Relapse prevention in patients with anxiety or depressive disorders

Krijnen-de Bruin, Esther

2021

document version
Publisher's PDF, also known as Version of record

RELAPSE PREVENTION IN PATIENTS WITH ANXIETY OR DEPRESSIVE DISORDERS

ESTHER KRIJNEN-DE BRUIN

Amsterdam UMC
Universitair Medische Centra
Department of Psychiatry, location VUmc

Relapse prevention in patients with anxiety or depressive disorders

Esther Krijnen-de Bruin

ISBN: 978-94-6423-298-1

Cover design & lay-out: Wendy Schoneveld || www.wenziD.nl
Printed by: ProefschriftMaken || Proefschriftmaken.nl

This thesis was prepared at the Department of Research and Innovation at GGZ inGeest, and the Department of Psychiatry, Amsterdam UMC, VU University Amsterdam, within the Amsterdam Public Health research institute.

Financial support for the publication and distribution of this thesis was kindly provided by the Department of Psychiatry, Amsterdam UMC, VU University Amsterdam.

VRIJE UNIVERSITEIT

Relapse prevention in patients with anxiety or depressive disorders

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor
aan de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. V. Subramaniam,
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de Faculteit der Geneeskunde
op donderdag 17 juni 2021 om 11.45 uur
in de aula van de universiteit,
De Boelelaan 1105

door

Esther Krijnen-de Bruin

geboren te Utrecht

Promotoren:	prof.dr. B.K.G. van Meijel prof.dr. A. van Straten
Copromotoren:	dr. A.D.T. Muntingh dr. N.M. Batelaan

CONTENTS

1

GENERAL INTRODUCTION

"My name is John and I am 55 years old. I am divorced and I have two adult children. I have experienced a depression twice. The first time was after my brother passed away. We got along well, and I was heartbroken. I was unable to talk about my feelings of grief with others, and instead focused on working as hard as I could. This led me to place too much pressure on myself, which resulted in me experiencing a burn-out in conjunction with severe symptoms of depression. The second time occurred when my wife and I had relationship issues. Over the years, we grew apart and were no longer able to live together. Ultimately, we decided to split up, which culminated in a very difficult period for me. During this time, my mother also became very ill, and I spent considerable time taking care of her. I've come to realize over the last several years that I have not spent enough time thinking about what I really want and what I care about. Rather, I focused too much on both the opinions and needs of others. In combination with these other life events, I was no longer able to sufficiently cope with the stress I was experiencing. Through therapy, I learned to listen to my own feelings and to do what is right for me. I have also become cognizant of the fact that I am vulnerable to developing symptoms of depression, and, as such, that I need to keep a close eye on myself. In doing so, I hope to prevent new symptoms. I drew up a relapse prevention plan, which lists activities that I can do whenever I feel that I am on the verge of relapsing. This helps me to focus on doing activities that I know are good for me, but that I simply do not always fancy doing, such as, for example, meeting friends, working out or cleaning my home. While both my family and my job are still incredibly important to me, I no longer let them take control of my life."

This is the case of John[1], a patient who is currently in remission from depression. Like many other patients who have experienced depressive episodes, there is a risk that he may relapse. John is aware of his vulnerability to relapse and thus tries to prevent this through employing relapse prevention strategies. This means that if John experiences an increase in his symptoms, he knows what to do in order to try and prevent a full-blown relapse.

It is evident from clinical practice and scientific literature that many patients who have experienced depression lack the relapse prevention strategies that are required to prevent relapse. This is partly due to the fact that relapse prevention is currently granted insufficient attention within the context of mental health care. Besides the prevention of depressive disorders – as mentioned in the case of John – the prevention of anxiety disorders also warrants closer attention, because these disorders are just as prevalent and have high recurrence rates. Given the aforesaid lack of attention to relapse prevention and the concurrence of anxiety and depressive disorders, the

1 The case of John is a hybrid case with a fictive name, based on multiple patients.

present thesis examines relapse prevention strategies for patients in remission from both anxiety and depressive disorders.

The introductory chapter of the thesis provides background information on anxiety and depressive disorders before proceeding to explicate the epidemiology, burden of disease and course of symptoms for anxiety and depressive disorders. Next, the chapter provides an overview of the common treatment methods for anxiety and depressive disorders, along with the opportunities for relapse prevention, the current organization of care related to relapse prevention, the role of mental health professionals (MHPs), and the expedience of applying self-management strategies to prevent relapses. Finally, the chapter outlines some of the limitations of current relapse prevention programs, before then providing a brief description of the GET READY relapse prevention program. The chapter closes by delineating the aims and outline of the thesis.

Anxiety and depressive disorders

Anxiety disorders are classified as a group of mental disorders that are characterized by anxiety and fear. These disorders, according to the classification of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [1], include panic disorder (with or without agoraphobia), agoraphobia, specific phobia, social phobia, generalized anxiety disorder, obsessive-compulsive disorder (OCD) and post-traumatic stress disorder (PTSD) (Table 1). Although OCD and PTSD have subsequently been reclassified within other categories in the DSM-5, the descriptions below correspond to their previous categorization in the anxiety disorders group in the DSM-IV.

Depressive disorders, including major depressive disorder and dysthymia, are characterized by a sad mood and loss of interest or pleasure (Table 1). For the purposes of this thesis, the decision was made to use the classifications from the DSM-IV, because at the start of the study, DSM-5 was not yet implemented in Dutch mental health care.

Table 1. Anxiety and depressive disorders according to DSM-IV.

Anxiety disorders according to DSM-IV

Panic disorder (with or without agoraphobia)
The most important characteristics of a panic disorder are recurrent, unexpected panic attacks, ongoing concern about experiencing a further panic attack as well as its possible implications and consequences, and a change of behavior related to the attacks. These panic attacks consist of short periods of intense fear or discomfort, accompanied by physical and psychological symptoms, which typically subside after 10 minutes. Panic disorders can be diagnosed both with or without agoraphobia. When patients experience a panic disorder with agoraphobia, they subsequently avoid certain situations or places to prevent a further attack.

Agoraphobia
Patients with agoraphobia experience anxiety over being in places or situations that are either difficult or embarrassing to escape from, or in which help is not available if they need it. More specifically, patients often experience extreme fear if they have to travel in a bus, train or car, are in a crowd or standing in a line, are on a bridge, or are outside on their own. These situations are typically either avoided, or endured with great distress.

Specific phobia
Patients with a specific phobia experience an excessive fear of specific objects, animals or situations. Exposure to these kind of stimuli induces an anxiety response. Frequent specific phobias are, for example, the fear of spiders, mice, elevators and flying. Most of the time these stimuli are avoided, and patients are cognizant of the fact that their fear is excessive or unreasonable.

Social phobia
Social phobia (or social anxiety disorder as it is also known) is characterized by a persistent fear towards social or performance-based situations. This is because patients with social phobia are afraid to humiliate or embarrass themselves, by, among other things, blushing or sweating. They ordinarily avoid social or performance-based situations, or attend and endure extreme distress. Patients recognize that their fear is excessive or unreasonable, but are simply unable to overcome it.

Generalized anxiety disorder
In most cases, patients who suffer from a generalized anxiety disorder experience excessive anxiety and worry towards a wide range of different situations or activities, for a period of at least six months. Patients find it incredibly difficult to control this worry, which is why they often experience additional symptoms, such as restlessness, irritability, sleep disturbance, distress, and impaired functioning.

Obsessive-compulsive disorder
Patients with an obsessive-compulsive disorder experience compulsive thoughts (obsessions) and/or other compulsions. Obsessions are recurrent and persistent thoughts, impulses or images that are experienced as intrusive and inappropriate, and cause anxiety and distress. An example of such thoughts would be a repeated thought that you may infect others or be infected by others, or a thought about hurting others. Ordinarily, patients try to control this disorder by engaging in compulsions, which are repetitive behaviors that seek to reduce distress or prevent a certain situation from occurring. Examples of such compulsions are cleaning, checking whether the door is locked or making sure things are positioned symmetrically.

Post-traumatic stress disorder
Patients with a post-traumatic stress disorder have been exposed to a traumatic event and subsequently experience negative consequences in their daily lives. Patients re-experience this traumatic event in manifold ways, such as, for example, via recurrent distressing dreams or intrusive, distressing recollections of the event. Patients often avoid situations, people or objects that remind them of the traumatic event. Moreover, patients routinely experience symptoms of increased arousal, which were not present prior to the trauma.

Depressive disorders according to DSM-IV

Major depressive disorder
A major depressive disorder (MDD) is characterized by (1) having a depressed mood, and/or (2) a loss of interest or pleasure in daily activities. In addition to this, patients display several of the following symptoms: (3) sleep problems, (4) fatigue, (5) feelings of worthlessness or excessive or inappropriate guilt, (6) problems in concentration or decision-making, (7) change in appetite or weight change, (8) psychomotor agitation or retardation, and (9) thoughts of death and suicide. In order to diagnose MDD, a patient must be experiencing at least five of the above nine symptoms. These symptoms should be present across the largest part of the day and occur on an almost daily basis, for at least a two-week period. Furthermore, MDD can result in impaired social, occupational and/or educational functioning.

Dysthymia
Dysthymia is classified as a more persistent and chronic form of depression, but with milder levels of symptoms. Symptoms are typically present for at least a two-year period.

Epidemiology and burden of disease

Around 615 million people globally are affected by anxiety and depressive disorders, which means that these disorders are among the most prevalent mental health disorders [2]. In the Netherlands, around 20% of the population experience an anxiety and/or depressive disorder over the course of their life [3].

Anxiety and depressive disorders place a heavy burden on people, insofar as these disorders are associated with a high level of disability and reduced quality of life, functioning and well-being [4–6]. Moreover, these disorders also cause a tremendous economic burden worldwide [7].

Anxiety and depressive disorders often coincide with one another [8]. Of all those patients that are currently diagnosed with an anxiety/depressive disorder, the vast majority (75-81%) have experienced a comorbid depressive/anxiety episode at least once in their life [9]. The comorbidity of these disorders has been found to be associated with long-term disability from work, increased absenteeism, longer duration of symptoms, and increased symptom severity [9,10].

Course of symptoms

Many patients with an anxiety and/or depressive disorder experience chronic symptoms. Chronicity levels range from 24.5% for patients with depression, up to 41.9% for patients with anxiety, and as high as 56.8% for patients with comorbid depression and anxiety [11]. Risk factors for anxiety and depression chronicity are early onset, high psychopathology, loss or adversity during childhood, longer duration of index episode, higher number of previous episodes, older age, and comorbid depression and anxiety [11–13]. Patients in remission from an anxiety or depressive

disorder are prone to relapse, with up to 57% of remitted patients experiencing a relapse of either their index disorder or another anxiety or depressive disorder within the first four years of remission [14]. The relapse rates among patients with anxiety disorders have been reported as ranging from 22% to 58% [11,15–17], while among patients with depressive disorders the relapse rates vary from 27% to 77% [18–21]. These reported differences in relapse rates may, in part, derive from variation in baseline symptoms, different definitions of relapse, different follow-up durations, and different treatments provided in the acute phase. Several risk factors for relapse have been identified in extant literature. Patients that achieve partial rather than full remission are at a higher risk of relapse [22,23]. With respect to patients with anxiety disorders, decreased functioning, anxiety sensitivity, and previous episodes of anxiety have been identified as risk factors for relapse [16,24]. Risk factors for relapse among patients with depressive disorders are, among other things, a high number of previous episodes, negative experiences in youth, and a prior severe depressive episode [25,26].

Remission and recovery

There is a long-standing debate in academic literature concerning how to define remission, partial remission and recovery. Full remission indicates that the patient no longer meets the DSM criteria for a particular disorder and experiences no more than minimal symptoms [27]. Partial remission also indicates that the patient no longer meets the DSM criteria for a disorder, but that they nevertheless continue to display minimal symptoms. While these aforesaid definitions by Frank et al. [27] are commonly used, they leave room for interpretation, insofar as it is often difficult in practice to determine whether someone is experiencing 'minimal symptoms' or 'more than minimal symptoms'.

An extensive array of questionnaires have been used to assess symptom severity, while a variety of cut-off points are used to define (partial) remission and relapse. For example, several studies classify patients as being in remission if they score <10 [28–30] on the Hamilton Depression Rating Scale-17 (HDRS-17), while others use a cut-off of <11 [31–33], or even <14 in some studies [34,35]. These examples underscore the heterogeneity of definitions used in research.

A further issue is that the term recovery is also frequently used in the literature to indicate that a longer period of remission has been achieved and that patients have subsequently entered into the maintenance phase [27] (Figure 1). If someone is recovered, then treatment will either be discontinued, or the focus of the treatment will shift to the prevention of a new episode of the disorder. As well as symptomatic recovery, people also recover their ability to function and participate in society, to return to work or study, and live their lives in accordance with their own preferences and standards. In this respect, recovery also refers to "a movement towards health

and meaning rather than avoidance of symptoms" [36]. In the present thesis, we use the term remission to indicate both full and partial remission and recovery. Remission implies that a patient no longer meets the criteria for a DSM disorder. Although these terms are primarily used in extant literature on depressive disorders, they are also applicable to anxiety disorders.

Relapse and recurrence

In parallel with the aforementioned debate about remission and recovery, there is a similar debate in the field pertaining to the use of the terms relapse and recurrence. Relapse is defined as "a return of symptoms satisfying the full syndrome criteria for an episode that occurs during the period of remission, but before recovery" [27] (Figure 1). The term 'recurrence' is often used alongside 'relapse' in extant literature. The difference between the two terms derives from their distinct timeframes: a relapse occurs after a period of remission in the continuation phase, while a recurrence occurs after a period of recovery within the maintenance phase (Figure 1). In this thesis, the term relapse is used to indicate both relapse and recurrence, as these terms are often used interchangeably in the literature [37].

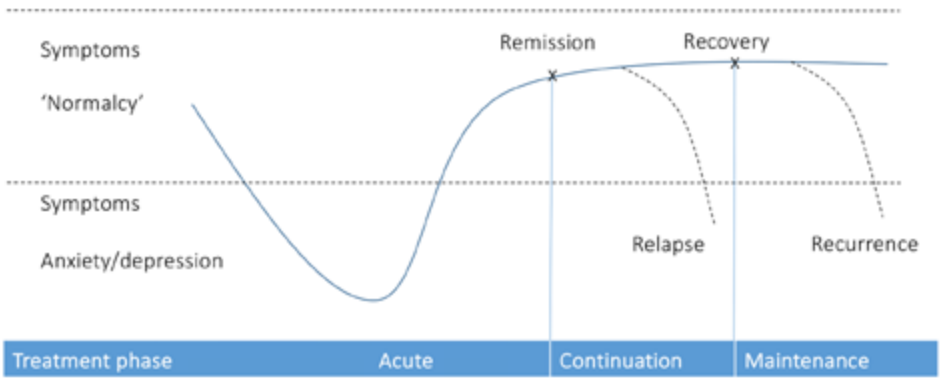

Figure 1. Overview of definitions. Modified based on criteria from Frank et al. [27].

Treatment

In recent decades, research has shown that many treatments for anxiety and depressive disorders in the acute phase are effective [38,39]. In accordance with national and international guidelines, the treatment for these disorders often consists of psychological and/or pharmacological treatments [40–43]. Out of the available psychological treatments, cognitive behavioral therapy (CBT) has received the most

attention from researchers. CBT aims to challenge and change negative thought patterns (cognitions), as these profoundly impact upon how people react to (stressful) situations, as well as how they behave and feel. Behavioral activation is also a critically important aspect of CBT, which focuses on increasing people's engagement in activities and decreasing their avoidant and isolating behaviors. CBT has been found to be effective in reducing symptoms for both anxiety and depressive disorders [44,45]. Other forms of evidence-based psychological treatments are psychodynamic therapy, interpersonal therapy, and mindfulness [38]. In clinical practice, a variety of treatments are used for patients with depressive disorders, while exposure therapy is the most common treatment for patients with anxiety disorders. Psychological and pharmacological treatments appear to be equally effective for patients with anxiety and depressive disorders [46]. In fact, a combination of both psychological and pharmacological treatments has been argued to be the most effective [47]. However, many patients favor psychological treatments over pharmacological treatments [48,49]. Motivation for this preference may stem from the fact that patients assume that psychological treatments solve the cause of the disorder, or it may be grounded in health concerns related to the side effects of medication [49,50].

Traditionally, treatments are provided by a professional via face-to-face (FTF) contact. However, in light of the outbreak of COVID-19 and ongoing lockdown measures, there has been a marked shift towards conducting treatments online. Ordinarily, online treatment consists of online E-health modules, personal feedback from a professional, and the possibility to exchange text messages via an online platform and engage in video calls. These E-health modules are based on regular treatment protocols and are divided into separate lessons. Their principal difference from traditional treatments is the delivery mode of the treatment. Specific advantages of online treatments are that they are easily accessible, potentially more cost-effective, facilitate multimedia interactivity, and enhance the possibilities for symptom monitoring [51,52].

Given that patients who have undergone treatment for anxiety and depressive disorders often experience relapse, and the risk of relapse increases with every new episode, one of the major challenges in terms of managing these disorders is the prevention of relapse [53]. Although national and international guidelines [40–43] stipulate that attention should be paid to relapse prevention over the course of treatment, it appears that this is often not the case in clinical practice. During informal conversations with therapists, some noted that during treatment they solely wanted to focus on positive aspects, rather than discussing 'negative' subjects such as a patient's vulnerability to relapse. This was found to be the same for patients themselves: therapists were under the impression that patients did not want to be confronted with their vulnerability to relapse. However, due to the high prevalence of relapse, paying special attention to relapse prevention is warranted.

Relapse prevention

After completing treatment in mental health care, patients who are vulnerable to relapse should be provided with relapse prevention strategies. Given the high relapse rates among patients with anxiety and depressive disorders, paying sufficient attention to relapse prevention is especially pertinent for this group of patients. Generally speaking, the guidelines recommend two relapse prevention strategies for patients who are in remission from anxiety and depressive disorders: 1) continuation of antidepressant medication (ADM), and 2) psychological relapse prevention interventions [41,54–56]. Although continuation of ADM after treatment in the acute phase has been shown to reduce relapse rates [57–59], not to mention that relapse rates are lower for those who continue to use ADM than for those who discontinue use [57,58], psychological relapse prevention interventions are potentially preferable to maintenance ADM (M-ADM) for the following reasons. First, M-ADM can often be accompanied by serious adverse effects [60], which, in turn, might lead to non-adherence [61]. Moreover, most patients have reservations about the long-term effects of using medication [62], while discontinuation of ADM has also been found to be challenging [57,58]. Second, given that patients prefer psychological treatments over pharmacological treatments [48,49], they may also prefer psychological interventions over M-ADM to prevent relapse. Finally, there is evidence to suggest that psychological relapse prevention interventions are more effective in preventing relapse than ADM [63].

The combination of ADM and psychological relapse prevention interventions appears to be a promising approach in this respect, albeit this approach needs to be tailored to individual patients [31]. For example, some patients might experience positive effects from M-ADM and, hence, no longer feel the need for additional psychological interventions. Others might prefer psychological interventions, because they feel these interventions target the underlying causes of their disorder, while others may experience the most benefit from a combination of M-ADM and psychological interventions. This serves to illustrate why relapse prevention strategies need to be customized to each patient, insofar as doing so is likely to enhance both adherence to, and the effectiveness of, the treatment.

Preventive cognitive therapy (PCT), CBT and mindfulness-based cognitive therapy (MBCT) are the predominant evidence-based psychological relapse prevention interventions for depressive disorders. All relapse prevention programs ordinarily consist of the following key 'ingredients': a relapse prevention or crisis management plan, symptom monitoring, psychoeducation, reinforcement of self-management strategies, feedback and homework exercises [64–67]. In most studies, psychological relapse prevention interventions are carried out in an outpatient mental health care setting. Most of these programs involve FTF contact, but programs using online formats are increasingly available [68]. Another format that acquires greater consideration is

a blended format, which offers both FTF contact and online components. While one major advantage of online sessions is that they are potentially (cost) effective, if little to no guidance is offered, then patients often find it difficult to adhere to the program [69–71]. Consequently, the combination of FTF contact and online sessions might constitute an effective approach to relapse prevention.

In contrast to the strong evidence base for relapse prevention in depressive disorders, only a handful of psychological relapse prevention randomized controlled trials (RCTs) have been conducted among patients with remitted anxiety disorders. For example, White et al. [81] found that patients who received maintenance CBT had lower relapse rates compared to those patients who only received assessment. Scholten et al. [82] concluded that there was no significant difference between the relapse rates for patients who received both CBT and discontinuation of ADM and those who only received discontinuation of ADM.

From a patient perspective, there appears to be a need for further support from professionals regarding relapse prevention [72,73]. Indeed, Muntingh et al. [72] found that patients prefer a relapse prevention program that includes regular FTF contact with a professional, flexible time investment based on their individual needs, and a personalized prevention plan.

Organization of care

In the Netherlands, there has been an emergent focus on the prevention of diseases – especially over the past decade – both in terms of preventing new disorders and recurring disorders. Consequently, self-management and recovery have taken on increased importance and been pinpointed as requiring attention, such as, for example, through E-mental health programs [74]. The impetus here is to provide effective care with the lowest possible intensity, which means that patients without a DSM disorder or who exhibit very mild symptoms receive care in primary care practices, patients with mild and moderate disorders receive care from the 'generalist basic' mental health services [GB-GGZ], while patients with severe and complex disorders receive care from specialized mental health care services [S-GGZ]. The rationale for this is that it would signal a partial shift away from treating patients in intensive, specialized mental health care services towards treatment in less intensive mental health services, including primary care. In order to support general practitioners (GPs) in primary care practices, a mental health professional (MHP) [POH-GGZ] is now available in most general practices. As described below, these MHPs can encourage patients to utilize self-management strategies in order to effectively cope with their disorder and its attendant consequences, and in terms of supporting remitted patients to prevent relapse.

Role of mental health professionals

Mental health care in primary care is primarily provided by MHPs, who consist of (community) mental health nurses, social workers or psychologists, and report to the GP. Given that GPs are ordinarily located nearby patients' homes, not to mention that these services are freely available, MHPs are easily approachable. Consequently, they play a pivotal role in terms of symptom monitoring, encouraging self-management, and, ultimately, relapse prevention [75].

In an ideal situation, therapists send a referral letter to the GP/MHP after patients have undergone treatment within specialized mental health care. The MHP would then contact the patient to organize a meeting. Patients can also contact the MHP after completing treatment to arrange a meeting. In this meeting, the MHP would discuss what the patient needs to do in the event of impending relapse, and provide them with self-management strategies that they can use. They will then collectively decide upon the frequency of their FTF contact. During these moments of FTF contact, shared decision-making between MHPs and patients is of vital importance for maintaining and empowering patients' mental health.

Today, MHPs are expected to provide relapse prevention programs to patients who are in remission from an anxiety or depressive disorder. However, research has shown that MHPs feel that they require additional tools to provide more effective relapse prevention programs [72].

Self-management

John: *"Last Monday I had an appointment with my mental health professional. Every 3 months I have a 'check-in appointment', in which we discuss how I am doing and how I have handled difficulties. On this occasion, we discussed strategies to stay mentally fit. For me, it always helps to visit friends, and I know I should keep doing this, even if I don't feel like doing it. My mental health professional challenged me to think of other things I can do to gain more control over my life. She suggested using self-management strategies, such as gaining more knowledge about my depression, keeping a diary to monitor my symptoms, engaging in activities such as sports, and building a routine of activities. Together we picked a few of these strategies that I could try out over the next 3 months. Although it is not always easy for me, it feels good to actively work on my recovery and to notice that I am feeling better. It especially helps me to routinely plan activities. What also helps is the knowledge that I have a check-in appointment with my mental health professional every 3 months, as she is very supportive, and we can evaluate my activities together."*

Given that the course of anxiety and depressive disorders often resemble the course of chronic diseases, a chronic disease care model is required [76]. Within a chronic care model, self-management plays an integral part in managing chronic diseases [77–79]. Self-management has been defined in manifold ways. Lorig [80] defines self-

management as "learning and practicing skills necessary to carry on an active and emotionally satisfying life in the face of a chronic condition" (p. 11), while Barlow et al. [81] define it as "the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and life style changes inherent in living with a chronic condition"(p. 178). A central theme within both of these definitions is enhancing individuals' abilities and skills to deal with a chronic disease, which includes, among other things, action planning, decision-making, and the formation of a patient-provider partnership [79].

In recent years, there has been an emergent recognition of the importance of recovery within mental health care [82,83]. With respect to recovering from mental health disorders, self-management has been identified as being of paramount importance [84–86], and, in fact, as being essential to the prevention of relapse. While this increased focus on recovery has hitherto principally been targeted at patients with severe mental disorders, it could also be applicable to patients with anxiety and depressive disorders, for whom the disorder has a chronic course. Generally speaking, patients with mental health disorders display a positive attitude towards employing self-management strategies as part of their recovery, and, indeed, most of them have the capability to use them [87,88]. However, it might not be as straightforward for all patients with anxiety and depressive disorders to employ the self-management strategies that are most appropriate for their personal situation. For example, it was found that patients with higher scores of anxiety and depressive symptoms after heart surgery, engaged in less self-management strategies [89]. Therefore, it is critically important to encourage and support patients to use self-management strategies that are particularly relevant for their specific situation. Doing so is vital, because research has shown that if self-management techniques are sufficiently utilized by patients, then this can reduce their symptoms and improve their overall functioning [90], which, in turn, helps to prevent a subsequent relapse.

Limitations of current relapse prevention programs

It is important to note that there are specific limitations with current psychological relapse prevention programs. First, there are no relapse prevention programs currently available that target both anxiety and depressive disorders, which is problematic given that these disorders are often comorbid and people often relapse into another disorder (i.e., from an anxiety disorder into a depressive disorder, and vice versa). Second, the programs are currently not specifically tailored to patients' individual preferences, which has been shown to increase acceptance and adherence towards the program, as well as it subsequent effectiveness [91]. Third, many programs continue to be provided solely in outpatient mental health care, despite the fact that primary care facilities are increasingly supposed to provide relapse prevention programs, with MHPs

taking a leading role. Fourth, to the best of our knowledge, no blended interventions for patients in remission from anxiety and depression are currently available, which once again is problematic insofar as this provides a promising approach.

GET READY program

In order to address these aforesaid limitations of current programs, we developed the GET READY relapse prevention program. GET READY stands for Guided E-healTh for RElapse prevention in Anxiety and Depression. The program focuses on patients who are in remission from anxiety disorders and/or depressive disorders. Patients' preferences were explicitly taken into account through the inclusion of regular FTF contact with professionals, flexible time investment from patients, and a personalized relapse prevention plan [72]. Furthermore, the relapse prevention program was specifically developed to be provided in primary care by MHPs. Alongside FTF contact between patients and MHPs, in which relapse prevention was discussed and a personalized relapse prevention plan was developed, the program also consisted of online E-health modules that were designed to encourage the use of self-management strategies. Finally, the program offered a mood and anxiety diary to patients, which enabled them to monitor their symptoms.

Aims and outline of the thesis

This thesis focuses on relapse prevention amongst patients with remitted anxiety and depressive disorders. Hence, it aims to contribute towards improving the quality of life for these patients. First, we conduct a systematic review and meta-analysis of extant psychological relapse prevention interventions, in order to assess their effectiveness for patients with remitted anxiety or depressive disorders. Next, we evaluate the newly developed GET READY relapse prevention program within several empirical studies. Finally, given our focus on the use of self-management strategies, we psychometrically test a newly developed self-management questionnaire. The thesis is structured as follows.

Chapter 2 presents the findings of our systematic review and meta-analysis of whether psychological relapse prevention interventions are effective in preventing relapse. Pubmed, PsycINFO and Embase were systematically searched for RCTs (n = 40) including patients with remitted anxiety or depressive disorders, who either received a psychological intervention to prevent relapse, or received treatment as usual. In addition, studies were included that compared psychological interventions in addition to M-ADM to M-ADM only. **Chapter 3** delineates the study protocol of the GET READY study. It describes the development, implementation and evaluation of the GET READY program. For the overall research project, a mixed-method study design was chosen to provide insight into patients' usage of the program (quantitative), the

association between usage intensity and the course of symptoms (quantitative), as well as the perspectives of users (both patients and MHPs) of the program (qualitative). **Chapter 4** presents the results of the quantitative evaluation of the GET READY program. A total of 113 patients participated in the GET READY study, by completing four questionnaires over the course of 9 months. The GET READY program was implemented by 54 MHPs across the Netherlands. Patients had access to the online modules and had FTF meetings with MHPs. Insight was gained into the usage intensity, course of symptoms, and the association between usage intensity and course of symptoms. **Chapter 5** reports the results of the qualitative evaluation of the GET READY program. This study aimed to shed light on both the perspectives of users (both patients and MHPs) of the GET READY program, and those factors that influenced the use and implementation of the GET READY program in general practice. Through conducting individual semi-structured interviews with pairs of patients and MHPs (N=26) and two additional focus groups, we gained insight into patients and MHPs' experiences and perspectives. In **Chapter 6**, the results of the exploratory and confirmatory factor analysis of the 'Assessment of Self-management in Anxiety and Depression' questionnaire (ASAD) are described. This questionnaire examined the self-management strategies utilized by 171 patients with (chronic or partially remitted) anxiety and depressive disorders, in order to examine the underlying factor structure and psychometric properties. Finally, **Chapter 7** provides a summary of the main findings of the research, before proceeding to discuss the results in context of extant literature and describe the implications for future research and clinical practice.

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. Washington, DC: Author; 2000.

2. World Health Organization. Investing in treatment for depression and anxiety leads to fourfold return [Internet]. 2016 [cited 2017 Jun 27]. Available from: http://www.who.int/mediacentre/news/releases/2016/depression-anxiety-treatment/en/

3. de Graaf R, ten Have M, van Gool C, van Dorsselaer S. Prevalence of mental disorders and trends from 1996 to 2009. Results from the Netherlands Mental Health Survey and Incidence Study-2. Soc Psychiatry Psychiatr Epidemiol [Internet] 2012 Feb 1;47(2):203–213. PMID:21197531

4. Alonso J, Angermeyer MCC, Bernert S, Bruffaerts R, Brugha TSS, Bryson H, Girolamo G, Graaf R, Demyttenaere K, Gasquet I, Haro JMM, Katz SJJ, Kessler RCC, Kovess V, Lepine JPP, Ormel J, Polidori G, Russo LJJ, Vilagut G, Almansa J, Arbabzadeh-Bouchez S, Autonell J, Bernal M, Buist-Bouwman MAA, Codony M, Domingo-Salvany A, Ferrer M, Joo SSS, Martinez-Alonso M, Matschinger H, Mazzi F, Morgan Z, Morosini P, Palacin C, Romera B, Taub N, Vollebergh WAAM. Disability and quality of life impact of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. Acta Psychiatr Scand [Internet] 2004 Jun;109(s420):38–46. PMID:15128386

5. Brenes GA, Penninx BWJH, Judd PH, Rockwell E, Sewell DD, Wetherell JL. Anxiety, depression and disability across the lifespan. Aging Ment Health [Internet] 2008;12(1):158–163. PMID:18297491

6. Buist-Bouwman MA, De Graaf R, Vollebergh WAM, Alonso J, Bruffaerts R, Ormel J, Angermeyer M, Bernert S, Brugha TS, De Girolamo G, Demyttenaere K, Gasquet I, Haro JM, Katz SJ, Kessler RC, Kovess V, Lépine JP, Polidori G, Vilagut G. Functional disability of mental disorders and comparison with physical disorders: A study among the general population of six European countries. Acta Psychiatr Scand 2006;113(6):492–500. PMID:16677226

7. Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications a systematic review and meta-analysis. JAMA Psychiatry 2015;72(4):334–341. PMID:25671328

8. Murphy JM, Horton NJ, Laird NM, Monson RR, Sobol AM, Leighton AH. Anxiety and depression: A 40-year perspective on relationships regarding prevalence, distribution, and comorbidity. Acta Psychiatr Scand 2004;109(5):355–375. PMID:15049772

9. Lamers F, Van Oppen P, Comijs HC, Smit JH, Spinhoven P, Van Balkom AJLM, Nolen WA, Zitman FG, Beekman ATF, Penninx BWJH. Comorbidity patterns of anxiety and depressive disorders in a large cohort study: The Netherlands Study of Depression and Anxiety (NESDA). J Clin Psychiatry 2011;72(3):342–348. PMID:21294994

10. Hendriks SM, Spijker J, Licht CMM, Hardeveld F, De Graaf R, Batelaan NM, Penninx BWJH, Beekman ATF. Long-term work disability and absenteeism in anxiety and depressive disorders. J Affect Disord [Internet] Elsevier; 2015;178:121–130. PMID:25805404

11. Penninx BWJH, Nolen WA, Lamers F, Zitman FG, Smit JH, Spinhoven P, Cuijpers P, de Jong PJ, van Marwijk HWJ, der Meer K van, Verhaak P, Laurant MGH, de Graaf R, Hoogendijk WJ, der Wee N van, Ormel J, van Dyck R, Beekman ATF. Two-year course of depressive and anxiety disorders: Results from the Netherlands Study of Depression and Anxiety (NESDA). J Affect Disord [Internet] 2011 Sep [cited 2017 Aug 9];133(1–2):76–85. [doi: 10.1016/j.jad.2011.03.027]

12. Brown GW, Moran P. Clinical and psychosocial origins of chronic depressive episodes. I: A community survey. Br J Psychiatry 1994;165(OCT.):447–456. PMID:7804658

13. Hoencamp E, Haffmans PMJ, Griens AMGF, Huijbrechts IPAM, Heycop ten Ham BF. A 3.5-year naturalistic follow-up study of depressed out-patients. J Affect Disord 2001;66(2–3):267–271. PMID:11578681

14. Scholten WD, Batelaan NM, Penninx BWJH, Balkom AJLM van, Smit JH, Schoevers RA, Oppen P van. Diagnostic instability of recurrence and the impact on recurrence rates in depressive and anxiety disorders. J Affect Disord [Internet] Elsevier; 2016 May [cited 2016 Jul 7];195:185–190. PMID:26896812

15. Bruce SE, Yonkers KA, Otto MW, Eisen JL, Weisberg RB, Pagano M, Shea MT, Keller MB. Influence of Psychiatric Comorbidity on Recovery and Recurrence in Generalized Anxiety Disorder, Social Phobia, and Panic Disorder: A 12-Year Prospective Study. Am J Psychiatry [Internet] American Psychiatric Publishing; 2005 Jun 1 [cited 2017 Jun 27];162(6):1179–1187. [doi: 10.1176/appi.ajp.162.6.1179]

16. Scholten WD, Batelaan NM, Van Balkom AJ, Penninx BWJH, Smit JH, Van Oppen P. Recurrence of anxiety disorders and its predictors. J Affect Disord Elsevier; 2013;147(1–3):180–185. PMID:23218248

17. Taylor JH, Jakubovski E, Bloch MH. Predictors of anxiety recurrence in the Coordinated Anxiety Learning and Management (CALM) trial. J Psychiatr Res [Internet] Elsevier Ltd; 2015 Jun [cited 2017 Aug 8];65:154–165. PMID:25896121

18. Conradi HJ, Bos EH, Kamphuis JH, de Jonge P, Gustavsson A, Svensson M, Jacobi F, Allgulander C, Alonso J, Beghi E, Dodel R, Ekman M, Faravelli C, Fratiglioni L, Gannon B, Jones DH, Jennum P, Jordanova A, Jönsson L, Karampampa K, Knapp M, Kobelt G, Kurth T, Lieb R, Linde M, Ljungcrantz C, Maercker A, Melin B, Moscarelli M, Musayev A, Norwood F, Preisig M, Pugliatti M, Rehm J, Salvador-Carulla L, Schlehofer B, Simon R, Steinhausen H-C, Stovner LJ, Vallat J-M, den Bergh P Van, van Os J, Vos P, Xu W, Wittchen H-U, Jönsson B, Olesen J. The ten-year course of depression in primary care and long-term effects of psychoeducation, psychiatric consultation and cognitive behavioral therapy. J Affect Disord [Internet] Elsevier B.V.; 2017 Oct [cited 2017 Aug 2];217(November 2016):174–182. [doi: 10.1016/j.jad.2017.03.064]

19. Gopinath S, Katon WJ, Russo JE, Ludman EJ. Clinical factors associated with relapse in primary care patients with chronic or recurrent depression. J Affect Disord 2007;101(1–3):57–63. PMID:17156852

20. Hardeveld F, Spijker J, De Graaf R, Hendriks SM, Licht CMM, Nolen WA, Penninx BWJH, Beekman ATF. Recurrence of major depressive disorder across different treatment settings: Results from the NESDA study. J Affect Disord [Internet] Elsevier; 2013 May [cited 2016 Jul 6];147(1–3):225–231. PMID:23218899

21. Yiend J, Paykel E, Merritt R, Lester K, Doll H, Burns T. Long term outcome of primary care depression. J Affect Disord [Internet] Elsevier B.V.; 2009 Nov [cited 2017 Aug 7];118(1–3):79–86. PMID:19246103

22. Paykel ES. Partial remission, residual symptoms, and relapse in depression. Dialogues Clin Neurosci 2008;10(4):431–437. PMID:19170400

23. Pintor L, Gastó C, Navarro V, Torres X, Fañanas L. Relapse of major depression after complete and partial remission during a 2-year follow-up. J Affect Disord 2003;73(3):237–244. PMID:12547292

24. Calkins AW, Otto MW, Cohen LS, Soares CN, Alison F, Hearon BA, Harlow BL. Psychosocial predictors of the onset of anxiety disorders in women: Results from a prospective 3-year longitudinal study. Anxiety 2009;23(8):1165–1169. [doi: 10.1016/j.janxdis.2009.07.022.Psychosocial]

25. Bockting CLH, Spinhoven P, Koeter MWJ, Wouters LF, Schene AH. Prediction of Recurrence in Recurrent Depression and the Influence of Consecutive Episodes on Vulnerability for Depression: A 2-Year Prospective Study. J Clin Psychiatry [Internet] [Physicians Postgraduate Press]; 2006 [cited 2017 Aug 10];67(5):747–755. Available from: http://www.psychiatrist.com/jcp/article/Pages/2006/v67n05/v67n0508.aspx

26. Hardeveld F, Spijker J, De Graaf R, Nolen WA, Beekman ATF. Recurrence of major depressive disorder and its predictors in the general population: results from The Netherlands Mental Health Survey and Incidence Study (NEMESIS). Psychol Med [Internet] Cambridge University Press; 2013 Jan 31 [cited 2016 Jul 7];43(1):39–48. PMID:23111147

27. Frank E, Prien RF, Jarrett RB, Keller MB, Kupfer DJ, Lavori PW, Rush AJ, Weissman MM. Conceptualization and Rationale for Consensus Definitions of Terms in Major Depressive Disorder. Arch Gen Psychiatry [Internet] 1991 Sep 1;48(9):851. PMID:1929776

28. Bockting CLH, Spinhoven P, Wouters LF, Koeter MWJ, Schene AH. Long-Term Effects of Preventive Cognitive Therapy in Recurrent Depression. J Clin Psychiatry [Internet] 2009 Dec 15;70(12):1621–1628. [doi: 10.4088/JCP.08m04784blu]

29. Jarrett RB, Kraft D, Doyle J, Foster BM, Eaves GG, Silver PC. Preventing Recurrent Depression Using Cognitive Therapy With and Without a Continuation Phase. Arch Gen Psychiatry [Internet] 2001 Apr 1;58(4):381. [doi: 10.1001/archpsyc.58.4.381]

30. Teasdale JD, Segal Z V., Williams JMG, Ridgeway VA, Soulsby JM, Lau MA. Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. J Consult Clin Psychol [Internet] 2000;68(4):615–623. [doi: 10.1037/0022-006X.68.4.615]

31. Bockting CLH, Klein NS, Elgersma HJ, van Rijsbergen GD, Slofstra C, Ormel J, Buskens E, Dekker J, de Jong PJ, Nolen WA, Schene AH, Hollon SD, Burger H. Effectiveness of preventive cognitive therapy while tapering antidepressants versus maintenance antidepressant treatment versus their combination in prevention of depressive relapse or recurrence (DRD study): a three-group, multicentre, randomised control. The Lancet Psychiatry [Internet] Elsevier Ltd; 2018 May;5(5):401–410. [doi: 10.1016/S2215-0366(18)30100-7]

32. Klein NS, Kok GD, Burger H, van Valen E, Riper H, Cuijpers P, Dekker J, Smit F, van der Heiden C, Bockting CLH. No Sustainable Effects of an Internet-Based Relapse Prevention Program over 24 Months in Recurrent Depression: Primary Outcomes of a Randomized Controlled Trial. Psychother Psychosom [Internet] 2018;87(1):55–57. PMID:29306953

33. Reynolds CF, Dew MA, Pollock BG, Mulsant BH, Frank E, Miller MD, Houck PR, Mazumdar S, Butters MA, Stack JA, Schlernitzauer MA, Whyte EM, Gildengers A, Karp J, Lenze E, Szanto K, Bensasi S, Kupfer DJ. Maintenance Treatment of Major Depression in Old Age. N Engl J Med [Internet] 2006 Mar 16;354(11):1130–1138. [doi: 10.1056/NEJMoa052619]

34. de Jonge M, Bockting CLH, Kikkert MJ, van Dijk MK, van Schaik DJF, Peen J, Hollon SD, Dekker JJM. Preventive cognitive therapy versus care as usual in cognitive behavioral therapy responders: A randomized controlled trial. J Consult Clin Psychol [Internet] 2019 Jun;87(6):521–529. [doi: 10.1037/ccp0000395]

35. Godfrin KA, van Heeringen C. The effects of mindfulness-based cognitive therapy on recurrence of depressive episodes, mental health and quality of life: A randomized controlled study. Behav Res Ther [Internet] Elsevier Ltd; 2010;48(8):738–746. [doi: 10.1016/j.brat.2010.04.006]

36. Clarke S, Oades LG, Crowe TP. Recovery in mental health: A movement towards well-being and meaning in contrast to an avoidance of symptoms. Psychiatr Rehabil J [Internet] 2012;35(4):297–304. [doi: 10.2975/35.4.2012.297.304]

37. Borges S, Chen Y-F, Laughren TP, Temple R, Patel HD, David PA, Mathis M, Unger E, Yang P, Khin NA. Review of Maintenance Trials for Major Depressive Disorder. J Clin Psychiatry [Internet] 2014 Mar 15;75(03):205–214. [doi: 10.4088/JCP.13r08722]

38. Bandelow B, Sagebiel A, Belz M, Görlich Y, Michaelis S, Wedekind D. Enduring effects of psychological treatments for anxiety disorders: meta-analysis of follow-up studies. Br J Psychiatry [Internet] Cambridge University Press; 2018 Jun 30;212(6):333–338. [doi: 10.1192/bjp.2018.49]

39. Cuijpers P. The Challenges of Improving Treatments for Depression. JAMA 2018 Dec;320(24):2529. [doi: 10.1001/jama.2018.17824]

40. Balkom A van, Vliet I van, Emmelkamp P, Bockting C, Spijker J, Hermens M, Meeuwissen J, namens de Werkgroep Multidisciplinaire richtlijnontwikkeling Angststoornissen/Depressie. Multidisciplinaire richtlijn Angststoornissen (3e revisie) [Internet]. Utrecht; 2013. Available from: https://assets-sites.trimbos.nl/docs/cc5b0f4e-9398-452d-8792-1453a38bf0a8.pdf

41. National Institute for Health and Care Excellence. The Nice Guideline on the Treatment and Management of Depression in Adults (updated edition) [Internet]. 2010. PMID:22132433

42. National Institute for Health and Care Excellence. Generalised anxiety disorder and panic disorder in adults: management [Internet]. 2011. Available from: www.nice.org.uk/guidance/cg113

43. Spijker J, Bockting C, Meeuwissen J, Vliet I van, Emmelkamp P, Hermens M, Balkom A van, namens de Werkgroep Multidisciplinaire richtlijnontwikkeling Angststoornissen/Depressie. Multidisciplinaire richtlijn Depressie (3e revisie). 2013.

44. Butler A, Chapman J, Forman E, Beck A. The empirical status of cognitive-behavioral therapy: A review of meta-analyses. Clin Psychol Rev [Internet] 2006 Jan;26(1):17–31. PMID:16199119

45. Norton PJ, Price EC. A Meta-Analytic Review of Adult Cognitive-Behavioral Treatment Outcome Across the Anxiety Disorders. J Nerv Ment Dis [Internet] 2007 Jun;195(6):521–531. [doi: 10.1097/01.nmd.0000253843.70149.9a]

46. Cuijpers P, Sijbrandij M, Koole SL, Andersson G, Beekman AT, Reynolds CF. The efficacy of psychotherapy and pharmacotherapy in treating depressive and anxiety disorders: a meta-analysis of direct comparisons. World Psychiatry [Internet] 2013 Jun;12(2):137–148. [doi: 10.1002/wps.20038]

47. Pampallona S, Bollini P, Tibaldi G, Kupelnick B, Munizza C. Combined Pharmacotherapy and Psychological Treatment for Depression. Arch Gen Psychiatry [Internet] 2004 Jul 1;61(7):714. [doi: 10.1001/archpsyc.61.7.714]

48. McHugh RK, Whitton SW, Peckham AD, Welge JA, Otto MW. Patient Preference for Psychological vs Pharmacologic Treatment of Psychiatric Disorders. J Clin Psychiatry [Internet] 2013 Jun 15;74(06):595–602. [doi: 10.4088/JCP.12r07757]

49. van Schaik DJF, Klijn AFJ, van Hout HPJ, van Marwijk HWJ, Beekman ATF, de Haan M, van Dyck R. Patients' preferences in the treatment of depressive disorder in primary care. Gen Hosp Psychiatry [Internet] 2004 May;26(3):184–189. [doi: 10.1016/j.genhosppsych.2003.12.001]

50. Angelo FN, Miller HE, Zoellner LA, Feeny NC. "I Need to Talk About It": A Qualitative Analysis of Trauma-Exposed Women's Reasons for Treatment Choice. Behav Ther 2008;39(1):13–21. PMID:18328866

51. Andersson G, Carlbring P, Ljótsson B, Hedman E. Guided Internet-Based CBT for Common Mental Disorders. J Contemp Psychother [Internet] 2013 Dec 21;43(4):223–233. [doi: 10.1007/s10879-013-9237-9]

52. Proudfoot J, Klein B, Barak A, Carlbring P, Cuijpers P, Lange A, Ritterband L, Andersson G. Establishing guidelines for executing and reporting internet intervention research. Cogn Behav Ther 2011;40(2):82–97. PMID:25155812

53. Howell CA. Preventing depression relapse: a primary care approach. Prim Care Ment Heal [Internet] 2004;2(3/4):151–156. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=106504004&site=ehost-live

54. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder [Internet]. 2010. Available from: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf

55. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Obsessive-Compulsive Disorder [Internet]. 2007. Available from: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/ocd.pdf

56. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Panic Disorder [Internet]. 2009. Available from: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/panicdisorder.pdf

57. Batelaan NM, Bosman RC, Muntingh A, Scholten WD, Huijbregts KM, van Balkom AJLM. Risk of relapse after antidepressant discontinuation in anxiety disorders, obsessive-compulsive disorder, and post-traumatic stress disorder: systematic review and meta-analysis of relapse prevention trials. BMJ [Internet] 2017;358. [doi: 10.1136/bmj.j3927]

58. Geddes JR, Carney SM, Davies C, Furukawa TA, Kupfer DJ, Frank E, Goodwin GM. Relapse prevention with antidepressant drug treatment in depressive disorders: a systematic review. Lancet [Internet] Elsevier; 2003 Feb 22 [cited 2016 Dec 2];361(9358):653–661. PMID:12606176

59. Sim K, Lau WK, Sim J, Sum MY, Baldessarini RJ. Prevention of Relapse and Recurrence in Adults with Major Depressive Disorder: Systematic Review and Meta-Analyses of Controlled Trials. Int J Neuropsychopharmacol [Internet] 2016 Feb;19(2):pyv076. PMID:26152228

60. Bet PM, Hugtenburg JG, Penninx BWJH, Hoogendijk WJG. Side effects of antidepressants during long-term use in a naturalistic setting. Eur Neuropsychopharmacol Elsevier; 2013;23(11):1443–1451. PMID:23726508

61. Ten Doesschate MC, Bockting CLH, Schene AH. Adherence to continuation and maintenance antidepressant use in recurrent depression. J Affect Disord [Internet] Elsevier B.V.; 2009;115(1–2):167–170. [doi: 10.1016/j.jad.2008.07.011]

62. Verbeek-Heida PM, Mathot EF. Better safe than sorry — why patients prefer to stop using selective serotonin reuptake inhibitor (SSRI) antidepressants but are afraid to do so: results of a qualitative study. Chronic Illn [Internet] 2006 Jun 29;2(2):133–142. [doi: 10.1177/17423953060020020801]

63. Biesheuvel-Leliefeld KEM, Kok GD, Bockting CLH, Cuijpers P, Hollon SD, van Marwijk HWJ, Smit F. Effectiveness of psychological interventions in preventing recurrence of depressive disorder: Meta-analysis and meta-regression. J Affect Disord [Internet] Elsevier; 2015 Mar 15 [cited 2016 Jul 7];174:400–410. PMID:25553400

64. Holländare F, Johnsson S, Randestad M, Tillfors M, Carlbring P, Andersson G, Engström I. Randomized trial of Internet-based relapse prevention for partially remitted depression. Acta Psychiatr Scand [Internet] Blackwell Publishing Ltd; 2011 Oct [cited 2017 May 30];124(4):285–294. [doi: 10.1111/j.1600-0447.2011.01698.x]

65. Kordy H, Wolf M, Aulich K, Bürgy M, Hegerl U, Hüsing J, Puschner B, Rummel-Kluge C, Vedder H, Backenstrass M. Internet-Delivered Disease Management for Recurrent Depression: A Multicenter Randomized Controlled Trial. Psychother Psychosom 2016;85(2):91–98. [doi: 10.1159/000441951]

66. Zwerenz R, Becker J, Knickenberg RJ, Siepmann M, Hagen K, Beutel ME. Online Self-Help as an Add-On to Inpatient Psychotherapy: Efficacy of a New Blended Treatment Approach. Psychother Psychosom 2017;86(6):341–350. [doi: 10.1159/000481177]

67. Kraft S, Wolf M, Klein T, Becker T, Bauer S, Puschner B. Text Message Feedback to Support Mindfulness Practice in People With Depressive Symptoms: A Pilot Randomized Controlled Trial. JMIR mHealth uHealth [Internet] 2017 May 2;5(5):e59. [doi: 10.2196/mhealth.7095]

68. Hennemann S, Farnsteiner S, Sander L. Internet- and mobile-based aftercare and relapse prevention in mental disorders: A systematic review and recommendations for future research. Internet Interv [Internet] Elsevier; 2018;14(August):1–17. [doi: 10.1016/j.invent.2018.09.001]

69. Beatty L, Binnion C. A Systematic Review of Predictors of, and Reasons for, Adherence to Online Psychological Interventions. Int J Behav Med 2016 Dec;23(6):776–794. [doi: 10.1007/s12529-016-9556-9]

70. Eysenbach G. The law of attrition. J Med Internet Res [Internet] 2005 [cited 2017 May 12];7(1):1–11. PMID:15829473

71. Kelders SM, Bohlmeijer ET, Van Gemert-Pijnen JE. Participants, Usage, and Use Patterns of a Web-Based Intervention for the Prevention of Depression Within a Randomized Controlled Trial. J Med Internet Res [Internet] Journal of Medical Internet Research; 2013 Aug 20 [cited 2017 May 10];15(8):e172. PMID:23963284

72. Muntingh ADT, Hoogendoorn AW, Van Schaik DJF, Van Straten A, Stolk EA, Van Balkom AJLM, Batelaan NM. Patient preferences for a guided self-help programme to prevent relapse in anxiety or depression: A discrete choice experiment. Eisenbarth H, editor. PLoS One [Internet] 2019 Jul 18;14(7):e0219588. [doi: 10.1371/journal.pone.0219588]

73. Nuijen J, Boerema I, Hermens M, Sinnema H, Veerbeek M, van Wijngaarden B, van Bon-Martens M, Boon B, Franx G, Ruiter M, van Splunteren P, Verhaak P. Versterking van de GGZ in de huisartsenpraktijk [Internet]. Trimbos Instituut; 2014. Available from: https://assets.trimbos.nl/docs/ef71d19b-a46b-4bd1-b7e0-f35f9f52e5a5.pdfISBN:9789052537535

74. Ministerie van Volksgezondheid Welzijn & Sport. Bestuurlijk akkoord toekomst GGZ 2013-2014 [Internet]. 2012. p. 1–19. Available from: www.vgct.nl/stream/bestuurlijk-akkoord-toekomst-ggz-2013-2014.pdf?

75. National Counsel Mental Health Professionals. Functie- & competentieprofiel "Praktijkondersteuner huisarts GGZ" 2020 [Job and competence profile "Mental Health Professional" 2020] [Internet]. 2020. Available from: https://www.poh-ggz.nl/wp-content/uploads/2020/03/Definitief-Functie-en-competentieprofiel-POH-GGZ-2020-versie-1.0-04032020.pdf

76. Collins PY, Patel V, Joestl SS, March D, Insel TR, Daar AS, Bordin IA, Costello EJ, Durkin M, Fairburn C, Glass RI, Hall W, Huang Y, Hyman SE, Jamison K, Kaaya S, Kapur S, Kleinman A, Ogunniyi A, Otero-Ojeda A, Poo M-M, Ravindranath V, Sahakian BJ, Saxena S, Singer PA, Stein DJ, Anderson W, Dhansay MA, Ewart W, Phillips A, Shurin S, Walport M. Grand challenges in global mental health. Nature [Internet] 2011 Jul 6;475(7354):27–30. [doi: 10.1038/475027a]

77. Bodenheimer T. Improving Primary Care for Patients With Chronic Illness. JAMA [Internet] 2002 Oct 9;288(14):1775. [doi: 10.1001/jama.288.14.1775]

78. Grypdonck M. Het leven boven de ziekte uittillen. Leiden: Spruyt Van Mantgem en de Does; 1999.

79. Lorig KR, Holman HR. Self-Management Education: History, Definition, Outcomes, and Mechanisms. Ann Behav Med 2003;26(1):1–7.

80. Lorig K. Self-management of chronic illness: A model for the future. Gener XVII 1993;3:11–14.

81. Barlow J, Wright C, Sheasby J, Turner A, Hainsworth J. Self-management approaches for people with chronic conditions: A review. Patient Educ Couns 2002;48(2):177–187. PMID:12401421

82. Casey B, Webb M. Imaging Journeys of Recovery and Learning: A Participatory Arts-Based Inquiry. Qual Health Res [Internet] 2019 May 19;29(6):833–845. [doi: 10.1177/1049732318804832]

83. Happell B. Determining the effectiveness of mental health services from a consumer perspective: Part 1: Enhancing recovery. Int J Ment Health Nurs [Internet] 2008 Apr;17(2):116–122. [doi: 10.1111/j.1447-0349.2008.00519.x]

84. Deegan PE. The importance of personal medicine: A qualitative study of resilience in people with psychiatric disabilities. Scand J Public Health [Internet] 2005 Oct 25;33(66_suppl):29–35. [doi: 10.1080/14034950510033345]

85. Sterling EW, von Esenwein SA, Tucker S, Fricks L, Druss BG. Integrating Wellness, Recovery, and Self-management for Mental Health Consumers. Community Ment Health J [Internet] 2010 Apr 23;46(2):130–138. [doi: 10.1007/s10597-009-9276-6]

86. Young SL, Ensing DS. Exploring recovery from the perspective of people with psychiatric disabilities. Psychiatr Rehabil J [Internet] 1999;22(3):219–231. [doi: 10.1037/h0095240]

87. Russell SJ, Browne JL. Staying well with bipolar disorder. Aust N Z J Psychiatry 2005 Mar;39(3):187–193. [doi: 10.1111/j.1440-1614.2005.01542.x]

88. Suto M, Murray G, Hale S, Amari E, Michalak EE. What works for people with bipolar disorder? Tips from the experts. J Affect Disord [Internet] 2010 Jul;124(1–2):76–84. [doi: 10.1016/j.jad.2009.11.004]

89. Fredericks S, Lapum J, Lo J. Anxiety, Depression, and Self-Management: A Systematic Review. Clin Nurs Res 2012;21(4):411–430. PMID:22473273

90. Levitt A, Mueser K, DeGenova J, Lorenzo J, Bradford-Watt D, Barbosa A, Karlin M, Chernick M. Randomized Controlled Trial of Illness Management and Recovery in Multiple-Unit Supportive Housing. Psychiatr Serv [Internet] 2009 Dec 1;60(12). [doi: 10.1176/appi.ps.60.12.1629]

91. Cuijpers P, van Straten A, Warmerdam L, van Rooy MJ. Recruiting participants for interventions to prevent the onset of depressive disorders: Possible ways to increase participation rates. BMC Health Serv Res [Internet] BioMed Central; 2010 Dec 25 [cited 2016 Jul 6];10(1):181. PMID:20579332

3

THE GET READY RELAPSE PREVENTION PROGRAM FOR ANXIETY AND DEPRESSION: A MIXED-METHODS STUDY PROTOCOL

PUBLISHED IN BMC PSYCHIATRY 2019, 19:1–11

Esther Krijnen-de Bruin, Anna D.T. Muntingh, Adriaan W. Hoogendoorn, Annemieke van Straten, Neeltje M. Batelaan, Otto R. Maarsingh, Anton J.L.M. van Balkom, Berno van Meijel

Abstract

Background

Since anxiety and depressive disorders often recur, self-management competencies are crucial for improving the long-term course of anxiety and depressive disorders. However, few relapse prevention programs are available that focus on improving self-management. E-health combined with personal contact with a mental health professional in general practice might be a promising approach for relapse prevention. In this protocol, the GET READY (Guided E-healTh for RElapse prevention in Anxiety and Depression) study will be described in which a relapse prevention program is developed, implemented and evaluated. The aim of the study is to determine patients' usage of the program and the associated course of their symptoms, to examine barriers and facilitators of implementation, and to assess patients' satisfaction with the program.

Methods

Participants are discharged from mental healthcare services, and are in complete or partial remission. They receive access to an E-health platform, combined with regular contact with a mental health professional in general practices. Online questionnaires will be completed at baseline and after 3, 6 and 9 months. Also, semi-structured qualitative individual interviews and focus group interviews will be conducted with patients and mental health professionals.

Discussion

This mixed-methods observational cohort study will provide insights into the use of a relapse prevention program in relation to the occurrence of symptoms, as well as in its implementation and evaluation. Using the results of this study, the relapse prevention program can be adapted in accordance with the needs of patients and mental health professionals. If this program is shown to be acceptable, a randomized controlled trial may be conducted to test its efficacy.

Trial registration

Retrospectively registered in the Netherlands Trial Register (NTR7574; 25 October 2018).

Keywords: Anxiety, Depression, Recurrence, Relapse prevention, Self-management, E-health, Mixed-methods research, Study protocol

Background

The course of anxiety and depressive disorders is often unfavorable, with chronic [1,2] or intermittent episodes of anxiety and/or depression [3] and a high risk of relapse. Percentages of 22-58 for anxiety [1,3–5] and 27-77 for depression [6–9] have been reported as relapse rates with higher rates in longer follow-up studies [1,6]. Furthermore, patients often achieve partial remission instead of full remission, and have residual symptoms [10]. The risk of relapse is higher for patients with a partial remission when compared to patients with full remission [11]. Moreover, even if remission is achieved, patients with residual symptoms have a three times higher risk of relapse than patients without residual symptoms [12]. Since anxiety and depression are often recurrent and patients remain vulnerable, these disorders should be approached as chronic diseases. Chronic care models, previously developed for other chronic diseases such as diabetes [13], can be applied. One essential element of chronic care models is the support of self-management [14]. Lorig [15] defined self-management as "learning and practicing skills necessary to carry on an active and emotionally satisfying life in the face of a chronic condition" (p.11). Self-management for anxiety and depression focuses on recovery and stabilization of symptoms, prevention of relapse, and improving functioning and quality of life [16,17]. People with recurrent anxiety and depression should be supported in performing self-management strategies.

One of the major challenges in the management of anxiety and depression symptoms is the prevention of relapse [18]. In their meta-analysis, Biesheuvel-Leliefeld et al. [19] concluded that relapse prevention strategies such as cognitive therapy or mindfulness-based cognitive therapy are effective in reducing relapse of depression. However, few relapse prevention programs are available for this patient group of depressed patients. In an empirical study from the same authors, the efficacy of a self-help preventive cognitive therapy combined with weekly telephone guidance in preventing depression was examined [20]. They demonstrated that this was significantly more effective than care as usual. To date, little is known about the efficacy of relapse prevention strategies for patients with anxiety disorders [21]. The fact that depression and anxiety are often comorbid, and relapse into another disorder frequently occurs (from anxiety to depression and vice versa), highlights the need to target both anxiety and depression in a single relapse prevention program.

Over the past two decades, it has been suggested that primary healthcare facilities should play a vital role in the long-term treatment of patients with anxiety and depression [22,23]. In the Netherlands, primary mental healthcare is usually provided by a mental health professional (MHP), working in a general practice and reporting to the general practitioner (GP). This MHP could be a (community) mental health nurse, a social worker or a (junior) psychologist. Since general practices are always located

close to where patients live, and the services are freely available, the MHPs are easily approachable. They can play a pivotal role in the monitoring of symptoms and the support of self-management, and therefore in the prevention of relapse. However, many MHPs are unfamiliar with relapse prevention interventions, including the use of supporting tools to monitor symptoms [24]. To encourage general practices to offer structured relapse prevention, while also supplying supporting tools for MHPs, the use of E-health could offer a solution. E-health tools can be easily tailored to the needs and preferences of patients, which is important for the tools' acceptability and effectiveness. Most (92%) of the MHPs in the Netherlands are already familiar with E-health [25]. If the use of E-health is embedded in personal contact with a MHP, it is likely to be more effective [26].

We therefore developed a relapse prevention program that can be offered in general practices by MHPs to patients with (partially) remitted anxiety or depression. This program aims to support self-management skills and provides tools for monitoring symptoms. The E-health modules can be individually tailored to the needs of patients, and is combined with regular contact with the MHP. The aim of the present study is to implement and evaluate this guided self-help online relapse prevention program for patients who are completely or partially in remission from anxiety and/or depressive disorders, and who previously received treatment in mental healthcare services. This study will provide insight into: 1) the extent to which patients make use of the relapse prevention program; 2) the factors that influence the use of the program; 3) the association between usage intensity and course of symptoms; 4) barriers and facilitators in implementation of the program; and 5) how patients evaluate the program.

Methods/design

The methods section is divided into three parts: 1) the development of the relapse prevention program; 2) the content of the relapse prevention program; and 3) the study design.

1. Development of the relapse prevention program

The program was developed using input from different studies. Muntingh et al. [27] examined preferences of patients regarding relapse prevention and revealed that patients prefer a relapse prevention program that is effective but not too time-consuming, taking up a maximum of one hour a week. Using a personal relapse prevention plan, in combination with regular contact with a professional (about once every three months)

was the most preferred relapse prevention strategy. The use of a relapse prevention plan as a practical aid for the early recognition and management of potential triggers and signs that indicate relapse is in accordance with the NICE guidelines [28]. According to several studies, relapse prevention should be flexible and tailored to the patient's individual situation and preferences in order to increase acceptability [29,30]. Our online program therefore consists of a personal relapse prevention plan and flexible E-health modules aiming at the promotion of self-management skills. The MHP can individually tailor the program in conjunction with the patient.

The initial format and underpinning of the relapse prevention program was discussed with academic experts, a panel of eight patients, and four MHPs. The content of the E-health modules was written by two expert psychologists, based on the principles of cognitive behavioral therapy (CBT). This therapy is effective in the treatment of anxiety and depression [31], and in preventing relapse in depression [19]. Some optional modules were added at the request of patients, such as healthy food and physical exercise. These modules contain psychoeducation and the ability to plan healthy behavior, with the aim of increasing physical and mental health. Preliminary versions of the E-health modules were reviewed by the members of the research team and E-health developers. Also, the patient panel reviewed the modules and provided feedback. This feedback was thoroughly discussed and processed by the researchers. For example: more lengthy text parts were placed in 'read more' menus, an overview page was created, and the possibility to print text was added. Finally, the adjusted content was released to the online platform.

2. Content of relapse prevention program

Online program

The online program consists of three basic components and 12 optional modules (see Figure 1). The three basic components are: 'Relapse psychoeducation', 'Relapse prevention plan', and 'Mood & anxiety diary'. As soon as the patient completes the module 'Relapse psychoeducation', the optional follow-up psychoeducation modules 'Depression', 'Anxiety' and 'Medication' will appear. Following the module 'Relapse prevention plan', the patient can choose which other optional modules he or she wishes to complete, based on own preferences and goals, thus offering the opportunity for the patient to customize treatment. The dotted lines in Figure 1 indicate that certain modules refer automatically to other optional follow-up modules.

The modules include short videos on what to expect in the module, written information, exercises, and clinical examples of fictional patients. In all modules except

the psychoeducation modules, patients have the possibility to ask for feedback from the MHP. For a more detailed overview of the contents of the E-health program, see Table 1.
It takes about 30-60 minutes to complete each module. In each module, patients draft plans related to the specific content of that module, and are encouraged to continue practicing, by offering the possibility to print out the plans.

Patients receive reminders via email regarding the completion of modules in the E-health platform. They also receive a newsletter every six weeks to keep them involved in the program by providing information about numbers of included patients, experiences of other patients and interesting articles or facts about anxiety and depression. The MHP has access to the patient's account, and can check whether the patient has been using the diary to monitor symptoms of anxiety and depression. Also, the MHP can monitor the patient's individual use of the different modules. In turn, MHPs can provide feedback on the completed modules and start a conversation in the E-health platform with the patient.

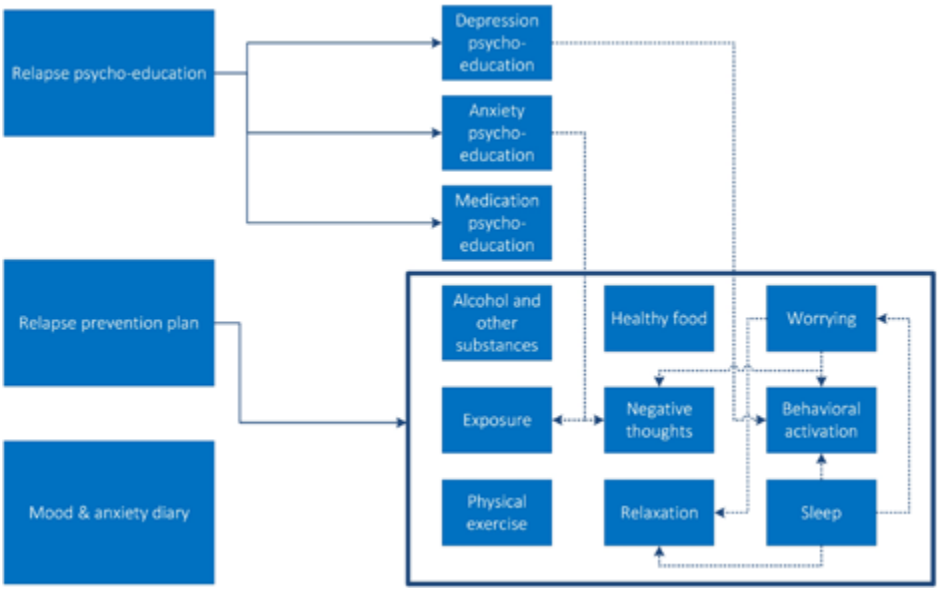

Figure 1. Content of E-health program.

Table 1. Overview of module content.

Module	Module content
Relapse	Information regarding relapse and relapse prevention Video: experiences of patients Overview of relapse prevention program
Relapse prevention plan	Formulating a relapse prevention plan Information about support from family/friends Choosing which optional modules to complete
Depression	Information regarding symptoms, differences in disorders, causes and prevalence of depression Links to websites for more information
Anxiety	Information regarding symptoms, differences in disorders, causes and prevalence of anxiety Links to websites for more information
Medication	Information regarding antidepressive medication Information regarding benzodiazepines
Alcohol and other substances	Information regarding use of alcohol and psychological symptoms Advice on how to reduce alcohol intake Information regarding other substances (marihuana and tobacco) and psychological symptoms Exercise: registering use of substances Exercise: motivation to change behavior Plan to change behavior
Exposure	Information on exposure Exercise: avoidance Plan for exposure
Physical exercise	Information regarding exercise Plan to increase physical exercise Links to websites for more information
Healthy food	Information on healthy food Advice on healthy food Plan to improve your diet
Negative thinking	Information on (un)helpful thoughts Exercise: make a thought schedule
Relaxation	Information regarding physical and psychological effects of relaxation Information regarding mindfulness Exercises in mindfulness Plan to increase mindfulness/relaxation
Worrying	Exercise and information on registering worrying Exercises on worrying
Behavioral activation	Information on importance of behavioral activation Information regarding physical and psychological effects of pleasurable activities Exercise: planning pleasurable activities
Sleep	Information regarding sleep and psychological symptoms Advice on how to improve sleep Exercise: completing a sleep diary Exercise: restoring your sleep rhythm Exercise: activities during the day

Role of MHP

The MHP and the patient will have at least one face-to-face contact during the nine-month period of the study, and are encouraged to meet each other every three months. During the first contact, the patient and MHP will start drawing up the relapse prevention plan (if not yet available) and decide on the frequency and number of contacts. In the follow-up contacts, the outcomes of the 'mood and anxiety diary', the use of the available modules and possible questions will be discussed. The time required for the first contact is 45 minutes, and 20 minutes for the follow-up contacts. The MHP can actively support the patient in using the online program and provide online feedback at the request of the patient.

3. Study design

In this mixed-methods observational cohort study, the relapse prevention program we developed will be implemented and evaluated. This program is targeted at patients who have been discharged from mental healthcare services, and are in complete or partial remission from an anxiety or depressive disorder. This relapse prevention program is called 'GET READY' and offers access to an E-health platform, combined with regular contact with a MHP for a period of nine months. General practices will be included in this study. Eligible patients completed mental health treatment for anxiety or depression and are in (partial) remission. Patients will complete online questionnaires at baseline, after 3, 6 and 9 months. In addition, individual interviews and focus group interviews will be held with patients as well as MHPs to evaluate the program and its implementation.

Definition of terms

Throughout the literature, several terms are used regarding relapse and remission. Based on the definitions described by Frank et al. [32], we will make use of three terms: the term 'relapse' refers to a return of full symptomatology in concordance with the DSM-IV criteria for a depressive or anxiety disorder [33]. The term 'full remission' indicates that no more than minimal symptoms are present and DSM-IV criteria for a disorder have not been fulfilled. In addition, 'partial remission' also indicates that DSM-IV criteria for a disorder have not been fulfilled, but that more than minimal symptoms are present.

Setting

This study will be performed in two settings:

1. General practices throughout the Netherlands, with the participation of approximately 50 MHPs. Patients follow the program at home via an E-health platform, accompanied by face-to-face contact with the MHPs.

2. Ambulatory mental healthcare services with the participation of eligible patients whose GP is not willing to participate in this study. A trained MHP will deliver the relapse prevention program using the same protocol as in the participating general practices.

Recruitment of MHPs

We aim to recruit 50 MHPs throughout the Netherlands. Recruitment will be done via telephone, letters, advertisements on websites for MHPs, and via the professional networks of the researchers. For the MHPs working in a general practice, the GP agrees that the MHP participates in this study. Informed consent will be obtained from the MHPs before inclusion.

Recruitment of participants

Patients will be recruited via general practices and mental healthcare services. Patients are eligible to participate when they have been treated for an anxiety disorder and/or a depressive disorder in mental healthcare services and are in full or partial remission, according to their clinician. To confirm the clinician's judgement regarding remission status, the Inventory of Depressive Symptomatology (IDS-SR) and the Beck Anxiety Inventory (BAI) will be administered at baseline [34,35]. Patients with scores > 39 on the IDS-SR and > 30 on the BAI are excluded from the study, since these scores indicate severe symptoms [36,37]. Inclusion criteria are: patients have completed their treatment for anxiety and/or depression within the last two years, have a score on the Global Assessment of Functioning scale (GAF) of 50 or higher, are at least 18 years old, and have sufficient command of the Dutch language. Patients are excluded if they participate in another structured psychological intervention, when they do not have access to the internet, or when the severity of a comorbid psychiatric disorder requires specialized treatment.

Recruitment via general practices

Each MHP is requested to include all patients that completed mental health treatment for anxiety and depression and meet the inclusion criteria. MHPs will be asked to identify eligible patients through their patient files. MHPs invite potentially eligible patients for a consultation to discuss participation in the study, to provide information about the study and to check whether patients meet the inclusion criteria. If interest is shown in the study, the researcher contacts the patient and sends the baseline questionnaire. When patients have completed the baseline questionnaire, they receive access to the E-health platform. Eight days after sending the invitation for login, the researchers check if the patient has logged in. If not, they contact the patient to offer technical or practical support.

Recruitment via mental healthcare services

Patients who completed their treatment and are recruited via mental healthcare services, will be contacted by the researchers directly. These patients will be supported during the GET READY program by a MHP working in the ambulatory mental healthcare.

Implementing the relapse prevention program

Training of the MHP

Each MHP participates in a four-hour training course, focusing on the background and relevance of relapse prevention in anxiety and depressive disorders and potential effective intervention strategies regarding relapse prevention. Next, the content and use of the E-health platform is explained. Finally, information is provided about the study protocol. This training course will be given by either a psychologist or psychiatrist (both part of the research team), together with the first author of this paper.

Support for the MHP

After completing the training course, MHPs will receive an information package, including a protocol in which the following topics are described: recruitment of patients, the content of the face-to-face contact with patients, instructions on how to complete the case registration forms, and a guide on the E-health platform, containing screenshots. The package also includes invitation and information letters for patients.

The researchers offer monthly individual consultation via phone to the MHPs to support them in recruiting patients, discuss possible issues, and answer additional questions. Every month the MHPs receive a newsletter to update them on the study and motivate them to continue including patients.

Quantitative data

Data collection – measurements

Patients are asked to complete four online questionnaires: at baseline (T0), after three months (T3), after six months (T6), and after nine months (T9). It takes approximately 20-30 minutes to complete the questionnaires. Patients receive email invitations and if they do not complete the questionnaire, weekly reminders are sent.

Next, patients are requested to complete the 'mood & anxiety diary' every week to rate their level of anxiety and depression. They can complete the diary on their smartphone or on a computer.

After each face-to-face contact, the MHP completes a case registration form. This form contains information on the duration and content of the face-to-face contact, clinical status description, and whether additional appointments were made.

Data collection – outcome measures

Use of relapse prevention program

Data will be collected regarding the use of the E-health platform data (number of logins, number of completed/uncompleted modules, and number of diary entries) and the frequency of contact with the MHPs, registered via the case registration forms.

Demographics and clinical variables

Sociodemographic characteristics and clinical variables of patients will be assessed at baseline, see Table 2. In addition, patients are asked to estimate their risk of relapse, and to indicate the expected effect of the program.

Self-management strategies

Self-management strategies will be measured using the 'Self-management in depression and anxiety' questionnaire. This questionnaire was developed during a study on self-management interventions for chronic anxiety and depression [38]. It consists of 45 items describing strategies that patients use to cope with anxiety and depression. Each item is rated on a 5-point Likert scale ranging from 1 (not at all) to 5 (a lot). The total score can be calculated by summing the individual scores.

Anxiety and depression scores

Anxiety severity will be measured by the Beck Anxiety Inventory (BAI), a 21-item tool, in which each item is rated on a 0 to 3 point scale, resulting in a total score between 0 to 63, with ≥ 30 indicating severe anxiety [34]. This tool is reported to have a good reliability [39] and validity [40].

The Anxiety Sensitivity Index (ASI) is a 16-item questionnaire for measuring anxiety sensitivity. Each item is rated on a 5-point Likert scale with scores from 0 (barely) to 4 (very much), with a total score ranging from 0 (no anxiety sensitivity) to 64 (severe anxiety sensitivity) [41]. The ASI is a reliable measure [42]. Anxiety sensitivity has been found to be a predictor for relapse in patients with remitted anxiety disorders [3].

The Inventory of Depressive Symptomatology – self-report (IDS-SR) is a 30-item questionnaire for measuring severity of depressive symptoms [35]. Each item is rated on a 0 to 3-point scale, and by summing 28 of the 30 items the total score ranges from 0 to 84, with ≥ 39 indicating severe depressive symptoms. The questionnaire has highly acceptable psychometric properties [43].

Anxiety and mood data are also collected in the weekly diary. Mood is measured by asking 'how would you rate your mood today?, from 1 (very sad) to 10 (very happy)'. Anxiety is measured by asking 'how would you rate the intensity of anxiety today?, from 1 (very relaxed) to 10 (very anxious/tense)'.

Functioning

General functioning and disability will be measured using the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0). This 36-item tool measures six domains: cognition, mobility, self-care, getting along, life activities and participation. Each item is rated on a 5-point Likert scale with scores from 0 (no difficulty) to 4 (extreme difficulty or cannot do). By using the 'item-response theory'-based scoring, the scores will range from 0 (no disability) to 100 (full disability) [44]. The WHODAS 2.0 is reported to have strong psychometric properties [45].

Healthcare use

Healthcare and medication use will be measured using an adjusted version of the Trimbos/iMTA Questionnaire for Costs Associated with Psychiatric Illness (TiC-P). Only psychotropic medication will be registered. Health care use is measured as the number of contacts with different healthcare providers. The TiC-P is a feasible and reliable instrument for measuring healthcare use and costs [46].

Satisfaction with the relapse prevention program

Satisfaction with the relapse prevention program will be assessed using the 'Satisfaction with treatment measure'. This 14-item measure provides insight into overall satisfaction, how helpful and useful patients valued the program, perceived support and effect [47]. Also patients will be asked to rate each online module. The original scale was translated into Dutch by the authors, with permission of the author.

Quantitative data analysis

For each of the quantitative research questions, a separate analysis will be performed using log data from the E-health platform, data from the case registration forms that have been completed by the MHPs, and data from the four questionnaires:

1) To what extent do patients use a tailored relapse prevention program?

The use of the tailored relapse prevention program will be described, focusing on different aspects of its use, such as the number of login sessions, the amount of time spent online, the number of completed modules, the number of diary entries, the number of sessions and the number of online and face-to-face conversations with the MHP. Descriptive statistics will be used to provide insight into these aspects of the use of the relapse prevention program.

2) What factors influence the use of the program?

The use of the tailored relapse prevention program may differ across patients, and may depend on age, education level and clinical situation. We will explore possible

Table 2. Information on data collection.

Research question	Type	Outcome measures	T0	T3	T6	T9	After study
1) To what extent do patients use a tailored relapse prevention program?	Quantitative	Use of the relapse prevention program (log data)	x	x	x	x	
		Case registration form					x
2) What factors influence the use of the program?	Quantitative	Demographic variables: - Gender - Age - Nationality - Ethnicity - Socioeconomic status - Marital status - Education - Employment status	x				
		Clinical variables: - Earlier treatment of depression and/or anxiety - Number of previous episodes - Age of onset of symptoms - Family history of depression and/or anxiety - Estimated risk of relapse - Estimated effect of the program	x				
		Self-management strategies	x			x	
3) What is the association between usage intensity and course of symptoms?	Quantitative	Use of the relapse prevention program (log data)	x	x	x	x	
		Case registration form					x
		BAI	x	x	x	x	
		ASI	x	x	x	x	
		IDS-SR	x	x	x	x	
		WHODAS 2.0	x	x	x	x	
		TiC-P	x	x	x	x	
		Weekly mood and anxiety diary	x	x	x	x	
4) What are barriers and facilitators in the implementation of the program?	Qualitative	Individual interviews					x
		Focus group interview					x
5) How do patients evaluate the program?	Qualitative	Satisfaction with treatment measure				x	
		Individual interviews					x
		Focus group interview					x

differences in usage between groups of patients systematically, considering sociodemographic factors, clinical symptoms and self-management strategies.

3) What is the association between usage intensity and course of symptoms?
Descriptive statistics will be used to provide insight into course of symptoms for 'high-use' participants and 'low-use' participants. In order to analyze the association between usage intensity and course of symptoms, multiple regression analyses will be performed. We will first analyze the change in anxiety severity from baseline to follow-up (9 months) with the following independent variables: intensity of E-health use, number of diary entries and number of contacts with the MHP. We will repeat these analyses for the depression outcomes. In addition, analyses will be performed using 'deterioration: yes or no' as outcome variable. Deterioration is defined as an increase of 1 standard deviation on the IDS-SR and/or on the BAI. The standard deviation will be calculated using data from the NESDA study [48], the study from Kok et al. [49], and the present study. This analysis will be performed using a time-lag model, in which the outcome will be assessed using determinants from an earlier measurement (deterioration at $time_t$ predicted by usage intensity at $time_{t-1}$), since we assume that usage intensity might influence whether deterioration occurs at a later point in time.

Because of the observational nature of the data, it will be difficult to draw conclusions about the effects of the relapse prevention program. However, we will conduct additional explorative analyses to estimate the association between usage intensity and course of symptoms. All data analysis will be performed using SPSS statistical analysis software.

Sample size

In order to determine the sample size, we assumed a moderate effect (r = 0.24 that corresponds to Cohen's d = 0.5) of the intensity of program use (X) on the change in symptoms of anxiety and depression (Y). Since this is a non-randomized study, we will use a set of covariates $\boldsymbol{W}$ to correct for selectivity in the uptake of the program. In applying the G*Power 3 software [50] to determine the sample size, we assume that the effect of X corresponds to a 6% of explained variance of Y (equivalent to the moderate effect, since $R^2 = r^2 = 0.24^2 = 0.06$) above the covariates $\boldsymbol{W}$ and assume a 6% reduction of the total variance in Y of the residual variance due to the use of covariates of $\boldsymbol{W}$, leading to a partial $R^2 = 0.06$ or, equivalently, an effect size of $f^2 = 0.0638$. Furthermore, setting $\alpha = 0.05$ and the power of $1 - \ = 0.80$, the sample size calculation shows that 126 patients are needed. Patients will be considered as drop-out when they refuse to complete questionnaires. With an estimated attrition of 20% (i.e. 80% complete at least one follow-up questionnaire), we aim to include 158 patients.

Qualitative data

Data collection – measurements

The individual interviews and focus group interviews are conducted to assess implementation and satisfaction with the program.

Individual interviews

Paired interviews will be conducted separately with patients and their MHPs in order to gain insight into both perspectives on one case. These paired interviews provide valuable insights regarding similarities and differences in experiences of MHPs and patients [51,52]. Purposive sampling will be used to select patients and realize sufficient variation in our sample with respect to gender, age, severity of symptoms, and use of the program [53]. Patients will be invited by email and telephone to participate in a semi-structured interview to evaluate their experience with the relapse prevention program. If willing to participate, their MHP will be invited as well. The interviews will be conducted by two researchers, who will prepare the interviews by performing two test interviews. A senior researcher will provide supervision and participate in the analysis. We aim to conduct 12-15 interviews with patients and 12-15 interviews with MHPs. The final number of interviews depends on when data saturation is achieved.

A topic guide is developed to support the interview process (see Appendix 3.1). This guide was drafted by the first author and reviewed by two experts, and inspired by the Consolidated Framework For Implementation Research (CFIR) [54]. Main topics are: experiences with the relapse prevention program, use of the relapse prevention program, useful and less useful aspects of the program, and suggestions to improve the program. Input from the E-health platform will be used, such as completed and uncompleted modules, use of the diary, and number of online conversations with the MHP. The topic guide will be evaluated and updated after conducting four interviews.

The MHPs of patients who participate in the interviews will also be invited by email and telephone to participate in an interview. Besides evaluating the program (research question 5), implementation barriers and facilitators will be discussed in these interviews (research question 4), see Appendix 3.2 for the topic guide.

These interviews will be conducted in a setting selected by participants and will take approximately 45 minutes.

Focus group interviews

After completing the individual interviews, two focus group interviews will be conducted, one with 8-10 patients and one with 8-10 MHPs. The goal of the focus group interviews is to present, test and discuss preliminary findings and conclusions from the individual interviews. A focus group interview is appropriate for this situation, since the group

interaction provides insight into topics of agreement and favorable and unfavorable topics, and experiences with the program can be shared [55]. A moderator will lead the group discussion, and an assistant moderator will take notes, observe and keep track of the time [56]. The input from the individual interviews will be used in these focus group interviews, to discuss desirable changes to the E-health program, in order to further improve its quality and usability. In order to obtain new perspectives on the evaluative data from the individual interviews, one half of the focus group participants will not have participated in a previous individual interview. The other half of the focus group members will be purposively selected from the patients and MHPs who previously participated in the individual interviews, where the selection is based on the diverging perspectives on using the relapse prevention program. These focus group interviews will be conducted in a mental healthcare facility and will take approximately 90 minutes.

Qualitative data analysis

For each of the qualitative research questions, a separate analysis will be performed:

4) What are barriers and facilitators in the implementation of the program?

The barriers and facilitators in the implementation of the program will be assessed through the semi-structured interviews and focus group interviews with the MHPs. These interviews will be audio recorded, and transcribed verbatim. Data will be sorted using the CFIR [54], which indicates five domains of implementation (intervention characteristics, outer setting, inner setting, characteristics of individuals and process). Data collection will alternate with data analysis and new topics will be discussed in the following interviews. Two researchers will independently openly code the first three interviews, compare the codes and draft a coding tree. The coding tree will be complemented through the following interviews. This data will be analyzed using thematic analysis [57], which means that the interviews will be coded for themes, these codes will then be sorted and analyses will be performed using software program MaxQDA. When reporting the data, quotations will be used to illustrate the findings.
During this process, multiple researchers will be involved in order to increase the validity and reliability [56]. From the beginning of data collection until the end of data analysis, detailed field notes will be documented, containing specific situations, reflections, and ideas and thoughts of the researchers [56]. In addition, a summary will be made of each interview, containing the most important findings.

5) How do patients evaluate the program?

The evaluation of the program will be assessed by the semi-structured interviews and focus group interviews with the patients. In addition, in the last follow-up questionnaire (T9), patients will be asked about their satisfaction with the program and to rate every

module they completed on a scale from 0-10. The data from the interviews and focus group interviews will be analyzed in the same way as described above (research question 4). Data from T9 will be analyzed using descriptive statistics.

Discussion

Providing relapse prevention for anxiety and depression is important, since these disorders are often chronic and recurrent. In this study we will implement and evaluate a newly developed relapse prevention program, specifically targeted at patients that are (partially) remitted from an anxiety disorder or depression. The mixed-methods approach in this study will provide valuable insights into how patients use the program, what influences the use of the program, how usage intensity influences symptoms and how patients evaluate the program. In addition, information on implementation will be provided which may be relevant for broad implementation of the program. The findings of this study can be used to further refine and adapt the program as preferred by patients and MHPs.

A strength of this study is that the relapse prevention program has been developed based on patient preferences and in close collaboration with patients. Additionally, this program is not only web-based, but also supplemented by contact with MHPs. Earlier research suggests that E-health can be especially effective when accompanied by therapist contact [58]. By using log data to establish the usage of the program, the actual use and usage behavior can be determined [59]. Furthermore, by using mixed methods, a complete view on the use of the program and its evaluation can be obtained [59].

This design is not appropriate to examine efficacy, since only within-group effect sizes can be determined, which might be considered a limitation of this study. However, the aim of this study was not to examine the efficacy of the program, but its acceptability. If the program is acceptable, a randomized controlled trial should be conducted to determine the efficacy of the program.

ABBREVIATIONS

MHP: mental health professional; CBT: cognitive behavioral therapy; DSM: diagnostic and statistical manual of mental disorders; GET READY: Guided E-healTh for RElapse prevention in Anxiety and Depression; BAI: Beck Anxiety Inventory; ASI: Anxiety Sensitivity Index; IDS-SR: Inventory of Depressive Symptomatology – self-report; WHODAS: World Health Organization Disability Assessment Schedule; TiC-P: Trimbos/iMTA Questionnaire for Costs Associated with Psychiatric Illness; CFIR: Consolidated Framework For Implementation Research

FUNDING

This study is funded by SIA-RAAK: The Taskforce for Applied Research, part of the Netherlands Organization for Scientific Research (NWO). The funder had no role in study design, data collection and analysis, interpretation of data, and preparation of the manuscript.

ACKNOWLEDGEMENTS

Not applicable.

References

1. Bruce SE, Yonkers KA, Otto MW, Eisen JL, Weisberg RB, Pagano M, Shea MT, Keller MB. Influence of Psychiatric Comorbidity on Recovery and Recurrence in Generalized Anxiety Disorder, Social Phobia, and Panic Disorder: A 12-Year Prospective Study. Am J Psychiatry [Internet] American Psychiatric Publishing; 2005 Jun 1 [cited 2017 Jun 27];162(6):1179–1187. [doi: 10.1176/appi.ajp.162.6.1179]

2. Verduijn J, Verhoeven JE, Milaneschi Y, Schoevers RA, van Hemert AM, Beekman ATF, Penninx BWJH. Reconsidering the prognosis of major depressive disorder across diagnostic boundaries: full recovery is the exception rather than the rule. BMC Med [Internet] BMC Medicine; 2017 Dec 12;15(1):215. PMID:29228943

3. Scholten WD, Batelaan NM, Van Balkom AJ, Penninx BWJH, Smit JH, Van Oppen P. Recurrence of anxiety disorders and its predictors. J Affect Disord Elsevier; 2013;147(1–3):180–185. PMID:23218248

4. Penninx BWJH, Nolen WA, Lamers F, Zitman FG, Smit JH, Spinhoven P, Cuijpers P, de Jong PJ, van Marwijk HWJ, der Meer K van, Verhaak P, Laurant MGH, de Graaf R, Hoogendijk WJ, der Wee N van, Ormel J, van Dyck R, Beekman ATF. Two-year course of depressive and anxiety disorders: Results from the Netherlands Study of Depression and Anxiety (NESDA). J Affect Disord [Internet] 2011 Sep [cited 2017 Aug 9];133(1–2):76–85. [doi: 10.1016/j.jad.2011.03.027]

5. Taylor JH, Jakubovski E, Bloch MH. Predictors of anxiety recurrence in the Coordinated Anxiety Learning and Management (CALM) trial. J Psychiatr Res [Internet] Elsevier Ltd; 2015 Jun [cited 2017 Aug 8];65:154–165. PMID:25896121

6. Conradi HJ, Bos EH, Kamphuis JH, de Jonge P. The ten-year course of depression in primary care and long-term effects of psychoeducation, psychiatric consultation and cognitive behavioral therapy. J Affect Disord Elsevier B.V.; 2017 Aug;217:174–182. [doi: 10.1016/j.jad.2017.03.064]

7. Gopinath S, Katon WJ, Russo JE, Ludman EJ. Clinical factors associated with relapse in primary care patients with chronic or recurrent depression. J Affect Disord 2007;101(1–3):57–63. PMID:17156852

8. Hardeveld F, Spijker J, De Graaf R, Hendriks SM, Licht CMM, Nolen WA, Penninx BWJH, Beekman ATF. Recurrence of major depressive disorder across different treatment settings: Results from the NESDA study. J Affect Disord [Internet] Elsevier; 2013 May [cited 2016 Jul 6];147(1–3):225–231. PMID:23218899

9. Yiend J, Paykel E, Merritt R, Lester K, Doll H, Burns T. Long term outcome of primary care depression. J Affect Disord [Internet] Elsevier B.V.; 2009 Nov [cited 2017 Aug 7];118(1–3):79–86. PMID:19246103

10. Van Londen L, Molenaar RP, Goekoop JG, Zwinderman AH, Rooijmans HG. Three- to 5-year prospective follow-up of outcome in major depression. Psychol Med England; 1998 May;28(3):731–735. PMID:9626729

11. Pintor L, Gastó C, Navarro V, Torres X, Fañanas L. Relapse of major depression after complete and partial remission during a 2-year follow-up. J Affect Disord 2003;73(3):237–244. PMID:12547292

12. Paykel ES, Ramana R, Cooper Z, Hayhurst H, Kerr J, Barocka A. Residual symptoms after partial remission: an important outcome in depression. Psychol Med England; 1995 Nov;25(6):1171–1180. PMID:8637947

13. Wagner EH, Austin BT, Davis C, Hindmarsh M, Schaefer J, Bonomi A. Improving Chronic Illness Care: Translating Evidence Into Action. Health Aff Health Affairs; 2001 Nov;20(6):64–78. [doi: 10.1377/hlthaff.20.6.64]

14. Von Korff M, Gruman J, Schaefer J, Curry SJ, Wagner EH. Collaborative Management of Chronic Illness Behavioral Principles. Ann Intern Med 1997;127(12):1097–102. PMID:9412313

15. Lorig K. Self-management of chronic illness: A model for the future. Gener XVII 1993;3:11–14.

16. van Balkom A, Oosterbaan D, Visser S, van Vliet I. Handboek Angststoornissen. Utrecht: De Tijdstroom uitgeverij BV; 2011.

17. Schene A, Sabbe B, Spinhoven P, Ruhé H. Handboek Depressieve stoornissen. 2nd editio. Utrecht: De Tijdstroom uitgeverij BV; 2016.

18. Howell CA. Preventing depression relapse: a primary care approach. Prim Care Ment Heal [Internet] 2004;2(3/4):151–156. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=106504004&site=ehost-live

19. Biesheuvel-Leliefeld KEM, Kok GD, Bockting CLH, Cuijpers P, Hollon SD, van Marwijk HWJ, Smit F. Effectiveness of psychological interventions in preventing recurrence of depressive disorder: Meta-analysis and meta-regression. J Affect Disord [Internet] Elsevier; 2015 Mar 15 [cited 2016 Jul 7];174:400–410. PMID:25553400

20. Biesheuvel-Leliefeld KEM, Dijkstra-Kersten SMA, van Schaik DJF, van Marwijk HWJ, Smit F, van der Horst HE, Bockting CLH. Effectiveness of Supported Self-Help in Recurrent Depression: A Randomized Controlled Trial in Primary Care. Psychother Psychosom [Internet] 2017;86(4):220–230. [doi: 10.1159/000472260]

21. Scholten WD, Batelaan NM, Van Oppen P, Smit JH, Van Balkom AJLM. Discontinuation of antidepressants in remitted anxiety disorder patients: The need for strategies to prevent relapse. Psychother Psychosom 2013;82(6):399–400. PMID:24080729

22. Von Korff M, Goldberg D. Improving outcomes in depression. BMJ 2001;323(October):948–949.

23. Katon W, Rutter C, Ludman EJ, Von Korff M, Lin E, Simon G, Bush T, Walker E, Unützer J. A Randomized Trial of Relapse Prevention of Depression in Primary Care. Arch Gen Psychiatry [Internet] American Medical Association; 2001 Mar 1 [cited 2017 Apr 10];58(3):241. PMID:11231831

24. Hermens MLM, Muntingh A, Franx G, Van Splunteren PT, Nuyen J. Stepped care for depression is easy to recommend, but harder to implement: Results of an explorative study within primary care in the Netherlands. BMC Fam Pract 2014;15(1):5. PMID:24400701

25. Krijgsman J, Swinkels I, Lettow B van, Jong J de, Out K, Friele R, Gennip L van. Meer dan techniek, eHealthmonitor 2016. Den Haag & Utrecht; 2016.

26. Baumeister H, Reichler L, Munzinger M, Lin J. The impact of guidance on Internet-based mental health interventions - A systematic review. Internet Interv [Internet] Elsevier B.V.; 2014;1(4):205–215. [doi: 10.1016/j.invent.2014.08.003]

27. Muntingh ADT, Hoogendoorn AW, Van Schaik DJF, Van Straten A, Stolk EA, Van Balkom AJLM, Batelaan NM. Patient preferences for a guided self-help program to prevent relapse in anxiety or depression: A discrete choice experiment. Eisenbarth H, editor. PLoS One [Internet] 2019 Jul 18;14(7):e0219588. [doi: 10.1371/journal.pone.0219588]

28. National Institute for Health and Care Excellence. The Nice Guideline on the Treatment and Management of Depression in Adults (updated edition) [Internet]. 2010. PMID:22132433

29. Boggs JM, Beck A, Felder JN, Dimidjian S, Metcalf CA, Segal Z V. Web-based intervention in mindfulness meditation for reducing residual depressive symptoms and relapse prophylaxis: A qualitative study. J Med Internet Res [Internet] JMIR Publications Inc.; 2014 [cited 2016 Jul 6];16(3):1–12. PMID:24662625

30. Notley C, Christopher R, Hodgekins J, Byrne R, French P, Fowler D. Participant views on involvement in a trial of social recovery cognitive-behavioral therapy. Br J Psychiatry [Internet] The Royal College of Psychiatrists; 2015 Feb [cited 2016 Jul 6];206(2):122–127. PMID:25431429

31. Butler A, Chapman J, Forman E, Beck A. The empirical status of cognitive-behavioral therapy: A review of meta-analyses. Clin Psychol Rev [Internet] 2006 Jan;26(1):17–31. PMID:16199119

32. Frank E, Prien RF, Jarrett RB, Keller MB, Kupfer DJ, Lavori PW, Rush AJ, Weissman MM. Conceptualization and Rationale for Consensus Definitions of Terms in Major Depressive Disorder. Arch Gen Psychiatry [Internet] 1991 Sep 1;48(9):851. PMID:1929776

33. American Psychiatric Association. DSM-IV Diagnostic and Statistical Manual of Mental Disorders. Am Psychiatr Assoc 1994;1–915. PMID:24413388

34. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. J Consult Clin Psychol [Internet] 1988;56(6):893–897. PMID:3204199

35. Rush AJ, Gullion CM, Basco MR, Jarrett RB, Trivedi MH. The Inventory of Depressive Symptomatology (IDS): psychometric properties. Psychol Med England; 1996 May;26(3):477–486. PMID:8733206

36. Beck AT, Steer RA. Beck anxiety inventory manual. Behav Res Ther. San Antonio, TX: The Psychological Corporation Harcourt Brace & Company; 1993.

37. Inventory of Depressive Symptomatology (IDS) and Quick Inventory of Depressive Symptomatology (QIDS) - Interpretation [Internet]. [cited 2018 May 22]. Available from: http://www.ids-qids.org/interpretation.html

38. Zoun MHH, Koekkoek B, Sinnema H, Muntingh ADT, van Balkom AJLM, Schene AH, Smit F, Spijker J. Effectiveness and cost-effectiveness of a self-management training for patients with chronic and treatment resistant anxiety or depressive disorders: design of a multicenter randomized controlled trial. BMC Psychiatry [Internet] BMC Psychiatry; 2016;16(1):216. PMID:27388878

39. De Ayala RJ, Vonderharr-Carlson DJ, Kim D. Assessing the reliability of the Beck Anxiety Inventory scores. Educ Psychol Meas 2005;65(5):836–850. [doi: 10.1177/0013164405278557]

40. Fydrich T, Dowdall D, Chambless DL. Reliability and validity of the beck anxiety inventory. J Anxiety Disord 1992;6(1):55–61. [doi: 10.1016/0887-6185(92)90026-4]

41. Reiss S, Peterson RA, Gursky DM, McNally RJ. Anxiety sensitivity, anxiety frequency and the predictions of fearfulness. Behav Res Ther [Internet] 1986;24(1):1–8. PMID:3947307

42. Rodriguez BF, Bruce SE, Pagano ME, Spencer MA, Keller MB. Factor structure and stability of the Anxiety Sensitivity Index in a longitudinal study of anxiety disorder patients. Behav Res Ther 2004;42(1):79–91.

43. Trivedi MH, Rush AJ, Ibrahim HM, Carmody TJ, Biggs MM, Suppes T, Crismon ML, Shores-Wilson K, Toprac MG, Dennehy EB, White B, Kashner TM. The Inventory of Depressive Symptomatology, Clinician Rating (IDS-C) and Self-Report (IDS-SR), and the Quick Inventory of Depressive Symptomatology, Clinician Rating (QIDS-C) and Self-Report (QIDS-SR) in public sector patients with mood disorders: a psych. Psychol Med [Internet] 2004 Jan 14;34(1):73–82. [doi: 10.1017/S0033291703001107]

44. WHO. WHO Disability Assessment Schedule 2.0 (WHODAS 2.0) [Internet]. 2018 [cited 2018 Aug 14]. Available from: http://www.who.int/classifications/icf/WHODAS2.0_36itemsSELF.pdf

45. Konecky B, Meyer EC, Marx BP, Kimbrel NA, Morissette SB. Using the WHODAS 2.0 to assess functional disability associated with DSM5 mental disorders. Am J Psychiatry [Internet] NIH Public Access; 2014 Aug [cited 2016 Dec 2];171(8):818–819. PMID:25082488

46. Bouwmans C, De Jong K, Timman R, Zijlstra-Vlasveld M, Van der Feltz-Cornelis C, Tan SS, Hakkaart-van Roijen L. Feasibility, reliability and validity of a questionnaire on healthcare consumption and productivity loss in patients with a psychiatric disorder (TiC-P). BMC Health Serv Res [Internet] 2013;13(1):217. PMID:23768141

47. Richards D, Murphy T, Viganó N, Timulak L, Doherty G, Sharry J, Hayes C. Acceptability, satisfaction and perceived efficacy of "Space from Depression" an internet-delivered treatment for depression. Internet Interv The Authors; 2016;5:12–22. [doi: 10.1016/j.invent.2016.06.007]

48. Penninx BWJH, Beekman ATF, Smit JH, Zitman FG, Nolen WA, Spinhoven P, Cuijpers P, De Jong PJ, Van Marwijk HWJ, Assendelft WJJ, Van Der Meer K, Verhaak P, Wensing M, De Graaf R, Hoogendijk WJ, Ormel J, Van Dyck R. The Netherlands Study of Depression and Anxiety (NESDA): rationale, objectives and methods. Int J Methods Psychiatr Res [Internet] Wiley-Blackwell; 2008 Sep;17(3):121–140. [doi: 10.1002/mpr.256]

49. Kok G, Burger H, Riper H, Cuijpers P, Dekker J, van Marwijk H, Smit F, Beck A, Bockting CLH. The Three-Month Effect of Mobile Internet-Based Cognitive Therapy on the Course of Depressive Symptoms in Remitted Recurrently Depressed Patients: Results of a Randomized Controlled Trial. Psychother Psychosom [Internet] 2015 Feb 21;84(2):90–99. PMID:25721915

50. Faul F, Erdfelder E, Lang A-G, Buchne, Buchner A, Buchne. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007;39(2):175–191. PMID:17695343

51. Bosman RC, Huijbregts KM, Verhaak PF, Ruhé HG, van Marwijk HW, van Balkom AJ, Batelaan NM. Long-term antidepressant use: a qualitative study on perspectives of patients and GPs in primary care. Br J Gen Pract [Internet] 2016 [cited 2017 Sep 14];66(651):e708–e719. [doi: 10.3399/bjgp16x686641]

52. Dikkers MF, Westerman MJ, Rubinstein SM, Van Tulder MW, Anema JR. Why neck pain patients are not referred to manual therapy: A qualitative study among Dutch primary care stakeholders. PLoS One [Internet] 2016;11(6):1–18. PMID:27311067

53. Coyle, I. T, Coyne IT. Sampling in qualitative research. Purposeful and theoretical sampling; merging or clear boundaries? J Adv Nurs [Internet] 1997;26(3):623–630. PMID:9378886

54. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci [Internet] 2009 Dec 7;4(1):50. PMID:19664226

55. Duggleby W. What about focus group interaction data? Qual Health Res 2005;15(6):832–840. PMID:15961879

56. Boeije H. Analyseren in kwalitatief onderzoek. 2nd ed. Amsterdam: Boom Lemma; 2014.

57. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol [Internet] 2006 Jan;3(2):77–101. PMID:223135521

58. Richards D, Richardson T. Computer-based psychological treatments for depression: A systematic review and meta-analysis. Clin Psychol Rev [Internet] Elsevier Ltd; 2012;32(4):329–342. PMID:22466510

59. Sieverink F, Kelders S, Poel M, van Gemert-Pijnen L. Opening the Black Box of Electronic Health: Collecting, Analyzing, and Interpreting Log Data. JMIR Res Protoc [Internet] 2017;6(8):e156. PMID:28784592

Appendix 3.1. Topic guide interview patient

Main questions	Additional questions
Introduction	Sign informed consent Introduce yourself Mention the duration of the interview (45 minutes) Ask permission to audio record the interview, and start the recording Mention that the name and personal data is saved separately from research data Mention the purpose of the interview
What is your experience with the relapse prevention program in general?	What were your expectations of the relapse prevention program? Could you tell more about the role of the MHP? · What did you expect from the MHP at the beginning of the study? · How did you experience the contacts? · How did you experience the support from the MHP? · In which way did the MHP help you to stay healthy? · What could be improved in the guidance from the MHP? · Who initiated the contact and how did you experience this? What is your experience with the E-health program? · Usability · Meeting your needs · Pleasure/satisfaction · Available choices · Use of language · Design · Time investment Did the program help you to stay healthy/without symptoms? · In which way did the program help you to stay healthy? How do you feel about the combination of E-health and having contact with the MHP?
What were the most useful and the least useful parts of the E-health program?	· Which modules did you complete? What made you choose these modules? · What were your motives concerning using or not using the modules? · Which modules were set up for you, but not completed? · Did you complete the diary? · How much did you use the message function within the program? · According to the questionnaires, your symptoms have decreased/ increased. How did you experience this?
What do you like about the relapse prevention program and what could be improved?	What is the most useful aspect of the relapse prevention program? What could be improved in the relapse prevention program? What did you miss in the relapse prevention program?
Completion	Are there other topics you would like to discuss? Do you have any questions? Would you like to receive the outcomes of the study? Would you be interested in participating in a focus group interview?

Appendix 3.2. Topic guide interview MHP

Main questions	Additional questions
Introduction	Sign informed consent Introduce yourself Explain which patient the interview is about Mention the duration of the interview (45 minutes) Ask permission to audio record the interview, and start the recording Mention that the name and personal data is saved separately from research data Mention the purpose of the interview
Practical questions	How many hours a week do you work as MHP? Do you work in multiple general practices? How many minutes does a regular contact last? How many MHPs/GPs are working in this general practice?
What is your experience with the relapse prevention program?	How did you offer the relapse prevention program to the patient? · How were follow-up contacts planned? · Who initiated the contact and how did you experience this? · How many contacts did you have? · What did you discuss during the contacts? · Did you stimulate the patient to use the relapse prevention program? In which way? · How did the program influence the health of the patient? · To what extent did the program meet the patients' symptoms? What did you expect from the patient at the beginning of the study? How did you offer the relapse prevention program to other patients? *What was it like to offer the relapse prevention program to the patient? What is your experience with the E-health program? · Usability/structure · Design · Use of language · Time investment · Aspects: what did you use/not use, experience with aspects, relapse prevention plan · Message function/providing feedback
What made it easier or harder to implement the relapse prevention program in the general practice?	The relapse prevention program itself: intervention characteristics · What did you think about the quality of the relapse prevention program? · Did you ever apply relapse prevention strategies before? How does this program compare to other strategies that you are familiar with? · *How complicated is the intervention? Factors within the general practice: inner setting · How could you apply the relapse prevention program in your 'normal work'? · Did you experience support from the general practice or GP? How? · In the general practice, what is the willingness to change? · How did having/not having time affect implementation? Characteristics of individuals · Did you feel confident offering the relapse prevention program? Why/why not? Process of implementation · Did you experience support from the research team? How? Influence from outer setting · Did you have contact with specialized mental healthcare services? What was the effect?

Main questions	Additional questions
What do you like about the relapse prevention program and what could be improved?	What is the most useful aspect of the relapse prevention program? What could be improved in the relapse prevention program? *What did you miss in the relapse prevention program? Would you use the relapse prevention program if available after completion of the study? What is needed?
Completion	Are there other topics you would like to discuss? Do you have any questions? Would you like to receive the outcomes of the study? Would you be interested in participating in a focus group interview?

* If not discussed yet, also ask this question

5

EVALUATION OF A BLENDED RELAPSE PREVENTION PROGRAM FOR ANXIETY AND DEPRESSION IN GENERAL PRACTICE: QUALITATIVE STUDY

PUBLISHED IN JMIR FORMATIVE RESEARCH 2021, 5:1–10

Esther Krijnen-de Bruin (shared first author), Jasmijn A. Geerlings (shared first author), Anna D.T. Muntingh, Willemijn D. Scholten, Otto R. Maarsingh, Annemieke van Straten, Neeltje M. Batelaan, Berno van Meijel

Abstract

Background

Existing studies have yet to investigate the perspectives of patients and professionals concerning relapse prevention programs for patients with remitted anxiety or depressive disorders in primary care. User opinions should be considered when optimizing the use and implementation of interventions.

Objective

This study aimed to evaluate the GET READY relapse prevention programs for patients with remitted anxiety or depressive disorders in general practice.

Methods

Semistructured interviews (N=26) and focus group interviews (N=2) with patients and mental health professionals (MHPs) in the Netherlands were performed. Patients with remitted anxiety or depressive disorders and their MHPs who participated in the GET READY study were interviewed individually. Findings from the interviews were tested in focus group interviews with patients and MHPs. Data were analyzed using thematic analysis.

Results

Participants were positive about the program because it created awareness of relapse risks. Lack of motivation, lack of recognizability, lack of support from the MHP, and symptom severity (too low or too high) appeared to be limiting factors in the use of the program. MHPs play a crucial role in motivating and supporting patients in relapse prevention. The perspectives of patients and MHPs were largely in accordance, although they had different perspectives concerning responsibilities for taking initiative.

Conclusions

The implementation of the GET READY program was challenging. Guidance from MHPs should be offered for relapse prevention programs based on eHealth. Both MHPs and patients should align their expectations concerning responsibilities in advance to ensure optimal usage. Usage of blended relapse prevention programs may be further enhanced by diagnosis-specific programs and easily accessible support from MHPs.

Keywords: Relapse prevention, Anxiety disorder, Depressive disorder, E-health, General practice, Qualitative research

Introduction

The high prevalence of anxiety and depressive disorders is a major public health problem, affecting 615 million people globally [1]. Although effective treatment interventions (psychological as well as pharmacological) are available [2–5], 57% of patients in remission from anxiety disorders or depression experience a relapse within 4 years [6]. Effective relapse prevention provided in general practice could increase quality of life, decrease the high burden of disease for patients with anxiety and depressive disorders, and prevent the need for treatment in a (more costly) specialized mental health care setting [7].

Existing knowledge about effective components of relapse prevention programs and effective ways of implementation remains limited. Several effective relapse prevention programs for patients with remitted depressive disorders were examined in a meta-analysis by Biesheuvel-Leliefeld et al [8], although few studies on relapse prevention concern patients with anxiety disorders [9–12]. A limited number of relapse prevention programs use eHealth, even though it offers improved access to evidence-based treatments [13]. Results concerning effectiveness in these guided eHealth studies for patients with remitted depressive disorders are conflicting: One reports a lower relapse rate after 2 years, while another does not [14,15]. Two other studies, both guided [16] and unguided [17], report a decrease in residual depressive symptoms after participating in an online relapse prevention intervention [16,17]. Variations in type of treatment, guidance, and the duration of the intervention might explain the conflicting results of these studies.

Knowledge concerning how patients and professionals value these programs is lacking. Also, knowledge regarding the appreciation of specific program components is missing. Additional insight into the valuation, feasibility, and usability of relapse prevention programs could allow optimization of such programs, as well as their implementation and use.

To our knowledge, no previous studies have investigated the perspectives of users concerning relapse prevention programs in general practice, although some do focus on users' perspectives regarding blended interventions (eHealth combined with face-to-face contact) for depression treatment. In a study on the perspectives of patients concerning a blended cognitive behavioral therapy program for depression, Urech et al [18] reported that patients appreciate the constant availability of the online program and the possibility of reflecting on their progress. At the same time, however, patients feel pressure to complete modules, experience a lack of flexibility, and have difficulty finding motivation to complete the online modules.

In addition to the patients' perspectives on relapse prevention interventions, it is important to consider the perspectives of the professionals providing the program:

If professionals do not support the intervention, patients are less likely to use it [19]. According to professionals, advantages of blended interventions include access to online content between face-to-face sessions for patients and the fact that the structure of the online format provides focus in the treatment. At the same time, however, professionals note that technical issues could be burdensome to patients, and they do not appreciate the limited possibility of customization for online programs [20].

This article describes findings from a qualitative study conducted as part of the GET READY (Guided E-healTh for RElapse prevention in Anxiety and Depression) study [21], in which a blended relapse prevention program tailored to the patients' preferences [22] was developed and tested. The overall aims of the GET READY study were to implement and evaluate the GET READY relapse prevention program. This program is offered by mental health professionals (MHPs) in general practices in the Netherlands to patients who are in remission from anxiety or depressive disorders.

The aim of the current study was to provide insight into the perspectives of users (both patients and MHPs) on the GET READY relapse prevention program, specifically regarding expectations of the program, attractiveness of the program, collaboration and communication between patients and MHPs, usability (especially in case of an increase of symptoms), and subjective effectiveness. In addition, the aim was to provide insight into factors that influence the use and implementation of the GET READY program in general practice.

Methods

Study design

We conducted a qualitative study as part of the GET READY study. First, semistructured individual interviews were conducted with pairs of patients and MHPs. We then conducted 2 focus group interviews—one with patients and one with MHPs—to reflect on the findings from the individual qualitative interviews. The COnsolidated criteria for REporting Qualitative studies guideline [23] was followed in reporting on this study. The completed checklist can be found in Appendix 5.1.

Sampling and recruitment for the qualitative study

For the individual interviews, purposive sampling was performed (based on sex, age, clinical variables, and place of residence) among all 113 patients participating in the GET READY intervention program, with the aim of including 12-15 patients and 12-15 of their MHPs. All patients enrolled in the GET READY study were at least in partial remission from an anxiety or depressive disorder and had completed treatment in specialized mental health care within the past 2 years. The researchers invited patients

to participate in the individual interviews by telephone or email. The MHPs of patients agreeing to participate were invited to participate as well. In the Netherlands, most general practices employ MHPs—with professional backgrounds in community mental health, social work, or psychology—to provide mental health services [24]. Besides screening, diagnostics, providing psychoeducation, and supporting self-management, one of their tasks is to support relapse prevention [25]. Patients whose MHPs declined to participate were not interviewed. By interviewing both the patient and their MHP, we aimed to gain insight into similarities and differences in perspectives within and between these groups.

For the 2 focus groups, patients and MHPs received invitations by email. Patients and MHPs participating in the individual interview could also participate in the focus group interviews.

All participants gave written informed consent and were offered a €25 (US $30.34) gift voucher for participating in the individual or the focus group interviews. The Medical Ethical Committee of the VU University Medical Center Amsterdam judged that ethical approval was not required according to Dutch legislation. The methods of the full GET READY study are described in detail in the study protocol [21]. The GET READY program consists of 3 core components: (1) relapse psychoeducation module, (2) relapse prevention plan, and (3) weekly diary in which patients can monitor their symptoms. Furthermore, 12 optional eHealth modules are offered. All modules are focused on promoting self-management skills, by providing information, exercises, videos, and examples of fictive patients. As described, this program is offered to patients by MHPs. Patients had at least one face-to-face contact with their MHP during the GET READY study and were encouraged to visit their MHP once every 3 months, for a period of 9 months. Further details about the GET READY intervention can be found in Appendix 5.2.

Data collection

The interviews were conducted individually with patients and MHPs by JG, EKB, and two Master's students in medicine. All researchers had prior experience with qualitative research. Separate topic lists were developed for patients and MHPs (see Appendix 5.3 and Appendix 5.4), based on the aims of the study, the content of the GET READY intervention, the Consolidated Framework for Implementation Research [26], and literature on qualitative research [27,28]. In short, the topic lists contained questions regarding expectations of the program, attractiveness of the program, collaboration and communication between patients and MHPs, usability (especially in case of an increase of symptoms), and subjective effectiveness of the relapse prevention program. The interviewers did not know the patients in advance. Although they were familiar with the researchers, the MHPs were encouraged to express all comments and criticism they might have.

The interviews were conducted in the patients' homes or the general practice location between February 2018 and February 2019. Each interview lasted about 45 minutes. Data collection and analysis occurred in an iterative process, with intermediate analyses guiding subsequent data collection [29]. Data were collected until data saturation was reached (ie, when no new themes emerged from the interviews).

After completing the individual interviews, 2 focus group interviews were conducted in June 2019 and September 2019 at the research clinic, one with patients and one with MHPs. These interviews were moderated by BM, an experienced researcher in the field of qualitative methodology. In the focus group interviews, preliminary findings from the individual interviews were presented, and input from participants was collected about their perceptions on remarkable findings in the data. Each focus group interview lasted about 90 minutes.

Individual interviews and focus group interviews were audio recorded, transcribed verbatim, and summarized. The transcripts were checked for accuracy (by reading and listening) and corrected as needed by EKB. Participants were anonymized from transcription to the reporting of the data, with only the interviewers having access to the identification key.

Data analysis

Data from the first sequence of individual interviews were analyzed according to the 6 steps of thematic analysis suggested by Braun and Clarke [29]. All interviews were read and re-read carefully, and initial ideas about the content of the data were recorded in the field notes (Step 1). All interviews were coded independently by 2 researchers using MAXQDA 12 [30] (EKB and JG or Master's student). This was followed by comparing the codes and resolving disagreements through discussion. After 3 interviews, a first draft of the coding tree was prepared, and it was supplemented or adjusted regularly, based on the intermediate analyses of data (Step 2). We searched the coded data for themes, which we subsequently reviewed and defined. Preliminary themes and subthemes were discussed within the project group. Coded segments were divided among the themes and read carefully, and relevant segments were selected. A summary was prepared for each theme (Steps 3, 4, and 5). The final step consisted of producing a comprehensive and detailed report of relevant segments for each theme and selecting the most compelling ones.

Results

Demographic and clinical characteristics

Demographic and clinical variables of the patients and MHPs are presented in Table 1. Our sample contained 13 pairs of patients and their MHPs, resulting in 26

individual interviews. One MHP was interviewed twice about 2 different patients. Seven patients participated in the focus group interview. None of the patients participated in both the individual and focus group interviews. Six MHPs participated in the other focus group interview, 2 of whom had also participated in an individual interview. Reasons for nonparticipation are provided in Appendix 5.5.

Table 1. Demographic and clinical characteristics of patients and mental health professionals (MHPs).

Characteristics		Individual interviews		Focus group interviews	
		Patients (n=13)	MHPs (n=12)	Patients (n=7)	MHPs (n=6)
Age range (years)		21-63	27-58	31-70	41-60
Age (years), n					
	20-39	6	4	2	0
	40-59	5	8	3	5
	≥60	2	0	2	1
Sex, n					
	Female	9	11	4	5
	Male	4	1	3	1
Diagnosis (in remission), n					
	Anxiety disorder	4	N/A[a]	2	N/A
	Depressive disorder	4	N/A	0	N/A
	Anxiety and depressive disorder	5	N/A	5	N/A

[a]N/A: not applicable.

Overview of the themes

Three central themes emerged from the data: "perceived value of the relapse prevention program," "usability of the relapse prevention program," and "need for guidance." Each theme is considered in detail in the following paragraphs, and an overview of the themes can be found in Table 2.

Perceived value of the relapse prevention program

The first theme emerging from the data was the "perceived value of the relapse prevention program." This theme was defined using 3 subthemes: (1) prior expectations, (2) evaluation of the program, and (3) factors inhibiting use of the program.

Table 2. Overview of the main themes and subthemes and a description of their content.

Main and subthemes	Content
Perceived value of the relapse prevention program	
Prior expectations	Positive expectations of patients and MHPs[a] before using the program increased motivation for use
Evaluation of the program	Attitudes towards the program and its (subjective) effects (eg, increased awareness of relapse risks)
Factors inhibiting use of the program	Specific factors that reduce motivation to use the program (eg, absence of current symptoms)
Usability of the relapse prevention program	Technical aspects, attractiveness, and reflection on choices in the design of the program (eg, positive or negative views about reminders)
Need for guidance	
Personal contact is essential	Added value of personal contact with MHP, prerequisite for active use of the program
Initiating contact	Belief that the other party (ie, patient or MHP) is responsible for taking initiative

[a]MHPs: mental health professionals.

Prior expectations

Prior expectations of the relapse prevention program and, by extension, motivation for its use were related to several factors, starting with the current level of symptoms experienced by patients, along with the perceived risk of relapse and the expectation that the relapse prevention program could relieve symptoms. MHPs mentioned that they noticed these factors in their patients, and patients also mentioned these factors. Patients who had current symptoms, a high perceived risk of relapse, and a belief that the program could help prevent relapse appeared to have a high motivation for active use of the program.

Evaluation of the program

Many patients mentioned the importance of the relapse prevention program following recovery from anxiety or depressive disorders. They particularly appreciated the active role assigned to the patients themselves within the program, thereby encouraging them to be active participants in their process to remain well. According to the patients, the program raised awareness of relapse risks:

> *I find it very useful to raise my own awareness, so that I become more aware of the impact I can have, and therefore be more active in my own recovery.*
> [34003, female, 42 years old]

The focus group with patients showed that, given the diversity of modules, the relapse prevention program had relevant components for all patients. Several patients explicitly mentioned that the program provided a sense of security and stability at times when they showed signs of impending relapse.

Factors inhibiting use of the program

Patients with few or very few symptoms believed that they would experience few, if any, benefits from participating in the program, thereby reducing their motivation to use or continue to use the program. Patients in this relatively stable situation found it more difficult to imagine the possibility of a future relapse, and they saw no immediate need to engage in active relapse prevention. On the other hand, having many symptoms could also hinder the use of the program, as a perceived lack of concentration and energy was a reason for decreased use.

According to MHPs, some patients feared that the use of the relapse prevention program could actually lead to dysregulation:

> *But at times I got the impression that people thought "yes, I'm doing well now" and that they were frightened that if they were to do something about their condition, they would feel less well.*
> [MHP 39, female]

Usability of the relapse prevention program

Many patients and MHPs considered the online modules inviting, due to their appealing layout and normalizing effect. They indicated that the program normalized vulnerability to relapse: Completing mental health care treatment does not mean that all the symptoms and problems have been overcome nor that aggravation of symptoms can be ruled out in the future. Several patients and MHPs found the program easy to use:

> *Thought it was really good. I thought it was well structured. Clear, simple to use for both the MHP and the patient.*
> [MHP 39, female]

The relapse prevention program provided MHPs with practical tools for cooperating with patients in relapse prevention. The patients were motivated by the targeted suggestions for choosing relevant modules, given their problems and needs at that time. Moreover, they felt that the content of the eHealth modules corresponded to previous treatment in specialized mental health care. Some patients appreciated receiving this information again, especially as they had forgotten some of the content. In contrast, some patients were annoyed by the repetition of information from previous

treatment. Some patients found the program's focus on anxiety and depression restrictive. In their opinion, this did not enhance recognizability, particularly for those who had experienced only 1 of the 2 disorders.

One adverse aspect of the practical usability was that patients had to log on to a computer to work with the online modules. The patients suggested that it would have been easier to use an app. Patients participating in the focus group regarded the pressure caused by the program (by reminders and mandatory fields) as unpleasant and often irritating. On the other hand, the reminders in the program were sometimes also seen as a necessary "stick," which actually helped patients to continue with the program.

Patients did not always agree with each other. While some appreciated the clarity of the eHealth program, others found navigating the online platform confusing, as they had no clear overview of the available modules. They would have preferred a more intuitive program:

> *I sometimes found the navigation on the site rather complicated. It wasn't very logical.* [25002, female, 40 years old]

This was confirmed by patients and MHPs participating in the focus groups.

Need for guidance

The third theme relates to the "Need for guidance." Both patients and MHPs considered the quality of the contact between patients and MHPs essential for effectiveness in preventing relapse.

Personal contact is essential

After patients started using the eHealth modules, patients and MHPs were encouraged to have personal contact with each other once every 3 months. Patients indicated that contact with their MHPs was particularly vital to helping them use or continue to use the eHealth modules in times of reduced stability.

Several patients reported having become aware of their current symptoms when preparing for their contact with their MHPs, because they knew that symptom levels would be discussed. The very prospect of the meeting seemed to increase awareness, which benefitted the focus of the conversation.

Both groups identified the combination of the eHealth program and the personal contact between patients and MHPs as a factor facilitating the use of the program. They noted that these elements complement and reinforce each other and that they would be of less value separately:

I don't think it's possible to do it just with eHealth. And only seeing an MHP wouldn't work either as this is just a snapshot in time and it's difficult to provide all the background information during that session. eHealth provides more background information, while the MHP gives practical tips.
[54001, female, 30 years old]

MHPs reported being happy to get patients started with eHealth modules, as this meant that the patients would have an active role in their own recovery:

It is good to be able to work with the relapse prevention program, in whatever form, in between the sessions and not just let it come down to those 30 or 40 minutes a month.
[MHP 25, male]

The combination of reminders from the eHealth program and the MHP provided an incentive for active use of the program. In the focus group interview with patients, it became apparent that patients receiving more support from an MHP appreciated the relapse prevention program more than patients who had received less or minimal support. The latter group indicated that they would have preferred to receive more support from the MHP in using the eHealth program.
The focus groups with patients and MHPs clearly indicated the importance of tailoring the level of support to individual patients, taking into account their coping styles and current symptom levels. The data further suggest the need to establish who will take primary responsibility when symptoms increase: Is the patient able to do this, or is active support by the MHP needed?

Initiating contact

During the focus group interviews, MHPs clearly differed from patients in their task interpretations. The MHPs strongly emphasized the patient's self-management skills, while patients expected MHPs to play a more active role if and when symptoms were to get worse. The capacity of MHPs was an impeding factor, placing limits on the active approach and support of patients. As a result, patients requiring more support were not always reached successfully:

Our consultation hour is busy enough, so if, for instance, someone doesn't show up twice in a row for an appointment, and you have called them, then that's it. After all, we have so many patients who can't wait to get an appointment, so that also plays a role.
[MHP 34, female]

Discussion

Principal findings

Both the patients and MHPs in our study were predominantly positive about the blended relapse prevention program. It created awareness of relapse risks, and users appreciated its usability and accessibility. Lack of motivation, lack of recognizability, lack of support from the MHP, and symptom severity (too low or too high) appeared to be limiting factors in the use of the program. The implementation of the program was thus challenging. Several patients and MHPs regarded the program as easy to use and clearly structured, although others referred to a lack of intuitive design and overview of modules. Patients and MHPs agreed that the combination of eHealth modules and face-to-face contact is essential. According to the respondents, the MHP plays a crucial role in motivating and supporting patients in the use of the relapse prevention program. Surprisingly, the level of agreement between MHPs and their patients was high. The paired interviews revealed no striking discrepancies within the pairs of patients and MHPs. However, the focus group interviews did reveal significant discrepancies, as MHPs assumed a certain level of self-management skills in patients, while patients articulated their limitations in this respect, expressing a desire for more direct and personalized support from their MHPs.

Limitations

This study has several limitations. One limitation of this study is the possibility of response bias, as patients knew the objectives of the study and might have given socially desirable answers. At the start of the interviews, we emphasized our openness to all feedback, including critical comments on the program. There was also a risk of selection bias, with participants who agreed to participate in the interviews possibly having been more positive towards the program than those who did not participate. Nonetheless, both positive and negative perspectives were explicitly discussed during the interviews. Furthermore, recall bias might have occurred, given the time elapsed between completing the program and the individual interview or focus group interview for some patients (range: 0-6 months for the individual interviews and 0-12 months for the focus group interviews). We noticed that some patients tended to forget which eHealth modules they had completed and whether they had received online feedback. To reduce this bias, patients could request an overview of their completed modules and number of feedback messages to and from the MHP during the interview. In addition, patients could remain engaged after the intervention period, as they received monthly newsletters about the study and still had access to the program. The longer duration between completion of the program and the focus group interviews was caused by the fact that the focus group interviews could be prepared and conducted only after all individual interviews were conducted and analyzed.

Comparison with prior work

The positive attitudes of MHPs and patients towards the program and the perceived increase in awareness of relapse risks are consistent with findings from previous research on relapse prevention for depression [31–33].

Our study revealed several factors influencing implementation, including motivation, recognizability, support received from the MHP, and symptom severity. Program use and implementation are facilitated by motivation and the perceived effectiveness of the program, as well as by the presence of current symptoms and the perceived high risk of future relapse. These findings are consistent with previous findings [34,35] demonstrating that motivation and perceived effectiveness increase adherence. On the contrary, lack of motivation impeded the use of the program, specifically in patients with few symptoms. A similar finding was suggested by Biesheuvel-Leliefeld et al [36], who may have found an indication of motivation issues among remitted patients, as they had major difficulties recruiting participants for their relapse prevention study. Another factor influencing use and implementation in our study was recognizability. This seems to correspond to findings reported by Gerhards et al [34] that patient perceptions that a program is not applicable to them act as a barrier to program usage. Our results further indicate that program implementation is determined by whether patients received support from their MHPs. This finding has also been reported in previous studies [31,33,34,37,38]. Accessible personal contact with and an active approach by the MHP appears to be the key to successful implementation of a program.

No unambiguous confirmation regarding the influence of symptom level on implementation and usage of relapse prevention programs was found in the literature. Interestingly, we found that both excessively low and excessively high perceived symptom levels hindered program use and implementation. According to a literature review on dropout from internet-based treatment, adult patients with few symptoms of any psychological disorder *and* those with more severe depressive symptoms were more likely to dropout from these treatments [39]. These findings might be generalizable to relapse prevention programs for anxiety and depressive disorders, as the setup of such internet-based treatments is similar to that of existing relapse prevention programs.

We identified different perspectives regarding responsibilities, with MHPs perceiving patients to be remitted and therefore relying on their self-management skills, while patients expected support and monitoring from their MHPs, particularly when symptoms worsened. A parallel finding is described in previous literature [40], with patients feeling that general practitioners should initiate contact, while general practitioners expect patients to contact them if needed. We found that these different expectations also exist between MHPs and patients, which has not been described before in the scientific literature.

Implications for practice and research

The present study highlights the importance of guidance in eHealth-based relapse prevention for anxiety and depression. The level of guidance from and engagement of the MHP emerged as crucial factors in the success of the relapse prevention program. The self-management skills of patients and desired level of support should thus be aligned in advance, particularly in case of worsening symptoms.

Because self-management skills might differ over time, among other things depending on symptoms, it is essential to discuss and align needs over the course of the contacts, possibly enhancing implementation of relapse prevention programs based on eHealth. Given the lack of studies specifically addressing associations between symptom levels and adherence to relapse prevention programs, further quantitative studies on this association are needed. One appropriate design could involve using Ecological Momentary Assessment [41] to assess symptom levels and log data from an eHealth platform to assess adherence.

When developing new relapse prevention interventions, attention should be paid to accessible guidance by professionals, accessibility through an app, along with a clear and intuitive, flexible structure for the eHealth component. Also, specific interventions for specific diagnoses might increase recognizability.

Conclusions

Our findings suggest that personalized guidance from MHPs should be offered for eHealth-based relapse prevention programs, taking into account the preferences of patients and their level of self-management competencies. Both MHPs and patients should align expectations and needs in advance, as well as during the intervention, in order to increase implementation and enable optimal usage.

ACKNOWLEDGMENTS

Funding for this study was provided by SIA-RAAK: The Taskforce for Applied Research, part of the Netherlands Organization for Scientific Research (NWO) and Stichting Stoffels-Hornstra. We are grateful to Master's students Annabel van der Hulst and Elise van der Laan for conducting and coding interviews and to all participants for taking the time and effort to participate in this study.

AUTHORS' CONTRIBUTIONS

EKB, AM, OM, AVS, NB, and BM designed the study. EKB and JG recruited participants for the interviews and focus group interviews. EKB and JG conducted interviews and were primary analysts of the data. BM moderated the focus group interviews. AM and BM consulted on the data analysis. EKB and JG wrote the first draft of the manuscript. All authors discussed interpretation of results and contributed to and approved the final manuscript.

ABBREVIATIONS

GET READY: Guided E-healTh for RElapse prevention in Anxiety and Depression
MHP: mental health professional

References

1. World Health Organization. Investing in treatment for depression and anxiety leads to fourfold return [Internet]. 2016 [cited 2017 Jun 27]. Available from: http://www.who.int/mediacentre/news/releases/2016/depression-anxiety-treatment/en/

2. Bandelow B, Sagebiel A, Belz M, Görlich Y, Michaelis S, Wedekind D. Enduring effects of psychological treatments for anxiety disorders: meta-analysis of follow-up studies. Br J Psychiatry [Internet] Cambridge University Press; 2018 Jun 30;212(6):333–338. [doi: 10.1192/bjp.2018.49]

3. Cuijpers P. The Challenges of Improving Treatments for Depression. JAMA 2018 Dec;320(24):2529. [doi: 10.1001/jama.2018.17824]

4. Cipriani A, Furukawa TA, Salanti G, Chaimani A, Atkinson LZ, Ogawa Y, Leucht S, Ruhe HG, Turner EH, Higgins JPT, Egger M, Takeshima N, Hayasaka Y, Imai H, Shinohara K, Tajika A, Ioannidis JPA, Geddes JR. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. Lancet [Internet] 2018 Apr;391(10128):1357–1366. [doi: 10.1016/S0140-6736(17)32802-7]

5. Bandelow B, Reitt M, Röver C, Michaelis S, Görlich Y, Wedekind D. Efficacy of treatments for anxiety disorders. Int Clin Psychopharmacol [Internet] 2015 Jul;30(4):183–192. [doi: 10.1097/YIC.0000000000000078]

6. Scholten WD, Batelaan NM, Penninx BWJH, Balkom AJLM van, Smit JH, Schoevers RA, Oppen P van. Diagnostic instability of recurrence and the impact on recurrence rates in depressive and anxiety disorders. J Affect Disord [Internet] Elsevier; 2016 May [cited 2016 Jul 7];195:185–190. PMID:26896812

7. Vos T, Haby MM, Barendregt JJ, Kruijshaar M, Corry J, Andrews G. The Burden of Major Depression Avoidable by Longer-term Treatment Strategies. Arch Gen Psychiatry [Internet] 2004 Nov 1;61(11):1097. [doi: 10.1001/archpsyc.61.11.1097]

8. Biesheuvel-Leliefeld KEM, Kok GD, Bockting CLH, Cuijpers P, Hollon SD, van Marwijk HWJ, Smit F. Effectiveness of psychological interventions in preventing recurrence of depressive disorder: Meta-analysis and meta-regression. J Affect Disord [Internet] Elsevier; 2015 Mar 15 [cited 2016 Jul 7];174:400–410. PMID:25553400

9. Hiss H, Foa EB, Kozak MJ. Relapse prevention program for treatment of obsessive-compulsive disorder. J Consult Clin Psychol [Internet] 1994;62(4):801–808. [doi: 10.1037/0022-006X.62.4.801]

10. Scholten WD, Batelaan NM, van Oppen P, Smit JH, Hoogendoorn AW, van Megen HJGM, Cath DC, van Balkom AJLM. The Efficacy of a Group CBT Relapse Prevention Program for Remitted Anxiety Disorder Patients Who Discontinue Antidepressant Medication: A Randomized Controlled Trial. Psychother Psychosom [Internet] 2018;87(4):240–242. [doi: 10.1159/000489498]

11. White KS, Payne LA, Gorman JM, Shear MK, Woods SW, Saksa JR, Barlow DH. Does maintenance CBT contribute to long-term treatment response of panic disorder with or without agoraphobia? A randomized controlled clinical trial. J Consult Clin Psychol [Internet] 2013;81(1):47–57. [doi: 10.1037/a0030666]

12. Wright J, Clum GA, Roodman A, Febbraro GAM. A Bibliotherapy Approach to Relapse Prevention in Individuals with Panic Attacks. J Anxiety Disord [Internet] 2000 Sep;14(5):483–499. [doi: 10.1016/S0887-6185(00)00035-9]

13. National Health Service. The Improving Access to Psychological Therapies Manual [Internet]. Natl Collab Cent Ment Heal. 2019 [cited 2020 Apr 6]. Available from: https://www.england.nhs.uk/wp-content/uploads/2019/12/iapt-manual-v3.pdf

14. Holländare F, A. Anthony S, Randestad M, Tillfors M, Carlbring P, Andersson G, Engström I. Two-year outcome of internet-based relapse prevention for partially remitted depression. Behav Res Ther [Internet] Elsevier Ltd; 2013 Nov [cited 2016 Jul 6];51(11):719–722. PMID:21401534

15. Klein NS, Kok GD, Burger H, van Valen E, Riper H, Cuijpers P, Dekker J, Smit F, van der Heiden C, Bockting CLH. No Sustainable Effects of an Internet-Based Relapse Prevention Program over 24 Months in Recurrent Depression: Primary Outcomes of a Randomized Controlled Trial. Psychother Psychosom [Internet] 2018;87(1):55–57. PMID:29306953

16. Kok G, Burger H, Riper H, Cuijpers P, Dekker J, van Marwijk H, Smit F, Beck A, Bockting CLH. The Three-Month Effect of Mobile Internet-Based Cognitive Therapy on the Course of Depressive Symptoms in Remitted Recurrently Depressed Patients: Results of a Randomized Controlled Trial. Psychother Psychosom [Internet] 2015 Feb 21;84(2):90–99. PMID:25721915

17. Hoorelbeke K, Koster EHW. Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Evidence from a double-blind randomized controlled trial study. J Consult Clin Psychol [Internet] 2017 Feb;85(2):135–146. PMID:27362792

18. Urech A, Krieger T, Möseneder L, Biaggi A, Vincent A, Poppe C, Meyer B, Riper H, Berger T. A patient post hoc perspective on advantages and disadvantages of blended cognitive behaviour therapy for depression: A qualitative content analysis. Psychother Res [Internet] 2019 Nov 8;29(8):986–998. [doi: 10.1080/10503307.2018.1430910]

19. Baumeister H, Reichler L, Munzinger M, Lin J. The impact of guidance on Internet-based mental health interventions - A systematic review. Internet Interv [Internet] Elsevier B.V.; 2014;1(4):205–215. [doi: 10.1016/j.invent.2014.08.003]

20. Titzler I, Saruhanjan K, Berking M, Riper H, Ebert DD. Barriers and facilitators for the implementation of blended psychotherapy for depression: A qualitative pilot study of therapists' perspective. Internet Interv [Internet] 2018;12:150–164. [doi: 10.1016/j.invent.2018.01.002]

21. Krijnen-De Bruin E, Muntingh ADT, Hoogendoorn AW, Van Straten A, Batelaan NM, Maarsingh OR, Van Balkom AJLM, Van Meijel B. The GET READY relapse prevention programme for anxiety and depression: A mixed-methods study protocol. BMC Psychiatry 2019;19(1). [doi: 10.1186/s12888-019-2034-6]

22. Muntingh ADT, Hoogendoorn AW, Van Schaik DJF, Van Straten A, Stolk EA, Van Balkom AJLM, Batelaan NM. Patient preferences for a guided self-help programme to prevent relapse in anxiety or depression: A discrete choice experiment. Eisenbarth H, editor. PLoS One [Internet] 2019 Jul 18;14(7):e0219588. [doi: 10.1371/journal.pone.0219588]

23. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Heal Care [Internet] 2007 Sep 16;19(6):349–357. PMID:17872937

24. Magnée T, de Beurs DP, Schellevis FG, Verhaak PF. Antidepressant prescriptions and mental health nurses: an observational study in Dutch general practice from 2011 to 2015. Scand J Prim Health Care [Internet] 2018;36(1):47–55. [doi: 10.1080/02813432.2018.1426145]

25. National Counsel Mental Health Professionals. Functie- & competentieprofiel "Praktijkondersteuner huisarts GGZ" 2020 [Job and competence profile "Mental Health Professional" 2020] [Internet]. 2020. Available from: https://www.poh-ggz.nl/wp-content/uploads/2020/03/Definitief-Functie-en-competentieprofiel-POH-GGZ-2020-versie-1.0-04032020.pdf

26. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci [Internet] 2009 Dec 7;4(1):50. PMID:19664226

27. Boeije H. Analyseren in kwalitatief onderzoek. 2nd ed. Amsterdam: Boom Lemma; 2014.

28. Baarda B, Bakker E, Fisher T, Julsing M, Peters V, van der Velden T, de Goede M. Basisboek Kwalitatief Onderzoek. Derde druk. Groningen/Houten: Noordhoff Uitgevers bv; 2013.

29. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol [Internet] 2006 Jan;3(2):77–101. PMID:223135521

30. VERBI Software. MAXQDA 12. Berling, Germany: VERBI Software; 2015.

31. Boggs JM, Beck A, Felder JN, Dimidjian S, Metcalf CA, Segal Z V. Web-based intervention in mindfulness meditation for reducing residual depressive symptoms and relapse prophylaxis: A qualitative study. J Med Internet Res [Internet] JMIR Publications Inc.; 2014 [cited 2016 Jul 6];16(3):1–12. PMID:24662625

32. Allen M, Bromley A, Kuyken W, Sonnenberg SJ. Participants' Experiences of Mindfulness-Based Cognitive Therapy: "It Changed Me in Just about Every Way Possible." Behav Cogn Psychother [Internet] 2009 Jul 10;37(4):413–430. PMID:19508744

33. Lillevoll KR, Wilhelmsen M, Kolstrup N, Høifødt RS, Waterloo K, Eisemann M, Risør MB. Patients' Experiences of Helpfulness in Guided Internet-Based Treatment for Depression: Qualitative Study of Integrated Therapeutic Dimensions. J Med Internet Res [Internet] 2013 Jun 20;15(6):e126. [doi: 10.2196/jmir.2531]

34. Gerhards SAH, Abma TA, Arntz A, de Graaf LE, Evers SMAA, Huibers MJH, Widdershoven GAM. Improving adherence and effectiveness of computerised cognitive behavioural therapy without support for depression: A qualitative study on patient experiences. J Affect Disord [Internet] 2011 Mar;129(1–3):117–125. [doi: 10.1016/j.jad.2010.09.012]

35. Cuijpers P, van Straten A, Warmerdam L, van Rooy MJ. Recruiting participants for interventions to prevent the onset of depressive disorders: Possible ways to increase participation rates. BMC Health Serv Res [Internet] BioMed Central; 2010 Dec 25 [cited 2016 Jul 6];10(1):181. PMID:20579332

36. Biesheuvel-Leliefeld KEM, Dijkstra-Kersten SMA, van Schaik DJF, van Marwijk HWJ, Smit F, van der Horst HE, Bockting CLH. Effectiveness of Supported Self-Help in Recurrent Depression: A Randomized Controlled Trial in Primary Care. Psychother Psychosom [Internet] 2017;86(4):220–230. [doi: 10.1159/000472260]

37. Kelders SM, Kok RN, Ossebaard HC, Van Gemert-Pijnen JE. Persuasive System Design Does Matter: a Systematic Review of Adherence to Web-based Interventions. J Med Internet Res [Internet] 2012 Nov 14 [cited 2017 May 12];14(6):e152. PMID:23151820

38. Apolinário-Hagen J, Kemper J, Stürmer C. Public Acceptability of E-Mental Health Treatment Services for Psychological Problems: A Scoping Review. JMIR Ment Heal [Internet] 2017;4(2):e10. PMID:28373153

39. Melville KM, Casey LM, Kavanagh DJ. Dropout from Internet-based treatment for psychological disorders. Br J Clin Psychol [Internet] 2010 Nov;49(4):455–471. [doi: 10.1348/014466509X472138]

40. Bosman RC, Huijbregts KM, Verhaak PF, Ruhé HG, van Marwijk HW, van Balkom AJ, Batelaan NM. Long-term antidepressant use: a qualitative study on perspectives of patients and GPs in primary care. Br J Gen Pract [Internet] 2016 [cited 2017 Sep 14];66(651):e708–e719. [doi: 10.3399/bjgp16x686641]

41. Shiffman S, Stone AA, Hufford MR. Ecological Momentary Assessment. Annu Rev Clin Psychol [Internet] United States; 2008 Apr;4(1):1–32. PMID:18509902

Appendix 5.1. COREQ checklist

		Location in manuscript (Section, page no.)
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Interviewer/facilitator Which author/s conducted the interview or focus group?	JG, EKB, AH (acknowledgements), EL (acknowledgements), BM	Page 121-122
2. Credentials What were the researcher's credentials? E.g. PhD, MD	EKB: MSc JG: MSc ADTM: PhD WDS: PhD ORM: MD, PhD AS: PhD NMB: MD, PhD BM: PhD AH: Master student EL: Master student	
3. Occupation What was their occupation at the time of the study?	EKB: PhD student; JG: psychologist and researcher; AM: psychologist and researcher; WS: psychotherapist and researcher; OM: general practitioner and researcher; AVS: Professor of Clinical Psychology; NB: psychiatrist and researcher; BVM: Professor of Mental Health Nursing.	
4. Gender Was the researcher male or female?	Males and Females	
5. Experience and training What experience or training did the researcher have?	All researchers had prior experience with qualitative research.	Page 121
Relationship with participants		
6. Relationship established Was a relationship established prior to study commencement?	No (patients) and yes (professionals)	Page 121
7. Participant knowledge of the interviewer What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	Participants were briefed about the purpose of the study	Appendix 5.3 & 5.4
8. Interviewer characteristics What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	None	

Appendix 5.1. Continued

		Location in manuscript (Section, page no.)
Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	Topic lists based on the Consolidated Framework for Implementation Research. Analyses conducted with thematic analysis.	Page 121-122
10. Sampling How were participants selected? e.g. purposive, convenience, consecutive, snowball	Purposive	Page 120
11. Method of approach How were participants approached? e.g. face-to-face, telephone, mail, email	Telephone or email	Page 120-121
12. Sample size How many participants were in the study?	36 participants	Page 122-123
13. Nonparticipation How many people refused to participate or dropped out? Reasons?	See Appendix 5.5	Appendix 5.5
Setting		
14. Setting of data collection Where was the data collected? e.g. home, clinic, workplace	Individual interviews: patients' homes, general practice location; Focus-group interview: research clinic	Page 122
15. Presence of non-participants Was anyone else present besides the participants and researchers?	No	
16. Description of sample What are the important characteristics of the sample? e.g. demographic data, date	See Table 1	Page 123
Data collection		
17. Interview guide Were questions, prompts, guides provided by the authors? Was it pilot tested?	Yes	Page 121, Appendix 5.3 & 5.4
18. Repeat interviews Were repeat interviews carried out? If yes, how many?	Yes, one MHP was interviewed twice, since two of his patients both agreed to participate	Page 123
19. Audio/visual recording Did the research use audio or visual recording to collect the data?	Individual interviews and focus-group interviews were audio recorded, transcribed verbatim and summarized.	Page 122

Appendix 5.1. Continued

		Location in manuscript (Section, page no.)
20. Field notes Were field notes made during and/or after the interview or focus group?	Yes	Page 122
21. Duration What was the duration of the interviews or focus group?	Individual interviews: 45 minutes Focus-group interviews: 90 minutes	Page 122
22. Data saturation Was data saturation discussed?	Yes	Page 122
23. Transcripts returned Were transcripts returned to participants for comment and/or correction?	No	
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders How many data coders coded the data?	4	Page 122
25. Description of the coding tree Did authors provide a description of the coding tree?	Yes	Page 122
26. Derivation of themes Were themes identified in advance or derived from the data?	Themes were derived from the data.	Page 122
27. Software What software, if applicable, was used to manage the data?	MAXQDA 12	Page 122
28. Participant checking Did participants provide feedback on the findings?	Yes, by performing the focus-group interviews.	Page 122
Reporting		
29. Quotations presented Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. participant number	Yes	Page 124-127
30. Data and findings consistent Was there consistency between the data presented and the findings?	Yes	
31. Clarity of major themes Were major themes clearly presented in the findings?	Yes	Page 123-127
32. Clarity of minor themes Is there a description of diverse cases or discussion of minor themes?	Yes	Page 124-127

Appendix 5.2. GET READY intervention

The GET READY relapse prevention program was developed for general practice and consists of several elements. First, patients are invited by their MHPs for a face-to-face session (F2F), in which an individual relapse prevention plan is discussed. Second, patients receive access to an E-health platform. Third, patients are monitored by their MHPs and can schedule regular F2F sessions. The E-health platform provides three basic components and 12 optional modules, which patients can select and prioritize according to their needs and preferences (Figure 5.2.1). Each module takes 20-30 minutes to complete. Based on module completion, pop-up suggestions appear about related modules that might be interesting to the patient. A diary is also available, in which patients monitor symptoms weekly. The diary is available via the computer and via an app. All other modules are accessible through the computer. All modules aim to promote self-management skills (e.g. seeking help in case of impending relapse or pro-active planning of healthy behavior to cultivate stability and psychological and physical wellbeing). Patients receive weekly reminders to complete the selected online modules, receiving feedback from their MHPs upon request.

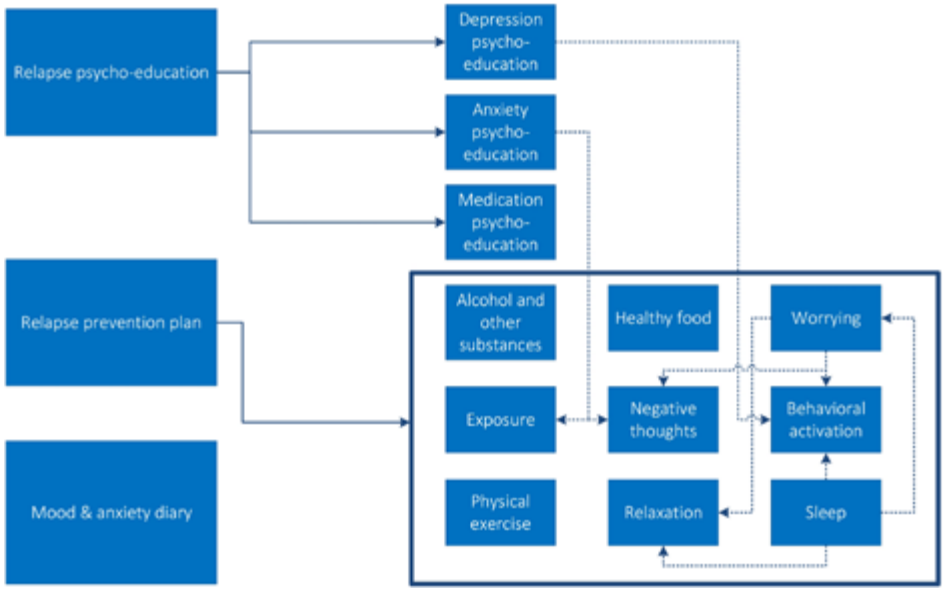

Figure 5.2.1. Overview of E-health modules, adapted from previous publication [21]. Dotted lines indicate that modules have overlapping themes and that modules can be easily opened from the other modules.

Appendix 5.3. Topic guide interview patient

Main questions	Additional questions
Introduction	Sign informed consent Introduce yourself Mention the duration of the interview (45 minutes) Ask permission to audio record the interview, and start the recording Mention that the name and personal data is saved separately from research data Mention the purpose of the interview
What is your experience with the relapse prevention program in general?	What were your expectations of the relapse prevention program? Could you tell more about the role of the MHP? · Did you already know the MHP at the beginning of the study? · What did you expect from the MHP at the beginning of the study? · How did you experience the contacts? · How did you experience the support from the MHP? · In which way did the MHP help you to stay healthy? · What could be improved in the guidance from the MHP? · Who initiated the contact and how did you experience this? · What did you expect from the MHP if symptoms worsened? What is your experience with the E-health program? · Usability · Meeting your needs · Pleasure/satisfaction · Available choices · Use of language · Design · Time investment Did the program help you to stay healthy/without symptoms? · In which way did the program help you to stay healthy? · If the program did not help: did other things help? · If you experienced a period of worsening symptoms: what would you have needed to use the program? How do you feel about the combination of E-health and having contact with the MHP? · If you had contacts with the MHP but did not use E-health: what motivated you to have contact with the MHP?
What were the most useful and the least useful parts of the E-health program?	· Which modules did you complete? What made you choose these modules? · What were your motives concerning using or not using the modules? · Which modules were set up for you, but not completed? · Did you complete the diary? · How much did you use the message function within the program? · According to the questionnaires, your symptoms have decreased/increased. How did you experience this?
What do you like about the relapse prevention program and what could be improved?	What is the most useful aspect of the relapse prevention program? What could be improved in the relapse prevention program? What did you miss in the relapse prevention program?
Completion	Are there other topics you would like to discuss? Do you have any questions? Would you like to receive the outcomes of the study? Would you be interested in participating in a focus group interview?

Appendix 5.4. Topic guide interview MHP

Main questions	Additional questions
Introduction	Sign informed consent Introduce yourself Explain which patient the interview is about Mention the duration of the interview (45 minutes) Ask permission to audio record the interview, and start the recording Mention that the name and personal data is saved separately from research data Mention the purpose of the interview
Practical questions	How many hours a week do you work as MHP? Do you work in multiple general practices? How many minutes does a regular contact last? How many MHPs/GPs are working in this general practice?
What is your experience with the relapse prevention program?	How did you offer the relapse prevention program to the patient? · How were follow-up contacts planned? · Who initiated the contact and how did you experience this? · How many contacts did you have? · What did you discuss during the contacts? · Did you already know the patient before the beginning of the study? · Did you stimulate the patient to use the relapse prevention program? In which way? · How did the program influence the health of the patient? · To what extent did the program meet the patients' symptoms? How did you offer the relapse prevention program to other patients? *What was it like to offer the relapse prevention program to the patient? What is your experience with the E-health program? · Usability/structure · Design · Use of language · Time investment · Aspects: what did you use/not use, experience with aspects, relapse prevention plan · Message function/providing feedback
What made it easier or harder to implement the relapse prevention program in the general practice?	The relapse prevention program itself: intervention characteristics · What did you think about the quality of the relapse prevention program? · Did you know the content of the modules? · Did you ever apply relapse prevention strategies before? How does this program compare to other strategies that you are familiar with? · How do you feel about the combination of contacts and E-health? · *How complicated is the intervention? Factors within the general practice: inner setting · How could you apply the relapse prevention program in your 'normal work'? · Did you experience support from the general practice or GP? How? · In the general practice, what is the willingness to change? · How did having/not having time affect implementation? Characteristics of individuals · Did you feel confident offering the relapse prevention program? Why/why not? Process of implementation · Did you experience support from the research team? How? Influence from outer setting · Did you have contact with specialized mental healthcare services? What was the effect?

Main questions	Additional questions
What do you like about the relapse prevention program and what could be improved?	What is the most useful aspect of the relapse prevention program? What could be improved in the relapse prevention program? *What did you miss in the relapse prevention program? Would you use the relapse prevention program if available after completion of the study? What is needed?
Completion	Are there other topics you would like to discuss? Do you have any questions? Would you like to receive the outcomes of the study? Would you be interested in participating in a focus group interview?

* If not discussed yet, also ask this question

Appendix 5.5. Reasons for nonparticipation

Initially, 35 patients were invited for the individual interviews. Of the 19 agreeing to participate, 13 (37%) were selected and interviewed. In all, 17 MHPs were invited for the individual interviews. Of the 14 agreeing to participate, 12 (71%) were selected and interviewed. Reasons for nonparticipation are presented in Table 5.5.1.

Table 5.5.1. Reasons for nonparticipation in individual interviews.

	Invited	Agreed to participate	Interviewed	Reasons for nonparticipation
Patients	35	19	13	Demographic variables overlapped with participating patients (N=6) First agreed to participate but later unreachable (N=6) Too difficult to talk about (N=2) Comorbid symptoms (N=2) MHPs did not wish to participate (leading to nonparticipation by patients) (N=2) No interest (N=2) No time (N=1) Did not use the program (N=1)
MHPs	17	14	12	No interest (N=2) Patient did not wish to participant (leading to nonparticipation by the MHP) (N=1) Already interviewed about another patient (N=1) Not reachable (N=1)

In all, 98 patients were asked to participate, and seven (7%) participated in the focus-group interview. Of the 50 MHPs invited to participate, six (12%) participated in the focus-group interview. Reasons for nonparticipation are presented in Table 5.5.2.

Table 5.5.2. Reasons for nonparticipation in the focus-group interview.

	Invited	Interviewed	Reasons for nonparticipation
Patients	98	7	No contact (N=55) No interest (N=16) No time (N=16) Not able to travel (N=2) Did not use the program (N=1) Too difficult to talk about (N=1)
MHPs	50	6	No contact (N=39) No interest (N=4) No time (N=1)

7

SUMMARY & GENERAL DISCUSSION

The primary aim of this thesis was to examine relapse prevention in patients with remitted anxiety and depressive disorders. Three specific aims were formulated: first, to examine – via a systematic review and meta-analysis – the effectiveness of current psychological relapse prevention interventions for patients with remitted anxiety or depressive disorders; second, to evaluate our newly developed GET READY relapse prevention program; and third, to psychometrically test a new measurement instrument for self-management strategies in patients with (chronic or partially remitted) anxiety and depressive disorders.

This chapter presents a summary of the main findings, which will be discussed in relation to extant literature, followed by a reflection on the findings. Methodological considerations are then addressed, before we proceed to delineate the implications of the research for clinical practice and future research. Finally, the chapter ends by providing an overall conclusion to the thesis.

Summary of the main findings

In **Chapter 2**, we conducted a systematic review and meta-analysis in order to examine the effectiveness of current psychological interventions aimed at preventing relapse among patients with remitted anxiety or depressive disorders. We focused on the effectiveness of stand-alone psychological relapse prevention interventions, as well as those interventions combined with maintenance antidepressant treatment (M-ADM) or antidepressant medication (ADM) discontinuation. In total, 7,324 papers were screened, with 40 studies subsequently being included. We demonstrated that for patients with remitted major depressive disorders (MDD), psychological interventions reduced the risk of relapse by 24% within the first 24 months (in comparison to treatment as usual (TAU)), and that this effect persisted for up to three years. When psychological interventions were offered in combination with M-ADM, the risk of relapse was also reduced by 24% within the first 24 months, in comparison to M-ADM alone. Due to the paucity of studies, no meta-analysis could be conducted regarding the effectiveness of psychological relapse prevention interventions that are combined with discontinuation of ADM. Similarly, we found that there was also a relative dearth of studies on relapse prevention for anxiety disorders, which, in turn, meant that no meta-analysis could be conducted for this patient group. In conclusion, psychological interventions were found to be effective for reducing the risk of relapse among patients with remitted MDD.

Chapters 3, 4 and 5 described the development, implementation and evaluation of the GET READY relapse prevention program. **Chapter 3** outlined the protocol of the GET READY study. The GET READY program was developed based on patient preferences, as well as in collaboration with professionals and a patient panel. The program included regular face-to-face (FTF) contact with a MHP in primary care, online

E-health modules (including drawing up a personalized relapse prevention plan), and a mood and anxiety diary, which allowed patients to monitor their symptoms. The study protocol describes both the quantitative and qualitative methods that were used to evaluate the GET READY relapse prevention program.

In **Chapter 4,** the usage of the GET READY program, course of symptoms of participants, and the association between usage intensity and course of symptoms was examined. These factors were investigated through conducting a pre-post study with 113 patients, who were either fully or partially in remission from anxiety and/or depressive disorders. Longitudinal data was collected over a 9-month period. It was observed that the core E-health modules, which focused on relapse psychoeducation and the relapse prevention plan, were used by 70-74% of the patients, while the optional modules were deemed to be elective and, as such, were used by less than 40% of the patients. According to a pre-defined usage intensity measure, around one in four patients were defined as 'regular users'. Generally speaking, the use of the self-management components of the program, such as online modules and the online 'mood & anxiety diary' decreased rapidly over time. Given that the study had a non-experimental design, no causal effect between the GET READY intervention and the severity of symptoms could be demonstrated. However, it appeared that most patients remained stable while participating in the GET READY intervention: a minority of participants (15%) experienced a relapse in their anxiety symptoms within the 9-month follow-up period, while 10% experienced a relapse in their depressive symptoms. Having more FTF contact with MHPs was significantly associated with higher anxiety and depressive scores. Other usage variables were not significantly associated with the course of symptoms. In **Chapter 5**, we described the results of a qualitative study about the implementation and evaluation of the GET READY intervention, from the perspective of both patients and MHPs. Individual interviews were conducted with pairs of patients (N=13) and MHPs (N=12), in order to highlight potential discrepancies between their respective accounts. After reflecting upon the findings of the individual interviews, two focus group interviews were subsequently conducted. These focus groups (comprising both patients and MHPs) showed that users were mostly positive about the GET READY intervention. Specifically, it was said that it created awareness of relapse risks, assigned an active role to patients themselves in relapse prevention, contained relevant components, and provided a sense of security and stability to patients. Alongside this, users also appreciated its usability and accessibility. However, the lack of motivation on the behalf of patients, lack of recognizability of the program due to its focus on both anxiety *and* depression, and the lack of support from MHPs limited the use of the program. Moreover, the use of the program was also negatively affected by both the number and severity of patients' symptoms. More specifically, those with few symptoms felt no need to engage in active relapse prevention, while

those with more severe symptoms experienced a lack of concentration and energy, and therefore made less use of the program. The combination of E-health modules and FTF contact was considered to be essential, and it appeared that MHPs played a crucial role in terms of motivating and supporting patients in the use of the E-health program. There were no marked discrepancies between the paired individual interviews with patients and MHPs. However, the focus group interviews did reveal significant discrepancies, insofar as MHPs expected patients to exercise a certain level of self-management skills when using the relapse prevention program, while patients articulated their limitations in this respect and expressed a desire for more direct and personalized support from their MHPs. In **Chapter 6,** we assessed the psychometric properties of a new questionnaire for measuring self-management strategies among patients with anxiety and depression: the 'Assessment of Self-management in Anxiety and Depression' (ASAD) questionnaire. Given that self-management is an increasingly important aspect in recovering from mental health disorders, focusing on self-management can also be expedient for relapse prevention. However, the burden of anxiety and depressive disorders potentially decreases people's ability to use self-management strategies, which is problematic given that employing these strategies can lead to a decrease in one's anxiety and depressive symptoms. Zoun et al. [1] developed the ASAD, because there was no Dutch self-management questionnaire for patients with anxiety and depressive disorders. In our study, the ASAD was completed by 171 participants across two samples. An exploratory and confirmatory factor analysis revealed three solid factors: Seeking support, Daily life strategies and Taking ownership. Furthermore, the factor analyses revealed that the number of questionnaire items could be reduced from 45 to 21. The evaluation indicated high levels of internal consistency and reliability for the 21 item ASAD short form (ASAD-SF). The identified factors can provide guidance for both patients and professionals with respect to what self-management strategies to apply.

Reflection on the main findings

Effectiveness of psychological relapse prevention interventions

Our systematic review and meta-analysis indicated that psychological interventions were effective in preventing relapse among patients with remitted MDD when compared to TAU, including when used in combination with M-ADM, leading to a 24% reduction in relapse rates (**Chapter 2)**.

This systematic review and meta-analysis extends the findings of previous research, insofar as it was the first study to demonstrate the additional effect to be gained from providing psychological interventions aimed at relapse prevention to patients using M-ADM up to and including 2 years after remission. This result is highly relevant given that many remitted patients use M-ADM and M-ADM in itself also affects relapse rates

[2]. We demonstrated that all patients who were receiving M-ADM after completion of their treatment benefited from additional psychological relapse prevention interventions for up to a 2-year period, and that it lowered the risk of relapse even more. This advice is currently not provided in international guidelines [3–6], while only one Dutch guideline suggests that a combination of medication and psychotherapy can be effective in preventing relapse for patients with severe symptoms or patients who have experienced three or more previous episodes [7].

In addition to this, our study revealed that there is a relative dearth of studies on relapse prevention interventions for patients with anxiety disorders. Hence, more research in this field is urgently needed to establish the effectiveness of psychological interventions aimed towards relapse prevention among patients with anxiety disorders.

Evaluation of the GET READY relapse prevention program

Our quantitative study **(Chapter 4**) revealed that – as expected – the core components of the online program were used more intensively than the optional components. This was consistent with data from other studies using E-health treatment programs [8,9]. Within our study, it appeared that the usage of the overall modules was rather low in comparison to other studies [10–13]. However, these other studies were not focused on the prevention of relapse per se, but rather on the treatment of anxiety and depressive disorders. Consequently, over the course of the treatment patients might have been more inclined to engage with the modules, as they felt that there was greater scope for improving their symptoms. In line with other studies, it was shown that the usage intensity of the E-health program decreased rapidly [14,15]. We considered this risk beforehand, which is why we sought to keep patients involved over a longer duration by sending them reminders and asking MHPs to motivate patients to use the program. Unfortunately, it appears that these efforts proved insufficient to keep patients engaged in the program.

At the start of our study, we hypothesized that patients should be able to have access to a relapse prevention program over a significant period of time, as the risk of relapse remains relatively stable over time, even years after reaching remission. Our intention was to provide an easily accessible relapse prevention tool that patients would either use more intensively if they were experiencing a deterioration of their symptoms, or less intensively when they were doing well. In addition, in response to patients' preferences [16], the GET READY program was offered in a non-committed and flexible way. While patients received recommendations regarding usage of the program and engaged in regular FTF contact with MHPs, they were not obliged to follow a certain protocol. Ultimately, the relatively low usage and rapid decrease of usage intensity is not consistent with the intended use of the program. In this respect, perhaps a more structured and time-intensive program with more frequent FTF contact with

MHPs might be better suited to keeping patients engaged, thereby increasing the effectiveness of the program. While we believe that it is important to follow patients' preferences, these findings potentially raise the question of whether following these preferences is necessarily the best way to go in terms of the effectiveness of such programs. Having said that, if patients' preferences are not sufficiently taken into account, then this is also likely to have a deleterious effect on adherence to the program. These considerations shed light on the difficult choices that must be made during the development of new relapse prevention programs. In conclusion, in order for relapse prevention programs to be effective, one must strike a balance between accounting for patients' preferences and guaranteeing sufficient exposure to the intervention.

It can be especially difficult to keep patients engaged in the case of relapse prevention. Indeed, previous relapse prevention studies [17–19] have highlighted low rates of participation, on the grounds that patients do not feel the need for such programs, do not feel at risk of relapse, do not expect interventions to be effective, or simply do not want to be confronted with their period of anxiety or depression [18–20]. These reasons were also reported in our qualitative study (**Chapter 5**).

Although the usage intensity was relatively low and decreased rapidly over time, generally speaking, it appeared that the patients who participated in the GET READY program remained stable over its duration. In fact, the relapse rates in our study were lower than those found in other relapse prevention studies [21,22]. Although no causal pathway could be established in this pre-post study, these results nevertheless may indicate that the GET READY program is equipped to potentially protect patients from relapse. These findings might be explained by the results from our qualitative study (**Chapter 5**), in which patients expressed that the program functioned as a 'safety net' for them, and that they found it comforting that they could easily contact their MHP if they needed to. Indeed, patients routinely mentioned that merely knowing that the MHP was available provided them with a sense of comfort. Patients also positively valued the combination of E-health modules and FTF contact and appreciated the support they received from their MHP. Furthermore, the mere fact that the program increased patients' awareness of the risk of relapse may have played a role in preventing relapses and keeping patients stable.

A significant positive association was found between the amount of FTF contact that patients had with their MHP and the severity of symptoms. This association remained significant when correcting for the anxiety and depressive symptoms one measurement prior. Since no causality could be established, interpreting this result is a complex issue. The most plausible explanation is that patients adequately responded to their initial symptoms by reaching out to their MHP, which is in accordance with a previous study that showed that patients with more severe symptoms were more likely

to reach out for help [23]. It is also possible that patients reached out too late, so that ultimately the support offered by the MHP was insufficient for averting relapse. This explanation is supported by findings from the qualitative study (**Chapter 5**), which showed that patients who experienced high symptom levels were less likely to use the program and, as such, less likely to have FTF contact with their MHP.

The results of our qualitative evaluation of the GET READY program (**Chapter 5**) revealed that patients and MHPs were generally positive about the GET READY program. The GET READY program was specifically tailored to the preferences of patients: it provided flexible modules, included regular FTF contact with a professional, gave them the opportunity to complete a personal relapse prevention plan, and required a low time investment [16]. It appeared that patients specifically appreciated these aspects of the GET READY program, as well as the ability to personalize their own program. The perceived increased awareness of relapse risks is consistent with previous research on relapse prevention in depression [24–26]. Several factors were identified that influenced the implementation of the program. In accordance with other studies, program use and implementation were facilitated by patients' motivation, the perceived effectiveness of the program, the presence of current symptoms and a perceived high risk of future relapse [19,27]. At the same time, we found that a lack of motivation and lack of current symptoms operated as barriers to using the program. In addition, the lack of support from MHPs was also cited as a barrier. Another factor influencing the use and implementation of the program was recognizability, which was also found in Gerhards et al.'s study [27]. That is to say, if patients do not perceive that a program is applicable to them, then this can form a barrier to them using the program. As a result of these factors in particular, implementing the GET READY program proved to be somewhat challenging, as is evidenced by the relatively low usage intensity and rapid decrease of usage described in **Chapter 4**.

In line with extant literature, this study found that receiving support from MHPs was beneficial in terms of the use and implementation of the relapse prevention program [24,26–29]; in particular, it appeared that the GET READY program was more likely to be successfully implemented if MHPs were accessible and actively engaged in personal contact with their patients. This stressed the importance of the role played by MHPs, which is discussed in greater detail later in this chapter.

We discovered an interesting mechanism with respect to the association between symptom level and usage, which was that both low and high symptom levels served as a barrier to usage of the program. These results support previous research, which describes that both adult patients with few symptoms of any psychological disorders *and* those with more severe depressive symptoms often dropout of treatment [30]. Patients with *just enough* symptoms are perhaps the easiest group to motivate to use the program, although it could also potentially benefit patients that have either a few

or many symptoms. It might be less important to target patients with only a few symptoms, insofar as they are at a lower risk of relapse [31]. However, patients with many symptoms might possibly be motivated to use the program via the use of persuasive techniques, such as emails, reminders, and additional support and guidance from their MHP.

We also identified different perspectives regarding responsibilities: MHPs perceived patients to be remitted and therefore relying on their self-management skills, while patients expected support and ongoing monitoring from their MHPs, especially when their symptoms worsened. Given that a similar finding was also identified in a study concerning patients and GPs [32], this result indicates that patients and health professionals (MHPs in this case) should seek to align their competencies, expectations and needs over the course of their FTF contact, in order to keep patients engaged.

Key themes in the self-management strategies used by patients with anxiety and depressive disorders

In the evaluation of the ASAD questionnaire, three consistent factors were identified: Seeking support, Daily life strategies and Taking ownership (**Chapter 6**).

When comparing our findings to previous studies that have assessed self-management questionnaires, the largest degree of overlap was found with respect to the following factors: Seeking support [33–35] and Daily life strategies [33–37]. Although less obvious, we also found some overlap with our third factor Taking ownership [33,35,38]. No important factors were identified in extant literature that were not found in our study.

The ASAD appeared to be an appropriate assessment tool for assessing the self-management strategies among patients with (chronic or partially remitted) anxiety and depressive disorders. Depending on their purpose for completing the ASAD, patients and professionals can choose which version of the ASAD to use. The 45-item ASAD contains all the self-management strategies of patients that were identified through the method of concept mapping. This version provides detailed insight into the potential self-management strategies that patients can use. However, some may consider the 45-item ASAD to be overly long. Hence, we conducted EFA and CFA to both reduce the number of items and reveal underlying factors, which led to the 21-item ASAD-SF. This short form of the ASAD reveals clusters of self-management strategies that patients do and do not apply. Specifically, the clustering of items in factors provides insight into how patients use self-management strategies with respect to 'Seeking support', 'Daily life strategies', and 'Taking ownership', which are considered to be important in self-management [33–38]. In the event of low scores on one or more of these factors on the 21-item ASAD-SF, specific intervention strategies could be employed by both patients and professionals to practice and improve the relevant

self-management skills from that cluster, or to use external resources in situations in which the further development of these skills is not possible. However, one must realize that when using the 21-item ASAD-SF, one also loses information with respect to the full spectrum of self-management strategies that patients use, insofar as items that did not correspond to the three factors were deleted. In conclusion, both the ASAD and the ASAD-SF can be used during relapse prevention interventions, as self-management strategies are integral to managing a chronic disease such as an anxiety or depressive disorder.

Methodological considerations

In this thesis, we adopted a broad perspective on relapse prevention for patients with remitted anxiety and/or depressive disorders by including a systematic review and meta-analysis, a quantitative study, a qualitative study and a psychometric study. However, the results of this thesis should be interpreted in the context of the following methodological considerations.

During the extraction of the data in our systematic review and meta-analysis (**Chapter 2**), it became apparent that manifold definitions of relapse and remission are used in the literature. Therefore, patients that are considered to be 'in remission' in one study might be considered as 'not in remission' in another study. The same issues apply to the term 'relapse'. Consequently, it is incredibly difficult to compare studies and populations with one another. Although there have been some efforts to establish an international consensus on defining these terms [39,40], these efforts require updating. In particular, an international consensus must be established with respect to the cut-off points for relapse and remission that are widely used in current questionnaires. Moreover, notwithstanding the need to develop a consensus regarding how to define depressive disorders, a consensus should also be reached regarding definitions for relapse and remission in anxiety disorders.

In the protocol paper (**Chapter 3**), we described the development of the GET READY intervention. Although it is deemed good practice to use a framework in the development of an intervention, such as, for example, the method of Intervention Mapping, no official framework was used in the development process of the GET READY intervention. However, we did adopt a systematic approach in the development process. Specifically, we considered input from a prior study on patient preferences [16], while the initial format and underpinning was discussed with experts, MHPs and patients. Preliminary versions of the E-health modules were reviewed by members of the research team, E-health developers and patients, and adapted accordingly. With respect to developing future relapse prevention programs, the Intervention Mapping method can be considered an appropriate approach, insofar as it facilitates a systematic planning process [41]. However, one should also take into account that Intervention

Mapping is a time-consuming method, with estimates suggesting that it takes up to 8 months of full-time work to conduct all the necessary steps for developing an intervention [42]. For pragmatic reasons (primarily, issues related to time), we opted to use the aforementioned approach rather than an official framework.

As aforesaid, the GET READY study (**Chapters 3, 4 & 5**) was a pre-post study. As such, this study provided insight into the acceptability, implementation, and adaptation of the program. In addition, we were able to explore the course of symptoms, as well as their association with the program usage, which, in turn, provided some indications as to the efficacy of the program. However, due to this feasibility design [43], the effectiveness of the intervention could not be established. This study should thus be considered as the first step towards conducting a RCT on the effectiveness of the GET READY intervention.

Another methodological consideration that should be considered is the possibility that selection bias occurred during the GET READY study (**Chapters 4 & 5**). One would assume that it was predominantly patients with a certain amount of motivation who agreed to participate in the study. At the same time, patients with a more avoidant self-management style might have been less inclined to participate in the study. Notably, it appeared that the participants in the GET READY study were, overall, highly educated and currently employed (**Chapter 4**). Although this was also the case in other web-based studies [44,45], it would be expedient to also reach out to patients with lower levels of educational achievement. One way to potentially do this might be to involve patients with lower levels of educational achievement in the developmental phase of relapse prevention programs, in order to ensure that the form and content of the program is feasible for this group. Of course, researchers could also seek to actively recruit these types of patients. Similarly, with respect to the qualitative study (**Chapter 5**), it is highly probable that those patients who agreed to participate in the interviews and focus group interviews held more positive attitudes towards the program.

Regarding the above consideration, it should be noted that recruiting patients for the GET READY study proved to be difficult, which resulted in a smaller sample size than we hoped for (**Chapter 4**). In this study, the most prominent method of recruitment was to ask MHPs to recruit their patients. However, it proved difficult to motivate MHPs to recruit patients for research purposes. One reason for this is that over half of the MHPs in the Netherlands experience their workload as being (very) high. On average, they have over 11 consultations a day [46]. Therefore, asking eligible patients to participate in this study was simply not always considered to be a priority for the MHPs. One alternative recruitment method might be to directly recruit patients to take part in the research via specialized mental health care services, as was done in our study and other relapse prevention studies [47]. However, this has become increasingly

difficult in recent years due to stricter privacy regulations. One way to facilitate this process might be to ask patients at the start of their treatment to consent to participating in research.

As well as this, it appeared that not many eligible patients agreed to participate. Unfortunately, we were unable to map precisely how many patients were asked to participate, and how many of those agreed to participate, due to the fact that MHPs did not record this information. Based on this, if researchers could directly contact patients themselves, then this would likely provide more insight into these response numbers.

We considered it a strength that we assessed the perspectives of both patients and MHPs on the GET READY program (**Chapter 5**). We found only two other qualitative studies on relapse prevention among patients with depressive symptoms, and in these cases only the perspective of patients was examined [24,25]. Other qualitative studies on perspectives towards the treatment of depression only included either the perspectives of patients [26,27,48] or therapists [49], but never both. In addition, it appeared that our study was the first to examine perspectives on a relapse prevention program that also focused on anxiety disorders, as other studies primarily focused only on depressive disorders.

Another strength of our study is that our qualitative data allowed for pairwise comparison, because we interviewed both patients and their MHPs. This provided the opportunity to study similarities and differences in their respective viewpoints about the same case. We also combined individual interviews with focus-group interviews, which contributed to data triangulation and thereby enhanced the credibility of our findings [50]. Given that differences in the accounts provided by patients and MHPs especially emerged in the focus-group interviews, this appeared to be a valuable addition to the individual interviews.

In this thesis, both quantitative (**Chapter 4**) and qualitative methods (**Chapter 5**) were employed to examine the GET READY program. This mixed-methods approach allowed us a more complete overview of both the use of the program and its evaluation, which, in turn, provided us with relevant suggestions for clinical practice and future research.

Implications for clinical practice

Relevance of relapse prevention

One of the main implications for clinical practice is that relapse prevention warrants more attention. During this study, it proved difficult to engage patients in the GET READY program. Currently, there appears to be a gap in knowledge and awareness regarding the risk of relapse among remitted patients, while no standard relapse prevention program is currently available for patients in remission from anxiety and

depressive disorders. Given that we have showed that psychological relapse prevention interventions for remitted depressed patients considerably reduces the risk of relapse (**Chapter 2**), it is our contention that relapse prevention programs should be available to all these patients. While this is in accordance with current guideline recommendations [3–6], it is far from the case in practice. Although psychological interventions are effective in preventing relapse among patients with depressive disorders, the question remains whether these interventions should be offered to all remitted patients, or only to those at high risk of relapse. Although it might be more cost-effective to specifically target those who are at high risk, clear indicators of precisely who is deemed to be at high risk are currently lacking.

One way to address the relevance of relapse prevention is through psychoeducation. Specifically, psychoeducation should focus on the risk of relapse and the effectiveness of relapse prevention interventions, in order to increase the motivation of patients to engage in relapse prevention programs. During psychoeducation, particular attention should be paid to engage patients with lower levels of educational achievement. For this purpose, simplified and literacy-adapted psychoeducation materials should be made available, along with using audiovisual methods. Psychoeducation could also be provided by professionals during treatment.

In order for professionals to be able to provide psychoeducation to their patients, they also need to increase their knowledge regarding the risk of relapse and the effectiveness of relapse prevention intervention. In this respect, it appeared that MHPs often lacked such knowledge prior to participating in this study. Therefore, professionals need to receive additional training on these aforesaid subjects. As part of this training, they must also be trained in how to work with existing relapse prevention programs and relapse prevention plans. This training could, for example, also be incorporated within both the initial and advanced education that these professionals undertake. As of June 2021, MHPs in the Netherlands are now obligated to be registered in a 'quality register', which requires them to both meet certain criteria for their formal education and to receive a certain amount of training every year. By incorporating relapse prevention into both their initial and advanced education, professionals' knowledge and skills of relapse prevention will be increased.

Professionals that are involved in guideline development could potentially also play a role in this process, insofar as they have the ability to make clear recommendations regarding relapse prevention. Informal conversations with MHPs during the GET READY study revealed that not all GPs agreed that providing relapse prevention was the task of MHPs. Although the guidelines on anxiety and depressive disorders generally recommend providing relapse prevention to remitted patients, the guidelines should provide more direction regarding the recommended setting for relapse prevention. Only the Dutch 'NHG quality standard depression' [7] clearly states that relapse

prevention should be provided in primary care settings. In light of the shift in the Netherlands towards providing effective care with the lowest possible level of intensity and as close as possible to the patients' place of residence, the primary care setting has become increasingly focused on the domain of (relapse) prevention [51]. This should be stressed more explicitly in the current guidelines.

Overall, the process of providing relapse prevention interventions to remitted patients could be enhanced by facilitating appropriate communication between professionals in specialized mental health care services and GPs/MHPs. As described in the Introduction of this thesis, in an ideal situation, the therapist in the mental health care setting should have already discussed the topic of relapse prevention with the patient and composed a relapse prevention plan with the patient during the course of their treatment. If patients complete their treatment in specialized mental health care, then their therapist should send a referral letter to the GP and/or contact the GP to discuss the treatment process and relapse prevention plan. In so doing, patients can be equipped with the right tools for relapse prevention after completion of their treatment. However, professionals in specialized mental health care also lack knowledge on the risk of relapse and relapse prevention. This should be addressed by providing (more) training on these topics to professionals working in specialized mental health care.

Role of the mental health professional

Another important implication for clinical practice is that personal support and guidance from MHPs is an essential component of effective relapse prevention (**Chapter 5**). This is because MHPs have the important task of monitoring and motivating patients to engage in relapse prevention, in order to ensure that patients receive timely support in the event of an impending relapse. In this study, patients appreciated being monitored by their MHP, while those who received less monitoring expressed the need for more intensive monitoring. Although most patients only had one additional FTF meeting after the initial FTF meeting, most patients indicated that regular meetings with their MHP were desirable. During this FTF contact, MHPs can use motivational interviewing techniques to motivate patients to engage in relapse prevention strategies. Indeed, research [24,26–29] has repeatedly shown that E-health based programs are more effective when a MHP is involved.

Most importantly, patients and MHPs should discuss and try to align their needs regarding self-management skills and their desired level of support, both at the beginning of their relationship and over the course of their relationship. Doing so enables each patient to be provided with a personalized and tailored approach, which most likely enhances the implementation and effectiveness of E-health based relapse prevention programs.

Role of the patient

For patients, it is important to focus on self-management strategies that they are actually capable of applying, in order to prevent relapse. According to our psychometric evaluation of the ASAD (**Chapter 6**), patients can self-manage their disorder by seeking support from professionals and important others (Seeking support), by maintaining a healthy lifestyle and engaging in activities (Daily life strategies), and by taking control and maintaining a focus on recovery (Taking ownership).

Moreover, patients should be aware that MHPs expect them to already possess a certain level of self-management competencies, which may or may not be in accordance with their actual competencies. This can lead patients to feel that they need more support from their MHP. Therefore, as aforementioned, patients should discuss their needs, self-management skills and desired level of support with their MHP.

Role of E-health

Our study has several implications for the role of E-health within clinical practice. In a similar vein to Muntingh et al.'s study [16], it appeared to be important to offer E-health in a personalized way. The GET READY program was designed in such a way that patients and MHPs could 'pick and choose' their preferred modules, which patients indicated that they valued. However, after completion of the initial module, the modules 'anxiety', 'depression' and 'medication' were automatically offered. As the program was focused on the prevention of both anxiety and depressive disorders, patients with only one of these disorders felt that the program did not completely apply to them (**Chapter 5**). Therefore, one might suggest that future relapse prevention programs should specifically focus on one diagnosis. However, given that anxiety and depressive disorders often coincide, one might also argue that a transdiagnostic approach is wholly justified [52]. Based on this, we therefore recommend to offer all optional modules without 'presets', and to provide patients with the opportunity to personalize the program themselves by choosing a program focused on anxiety, depression or both disorders. One would expect this to strengthen acceptance and adherence to the program, and, ultimately, increase its effectiveness [19]. At the same time, as aforementioned, one should keep in mind that a more structured and time-intensive program might be better suited to keeping patients engaged. Perhaps, patients and MHPs can decide together which modules to choose, along with the required level of support needed from the MHP to remain engaged in these modules.

Therefore, in line with the above recommendations, E-health modules should be tailored to patients' preferences, as well as to their individual self-management skills. To create awareness of the available self-management skills and competencies, after they first login, patients should then have the option to either complete the ASAD (if a detailed description of self-management strategies is required) or the ASAD-SF (if a

shorter version is preferred that provides insight into important clusters of self-management) (**Chapter 6**). In so doing, it can be identified which self-management skills require specific attention for further development. In line with this assessment, suitable modules can then be set up and the appropriate level of support required from the MHP can also be planned and executed.

This is important because this study clearly indicated that patients prefer professional support in addition to receiving E-health modules (**Chapter 5**). After completing treatment in specialized mental health care, patients should thus receive guidance in relapse prevention from their MHP. When FTF meetings are combined with E-health modules, these can enhance each other in such a way that ultimately contributes to the effectiveness of the relapse prevention program. This recommendation is supported by both extant literature and the patients in our study who especially valued this combination.

Recommendations for future research

The findings of this thesis imply several recommendations for future research. First, this thesis (specifically **Chapter 2)** has demonstrated that there is a significant lack of studies on relapse prevention among patients with remitted anxiety disorders. We feel that additional studies in this area should be conducted. In addition, this chapter has also shown that there is a relative dearth of studies exploring the use of relapse prevention interventions during the discontinuation of ADM. Given that most patients do not prefer to use medication in the long term [53], and the risk of relapse during discontinuation is high [54], relapse prevention interventions may be able to support patients during the discontinuation of ADM.

Second, in order to examine the efficacy of the GET READY intervention, a RCT should be conducted. However, we recommend adapting the GET READY program according to the preferences expressed by patients (**Chapter 5**). Most importantly, the program should be accessible through a mobile app, as well as having a clear, intuitive and flexible structure for the E-health component, and should allow users to personalize it based on their disorder. To increase patients' engagement in the program, more frequent FTF contact with MHPs is likely necessary. Preferably, the follow-up duration of this RCT should be at least 2 years, as this will provide greater insight into the course of symptoms over a longer period of time, and allow for greater comparison with other studies. During the patient recruitment phase of the RCT, particular attention should be paid to the variability of patients' characteristics in the sample, especially regarding their level of educational achievement. In order to gain more insight into the association between course of symptoms and usage, Ecological Momentary Assessment (EMA) could be used in the RCT [55]. In addition, this RCT could be supplemented with a cost-effectiveness study, based on our contention that relapse prevention is a cost-effective intervention strategy.

Third, as outlined in the Introduction of this thesis, self-management can be considered as part of the chronic care model, and, as such, may be essential in preventing relapse. However, one could raise the question of whether self-management is feasible for every patient with remitted anxiety and depressive disorders. In this study, it appeared that self-management could not be expected from every patient, given the low usage intensity and rapid decrease in usage. In particular, patients with low and high symptom levels might require additional guidance and motivation from MHPs to engage in relapse prevention (**Chapter 5**). Further research into prerequisites for patients with anxiety and depressive disorders to engage self-management strategies is recommended for their effective application.

Fourth, given that the psychometric evaluation of the ASAD indicated that the 21-item version was appropriate (**Chapter 6**), this version should be further explored and validated among a sample of patients with chronic and/or remitted anxiety and depressive disorders. Furthermore, it would be interesting to relate self-management styles, as assessed by the ASAD-SF, to the course of symptoms and the effectiveness of relapse prevention.

Concluding remarks

This thesis focused on relapse prevention among patients with remitted anxiety and depressive disorders. As demonstrated in this thesis, patients in remission from depressive disorders should receive psychological relapse prevention interventions. Greater attention should be paid to developing, implementing and evaluating relapse prevention interventions among patients with anxiety disorders. Although patients were generally positive about the GET READY relapse prevention program, the implementation of the program proved to be challenging, primarily due to a lack of motivation among patients and a lack of support from MHPs. Therefore, psychoeducation focused on the risk of relapse and the effectiveness of psychological relapse prevention interventions should receive more attention in mental health care and the GET READY program may be intensified to attain effectiveness. MHPs appear to have a crucial role to play in implementing relapse prevention programs, and should seek to tailor their support and guidance to the expressed needs and self-management skills of patients. Although usage of the GET READY relapse prevention program was relatively low compared to similar programs, patients mostly remained stable during their participation in the study. This might indicate that the program is capable of potentially protecting patients from relapse. However, a RCT is needed to validate this particular finding.

References

1. Zoun MHH, Koekkoek B, van Grieken R, Sinnema H, Smit F, Spijker J. Self-management strategies in chronic anxiety and depression from the patients' perspective: development and results of a self-management questionnaire. In preparation.

2. Geddes JR, Carney SM, Davies C, Furukawa TA, Kupfer DJ, Frank E, Goodwin GM. Relapse prevention with antidepressant drug treatment in depressive disorders: a systematic review. Lancet [Internet] Elsevier; 2003 Feb 22 [cited 2016 Dec 2];361(9358):653–661. PMID:12606176

3. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Obsessive-Compulsive Disorder [Internet]. 2007. Available from: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/ocd.pdf

4. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Panic Disorder [Internet]. 2009. Available from: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/panicdisorder.pdf

5. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder [Internet]. 2010. Available from: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf

6. National Institute for Health and Care Excellence. The Nice Guideline on the Treatment and Management of Depression in Adults (updated edition) [Internet]. 2010. PMID:22132433

7. NHG-werkgroep Depressie. NHG-Standaard Depressie (M44) [Internet]. 2019. Available from: https://richtlijnen.nhg.org/files/pdf/54_Depressie_mei-2019.pdf

8. Arden-Close EJ, Smith E, Bradbury K, Morrison L, Dennison L, Michaelides D, Yardley L. A Visualization Tool to Analyse Usage of Web-Based Interventions: The Example of Positive Online Weight Reduction (POWeR). JMIR Hum Factors [Internet] 2015 [cited 2017 May 10];2(1):e8. PMID:27026372

9. Holländare F, Johnsson S, Randestad M, Tillfors M, Carlbring P, Andersson G, Engström I. Randomized trial of Internet-based relapse prevention for partially remitted depression. Acta Psychiatr Scand [Internet] Blackwell Publishing Ltd; 2011 Oct [cited 2017 May 30];124(4):285–294. [doi: 10.1111/j.1600-0447.2011.01698.x]

10. Donkin L, Hickie IB, Christensen H, Naismith SL, Neal B, Cockayne NL, Glozier N. Rethinking the Dose-Response Relationship Between Usage and Outcome in an Online Intervention for Depression: Randomized Controlled Trial. J Med Internet Res 2013 Oct;15(10):e231. [doi: 10.2196/jmir.2771]

11. Hilvert-Bruce Z, Rossouw PJ, Wong N, Sunderland M, Andrews G. Adherence as a determinant of effectiveness of internet cognitive behavioural therapy for anxiety and depressive disorders. Behav Res Ther 2012 Aug;50(7–8):463–468. [doi: 10.1016/j.brat.2012.04.001]

12. Van Gemert-Pijnen JEWC, Kelders SM, Bohlmeijer ET. Understanding the usage of content in a mental health intervention for depression: An analysis of log data. J Med Internet Res [Internet] 2014 Jan 31;16(1):1–16. [doi: 10.2196/jmir.2991]

13. Van Straten A, Cuijpers P, Smits N. Effectiveness of a web-based self-help intervention for symptoms of depression, anxiety, and stress: Randomized controlled trial. J Med Internet Res 2008;10(1):1–11. PMID:18364344

14. Eysenbach G. The law of attrition. J Med Internet Res [Internet] 2005 [cited 2017 May 12];7(1):1–11. PMID:15829473

15. Kelders SM, Bohlmeijer ET, Van Gemert-Pijnen JE. Participants, Usage, and Use Patterns of a Web-Based Intervention for the Prevention of Depression Within a Randomized Controlled Trial. J Med Internet Res [Internet] Journal of Medical Internet Research; 2013 Aug 20 [cited 2017 May 10];15(8):e172. PMID:23963284

16. Muntingh ADT, Hoogendoorn AW, Van Schaik DJF, Van Straten A, Stolk EA, Van Balkom AJLM, Batelaan NM. Patient preferences for a guided self-help programme to prevent relapse in anxiety or depression: A discrete choice experiment. Eisenbarth H, editor. PLoS One [Internet] 2019 Jul 18;14(7):e0219588. [doi: 10.1371/journal.pone.0219588]

17. Scholten WD, Batelaan NM, Van Oppen P, Smit JH, Van Balkom AJLM. Discontinuation of antidepressants in remitted anxiety disorder patients: The need for strategies to prevent relapse. Psychother Psychosom 2013;82(6):399–400. PMID:24080729

18. Apil SRA, Hoencamp E, Haffmans JPM, Spinhoven P. A stepped care relapse prevention program for depression in older people: A randomized controlled trial. Int J Geriatr Psychiatry 2012;27(6):583–591. PMID:21766336

19. Cuijpers P, van Straten A, Warmerdam L, van Rooy MJ. Recruiting participants for interventions to prevent the onset of depressive disorders: Possible ways to increase participation rates. BMC Health Serv Res [Internet] BioMed Central; 2010 Dec 25 [cited 2016 Jul 6];10(1):181. PMID:20579332

20. van der Weele GM, de Jong R, de Waal MWM, Spinhoven P, Rooze HAH, Reis R, Assendelft WJJ, Gussekloo J, van der Mast RC. Response to an unsolicited intervention offer to persons aged ≥ 75 years after screening positive for depressive symptoms: a qualitative study. Int Psychogeriatrics [Internet] 2012 Feb 16;24(2):270–277. [doi: 10.1017/S1041610211001530]

21. Hardeveld F, Spijker J, De Graaf R, Hendriks SM, Licht CMM, Nolen WA, Penninx BWJH, Beekman ATF. Recurrence of major depressive disorder across different treatment settings: Results from the NESDA study. J Affect Disord [Internet] Elsevier; 2013 May [cited 2016 Jul 6];147(1–3):225–231. PMID:23218899

22. Taylor JH, Jakubovski E, Bloch MH. Predictors of anxiety recurrence in the Coordinated Anxiety Learning and Management (CALM) trial. J Psychiatr Res [Internet] Elsevier Ltd; 2015 Jun [cited 2017 Aug 8];65:154–165. PMID:25896121

23. ten Have M, de Graaf R, Vollebergh W, Beekman A. What depressive symptoms are associated with the use of care services? J Affect Disord [Internet] 2004 Jun;80(2–3):239–248. [doi: 10.1016/S0165-0327(03)00132-0]

24. Boggs JM, Beck A, Felder JN, Dimidjian S, Metcalf CA, Segal Z V. Web-based intervention in mindfulness meditation for reducing residual depressive symptoms and relapse prophylaxis: A qualitative study. J Med Internet Res [Internet] JMIR Publications Inc.; 2014 [cited 2016 Jul 6];16(3):1–12. PMID:24662625

25. Allen M, Bromley A, Kuyken W, Sonnenberg SJ. Participants' Experiences of Mindfulness-Based Cognitive Therapy: "It Changed Me in Just about Every Way Possible." Behav Cogn Psychother [Internet] 2009 Jul 10;37(4):413–430. PMID:19508744

26. Lillevoll KR, Wilhelmsen M, Kolstrup N, Høifødt RS, Waterloo K, Eisemann M, Risør MB. Patients' Experiences of Helpfulness in Guided Internet-Based Treatment for Depression: Qualitative Study of Integrated Therapeutic Dimensions. J Med Internet Res [Internet] 2013 Jun 20;15(6):e126. [doi: 10.2196/jmir.2531]

27. Gerhards SAH, Abma TA, Arntz A, de Graaf LE, Evers SMAA, Huibers MJH, Widdershoven GAM. Improving adherence and effectiveness of computerised cognitive behavioural therapy without support for depression: A qualitative study on patient experiences. J Affect Disord [Internet] 2011 Mar;129(1–3):117–125. [doi: 10.1016/j.jad.2010.09.012]

28. Kelders SM, Kok RN, Ossebaard HC, Van Gemert-Pijnen JE. Persuasive System Design Does Matter: a Systematic Review of Adherence to Web-based Interventions. J Med Internet Res [Internet] 2012 Nov 14 [cited 2017 May 12];14(6):e152. PMID:23151820

29. Apolinário-Hagen J, Kemper J, Stürmer C. Public Acceptability of E-Mental Health Treatment Services for Psychological Problems: A Scoping Review. JMIR Ment Heal [Internet] 2017;4(2):e10. PMID:28373153

30. Melville KM, Casey LM, Kavanagh DJ. Dropout from Internet-based treatment for psychological disorders. Br J Clin Psychol [Internet] 2010 Nov;49(4):455–471. [doi: 10.1348/014466509X472138]

31. Paykel ES, Ramana R, Cooper Z, Hayhurst H, Kerr J, Barocka A. Residual symptoms after partial remission: an important outcome in depression. Psychol Med England; 1995 Nov;25(6):1171–1180. PMID:8637947

32. Bosman RC, Huijbregts KM, Verhaak PF, Ruhé HG, van Marwijk HW, van Balkom AJ, Batelaan NM. Long-term antidepressant use: a qualitative study on perspectives of patients and GPs in primary care. Br J Gen Pract. 2016 Oct;66(651):e708-19. [doi: 10.3399/bjgp16X686641]. Epub 2016 Aug 15. PMID: 27528709

33. Coulombe S, Radziszewski S, Trépanier SG, Provencher H, Roberge P, Hudon C, Meunier S, Provencher MD, Houle J. Mental health self-management questionnaire: Development and psychometric properties. J Affect Disord [Internet] Elsevier; 2015;181:41–49. PMID:25917292

34. Smith D, Harvey P, Lawn S, Harris M, Battersby M. Measuring chronic condition self-management in an Australian community: factor structure of the revised Partners in Health (PIH) scale. Qual Life Res Springer International Publishing; 2017;26(1):149–159. PMID:27432251

35. Villaggi B, Provencher H, Coulombe S, Meunier S, Radziszewski S, Hudon C, Roberge P, Provencher MD, Houle J. Self-Management Strategies in Recovery From Mood and Anxiety Disorders. Glob Qual Nurs Res [Internet] 2015 Nov 5;2:233339361560609. [doi: 10.1177/2333393615606092]

36. van Grieken RA, Kirkenier ACE, Koeter MWJ, Schene AH. Helpful self-management strategies to cope with enduring depression from the patients' point of view: A concept map study. BMC Psychiatry 2014;14(1):1–9. PMID:25495848

37. van Grieken RA, Kirkenier ACE, Koeter MWJ, Nabitz UW, Schene AH. Patients' perspective on self-management in the recovery from depression. Heal Expect [Internet] 2015 Oct;18(5):1339–1348. PMID:23910797

38. Schreurs P, Willige G van de, Tellegen B, Brosschot J. De Utrechtse Coping Lijst: UCL-handleiding [Utrecht Coping List: UCL manual]. Lisse: Swets & Zeitlinger; 1988.

39. Frank E, Prien RF, Jarrett RB, Keller MB, Kupfer DJ, Lavori PW, Rush AJ, Weissman MM. Conceptualization and Rationale for Consensus Definitions of Terms in Major Depressive Disorder. Arch Gen Psychiatry [Internet] 1991 Sep 1;48(9):851. PMID:1929776

40. Tohen M, Frank E, Bowden CL, Colom F, Ghaemi SN, Yatham LN, Malhi GS, Calabrese JR, Nolen WA, Vieta E, Kapczinski F, Goodwin GM, Suppes T, Sachs GS, Chengappa KR, Grunze H, Mitchell PB, Kanba S, Berk M. The International Society for Bipolar Disorders (ISBD) Task Force report on the nomenclature of course and outcome in bipolar disorders. Bipolar Disord [Internet] 2009 Aug;11(5):453–473. PMID:19624385

41. Kok G. A practical guide to effective behavior change How to apply theory- and evidence-based behavior change methods in an intervention. Eur Heal Psychol [Internet] 2014;16(5):156–170. [doi: 10.31234/osf.io/r78wh]

42. McEachan RR, Lawton RJ, Jackson C, Conner M, Lunt J. Evidence, Theory and Context: Using intervention mapping to develop a worksite physical activity intervention. BMC Public Health [Internet] 2008 Dec 22;8(1):326. [doi: 10.1186/1471-2458-8-326]

43. Bowen DJ, Kreuter M, Spring B, Cofta-Woerpel L, Linnan L, Weiner D, Bakken S, Kaplan CP, Squiers L, Fabrizio C, Fernandez M. How We Design Feasibility Studies. Am J Prev Med [Internet] 2009 May;36(5):452–457. PMID:19362699

44. Torrent-Sellens J, Díaz-Chao Á, Soler-Ramos I, Saigí-Rubió F. Modelling and predicting eHealth usage in Europe: A multidimensional approach from an online survey of 13,000 European Union Internet Users. J Med Internet Res 2016;18(7):1–19. [doi: 10.2196/jmir.5605]

45. Kontos E, Blake KD, Chou WYS, Prestin A. Predictors of ehealth usage: Insights on the digital divide from the health information national trends survey 2012. J Med Internet Res 2014;16(7):1–16. PMID:25048379

46. Magnée T, Sinnema H, van Weelderen G, Nuijen J, Kenter A. Hoe denken poh's-ggz over hun werk? Huisarts Wet 2020;63(5):34–41. [doi: 10.1007/s12445-020-0571-3]

47. Biesheuvel-Leliefeld KEM, Dijkstra-Kersten SMA, van Schaik DJF, van Marwijk HWJ, Smit F, van der Horst HE, Bockting CLH. Effectiveness of Supported Self-Help in Recurrent Depression: A Randomized Controlled Trial in Primary Care. Psychother Psychosom [Internet] 2017;86(4):220–230. [doi: 10.1159/000472260]

48. Urech A, Krieger T, Möseneder L, Biaggi A, Vincent A, Poppe C, Meyer B, Riper H, Berger T. A patient post hoc perspective on advantages and disadvantages of blended cognitive behaviour therapy for depression: A qualitative content analysis. Psychother Res [Internet] 2019 Nov 8;29(8):986–998. [doi: 10.1080/10503307.2018.1430910]

49. Titzler I, Saruhanjan K, Berking M, Riper H, Ebert DD. Barriers and facilitators for the implementation of blended psychotherapy for depression: A qualitative pilot study of therapists' perspective. Internet Interv [Internet] 2018;12:150–164. [doi: 10.1016/j.invent.2018.01.002]

50. Portney LG, Watkins MP. Foundations of Clinical Research: Applications to Practice [Internet]. 3rd ed. New Jersey: Pearson/Prentice Hall; 2009. Available from: https://books.google.nl/books?id=apNJPgAACAAJ ISBN:9780131716407

51. Ministerie van Volksgezondheid Welzijn & Sport. Bestuurlijk akkoord toekomst GGZ 2013-2014 [Internet]. 2012. p. 1–19. Available from: www.vgct.nl/stream/bestuurlijk-akkoord-toekomst-ggz-2013-2014.pdf?

52. Spijker J, Muntingh A, Batelaan N. Advice for Clinicians on How to Treat Comorbid Anxiety and Depression. JAMA Psychiatry [Internet] 2020 Jun 1;77(6):645. [doi: 10.1001/jamapsychiatry.2020.0601]

53. Verbeek-Heida PM, Mathot EF. Better safe than sorry — why patients prefer to stop using selective serotonin reuptake inhibitor (SSRI) antidepressants but are afraid to do so: results of a qualitative study. Chronic Illn [Internet] 2006 Jun 29;2(2):133–142. [doi: 10.1177/17423953060020020801]

54. Sim K, Lau WK, Sim J, Sum MY, Baldessarini RJ. Prevention of Relapse and Recurrence in Adults with Major Depressive Disorder: Systematic Review and Meta-Analyses of Controlled Trials. Int J Neuropsychopharmacol [Internet] 2016 Feb;19(2):pyv076. PMID:26152228

55. Shiffman S, Stone AA, Hufford MR. Ecological Momentary Assessment. Annu Rev Clin Psychol [Internet] United States; 2008 Apr;4(1):1–32. PMID:18509902

NEDERLANDSE SAMENVATTING
DUTCH SUMMARY

Achtergrond en doelstellingen

Veel mensen krijgen in hun leven te maken met angst- of depressieve klachten. Wanneer deze klachten het leven gaan beheersen, kunnen dit stoornissen worden. Angststoornissen worden gekenmerkt door het ervaren van ernstige angst en bezorgdheid. In dit proefschrift komen angststoornissen aan bod, die in de 'Diagnostic and Statistical Manual of Mental Disorders' (DSM) beschreven zijn: paniekstoornis (met of zonder agorafobie), agorafobie, specifieke fobie, sociale fobie (ook wel sociale angststoornis), gegeneraliseerde angststoornis, obsessieve-compulsieve stoornis en posttraumatische stressstoornis. Naast aandacht voor angststoornissen is er in dit proefschrift ook aandacht voor depressieve stoornissen. Deze kenmerken zich door een sombere stemming en het verlies van interesse of plezier in het leven. In dit proefschrift komen de depressie en dysthyme stoornis aan bod. Een dysthyme stoornis is een langdurige milde depressie.

Wereldwijd behoren angst- en depressieve stoornissen tot de meest voorkomende psychische stoornissen. In Nederland krijgt één op de vijf mensen ooit in het leven te maken met een angst- en/of depressieve stoornis. Dit heeft een grote impact op hun kwaliteit van leven, het functioneren en het welbevinden. Angst- en depressieve stoornissen komen vaak samen voor: mensen die ooit een angststoornis hebben gehad, hebben ook vaak ooit een depressieve stoornis gehad, en andersom.

Er is veel onderzoek verricht naar het behandelen van angst- en depressieve stoornissen. Vaak bestaat de behandeling uit een psychologische en/of medicamenteuze behandeling. Eén van de psychologische behandelingen die veel is onderzocht, is cognitieve gedragstherapie (CGT). CGT blijkt effectief te zijn in het behandelen van angst- en depressieve stoornissen. Behandeling met medicatie blijkt ongeveer even effectief te zijn in het verlagen van angst- en depressieve klachten. Een combinatie van beiden blijkt het meest effectief te zijn. Vaak geven patiënten echter de voorkeur aan psychologische behandeling, bijvoorbeeld vanwege zorgen over bijwerkingen van medicatie. Psychologische behandelingen worden doorgaans via persoonlijk contact gegeven, waarbij de patiënt en hulpverlener elkaar 'live' zien. Echter, vanwege COVID-19 lijken er steeds meer van deze behandelingen online gegeven te worden. Online behandelingen kenmerken zich veelal door de inzet van E-health-modules, persoonlijke feedback van een hulpverlener en de mogelijkheid om berichten uit te wisselen. De voordelen van online behandeling kunnen o.a. zijn dat het gemakkelijk toegankelijk is, dat symptomen effectief gemonitord kunnen worden via E-health toepassingen en dat het mogelijk meer kosteneffectief is.

Wanneer patiënten herstellen van een angst- of depressieve stoornis, wordt gesproken van remissie (remission) of herstel (recovery). Hoewel er veel variatie is in hoe deze termen gebruikt worden in de literatuur, geven beide termen aan dat patiënten niet meer voldoen aan de DSM-criteria voor de stoornis. Maar ook als patiënten hersteld zijn van een angst- of depressieve stoornis, kunnen zij een terugval ervaren. Voor terugval zijn er ook twee termen te vinden in de Engelstalige literatuur: 'relapse' en 'recurrence'. Beide wijzen op een terugkeer van klachten, die zo ernstig zijn dat men (opnieuw) spreekt van een DSM-stoornis. Patiënten die hersteld zijn van een angst- of depressieve stoornis hebben 57% kans om binnen vier jaar een terugval te ervaren. Dit kan een terugval zijn in dezelfde stoornis, maar mensen die eerst een depressieve stoornis hadden, kunnen ook een angststoornis ontwikkelen (en andersom). Terugvalcijfers zijn dus hoog. Er zijn enkele risicofactoren bekend die de kans op terugval verhogen. Patiënten die niet geheel maar gedeeltelijk herstellen, hebben meer kans op terugval. Ook is er een grote kans op terugval wanneer men minder goed functioneert in psychosociaal opzicht, en ook wanneer men meerdere en ernstigere episodes van de stoornis heeft ervaren.

Aangezien veel mensen die een behandeling hebben ontvangen voor hun angst- en/of depressieve stoornis alsnog te maken krijgen met een terugval, is één van de grootste uitdagingen het voorkomen van terugval. Momenteel is er nog te weinig aandacht voor terugvalpreventie in de geestelijke gezondheidszorg. Terugvalpreventie bestaat vaak uit: 1) het continueren van antidepressiva, en 2) psychologische terugvalpreventie-interventies. Het is belangrijk dat patiënt en hulpverlener overeenkomen welke manier van terugvalpreventie gebruikt wordt, aangezien dit de therapietrouw, en daarmee effectiviteit ten goede komt. Er is veel onderzoek gedaan naar psychologische terugvalpreventie-interventies bij depressieve stoornissen, maar in veel mindere mate bij angststoornissen.

In Nederland is de focus de laatste jaren steeds meer verschoven van het behandelen van ziektes naar het voorkomen ervan. Zorg wordt zo laagdrempelig mogelijk aangeboden, wat ook geldt voor psychologische zorg. Bij deze ontwikkeling past de opkomst van de praktijkondersteuner huisarts GGZ (POH-GGZ). Deze hulpverlener ondersteunt de huisarts bij het bieden van psychologische zorg. POH-GGZ zijn dan ook de aangewezen hulpverleners om terugvalpreventie aan patiënten aan te bieden. Daarbij leggen zij een focus op het zelfmanagementvermogen van patiënten, oftewel: wat kunnen patiënten zelf doen om op een constructieve manier met hun symptomen om te gaan?

Huidige terugvalpreventieprogramma's hebben enkele beperkingen. Ten eerste zijn ze niet toegespitst op zowel angst- en depressieve stoornissen. Ten tweede worden deze programma's nog nauwelijks aangeboden via de huisartsenpraktijk. Ten slotte zijn ze niet specifiek afgestemd op de voorkeuren van patiënten. Als antwoord op deze

beperkingen is het GET READY terugvalpreventieprogramma ontwikkeld. Dit is gericht op patiënten die hersteld zijn van een angst- en/of depressieve stoornis. De voorkeuren van patiënten zijn meegenomen in de ontwikkeling van dit programma. Het programma bestaat uit verschillende E-health modules die gepaard gaan met persoonlijke contacten met een POH-GGZ in de huisartsenpraktijk. Daarnaast is er een persoonlijk terugvalpreventieplan. Patiënten kunnen hierbij ook een angst- en stemmingsdagboek invullen. Hun angst- en stemmingsniveau kan zo effectief gemonitord worden.
Het overkoepelende doel van dit proefschrift is om terugval te voorkomen bij patiënten die hersteld zijn van een angst- en/of depressieve stoornis, en daarmee hun kwaliteit van leven te verbeteren. Om dit doel te kunnen bereiken zijn verschillende onderzoeken uitgevoerd Ten eerste werd via een literatuuronderzoek de effectiviteit van psychologische terugvalpreventie-interventies onderzocht. Ten tweede werd het nieuw ontwikkelde GET READY programma en de implementatie ervan geëvalueerd. Als laatste werden de psychometrische eigenschappen van een zelfmanagementvragenlijst voor patiënten met angst- en depressieve klachten onderzocht.

Resultaten

In **Hoofdstuk 2** wordt een systematische literatuur-overzichtsstudie en meta-analyse beschreven, die is uitgevoerd om de effectiviteit van psychologische terugvalpreventie-interventies voor patiënten met herstelde angst- en depressieve stoornissen te onderzoeken. Er is gekeken naar de effectiviteit van psychologische terugvalpreventie-interventies als aparte interventie, maar ook wanneer deze gecombineerd werden met een onderhoudsbehandeling van antidepressiva, of werden gecombineerd met het afbouwen van antidepressiva. In totaal werden er 7.324 artikelen gescreend, en werden er uiteindelijk 40 artikelen geïncludeerd. Hieruit bleek dat het ontvangen van een psychologische interventie de kans op terugval voor patiënten die hersteld waren van een depressieve stoornis met 24% verminderde ten opzichte van mensen die gebruikelijke zorg ontvingen. Dit effect kwam het duidelijkst naar voren in de eerste 24 maanden, maar het effect bleef zelfs na drie jaar zichtbaar. Wanneer psychologische interventies en antidepressiva werden gecombineerd, leidde dit ook tot 24% minder kans op terugval, vergeleken met wanneer er enkel antidepressiva werden gegeven. Dit effect was in de eerste 24 maanden zichtbaar. Er kon geen meta-analyse worden uitgevoerd naar het gecombineerde effect van psychologische interventies en het afbouwen van antidepressiva, omdat er te weinig studies over dit onderwerp beschikbaar waren. Tevens kon er, vanwege een gebrek aan studies, geen meta-analyse uitgevoerd worden naar de effectiviteit van psychologische interventies voor patiënten die hersteld zijn van een angststoornis. De conclusie van dit hoofdstuk is dat psychologische interventies effectief zijn in het verminderen van de kans op terugval voor patiënten die hersteld zijn van een depressieve stoornis.

Hoofdstukken 3, 4 en 5 beschrijven de ontwikkeling, implementatie en evaluatie van het GET READY terugvalpreventieprogramma. **Hoofdstuk 3** beschrijft het protocol van de GET READY studie, waarin het GET READY terugvalpreventieprogramma werd aangeboden aan patiënten. Het programma is ontwikkeld in samenspraak met professionals en met een panel van patiënten. Het protocol beschrijft zowel de kwantitatieve als de kwalitatieve methoden die gebruikt zijn om het GET READY programma te evalueren.

In **Hoofdstuk 4** wordt het gebruik van het GET READY programma, het beloop van klachten en het verband tussen deze twee factoren beschreven. Deze factoren werden in kaart gebracht bij 113 patiënten die geheel of gedeeltelijk hersteld waren van een angst- en/of depressieve stoornis. Er is longitudinale data verzameld over een periode van negen maanden. De kernmodules in het E-health programma – zijnde het terugvalpreventieplan en de psycho-educatiemodule over terugvalpreventie – werden gebruikt door 70-74% van de patiënten, terwijl de optionele modules gebruikt werden door minder dan 40% van de patiënten. Ongeveer een kwart van de patiënten gebruikte het programma relatief vaak ten opzichte van de rest van de patiënten die er relatief weinig gebruik van maakten. Over het algemeen nam het gebruik van de zelfmanagementonderdelen van het terugvalpreventieprogramma snel af na de start van de follow-up-periode. Aangezien de studie niet experimenteel was, kon er geen oorzakelijk verband worden aangetoond tussen het gebruik van het GET READY programma en de ernst van de symptomen. Wel bleek dat de meeste patiënten die deelnamen aan het programma stabiel bleven: een minderheid van 15% ervaarde een terugval in angstsymptomen in de negen maanden van de studie, en 10% ervaarde een terugval in depressieve symptomen. Patiënten met meer persoonlijke contacten met hun POH-GGZ, hadden significant meer angst- en depressieve klachten. Andere gebruiksvariabelen toonden geen significant verband met het beloop van de klachten.

In **Hoofdstuk 5** zijn de resultaten beschreven van een kwalitatieve studie naar de implementatie en evaluatie van het GET READY programma, dit vanuit het perspectief van zowel de patiënt als de POH-GGZ. Daarvoor werden gepaarde individuele interviews afgenomen bij patiënten (N=13) en hun POH-GGZ (N=12). Door deze gepaarde interviews konden eventuele verschillen in de perspectieven aan het licht komen betreffende een en dezelfde casus. Aanvullende op de individuele interviews zijn er ook twee focusgroep-interviews uitgevoerd, één met patiënten en één met POH-GGZ. De interviews toonden aan dat de meeste gebruikers positief waren over het GET READY programma. Specifiek werd genoemd dat het een bewustzijn van risico op terugval teweegbracht en dat het programma bijdroeg aan het innemen van een actieve rol van patiënten in hun eigen herstel. Het werd ervaren als een vangnet voor eventuele terugval in de periode na eerder herstel. Daarnaast waardeerden patiënten de gebruiksvriendelijkheid en toegankelijkheid van het programma. Echter waren er

ook factoren die het gebruik van het programma belemmerden: het gebrek aan motivatie van patiënten, het gebrek aan herkenbaarheid van het programma (omdat het zich op zowel angst als depressie richtte), en het gebrek aan ervaren steun van de POH-GGZ. Ook bleek dat het gebruik van het programma negatief beïnvloed werd door het aantal en de ernst van de symptomen van patiënten. Patiënten met slechts lichte symptomen hadden er weinig behoefte aan om actief met terugvalpreventie bezig te zijn, terwijl patiënten met meer ernstige symptomen, mede door een gebrek aan concentratie en energie, het programma eveneens minder gebruikten. Het combineren van de E-health modules met de persoonlijke contacten met de POH-GGZ werd als essentieel gezien, door zowel patiënten als POH-GGZ. De POH-GGZ speelde een heel belangrijke rol in het motiveren en steunen van patiënten om met E-health aan de slag te gaan. Uit de gepaarde interviews kwamen geen opvallende verschillen in perspectieven naar voren, maar deze werden in de focusgroepen wel opgemerkt. Zo bleek dat POH-GGZ van patiënten verwachten dat zij een zekere mate van zelfmanagementvaardigheden hadden ten aanzien van het gebruik van het terugvalpreventieprogramma, terwijl patiënten juist aangaven deze vaardigheden niet altijd te bezitten. Zij hadden behoefte aan meer directe en persoonlijke steun van hun POH-GGZ.

In **Hoofdstuk 6** worden de resultaten gepresenteerd van een onderzoek naar de psychometrische eigenschappen van een nieuwe vragenlijst die gericht is op zelfmanagementvaardigheden van patiënten met angst- en depressieve stoornissen: de 'Assessment of Self-management in Anxiety and Depression' (ASAD) vragenlijst. Deze vragenlijst bestaat uit 45 items en kan gebruikt worden door zowel patiënten als professionals, om zelfmanagementvaardigheden in kaart te brengen. Aangezien zelfmanagement in toenemende mate belangrijk is in het herstel van psychische stoornissen, lijkt een focus op zelfmanagement in het kader van terugvalpreventie gerechtvaardigd. Tegelijkertijd blijkt echter ook dat de last van angst- en depressieve stoornissen mogelijk het gebruik van zelfmanagementvaardigheden juist vermindert. De ASAD is ontwikkeld omdat er nog geen Nederlandse zelfmanagementvragenlijst beschikbaar was voor patiënten met angst- en depressieve stoornissen. In onze studie werd de ASAD door in totaal 171 mensen ingevuld. Zowel een exploratieve als een confirmatieve factoranalyse lieten zien dat er drie solide factoren aanwezig waren in de vragenlijst: het zoeken van steun, dagelijkse levensstrategieën en het nemen van eigenaarschap. Verder bleek uit de uitgevoerde analyses dat het aantal items verminderd kon worden van 45 naar 21. De evaluatie wees op een hoog niveau van interne consistentie en betrouwbaarheid voor de 21 items van de ASAD 'short form' (ASAD-SF).

Conclusies

Eén van de belangrijkste conclusies naar aanleiding van dit proefschrift is dat terugvalpreventie bij angst- en depressieklachten meer aandacht verdient: patiënten die (grotendeels) hersteld zijn van deze stoornissen zouden naast eventuele medicamenteuze ondersteuning (onderhoudsmedicatie) ook psychologische terugvalpreventie-interventies moeten ontvangen. Er is meer aandacht nodig voor de ontwikkeling, implementatie en evaluatie van deze interventies voor deze patiënten. Hoewel patiënten overwegend positief waren over het GET READY terugvalpreventieprogramma, bleek de implementatie ervan uitdagend, voornamelijk vanwege een gebrek aan motivatie bij patiënten en gebrek aan ervaren steun van de POH-GGZ. Daarom zou er in de gezondheidszorg meer voorlichting gegeven moeten worden over de risico's op terugval, aan zowel patiënten als de POH-GGZ. POH-GGZ hebben een belangrijke rol in het implementeren van terugvalpreventieprogramma's, waarbij het essentieel is dat zij de mate van ondersteuning en begeleiding afstemmen op de zelfmanagementvaardigheden en behoeften van de patiënt. Hoewel het GET READY terugvalpreventieprogramma relatief weinig gebruikt werd, bleek toch dat de meeste patiënten gedurende het onderzoek stabiel bleven in de klachten. Dit zou kunnen betekenen dat het programma mensen voor terugval zou kunnen behoeden. Om dit resultaat te bevestigen, zou een gerandomiseerd onderzoek met een controlegroep uitgevoerd moeten worden.

CURRICULUM VITAE

Esther Krijnen- de Bruin was born on July 2nd 1989 in Utrecht, the Netherlands. After completing her secondary education at De Passie in Utrecht, she had a gap year, doing voluntary work in Kenya. In 2011 she completed her bachelor's degree in nursing at Christelijke Hogeschool Ede. From 2011 to 2012 she was a nursing trainee at the department of child and youth psychiatry and at the department for patients with (early) psychosis at UMC Utrecht, and she kept working as a psychiatric nurse until 2015. In addition, she studied Health Sciences at the VU University Amsterdam, with the specialization 'Prevention and Public Health'. In 2014 she obtained her master's degree. From 2015 to 2016 she worked as a Clinical Trial Assistant at Julius Clinical in Zeist. In 2016 she started working as a PhD student at GGZ inGeest/Department of Psychiatry of the Amsterdam UMC, location VUmc, also affiliated with Inholland University of Applied Sciences. Her research has been embedded in the 'Academische Werkplaats Angst' and focused on relapse prevention for patients with remitted anxiety and depressive disorders. In 2021 she started to work as a lecturer in scientific training at Inholland University of Applied Sciences, in which she also focuses on the development of 'Leer- en innovatienetwerken' in mental health care, networks in which science, practice and education is connected.

DISSERTATION SERIES

Department of Psychiatry, Amsterdam University Medical Centers

N.M. (Neeltje) Batelaan (2010). Panic and Public Health: Diagnosis, Prognosis and Consequences. Vrije Universiteit Amsterdam. ISBN: 978-90-8659-411-5.

G.E. (Gideon) Anholt (2010). Obsessive-Compulsive Disorder: Spectrum Theory and Issues in Measurement. Vrije Universiteit Amsterdam.

N. (Nicole) Vogelzangs (2010). Depression & Metabolic Syndrome. Vrije Universiteit Amsterdam. ISBN: 978-90-8659-447-4.

C.M.M. (Carmilla) Licht (2010). Autonomic Nervous System Functioning in Major Depression and Anxiety Disorders. Vrije Universiteit Amsterdam. ISBN: 978-90-8659-487-0.

S.A. (Sophie) Vreeburg (2010). Hypothalamic-Pituitary-Adrenal Axis Activity in Depressive and Anxiety Disorders. Vrije Universiteit Amsterdam. ISBN: 978-90-8659-491-7.

S.N.T.M. (Sigfried) Schouws (2011). Cognitive Impairment in Older Persons with Bipolar Disorder. Vrije Universiteit Amsterdam. ISBN: 978-90-9025-904-8.

P.L. (Peter) Remijnse (2011). Cognitive Flexibility in Obsessive-Compulsive Disorder and Major Depression – Functional Neuroimaging Studies on Reversal Learning and Task Switching. Vrije Universiteit Amsterdam. ISBN: 978-90-6464-449-8.

S.P. (Saskia) Wolfensberger (2011). Functional, Structural, and Molecular Imaging of the Risk for Anxiety and Depression. Vrije Universiteit Amsterdam. ISBN: 978-90-8659-536-5.

J.E. (Jenneke) Wiersma (2011). Psychological Characteristics and Treatment of Chronic Depression. Vrije Universiteit Amsterdam. ISBN: 978-94-9121-150-8.

P.D. (Paul David) Meesters (2011). Schizophrenia in Later Life. Studies on Prevalence, Phenomenology and Care Needs (SOUL Study). Vrije Universiteit Amsterdam. ISBN: 978-90-8659-563-1.

R. (Ritsaert) Lieverse (2011). Chronobiopsychosocial Perspectives of Old Age Major Depression: a Randomized Placebo Controlled Trial with Bright Light. Vrije Universiteit Amsterdam. ISBN: 978-90-8570-858-2.

A. (Adrie) Seldenrijk (2011). Depression, Anxiety and Subclinical Cardiovascular Disease. Vrije Universiteit Amsterdam. ISBN: 978-94-6191-052-3.

Y. (Yuri) Milaneschi (2012). Biological Aspects of Late-life Depression. Vrije Universiteit Amsterdam. ISBN: 978-90-8659-608-9.

L. (Lynn) Boschloo (2012). The Co-occurrence of Depression and Anxiety with Alcohol Use Disorders. Vrije Universiteit Amsterdam. ISBN: 978-94-6191-327-2.

D. (Didi) Rhebergen (2012). Insight into the heterogeneity of depressive disorders. Vrije Universiteit Amsterdam. ISBN: 978-94-6191-387-6.

T.M. (Michiel) van den Boogaard (2012). The Negotiated Approach in the Treatment of Depressive Disorders: the impact on patient-treatment compatibility and outcome. Vrije Universiteit Amsterdam. ISBN: 978-90-8891-495-9.

M. (Marjon) Nadort (2012). The implementation of outpatient schema therapy for borderline personality disorder in regular mental healthcare. Vrije Universiteit Amsterdam. ISBN: 978-94-6191-463-7.

U. (Ursula) Klumpers (2013). Neuroreceptor imaging of mood disorder related systems. Vrije Universiteit Amsterdam. ISBN: 978-94-6191-575-7.

E. (Ethy) Dorrepaal (2013). Before and beyond. Stabilizing Group treatment for Complex posttraumatic stress disorder related to child abuse based on psycho-education and cognitive behavioral therapy. Vrije Universiteit Amsterdam. ISBN: 978-94-6191-601-3.

K. (Kathleen) Thomaes (2013). Child abuse and recovery. Brain structure and function in child abuse related complex posttraumatic stress disorder and effects of treatment. Vrije Universiteit Amsterdam. ISBN: 978-94-6191-600-6.

K.M.L.(Klaas) Huijbregts (2013). Effectiveness and cost-effectiveness of the implementation of a collaborative care model for depressive patients in primary care. Vrije Universiteit Amsterdam. ISBN: 978-90-9027404-1.

T.O. (Tessa) van den Beukel (2013). Ethnic differences in survival on dialysis in Europe. The role of demographic, clinical and psychosocial factors. Vrije Universiteit Amsterdam. ISBN: 978-94-6108410-1.

A. (Agnes) Schrier (2013). Depression and anxiety in migrants in the Netherlands. Population studies on diagnosis and risk factors. Vrije Universiteit Amsterdam. ISBN: 978-94-6191-719-5.

B. (Barbara) Stringer (2013). Collaborative Care for patients with severe personality disorders. Challenges for the nursing profession. Vrije Universiteit Amsterdam. ISBN: 978-94-6191-809-3.

C.M. (Caroline) Sonnenberg (2013). Late life depression: sex differences in clinical presentation and medication use. Vrije Universiteit Amsterdam. ISBN: 978-94-6191-866-6.

Z. (Zsuzsika) Sjoerds (2013). Alcohol dependence across the brain: from vulnerability to compulsive drinking. Vrije Universiteit Amsterdam. ISBN: 978-90-8891-695-3.

V.J.A. (Victor) Buwalda (2013). Routine Outcome Monitoring in Dutch Psychiatry: Measurement, Instruments, Implementation and Outcome. Vrije Universiteit Amsterdam. ISBN: 978-94-6191-905-2.

J.G. (Josine) van Mill (2013). Sleep, depression and anxiety: an epidemiological perspective. Vrije Universiteit Amsterdam. ISBN: 978-94-6108-525-2.

S. (Saskia) Woudstra (2013). Framing depression in a SN[a]Pshot: Imaging risk factors of MDD. Vrije Universiteit Amsterdam. ISBN: 978-90-8891-751-6.

N.C.M. (Nicole) Korten (2014). Stress, depression and cognition across the lifespan. Vrije Universiteit Amsterdam. ISBN: 978-94-6108-748-5.

M.K. (Maarten) van Dijk (2014). Applicability and effectiveness of the Dutch Multidisciplinary Guidelines for the treatment of Anxiety Disorders in everyday clinical practice. Vrije Universiteit Amsterdam. ISBN: 978-94-92096-00-5.

I.M.J. (Ilse) van Beljouw (2015). Need for Help for Depressive Symptoms from Older Persons Perspectives: The Implementation of an Outreaching Intervention Programme. Vrije Universiteit Amsterdam. ISBN: 978-94-6259-496-8.

A.M.J. (Annemarie) Braamse (2015). Psychological aspects of hematopoietic stem cell transplantation in patients with hematological malignancies. Vrije Universiteit Amsterdam. ISBN: 978-94-6259-594-1.

A. (Annelies) van Loon (2015). The role of ethnicity in access to care and treatment of outpatients with depression and/or anxiety disorders in specialised care in Amsterdam the Netherlands. Vrije Universiteit Amsterdam. ISBN: 978-94-90791-34-6.

C. (Chris) Vriend (2015). (Dis)inhibition: imaging neuropsychiatry in Parkinson's disease. Vrije Universiteit Amsterdam. ISBN: 978-94-6295-115-0.

A.M. (Andrea) Ruissen (2015). Patient competence in obsessive compulsive disorder. An empirical ethical study. Vrije Universiteit Amsterdam. ISBN: 978-90-6464-856-4.

H.M.M. (Henny) Sinnema (2015). Tailored interventions to implement guideline recommendations for patients with anxiety and depression in general practice. Vrije Universiteit Amsterdam. ISBN: 978-94-6169-653-3.

T.Y.G. (Nienke) van der Voort (2015). Collaborative Care for patients with bipolar disorder. Vrije Universiteit Amsterdam. ISBN: 978-94-6259-646-7.

W. (Wim) Houtjes (2015). Needs of elderly people with late-life depression; challenges for care improvement. Vrije Universiteit Amsterdam. ISBN: 978-94-6108-985-4.

M. (Marieke) Michielsen (2015). ADHD in older adults. Prevalence and psychosocial functioning. Vrije Universiteit Amsterdam. ISBN: 978-90-5383-132-8.

S.M. (Sanne) Hendriks (2016). Anxiety disorders. Symptom dimensions, course and disability. Vrije Universiteit Amsterdam. ISBN: 978-94-6259-963-5.

E.J. (Evert) Semeijn (2016). ADHD in older adults; diagnosis, physical health and mental functioning. Vrije Universiteit Amsterdam. ISBN: 978-94-6233-190-7.

N. (Noera) Kieviet (2016). Neonatal symptoms after exposure to antidepressants in utero. Vrije Universiteit Amsterdam. ISBN: 978-94-6169-794-3.

W.L. (Bert) Loosman (2016). Depressive and anxiety symptoms in Dutch chronic kidney disease patients. Vrije Universiteit Amsterdam. ISBN: 987-94-6169-793-6.

E. (Ellen) Generaal (2016). Chronic pain: the role of biological and psychosocial factors. Vrije Universiteit Amsterdam. ISBN: 978-94-028-0032-6.

D. (Dóra) Révész (2016). The interplay between biological stress and cellular aging: An epidemiological perspective. Vrije Universiteit Amsterdam. ISBN: 978-94-028-0109-5.

F.E. (Froukje) de Vries (2016). The obsessive-compulsive and tic-related brain. Vrije Universiteit Amsterdam. ISBN: 978-94-629-5481-6.

J.E. (Josine) Verhoeven (2016). Depression, anxiety and cellular aging: does feeling blue make you grey? Vrije Universiteit Amsterdam. ISBN: 978-94-028-0069-2.

A.M. (Marijke) van Haeften-van Dijk (2016). Social participation and quality of life in dementia: Implementation and effects of interventions using social participation as strategy to improve quality of life of people with dementia and their carers. Vrije Universiteit Amsterdam. ISBN: 978-94-6233-341-3.

P.M. (Pierre) Bet (2016). Pharmacoepidemiology of depression and anxiety. Vrije Universiteit Amsterdam. ISBN: 978-94-6299-388-4.

M.L. (Mardien) Oudega (2016). Late life depression, brain characteristics and response to ECT. Vrije Universiteit Amsterdam. ISBN: 978-94-6295-396-3.

H.A.D. (Henny) Visser (2016). Obsessive-Compulsive Disorder; Unresolved Issues, Poor Insight and Psychological Treatment. Vrije Universiteit Amsterdam. ISBN: 978-94-028-0259-7.

E.C. (Eva) Verbeek (2017). Fine mapping candidate genes for major depressive disorder: Connecting the dots. Vrije Universiteit Amsterdam. ISBN: 978-94-028-0439-3.

S. (Stella) de Wit (2017). In de loop: Neuroimaging Cognitive Control in Obsessive-Compulsive Disorder. Vrije Universiteit Amsterdam. ISBN: 978-90-5383-225 7.

W.J. (Wouter) Peyrot (2017). The complex link between genetic effects and environment in depression. Vrije Universiteit Amsterdam. ISBN: 978-94-6182-735-7.

R.E. (Rosa) Boeschoten (2017). Depression in Multiple Sclerosis: Prevalence Profile and Treatment. Vrije Universiteit Amsterdam. ISBN: 978-94-028-0474-4.

G.L.G. (Gerlinde) Haverkamp (2017). Depressive symptoms in an ethnically DIVERSe cohort of chronic dialysis patients: The role of patient characteristics, cultural and inflammatory factors. Vrije Universiteit Amsterdam. ISBN: 978-94-6233-528-8.

T.J. (Tjalling) Holwerda (2017). Burden of loneliness and depression in late life. Vrije Universiteit Amsterdam. ISBN: 978-94-6233-598–1.

J. (Judith) Verduijn (2017). Staging of Major Depressive Disorder. Vrije Universiteit Amsterdam. ISBN: 978-94-6299-597-0.

C.N. (Catherine) Black (2017). Oxidative stress in depression and anxiety disorders. Vrije Universiteit Amsterdam. ISBN: 978-94-6299-672-4.

J.B. (Joost) Sanders (2017). Slowing and Depressive Symptoms in Aging People. Vrije Universiteit Amsterdam. ISBN: 978-94-6233-650-6.

W. (Willemijn) Scholten (2017). Waxing and waning of anxiety disorders: relapse and relapse prevention. Vrije Universiteit Amsterdam. ISBN: 978-94-6299-606-9.

P. (Petra) Boersma (2017). Person-centred communication with people with dementia living in nursing homes; a study into implementation success and influencing factors. Vrije Universiteit Amsterdam. ISBN: 978-94-6233-725-1.

T.I. (Annet) Bron (2017). Lifestyle in adult ADHD from a Picasso point of view. Vrije Universiteit Amsterdam. ISBN: 978-94-6299-685-4.

S.W.N. (Suzan) Vogel (2017). ADHD IN ADULTS: seasons, stress, sleep and societal impact. Vrije Universiteit Amsterdam. ISBN: 978-94-6299-673-1.

R.(Roxanne) Schaakxs (2018). Major depressive disorder across the life span: the role of chronological and biological age. Vrije Universiteit Amsterdam. ISBN: 978-94-6299-819-3.

J.J. (Bart) Hattink (2018). Needs-based enabling- and care technology for people with dementia and their carers. Vrije Universiteit Amsterdam. ISBN: 978-94-6295-880-7.

F.T. (Flora) Gossink (2018). Late Onset Behavioral Changes differentiating between bvFTD and psychiatric disorders in clinical practice. Vrije Universiteit Amsterdam. ISBN: 978-94-6295-899-9.

R. (Roxanne) Gaspersz (2018). Heterogeneity of Major Depressive Disorder. The role of anxious distress. Vrije Universiteit Amsterdam. ISBN: 978-94-028-1076-9.

M.M. (Marleen) Wildschut (2018). Survivors of early childhood trauma and emotional neglect: who are they and what's their diagnosis? Vrije Universiteit Amsterdam. ISBN: 978-94-6332-401-4.

J.A.C. (Jolanda) Meeuwissen (2018). The case for stepped care. Exploring the applicability and cost-utility of stepped-care strategies in the management of depression. Vrije Universiteit Amsterdam. ISBN: 978-90-5383-359-9.

D.S. (Dora) Wynchank (2018). The rhythm of adult ADHD. On the relationship between ADHD, sleep and aging. Vrije Universiteit Amsterdam. ISBN: 978-94-6375-034-9.

M.J.(Margot) Metz (2018). Shared Decision Making in mental health care: the added value for patients and clinicians. Vrije Universiteit Amsterdam. ISBN: 978-94-6332-403-8.

I.(Ilse) Wielaard (2018). Childhood abuse and late life depression. Vrije Universiteit Amsterdam. ISBN: 978-94-6380-072-3.

L.S.(Laura) van Velzen (2019). The stressed and depressed brain. Vrije Universiteit Amsterdam. ISBN: 978-94-6380-062-4.

S. (Sonja) Rutten (2019). Shedding light on depressive, anxiety and sleep disorders in Parkinson's disease. Vrije Universiteit Amsterdam. ISBN: 978-94-6380-176-8.

N.P.G. (Nadine) Paans (2019). When you carry the weight of the world not only on your shoulders. Factors associating depression and obesity. Vrije Universiteit Amsterdam. ISBN: 978-94-6380-141-6.

D.J. (Deborah) Gibson-Smith (2019). The Weight of Depression. Epidemiological studies into obesity, dietary intake and mental health. Vrije Universiteit Amsterdam. ISBN: 978-94-6380-144-7.

C.S.E.W. (Claudia) Schuurhuizen (2019). Optimizing psychosocial support and symptom management for patients with advanced cancer. Vrije Universiteit Amsterdam. ISBN: 978-94-6323-468-9.

M.X. (Mandy) Hu (2019). Cardiac autonomic activity in depression and anxiety: heartfelt afflictions of the mind. Vrije Universiteit Amsterdam. ISBN: 978-94-6380-206-2.

J.K.(Jan) Mokkenstorm (2019). On the road to zero suicides: Implementation studies. Vrije Universiteit Amsterdam. ISBN: 978-94-6361-224-1.

S.Y. (Sascha) Struijs (2019). Psychological vulnerability in depressive and anxiety disorders. Vrije Universiteit Amsterdam. ISBN: 978-94-6380-244-4.

H.W. (Hans) Jeuring (2019). Time trends and long-term outcome of late-life depression: an epidemiological perspective. Vrije Universiteit Amsterdam. ISBN: 978-94-6380-228-4.

R. (Ruth) Klaming Miller (2019). Vulnerability of memory function and the hippocampus: Risk and protective factors from neuropsychological and neuroimaging perspectives. Vrije Universiteit Amsterdam. ISBN: 978-94-6182-955-5.

P.S.W. (Premika) Boedhoe (2019) The structure of the obsessive-compulsive brain – a worldwide effort. Vrije Universiteit Amsterdam. ISBN: 978-94-6380-329-8.

C.S. (Carisha) Thesing (2020). Fatty acids in depressive and anxiety disorders: fishing for answers. Vrije Universiteit Amsterdam. ISBN: 978-94-6375-846-8.

R.D. (Richard) Dinga (2020). Evaluation of machine learning models in psychiatry. Vrije Universiteit Amsterdam.

M. (Mayke) Mol (2020). Uptake of internet-based therapy for depression: the role of the therapist. Vrije Universiteit Amsterdam. ISBN: 978-94-6416-150-2.

R.C. (Renske) Bosman (2020). Improving the long-term prognosis of anxiety disorders: Clinical course, chronicity and antidepressant use. Vrije Universiteit Amsterdam. ISBN: 978-94-6375-736-2.

R.W. (Robbert) Schouten (2020). Anxiety, depression and adverse clinical outcomes in dialysis patients. Should we do more? Vrije Universiteit Amsterdam. ISBN: 978-94-6416-179-3.

T.T. (Trees) Juurlink (2021). Occupational functioning in personality disorders: a quantitative, qualitative and semi-experimental approach. Vrije Universiteit Amsterdam. ISBN: 978-94-6421-117-1.

I.P.H. (Ires) Ghielen (2021). Surfing the waves of Parkinson's disease. Understanding and treating anxiety in the context of motor symptoms. Vrije Universiteit Amsterdam. ISBN: 978-94-6416-493-0.

L.K.M. (Laura) Han (2021). Biological aging in major depressive disorder. Vrije Universiteit Amsterdam. ISBN: 978-94-93184-91-6.

E. (Esther) Krijnen-de Bruin (2021). Relapse prevention in patients with anxiety or depressive disorders. Vrije Universiteit Amsterdam. ISBN: 978-94-6423-298-1