2012; Kuester, Niemeyer, & Knaevelsrud, 2016; Macea, Gajos, Daglia Calil, & Fregni, 2010; Riper et al., 2014; Zachariae, Lyby, Ritterband, & O'Toole, 2015). See Table 1 for an overview of effects based on a meta-analysis of randomized controlled trials. The body of evidence for other mental disorders, by contrast, is still largely unclear, although promising initial results exist from individual randomized controlled studies, for example for obsessive-compulsive (E. Andersson, Enander, Andrén, et al., 2012b; Herbst et al., 2014; Lenhard et al., 2017; Storch et al., 2011), psychotic (Gottlieb et al., 2013; Harper, 2013), body dysmorphic disorders (Enander et al., 2016) or bipolar disorders (Hidalgo-Mazzei et al., 2015), male- and female sexual dysfunction, Tinnitus, Complicated grief, pathologic gambling (Luquiens et al., 2016).

Most of the interventions evaluated up to this point have been aimed at adults as a target group. However, in recent years, the number of studies which investigate possible potential for the treatment of mental disorders in children and adolescents has increased. In one such meta-analysis based on 14 RCT studies, Ebert and colleagues discovered a significant medium to large effect size ( $d = 0.72$ ) in the treatment of anxiety disorders and/or depression with IMIs in children and adolescents.

Table 1 gives an overview of the effectiveness of IMIs for different mental health disorders based on meta-analytical findings.

### Table 1!

#### IMIs compared to face-to-face treatments

The great potential of IMIs is not solely based on studies in which these approaches were evaluated in comparison to (mostly) untreated control groups, but rather also in direct comparison to face-to-face therapy. In a meta-analysis based on 13 RCTs in various disorders (depression, social phobias, tinnitus, panic disorders, sexual dysfunction, specific phobias, among others), Andersson and colleagues found on average no differences in the mean effect size between face-to-face psychotherapy and IMIs which were



designed as a therapist-assisted CBT-based stand-alone intervention (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014). The results were confirmed on a disorder-specific level in a recent Cochrane review for the treatment of anxiety disorders in adults (Olthuis, Watt, Bailey, Hayden, & Stewart, 2015) and a meta-analysis by Andersson for the treatment of depression (G. Andersson, Topococo, Havik, & Nordgreen, 2016). Even if the current number of RCTs evaluating IMIs in direct comparison to classical on-site psychotherapy is limited, the results so far suggest that both types of intervention may achieve equivalent treatment successes. However, it must be mentioned that the limitation applies only to patients who are potentially willing to participate in both face-to-face and Internet-based treatment. Such self-help treatments and programs are not necessarily an adequate treatment option for all affected people (Ebert, Berking, et al., 2015), and face-to-face psychotherapy is likewise not necessarily an attractive form of intervention for all (Andrade et al., 2014).

Significantly less evidence exists regarding the benefits of IMIs as intervention in combination with face-to-face psychotherapy (blended) in comparison to the body of evidence supporting stand-alone intervention. However, initial meta-analytic findings point to the fundamental potential that the efficacy of traditional face-to-face therapy might actually increase with IMIs. Lindheim and colleagues discovered through 10 RCTs that a mobile component, used as a supplemental element in treatment (e.g. SMS to support behavior changes between therapy sessions), could considerably increase the effectiveness of psychological intervention in comparison to solely on-site intervention (SMD= 0.27) (Lindheim, Bennett, Rosen, & Silk, 2015). However, research regarding the optimal integration of IMIs into on-site therapy and the use of such intervention to increase the effectiveness of psychotherapy is still in its infancy. Also with regard to the potential of such approaches saving clinicians time, only a few studies have so far compared blended vs. non-blended concepts in RCT studies. A recent systematic review (Erbe, Eichert & Ebert, under review) identified three trials that showed that blended concepts were able to reduce clinicians' time by 50 – 86 % without reducing the efficacy of the therapy (Kenwright, Liness, & Marks, 2001; Marks, Kenwright, McDonough, Whittaker, & Mataix-Cols, 2004; Wright et al., 2005). However, a number of large scale studies across Europe are currently being conducted (Kleiboer et al., 2016; Kooistra et al., 2014; Romijn et al., 2015) which will provide valuable insight into the potential of blended-concepts for the treatment of mental health disorders.

In addition to findings from randomized clinical trials, there is accumulating evidence for a number of disorders that [therapist-assisted] IMIs can result also in clinically relevant changes when implemented in routine clinical practice (Andrews & Williams, 2014; El Alaoui, Hedman, Kaldø, et al., 2015; El Alaoui, Hedman, Ljótsson, & Lindefors, 2015; Hedman et al., 2014; Williams, O'Moore, Mason, & Andrews,

2014).

### **The therapist in IMIs**

The therapeutic relationship is a well-known vital component of the effectiveness of Face-to-face psychotherapy. But which role does the therapist have in the realm of IMIs, and does this “impersonal” Internet medium allow for the development of such a relationship? Despite the qualitative and quantitative reduction of overall therapeutic contact and the absence of social and non-verbal signals, previous studies indicate that high quality and comparable therapeutic relationships can be fostered with IMIs just as in face-to-face settings (G. Andersson, Paxling, Wiwe, et al., 2012; Bengtsson, Nordin, & Carlbring, 2015; Cook & Doyle, 2002; Ebert, Hannig, et al., 2013; Preschl, Maercker, & Wagner, 2011). In a study evaluating the Internet-based method “Interapy”, it was found that 88% of patients characterized their online contact with therapists as “pleasant”, while 80% considered the fact that the therapeutic contact took place exclusively on the Internet “positive” (Lange et al., 2003). Similar results can be found based on standardized instruments for assessing the quality of relationships within therapist-assisted IMIs for the treatment of depression, GAS, social phobias, panic disorder and PTSD (G. Andersson, Paxling, Wiwe, et al., 2012; Knaevelsrud & Maercker, 2006).

But is a therapist in Internet-based contexts at all necessary, or will fully automated self-help programs be sufficient for the majority of patients in the future?

The previous findings clearly show that IMIs with therapeutic accompaniment have a significantly greater therapeutic success than IMIs without therapist guidance (Baumeister, Reichler, Munzinger, & Lin, 2014; Klein & Berger, 2013; Palmqvist, Carlbring, & Andersson, 2007). Baumeister and colleagues reported in a systematic review that IMIs with accompanying therapeutic support had a significantly lower dropout rate (odds ratio = 2.67), had more implemented modules per intervention ( $g = 0.52$ ), and achieved great reduction of symptoms ( $g = -0.27$ ) than IMIs without such support.

The relevance of therapeutic contact is also shown through a meta-analysis of IMIs conducted by Richards and Richardson, which produced an average efficacy of  $d = 0.36$  and  $d = 0.78$  with and without support, respectively, in the treatment of depression (Richards and Richardson, 2012).

Although these and other works demonstrate significant effects for unaccompanied self-help intervention, it must nevertheless be mentioned that the studies were based exclusively on randomized clinical trials which bring a per se rather high structuring of patients with it that is usually not to be found in routine clinical care. Since the securing of commitment represents an adherence-promoting element

in self-help interventions, it can be assumed that the effect sizes for pure self-help intervention under laboratory conditions are significantly overestimated for their potential in routine care. Such an assumption is supported by studies in which no additional benefit of unaccompanied, pure self-help programs compared to the standard treatment was found (Littlewood et al., 2015), further emphasizing the importance of a clear concept for ensuring adherence to IMIs, such as through routine therapeutic support (Jones et al., 2015).

Regarding the dose-efficacy relation, two review articles suggest that the effectiveness of IMIs rises with increased support time, whereas Andersson and colleagues conclude that an increase of therapist time beyond 100 minutes per patient within a 10-week IMI has no incremental additional effect on the efficacy (G. Andersson, Carlbring, Berger, Almlöv, & Cuijpers, 2009; Johansson & Andersson, 2012; Palmqvist et al., 2007).

## **Cost-Effectiveness**

### **Limitations and possible negative effects**

As with any other method, it is important to take into account the limitations and risks involved with IMIs alongside all of the potential benefits of the procedure. At this stage, however, no reliable empirical information is available on contraindications for IMIs. It is often argued that in the context of stand-alone methods without therapeutic support, the ability to assess the risk and respond adequately to emergencies (such as suicide) is restricted, since nonverbal cues are missing that help to assess whether dissociation of suicidal thoughts is possible. Therefore, acute suicidality is considered often as a criterion for exclusion in many cases. However, various current empirical studies show that IMIs can also be used effectively in the treatment of suicidal patients, in general, and can reduce suicidal tendencies considerably (Christensen et al., 2013; Mewton & Andrews, 2014). However, worryingly many apps available in the app stores lack empirical support (Aguirre, McCoy, & Roan, 2013) and overall more research is clearly needed to determine under what circumstances such approaches can also be safely used for patients with suicidal ideation.

Little more can be said about further possible negative effects of IMIs at this stage (Rozental et al., 2014). Potential risks and negative effects include, depending on the illness, the following points, among others: (1) limited ability to timely identify patients prone to self-injury; (2) imprecise diagnosis; (3) the development of a reduced health-related self-efficiency if participants should not be successful with

using a stand-alone IMI; (4) the development of negative attitudes towards psychological interventions in general in non-responders; (5) an excessive demand or mental overload of those concerned in the autonomous administration of therapeutic methods; and, 6) the development of a technological and therapeutic dependency (e.g. a patient with agoraphobia feeling insecure to be in public spaces without the possibility to rely on his or her iPhone for symptom control in case issues arise); (7) a possible worsening of symptoms in subgroups of patients. Although initial studies address this subject (Boettcher, Rozental, Andersson, & Carlbring, 2014; Ebert, Donkin, et al., 2016; Ebert, Lehr, Baumeister, et al., 2014; Rozental, Boettcher, Andersson, Schmidt, & Carlbring, 2015), possible negative effects of such interventions cannot be ruled at present and there is an urgent need for further research.

With regard to a potential deterioration of symptoms in subgroups of patients, a recent individual patient data meta-analysis by Ebert and colleagues (Ebert, Donkin, et al., 2016) showed the mean risk for a symptom deterioration was significantly lower in participants of internet-based guided self-help for depression compared to controls. They found no subgroup of participants with an increased risk for deterioration, although education moderated effects on deterioration; with patients with low education displaying a higher risk for deterioration, than patients with higher education. This indicates that treatment and symptom progress of patients with low education should be closely monitored, as some patients might face an increased risk for symptom deterioration.

## **Professional, confidentiality, and ethical aspects**

### *Ethical Aspects*

From an ethical point of view, both risks and opportunities may arise from the use of IMIs. Central concerns about IMIs deal mainly with the risks in the course of diagnosis and of treatment. Moreover, there are concerns about the quality of many programs, as these are not currently subject to uniform quality assurance. Furthermore, the prospects of IMIs are frequently discussed in the context of positive empirical evidence which suggests that the withholding of IMIs as a complementary treatment option for afflicted persons is ethically questionable. As outlined above, findings show that, for many disorders, IMIs have good impact that is comparable to the respective gold standard of care. In addition, IMIs have the ability to reach groups that may not want to take part in conventional treatment for such reasons as a sense of stigma, the availability of a therapist, health restrictions, or a preference for self-help. Accordingly, within the discussion, it is important to differentiate whether an IMI is meant as supplementary or replacement of treatment. While clarification of the legal aspects still apply to the

former, the mostly economically led discussion of IMIs as a replacement for conventional treatment is seen ethically far more critically.

In terms of quality of IMIs, separate consideration of those offers described in this article- ideally scientifically evaluated self-help programs- and the variety of commercial, non-science-based treatment sites on the Internet must be taken. Total commercialization of the market can be seen as problematic, because the quality of the commercial offers in many cases cannot be guaranteed or is transparent to users. Ethical guidelines featuring high-quality, reputable IMIs are needed in order to protect persons concerned against dubious offers and to provide guidance in selecting effective programs. Mandatory regulations for quality assurance, however, do not exist at present on a European level and only in with regard to some indications in some European countries on a national level, such as the UK and the Netherlands. Recently however, initial attempts are being made to improve this lack of quality assurance by the development of an EU-wide platform for e-mental health innovation and implementation (Interreg North-West Europe, 2016). Although this so-called eMEN program will only be completed by 2019. Conceivably, in the long-term, only IMIs which demonstrate the highest possible patient safety and desired quality of care and that have been shown in randomized clinical trials to be effective would be systematically integrated into health care. Desirably, this would lead to the costs borne by the service providers being taken over by national health care systems as well, as is the case with other medical products.

### *Confidentiality Aspects*

Specific control measures for confidentiality aspects, data protection management and ethical issues are determined by on a national level in Europe law. Examples for relevant regulations on a European level include the following: the EU Good Clinical Practice Directive (2001/20/EC); the charter of fundamental rights of the EU (2000/C 364/01); Directive 95/46/EC (amendment 2003) of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the protection of privacy, storing of personal data and on the free movement of such data; Directive 95/46/EC on the protection of individuals with regard to processing of personal data and on the free movement of such data Council Directive 83/570/EEC amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC dealing with proprietary medicinal products.

Examples for relevant areas of data protection include among others, measures relating to 1) access control; 2) admittance control; 3) disclosure control; 4) input control; 5) commission control; 6) availability check; and 8) separation of data according to purpose. As the former items indicate, the scope of data protection management covers not only the legal field but also relates to aspects of

technology and organization. Examples of these include professional protection (with firewalls implemented as a hardware solution) and the performance of backups on a regular basis. In addition, personal data and communications should always be transmitted and stored in encrypted form; and communication over insecure channels such as email should not be used, as there can be no assurance of the prevention of unauthorized access to the communication history. In order to meet these extensive measures in the development and implementation of IMIs, the consultation of experts in the field of data protection is recommended. However, at the moment there are no clear guidelines on quality criteria with regard to data protection, or data safety across Europe.

### **Implementation in routine care**

While IMIs are established as part of routine care in some European countries, such as the Netherlands, Sweden, Norway and the UK, IMIs are less-widely integrated in the mental health care in most other European countries. In some countries, such as Germany the implementation is restricted by professional legal regulations, such as the forbid to carry out psychotherapy fully online without a personal contact. In other countries IMIs are yet not part of the reimbursement system. Hence IMIs are used so far across Europe mainly within defined pilot projects such as the Mastermind project which aims to implement IMIs for depression in 11 European countries (Vis et al., 2015).

The WHO has among others identified barriers to implementation of IMI's in routine care. First, there is a lack of recognition of technology as an approach to health assessment and treatment. This is reflected in limited or no reimbursement for contact between therapists and patients in the health services. Second there is still limited knowledge about the health effects of IMI's for mental health disorders. Even though there is now an app for most psychological disorders and complaints available in app stores, only a few is tested in randomized controlled trials. This makes health professionals uncertain about benefits and risks related to available IMI's. Hence more effort is needed to transform evidence-based interventions that have been systematically tested in research settings to being routinely available for clinicians. Maybe as a consequence of the first two, there is a lack of prioritization of IMI's for mental health disorders in the health care services. While modern somatic medicine is dependent on advanced technology the field of mental health has not started to prioritize digitalizing mental health services at local, regional, national nor international levels. In countries dominated by a large public health sector, the lack of integration with existing IT systems in the sector, such as EPJ's, are a barrier to the implementation of IMI's. Although there are exceptions, the UK government has recently announced (Hunt, 2017) increases in funding for mental health and one of the key points in the paper was to expand

digital mental health provision with a £68 million investment to support a pilot in online therapy, the development of apps and the provision of advice for medical practitioners. Hundreds of IT-systems co-exists in the health sector, therefore integration with existing systems are often prerequisite for implementing new systems. Taken together, these barriers need to be addressed at an international and national level in order to facilitate the dissemination of evidence-based and secure programs throughout Europe.

## **Conclusion**

IMIs are flexible, technically diverse methods which lend themselves to a variety of application areas and indications of varying degrees of severity. As empirical findings on the impact of human support clearly suggest, IMIs are seen less as a substitute for conventional psychotherapeutic interventions, and should rather be understood more as a useful addition to the treatment spectrum. IMIs have an ability to reach target groups in a way not yet achieved by classical on-site activities, and can also accompany conventional psychotherapy and thereby reduce cost or increase effectiveness.

Initial findings suggest the effectiveness of stand-alone IMI-based therapy in routine conditions, although further research is needed. Unlike for illnesses such as anxiety and depression, though, the evidence base of IMIs for many other disorders is fragmented. Little is known about how blended IMIs concepts and Face-to-Face services can be optimally combined in order to improve the effectiveness of current psychotherapeutic methods. The continued use of IMIs in routine care raises a number of relevant questions; how to maximize the full potential of such approaches, on the one hand, while ensuring patient safety, positive outcomes and certainty of care on part of the leading therapists on the other. An important next step will be to develop standards for data protection and quality control within such approaches, as well as standards to ensure patient safety in crisis situations. Likewise, financing models on national levels that allow both patients and therapists to benefit from IMIs must be developed. Moreover as the potential of such approaches can only be fully exploited if not only patients want them, but also only if therapists use them. Hence there is a need for studies that evaluate how to overcome patients and therapist's common prejudices and negative opinions about the use of technologies in clinical settings.

Once these basic structural questions have been elucidated it will be possible to benefit fully from the vast potential of IMIs for the further improvement of health care systems across Europe.





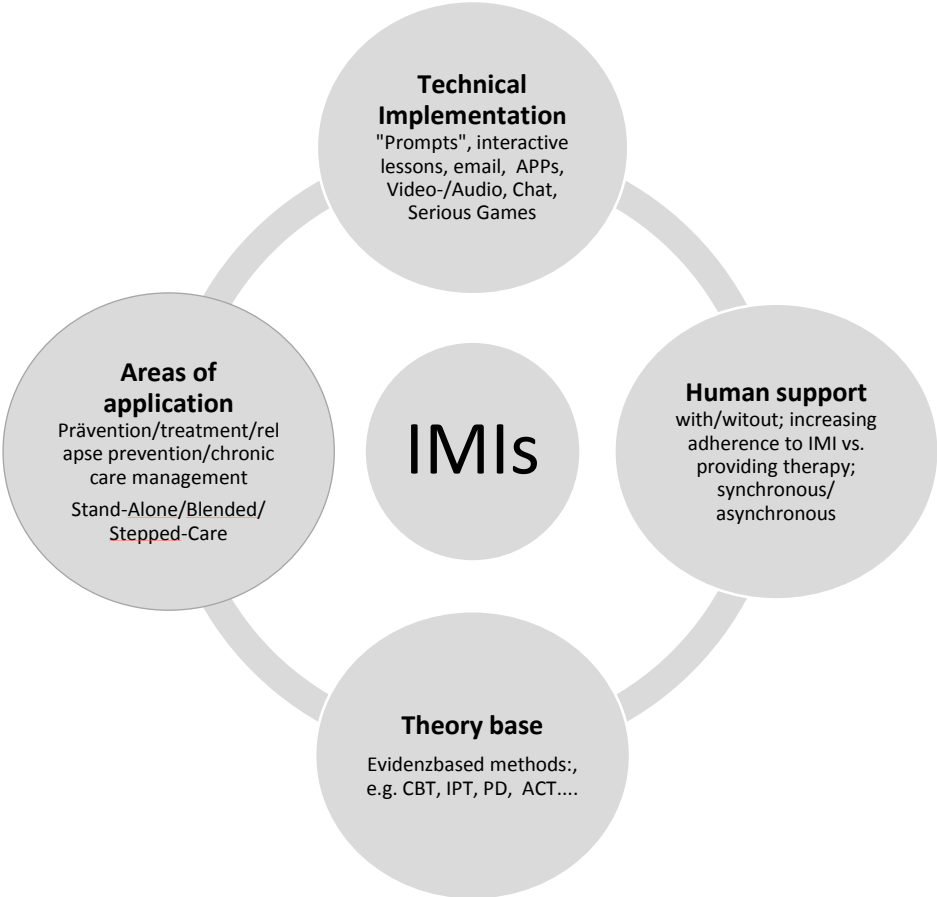
Table 1: Efficacy of IMIs based on meta-analyses

Target population	SMD	[95 % CI]	N	NNT
<b>Adults</b>				
Depressive Disorders (Richards & Richardson, 2012b)	0.56	[0.41,0.71]	19	3.25
Panic Disorders (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010a)	0.83	[0.45,1.21]	6	2.26
Social Phobias (Andrews et al., 2010b)	0.92	[0.74,1.09]	8	2.07
General Anxiety Disorders (Richards et al., 2015)	0.91	[0.56,1.25]	8	2.08
PTSD (Kuester, Niemeyer, & Knaevelsrud, 2016)	0.95	[0.56,1.43]	8	2.01
Insomnia (Zachariae, Lyby, Ritterband, & O'Toole, 2015)	1.09	[0.74,1.45]	8	1.79
Hazardous Alcohol Use (Riper et al., 2014)	0.2	[0.13,0.27]	16	8.93
OCD (own calculations) <sup>1</sup>	0.90	[0.66,1.19]	3	2.10
Eating Disorders (Melioli et al., 2016)	0.30 <sup>2</sup>	[0.02,0.57]	12	5.95
Chronic Pain (Buhrman, Gordh, & Andersson, 2016)	0.42	[0.28,0.55]	15	4.27
Physical Activity (Davies et al., 2012)	0.14-0.37	[0.09,0.10]	34	12.82-4.85
Irritable Bowel Syndrome (Hedman, Ljótsson, & Lindefors, 2012)	1.20	[0.57-1.84]	4	
	<b>MD</b>	<b>[95 % CI]</b>	<b>N</b>	
Weight [mobile only] (Flores Mateo, Granado-Font, Ferré-Grau, & Montaña-Carreras, 2015)	1.04 kg	[1.75,0.03]	12	
	<b>RR</b>	<b>[95 % CI]</b>	<b>N</b>	
Smoking	1.60	[1.15–2.21]	40	
<b>Children &amp; Adolescents</b>				
Depression (Ebert, Zarski, et al., 2015)	0.76	[0.41,1.12]	4	2.44
Anxiety (Ebert, Zarski, et al., 2015)	0.68	[0.45,0.92]	7	2.70

<sup>1</sup> Own calculations (Hedges' g using Comprehensive Meta-Analyses 2.0) based on primary study results of Andersson, Enander, Andrés, et al. (E. Andersson, Enander, Andrés, et al., 2012a) Herbst et al. (Herbst et al., 2014) und (Lenhard et al., 2016). <sup>2</sup> Purging.

SMD = standardized mean difference (Cohens' d / Hedges' g); CI = Confidence Interval; MD = Mean difference; RR = relative risk; N = number of primary studies included in the meta-analysis; NNT = numbers needed to be treated in order to achieve one treatment response. PTSD = Posttraumatic Stress Disorder.

**Figure 1** Central Aspects of Internet- and mobile-based Interventions.



- Aguirre, R. T. P., McCoy, M. K., & Roan, M. (2013). Development Guidelines from a Study of Suicide Prevention Mobile Applications (Apps). *Journal of Technology in Human Services, 31*(3), 269–293. <http://doi.org/10.1080/15228835.2013.814750>
- Andersson, E., Enander, J., Andrén, P., Hedman, E., Ljótsson, B., Hursti, T., ... Rück, C. (2012a). Internet-based cognitive behaviour therapy for obsessive-compulsive disorder: a randomized controlled trial. *Psychological Medicine, 42*(10), 2193–203. <http://doi.org/10.1017/S0033291712000244>
- Andersson, E., Enander, J., Andrén, P., Hedman, E., Ljótsson, B., Hursti, T., ... Rück, C. (2012b). Internet-based cognitive behaviour therapy for obsessive-compulsive disorder: a randomized controlled trial. *Psychological Medicine, 42*(10), 2193–2203. <http://doi.org/10.1017/S0033291712000244>
- Andersson, G., Carlbring, P., Berger, T., Almlöv, J., & Cuijpers, P. (2009). What makes Internet therapy work? *Cognitive Behaviour Therapy, 38 Suppl 1*, 55–60. <http://doi.org/10.1080/16506070902916400>
- Andersson, G., Paxling, B., Roch-Norlund, P., Ostman, G., Norgren, A., Almlöv, J., ... Silverberg, F. (2012). Internet-Based Psychodynamic versus Cognitive Behavioral Guided Self-Help for Generalized Anxiety Disorder: A Randomized Controlled Trial. *Psychotherapy and Psychosomatics, 81*(6), 344–355. <http://doi.org/10.1159/000339371>
- Andersson, G., Paxling, B., Wiwe, M., Vernmark, K., Felix, C. B., Lundborg, L., ... Carlbring, P. (2012). Therapeutic alliance in guided internet-delivered cognitive behavioural treatment of depression, generalized anxiety disorder and social anxiety disorder. *Behaviour Research and Therapy, 50*(9), 544–50. <http://doi.org/10.1016/j.brat.2012.05.003>
- Andersson, G., Topooco, N., Havik, O., & Nordgreen, T. (2016). Internet-supported versus face-to-face cognitive behavior therapy for depression. *Expert Review of Neurotherapeutics, 16*(1), 55–60. <http://doi.org/10.1586/14737175.2015.1125783>
- Andrade, L. H., Alonso, J., Mneimneh, Z., Wells, J. E., Al-Hamzawi, A., Borges, G., ... Kessler, R. C. (2014). Barriers to mental health treatment: results from the WHO World Mental Health surveys. *Psychological Medicine, 44*(6), 1303–17. <http://doi.org/10.1017/S0033291713001943>
- Andrews, G., Cuijpers, P., Craske, M. G., McEvoy, P., & Titov, N. (2010a). Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: a meta-analysis. *PloS One, 5*(10), e13196. <http://doi.org/10.1371/journal.pone.0013196>
- Andrews, G., Cuijpers, P., Craske, M. G., McEvoy, P., & Titov, N. (2010b). Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: a meta-analysis. *PloS One, 5*(10), e13196. <http://doi.org/10.1371/journal.pone.0013196>
- Andrews, G., & Williams, A. D. (2014). INTERNET PSYCHOTHERAPY AND THE FUTURE OF PERSONALIZED TREATMENT. *Depression and Anxiety, 31*(11), 912–915. <http://doi.org/10.1002/da.22302>
- Baumeister, H., Reichler, L., Munzinger, M., & Lin, J. (2014). The impact of guidance on Internet-based mental health interventions — A systematic review. *Internet Interventions, 1*(4), 205–215. <http://doi.org/10.1016/j.invent.2014.08.003>
- Bengtsson, J., Nordin, S., & Carlbring, P. (2015). Therapists' Experiences of Conducting Cognitive Behavioural Therapy Online vis-à-vis Face-to-Face. *Cognitive Behaviour Therapy, 1*–10. <http://doi.org/10.1080/16506073.2015.1053408>
- Berger, T., & Andersson, G. (2009). Internetbasierte Psychotherapien: Besonderheiten und empirische

Evidenz. *PPmP - Psychotherapie · Psychosomatik · Medizinische Psychologie*, 59(03/04), 159–170.  
<http://doi.org/10.1055/s-0028-1090162>

- Berto, P., D'Ilario, D., Ruffo, P., Di Virgilio, R., & Rizzo, F. (2000). Depression: cost-of-illness studies in the international literature, a review. *The Journal of Mental Health Policy and Economics*, 3(1), 3–10.
- Bockting, C. L. H., Kok, G. D., van der Kamp, L., Smit, F., van Valen, E., Schoevers, R., ... Beck, A. T. (2011). Disrupting the rhythm of depression using Mobile Cognitive Therapy for recurrent depression: randomized controlled trial design and protocol. *BMC Psychiatry*, 11, 12.  
<http://doi.org/10.1186/1471-244X-11-12>
- Boettcher, J., Rozentel, A., Andersson, G., & Carlbring, P. (2014). Side effects in Internet-based interventions for Social Anxiety Disorder. *Internet Interventions*, 1(1), 3–11.  
<http://doi.org/10.1016/j.invent.2014.02.002>
- Buhrman, M., Gordh, T., & Andersson, G. (2016). Internet interventions for chronic pain including headache: A systematic review. *Internet Interventions*, 4, 17–34.  
<http://doi.org/10.1016/j.invent.2015.12.001>
- Buntrock, C., Ebert, D. D., Lehr, D., Cuijpers, P., Riper, H., Smit, F., & Berking, M. (2014). Evaluating the efficacy and cost-effectiveness of web-based indicated prevention of major depression: design of a randomised controlled trial. *BMC Psychiatry*, 14, 25. <http://doi.org/10.1186/1471-244X-14-25>
- Clement, S., Schauman, O., Graham, T., Maggioni, F., Evans-Lacko, S., Bezborodovs, N., ... Thornicroft, G. (2015). What is the impact of mental health-related stigma on help-seeking? A systematic review of quantitative and qualitative studies. *Psychological Medicine*, 45(1), 11–27.  
<http://doi.org/10.1017/S0033291714000129>
- Cook, J. E., & Doyle, C. (2002). Working alliance in online therapy as compared to face-to-face therapy: preliminary results. *Cyberpsychology & Behavior : The Impact of the Internet, Multimedia and Virtual Reality on Behavior and Society*, 5(2), 95–105.
- Cuijpers, P., & Smit, F. (2002). Excess mortality in depression: a meta-analysis of community studies. *Journal of Affective Disorders*, 72(3), 227–36.
- Cuijpers, P., van Straten, A., Andersson, G., & van Oppen, P. (2008). Psychotherapy for depression in adults: a meta-analysis of comparative outcome studies. *Journal of Consulting and Clinical Psychology*, 76(6), 909–22. <http://doi.org/10.1037/a0013075>
- Davies, C. A., Spence, J. C., Vandelanotte, C., Caperchione, C. M., Mummery, W., Norman, G., ... Bauman, A. (2012). Meta-analysis of internet-delivered interventions to increase physical activity levels. *International Journal of Behavioral Nutrition and Physical Activity*, 9(1), 52.  
<http://doi.org/10.1186/1479-5868-9-52>
- Donker, T., Batterham, P. J., Warmerdam, L., Bennett, K., Bennett, A., Cuijpers, P., ... Christensen, H. (2013). Predictors and moderators of response to internet-delivered Interpersonal Psychotherapy and Cognitive Behavior Therapy for depression. *Journal of Affective Disorders*, 151(1), 343–351.
- Ebert, D. D., Berking, M., Cuijpers, P., Lehr, D., Pörtner, M., & Baumeister, H. (2015). Increasing the acceptance of internet-based mental health interventions in primary care patients with depressive symptoms. A randomized controlled trial. *Journal of Affective Disorders*.  
<http://doi.org/10.1016/j.jad.2015.01.056>
- Ebert, D. D., Buntrock, C., Cuijpers, P., K, van Z., P, C., C, B., ... H, B. (2016). Online Intervention for

Prevention of Major Depression —Reply. *JAMA*, 316(8), 881.  
<http://doi.org/10.1001/jama.2016.9586>

- Ebert, D. D., Donkin, L., Andersson, G., Andrews, G., Berger, T., Carlbring, P., ... Cuijpers, P. (2016). Does Internet-based guided-self-help for depression cause harm? An individual participant data meta-analysis on deterioration rates and its moderators in randomized controlled trials. *Psychological Medicine*, 46(13), 2679–93. <http://doi.org/10.1017/S0033291716001562>
- Ebert, D. D., Gollwitzer, M., Riper, H., Cuijpers, P., Baumeister, H., & Berking, M. (2013). For whom does it work? moderators of outcome on the effect of a transdiagnostic internet-based maintenance treatment after inpatient psychotherapy: randomized controlled trial. *Journal of Medical Internet Research*, 15(10), e191. <http://doi.org/10.2196/jmir.2511>
- Ebert, D. D., Hannig, W., Tarnowski, T., Sieland, B., Götzky, B., & Berking, M. (2013). Web-based rehabilitation aftercare following inpatient psychosomatic treatment. *Die Rehabilitation*, 52(3), 164–72. <http://doi.org/10.1055/s-0033-1345191>
- Ebert, D. D., Lehr, D., Baumeister, H., Boß, L., Riper, H., Cuijpers, P., ... Berking, M. (2014). GET.ON Mood Enhancer: efficacy of Internet-based guided self-help compared to psychoeducation for depression: an investigator-blinded randomised controlled trial. *Trials*, 15(1), 39. <http://doi.org/10.1186/1745-6215-15-39>
- Ebert, D. D., Lehr, D., Smit, F., Zarski, A.-C., Riper, H., Heber, E., ... Berking, M. (2014). Efficacy and cost-effectiveness of minimal guided and unguided internet-based mobile supported stress-management in employees with occupational stress: a three-armed randomised controlled trial. *BMC Public Health*, 14, 807. <http://doi.org/10.1186/1471-2458-14-807>
- Ebert, D. D., Nobis, S., Lehr, D., Baumeister, H., Riper, H. M., Auerbach, R. P., ... Berking, M. (2016). The 6-month effectiveness of Internet-based guided self-help for depression in adults with Type 1 and 2 diabetes mellitus. *Diabetic Medicine*. <http://doi.org/10.1111/dme.13173>
- Ebert, D. D., Tarnowski, T., Gollwitzer, M., Sieland, B., & Berking, M. (2013). A transdiagnostic internet-based maintenance treatment enhances the stability of outcome after inpatient cognitive behavioral therapy: a randomized controlled trial. *Psychotherapy and Psychosomatics*, 82(4), 246–56. <http://doi.org/10.1159/000345967>
- Ebert, D. D., Zarski, A.-C., Christensen, H., Stikkelbroek, Y., Cuijpers, P., Berking, M., & Riper, H. (2015). Internet and computer-based cognitive behavioral therapy for anxiety and depression in youth: a meta-analysis of randomized controlled outcome trials. *PloS One*, 10(3), e0119895. <http://doi.org/10.1371/journal.pone.0119895>
- El Alaoui, S., Hedman, E., Kaldo, V., Hesser, H., Kraepelien, M., Andersson, E., ... Lindefors, N. (2015). Effectiveness of Internet-based cognitive-behavior therapy for social anxiety disorder in clinical psychiatry. *Journal of Consulting and Clinical Psychology*, 83(5), 902–14. <http://doi.org/10.1037/a0039198>
- El Alaoui, S., Hedman, E., Ljótsson, B., & Lindefors, N. (2015). Long-term effectiveness and outcome predictors of therapist-guided internet-based cognitive-behavioural therapy for social anxiety disorder in routine psychiatric care. *BMJ Open*, 5(6), e007902. <http://doi.org/10.1136/bmjopen-2015-007902>
- Enander, J., Andersson, E., Mataix-Cols, D., Lichtenstein, L., Alström, K., Andersson, G., ... Rück, C. (2016). Therapist guided internet based cognitive behavioural therapy for body dysmorphic disorder: single

blind randomised controlled trial. *BMJ*, 352.

- Essau, C. A. (2005). Frequency and patterns of mental health services utilization among adolescents with anxiety and depressive disorders. *Depression and Anxiety*, 22(3), 130–7. <http://doi.org/10.1002/da.20115>
- Flores Mateo, G., Granado-Font, E., Ferré-Grau, C., & Montaña-Carreras, X. (2015). Mobile Phone Apps to Promote Weight Loss and Increase Physical Activity: A Systematic Review and Meta-Analysis. *Journal of Medical Internet Research*, 17(11), e253. <http://doi.org/10.2196/jmir.4836>
- Garcia-Palacios, A., Hoffman, H., Carlin, A., Furness, T. A., & Botella, C. (2002). Virtual reality in the treatment of spider phobia: a controlled study. *Behaviour Research and Therapy*, 40(9), 983–93.
- Golkaramnay, V., Bauer, S., Haug, S., Wolf, M., & Kordy, H. (2007). The exploration of the effectiveness of group therapy through an Internet chat as aftercare: a controlled naturalistic study. *Psychotherapy and Psychosomatics*, 76(4), 219–25. <http://doi.org/10.1159/000101500>
- Gottlieb, J. D., Romeo, K. H., Penn, D. L., Mueser, K. T., Chiko, B. P., Anonymous, ... Everitt, B. (2013). Web-based cognitive-behavioral therapy for auditory hallucinations in persons with psychosis: a pilot study. *Schizophrenia Research*, 145(1–3), 82–7. <http://doi.org/10.1016/j.schres.2013.01.002>
- Greenberg, P. E., & Birnbaum, H. G. (2005). The economic burden of depression in the US: societal and patient perspectives. *Expert Opinion on Pharmacotherapy*, 6(3), 369–76. <http://doi.org/10.1517/14656566.6.3.369>
- Harper, K. M. (2013). *An Investigation of an Internet-based cognitive behavioral Therapy Program for auditory hallucinations*. University of North Carolina at Chapel Hill.
- Hedman, E., Ljótsson, B., Kaldø, V., Hesser, H., El Alaoui, S., Kraepelien, M., ... Lindefors, N. (2014). Effectiveness of Internet-based cognitive behaviour therapy for depression in routine psychiatric care. *Journal of Affective Disorders*, 155, 49–58. <http://doi.org/10.1016/j.jad.2013.10.023>
- Hedman, E., Ljótsson, B., & Lindefors, N. (2012). Cognitive behavior therapy via the Internet: a systematic review of applications, clinical efficacy and cost-effectiveness. *Expert Review of Pharmacoeconomics & Outcomes Research*, 12(6), 745–64. <http://doi.org/10.1586/erp.12.67>
- Henderson, C., Evans-Lacko, S., & Thornicroft, G. (2013). Mental illness stigma, help seeking, and public health programs. *American Journal of Public Health*, 103(5), 777–80. <http://doi.org/10.2105/AJPH.2012.301056>
- Herbst, N., Voderholzer, U., Thiel, N., Schaub, R., Knaevelsrud, C., Stracke, S., ... Külz, A. K. (2014). No talking, just writing! Efficacy of an Internet-based cognitive behavioral therapy with exposure and response prevention in obsessive compulsive disorder. *Psychotherapy and Psychosomatics*, 83(3), 165–75. <http://doi.org/10.1159/000357570>
- Hidalgo-Mazzei, D., Mateu, A., Reinares, M., Matic, A., Vieta, E., & Colom, F. (2015). Internet-based psychological interventions for bipolar disorder: Review of the present and insights into the future. *Journal of Affective Disorders*, 188, 1–13. <http://doi.org/10.1016/j.jad.2015.08.005>
- Hofmann, S. G., & Smits, J. A. J. (2008). Cognitive-behavioral therapy for adult anxiety disorders: a meta-analysis of randomized placebo-controlled trials. *The Journal of Clinical Psychiatry*, 69(4), 621–32.

- Hunt, J. (2017). Mental Health: Written statement HCWS397 to UK Parliament 9<sup>th</sup> January 2017. Accessed on 9/1/17 from <http://www.parliament.uk/business/publications/written-questions-answers-statements/written-statement/Commons/2017-01-09/HCWS397/>
- Johansson, R., & Andersson, G. (2012). Internet-based psychological treatments for depression. *Expert Review of Neurotherapeutics*, 12(7), 861–9; quiz 870. <http://doi.org/10.1586/ern.12.63>
- Johansson, R., Hesser, H., Ljótsson, B., Frederick, R. J., & Andersson, G. (2012). Transdiagnostic, affect-focused, psychodynamic, guided self-help for depression and anxiety through the internet: study protocol for a randomised controlled trial. *BMJ Open*, 2(6). <http://doi.org/10.1136/bmjopen-2012-002167>
- Jones, M., Ebert, D. D., Berger, T., Botella, C., Riper, H. ., & Consortium, I.-C. (2015). Why didn't patients use it? Engagement is the real story in Gilbody et al. (2015), not effectiveness. *BMJ, Response t*.
- Kenwright, M., Liness, S., & Marks, I. (2001). Reducing demands on clinicians by offering computer-aided self-help for phobia/panic. Feasibility study. *The British Journal of Psychiatry : The Journal of Mental Science*, 179, 456–9.
- Kessler, D., Lewis, G., Kaur, S., Wiles, N., King, M., Weich, S., ... Peters, T. J. (2009). Therapist-delivered internet psychotherapy for depression in primary care: a randomised controlled trial. *The Lancet*, 374(9690), 628–634.
- Kessler, R. C., Aguilar-Gaxiola, S., Alonso, J., Chatterji, S., Lee, S., Ormel, J., ... Wang, P. S. (2009). The global burden of mental disorders: an update from the WHO World Mental Health (WMH) surveys. *Epidemiologia E Psichiatria Sociale*, 18(1), 23–33.
- Kleiboer, A., Smit, J., Bosmans, J., Ruwaard, J., Andersson, G., Topooco, N., ... Moher, D. (2016). European COMPARative Effectiveness research on blended Depression treatment versus treatment-as-usual (E-COMPARED): study protocol for a randomized controlled, non-inferiority trial in eight European countries. *Trials*, 17(1), 387. <http://doi.org/10.1186/s13063-016-1511-1>
- Klein, J. P., & Berger, T. (2013). Internetbasierte psychologische Behandlung bei Depressionen. *Verhaltenstherapie*, 23(3), 149–159. <http://doi.org/10.1159/000354046>
- Knaevelsrud, C., & Maercker, A. (2006). Does the quality of the working alliance predict treatment outcome in online psychotherapy for traumatized patients? *Journal of Medical Internet Research*, 8(4), e31. <http://doi.org/10.2196/jmir.8.4.e31>
- Kohn, R., Saxena, S., Levav, I., & Saraceno, B. (2004). The treatment gap in mental health care. *Bulletin of the World Health Organization*, 82(11), 858–66. <http://doi.org/S0042-96862004001100011>
- Kok, G., Bockting, C., Burger, H., Smit, F., & Riper, H. (2014). Mobile Cognitive Therapy: Adherence and acceptability of an online intervention in remitted recurrently depressed patients. *Internet Interventions*, 1(2), 65–73. <http://doi.org/10.1016/j.invent.2014.05.002>
- Kooistra, L. C., Wiersma, J. E., Ruwaard, J., van Oppen, P., Smit, F., Lokkerbol, J., ... Riper, H. (2014). Blended vs. face-to-face cognitive behavioural treatment for major depression in specialized mental health care: study protocol of a randomized controlled cost-effectiveness trial. *BMC Psychiatry*, 14(1), 290. <http://doi.org/10.1186/s12888-014-0290-z>
- Kuester, A., Niemeyer, H., & Knaevelsrud, C. (2016). Internet-based interventions for posttraumatic stress: A meta-analysis of randomized controlled trials. *Clinical Psychology Review*, 43, 1–16. <http://doi.org/10.1016/j.cpr.2015.11.004>



- Lenhard, F., Andersson, E., Mataix-Cols, D., Rück, C., Vigerland, S., Högström, J., ... Serlachius, E. (2016). Therapist-Guided, Internet-Delivered Cognitive-Behavioral Therapy for Adolescents With Obsessive-Compulsive Disorder: A Randomized Controlled Trial. *Journal of the American Academy of Child & Adolescent Psychiatry*. <http://doi.org/10.1016/j.jaac.2016.09.515>
- Lenhard, F., Andersson, E., Mataix-Cols, D., Rück, C., Vigerland, S., Högström, J., ... Serlachius, E. (2017). Therapist-Guided, Internet-Delivered Cognitive-Behavioral Therapy for Adolescents With Obsessive-Compulsive Disorder: A Randomized Controlled Trial. *Journal of the American Academy of Child & Adolescent Psychiatry*, 56(1), 10–19.e2. <http://doi.org/10.1016/j.jaac.2016.09.515>
- Lin, J., Ebert, D. D., Lehr, D., Berking, M., & Baumeister, H. (2013). [Internet based cognitive behavioral interventions: state of the art and implementation possibilities in rehabilitation]. *Die Rehabilitation*, 52(3), 155–63. <http://doi.org/10.1055/s-0033-1343491>
- Lin, J., Lüking, M., Ebert, D. D., Buhrman, M., Andersson, G., & Baumeister, H. (2015). Effectiveness and cost-effectiveness of a guided and unguided internet-based acceptance and commitment therapy for chronic pain: Study protocol for a three-armed randomised controlled trial. *Internet Interventions*, 2(1). <http://doi.org/10.1016/j.invent.2014.11.005>
- Lin, J., Sander, L., Paganini, S., Schlicker, S., Mittag, O., Berking, M., ... Baumeister, H. (n.d.). Effectiveness and cost-effectiveness of a guided internet- and mobile-based depression intervention for individuals with chronic back pain: protocol of a multi-centre randomised controlled trial. in progress.
- Lindhiem, O., Bennett, C. B., Rosen, D., & Silk, J. (2015). Mobile Technology Boosts the Effectiveness of Psychotherapy and Behavioral Interventions: A Meta-Analysis. *Behavior Modification*, 39(6), 785–804. <http://doi.org/10.1177/0145445515595198>
- Littlewood, E., Duarte, A., Hewitt, C., Knowles, S., Palmer, S., Walker, S., ... Gilbody, S. (2015). A randomised controlled trial of computerised cognitive behaviour therapy for the treatment of depression in primary care: the Randomised Evaluation of the Effectiveness and Acceptability of Computerised Therapy (REEACT) trial. *Health Technology Assessment (Winchester, England)*, 19(101), 1–174. <http://doi.org/10.3310/hta191010>
- Luquiens, A., Tanguy, M.-L., Lagadec, M., Benyamina, A., Aubin, H.-J., & Reynaud, M. (2016). The Efficacy of Three Modalities of Internet-Based Psychotherapy for Non-Treatment-Seeking Online Problem Gamblers: A Randomized Controlled Trial. *Journal of Medical Internet Research*, 18(2), e36. <http://doi.org/10.2196/jmir.4752>
- Luxton, D. D. (2016). *Artificial intelligence in behavioral and mental health care*. (Luxton D, Ed.). Elsevier.
- Mack, S., Jacobi, F., Gerschler, A., Strehle, J., Höfler, M., Busch, M. A., ... Wittchen, H.-U. (2014). Self-reported utilization of mental health services in the adult German population - evidence for unmet needs? Results of the DEGS1-Mental Health Module (DEGS1-MH). *International Journal of Methods in Psychiatric Research*. <http://doi.org/10.1002/mpr.1438>
- Mak, W. W. S., Chan, A. T. Y., Cheung, E. Y. L., Lin, C. L. Y., & Ngai, K. C. S. (2015). Enhancing Web-based mindfulness training for mental health promotion with the health action process approach: randomized controlled trial. *Journal of Medical Internet Research*, 17(1), e8. <http://doi.org/10.2196/jmir.3746>
- Marks, I. M., Kenwright, M., McDonough, M., Whittaker, M., & Mataix-Cols, D. (2004). *Saving clinicians' time by delegating routine aspects of therapy to a computer: a randomized controlled trial in*

*phobia/panic disorder. Psychological Medicine* (Vol. 34). Cambridge Univ Press.

- Mayo-Wilson, E., & Montgomery, P. (2013). Media-delivered cognitive behavioural therapy and behavioural therapy (self-help) for anxiety disorders in adults. *The Cochrane Database of Systematic Reviews*, 9, CD005330. <http://doi.org/10.1002/14651858.CD005330.pub4>
- Melioli, T., Bauer, S., Franko, D. L., Moessner, M., Ozer, F., Chabrol, H., & Rodgers, R. F. (2016). Reducing eating disorder symptoms and risk factors using the internet: A meta-analytic review. *International Journal of Eating Disorders*, 49(1), 19–31. <http://doi.org/10.1002/eat.22477>
- Merry, S. N., Stasiak, K., Shepherd, M., Frampton, C., Fleming, T., & Lucassen, M. F. G. (2012). The effectiveness of SPARX, a computerised self help intervention for adolescents seeking help for depression: randomised controlled non-inferiority trial. *BMJ (Clinical Research Ed.)*, 344, e2598.
- Nobis, S., Lehr, D., Ebert, D. D., Baumeister, H., Snoek, F., Riper, H., & Berking, M. (2015). Efficacy of a Web-Based Intervention With Mobile Phone Support in Treating Depressive Symptoms in Adults With Type 1 and Type 2 Diabetes: A Randomized Controlled Trial. *Diabetes Care*. <http://doi.org/10.2337/dc14-1728>
- Olthuis, J. V., Watt, M. C., Bailey, K., Hayden, J. A., & Stewart, S. H. (2015). Therapist-supported Internet cognitive behavioural therapy for anxiety disorders in adults. *The Cochrane Database of Systematic Reviews*, 3, CD011565. <http://doi.org/10.1002/14651858.CD011565>
- Palmqvist, B., Carlbring, P., & Andersson, G. (2007). Internet-delivered treatments with or without therapist input: does the therapist factor have implications for efficacy and cost? *Expert Review of Pharmacoeconomics & Outcomes Research*, 7(3), 291–7. <http://doi.org/10.1586/14737167.7.3.291>
- Preschl, B., Maercker, A., & Wagner, B. (2011). The working alliance in a randomized controlled trial comparing online with face-to-face cognitive-behavioral therapy for depression. *BMC Psychiatry*, 11(1), 189. <http://doi.org/10.1186/1471-244X-11-189>
- Richards, D., & Richardson, T. (2012a). Computer-based psychological treatments for depression: a systematic review and meta-analysis. *Clinical Psychology Review*, 32(4), 329–42. <http://doi.org/10.1016/j.cpr.2012.02.004>
- Richards, D., & Richardson, T. (2012b). Computer-based psychological treatments for depression: a systematic review and meta-analysis. *Clinical Psychology Review*, 32(4), 329–42. <http://doi.org/10.1016/j.cpr.2012.02.004>
- Richards, D., Richardson, T., Timulak, L., & McElvaney, J. (2015). The efficacy of internet-delivered treatment for generalized anxiety disorder: A systematic review and meta-analysis. *Internet Interventions*, 2(3), 272–282. <http://doi.org/10.1016/j.invent.2015.07.003>
- Riper, H., Blankers, M., Hadiwijaya, H., Cunningham, J., Clarke, S., Wiers, R., ... Cuijpers, P. (2014). Effectiveness of Guided and Unguided Low-Intensity Internet Interventions for Adult Alcohol Misuse: A Meta-Analysis. *PloS One*, 9(6), e99912. <http://doi.org/10.1371/journal.pone.0099912>
- Romijn, G., Riper, H., Kok, R., Donker, T., Goorden, M., Roijen, L. H. Van, ... Koning, J. (2015). Cost-effectiveness of blended vs . face-to- face cognitive behavioural therapy for severe anxiety disorders : study protocol of a randomized controlled trial. *BMC Psychiatry*, 1–10. <http://doi.org/10.1186/s12888-015-0697-1>
- Rozental, A., Andersson, G., Boettcher, J., Ebert, D. D., Cuijpers, P., Knaevelsrud, C., ... Carlbring, P. (2014). Consensus statement on defining and measuring negative effects of Internet interventions.

*Internet Interventions*, 1(1), 12–19. <http://doi.org/10.1016/j.invent.2014.02.001>

- Rozental, A., Boettcher, J., Andersson, G., Schmidt, B., & Carlbring, P. (2015). Negative effects of internet interventions: a qualitative content analysis of patients' experiences with treatments delivered online. *Cognitive Behaviour Therapy*, 44(3), 223–36. <http://doi.org/10.1080/16506073.2015.1008033>
- Saarni, S. I., Suvisaari, J., Sintonen, H., Pirkola, S., Koskinen, S., Aromaa, A., & Lönnqvist, J. (2007). Impact of psychiatric disorders on health-related quality of life: general population survey. *The British Journal of Psychiatry : The Journal of Mental Science*, 190, 326–32. <http://doi.org/10.1192/bjp.bp.106.025106>
- Smit, F., Cuijpers, P., Oostenbrink, J., Batelaan, N., de Graaf, R., & Beekman, A. (2006). Costs of nine common mental disorders: implications for curative and preventive psychiatry. *The Journal of Mental Health Policy and Economics*, 9(4), 193–200.
- Storch, E. A., Caporino, N. E., Morgan, J. R., Lewin, A. B., Rojas, A., Brauer, L., ... Murphy, T. K. (2011). Preliminary investigation of web-camera delivered cognitive-behavioral therapy for youth with obsessive-compulsive disorder. *Psychiatry Research*, 189(3), 407–12. <http://doi.org/10.1016/j.psychres.2011.05.047>
- Ustün, T. B., Ayuso-Mateos, J. L., Chatterji, S., Mathers, C., & Murray, C. J. L. (2004). Global burden of depressive disorders in the year 2000. *The British Journal of Psychiatry : The Journal of Mental Science*, 184, 386–92.
- Van Daele, T., & Vanhoomissen, T. (2015). Portable technology in mental healthcare. *De Psycholoog*, 34–39.
- Vis, C., Kleiboer, A., Prior, R., Bønes, E., Cavallo, M., Clark, S. A., ... Riper, H. (2015). Implementing and up-scaling evidence-based eMental health in Europe: The study protocol for the MasterMind project. *Internet Interventions*, 2(4). <http://doi.org/10.1016/j.invent.2015.10.002>
- Whiteford, H. a., Degenhardt, L., Rehm, J., Baxter, A. J., Ferrari, A. J., Erskine, H. E., ... Vos, T. (2013). Global burden of disease attributable to mental and substance use disorders: Findings from the Global Burden of Disease Study 2010. *The Lancet*, 382, 1575–1586. [http://doi.org/10.1016/S0140-6736\(13\)61611-6](http://doi.org/10.1016/S0140-6736(13)61611-6)
- Williams, A. D., O'Moore, K., Mason, E., & Andrews, G. (2014). The effectiveness of internet cognitive behaviour therapy (iCBT) for social anxiety disorder across two routine practice pathways. *Internet Interventions*, 1(4), 225–229. <http://doi.org/10.1016/j.invent.2014.11.001>
- Wittchen, H.-U., Jacobi, F., Rehm, J., Gustavsson, A., Svensson, M., Jönsson, B., ... Steinhausen, H.-C. (2011). The size and burden of mental disorders and other disorders of the brain in Europe 2010. *European Neuropsychopharmacology : The Journal of the European College of Neuropsychopharmacology*, 21(9), 655–79. <http://doi.org/10.1016/j.euroneuro.2011.07.018>
- Wright, J. H., Wright, A. S., Albano, A. M., Basco, M. R., Goldsmith, L. J., Raffield, T., & Otto, M. W. (2005). Computer-assisted cognitive therapy for depression: maintaining efficacy while reducing therapist time. *The American Journal of Psychiatry*, 162(6), 1158–64. <http://doi.org/10.1176/appi.ajp.162.6.1158>
- Zachariae, R., Lyby, M. S., Ritterband, L., & O'Toole, M. S. (2015). Efficacy of Internet-delivered cognitive-behavioral therapy for insomnia – a systematic review and meta-analysis of randomized controlled trials. *Sleep Medicine Reviews*, 30, 1–10. <http://doi.org/10.1016/j.smr.2015.10.004>

Zachrisson, H. D., Rödje, K., & Mykletun, A. (2006). Utilization of health services in relation to mental health problems in adolescents: a population based survey. *BMC Public Health*, 6, 34.  
<http://doi.org/10.1186/1471-2458-6-34>

Zarski, A.-C., Lehr, D., Berking, M., Riper, H., Cuijpers, P., & Ebert, D. D. (2016). Adherence to Internet-Based Mobile-Supported Stress Management: A Pooled Analysis of Individual Participant Data From Three Randomized Controlled Trials. *Journal of Medical Internet Research*, 18(6), e146.  
<http://doi.org/10.2196/jmir.4493>