UNIVERSITY OF TWENTE

Faculty of Behavioral and Management Sciences

Master thesis (10 EC)

Universal, Selective and Indicated Prevention of Anxiety disorders in adults: a Systematic Review

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2017/2018

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Summary

Introduction. The field of the prevention of anxiety disorders in adults is in a premature state compared to the prevention of other mental disorders, which is why the current scientific status of universal, selective and indicated prevention programs for anxiety in adults needs to be updated.

Objective. The aim of the present study was to explore recent developments within the field of prevention of anxiety in adult populations.

Method. A systematic review of the electronic databases Scopus, Web of Science, PsycINFO and Cochrane Library was conducted, including articles published between 2000 and January 2018. Eligibility criteria were (1) interventions described or designed as universal, selective and indicated prevention programs, (2) targeting anxiety symptoms, (3) focusing on adult populations (>18) and (4) studies designed as randomized controlled trials (RCTs) that examined the effectiveness of the interventions. The recruitment and selection procedures were extracted for the identification of prevention type. Outcomes for anxiety measures were extracted, as well as the structure and the content of the preventive interventions.

Results. Eleven studies (n = 2661 participants, 75.5% female) that examined the effects of preventive interventions based on Positive Psychology, ACT, and CBT for adult populations met eligibility criteria. The categorization into universal, selective and indicated prevention turned out to be problematic and lead to the categorization of additional mixed recruitment approaches. Nine studies found significant effects for preventive interventions, including one universal (d = 0.43 to 0.66), one selective (d = 0.13 to 0.74), three indicated prevention programs (d = 0.20 to 0.68; NNT = 5) and four mixed recruitment approaches (d = 0.32 to 0.87).

Conclusion. This systematic review demonstrated that the conceptualization of universal, selective and indicated prevention still suffers from issues concerning the implementation in practice. Nevertheless, effective preventive interventions based on positive psychological, acceptance and commitment and cognitive behavioral approaches were identified. Due to the fact that these effects were measured in populations mostly consisting of higher educated females, future research that focuses on a broader public is recommended.

Key words: Universal, Selective, Indicated, Prevention, Anxiety, Adult

Samenvatting

Inleiding. Het veld van de preventie van angststoornissen bij volwassenen verkeert in een vroeg stadium in vergelijking met de preventie van andere psychische stoornissen. Daarom moet de huidige wetenschappelijke status van universele, selectieve en geïndiceerde preventieprogramma's voor angst bij volwassenen worden bijgewerkt.

Doelstelling. Het doel van deze studie was om recente ontwikkelingen op het gebied van preventie van angst bij volwassen populaties te onderzoeken.

Methode. Een systematische review van de elektronische databases Scopus, Web of Science, PsycINFO en Cochrane Library werd uitgevoerd, inclusief artikelen die zijn gepubliceerd tussen 2000 en januari 2018. Inclusiecriteria waren (1) interventies die beschreven of ontworpen zijn als universele, selectieve en geïndiceerde preventieprogramma's, (2) interventies gericht op angstsymptomen, (3) interventies gericht op volwassen populaties (>18) en (4) studies ontworpen als RCT's die de effectiviteit van de interventies onderzochten. De wervings- en selectieprocedures werden geëxtraheerd voor de identificatie van het preventietype. Uitkomsten voor angst werd geëxtraheerd, evenals de structuur en de inhoud van de preventieve interventies.

Resultaten. Elf studies (n = 2661 deelnemers, 75,5% vrouwelijk) die de effecten van preventieve interventies gebaseerd op positieve psychologie, ACT en CGT voor volwassen populaties bestudeerden, voldeden aan de inclusiecriteria. De indeling in universele, selectieve en geïndiceerde preventie bleek problematisch en leidde tot de indeling van een aanvullende categorie van gemengde wervingsbenaderingen. Negen studies vonden significante effecten voor preventieve interventies, waaronder één universele (d = 0.43 tot 0.66), één selectieve (d = 0.13 tot 0.74), drie geïndiceerde preventieprogramma's (d = 0.20 tot 0.68; NNT = 5) en vier gemengde wervingsbenaderingen (d = 0.32 tot 0.87).

Conclusie. Deze systematische review toonde aan dat de conceptualisering van universele, selectieve en geïndiceerde preventie nog steeds problemen heeft met betrekking tot de implementatie in de praktijk. Desalniettemin werden effectieve preventieve interventies geïdentificeerd op basis van positieve psychologische, acceptatie en commitment en cognitieve gedragsbenaderingen. Vanwege het feit dat deze effecten werden gemeten in populaties die meestal uit hoger opgeleide vrouwen bestonden, wordt toekomstig onderzoek dat zich richt op een breder publiek aanbevolen.

I. Introduction

According to recent assessments of the global burden of mental disorders, anxiety disorders belong to the most diagnosed affective disorders next to depression (Wittchen, Jacobi, Rehm, Gustavsson, ...& Fratiglioni, 2011; Mokdad, 2015; World Health Organization, 2017). The World Health Organization (2017) stated that an estimated 3.6% of the global population, which equals 264 million people worldwide, were newly diagnosed with an anxiety disorder in 2015, following shortly after diagnoses of depression (4.4%, 322 million people worldwide). In Europe, anxiety disorder belongs to the most frequent diagnosis with 14.0% of the population affected, which equals 61.3 million individuals (Wittchen et al., 2011). Due to the growth and ageing of the world population, these numbers have increased 14.9% since 2005, underscoring the need of a preventive approach to address this issue (Hay, 2017; WHO, 2015; WHO, 2017). However, evidence suggests that the prevention of anxiety disorders in adult populations is a field of study that is in a premature state compared to other fields of prevention (Meijer, Smit, Schoemaker, & Cuijpers, 2006). The explanation for the prematurity of this field can be found in several reasons.

First, conceptual issues have been reported with regard to prevention of anxiety in general, such as the choice of terminology for different types of prevention (Dozois, 2004). The framework of primary, secondary and tertiary prevention as proposed by Caplan (1964), which is often used in medical health services, is not applicable without inconsistencies to mental health services according to Haggerty and Mrazek (1994). This framework refers to prevention from a medical perspective, including treatment opportunities in order to decrease the risk of developing a disorder (Haggerty & Mrazek, 1994). For instance, treatment with pharmacological substances such as vaccines can be regarded as a form of prevention, although it is in fact a sort of treatment that aims to reduce the risk of the occurrence of a disorder (Hawn, Day, Scriba, Hatherill, … & Self, 2014). Due to the fact that many mental, emotional and behavioral problems can themselves be regarded as risk factors for the development of other disorders or disabilities, this framework is not applicable to the definition of mental health prevention (O'Connell, Boat, & Warner, 2009). Therefore, an alternative framework for mental health prevention was recommended by Gordon (1987), covering the three levels of universal, selective and indicated prevention (as cited in Haggerty & Mrazek, 1994; Dozois, 2004; O'Connell et al., 2009). According to Haggerty and Mrazek (1994), these three levels refer to three different target groups. In particular, these are the general population, population groups with an above average risk for developing a disorder and individuals at high risk who have been identified with minimal but clinically relevant symptoms of a disorder (Haggerty & Mrazek, 1994).

The second reason for the prematurity of the field of anxiety disorder prevention in adult populations is the lack of evidence. No clear evidence for effective universal or selective prevention programs targeting anxiety symptoms for general adult populations has been found yet, indicating that there is a lack of knowledge with regard to this field (Conley Durlak, Shapiro, Kirsch, & Zahniser, 2016; Cuijpers Reynolds, Donker, Li, ... , & Beekman, 2011; Meijer et al., 2006). Research on the prevention of anxiety disorders in adult populations is in general scarce compared to the amount of research available on the prevention of anxiety in children or the prevention of depressive disorders (Cuijpers, et al., 2012; Meijer et al., 2006). This scarcity can be explained by the fact that scientific interest for this particular field has started growing within the last three decades (Haggerty & Mrazek, 1994; WHO, 2004). Given the fact that general mental health prevention started scientifically in 1909, this timespan is rather short (Haggerty & Mrazek, 1994; Aigner, 2011; WHO, 2004). The implementation of empirical research on mental health prevention programs began in the 1980's and focused mainly on the target group of children (Haggerty & Mrazek, 1994). The reason therefore is the fact that these preventive programs were designed based on the assumption that the onset of anxiety would mostly be found during childhood (Roza, Hofstra, Ende, & Verhulst, 2003). Nevertheless, recent evidence suggests that many people develop anxiety disorders at a later stage of their life than childhood or adolescence (WHO, 2004; Cuijpers et al., 2011).

This evidence covers the third issue, which is in particular the fact that the lines of the age of onset (AOO) are blurred among various types of anxiety disorders (Bandelow & Michaelis, 2015). The proper estimation of the age group that needs to be targeted is essential for the design of interventions because it impacts the structure and the delivery of the intervention (Kessler, Amminger, Aguilar-Gaxiola, Alonso, Lee, & Ustun, 2007). Recent evidence on estimated AOO of anxiety disorders displayed that the estimated median AOO for specific phobias is 7 years, followed by agoraphobia with panic attacks with an estimated median AOO of 20 years, panic disorders with a median AOO of 24 years and Generalized Anxiety disorder (GAD) with a median AOO of 31 years (Bandelow & Michaelis, 2015; Kessler et al., 2007). A systematic review that included all these age groups has not been conducted yet because most of the reviews focused particularly on one specific type of anxiety disorder, intervention program or population group (Conley et al., 2016; Cuijpers, Smit, Lebowitz, & Beekman, 2011).

This was illustrated in a recent systematic review that focused on the effectiveness of prevention programs for anxiety in adults aged 45 to 75 years, thus neglecting all adults aged 18 to 44 years. Only studies that were designed as randomized controlled trials (RCTs) in primary health care settings conducted until 2015 were included in the analysis (Garcia-Campayo, del Hoyo, Valero, Yus, Esteban, Guedea, & Botaya, 2015). From the initially

selected articles (N = 139), no article was eligible for analysis according to the authors due to their exclusion criteria. This means that to the author's knowledge, no high quality studies that tested the effectiveness of preventive interventions for anxiety disorders in adults within primary health care settings were conducted until 2015 (Garcia-Campayo et al., 2015). Therefore, a synthesis of recent findings covering the prevention of anxiety disorders in the general adult population is missing.

Moreover, treatment opportunities for anxiety disorders also suffer from various issues (Dozois, 2004; Corrigan, Druss, & Perlick, 2014). These issues have to do with stigmatization as well as practical issues, such as poor access to treatment, treatment-gaps or the experience of long delays prior to treatment access (Corrigan et al., 2014). Further, negative treatment- and care experiences seem to account for the biggest amount of dropouts and attrition of participants (Bados, Balaguer, & Saldaña, 2007; WHO, 2015; Corrigan et al., 2014). Especially the risk of stigma seems to be a problem that does not only concern the field of treatment but also the field of prevention.

Evidence has shown that only a small part of the population actually seeks professional help due to the fear of being stigmatized (Ociskova, Prasko, & Sedlackova, 2013). According to a Dutch study on the risk of stigma in preventive services within primary health care settings, the participation rates of adults with anxiety symptoms in preventive interventions were too low to measure any effects (Batelaan, Smit, Cuijpers, van Marwijk, Terluin, & van Balkom, 2012). According to Batelaan et al. (2012), the willingness to be screened turned out to be low within the sample of initially recruited individuals. Only 17.3% out of 2454 recruited individuals participated in the screening process (Batelaan et al., 2012). Unfortunately, the assessment resulted in a higher risk of stigmatization, because Participants were labeled as "high risk"-individuals in order to be eligible for the prevention program. This in turn led to large numbers of dropout and unwillingness to participate (Batelaan et al., 2012).

Hence, people who could have profited from preventive interventions were not sufficiently reached. This is unfavorable because once manifested, an untreated anxiety disorder can last many years and affect different levels of the daily life of sufferers (Olatunji, Cisler, Tolin, 2007). The importance of addressing psychological problems as soon as possible has already been emphasized throughout the literature, and the problem of stigma needs to be overcome for a preventive intervention to be effective within primary care settings (Batelaan et al., 2012). Well-functioning and non-stigmatizing prevention programs could offer solutions for these problems, making preventive approaches and treatment approaches equally important (Mental Health Foundation, 2016). However, an update of the literature on this topic is needed, and the aim of the present study was to provide such an update. Therefore, findings of the most recent meta-analyses and reviews of preventive

interventions for anxiety disorders in adult populations were summarized with regard to universal, selective and indicated preventive interventions to provide an overview over the current scientific status of this field.

Universal Prevention

Universal prevention programs aim to offer interventions that are accessible for the entire population, including people who have not been diagnosed yet with a mental disorder and who do not suffer from symptoms at all (Beretty, 2013; Stockings, Degenhardt, Dobbins, Lee, … & Patton, 2016). According to the Dutch national guidelines for depression, universal mental health prevention aims to support optimal mental health, job satisfaction, resilience, social skills, self-efficacy and security (Wamel, Takkenkamp, Meeuwissen, Voordouw, & Verburg, 2005). In order to reach a population group with broad age ranges and various characteristics, these types of prevention programs are required to be non-stigmatizing open access programs for interested individuals. As stated earlier, these requirements turned out to be problematic for the prevention of anxiety within primary care settings (Batelaan et al., 2012; Garcia-Campayo et al., 2015). Nevertheless, some studies have examined the effectiveness of prevention programs for anxiety disorders in adult populations outside primary care settings.

One of these studies was a review that examined the possibilities of prevention of anxiety disorders in the late stages of life. In this review, universal preventive interventions were not discussed because these were not developed systematically or tested in well-designed trials (Cuijpers et al., 2011). This is not surprising because most of the people in the age group of seniors already suffer from a general medical or mental disorder (Cuijpers et al., 2011). Therefore, only a small part of this age group would be eligible for a universal preventive intervention.

However, a meta-analysis published in 2016 showed significant effects of universal and indicated prevention programs for anxiety disorders in higher education students, implemented through Technology-Delivered Interventions (TDI) (Conley et al., 2016). The intervention elements implemented in the studies were *cognitive behavioral therapy (CBT), mindfulness-interventions, psycho-education, social skills training, relaxation techniques, online support group interventions* and other, unique interventions such as *concreteness training, emotion perception training* and *interactive gaming* (Conley et al., 2016). The CBT elements that were implemented in these preventive interventions contained *monitoring and modifying cognitions, identifying emotions* and *changing behaviors in order to improve adjustment*. Psycho-educational elements provided information on how to cope with stress or mental health issues, and relaxation techniques were based on progressive muscle relaxation (Conley et al., 2016). The authors of this meta-analysis pointed out that the factor 'skill

training' in particular demonstrated a strong pattern of effects on depression, anxiety, stress and interpersonal relationships in universal as well as indicated prevention programs (Conley et al., 2016).

Selective Prevention

Selective prevention programs aim to reach people who are at above average risk of developing an anxiety disorder (Stockings et al., 2016; Cuijpers et al., 2011). These are in particular groups consisting of individuals that share risk factors, such as the experience of difficulties in interactions between another individual, a group or the environment in general (Wamel et al., 2005). Selective prevention programs focus on empowering protective factors in individuals of groups defined as at above average risk (Wamel et al., 2005). In order to identify individuals eligible for selective prevention, a risk status assessment based on specific risk- and vulnerability factors needs to be conducted (Dozois, 2004; WHO, 2015). These risk- and vulnerability factors can be defined as the cognitive mechanisms that influence the development of an anxiety disorder (Dozois, 2004). Examples of recently researched risk factors are the cognitive mechanisms of anxiety sensitivity, emotional regulation difficulties and self-efficacy beliefs (Gallagher, Payne, White, Shear, … & Barlow, 2013). Elevated levels of anxiety sensitivity, high levels of emotional regulation difficulties and low self-efficacy together can lead to a vicious circle of anxiety (Gallagher et al., 2013). This can put a person into constant enhanced sensitivity levels of the perception of threat, which can result in a chronic "fight or flight"-mode (Aigner, 2011). Within this mode, a person is more likely to perceive bodily sensations more intense and threatening than average and is therefore at above average risk of developing an anxiety disorder (Aigner, 2011).

Risk- and vulnerability factors are complex, variable and highly dependent on circumstances of the individual such as age, personal environment and socio-economic status (Dozois, 2004). They are essential but highly subjective target points for an intervention and they change constantly throughout life, which is why they require to be assessed on an individual level (WHO, 2015; Dozois, 2004). Examples found in the literature of people at risk were widows, victims of abuse, caregivers and (older) adults without a social network or with chronic general medical illnesses (Wamel et al., 2005; Cuijpers et al., 2011). However, evidence has shown that the identification of risk- and vulnerability factors for anxiety disorders is still a major challenge within research in this field, because these factors can be highly diverse across different population groups (Dozois, 2004; WHO, 2015).

According to Cuijpers et al. (2011), very few studies on selective prevention of anxiety symptoms in adults were conducted with no significant effects. Other reviews and meta-analyses reported no selective prevention programs at all in their analyses, and most of

the studies that found significant effects of selective prevention programs were designed for children (Meijer et al., 2006; Conley et al., 2016; Stockings et al., 2016).

Indicated Prevention

Indicated prevention programs address people who display sub-threshold symptoms or a history of mental illness but no recent diagnosis of a full-blown mental disorder (Stockings et al., 2016; Cuijpers et al., 2011). This includes all individuals with mild to moderate symptoms, not meeting the diagnostic criteria for a full-blown disorder yet (van Balkom, Van Vliet, Emmelkamp, Bockting, ..., & Meeuwissen, 2011). The aim of indicated prevention is an early detection of symptoms in order to be able to offer help at an early stage of symptom development (Wamel et al., 2005). Recent reviews and meta-analyses found supporting evidence for positive effects of indicated preventive interventions (Cuijpers et al, 2011; Conley et al., 2016; Meijer et al., 2006). In particular, the effects of indicated prevention programs for student populations were two times higher than similar universal prevention programs. Indicated CBT-based skill-training interventions displayed significant positive effects for depression, anxiety, stress, health, self-perceptions, interpersonal relationships and significant negative effects for spirituality (Conley et al., 2016). These interventions mostly consisted of *psycho-educational elements, interoceptive exposure, in vivo or in virtuo exposure* and elements containing *relapse-prevention* (van Balkom et al., 2013).

In population groups of elderly people, significant reductions of depressive as well as anxiety symptoms were found when the interventions were delivered through Stepped care (Cuijpers et al., 2011; Conley et al., 2016). Indicated preventive interventions based on Stepped care consisted of four steps, mostly containing the elements (1) psycho-education, (2) psychosocial support and self-help or e-mental health interventions, CBT in the case of non-effectiveness, (3) evaluation of the intervention, and (4) Pharmacotherapy in the case of non-effectiveness. It is important to note that these steps vary according to the type of anxiety disorder that is targeted (van Balkom et al., 2013).

Most of the published indicated prevention programs that were randomized controlled trials (RCTs) targeted adults with panic symptoms (Meijer et al., 2006). Fewer studies focused on populations with social phobic symptoms, high levels of stress and generalized anxiety disorder symptoms (Meijer et al., 2006).

Aim Of Present Review

This summary indicates that there are still gaps in the literature concerning prevention programs for anxiety in general adult populations (Cuijpers, et al., 2011; Meijer et al., 2006; Garcia-Campayo et al., 2015). Little to no information about universal or selective interventions for general adult populations was available throughout the literature (Conley et

al., 2016; Cuijpers et al., 2011; Meijer et al., 2006). Only indicated prevention programs had sufficient support for effectiveness, although focusing mainly on student populations and elderly people, with interventions mainly based on CBT (Cuijpers et al., 2011; Conley et al., 2016; Meijer et al., 2006). The present review therefore examined recent developments with regard to effective prevention programs for anxiety in general adult populations. In order to get a broad overview over developments within this field, high-quality studies conducted between 2000 and 2017 were analyzed. Furthermore, it was examined whether theoretical bases other than CBT were implemented within prevention programs and how these interventions were structured. The review question examined in this systematic review was therefore

Which types of preventive interventions (universal, selective, indicated) targeting anxiety symptoms in adult populations have been (further) developed and tested on effects?

Additionally, special attention was paid to the structure of the interventions and possible moderators or mediators that contributed to the effectiveness of preventive interventions.

II. Methods

A systematic literature review was conducted by the author with supervision of two experts on the field of prevention of anxiety disorders (P. M. & P. K.). The methods used within this systematic review were based on the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses, Liberati, Altman, Tetzlaff, Mulrow, ... , & Moher, 2009) and meta-analysis guidelines (Cuijpers, 2016). An expert in the field of systematic reviews was consulted for the development of the search string. A PICO statement (Populations, Interventions, Comparators, Outcomes) was developed in order to build the search string and to analyze the extracted data (Schardt, Adams, Owens, Keitz, & Fontelo, 2007). The approach of a narrative synthesis was used as review strategy in order to synthesize the literature with additional findings (Popay, Roberts, Sowden, Petticrew, Arai, Rodgers, ... & Duffy, 2006).

Eligibility criteria

The present review included high-quality studies that concentrated on the effectiveness of prevention programs for anxiety disorders in adult populations, irrespective of the type of setting. Inclusion criteria were therefore (1) interventions that have been described or designed as universal, selective or indicated prevention programs or as an early intervention program., (2) studies that implemented anxiety outcome measure instruments, measuring effects on anxiety symptoms as primary or secondary outcome, (3) interventions designed for adult population groups aged above 18 years, and (4) studies conducted as RCT. In particular, interventions were identified as universal prevention when they provided access for the general population with no present symptoms of anxiety. Requirements for the identification of a selective prevention intervention were access for at-risk populations including measurements for the selection of participants. Indicated preventive interventions were characterized as interventions that provided access for populations with a history of mental illness and/or mild to moderate symptoms of anxiety but no recent full-blown diagnosed anxiety disorder. Additionally, studies were included when published in English language between 2000 and January 2018. Studies that met all of these requirements were selected for further analysis.

Exclusion criteria were (1) not containing any type of the three preventive interventions (universal, selective, indicated) and (2) targeting children or adolescents. Additionally, (3) pilot studies, study designs without measurements of effect and meta-analyses or reviews were excluded from the analysis.

Data sources and search strategy

A broad comprehensive literature search was conducted within four electronic bibliographic databases. The electronic databases Scopus, PsychINFO, Cochrane Library and

Web of Science were systematically searched between November 2017 and February 2018 by the author. Access to the databases was provided through the University of Twente. In accordance with the PICO statement developed for this search, the basis of the search terms included 'adult' for the population of interest; 'universal, selective or indicated prevention' and 'early intervention' for the interventions of interest; and 'anxiety' as an outcome measure. The records were limited to publications between 2000 and 2017 and to studies written in English. These limitations were set through the search pages of Cochrane Library and PsycINFO by limiting the search to records published between 2000 and 2017. Within the two databases Web of Science and Scopus, all studies published earlier than 2000 were excluded through the adjustment bar. In addition, a reference search of relevant records that were found with this search strategy was conducted in order to identify possible relevant records that were not identified yet through the search query. A full display of the final search queries used within this systematic search can be reviewed in Table 1.

Table 1. Search queries

Date	Database/Set	Query	Hits
17-02-2018	Scopus	TITLE ("Universal Prevention" OR "Selective Prevention" OR "Indicated Prevention" OR "early intervention") AND ("Anxiety disorder" OR anxiety) AND (adults OR adult)	274
17-02-2018	PsycINFO	TI ("universal prevention" OR "selective prevention" OR "indicated prevention" OR "early intervention") AND (adults OR adult) AND (anxiety disorders OR anxiety)	44
17-02-2018	Cochrane Library	("universal prevention" OR "selective prevention" OR "indicated prevention" OR "early intervention") AND (adults OR adult) AND (anxiety disorders OR anxiety)	116
17-02-2018	Web of Science	TS=("universal prevention" OR "selective prevention" OR "indicated prevention" OR "early intervention") AND TS=(anxiety*) AND TS=(adult*)	215

Selection of studies

After removing the duplicates through the use of a reference management tool (Endnote X7), a manual search for duplicates was conducted in order to ensure the accuracy of this exclusion. Then, the titles and abstracts of the remaining records were screened through the use of Endnote and additional manual screening on the terms 'prevention', 'anxiety' or 'adult'. The excluded records were grouped into 'children and adolescents', 'no prevention program', 'pilot- and design studies', 'protocols', and ' meta-analyses and reviews'. After this selection process, the full-texts of the selected records were screened on eligibility. Finally, the records that were included in the analysis were examined and the data was extracted.

Data extraction

The data was extracted by the author according to the guidelines of Cuijpers (2014) and synthesized through the method of narrative synthesis (Popay et al., 2006). This included the extraction of information about participants (recruitment, selection processes, target group), interventions (structure of the intervention, study design) and information about the outcomes (effects of the interventions). The aim of a narrative synthesis approach is to identify factors that explain the differences in direction and size of effects across studies in a narrative way (Popay et al., 2006). The main factors of interest of the present study were the characteristics of participants in terms of risk status, recruitment and selection processes, program content and delivery and program outcomes for the three types of preventive interventions. As the focus was on qualitative aspects rather than on quantitative, a narrative synthesis approach was considered the most appropriate approach for this systematic review.

The first step in the process of data extraction was to extract available information about the selection procedures of the included preventive interventions in order to identify them as universal, selective or indicated prevention programs. Therefore, the study characteristics of each study were tabulated, including year of publication, country of publication, study objectives, the target group, recruitment and the selection processes and instruments used to measure effects. A grouping of the records into universal, selective and indicated prevention was done through the analysis of recruitment and selection criteria of participants. Then, the interventions were described in terms of the theoretical basis for the intervention, the structure including the number of sessions of the intervention, the content and delivery of the intervention and the effective elements, such as instruments that were used and concepts that were measured. Follow-ups and dropout numbers were summarized for each selected study. Further, the risk of bias and the quality of the studies were assessed.

Quality assessment

For the assessment of the risk of bias and the quality of conduct with regard to the included studies, the *Cochrane Collaboration's tool for assessing risk of bias* (Higgins, 2011) was used. This tool helps researchers to judge the risk of bias within a study through the differentiation between five different types of biases. These biases are (1) Selection bias and confounding including biased allocation to interventions, (2) Performance bias due to knowledge of the allocated interventions by participants and personnel during the study, (3) Attrition bias due to amount, nature or handling of incomplete outcome data, (4) Detection bias due to knowledge of the allocated interventions by outcome assessors, and (5) Reporting bias due to selective outcome reporting. The selected articles were rated with "low risk of bias", "high risk for bias", or "unclear risk of bias" (Higgins, 2011). For a detailed outline of

the questions answered with regard to bias and quality control, see Higgins, 2011, p. 181, Table 8.5.a.

III. Results

The search string was applied on the four databases and resulted in 649 records. Additional hand-search of the references of relevant records resulted in 3 more matching records. Another 4 records were collected through consultation of experts in the field of anxiety disorders and psychological interventions, resulting in a total of 656 records. After removing the duplicates (N=325), 331 records were identified. The abstracts of these records were screened on eligibility. 114 records were excluded because they focused on the target group children and adolescents, 74 records did not focus on anxiety and 58 records did not contain any kind of preventive intervention. Nine records were excluded because they were pilot or design studies with no effect measurement, 17 studies were excluded because they were study protocols and 33 records were excluded because they were meta-analyses or reviews. The full-texts of the remaining 26 records were retrieved and screened. Fifteen records were excluded during the data extraction process because they focused mainly on Post-traumatic Stress disorder (PTSD). According to the DSM-V, PTSD was separated from anxiety disorders and classified as a type of traumatic stress disorder (Resick & Miller, 2009). The remaining 11 records were considered relevant for further full-text analysis. They were analyzed with the focus on the three types of preventive interventions, the population group, the baseline and outcome measurements and the effectiveness. Figure 1 displays the selection process in a flow chart.

Figure 1. PRISMA Flowchart Search Strategy

Identification

Records identified through database searching
Scopus n = 274
PsycINFO n = 44
WOS = 215
Cochrane Library n = 116

Additional records identified through other sources
Experts n = 4
Reference search n = 3

Records after duplicates removed
n = 331

Screening

Records screened
n = 331

Records excluded
n = 114 (children & adolescets)
n = 74 (no anxiety)
n = 58 (no prevention)
n = 9 (pilot & design studies)
n = 17 (protocols)
n = 33 (meta-analyses/reviews)

Eligibility

Full-text articles assessed for eligibility
n = 26

Full-text articles excluded, with reasons
n = 15 (focus on PTSD)

Included

Studies included in qualitative synthesis
n = 11

Study Characteristics

The 11 selected articles contained RCTs that were conducted in Europe (N=7), the USA (N=1), Asia (N=1) and Oceania (N=2). Seven studies were conducted and published in the Netherlands, one study was conducted in Texas (USA), another study was conducted in China, and 2 studies were conducted in Australia. Table 2 shows the study characteristics of

the selected articles, including recruitment and selection procedures of participants in the studies. The articles are numbered from one to 11 and will be referred to according to their numbering in the following.

Five studies were conducted during the last five years (2; 3; 4; 9; 11), five studies were conducted between five and ten years ago (1; 5; 6; 8; 10) and one study was conducted fifteen years ago (7). The 11 articles focused on nine different interventions, containing principles of Cognitive behavioral therapy (CBT), Acceptance and Commitment Therapy (ACT), and Positive Psychology (PP). From the 11 articles, seven focused on interventions based on CBT, including psycho-education, Interpersonal Therapy (IPT), and Problem-Solving Therapy (PST) and the self-help course "Coping with depression" (CWD; 3; 4; 5; 7; 8; 10; 11). Two articles reported the implementation of ACT-based interventions (1; 6), and the remaining two articles reported the implementation of interventions based on PP (2; 9).

From the seven articles with interventions based on CBT, four articles focused on depression and anxiety in general (4; 5; 10; 11), two articles focused on panic disorder (7; 8), and one article focused on generalized anxiety disorder (3). The two articles that were based on ACT focused on depression and anxiety in general and the two articles that were based on PP also focused on anxiety in general. Participants that were included in the studies were adults aged between 17 and 84 years from various population groups, such as students, elderly people, a Chinese clinical population and self-selected individuals with various levels of anxiety or depressive symptoms.

The mean age of the participants of all included studies ranged from a mean age of 20.73 years with a standard deviation (SD) of 6.29 up to a mean age of 84.0 years (SD = 6.7). Although 17 years falls out of the range of the present review, this study was included in the analysis due to the fact that the mean age of the subjects included was higher in the actual sample (mean = 20.73 years, SD = 6.29) than in the initially recruited sample (mean = 19.92 years, SD = 4.78). The higher mean age in the included sample may be seen as an indicator that more participants above 18 years of age participated in this study. The actual age range of participants included in the study was not reported.

Screening instruments used in order to select participants within the eleven articles were instruments that measured depressive symptoms (*the Center for Epidemiologic Studies Depression Scale*, CES-D; Radloff, 1977; *Beck's depression Inventory*, BDI, Beck & Steer, 1993), general mental health and well-being (*the Mental Health Continuum-Short form*, MHC-SF, Lamers, Westerhof, Bohlmeijer, ten Klooster, & Keyes, 2011), and specific anxiety symptoms (*Generalized Anxiety Disorder 7*, GAD-7, Spitzer, Kroenke, Williams, & Löwe, 2006; *Beck's anxiety inventory*, BAI, Beck & Steer, 1987; *the Hospital Anxiety and Depression Scale*, HADS, Zigmond & Snaith, 1983, Bjelland, Dahlb, Haugc, & Neckelmanns, 2002; *the Anxiety Sensitivity Index*, ASI, Peterson & Reiss, 1992; *the Panic*

Disorder Severity Scale - self report, PDSS-SR, Shear, Rucci, Williams, Frank, Grochocinski, Vander Bilt, ... & Wang, 2001).

Table 2. Study Characteristics

#	Authors, Year, Location	Aim of the study	Target group & Recruitment	Selection of participants
1	Bohlmeijer, Fledderus, Rokx, & Pieterse, 2011 (Netherlands)	Examining the efficacy of an ACT-based self-help book "living to the full" as an early community intervention	People aged 18 years or older (mean 49.0 years, SD = 10.7) with clinically relevant depressive symptoms; Recruitment through press articles, leaflets, posters and psychologists at 7 mental health institutions in the Netherlands	Assessment of mental health through interview with trained psychologists, included with mild to moderate depressive symptoms
2	Bolier, Haverman, Kramer, Westerhof, Riper, Walburg, Boon, & Bohlmeijer, 2013 (Netherlands)	Examining the effects of online self-help online intervention "Psyfit" (based on positive psychology) on well-being and depressive/anxiety symptoms	Mildly depressed adults aged 21 years or older (mean 43.2 years, SD 11.8) from the general population; Recruitment through social media, banners, information brochures and regional newspapers ("Would you like to increase your mental fitness? Improve your mental fitness and participate in our study of an online self-help program.", p.3)	Selection based on CES-D score between 10 and 24 (non-clinical + clinical) and languishing or moderate levels of well-being on MHC-SF (mild to moderate depressive symptoms)
3	Christensen, Batterham, Mackinnon, Griffiths, Kalia Hehir, Kenardy, Gosling, & Bennett, 2014 (Australia)	Evaluate the effectiveness of the web-based intervention "iChill" based on CBT for the prevention of generalized anxiety disorder (GAD) in young adults	Young adults aged 18 to 30 years (mean 25.6 years, SD = 3.2); Recruitment via the Australian electoral roll	A score above 5 on the GAD-7 but no current diagnosis of GAD (mild to moderate anxiety)
4	Cukrowicz, Smith, Hohmeister, & Joiner, 2014 (USA, Texas)	Explore the potential moderators that have an impact on the effectiveness of the CBASP program (based on CBT and IPT) in a student population	Individuals entrenched in highly social environments: Undergraduate university students aged between 18 and 21 years (mean 19.2 years, SD = 1.5), received course credits for participation	A score lower or equal to 18 on BAI and BDI (no current significant symptoms of anxiety or depressive disorders)
5	Dozeman, van Schaik, van Marwijk, Stek, Beekman, & van der Horst, 2011 (Netherlands)	Explore the feasibility and effectiveness of the module "activity scheduling" from the self-help course "Coping with depression" (CWD) as guided self-help intervention for the prevention of depression and anxiety in elderly people	Residents of homes for elderly people living alone or together with a spouse, (mean 84.0 years, SD = 6.8)	A score of 8 or higher on the CES-D, no current diagnosis of depression or anxiety disorder (minimal to mild symptoms)
6	Fledderus, Bohlmeijer, Pieterse, & Schreurs, 2011 (Netherlands)	Explore the effectiveness of the ACT-based self-help book "living to the full" with two different levels of e-mail support through counselors	Individuals aged 18 years or older (mean 42.5 years, SD = 11.1) from the general population with mild to moderate depressive and anxiety symptoms, recruited via advertisements placed in newspapers	A score between 10 and 39 on the CES-D (non-clinical + clinical individuals) and between 3 and 15 on the HADS-A (non-cases as well as mild to moderate depressive/ anxiety symptoms)
7	Kenardy, McCafferty, & Rosa, 2003 (Australia)	Investigate the efficacy of the Online Anxiety Prevention Program based on SERENA software on first-year psychology students with high	First year psychology students from the University of Queensland (Brisbane, Australia), aged 17-51 years (mean 20.7 years, SD = 6.3)	Cut off score of 24 within the top third scores on the ASI (high anxiety sensitivity levels)

anxiety sensitivity

8	Meulenbeek, Willemse, Smit, van Balkom, Spinhoven, Cuijpers, 2010 (Netherlands)	Examination of the effectiveness of the early group intervention "Don't Panic" for panic symptoms	Self-referred Individuals over 18 years (mean 42.0 years, SD = 12.4) presenting with subthreshold or mild panic disorder	Below the cut-off score of 13 on the PDSS-SR (mild to moderate symptoms)
9	Schotanus-Dijkstra, Drossaert, Pieterse, Boon, Walburg, & Bohlmeijer, 2017 (Netherlands)	Examination of the efficacy of the self-help book 'This is your life' based on positive psychology	Self-selected adults above 18 years (mean 47.8 years, SD = 10.9), who were willing to invest 4 hours per week in the program, recruitment via advertisements placed in national newspapers and in an online psychology newsletter	Excluded when flourishing on the MHC-SF; included with a score below 10 on the HADS-A or HADS-D (mild symptoms)
10	Van't Veer-Tazelaar, van Marwijk, van Oppen, van Hout, van der Horst, Cuijpers, Smit, & Beekman, 2009 (Netherlands)	Reassessment of the effectiveness of a Stepped-Care model based on CBT and CWD for elderly people in primary health care setting	Elderly people aged 75 or older (mean 81.4 years, SD = 3.7) from a large prevention project "Preventive Intervention for Frail Elderly" (PIKO)	Subthreshold depression or anxiety, score equal to or above 16 on the CES-D (moderate symptoms)
11	Zhang, Lewis, Araya, Tang, Mak, Cheung, Mercer, Griffiths, Woo, Lee, Kung, Lam, Yip, & Wong, 2014 (China)	Examination of the effectiveness of the Stepped Care model based on PST for preventing anxiety and depression in a Chinese sample	Chinese people aged 18 years or older (mean 33.4 years); Recruitment: 1) patients in GOPCs* approached by trained research assistant, 2) staff distributed questionnaires, 3) patients that returned questionnaires checked on eligibility by research assistant	A score equal to or above 16 on the CES-D (moderate symptoms) or a score of equal or above 6 on the HADS-A, not fulfilling criteria for full-blown anxiety or depressive disorder (< mild symptoms)

Notes. **CES-D** = Center for Epidemiologic Studies Depression Scale; **MHC-SF**= Mental Health Continuum-Short Form; **GAD-7**= Generalized Anxiety Disorder 7; **BDI**= Beck's Depression Inventory; **BAI**= Beck's Anxiety Inventory, **ASI**= Anxiety Sensitivity Index; **PDSS-SR**= The Panic Disorder Severity Scale- Self Report, **HADS-A**= Hospital Anxiety and Depression Scale – anxiety section, **PST** = Problem Solving Therapy, **CWD** = "Coping with Depression". *GOPCs = General Outpatient Clinics

Grouping into Universal, Selective or Indicated Prevention Program

In order to group the interventions into the categories of universal, selective or indicated prevention, recruitment and selection criteria for the eleven studies were analyzed. Recruitment from the general population belongs to one of the main eligibility criteria of a universal prevention program; the second criterion is no current experience of symptoms and no history of an anxiety disorder. Four of the 11 selected studies recruited participants through the use of newspapers and various other open-access media from the general population (1; 2; 6; 9). Of these four studies, one concentrated on people with moderate symptoms of depression (1), which is an eligibility criterion for an indicated prevention program. Two studies concentrated on people that were not flourishing according to the MHC-SF and included non-cases as well as cases measured through scores between 3 and 15 on the HADS and a score between 10 and 24 or between 10 and 39 on the CES-D (2; 6). One

concentrated on non-flourishers assessed through the MHC-SF with a score below 10 on the HADS, which indicates non-cases as well as mild symptoms of anxiety (9). Based on these selection criteria, one study was categorized as universal prevention program (9), two were categorized as fulfilling the criteria for universal as well as indicated prevention programs (2; 6) and one was categorized as indicated prevention program (1).

People at above average risk of developing an anxiety disorder due to shared risk factors are the target group of selective prevention programs. One of the eleven studies recruited participants through a national electoral roll (3) based on a score above 5 on the GAD-7, which indicates mild to moderate symptoms of anxiety. Further, this study did not exclude participants that were currently under medication of antidepressants or benzodiazepines. Based on these criteria, this population was categorized as a high-risk group for the development of an anxiety disorder, including cases with a history of GAD (24.2%, 135/558). Two of the eleven studies concentrated on university students as at risk-target group. Of these studies, one study (4) selected participants based on a score lower than or equal to 18 on the Beck's Anxiety Inventory (BAI; Beck & Steer, 1993) and the Beck's Depression Inventory (BDI; Smarr & Keefer, 2011), which is the cut-off score for mild symptoms of anxiety and minimal symptoms of depression (Julian, 2011; Smarr & Keefer, 2011). One study that concentrated on people that live in homes for elderly based the selection of participants on a cut-off score of 8 or higher on the CES-D, which includes non-clinical as well as clinical cases of depressive symptoms (5). Due to the fact that people who live in homes for the elderly are classified as at above average risk for developing a mental disorder, this study could be categorized as selective as well as indicated prevention program. Another article described a specific intervention for panic disorder (8), targeting people with a cut-off score below 13 on the Panic Disorder Severity Scale (PDSS-SR; Houck, Spiegel, Shear, & Rucci, 2002). This score indicates non-cases as well as cases with mild to moderate symptoms of panic disorder, which belongs to the scope of either selective or indicated prevention program or even treatment. In sum, one study was categorized as selective prevention program and three studies were categorized as selective as well as indicated prevention program.

Eligibility criteria for participants of an indicated prevention program are people who display sub-threshold symptoms or a history of mental illness, which equals mild to moderate symptoms. One study was already categorized as indicated prevention program due to selection criteria (1). Another study focused on a student population (7) and was described as an indicated prevention program, with a cut off score of 24 within the top third scores on the Anxiety Sensitivity Index (ASI; Peterson & Reiss, 1992). According to Kenardy et al. (2003), the subjects included in the study had a mean score of 30.75 on the ASI. This score is in the range of the mean scores for subjects with a panic disorder, ranging between 30.5 and 36.4.

This cut-off score indicates that this intervention was also used as treatment. Additional two studies were categorized as indicated prevention program, both selecting participants based on a score above 16 on the CES-D. One of these studies concentrated on elderly people, the other concentrated on clinical populations from all age groups. Based on these findings, four studies were categorized as indicated prevention program.

According to the predefined eligibility criteria for the three intervention types, one intervention that was based on positive psychology was categorized as a universal prevention approach (9); one intervention that was based on CBT was categorized as selective prevention approach (4); and four studies with one study based on ACT and three studies based on CBT were categorized as indicated prevention approach (1; 7; 10; 11). Five studies were categorized as mixed approaches of universal and indicated prevention (2; 6) or selective and indicated prevention (3; 5; 8). Additionally, three studies included participants with scores in the range of diagnosed clinical populations with mild to moderate symptoms of depression and anxiety (6; 7; 8). One of these studies stated that the preventive intervention was also used as treatment program in a separate treatment group (8).

Table 3. Universal or Indicated Prevention programs

#	Theoretical basis	Structure of Intervention	Content and delivery	n, FU and drop-outs	Population characteristics	Program outcomes	Risk of Bias
9	"This is your life" positive psychological self-help book; multicomponent well-being intervention	2 – armed RCT (self-help book with email support vs. waitlist control); 8 modules within 9 weeks, reading 1 module per week and practicing min. 2 recommended exercises for each module; 8 to 12 weeks time to complete program individually with weekly email support from personal counselor	Guidance through 5 Master students and the author; each module consisted of psycho-education and evidence-based PP exercises concerning 6 key components of well-being: (1) positive emotions, (2) discovering and using strengths (2 modules), (3) optimism and hope, (4) self-compassion, (5) resilience, (6) positive relations (two modules)	n = 275 randomized; N = 253 (92.0%) completed 3 months FU; n = 237 (86.2%) completed 6 months FU; more drop-outs in I (19.7%) than in C (10.9%, higher baseline anxiety symptoms); 25.1% drop out after 12 months	n = 236 (85.8%) female; n = 205 (74.5 %) higher educated; n = 188 (68.4%) paid employment	ITT; moderate effects on MHC-SF after 12 months; large effects on HADS-A after 12 months; Moderator: neuroticism (low neuroticism = more benefit); Cohen's d = 0.63 for anxiety outcomes	0 (Initially planned 3 armed trial; randomization through author)
2	"Psyfit" online intervention, elements of mindfulness, CBT, Problem-Solving therapy, aimed to improve overall well-being based on positive psychology	2 – armed RCT (access to Psyfit vs. waitlist control); 6 modules, each module 4 lessons-program completed within 8 weeks individually; Assessment PO: MHC-SF, WHO-5; assessment SO: CES-D, HADS-A, MOS-SF-36	1) personal mission statement and setting your goals, (2) positive emotions, (3) positive relationships, (4) mindfulness, (5) optimistic thinking, and (6) mastering your life	n = 284 randomized: I=143 and C=141; 2 months FU: n = 214: I=95, C=119; 6 months FU N=198: I=89, C=109; drop out 30.3% after 6 months;	n = 226 (79.6%) female; n = 208 (73.2%) higher educated; n = 214 (75.4%) paid employment	ITT; Small effects: after 2 months, significant positive effects on PO: WHO-5, non-significant positive trend on MHC-SF; and SO: CES-D, HADS-A, MOS-F; After 6 months, significant effects for SO: HADS-A, CES-D; subgroup effect: significant positive results for higher education; non-significant trend: more effect for participants >45; Cohen's d = 0.32 to 0.35 for anxiety outcomes in mildly depressed individuals	+ (no description of allocation concealment)
6	"Living to the full" self-help book based on principles of ACT for reducing depressive and anxiety symptoms and increase positive mental health	3 – armed RCT: ACT – email, ACT – minimal email, Waitlist control; 9 modules divided into 3 parts: (1) reflecting on avoidance and control strategies; (2) cognitive defusion and experiencing self as context; (3) becoming aware of most important personal values & making decisions based on these; 1 module per week; daily mindfulness exercises completed individually	Guidance through 5 trained Master students; six core processes of ACT that promote psychological flexibility: (1) acceptance, (2) cognitive defusion, (3) contact with the present moment, (4) self as context, (5) choosing values in different life domains, (6) commitment to choices based on values	n = 340 at post-intervention (drop-out 9.6%) n = 204 at 5 months FU; drop out I = 22 (17.6%); total drop out 45.7% after 5 months	n = 262 (77.1%) female; n = 325 (95.6%) higher educated;	ITT; Moderate to large effects at post-intervention (after 3 months), positive effects on SO: HADS-A; MHC-SF; FFMQ, AAQ-II; large effects on EA; Cohen's d = 0.80 to 0.87 for anxiety outcomes in individuals with and without depressive symptoms	+

Note. **PO** = Primary Outcomes; **SO** = Secondary Outcomes; **I** = Intervention group; **C** = Control group; **n** = total number of participants; **FU** = Follow-Up; **+** = low risk of bias; **0** = unclear risk of bias; **-** = high risk of bias; **EA** = Experiential avoidance; **WHO-5** = Well-being Index ; **CES-D** = Center for Epidemiologic Studies Depression Scale; **HADS – A** = Hospital Anxiety and Depression Scale – anxiety Subscale; **MHC-SF** = Mental Health Contiuum-Short Form; **MOS-F** = ; **FFMQ** = Five Facet Mindfulness Questionnaire; **AAQ – II** = Acceptance and Action Questionnaire – II

Contents and Structure of Universal (or indicated) prevention programs

One study was mainly identified as a universal prevention program implementing a positive psychological self-help book based on well-being interventions ("This is your life", 9). Two studies matched the definition of universal as well as indicated prevention, implementing an online self-help intervention implementing evidence-based positive psychological exercises with elements of mindfulness, CBT and Problem-Solving Therapy ("Psyfit", 2) and another self-help book based on Acceptance and Commitment Therapy ("Living to the full", 6).

Two of these studies were 2-armed RCTs with a positive psychological approach that aimed to improve well-being (9; 2) and one study was a 3-armed RCT based on ACT that aimed to reduce depressive and anxiety symptoms and increase positive mental health (6). One study had an intervention group that received email support and a waitlist-control group (9); the second study had an online intervention with no additional email support (2); the third study had an intervention group with extensive email support with an average of 9 minutes of counseling, an intervention group with minimal email support with an average of 3 minutes of counseling and a waitlist-control group (6). The structure of the interventions used in these studies varied from eight modules completed individually within nine weeks guided by five master students (9), six modules with each module containing a four-lessons program to be completed individually within eight weeks (2) and nine modules divided into three parts to be completed individually within nine weeks, also guided by five master students.

The self-help book described in the universal prevention approach in study 9 included psycho-education as well as evidence-based positive psychological exercises. The positive psychological exercises contained the six core components of well-being, particularly *positive emotions, discovering and using strengths, optimism and hope, self-compassion, resilience and positive relations*. The online intervention described in study 2 contained modules such as *personal mission statement and setting your goals, positive emotions, positive relationships, mindfulness, optimistic thinking and mastering your life*. The self-help book implemented in study 6 concentrated on six core processes of ACT that promote psychological flexibility such as *acceptance, cognitive defusion, contact with the present moment, self as context, choosing values in different life domains and commitment to choices based on these values*. A summary of the universal prevention programs and the mixed approaches of universal or indicated prevention can be reviewed in Table 3.

Effects of Universal (or indicated) prevention interventions

A total of 877 participants were initially randomized in the three studies, with a mean of 292 participants per study. The drop-out percentages ranged from 25.1% after 12 months

(9), 30.3% after 6 months (2) and 45.7% after 5 months follow-up (6). The population of these three studies consisted mostly of higher educated females who where paid employed. Possible moderators identified in these studies were (9) more benefit for people with low scores of neuroticism; and (2) more effects for people aged above 45 years. One study found large effects on the mechanism of experiential avoidance (EA) as a mediator (6). All of the three interventions based their calculations on intention-to-treat (ITT) analyses and effect sizes were indicated through the calculation of Cohen's d. The interpretation of these effect sizes was based on a meta-analysis on the efficacy of psychological treatment, with 0 to 0.32 interpreted as small effect sizes, 0.33 to 0.55 interpreted as moderate effect sizes and 0.56 to 1.2 interpreted as large effect sizes (Lipsey & Wilson, 1993).

The effects that were calculated within these three studies varied from small to large effect sizes, with large effects on anxiety symptoms measured through the HADS-A in study 6 and study 9 (Cohen's d = 0.63 to 0.87). Study 2 calculated small to moderate effect sizes for anxiety symptoms, indicating that more adherence equals larger effects.

Quality assessment and Risk of Bias

The assessment of the quality of the three studies revealed that two studies had a low risk of bias (6) and one study had an unclear risk of bias. This one study was initially planned to be conducted as a 3-armed RCT (9). Another possible source of risk of bias in study 9 was the selection, because of the fact that the author was responsible of randomization, enrollment and assignment of participants to groups. Further, the group of self-selected participants mostly consisted of higher educated women, decreasing the generalizability of the effects. For these reasons, the quality for this study was rated as unclear risk of bias due to the given limitations. The other two articles were at low risk of bias and yielded small and moderate to large effects on anxiety outcomes for higher-educated female participants with mild to moderate symptoms (6).

Table 4. Selective or Indicated Prevention programs

#	Theoretical basis	Structure of intervention	Content and delivery	n, FU and drop-outs	Participants	Program outcomes	Risk of Bias
3	Anxiety and Worry modules of the "e-Couch", containing psycho-education, CBT, relaxation and physical activity promotion	5 arm RCT; 10 weeks, 5 conditions: active website; active website with email reminders; active website with phone reminders; control website with phone reminders; control website; assessment PO through GAD-7, MINI; assessment SO through ASI, Days out of Role due to anxiety, CES-D, PSWQ	Web-based multimedia intervention with modules: week 1-2 = psycho-education, week 3-7 = CBT toolkits, week 8 = PMR, week 9 = Mindfulness meditation, week 10 = physical activity	n = 558 randomized; n = 360 completed post-test (35% attrition); n = 303 completed 6 months FU; n = 264 completed 12 months FU; 52.7% drop out	n = 450 (80.6%) female; 341 (62.0%) full-time employment	ITT; No effects on PO: GAD 7 scores reduced at post-test & 6 months FU but returned to baseline levels after 12 months, no improvement on MINI; Significant effects (active/email condition) on SO: Significant decrease of ASI scores at post-test and 6 months FU; significant decrease of Days out of Role due to anxiety at 12 months FU; CES-D and PSWQ scores significantly lower at post-test; Cohen's d = 0.3 (post hoc)	+
4	Computer-based cognitive-behavioral psycho-education model as intervention, CBASP (focus on interpersonal interactions)	2 arm RCT; 1 program, 6 segments of 20 min each; session with groups between 2 and 27 participants; weekly reminders during 8 weeks after intervention; baseline assessment (30 min): BAI, BDI, PANAS, STAI-S	1) psycho-education, 2) purpose of CBT principles, 3) CBASP as intervention model, 4) 5 steps of CBASP, 5) generalization of these principles, 6) review; additional take-home information based on the session	n = 238 completed baseline assessment, n = 23 did not complete follow-up, n = 50 excluded because of moderate to severe symptoms, n = 165 included in analysis; 30.0% drop out	n = 116 (70.3%) female	Small to large effects after 2 months, lower levels of depression, anxiety, negative affect when outcomes on BDI, BAI, insomnia and PTSD were low; Cohen's d = 0.13 to 0.74 (d = 0.13 on STAI-S, d = 0.50 on BAI, d = 0.74 on PANAS-PA)	+
5	Guided self-help: Activity Scheduling, a module retrieved from the self-help course *Coping with depression*	2 arm RCT; 4 steps,: 1 months watchful waiting, assessment PO: CES-D, HADS-A; assessment SO: Tic-P	Behavioral treatment in which participants can monitor their mood and design a pleasurable activity plan	n = 185 randomized; after 1 months FU: n = 129, I=67, C=62; Self-help course offered to I=51, C=56; n = 14 completed all 4 steps; 92.4% drop out	n = 96 (74.7%) female; n = 31 (23.9%) educated beyond high school	ITT; non-significant small effects after 3 months, no significant difference between I and C, trend of larger effects for completers compared to usual care; Cohen's d = 0.18 to 0.48	+
8	Don't Panic-course based on CBT	2 arm RCT; 8 weeks, weekly group sessions of 2 hours, consisting of 6-12 participants per group; assessment PO: PDSS-SR, MINI-Plus-Panic disorder, MINI-Plus-Agoraphobia,; assessment SO: HADS-A, Mobility Inventory, BDI-II	Delivery through clinician or prevention specialist (with course manual), workbook for participants; Course elements: 1) psycho-education, 2) lifestyle changes, 3) stress management, 4) relaxation training, 5) cognitive restructuring, 6) interoceptive exposure, 7) 'in vivo' exposure and 8) relapse prevention techniques	n = 217 randomized: I = 109, C = 108; n = 82 completed above or equal 6 sessions, n = 106 completed Diagnostic interview at post-intervention, n = 96 completed self measures at post-intervention, n = 99 completed FU at 6 months; 9% drop out	n = 154 (71.0%) female; n= 151 (70.0%) paid employment; mean 14.04 years of education (SD = 3.26)	ITT; Beneficial (moderate to large) effects on reduction of panic severity levels after 3 and 9 months, measured through PDSS-SR, MINI; SO effects on BDI-II, Mobility Inventory; Cohen's d = 0.68 (PDSS-SR), 0.59 (HADS-A)	+

Note. **PO** = Primary Outcome; **SO** = Secondary Outcome; **ITT** = Intention to treat; **I** = Intervention group; **C** = control group; **N** = total number of participants; **FU** = Follow-up; **CES-D** = Center for Epidemiologic Studies Depression Scale; **HADS-A** = Hospital Anxiety and Depression Scale – anxiety subscale; **Tic-P** = Trimbos/iMTA Questionnaire for Costs Associated with Psychiatric Illness*;* **CBT** = Cognitive Behavioral Therapy; **PMR** = Progressive Muscle Relaxation; **PSWQ** = Penn State Worry Questionnaire; **CBASP** =Cognitive-Behavioral Analysis System of Psychotherapy; **PHQ-9** = Patient Health Questionnaire-9 (self-reported depression); **BDI** = Beck's depression inventory; **BAI** = Beck's anxiety inventory; **PTSD** = Post-traumatic stress disorder

Content and Structure of Selective (or Indicated) prevention programs

One study was categorized as selective prevention program based on CBT for a student population targeting mild anxiety symptoms (4). This study implemented a computer-based intervention program based on the cognitive behavioral analysis system of psychotherapy, abbreviated with CBASP. Three studies were categorized as either selective or indicated prevention program (3; 5; 8).

One of these studies consisted of an online-intervention named "iChill" with anxiety and worry modules from the "e-Couch", containing elements of psycho-education, CBT, relaxation and physical activity promotion (3). The second study consisted of a guided self-help course in activity scheduling, a module retrieved from the self-help course CWD (Haringsma, Engels, Cuijpers, & Spinhoven, 2006). This study aimed to improve depressive and anxiety symptoms (5). The third study consisted of the "Don't Panic" course for panic disorders that was delivered through a clinician and a prevention specialist based on a standardized course manual within eight weekly group sessions of two hours (8).

Three of these studies were designed as 2-armed RCTs (4; 5; 8); and one study was designed as a 5-armed RCT with three active website groups with either no reminder, email reminder or phone reminder and two control groups with no reminder and phone reminder (3). The web-based online intervention in study 3 consisted of six segments of 20 minutes each with the modules *psycho-education, CBT toolkits, Progressive Muscle Relaxation, Mindfulness meditation and physical activity* that had to be completed individually during ten weeks. The computer-based intervention CBASP in study 4 is a program that was originally developed as an intervention for chronic depression. The main focus of this intervention lies in interpersonal interactions. The aim of this intervention was to help people identify the connections between their thoughts, behaviors and situational outcomes through individual completion of the modules *psycho-education, purpose of CBT principles, CBASP as intervention model, 5 steps of CBASP, generalization of these principles, review* and additional take-home information based on each session (4). Study 5 consisted of four steps of behavioral treatment in which participants were individually guided by trained coaches in the monitoring of mood and in the design of a pleasurable activity plan after a month of watchful waiting. The course elements of the "Don't Panic" course contained *psycho-education, lifestyle changes, stress management, relaxation training, cognitive restructuring, interoceptive exposure, in vivo exposure* and *relapse prevention techniques*, delivered within groups of 6 to 12 participants per group (8). A summary of these findings can be reviewed in Table 4.

Effects of Selective (or indicated) prevention interventions

A total of 1198 participants were initially randomized within these four studies, with

558 participants in study 3, 238 participants in study 4, 185 participants in study 5 and 217 participants in study 8. The population groups of these four studies consisted mainly of female participants (mean 74.2%), with two student populations, one elderly population with only 31 (23.9%) participants that were educated beyond high school and a population consisting of employed participants that were mostly female with a mean of 14 years of education (8). Possible moderators were not identified within these studies. Instead, effects were found for (3) lower levels of anxiety sensitivity and a significant decrease of days out of role due to anxiety; (4) lower levels of depression, anxiety, and negative affect when outcomes on the BDI, the BAI, levels of insomnia and levels of PTSD were low; (5) no significant differences between the intervention group and the control group but a trend of positive effects for completers compared to usual care; and (8) reduction of panic severity.

Dropout percentages for these three studies ranged from 9% after nine months in the "Don't Panic" course intervention (8), 30.0% two months after the CBASP course (4), to 52.7% after twelve months (3) up to 92.4% after three months (5). Three studies analyzed their results based on ITT (3; 5; 8), and two of these three studies reported a calculation of Cohen's d on specific scales. One of these studies found non-significant but small to moderate effect sizes for anxiety, ranging from 0.18 to 0.48 on the HADS-A and small to large effects for depression, ranging from 0.08 to 0.60 on the CES-D (5). Study 8 reported effect sizes ranging from 0.44 on the Mobility Inventory up to 0.68 on the PDSS-SR, indicating moderate to large effects between groups. Study 3 reported a post-hoc calculation of Cohen's d, indicating small effects with a score of 0.30. The analyses in study 4 were not based on ITT, but Cohen's d for post-intervention effect sizes was calculated and ranged from small effects on the State and trait anxiety index (STAI-S, Spielberger, Gorsuch, & Lushene, 1970, $d = 0.13$) and medium effects on the BAI ($d = 0.50$) to large effects with $d = 0.74$ on the Positive and negative affect scale (PANAS-PA, Watson, Clark & Tellegen, 1988).

Quality Assessment and Risk of Bias

The quality assessment of these four studies yielded a low risk of bias for all of these studies. Two of these selective (or indicated) prevention studies had small to large effects on anxiety outcomes for populations that mostly consisted of female students.

Table 5. Indicated prevention programs

#	Theoretical basis	Structure of intervention	Content and delivery	n, FU and drop-outs	Participants	Program Outcomes	Risk of Bias
1	"Living to the full", ACT intervention: behavioral therapy focused on decreasing EA; 6 core processes	2 arm RCT; 8 weekly group sessions of 2 hours; assessment PO: CES-D; assessment SO: HADS-A, CIS, AAQ-II	Delivered through 7 teams of 2 licensed psychologists; all sessions contain mindfulness skills; session 1: basic principles of ACT; session 2-3: reflection of avoidance and control strategies; session 4-6: cognitive defusion & experiencing self as context; session 7-8:becoming aware of personal values	n = 93 randomized; I = 49 and C = 44 completed baseline assessment; I = 39 and C = 42 completed post-treatment assessment, I=36 and C=41 completed 4 months FU; 14.3% drop out	n = 76 (81.7%) female; n = 37 (39.8%) > 16 years of education; n = 49 (52.7%) paid employment	ITT; Moderate to large effects, significant at post-treatment and 3 months FU, PO: significantly lower scores on CES-D; SO: significant with moderate effect sizes on HADS-A, CIS, AAQ-II; moderate effect sizes for reduction of EA; Cohen's d = 0.52-0.67	+
7	Online Anxiety Prevention Program based on CBT from SERENA software, a form of computer-assisted treatment of Panic disorder	2 arm RCT; 6 individual sessions, no time-limits, recommendation to spend 5 to 7 days on each session for maximum benefit; assessment PO through ASI, BSQ, ACQ, CCQ, CES-D	Sessions incorporate psycho-education about anxiety, relaxation training, interoceptive exposure, cognitive restructuring. Each session requires individual covering of program material, practicing a specific set of skills and recording progress daily	n = 83 randomized: I = 43, C = 40; N=8 drop-outs, n = 1 excluded (extremely high post-intervention scores). Final sample: I = 36, C = 38; 10.84% drop out (significantly higher scores on ASI)	n = 65 (61.7%) female	Moderate global treatment effect: positive effect on ACQ, CCQ, CES-D after 6 weeks; interaction effects in medium range = 0.20	0 (technical problems with program impaired monitoring)
10	Stepped Care based on principles of CBT	2 arm RCT; Stepped Care with permanent access to usual care including 4 steps, each step 3 months, individual intervention; 3 visits and 2 phone calls of trained district nurses, PO assessment: MINI; SO assessment: CES-D, HADS-A (7 items), MOS-SF-36, Tic-P, GGZ-Thermometer	Delivered through trained district nurses, coaching by district psychiatric nurses (maximum 7 sessions); 1) Watchful waiting, 2) biblio-therapeutic self-help intervention based on CBT, CWD, 3) PST 4 sessions à 45 minutes, 4) referral to primary care physician	n = 170 randomized: I = 86, C = 84; at 6 months FU: I = 66, C = 77; at 12 months FU: I = 62, C = 76; at 18 months FU: I = 60, C = 74; at 24 months FU: I = 59, C = 70; 24.1% drop out after 24 months	n = 125 (74.0%) female; n = 46 (27.0%) higher education (beyond secondary school); n = 81 (48.0%) chronic diseases	ITT; Effective over a 24 months period in halving the incidence rate of depression and anxiety in elderly people, measured through CES-D and MINI; NNT = 5	+ (allocation concealment)
11	Stepped Care Program in China based on principles of CBT; adapted from the Netherlands	2 arm RCT; Stepped Care with permanent access to usual care; coaching by social worker (max 6 sessions); PO assessment: SCID; SO assessment: CES-D, HADS, MOS-SF-12,CAHPS, MSPSS	1) Watchful waiting, 2) Telephone counseling – self-help instruction coached by a professional, 3) Face-to-face PST, 4) Consultation by primary care doctors	n = 240 randomized: I = 121, C = 119; drop out after 3 months (watchful waiting): I = 109, C = 103; after 6 months FU: I = 104, C = 97; after 9 months FU: I = 97, C = 93; after 12 months FU: I = 86, C = 83; after 15 months FU: I = 104, C = 101; Final analysis I = 113, C = 111; 29.6% drop out after 12 months; 6.7% drop out after 15 months	74.2% female; 21.3% higher educated; 39.2% employment	ITT; No significant effects on PO; Non-significant positive effects on SO: CES-D	0 (high number of declines, performance)

Notes. **N** = total number of participants, **I** = Intervention group; **C** = Control group; **PO** = Primary Outcomes, **SO** = Secondary Outcomes; **FU**= Follow-up; **ITT** = Intention-to-treat; **ACT**= Acceptance and Commitment Therapy; **EA**= Experiential Avoidance; **CES-D** = Center for Epidemiologic Studies Depression Scale, **HADS-A** = Hospital Anxiety and Depression Scale-Anxiety; **CIS** = Checklist Individual Strength; **AAQ-II** = Acceptance and Action Questionnaire-II; **Tic-P** = Trimbos/iMTA Questionnaire for Costs Associated with Psychiatric Illness; **ASI** = Anxiety Sensitivity Index; **BSQ** = Body Sensations Questionnaire; **ACQ** = Agoraphobic Cognitions Questionnaire; **CCQ** = Catastrophic Cognitions Questionnaire, **BDI-II** = Beck Depression Inventory-Second Edition; **CWD** = Coping With Depression; **PST** = Problem-Solving-Treatment; **MINI** = Mini Neuropsychiatric Interview; **MOS-SF-36** = Medical Outcomes Study Short form 36 (quality of life); **GGZ-Thermometer** = Institution of Mental Health; **SCID** = Structured Clinical Interview; **CAHPS** = Consumer Assessment of Healthcare Providers and Systems; **MSPSS** = Multidimensional Scale of Perceived Social Support.

Content and Structure of Indicated prevention programs

A total of four studies were categorized as indicated prevention program, with one intervention based on ACT for the general adult population ("Living to the full"; 1) and three studies based on CBT for general and specific adult populations (7; 10; 11). The intervention based on ACT consisted of a self-help book and was guided from seven teams of two licensed psychologists within eight weekly group sessions of two hours each (1). One of the studies based on CBT contained an online anxiety prevention program for university students (7). This program is based on the SERENA software, which is a type of computer-assisted individual treatment program designed for panic disorder consisting of six sessions. The remaining two studies consisted both of Stepped Care programs based on the principles of CBT, including four steps of individual treatment. These steps contained the elements *empowerment, individualized preventive activities, outcome monitoring and stepping up from lower, less intensive to higher, more intensive levels of preventive activities based on monitored outcomes* (10; 11). They were delivered through trained district psychiatric nurses within a timespan of one year, with three months of time for one step within the intervention. One of the Stepped-Care programs implemented the self-help course CWD within a population group of 75 years and older (10) and one implemented PST as a clinical trial for adults in China (11).

All four studies were structured as 2-armed RCTs, with two studies implementing an intervention group and a waitlist-control group (1; 7) and two studies implementing an intervention group and a usual care group (10; 11). The ACT intervention contained sessions with *basic principles of ACT, reflection of avoidance and control strategies, cognitive defusion, experiencing self as context* and *becoming aware of personal values* (1). The online anxiety prevention program contained sessions that incorporated *psycho-education about anxiety, relaxation training, interoceptive exposure* and *cognitive restructuring* (7). The two Stepped care interventions contained the elements *watchful waiting, biblio-therapeutic self-help intervention based on CBT, Problem solving therapy* and *referral to primary care physician* (10; 11).

Effects of Indicated prevention Interventions

A total of 586 participants were randomized within the four indicated prevention studies, with 93 participants in study 1, 83 participants in study 7, 170 participants in study 10 and 240 participants in study 11. The populations of these four studies consisted mostly of females (mean 72.5%). One study included students (7) and a minority of participants included in the other three studies were higher educated (1; 10; 11, mean 29.4%). Employment status was outlined in two studies, with 39.2% employed participants in study 11 and 52.7% employed participants in study 1. One study identified experiential avoidance

as a possible moderator of effects (1). Other significant effects were positive effects on maladaptive cognitions about the consequences of anxiety (7). Two studies focused only on general effects of the Stepped-Care process on anxiety outcomes (10; 11).

The dropout percentages of the studies ranged from 10.8% in the online anxiety prevention program for students (7); 17.2% after four months in the "living to the full" ACT intervention (1) and 24.2% after 24 months in a stepped care program for elderly people. Study 11 reported 29.6% dropout after twelve months in a stepped care program for a Chinese population of adults. However, this study also reported low numbers of participants that actually received the intervention. The actual number of included participants for analysis was based on the inclusion of newly eligible participants.

Three studies based their analyses on ITT (1; 10; 11). One of these three studies reported the calculation of Cohen's d with moderate to large effect sizes on anxiety outcomes (0.52 to 0.67, study 1). The other two studies did not calculate effect sizes (10; 11). Instead, one of these studies (10) calculated the number needed to treat of 5 (95% CI = 3-16), indicating that the onset of an depressive or anxiety disorder was prevented in one of five participants with an odds-ratio of 0.44 (95% CI, 0.21-0.95). The other study (11) calculated outcomes on the scales used to assess symptoms and hazard ratios for the mean disease free time, indicating that no significant differences were found between Stepped care and care as usual. Additionally, the authors stated a lack of statistical power due to the great number of dropouts and declines of participants. However, a positive trend was found for anxiety outcomes, but the post-hoc calculation yielded a power of 41%, which indicates that the sample size was too small to detect significant effects of the intervention. One study reported effect sizes calculated with the eta-square ($\eta2 = 0.20$), indicating a medium interaction effect between condition and time on anxiety outcomes (7).

Quality Assessment and Risk of Bias

The quality assessment yielded that two of the four studies were at a low risk of bias (1; 10) and two studies had an unclear risk of bias due to several reasons (7; 11). One of these studies reported technical problems with the program, which impaired monitoring due to loss of data (7). The second study reported that only a small number of 28 participants actually received the intervention because a large part of the participants declined the intervention or were not eligible anymore due to low levels of symptoms (11). This study suffered mostly from problems concerning the adaptation of a Dutch intervention into a Chinese population. In sum, two indicated prevention program at low risk of bias reported significant moderate to large effect sizes on anxiety outcomes within an adult population (1) and sustained effects over 24 months (10).

IV. Discussion

In the current study, a systematic review of the recent literature on universal, selective and indicated prevention of anxiety disorders in adults was conducted. This review examined the developments of anxiety disorder prevention programs for general adult populations. The systematic search led to the identification of eleven RCTs that met the eligibility criteria of prevention programs targeting anxiety in adults. These eleven articles included a total of 2661 participants, with a mean percentage of 75.5% females. They examined the effects of nine different preventive interventions based on CBT, ACT and Positive Psychology for individuals with symptoms as well as individuals without symptoms of anxiety. The theoretical categorization of universal, selective and indicated prevention turned out to be problematic to implement in practice, especially for universal and selective prevention programs. Thus, the interventions had to be categorized as one universal, one selective, four indicated preventive interventions and five mixed recruitment preventive interventions. Eight of these studies displayed significant effects on decreasing anxiety levels through preventive interventions. The quality assessment of the eleven RCTs yielded a reasonable methodological quality across the studies according to Higgins, 2011. Therefore, it can be concluded that research on prevention of anxiety in adults has made progress but still seems to be in a developmental state regarding the small number of interventions that met eligibility criteria for the analysis.

Principal findings

The first review question aimed to examine which sorts of interventions in terms of universal, selective and indicated prevention approaches targeting anxiety in adults were newly or further developed and tested on effects. The analysis of the recruitment and selection procedures of the studies showed that the lines of eligibility between the three levels of prevention were often blurred, with some studies that not only analyzed preventive effects of the intervention but also treatment effects. It appeared that the lines of the recruitment and selection procedures were not as straight in practice within all of these studies as they were defined theoretically through the eligibility criteria. Thus, five studies could not definitely be categorized as a specific type of prevention program but as a mix of either universal or indicated prevention and selective or indicated prevention. These five studies were therefore categorized as mixed approaches targeting population groups without as well as with mild to moderate symptoms of anxiety (Bolier et al., 2013; Christensen et al., 2014; Dozeman et al., 2011; Fledderus et al., 2011; Meulenbeek et al., 2010). The remaining six studies were better adjusted to the theoretical framework and were therefore categorized as one universal prevention approach, one selective prevention approach and four indicated prevention

approaches.

These findings did not only demonstrate that progress has been made with regard to research on this field but also pointed out difficulties concerning the implementation of this theoretical framework in practice. In particular, these difficulties arose with regard to the cut-off scores of participants on clinical questionnaires. Scores above a specific cut-off point can be seen as a criterion for indicated prevention due to the fact that individuals with higher scores on clinical questionnaires can be included. Scores below a specific cut-off point, however, can therefore be categorized as criterion for either selective or universal prevention. Thus, the categorization of a preventive intervention as either universal or selective prevention became problematic in practice due to the fact that no clear cut-off points were defined yet for the implementation of these interventions. Additionally, the cut-off scores for detectable symptoms on clinical questionnaires vary across different population groups, underscoring the problematic categorization of the level of prevention (Vilagut, Forero, Barbaglia, & Alonso, 2016). In the current review, various different cut-off scores that were above, below or between specific scores on clinical questionnaires were identified within the included studies. Therefore, the categorization into universal, selective or indicated prevention was not only based on cut-off scores but also on recruitment procedures of participants. This, in turn, led to the categorization of mixed approaches.

Former reviews and meta-analyses reported that no effect-studies were conducted yet that implemented universal and selective prevention programs in general adult populations (Cuijpers et al., 2011; Meijer et al., 2006; Conley et al., 2016). Moreover, none of these studies outlined a description of the cut-off scores on clinical questionnaires for individuals included in the studies either. Thus, the current review contributed to a better understanding of the problems that may arise in practice concerning the categorization of the three levels of prevention.

Another focus of this review was to examine which types of prevention programs were effective, whether specific moderators or mediators were examined and how the prevention programs were structured. The analysis of the intervention effects yielded that nine of the eleven studies measured significant positive effects on anxiety outcomes, ranging from small to large effects, measured after 6 weeks up until after 24 months. In particular, these were one study focusing on universal prevention based on positive psychology, one study focusing on selective prevention based on CBASP containing elements from CBT and IPT, five mixed approaches based on CBT and ACT and three studies focusing on indicated prevention based on CBT. Former reviews and meta-analyses only outlined interventions based on CBT and Stepped Care (Cuijpers et al., 2011; Meijer et al., 2006; Conley et al., 2016). Thus, these findings demonstrated that the approaches of positive psychology and

ACT are additional effective approaches with regard to prevention of anxiety disorders in adults.

The effective prevention programs were structured as self-help programs with either a self-help book, an online website or guided self-help with practitioner support or a mix of these delivery forms. Further, the only possible moderators or mediators identified in these studies were the mechanism of experiential avoidance in an acceptance and commitment-based indicated approach and scores on the neuroticism scale of the Big Five in a positive psychological universal approach (Schotanus-Dijkstra et al., 2017; Bohlmeijer et al., 2010). This turned out to be rather surprising due to the fact that the identification of risk- and vulnerability factors are essential in defining the target group for a selective prevention. However, the predictive power of experiential avoidance for individuals with generalized anxiety disorder was also supported elsewhere (Eustis, Hayes-Skelton, Roemer, & Orsillo, 2016), as well as supporting evidence for the association of anxiety with neuroticism (Paulus, Vanwoerden, Norton, & Sharp, 2016). According to Paulus et al. (2016), neuroticism and anxiety are associated via the factor of shame, and the universal prevention program identified in this review stated that low neuroticism scores accounted for more positive results on anxiety outcomes (Schotanus-Dijkstra et al., 2017). The positive effects of this intervention were therefore found in individuals that were not ashamed to participate, which was a big part of the included population. This means that a positive psychological approach may be promising with regard to the solution of the problem of stigma in prevention and treatment interventions.

According to Ociskova et al. (2013), traditional prejudices about mental disorders that result in stigmatization problems still play a major role in the western society. The risk of stigma still exists within different contexts, such as labeling through physicians, fear of labeling from family members and self-stigmatization (Ociskova et al., 2013). Fear of stigma seems to be a common reason among individuals with anxiety symptoms to avoid seeking help, which in turn worsens their symptoms (Ociskova et al., 2013). Additionally, families of affected individuals might also try to avoid seeking professional help by providing the affected family member with everything to enable avoidant behavior (Ociskova et al., 2013). It was further stated that different forms of media and articles in tabloids contribute to the negative way mentally ill people are being perceived from the society (Ociskova et al., 2013). Therefore, a non-stigmatizing open-access approach that includes individuals without as well as with symptoms could be a contribution towards a paradigm shift in the perception of mental health and mental illness within the society and the media.

A possible basis for such a non-stigmatizing approach can be found in the two-continua model of mental health that also builds the basis of positive psychology (Westerhof & Keyes, 2009). This model states that mental health cannot only be defined by the absence

of mental illness, but rather describes the state of well-being in an individual that has the capacities to grow mentally (Westerhof & Keyes, 2009). With this perspective in mind, the focus on anxiety as a disorder could be redirected towards a more positive perspective of possibilities to grow as a human being through preventive approaches. Open access for the general population to positive psychological prevention programs could therefore contribute to a broader acceptance and understanding of mental disorders and thereby lower the fear of stigma in individuals. Overall, the current review pointed out that significant positive effects for universal and selective prevention were found, giving support for evidence on well-functioning prevention programs.

Quality of the evidence

The eleven selected studies were all RCTs, which is a general indicator for a study of high quality. However, six studies were rated as being at unclear risk of bias according to the rating scheme of Higgins (2011). According to this scheme, blinding of participants as well as blinding of assessors needs to be granted for clean research. In practice, blinding is barely possible due to the fact that most of the participants recognize whether or not they received an intervention. Therefore, this criterion was neglected in the quality rating process of the current review. Issues concerning blinding processes became evident through the analysis of the included studies. Most of the studies mentioned difficulties during the blinding process, and some studies outlined no description of this process at all. In particular, these were the universal prevention self-help program "This is your life" (Schotanus-Dijkstra et al., 2017); the online self-help intervention "Psyfit", categorized as mixed universal or indicated approach (Bolier et al., 2013); the guided self-help intervention categorized as mixed selective or indicated approach of Activity scheduling (Dozeman et al., 2011) and one indicated prevention program, Stepped Care for residents of homes for elderly people (Van't Veer-Tazelaar et al., 2009).

The universal prevention program reported that randomization and allocation to conditions was not done by an independent researcher but by the first author of this study (Schotanus-Dijkstra et al., 2017). Further, performance issues arose during the implementation of the study regarding the fact that the initial plan was to conduct a three-armed trial with an additional intervention group. The mixed prevention approach of the "Psyfit" online intervention encountered similar issues with regard to blinding (Bolier et al., 2013). In this study, no description of allocation concealment for the included individuals was reported, which would normally indicate a possible risk of bias with regard to the blinding of participants. The mixed approach intervention with the intervention "Activity scheduling" also reported that the blinding of participants was not possible. One study that was categorized as indicated prevention program reported that blinding procedures were not

completely transparent during clinical interviews (Van't Veer-Tazelaar et al., 2009).

Other sources of possible risk of bias were identified in additional two studies, consisting of technical issues with the program in the online self-help anxiety prevention program (Kenardy et al., 2003); and performance issues in Stepped Care in a Chinese clinical population (Zhang et al., 2014). In the Stepped Care approach for the general clinical population in China, high attrition rates and non-adherence to the intervention were reported (Zhang et al., 2014). This study aimed to implement a Stepped Care approach for the prevention of anxiety symptoms in a Chinese population for the first time. One possible explanation for the non-effectiveness of this intervention and non-adherence of participants can be found in the differences of intercultural communication between a Chinese and a Dutch population (Kim, Pan, & Park, 1998).

Hall and Hall (2001) stated that cultures could be categorized as either high-context- or low-context cultures due to essential differences in communication. A high-context culture describes cultures with individuals who closely interact with important people in their environment on a regular basis (Hall & Hall, 2001). Therefore, little communicative information is needed in order to interpret messages from important others, because little information about the context needs to be provided in order to understand each other. Examples of such high-context cultures are the Japanese, the Arab and a big part of the eastern Mediterranean cultures (Hall & Hall, 2001). In a low-context culture, such as the American, Western and Northern European cultures, additional contextual information is needed in order to make sophisticated decisions (Hall & Hall, 2001). Thus, a preventive approach needs to be sensitive with regard to cultural differences in communication in order to be accepted by a broad population group.

Limitations & Potential biases in the review process

The present systematic review was conducted according to the guidelines for meta-analyses and the PRISMA statement (Cuijpers, 2016; Liberati et al., 2009). According to Cuijpers (2016), a systematic review should preferably be conducted by two independent researchers. Therefore, one limitation of the current study could be the fact that the author alone conducted the systematic search, the selection and the analysis of the records. Another possible limitation within the current study is the small number of articles included in the analysis. Although this study showed that some progress was made especially with regard to the development of universal and selective prevention programs, the evaluation of this progress was only based on the outcomes of eight effective prevention programs. One possible reason for this low number of included records may be the specificity of the systematic search. In the current study, the focus was mainly on preventive interventions conceptualized as universal, selective and indicated prevention, as proposed by Gordon

(1987). Therefore, possible relevant records that did not use the same terminology for different levels of prevention may have been missed through this search. This was also supported by the terminology used within the selected articles, as most of the studies described the intervention as an "early intervention" or simply as "preventive intervention". Only one study of the selected articles referred to the implemented intervention as "indicated prevention for anxiety disorders" (Kenardy et al., 2003). Additionally, not all of the preventive interventions that were included in former reviews were found through this search strategy.

The fact that only RCTs were included in the systematic search can be seen as strength but also as a possible limitation of the present study. Evidence suggests that RCTs are not in all cases superior to observational studies or other study designs (Concato, Shah, & Horwitz, 2000). In fact, a review that compared the methodological quality of RCTs with the methodological quality of observational studies found that RCTs had more heterogeneity in their results than observational studies (Concato et al., 2000). This means that the point estimates had more variability, sometimes even representing contradictory results (Concato et al., 2000). On a broad scale, RCTs were often discordant with large, simple trials, which means that RCTs do not always equal the gold standard for clinical implementation (Concato et al., 2000). Therefore, most of the RCTs are too specific due to methodological requirements and can therefore not be expected to find results that are generalizable to a broad population (Concato et al., 2000).

The qualitative nature of this systematic review can also be seen as a kind of limitation. Due to the fact that participant numbers were relatively high for most of the analyzed interventions, a meta-analysis conducted with the selected articles of this study could have given more insights to the nature of the measured effects and the heterogeneity of the studies. For the present review, this means that the outcomes of the interventions seem to be promising, but an evaluation through future meta-analyses is needed in order to confirm the robustness of the effects.

Overall completeness and applicability of evidence
The evidence evaluated within the present systematic review indicates that the field of prevention of anxiety in adults has made promising progress. However, there are still some gaps that need to be filled through further evaluation of preventive interventions. One major finding across all included articles was the fact that mainly higher educated women from western cultures participated in the studies. This factor impedes the generalizability of the current findings, as population groups that differ significantly from this specific population group were not assessed throughout the studies. Nevertheless, the effects for this population group were mostly consistent across the selected studies, which means that these findings

may be generalizable to a part of the western higher-educated female adult population.

Another finding was the fact that no specific risk factors were described or examined for the implementation within selective prevention programs as was expected based on the eligibility criteria. One approach for examining risk factors within specific population groups was to determine groups that are at a higher risk for the development of an anxiety disorder based on shared risk factors. Due to the fact that comorbidity between depression and anxiety disorders is common, the determination of risk and protective factors for both depression and anxiety could lead to a better understanding of the factors that have an impact on the development of these mental disorders (Wuthrich & Rapee 2013; Pumar, Grey, Walsh, Yang, Rolls, & Ward, 2014). The findings of the present review support the necessity of this determination, because the majority of included studies not only assessed anxiety outcomes but also outcomes on depressive symptoms.

Moreover, the approach of targeting protective factors for anxiety as well as depressive symptoms within a preventive intervention would be promising. In particular, the factor well-being seems to be a promising protective factor for both depression and anxiety disorders within positive psychological approaches (Takebayashi, Tanaka, Sugiura, & Sugiura, 2017). Within the factors of well-being that could buffer or even decrease anxiety symptoms, self-compassion is found to be a powerful protective mechanism (Trompetter, de Kleine, Bohlmeijer, 2016). Self-compassion is the ability to experience broadened and more understanding thoughts and feelings towards the self. It basically covers the concept of self-love and has a positive impact on emotional regulation strategies (Trompetter et al., 2016). Self-compassion skills aid the process of emotional regulation by creating the basis that stressors are momentary, controllable and less aversive (Trompetter et al., 2016). This can result in higher levels of well-being, which in turn can decrease the risk of developing an anxiety or depressive disorder. By concentrating not only on mental illness but also on mental fitness, as proposed by the two-continua model of mental health, the risk of stigma in preventive as well as treatment interventions could be lowered (Keyes, 2002; Westerhof et al., 2009). Further, a positive approach would reach more individuals such as family members, friends or colleagues of affected individuals, which could in turn prevent the aversive support they naturally provide.

Future Recommendations

The necessity of a protective factor approach was supported through the current review. In particular, guided positive psychological self-help approaches that targeted depressive as well as anxiety symptoms yielded promising effects for both anxiety and depressive outcomes. Therefore, positive psychological approaches that focus on the enhancement of well-being could offer a promising solution for the issues concerning the

conceptualization of preventive interventions. One example of a positive psychological intervention that was originally designed as a treatment intervention but could also serve as a universal prevention program is the well-being therapy. This therapy is based on the assumption that high levels of well-being function in a protective way with regard to the development of anxiety disorders. Well-being therapy focuses on the six dimensions *autonomy, personal growth, environmental mastery, purpose in life, positive relations and self-acceptance* and aims to enhance the quality of life of a person (Fava & Ruini, 2003). In this context, a preventive intervention with positive psychological elements would not have to label anyone.

One major recommendation for future research is therefore to validate the effectiveness of positive psychological interventions as prevention program within various population groups. Another recommendation for future research is to examine possible protective factors for anxiety disorders within already developed positive psychological interventions in order to enhance the adherence and acceptability of preventive interventions. Additionally, a validation of the long-term effects of these interventions was only given in one of eleven studies. More long-term studies for preventive interventions are therefore recommended for future research.

Conclusion

Placing the present findings into a greater context, it becomes evident that the prevention of anxiety disorders in adult populations has made considerable progress, but problems concerning the conceptualization of preventive interventions were still present. The current systematic review demonstrated the problems that arose with regard to the categorization of preventive interventions that need to be solved. Nevertheless, it was also demonstrated that effective preventive interventions for anxiety in adult populations based on CBT, ACT and positive psychology were found. Due to the fact that the populations of these studies consisted mostly of higher educated females, these effects cannot be generalized to various population groups. Future research should therefore examine the effects of these or similar interventions in broad population groups. As demonstrated in this review, the interventions should also be sensitive to various contexts of intercultural communication in order to achieve high adherence.

V. References

Note. References marked with * were studies included in the analysis.

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