Summary

Depression and anxiety disorders are highly prevalent mental disorders and are associated with serious functional impairments, losses in quality of life, high economic costs and high levels of service use. Chapter 1 states that this makes the treatment of depression and anxiety important. A wide range of effective treatments (e.g. cognitive behavioral therapy, exposure therapy, pharmalogical treatments) exist, but despite their proven effectiveness depression and anxiety disorders often remain untreated. Rates of treatment seeking are low and when patients do seek treatment the treatments are not easily accessible. Due to scarce health care resources, limited availability of trained clinicians, long waiting lists, stigma and costs related to treatment, less than half of individuals with mental disorders receive treatment. This is even less in adolescents, older adults and individuals with lower socioeconomic status and from ethnic minorities. The need for a further reduction of the disease burden of common mental disorders is high, but several of the before mentioned issues pose a barrier to the uptake of effective treatments.

Regular psychological treatment, delivered in individual face-to-face sessions, is an effective, but expensive mode of treatment delivery. It takes up a lot of clinician time and other resources. With the current prevalence rates of depression and anxiety disorders, there is a high demand for psychological treatment, but too little supply. In addition, the national health care budget in the Netherlands is shrinking, which has a major impact on the resources available for mental health care and puts pressure on mental health care providers to offer (cost-)effective treatments.

Internet-based treatments are often proposed as a cost-effective way of treatment delivery. These interventions make use of the same principles as traditional face-to-face treatment, but the difference is that the therapeutic content, which is usually based on evidence-based treatment models, is provided via the Internet on computers, tablets or smartphones. The structure of the Internet interventions is similar to that of regular face-to-face treatments; content and assignments are dispatched in (weekly) sessions and the goal is that patients will practice and apply the techniques in their daily lives. Internet-based treatments can be provided with some level of contact with a clinician or coach, via email or a secure messaging system within the intervention platform, or via telephone calls. These interventions are referred to as guided Internet interventions. Internet interventions can also be entirely self-guided. In that case, the users are expected to work through the intervention by themselves and receive no feedback on (homework) assignments.
Although research groups have examined the efficacy of Internet-delivered treatments for a while now, this mode of treatment delivery has not been extensively researched in actual outpatients clinics, as e-mental health services are usually found outside of regular mental health services. Despite of the proposed advantages of Internet treatment it is still not a very commonly used mode of treatment delivery for outpatients and the (cost-)effectiveness in regular outpatient clinics has not been studied yet. 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 **Chapter 2** of this thesis Internet-based PST was offered during the waitlist at an outpatient clinic in an observational study. Due to limited resources, patients in the Netherlands often have to wait for a minimum of six weeks after registration for mental health care to receive their first treatment session. Offering guided online treatment might be an effective solution to reduce waiting time and to increase patient outcomes at relatively low cost. In this study we reported on the (1) uptake of the Internet treatment, which was defined as the percentage of patients who accept the offer of online treatment during waiting for face-to-face treatment and the percentage who declined, (2) the demographic and clinical profile of patients who preferred online treatment, and (3) symptom reduction.

The results showed that 53% of the patients preferred to start with Internet-based PST over waiting for face-to-face treatment (care as usual). The study also showed that patients who chose to start with Internet treatment were more often female, and they were younger and lower educated, compared to those who wished to remain on the waitlist. This is contrary to the characteristics of participants in previous Internet trails, who were more often higher educated. There were, however, no baseline differences in levels of clinical symptoms between the groups. Patients mentioned: the fear that personal information was not save on the Internet; the wish of talking to a therapist instead of a computer and the lack of computer skills, as reasons not to take up Internet treatment.

With regard to reductions in symptoms, the results showed that patients who carried out the Internet-delivered intervention during the waitlist time had lower levels of depression and anxiety after 5 weeks, compared to the patients that had waited 5 weeks for face-to-face treatment. Large between-group effect sizes were observed for depression, anxiety and quality of life, but not for burn-out symptoms. We concluded that the results are encouraging with respect to patients’ acceptability of Internet treatments in regular outpatient clinics. However, due to the nature of the study, which was observational, it is not possible to draw firm conclusions about the effectiveness of offering internet treatment during waitlist.
Chapter 3 described the design of a randomized controlled trial. The study was designed to evaluate the clinical and economical effects of a guided Internet-based self-help intervention, when offered to patients with major depressive disorder on a waiting list for psychotherapy in regular outpatient clinics. At the start of this waiting list period patients were randomized and either (a) received a guided Internet-based intervention or (b) remained on the waitlist and received a self-help book without additional guidance for motivational purposes. Both the 5-week Internet-based guided self-help intervention and the self-help booklet were based on problem solving treatment. After the intervention patients were allowed to start with regular face-to-face treatment at the clinics. Costs and effects were measured at baseline, at 8 weeks, 6 months and 12 months. The primary outcome was symptoms of depression, as measured by the CES-D. Secondary outcome measures were the number of face-to-face sessions, absence of work, and health care uptake in general. Additional outcome measures were levels of anxiety, insomnia, quality of life and mastery. We hypothesized that by starting with the guided Internet-based intervention during the waiting list, the clinical effects of the treatment would be maintained, with less uptake of face-to-face treatment after the intervention and a reduction in the costs of treatment.

Chapter 4 described the short-term effectiveness of Internet-based PST in outpatient clinics. A total of 269 participants were randomized to the intervention group (n=136) or the control group (n=133). The analyses showed that Internet-based PST was not more effective in reducing symptoms of depression than receiving an unguided self-help book before onset of face-to-face treatment at outpatient clinics. The effect sizes were smaller than those generally found in Internet trials for depression and the adherence rates were low. Only 12.5% of the Internet intervention group completed the entire course. However, both the intervention group as the control group demonstrated significant improvements in depressive symptoms from pre- to posttest.

Chapter 5 described the long-term outcomes of the RCT and examined the cost-effectiveness of the Internet intervention. There were no statistically significant differences between the two groups with regard to clinical outcomes. The results, based on a societal perspective, also showed that offering an Internet-based intervention to those on waiting list for face-to-face treatment was not cost-effective in comparison with usual care. It was hypothesized that patients who received the Internet intervention would use less mental healthcare services (e.g. fewer face-to-face sessions) leading to lower costs. This was not confirmed. In contrast, patients in the intervention group had on average more face-to-face sessions and more minutes with healthcare professionals than those in the control group.
Sensitivity analysis from the perspective of the mental healthcare provider showed that there was a high probability of the intervention being cost-effective in comparison with usual care. Despite the higher number and duration of these sessions, the intervention group was associated with statistically non-significantly lower costs compared to usual care group, due to the uptake of less expensive mental healthcare services in the clinic. Thus from the perspectives of mental healthcare provider, offering Internet-based treatment to patients on a waiting list for face-to-face treatment may be considered cost-effective.

In Chapter 6 we evaluated the costs and effects of blended treatment (combination of Internet sessions with face-to-face sessions) versus standard face-to-face treatment in routine care for patients with depression or anxiety disorder. We examined routine data from a mental health clinic which was one of the first in the Netherlands to implement blended treatment. The results showed that only a few professionals used blended treatments. Functioning of patients who received blended treatment did not improve significantly more than those who received only face-to-face treatment. Blended treatment resulted in longer treatment durations and subsequently higher costs compared to standard face-to-face treatments, as the Internet sessions were added on top of the face-to-face treatments in this outpatient clinic.

The finding that blended care leads to more treatment time and costs was unexpected and might be explained by the suboptimal implementation of blended care. The study illustrated that integrating Internet treatments into existing mental health services is challenging and that offering these interventions in routine practice do not automatically lead to a more efficient way of using the scarce therapeutic resources. Previous research in the field of implementation science shows that interventions or new treatment modalities will not be effective if not implemented well. We recommended that mental health services need to have stronger implementation procedures, e.g. treatment protocols and ongoing support for clinicians should be offered in order to assist implementation of these treatments and to maximize benefits. Furthermore awareness of clinician’s attitudes and barriers to use of Internet treatments should be carefully considered in developing training and online treatment (tools).

The aim of Chapter 7 of this thesis was to identify predictors of clinical response to self-guided Internet-delivered treatment for depression and anxiety. Self-guided Internet interventions can be effective in treating depression and anxiety, but little robust information is known about the factors that determine effectiveness. 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. In this exploratory study participant characteristics (e.g. gender, age, educational level, marital status, and vocational status), the clinical characteristics (e.g., neuroticism and symptom severity) and the treatment related variables of treatment (e.g. credibility, expectancy and adherence) were examined as predictors of treatment response to self-guided Internet-based treatment. Clinical response was defined in three different ways (reliable improvement, reliable recovery and 50% symptom reduction). The study used the data (N=203) of a previous randomized controlled trial (RCT),

The only stable predictor in this study that predicted favourable outcome, across time for the different definitions outcome, was treatment credibility. Patients with higher levels of credibility were more likely to reliable improve, reliable recover and to half their symptoms. Previous studies identified credibility as a significant predictor of both outcome and adherence for social anxiety disorder. 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. In addition, medication use and higher scores of depression were associated with worse treatment response in patients with anxiety, while higher neuroticism and credibility ratings were associated with better response. In depression, credibility was the only stable predictor of outcome. Although the results did not identify predictors for all outcome measures at all the different time points, we were able to replicate treatment credibility as a predictor of outcome in self-guided treatment.

Chapter 8 provides the general discussion of this thesis. 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. However, the question remained 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. 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. More than half of all participants preferred Internet treatment over waiting for treatment (care-as-usual), 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 the studies in outpatient clinics 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. The adherence rates in our trial also compare poorly to those in other Internet-delivered CBT trials in the routine care, which could indicate that this particular Internet-delivered PST intervention is not a good match for depressed patients in outpatient clinics. With regard to treatment satisfaction, most patients were moderately satisfied with the intervention. 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.

The second question this thesis examined was whether Internet-based PST in outpatient clinics was effective. The results of the studies in this thesis showed that guided Internet-based PST was not more effective than being on the waitlist with a self-help book at outpatient clinics. However, considering the larger clinical effects in the analysis of the subgroup with high adherence future studies should aim to improve the adherence of the participants on the Internet-based intervention. For further use of this intervention, we recommend adjusting it to today’s technology standards in order to increase adherence and treatment satisfaction, and effectiveness.

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 during the waitlist was not (cost-)effective and by blending Internet and face-to-face treatments treatment time and costs increased without additional health benefits.

In sum, 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 in regular mental health care. However, taking into account that there is much evidence for the efficacy of Internet-based treatments it is too early to draw firm conclusions about the effectiveness of these treatments in regular outpatient clinics as a whole.