CHAPTER 8

General discussion
Introduction

Depressive and anxiety disorders annually affect 700 million people worldwide [1, 2]. Their impact on patients’ life is enormous as depression and anxiety are associated with serious functional impairments in the educational, social and occupational domains, together with losses in quality of life, high economic costs and high levels of service use [3].

When patients seek treatment at outpatient clinics they are often confronted with long waiting lists. Mental health clinics recognize this problem and because of the increasing number of patients seeking help, several initiatives are undertaken to use the Internet to deliver interventions to improve the accessibility and efficiency of treatments, not in the last place as an effort to contain the costs of mental health care. One such initiative is offering Internet-based PST during the waiting list in regular outpatient mental health clinics. The idea is that patients can be treated faster with Internet treatments, which will reduce indirect costs caused by absenteeism and presenteeism, as patients can get immediate access to treatment, and that less expensive Internet treatment will partly replace expensive face-to-face sessions.

Another initiative that is becoming increasingly popular in the Netherlands is to combine Internet treatments with face-to-face consultations, rather than to offer Internet treatments on its own. This method, blended care, implies that part of the treatment is delivered face-to-face at the clinic, while other parts are delivered through online treatment sessions. The idea is that blended care maximizes outcomes as patients can do part of their treatment online at home where they have unlimited access to records of communication with the clinician, treatment materials and exercises, while in the face-to-face sessions the clinicians can respond to the more complex problems of the patient in real time, have the opportunity to detect misunderstandings and ruptures in therapeutic contact, and can observe the patient in the consulting room. The idea behind blended care is that it combines the best of both treatment delivery systems, while being less disruptive to the organization of care, compared to stand-alone internet treatments.

Despite of the proposed advantages of Internet treatments and studies that have shown that Internet-based guided interventions have comparable effect sizes to face-to-face treatments [4-7], it is still not a very commonly used mode of treatment delivery in regular mental health clinics and the (cost-)effectiveness in regular outpatient clinics has not been studied extensively. Clinical effectiveness and cost-effectiveness are important when evaluating whether a new technology should be implemented into routine clinical practice.

This thesis aimed to extend upon the existing literature on Internet-based interventions and to examine the effects and costs of Internet-based treatments in outpatient clinics. In this
final chapter the main findings of the studies are discussed, considering methodological limitations that need to be taken into account when interpreting the findings and recommendation for future research are given.

**General discussion**

The main focus of this thesis was on Internet interventions in regular mental health care. From previous studies we know that Internet interventions can be effective in reducing symptoms of depression and anxiety and there is even evidence that guided Internet-delivered CBT can be as effective as face-to-face CBT [9, 12, 13]. Direct comparisons between guided iCBT and face-to-face CBT show that guided iCBT produces similar overall effects [10,14]. However, the question remains whether Internet-delivered treatments can be effectively disseminated and implemented into regular mental health clinics, and whether the results found in previous Internet trials generalize to clinical populations in regular outpatient care.

Research trials often have different procedures of participant recruitment and also different selection, supervision and training of therapists compared to actual clinical practice [15]. Self-reference to Internet trials and particularly the use of subclinical samples differs from actual patients diagnosed with a DSM disorder, seeking treatment in regular outpatient clinics. A common finding in Internet trials is that the study participants are higher educated than the participants from the general population [16]. These observations raise uncertainty with regard to the effects of Internet interventions on more diverse and/or complex populations as seen in regular outpatient clinics. Also, a large part of the current body of evidence on Internet interventions is based on the examination of subclinical samples who were either randomized to an Internet intervention or a pure waitlist condition. That study design might not necessarily be similar to routine clinical practice. This thesis examined outcomes from the use of Internet-based treatments as part of routine mental healthcare. We reported on the results of Internet-based PST as a first step of treatment in routine mental healthcare in chapter 2, 4 and 5, and the results of blended treatment chapter 6.

The first question this thesis addressed was whether the Internet-based PST intervention was acceptable for patients in outpatient care. We distinguished three aspects of acceptability, 1) treatment preference, 2) treatment adherence and 3) treatment satisfaction.

With regard to treatment preference, 53% of all eligible patients in the observational study in chapter 2 preferred to start with Internet treatment over waiting for face-to-face treatment, which was the usual care. Reasons for not starting with Internet treatment were: the
fear that personal information was not safe on the Internet, the wish of talking to a therapist instead of a computer and the lack of computer skills. At the time the study was executed (2011), Internet treatment was not well known to patients and clinicians. However, still more than half of all participants did prefer to start with Internet treatment, we see this as an promising fact. If only a small proportion of patients prefers Internet treatment, this could already take the pressure of the healthcare system.

With regard to adherence, the rates of adherence to the Internet PST intervention can be interpreted as a cause of concern for the acceptability of Internet treatment in outpatient care. In both studies in outpatient clinics (chapter 2 and chapter 4) the adherence rates are far lower than rates found in previous research trials of the same Internet intervention with subclinical samples from the general population. In these previous trials, which examined self-referred participants from the community, 55.7% [17] and 65% [18] completed ≥3 sessions and 37.5% [17] and 55% [18] completed the entire intervention. These rates are much higher than the adherence rates in our randomized controlled trial in outpatients clinics (chapter 4) (34.6% completed ≥3 sessions and 12.5% the entire intervention). The adherence rates in our trial also compare poorly to those in other Internet-delivered CBT trials in the routine care [19, 20], which could indicate that this particular Internet-delivered PST intervention doesn’t meet the needs of all depressed patients in outpatient clinics. When outpatients were offered the choice of starting with Internet-based PST (chapter 2), the adherence rates are somewhat higher (65.5% completed 3 or more sessions, and 18.2% the entire intervention). This might indicate that the outpatients choosing to start with Internet treatment could have been more motivated, had a more positive attitude towards Internet treatment and/or found the treatment more credible as they actively chose this treatment option over care as usual. In all, the low adherence to the Internet intervention is a cause of concern and should be improved before further use of this intervention in outpatient care.

Adherence can be boosted by improved design of the Internet treatment (e.g. usability, interface) and the tailoring of interventions to the needs of the patient. The Internet-based PST intervention was very limited in personalization and interactivity, and the user interface did not live up to today’s technology and website design. Also, the pace of completing one session a week may have been too rapid and patients needed more time to complete sessions.

Another explanation for the low adherence may be found in the symptoms of the study sample. The patients might have been too severely ill to work largely independent on the Internet intervention. Depression is associated with low levels of energy and difficulties in concentration and might have caused reasons for discontinuation.
With regard to treatment satisfaction, in the RCT in chapter 4 the post-test completers were in all moderately satisfied with the intervention. Participants were mostly satisfied with the quality of the feedback, and half of the intervention group participants thought the intervention was useful to them.

In all, these three aspects of acceptability indicate that patients are open to the idea of being treated over the Internet, but also indicate that the Internet-based PST intervention was not very engaging. If this intervention was to be further used, we recommend adjusting it to today’s technology standards, with possibilities for interaction, a user friendly interface and tailored treatment, in order to increase adherence and treatment satisfaction.

The second question this thesis examined was whether Internet-based PST in outpatient clinics was effective. The RCT in this thesis (chapter 4) compared starting with Internet-based PST in outpatient clinics against an active control group that received a self-help booklet during the waiting list for face-to-face treatment. Both groups improved substantially, demonstrating high within-group effect sizes from pre- to post-test. However the between group effect sizes were small and the adherence rates low. Internet-delivered PST was not more effective than an active control condition for depressed outpatients. This result is not in line with other research. Since the start of the studies in this thesis, more research has been done in regular care for example in the Internet psychiatry unit in Sweden [20] and in primary care settings in Norway [21]. These studies show that the effect sizes for guided Internet treatment are equivalent to those found in previous Internet trails [8, 9]. The difference in result might be explained by several factors. One explanation relates to the difference in treatment model. Even though the most common psychological face-to-face therapies show very little or no differences in effect [22], this might be different for Internet-delivered treatments. Most Internet trials have examined iCBT interventions. These interventions differ from our PST intervention in terms of content and duration (8-15 weeks for iCBT versus 5 weeks for PST). Perhaps the duration of our Internet-based PST too short to achieve substantial changes in symptoms of depression.

Another explanation relates to the way our intervention was offered to patients, which differed substantially from other Internet trials. In the Swedish clinic participants received a face-to-face diagnostic assessment before the start of treatment, the Internet treatment was guided by licensed psychologists and the treatment was offered as a standalone Internet treatment, not to be followed up by face-to-face sessions [20]. In our studies in chapter 2 and chapter 4 a face-to-face appointment was already scheduled at the clinics, which might have diminished adherence to the intervention. In both the study in chapter 2 as chapter 4 the
Internet treatment was administered by staff from the university, not the professionals at the clinic. The treatment was not well integrated as part of regular care at the clinics. Patients may have regarded the treatment as a second-best option to face-to-face treatment, and staff at the clinic may have been less aware of the Internet treatment.

A final but important explanation for the low effect sizes, is the amount of exposure the patients had to the Internet intervention. The majority of patients only completed one or two Internet sessions. This makes it hard to conclude that the intervention is not effective, as it shows that patients were not using of the intervention. Without exposure to the treatment content, a patient cannot be expected to make substantial improvements. Considering the larger clinical effects in the analysis of the subgroup with high adherence (chapter 5), future studies should aim to improve the adherence of the participants on the Internet-based intervention.

The third question this thesis aimed to address was whether Internet treatment in outpatient care was cost-effective. The studies in this thesis showed that adding Internet treatments to routine outpatient care did not lead to more (cost-)effective way of treating outpatients. Starting with Internet-based PST (chapter 4 and 5) during the waitlist was not (cost-)effective and by blending Internet and face-to-face treatments (chapter 6) treatment time and costs increased without resulting in additional health benefits. Furthermore, the observational study in chapter 2 and RCT in chapter 5 showed that despite the improvement rates after Internet-based PST, participants started face-to-face treatment at the outpatient clinic. The general idea behind offering Internet treatment during the waitlist in routine care is that it leads to more efficient treatment (better use of waiting time) and less uptake of (more expensive) face-to-face sessions. For this reason insurance companies and governments stimulate the use of Internet treatments [24] by means of awarding bonuses to clinics that implement e-Health solutions. The cost analysis in chapter 5 showed that the Internet intervention was not considered cost-effective as compared to enhanced usual care for patients waiting for face-to-face treatment at outpatient clinics from a societal perspective. However, there was a high probability that the intervention was cost-effective from the perspective of the mental healthcare provider. We hypothesized that patients who received the Internet-based intervention would use less mental healthcare services (e.g. less face-to-face sessions) resulting in lower costs, this was not confirmed, on the contrary, patients in the intervention group had on average two more face-to-face sessions and spent 27 more minutes with healthcare professionals than those in the control group. However, despite the higher number and duration of sessions, outpatient clinic costs in the intervention group were lower.
than in the control group. Thus, the patients who received the Internet-based intervention used less expensive mental healthcare services like for example group sessions and less expensive clinicians.

Evidence from previous controlled studies indicate that Internet-based treatments have a high probability of being cost-effective in comparison with control conditions at relatively low ceiling ratios [25, 26]. These studies included self-referred participants from the general population or patients from primary care. In addition, one study used as a comparator a waiting-list control group [26]. In contrast with the previous studies, the current study comprised severely depressed outpatients, who afterwards received face-to-face treatment. In sum, even though we found evidence that from the perspective of the mental health provider this Internet-based intervention could be cost-effective, the overall results showed that from a societal perspective it was not.

The fourth question this thesis addressed was whether clinicians would carry out Internet treatments. If Internet treatments are to have an impact on mental health care, clinicians and patients must be aware of existing evidence-based Internet interventions, and be able and willing to use them. Clinicians are not always positive about Internet interventions [37]. Blended care is often suggested to be more well received than standalone Internet treatments. However, the uptake of blended treatment in chapter 6 was low and this view might be too optimistic. Only a minority of the trained therapists (18%) actually offered blended care and they offered it to only a small part of their caseload. Barriers for the dissemination of blended care might be that the clinicians in this sample were still learning how to use the tools due to insufficient training and the lack of established pathways and treatment protocols, or that despite the training the therapists might not have been convinced of the advantages of blended treatment, and/or that they had difficulties explaining the platform and treatment to their patients.

What we learned from the study in chapter 6 is that the awareness of clinician’s attitudes and barriers to use of Internet treatments should be carefully considered in implementing Internet-delivered treatments. Treatment protocols and ongoing support for clinicians should be offered in order to assist implementation of these treatments and to maximize benefits [23]. In order to treat a substantial part of the patients via the internet, it seems necessary to train a larger percentage of therapists more intensively and also, for example, therapists with lower qualifications. A recent review showed that the level of experience and qualifications of clinician performing Internet-based treatment was of less importance in the outcome of treatment, but that the skills needed for Internet interventions
differ from skills needed in conventional treatments [36]. The authors of this review also suggest that the training of therapists might be an important effect moderating factor. It is therefore important to offer more extensive training in which clinicians are able to master the specific skills needed for Internet treatment.

Today, the mental health workers are extensively trained in providing regular face-to-face treatment. This has been the focus of their education for years and a lot of emphasis is put on developing a good therapeutic relation, on clinical observation and on regular psychotherapies. In order to increase the impact of Internet treatments, the reservations and skepticism of clinicians towards Internet treatments should be addressed. This can be done during the training of mental health workers. Putting more focus on low intensity treatments, Internet-based treatments, mobile health (mHealth) applications should provide mental health workers with more knowledge and skills regarding these types of treatment. Furthermore, for mental health organizations it is important to invest in the training of staff, the development of treatment protocols and a secure web platform in order to maximize the potential of Internet treatments in routine care. Treating patients via the Internet requires alterations in the therapeutic role, the infrastructure of the organization, and should be supported by the management for example with adequate supervision.

The last question this thesis addressed was related to predictors of outcome. One challenge facing the safe adoption of Internet interventions, particularly in self-guided formats, is a clear understanding of the intervention features and participant characteristics associated with treatment adherence and clinical outcomes. The study in chapter 7 aimed to identify predictors of clinical response to self-guided Internet-delivered treatment for depression and anxiety. The only stable predictor in this study that predicted favourable outcome, across time for the different definitions outcome, was high initial treatment credibility. This study showed that treatment credibility is related to outcome in both depression and generalized anxiety. Higher treatment credibility might be of special importance to self-guided treatments as patients are required to do the treatment without extra guidance from a therapist or coach. Patients who think this treatment might suit them, may work more independently than those who have a less clear formulation of their needs. Although the results of the study did not identify predictors for all outcome measures at all the different time points and more research is needed, we were able to replicate treatment credibility as a predictor of outcome in self-guided treatment.
Methodological Considerations and Limitations

The previous chapters of this thesis already discussed several limitations. This paragraph addresses another two important limitations.

Study design

The studies in chapter 2 and chapter 6 were observational, which means that we had no control over the composition of the groups and couldn’t randomize the allocation of participants. Randomization controls for bias by attempting to balance factors that affect outcomes across study groups. Without randomization the study is more prone to selection bias. The lack of randomization made it in chapter 2 not possible to determine whether the intervention itself was the factor that caused the improvement of the dependent variables, or whether the findings could be due to nonspecific factors (e.g. patients’ readiness to change, spontaneous improvement, treatment credibility) or baseline differences and may not be attributed to the Internet intervention itself.

However, the observational studies offered some advantages over clinical trials. For example the studies were able to evaluate the real-world applicability of evidence derived from randomized controlled trials. It provided information about whether or not outpatients would choose the option of starting with Internet treatment and what their characteristics were.

In chapter 4 and 5 the randomized design was a strength, however, it was impaired by offering the control group a self-help book. At the time it was deemed a necessary compromise for ethical reasons. The book was sent without further instructions or expectations. While there are exceptions, especially with newer self-guided treatments, most research find a small effect size for unguided bibliotherapy and significantly larger effect sizes for guided Internet interventions. For example, a meta-analyses had shown that self-help without any form of guidance resulted in only small effect sizes for participants with increased levels of depressive symptoms (d=0.28 [27] and d=0.06 [28]). Two other more recent meta-analysis also showed that unguided interventions had a significantly lower effect size compared to guided interventions. Andersson and Cuijpers [9] found an effect size of d=0.25 for unguided interventions and d=0.61 for guided self-help and Richard and Richardson [6] found an effect size of d=.36 for unguided interventions and d=.78 for therapist-supported studies. Based on this evidence, we would have found differences in effects between the two groups as the trial was powered to detect an effect size of d >0.40 as
statistically significant. However, we found no difference in any of the outcome measures, so we could not demonstrate the effectiveness of this particular Internet intervention in outpatient clinics. It would be interesting to have included a third group that received no treatment during the waiting list time in the outpatient clinics (care as usual).

**Implementation**

Previous research in the field of implementation science shows that interventions or new treatment modalities will not be effective if not implemented well [29]. In chapter 2, 4 and 5 of this thesis, the Internet intervention was carried out by staff from the university, not staff from the outpatient clinics. A challenge identified when designing the trial (chapter 3) was the extent the outpatient staff would take into account that patients might already have acquired skills and knowledge due to the Internet intervention, so that there might be no need to start patients on a fixed number of face-to-face sessions as prescribed by the standard treatment protocol. We aimed that only those patients who require additional treatment would be seen face-to-face, because otherwise the addition of the Internet interventions would be ineffectual in lowering treatment costs.

Although clinicians and staff at the outpatient clinics were informed about the details of the Internet program before and during trial, and received information about how many sessions their patients had already completed with the Internet course (before the onset of face-to-face treatment) we do not know how that information changed treatment decisions. Furthermore, the Internet intervention might have been more valid to patients and staff if it was offered at the outpatient clinic, not at the university, by staff from the outpatient clinic, not independent researchers.

In chapter 6 the blended treatment was offered by staff from the outpatient clinic. However, as argued in that chapter, suboptimal implementation of blended care might explain the finding that blended treatment was more expensive, without having additional health benefits. The clinical staff received only a short training in blended treatment, no guidelines on how to incorporate Internet sessions or which patients were eligible were in place. Furthermore, it was left to the therapist to decide how many online sessions would be used, and how many face-to-face, and what to discuss in both.

In order to aid dissemination of a new treatment modality, in this case blended care, it is necessary to create proper manuals and treatments protocols and more importantly to train clinicians in mastering the skills needed for the new intervention. Quality implementation does not happen automatically, but requires more effort than just a short training of staff.
Providing ongoing (technical) support for the clinicians executing the new treatment might increases the likelihood for a new treatment to be effective in routine care [30]. More efforts should be made to examine how the treatment can be optimized at organization level, clinician level, and patient level.

**Recommendations for future research**

Based on the studies in this thesis, some advice for future research can be given. It is necessary that, before implementation in regular clinics, the costs and effects of Internet treatments in routine care is examined, together with optimal implementation strategies. More studies need to be carried out in regular mental health clinics to demonstrate the (cost-) effectiveness or ineffectiveness of Internet-delivered interventions and other information technologies (e.g. mHealth, apps, wearables) for different patients and disorders at different times in treatment (e.g. at the start, during or after treatment or as stand-alone treatments). Research should focus on gaining knowledge about how these interventions work in real-world settings and should evaluate the effectiveness of implementing Internet treatments in routine care on health system outcomes. The European study MASTERMIND currently examines barriers and facilitating factors of implementation of Internet-delivered treatments on large scale in different settings. Understanding these factors, on organization, clinician and patient level, is crucial for optimizing the implementation of promising Internet treatments in routine care.

With regard to blended care, research needs to strengthen the evidence base first and subsequently explore if and how blended treatment can be effectively offered in routine mental health care. Research to the effectiveness and efficiency of blended care has only just began [31]. We do not yet know what the optimal dosage of Internet combined with face-to-face treatments is, and which treatment elements can best be offered online and which face-to-face. At the moment the European study e-COMPARED examines these issues and aims to provide evidence-based recommendations on how blended care can be integrated into routine healthcare and outpatients clinics.

Another important question is whether all patients should be offered Internet-based treatment. It is possible that some patients are better suited for face-to-face treatment, as well as the other way around, with some being better suited for Internet treatments. Studies are needed that can identify patients with a high risk of poor response to Internet-based treatment, so that they can be offered other types of treatment in other formats or other types and/or intensity of guidance. Furthermore, we need to identify who will benefit from what type of
intervention and why. This relates to identifying predictors, moderators and mediators of treatment outcome. The literature on predictors of treatment outcome is growing, but findings are inconsistent with clinical characteristics such as symptom level, gender, and age not being consistently related to outcome. Also, the lack of robust knowledge about adverse events related to Internet-delivered treatment may have left clinicians hesitant about potential harmful effects of these interventions and might have caused a barrier of to deploy Internet interventions. More research in the domains of predictors and adverse events is necessary. However, research on predictors of response to Internet-delivered treatments is challenging, conceptually and methodological. Due to the restrictive inclusion and exclusion criteria in research trials, diagnostic assessment based on self-report questionnaires, and the use of a research sample, the variance in the predictors might be small. Further research would benefit from a replication of predictor studies, including large samples. Information on predictors and negative outcomes may facilitate implementation of Internet-based treatments for both patients as clinicians.

A final, but essential recommendation is that patients’ needs require more attention. A neglected factor in Internet research is patient preferences regarding treatment ingredients and modalities. Nowadays, patients often get a non-personalized, non-interactive, and fixed Internet intervention, that in addition is developed with limited resources and lacks an engaging user interface. Internet interventions in routine care should be in line with the user requirements, should be able to adapt to what patients want and to what patient need (e.g. based on patients educational level, motivation and symptom levels). Meeting the needs of patients should increase motivation for and adherence to treatment. Future research could focus on ways to minimize attrition and increase adherence, especially as adherence is correlated with outcome in cognitive therapy [27].
In conclusion

A new mode of treatment delivery can be viewed as suitable for large scale dissemination when it has been shown to be acceptable to patients, clinicians and health systems, efficacious, effective, health economically evaluated and possible to administer in the desired setting. In this thesis, we could not demonstrate the (cost-)effectiveness of guided Internet-based problem solving treatment for depressed outpatients. Together with the low rates of adherence, we do not recommend the dissemination of this particular Internet intervention as such in regular mental health care.

However, taking in to account that there is much evidence for the efficacy of Internet-based treatments, especially for iCBT, it is too early to draw firm conclusions about the effectiveness of Internet treatments in regular outpatient clinics as a whole. Internet interventions have proven their effectiveness in trials comparing no intervention with Internet interventions, which is of major importance as many individuals do not receive any intervention or treatment. While several countries are increasingly offering Internet treatments in clinical practice in order to reduce the burden of psychological disorders and to save treatment costs, more research is needed to that examines Internet interventions in routine care. Only then can we draw firm conclusions about the value of Internet-based interventions for a wider group of patients in regular mental health care.
References


