Doctoral Programme in Psychology

Escuela de Doctorado de la Universitat Jaume I

EFFECTIVENESS OF A TRANSDIAGNOSTIC INTERNET-BASED PROTOCOL FOR THE TREATMENT OF EMOTIONAL DISORDERS IN PUBLIC SPECIALIZED MENTAL HEALTH CARE

DOCTORAL DISSERTATION

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Castellón de la Plana, January 2019

The current doctoral thesis has been supported by a PhD grant from the Ministerio de Cultura, Educación y Deporte (Spain) (FPU00576/13) and the Institute of Health Carlos III (ISCiii) CIBERobn is an initiative of ISCIII.
The publication of articles in open access journals has been possible thanks to the support of CIBER, CIBER Fisiopatología de la Obesidad y Nutrición-ISCIII CB06/03/0052 and the Ministerio de Economia y Competitividad (Plan Nacional I + D + I. PSI2014-54172-R).

"It is widely believed that misjudgment produces dysfunction. Certainly, gross miscalculation can create problems. However, optimistic self-appraisals of capability that are not unduly disparate from what is possible can be advantageous, whereas veridical judgments can be self-limiting. When people err in their self-appraisals, they tend to overestimate their capabilities. This is a benefit rather than a cognitive failing to be eradicated. If self-efficacy beliefs always reflected only what people could do routinely, they would rarely fail but would not mount the extra effort needed to surpass their ordinary performances".

ALBERT BANDURA (1989)

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Presentation

This doctoral thesis is a compendium of research articles. At the moment of the preparation of this thesis, four of these papers have already been published, and the rest have been submitted to indexed scientific journals for its publication.

Following Royal Decree 99/2011, which sets forth the regulations about doctorate studies in Spain, in order to obtain the degree of International Doctor, the current doctoral thesis has been fully written in English.

Chapter 1. General Introduction

General introduction

This chapter presents a general preface to the doctoral thesis. The main goal of this thesis was to develop and test in a randomized controlled trial a psychological intervention for anxiety and depressive disorders (i.e. emotional disorders) in Spanish public specialized mental health care. To this end, two general approaches were undertaken. The first is the use of Information and Communication Technologies (ICTs) and, more specifically, the Internet, to provide psychological interventions. The second is the adoption of a mechanistically, cognitive behavioral therapy (CBT) transdiagnostic approach to the treatment of emotional disorders.

The general introduction starts highlighting the burden of emotional disorders, as well as the need for evidence-based treatments to address this alarming public health problem. Next, a review of the literature about the efficacy of disorder-specific CBT is briefly outlined, followed by a description of the barriers for the use of these protocols. This is followed by a section that underscores the challenges of current public mental health services regarding the treatment of emotinal disorders, both globally and in Spain. The next sections focus on transdiagnostic treatments and Internet-delivered interventions, and in how they can help to decrease the burden of anxiety and depressive disorders, with a particular emphasis in public specialized mental health care. The general introduction ends with a description of the general aim and the specific aims pursued in each chapter.

The burden of emotional disorders

Anxiety and depressive disorders (referred to as emotional disorders) negatively affect the lives of millions of people across the globe (Baxter, Scott, Vos, & Whiteford, 2013; Kohn, Saxena, Levav, & Saraceno, 2004; Steel et al., 2014). Regarding anxiety, the lifetime prevalence of an anxiety disorder has been estimated at 28.8% (Kessler et al., 2005), whereas the 12-month prevalence has been estimated at 18.1% (Kessler, Chiu, Demler, Merikangas, & Walters, 2005). Anxiety disorders are associated with important costs (Andlin-Sobocki & Wittchen, 2005), disability (Baxter, Vos, Scott, Ferrari, & Whiteford, 2014; Hendriks et al., 2014), and worse psychosocial functioning and quality of life (Mendlowicz & Stein, 2000; Rapaport, Clary, Fayyad, & Endicott, 2005). Along with anxiety disorders, depressive disorders are some of the most prevalent and disabling psychological disorders among the adult population (Ferrari et al., 2013). Only for major depressive disorder, the literature has shown a lifetime prevalence of 16.6% (Kessler et al., 2005a) and a 12-month

prevalence of 6.7% (Kessler et al., 2005b). Similarly to anxiety disorders, depression is associated with substantial impairment (Ferrari et al., 2013), chronicity (Andrews, 2001; Richards, 2011), and increased mortality (Cuijpers & Smit, 2002), as well as high personal, social, and economic costs (Cuijpers, Beekman, & Reynolds, 2012). In Spain, the lifetime prevalence for mood and anxiety disorders among patients attending primary care settings has been estimated at 35.8% and 25.6%, respectively (Roca et al., 2009).

Another important characteristic related to emotional disorders is the high comorbidity rates among these conditions (i.e. when two or more psychological disorders co-occur in the same patient). The literature has shown the high current and lifetime comorbidity rates between anxiety disorders (Kroenke, Spitzer, Williams, Monahan, & Löwe, 2007), and between anxiety and depression (Brown, Campbell, Lehman, Grisham, & Mancill, 2001), with estimates that range from 40 to 80%. Moreover, higher comorbidity rates usually lead to greater severity (Kessler et al., 2005b), poorer quality of life (Rapaport et al., 2005), higher chronicity rates (Hofmeijer-Sevink et al., 2012), and a worse clinical course (Bruce, Machan, Dyck, & Keller, 2001; Sherbourne & Wells, 1997). Thus, the development of assessment and treatment strategies for patients with anxiety and depression, as well as for patients with comorbid presentations of these disorders, is of paramount importance for research and clinical practice.

In the past few decades, research efforts have been devoted to developing and testing evidence-based psychological treatments for different mental health problems. From the range of treatment approaches, Cognitive Behavioral Treatments (CBT) are those with the most evidence found for their efficacy and effectiveness in the treatment of multiple mental disorders, with a substantial proportion of this research focused on the treatment of depression and anxiety disorders. Data on the efficacy and effectiveness of these interventions have been shown in numerous systematic reviews for both traditional (i.e. face-to-face psychotherapy) (Cuijpers, van Straten, & Warmerdam, 2007; Hofmann & Smits, 2008; Olatunji, Cisler, & Deacon, 2010) and computerized CBT (i.e. computer- and Internet-delivered treatments) (Andrews et al., 2018; Richards & Richardson, 2012; Spek et al., 2007; Warmerdam, Van Straten, Twisk, Riper, & Cuijpers, 2008) and summarized in books and manuals about evidence-based treatments (Nathan & Gorman, 2015). There is extensive research showing the efficacy and effectiveness of disorder-specific CBT (i.e. a specific protocol to target a specific disorder) for the treatment of depression (Cuijpers, van Straten, Andersson, & van Oppen, 2008; Hollon & Ponniah, 2010), generalized anxiety disorder (GAD) (Borkovec & Ruscio, 2001; Covin, Ouimet, Seeds, & Dozois, 2008),

panic disorder (PD) and agoraphobia (AG) (David H. Barlow, Craske, Cerny, & Klosko, 1989; Mitte, 2005), social anxiety disorder (SAD) (Mayo-Wilson et al., 2014), and obsessive-compulsive disorder (OCD) (Öst, Havnen, Hansen, & Kvale, 2015). Data on the efficacy and effectiveness of CBT protocols have been shown across age groups and settings, such as community samples and university students, as well as primary and specialized care (Cartwright-Hatton, Roberts, Chitsabesan, Fothergill, & Harrington, 2004; Cuijpers et al., 2013; Stewart & Chambless, 2009).

Disorder-specific CBT protocols are effective but have important shortcomings

In the past few decades, a large number of CBT protocols for both anxiety and depressive disorders have been developed and tested in clinical trials. However, whereas disorder-specific CBT has shown its efficacy for anxiety and depressive disorders, there are a number of barriers regarding these protocols that limit their utility. The first drawback stems from the high comorbidity rates observed among the emotional disorders. Because each disorder-specific treatment focuses on a specific set of symptoms, comorbid disorders are not directly targeted in these protocols (McManus, Shafran, & Cooper, 2010). Although several ways to address comorbidity have been proposed (e.g. sequential application of treatments), the literature does not support the utility of these strategies (e.g. McManus et al., 2010). Second, subthreshold symptoms of clinical entity that do not meet diagnostic criteria for one disorder or another are not usually targeted by disorder-specific protocols (Barlow, Allen, & Choate, 2004). Third, disorder-specific protocols do not target disorders that do not fit a specific nosological category, i.e. anxiety and depression "not otherwise specified" (NOS), even though these disorders may also have clinical significance and, therefore, should be addressed with appropriate treatment (Brown et al., 2001). Finally, disorder-specific protocols are costly in terms of training because clinicians have to be trained in one specific protocol for each of the different emotional disorders (McHugh, Murray, & Barlow, 2009).

The barriers to the treatment of emotional disorders in public specialized mental health care

In Spain, the two main public providers of mental health care are primary and specialized care. Mental health care in our country is based on a model in which the patient has a first consultation with a primary care general practitioner (GP), who typically prescribes medication (e.g.

antidepressants or anxyolitics), even when the patient presents with mild to moderate levels of anxiety or depression. When the medication is not effective or when the GP judges that the case is difficult or severe enough to require specialized attention, the patients are referred to specialized mental health care or *mental health units,* where they receive treatment from a psychiatrist and/or a clinical psychologist. This model differs from the so-called *stepped care model*, in which patients with mild to moderate depression and anxiety disorders are prescribed low intensity interventions, such as guided self-help and computerized CBT. This model has been successfully implemented in countries such as the United Kingdom in response to the movement *Improving Access to Psychological Therapies* (IAPT) (Clark et al., 2009). Specialized mental health care in Spain is provided by psychiatrists and clinical psychologists with the highest degree of specialization in the assessment, diagnosis, and treatment of psychological disorders. Therefore, patients in this setting receive the best therapeutic option that can be provided by the national public health system. However, current mental health units face a number of barriers that affect both the quantity and quality of the services delivered in these centers. First, in Spain, most of the patients attending public mental health services, such as mental health units, suffer from anxiety and depressive disorders (Montilla, González, Retolaza, Dueñas, & Alameda, 2002). Second, the literature has shown that a lack of resources tends to characterize mental health services in developed countries, resulting in limitations in providing adequate treatment or follow-up care (Wang et al., 2007). For instance, compared to other European countries, in Spain, the number of clinical psychologists in the public mental health care system is very low, with a ratio of around 4 of these professionals per 100000 inhabitants (Palacios, Fraga, Hoyas, Laíz, & Rodríguez, 2006). It is therefore not surprising that the data in Spain show that a substantial proportion of patients have to wait longer than 45 days until the first consultation with a clinical psychologist or a psychiatrist (Martín-Jurado, de la Gándara, Carbajo, Moreira, & Sánchez-Hernández, 2012). Likewise, a study by Fernández et al. (2006) concluded that only one third of the treatments provided to patients who attend public services to seek mental health treatment in Spain meet minimal adequacy criteria. Finally, other authors have highlighted the treatment gap present in mental health care, that is, the proportion of patients with mental disorders who do not receive treatment in mental health services, especially those with anxiety and mood disorders (Fernández et al., 2006; Kohn et al., 2004). In sum, these data point to the need to improve the quality of mental health services. In this task, the role of clinical research in this setting is of vital importance.

On the other hand, the barriers mentioned in the previous section regarding disorder-specific protocols might be particularly evident when

these protocols are administered in clinical contexts such as public specialized mental health care. First, because it is an ecological setting (i.e. patients are not selected based on eligibility criteria), the clinical presentations of the patients attending these centers are generally more heterogeneous, including more patients with comorbidity, subthreshold symptoms, and NOS diagnoses (i.e. anxiety and depression NOS), which impedes their adequate treatment using disorder-specific protocols. Second, patients attending mental health units normally have to face long waitlists to receive treatment. In this sense, the literature shows that most disorder-specific evidence-based treatments for anxiety and depression work, among other reasons, because they are delivered regularly (e.g. on a weekly basis) (Nathan & Gorman, 2015). However, the frequency of the visits in mental health units is generally lower. For instance, in Spain the frequency of the sessions for patients attending these units is around once a month (González-González et al., 2014). Thus, this lower frequency of sessions may negatively impact the effective delivery of manualized evidence-based treatments in these centers. Finally, the work of clinical psychologists in mental health units in Spain is not restricted to anxiety and depressive disorders, but rather includes a wide range of clinical presentations (Echeburúa, Salaberría, de Corral, & Cruz-Sáez, 2012), which means that these professionals require the knowledge and skills to treat a myriad of psychological problems. Therefore, training clinicians in the different disorder-specific protocols required for each emotional disorder can become a real challenge under these circumstances. In fact, it does not come as a surprise that training clinicians has been highlighted as a major difficulty in the dissemination and implementation of evidence-based treatments in clinical settings (McHugh & Barlow, 2010). In response to the limitations of disorder-specific protocols, new lines of research have emerged that could help to overcome some of these challenges. A characteristic example of this research is the transdiagnostic approach for the treatment of emotional disorders, which has experienced rapid growth in the past fifteen years. This approach is described in the following sections.

The transdiagnostic approach to the treatment of emotional disorders

In recent years, there has been great interest in treatment strategies (referred to as transdiagnostic treatments) that might be more widely effective across these diverse mental health disorders. Transdiagnostic treatments “apply the same underlying treatment principles across mental disorders, without tailoring the protocol to specific diagnoses” (McManus et al., 2010, p. 4). In general terms, unlike disorder-

specific protocols, transdiagnostic treatments are based on the premise that the commonalities of psychological disorders outweigh their differences, and that the observed differences (symptoms) are specific manifestations of broader, underlying common psychopathological processes (Barlow, Sauer-Zavala, Carl, Bullis, & Ellard, 2013; Barlow et al., 2004; Harvey, Watkins, Mansell, & Shafran, 2004; Mansell, Harvey, Watkins, & Shafran, 2009; Meidlinger & Hope, 2017). Research on transdiagnostic treatments and processes has attracted researchers' interest in recent years, and this interest has been manifested in several ways. For example, a special issue entitled "Transdiagnostic Approaches" was published in the Journal of Anxiety Disorders, which presented a series of articles focused on recent developments in the field of transdiagnostic treatments for emotional disorders (Norton, 2017). Similarly, in our country some researchers have manifested their interested in this topic (Sandín, 2012), and a number of randomized controlled trials are currently being conducted to study the efficacy of transdiagnostic treatments in both community (Díaz-García et al., 2017) and specialized care settings (Osma et al., 2018). Finally, at the "Conference on Transdiagnostic Approaches to Mental Health Challenges", held in Cambridge, UK, on September (2018), the most recent advances and future research directions were presented by leading researchers in the field of transdiagnostic treatments, helping to consolidate the interest in the study of the transdiagnostic approach to the scientific understanding, assessment, and treatment of emotional disorders.

The transdiagnostic approach has directly influenced both research focused on common psychopathological processes across diagnoses (Harvey et al., 2004) and the development of treatments and their application in multiple randomized controlled trials over the past fifteen years (e.g. Barlow et al., 2017; Dear et al., 2015; Erickson, Janeck, & Tallman, 2007; Farchione et al., 2012; Norton & Hope, 2005). Several meta-analytic reviews have shown that transdiagnostic treatments are effective in comparison with control groups (Newby, McKinnon, Kuyken, Gilbody, & Dalgleish, 2015; Newby et al., 2016; Păsărelu, Andersson, Bergman Nordgren, & Dobrean, 2017; Reinholt & Krogh, 2014), with pooled effect sizes (Hedges' g) in the moderate to large range for overall measures of anxiety (.65 to .82) and depression (.79 to .84), and moderate effects on quality of life measures (.46 to .56). In addition, another meta-analysis revealed that there are no differences in efficacy between transdiagnostic treatments and disorder-specific protocols (Pearl & Norton, 2017). There is, therefore, a growing body of evidence indicating that transdiagnostic treatments are effective in improving anxiety and depression, as well as quality of life.

The first author to apply a transdiagnostic approach was Fairburn (Fairburn & Harrison, 2003), with a particular focus on the transdiagnostic treatment of eating disorders. For instance, within this model, the overvaluation of shape and weight is viewed as a core process that is common to all the eating disorders (i.e. bulimia nervosa, anorexia nervosa, and atypical eating disorders), and therefore the treatment is developed to directly address this common vulnerability. The counterpart for emotional disorders is the Unified Protocol (UP) developed by Barlow (Barlow et al., 2004; Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010). Both the theoretical rationale and the treatment protocol are described below.

Transdiagnostic treatments can be classified according to several characteristics. First, regarding the number of disorders that transdiagnostic protocols cover, these treatments may range from those targeting two disorders (Bolton et al., 2014; Wetherell et al., 2009) to those targeting multiple anxiety and/or depressive disorders (Boettcher et al., 2014; Farchione et al., 2012). Second, whereas some transdiagnostic protocols focus on the treatment of anxiety disorders alone (Nordgren et al., 2014), others address both anxiety and depressive disorders (Titov et al., 2011). Transdiagnostic treatments may also be classified according to other characteristics, such as the delivery format (e.g. face-to-face vs. Internet-delivered treatments; group vs. individual); however, one of the most important features in classifying transdiagnostic protocols is probably the treatment approach used.

According to Sauer-Zavala et al. (2017), transdiagnostic protocols can be classified in three broad categories depending on the treatment approach adopted by each: a) transdiagnostic treatments based on *universally applied therapeutic principles*; b) transdiagnostic *modular treatments*; and c) transdiagnostic treatments based on *shared mechanisms*. In short, transdiagnostic interventions within the first approach are *top-down* strategies to be applied across a wide range of diagnoses. However, they do not pay attention to the specific mechanisms underlying these disorders. Rather, the distinct characteristic of this approach is that a theoretical model is first developed and then applied to a wide range of psychological disorders. Examples of this approach include humanistic, psychodynamic, and “third wave” therapies (e.g. Mindfulness-based treatments, and Acceptance and Commitment Therapy). In contrast, the main characteristic of transdiagnostic modular treatments is that the treatment is developed based on the selection of evidence-based strategies and techniques. However, as in the first approach, the rationale for modular treatments is not the selection of treatment strategies based on mechanisms underlying all the emotional disorders. Instead, this approach to treatment is based on the selection of treatment strategies that have been shown to work for each problem. An

example of a treatment in this category is CETA (Common Elements Treatment Approach), a modular treatment designed for depression and anxiety (Murray et al., 2013). In CETA, the treatment strategies are selected from a bank of empirically supported components as varied as psychoeducation, behavioral activation, relaxation, exposure, and suicide management. Moreover, the specific strategies and their dose, as well as the order in which they are implemented, depend on the characteristics of each patient. Finally, unlike the other two approaches, the goal of transdiagnostic treatments based on shared mechanisms is to address the common psychopathological processes responsible for the development and maintenance of a specific range of disorders, assuming a causal relationship between these processes and the manifestation of the emotional, cognitive, and physiological phenomenology characteristic of each emotional disorder. The most representative example of a treatment based on a mechanistically transdiagnostic approach is probably the Unified Protocol (UP) (Barlow et al., 2011a, 2011b). A number of advantages have been attributed to transdiagnostic treatments based on this approach. First, the assumption of a core psychopathology across emotional disorders can help to explain the high levels of comorbidity among these disorders and provide a treatment strategy with the potential to more effectively treat comordid presentations (Mansell, Harvey, Watkins, & Shafran, 2008). Second, only one protocol is needed for a range of disorders, which means lower costs in terms of training and is consequently beneficial for both dissemination and implementation (McEvoy, Nathan, & Norton, 2009). Third, rather than focusing on disorder-specific symptoms, mechanistically transdiagnostic treatments address core processes that are hypothesized to be responsible for the maintenance vulnerability processes across emotional disorders. It is assumed that by targeting these common processes, larger and more lasting clinical changes can be expected in these disorders (Sauer-Zavala et al., 2017).

A more detailed review of the different transdiagnostic approaches is beyond the scope of this work (for a comprehensive review see Sauer-Zavala et al., 2017). Thus, this dissertation will focus on the last approach described, that is, the mechanistically transdiagnostic approach. Because the principal objective of the current doctoral thesis was to test a transdiagnostic intervention mainly focused on the dimension of neuroticism and the regulation of negative affectivity, in the following sections we describe the rationale and specific psychopathological processes and intervention strategies supporting the transdiagnostic treatment protocol designed and tested in this work. First, the *Theory of triple vulnerability* is presented as the theoretical model underlying the treatment approach adopted in this doctoral thesis, as well as the links

between this model and the difficulties in emotion regulation shown in emotional disorders. Second, the Unified Protocol, a treatment protocol derived from this theoretical model, is described. Third, the utility of Dialectical Behavior Therapy (DBT) for the transdiagnostic treatment of emotional disorders is outlined. Finally, as a secondary objective we also establish the basis for including components focused on the regulation of positive affectivity. Specifically, a pilot study was conducted to explore the utility of adding intervention modules targeting positive affectivity to a transdiagnostic protocol with traditional components for the regulation of negative affectivity (e.g. cognitive restructuring, exposure procedures). The last section explains the rationale for this approach.

The theory of triple vulnerability

A number of cognitive, behavioral, and emotional constructs have been found to play a transdiagnostic role in emotional disorders. These processes include, but are not limited to, intolerance to uncertainty (Mahoney & McEvoy, 2012), thought suppression (Aldao & Nolen-Hoeksema, 2010), rumination (Ehring & Watkins, 2008), perfectionism (Egan, Wade, & Shafran, 2011), anxiety sensitivity (Boswell et al., 2013), and behavioral avoidance and safety behaviors (Clark, 2009; Schmidt et al., 2012). Among these constructs, neuroticism is a transdiagnostic process that has been consistently associated with both anxiety and depressive disorders (Barlow, Ellard, Sauer-Zavala, Bullis, & Carl, 2014; Brown & Barlow, 2009; Harvey et al., 2004).

The *Theory of triple vulnerability*, formulated by Barlow (2000), is a dimensional model that integrates the personality construct of neuroticism as a key feature to understand both the origin and the perpetuation of emotional disorders. This model provides a conceptual framework for understanding emotional disorders, with contributions from the fields of genetics, personality, cognitive research and neuroscience, and emotion and learning theories. According to this theory, three types of vulnerabilities or *diatheses* can be distinguished that influence both the onset and maintenance of emotional disorders. The first, a *general biological vulnerability*, is described as a genetically or heritable tendency to experience negative emotions (also called neuroticism or “general neurotic syndrome”). The second, a *general psychological vulnerability,* is caused by early childhood experiences in stressful environments, leading to a sense of unpredictability and uncontrollability that interferes with the development of effective coping strategies and self-efficacy. Finally, the third vulnerability is a *specific psychological vulnerability*, by virtue of which an individual learns that some situations, objects, or internal states (e.g. thoughts, physical sensations) are dangerous, even when there is no

reasonable association between them. The combination of these three diatheses would account for the emergence of the different anxiety and depressive disorders.

These vulnerabilities or diatheses have been intimately linked to the difficulties in emotion regulation shown by individuals with emotional disorders, especially with regard to neuroticism (Barlow, Sauer-Zavala, Carl, Bullis, & Ellard, 2013) and low positive affect (Carl, Soskin, Kerns, & Barlow, 2013). Emotion regulation has been defined as an individual's attempts to affect the types of emotions experienced, and when and how these emotions are expressed and experienced (Gross et al., 1998). In addition, an individual may use emotion regulation to increase or maintain an emotion (i.e. up-regulation) or to decrease his/her emotions (i.e. down-regulation). The strategies used to regulate emotion may be behavioral (e.g. problem solving, avoidance) or cognitive (reappraisal, suppression), and they can be more or less adaptive for the individual's psychological and interpersonal functioning. For instance, *reappraisal* is a cognitive emotion regulation strategy used to change the meaning of an emotion-eliciting situation in a way that promotes adaptation, whereas *suppression* entails the attempt to hide, inhibit, or decrease ongoing emotion-expressive behavior, leading to increased distress and worse psychological functioning (Gross & John, 2003). Difficulties in the regulation of both negative and positive emotions have emerged in research as a common feature in depression and anxiety disorders (Campbell-Sills & Barlow, 2007; Campbell-Sills, Ellard, & Barlow, 2014; Sloan, Moulding, Bryce, Mildred, & Staiger, 2017). Based on this theoretical framework, David H. Barlow developed The Unified Protocol (UP), a transdiagnostic CBT protocol for anxiety and depressive disorders (Ellard et al., 2010) that emphasizes the role of emotion regulation in the maintenance of these disorders. A detailed description of the protocol, as well as the evidence supporting its efficacy, is summarized in the following section.

The Unified Protocol

The Unified Protocol for the Transdiagnostic Treatment of Emotional Disorders (UP) is a manualized, mechanistically transdiagnostic CBT protocol for the treatment of anxiety and depressive disorders, whose principal goal is to teach patients adaptive ways to regulate their emotions. The UP contains the following five core treatment modules: a) present-focused emotional awareness, b) cognitive flexibility, c) identification and prevention of emotional avoidance patterns, d) increasing awareness and tolerance of physical sensations, and e) graded (interoceptive and situational) exposure. The protocol includes two additional modules,

focused on motivation for change and psychoeducation about emotional experiences, and a relapse prevention module at the end of the treatment. UP manuals for both patient and therapist have been published (Barlow et al., 2011a, 2011b) and translated into Spanish (Barlow et al., 2016).

The efficacy of the UP has been shown in two randomized controlled trials. The first compared the efficacy of the UP to a waitlist control group. At post-treatment, the between-group comparison yielded a moderate effect size for anxiety (Hedges's g = .56) and a large effect for depression (Hedges's g = 1.11) and work and social adjustment (Hedges's g = 1.09), and these effects were maintained in the long term (Bullis, Fortune, Farchione, & Barlow, 2014). Five years later, the results of a second larger randomized controlled trial comparing the UP to disorder-specific CBT protocols showed that there were no differences in efficacy between the transdiagnostic and disorder-specific approaches on generic measures of anxiety and depression (Barlow et al., 2017), as well as on measures of comorbid anxiety disorders (Steele et al., 2018). Moreover, preliminary data have been published that support the efficacy of the UP in improving the temperament dimensions of behavioral inhibition and behavioral activation (Carl, Gallagher, Sauer-Zavala, Bentley, & Barlow, 2014).

The UP has also been tested in other populations and using different delivery formats. For instance, there is preliminary evidence suggesting the efficacy of the UP for anxiety and depression delivered in a group format (Bullis et al., 2015; Laposa, Mancuso, Abraham, & Loli-Dano, 2017), for comorbid bipolar disorders and anxiety (Ellard et al., 2017), and for the treatment of anxiety and depression in adolescents (Ehrenreich-May et al., 2017). Furthermore, cross-cultural studies with the UP have been carried out (de Ornelas Maia, 2015; Ito et al., 2016; Mohsenabadi, Zanjani, Shabani, & Arj, 2018), and ongoing randomized controlled trials are being conducted to study the efficacy of the UP, for example, in Spain (Osma et al., 2018) and Japan (Ito et al., 2016). In summary, the literature on the UP suggests that a mechanistically transdiagnostic approach can be effective across categories of emotional disorders, outcome measures, delivery formats, and age groups.

Using Dialectical Behavioral Therapy to regulate emotions in anxiety and depressive disorders

Emotion regulation difficulties play a pivotal role under the umbrella of Dialectical Behavioral Therapy (DBT) (Linehan, 1993). Although DBT was initially developed as a theoretical model and treatment strategy for understanding and treating borderline personality disorder, more recently, it has been proposed that DBT may also be useful for treating patients

with anxiety and depressive disorders because these individuals show patterns of emotion dysregulation that may benefit from the emotion regulation skills present in DBT (Neacsiu, Bohus, & Linehan, 2015; Neacsiu, Herr, Fang, Rodriguez, & Rosenthal, 2015). For instance, one of the targets in DBT is the regulation of emotion expression and the action tendencies linked to these emotions. A DBT technique proposed to improve this regulation strategy is the *opposite action. This* strategy is based on the idea that, in order to change the nature and intensity of a specific emotion, individuals have to engage in behaviors or *actions* opposite to those associated with the unwanted emotions. Another skill central to DBT is *mindfulness*. For instance, mindfulness skills in DBT include "what skills" (observing, describing, and participating) and "how skills" (non-judgmentally, one-mindfully, and effectively). Overall, these techniques are aimed at teaching the ability to observe and describe one's emotional experiences in a nonjudgmental way, trying to focus on the present moment (Linehan, 1993). In this regard, another important element of DBT linked to mindfulness skills is the concept of *radical acceptance*. This concept implies that, in order to reduce unnecessary emotional suffering, individuals should aim for the complete and nonjudgmental acceptance of experiences, embracing reality "as it is" (Linehan, 1993). DBT skills have been adapted and applied to different emotional disorders, including post-traumatic stress disorder (Bohus et al., 2014), depression (Berking, Ebert, Cuijpers, & Hofmann, 2013), and mixed anxiety and depression (Neacsiu et al., 2014), suggesting that the inclusion of treatment strategies based on the emotion regulation DBT skills may be used transdiagnostically to improve symptoms of anxiety, depression, and emotion dysregulation in patients suffering from anxiety and depressive disorders.

The regulation of positive affectivity as a treatment target in transdiagnostic treatments

In the previous sections, the role of pathological factors such as neuroticism or emotion dysregulation in anxiety and depressive disorders has been highlighted. However, a more complete picture for understanding and treating these disorders is not possible without the consideration of positive affectivity (Carl et al., 2013; Eisner, Johnson, & Carver, 2009; Headey, Kelley, & Wearing, 1993; Watson, Clark, & Carey, 1988).

There is a growing body of research linking positive affectivity to anxiety and depressive disorders. First, low levels of positive affectivity have been associated with most emotional disorders (Kotov, Gamez, Schmidt, & Watson, 2010). For instance, structural equations have shown

the association between low levels of positive affectivity and emotional disorders such as depression (Clark & Watson, 1991), social anxiety disorder (Brown, Chorpita, & Barlow, 1998), and agoraphobia (Rosellini, Lawrence, Meyer, & Brown, 2010). Second, individuals with depression are more prone to using maladaptive strategies to regulate positive affectivity. For example, a study found that depressed individuals tend to engage in *dampening* (i.e. an emotion regulation strategy used to decrease the intensity of positive emotional states) more frequently than healthy individuals (Werner-Seidler, Banks, Dunn, & Moulds, 2013). Third, deficits in the regulation of positive affectivity seem to worsen the clinical course of individuals with depression (Shankman, Nelson, Harrow, & Faull, 2010). Fourth, a review focused on positive emotion regulation in emotional disorders revealed different patterns of disturbances with regard to the regulation of positive emotions in individuals with anxiety and depression. For example, the review showed that whereas patients with depression are more likely to exhibit deficits such as decreased reward sensitivity and positive imagery difficulties, individuals with anxiety and related disorders (e.g. generalized anxiety disorder, agoraphobia, panic disorder, social anxiety, and obsessive-compulsive disorder) more often display deficits such as stronger biases toward negative stimuli and increased avoidance motivation (Carl et al., 2013). A comprehensive review of the deficits in emotion regulation shown by both anxiety and depressive disorders can be found in Carl et al. (2013).

The study of protective factors is not new in the literature. The emphasis on promoting these factors has long been acknowledged by leading researchers in the field (Bandura, 1977; Rutter, 1985; Seligman & Csikszentmihalyi 2000; Taylor, & Brown, 1988). With regard to positive affectivity, its study in relation to different indicators of health and optimal functioning is abundant in the literature. For instance, positive affectivity has been associated with better physical (Cohen & Pressman, 2006) and psychological health (Livingstone & Srivastava, 2012), general well-being (Lyubomirsky, King, & Diener, 2005), healthier lifestyles (Kobau et al., 2011), better interpersonal functioning (Garland et al., 2010), and enhanced cognitive performance (Rowe, Hirsh, & Anderson, 2007). Additionally, the promotion of positive emotion functioning has been linked to increased resilience (Tugade & Fredrickson, 2007), i.e., the ability of individuals to cope with and learn from stressful events in life, a factor that is believed to play a protective role across psychopathologies, including anxiety and depressive disorders (Luthar, Cicchetti, & Becker, 2000; Southwick, Vythilingam, & Charney, 2005). Furthermore, recent efforts to identify protective factors have linked positive affectivity to the construct of *Openness to the future*, a prospective protective factor defined by the authors as “an active cognitive-affective mood state that involves positive

expectations about what life may bring, a sense of competence and ability to cope with events, the anticipation, planning and perseverance to reach an outcome even in the face of adversity, and the acceptance of what cannot be resolved or predicted" (Botella et al., 2018 p. 2). Based on the breadth of the data, it appears logical that the development of treatment strategies to up-regulate positive affectivity should not be neglected.

To date, research on the transdiagnostic approach has mainly focused on deficits and negative psychological functioning (Barlow et al., 2017; Dear et al., 2015; Norton & Hope, 2005; Titov et al., 2011), and less attention has been paid to the promotion of flourishing and protective factors such as positive affectivity. However, more recently, the study of positive affective regulation from a transdiagnostic perspective has gained renewed interest among researchers. For instance, Taylor, Lyubomirsky, and Stein (2017) pilot-tested the efficacy of a transdiagnostic intervention based on positive psychology interventions (PPIs) for anxiety and depressive disorders, with results suggesting their usefulness on measures of anxiety and depression, as well as positive and negative affectivity. Another possible strategy is to add strategies to up-regulate positive affectivity to the existing transdiagnostic protocols, mainly focused on down-regulating negative affectivity. A study by Carl, Gallagher, and Barlow, (2018) illustrates this point. In this study, the authors presented a module for the regulation of positive affectivity to be applied transdiagnostically across anxiety and depressive disorders. According to the authors, the module can be implemented in a flexible way, either integrated into a modular treatment program, or as an adjunct for patients who show deficits in positive emotions at post-treatment. Although promising, the results of this emerging research are only preliminary, and thus more research is needed to further explore the potential of these strategies in improving emotional disorders.

The use of Information and Communication Technologies to improve mental health: Internet-delivered interventions

The main objective of this doctoral thesis was to explore the effectiveness of a transdiagnostic Internet-delivered protocol for emotional disorders. Therefore, in the following sections, both the rationale and the most relevant research on the topic of Internet interventions are set forth.

Research on Internet-delivered psychological interventions has blossomed in the past two decades (Andersson, 2016, 2018). The number of clinical trials testing the efficacy and effectiveness of Internet-delivered CBT (ICBT) has increased exponentially in recent years. A number of meta-analyses have shown that Internet-delivered treatments are effective

for both anxiety and depressive disorders in comparison with control groups (Andrews et al., 2018; Richards & Richardson, 2012; Spek et al., 2007), and that there are no differences in efficacy between ICBT and face-to-face CBT (Carlbring, Andersson, Cuijpers, Riper, & Hedman-Lagerlöf, 2018). Moreover, in terms of cost-effectiveness, the literature has shown promising data in favor of Internet-delivered interventions, compared to more traditional ways of delivering therapy (e.g. face-to-face treatments) (Donker et al., 2015). In Spain, a number of studies have shown the efficacy of Internet-delivered treatments for depression (Mira et al., 2017; Montero-Marín et al., 2016), and others for the treatment of anxiety and depression are underway (e.g. Campos et al., 2016; Díaz-García et al., 2017; Rachyla et al., 2018). In sum, there is extensive evidence in the literature indicating the efficacy and (potential) cost-effectiveness of these treatments.

Internet-delivered interventions have been found to have several advantages for users, clinicians, and researchers. For users, the most commonly mentioned advantages include increased access to evidence-based treatments (e.g. individuals living in rural areas) (Griffiths & Christensen, 2007), the possibility of receiving treatment without the stigma typically associated with mental disorders (Griffiths, Lindenmeyer, Powell, Lowe, & Thorogood, 2006), a shorter waiting time to receive treatment (Spurgeon & Wright, 2010), and greater convenience compared to other delivery formats such as face-to-face psychotherapy (e.g. patients do not have to attend a center or facility to receive treatment) (Griffiths et al., 2006). For researchers and clinicians, the potential advantages of Internet interventions include, but are not limited to, easier participant recruitment and data collection about the patients (Andersson & Titov, 2014), reductions in the workload of mental health professionals (Musiat & Tarrier, 2014), and increased cost-effectiveness (Donker et al., 2015).

An important aspect of Internet-delivered treatments is the type and degree of guidance provided to the patients. ICBT can be delivered with some type of clinician or therapist support or completely self-guided. Moreover, support in guided ICBT can be provided in many ways, such as phone calls, emails, chat, and/or videoconference. In general terms, the literature suggests that guided ICBT frequently leads to better outcomes than unguided ICBT (Baumeister, Reichler, Munzinger, & Lin, 2014; Palmqvist, Carlbring, & Andersson, 2007). In this regard, a systematic review on the efficacy of Internet-delivered treatments for depression showed a linear relationship between the degree of clinician contact and the magnitude of the outcomes, with the largest effect sizes observed for the treatments where there was therapist contact both before and during the treatment, and the smallest effect sizes for those where there was no contact between patients and the providers of support (Richards &

Richardson, 2012). Although there is research indicating that unguided ICBT can lead to similar results as guided ICBT, at least for some patients (Karyotaki et al., 2017), in general, it is widely assumed that Internet interventions work better if some type of support is delivered to the patients. In addition, the degree of support or contact provided to the patients has also been linked to the rates of adherence and attrition from these treatments, as dropout rates have been found to be higher in unguided Internet-delivered treatments (Richards & Richardson, 2012). Apart from the indicators of efficacy, which are of undeniable importance, given the higher drop-out rates in Internet-delivered interventions compared to face-to-face treatments (van Ballegooijen et al., 2014), indicators of adherence and attrition should be given equal importance in research on these treatments. In order to enhance the value of Internet-delivered interventions, efforts should be made to decrease the percentage of participants who decide to drop out from these treatments.

In the field of transdiagnostic treatments for emotional disorders, the literature has shown the efficacy of Internet-delivered treatments in comparison with control groups (Newby et al., 2016), and that transdiagnostic Internet-delivered treatments might be as effective as transdiagnostic face-to-face treatments (Newby et al., 2015). However, most of the evidence about the efficacy and effectiveness of transdiagnostic treatments comes from studies conducted in community settings (e.g. Farchione et al., 2012; Dear, et al., 2015) and, less commonly, in primary care (e.g. Berger et al., 2016). However, in spite of the compelling data showing the prevalence and lack of adequate coverage of anxiety and depressive disorders in specialized mental health care, to our knowledge, the way transdiagnostic Internet-delivered treatments work in this setting has not yet been explored in the literature. Hence, the aforementioned problems associated with the delivery of mental health services in public specialized mental health (e.g. long waiting times to access therapy, low number of clinical psychologists in public mental health services, and so on) strongly suggest that a change in the way mental health services are provided is needed. Some authors have highlighted the usefulness of ICTs, such as the Internet, to bridge this gap, in order to provide evidence-based treatments that are more accessible for all of the population in need (Kazdin, 2015; Kazdin & Blase, 2011). Consistent with this view, the benefits of a transdiagnostic approach (i.e. less training is needed because only one treatment protocol is used to address various psychological disorders, which might lead to greater coverage of the demand for treatments in these services) may be enhanced by using an Internet-delivered format in order to improve access by people for whom face-to-face treatments are not available.

Aims of the current doctoral thesis

General aim

With the aforementioned in mind, the **general aim** of this doctoral thesis was to develop a transdiagnostic Internet-delivered protocol for the treatment of emotional disorders to be tested in an RCT, compared to treatment as usual as provided in public specialized mental health care.

Specific aims

The **specific aims** of the current doctoral thesis are described in the following lines. First**,** a systematic review focused on transdiagnostic treatments for anxiety and depressive disorders is presented in **Chapter 2**. It sought to answer the following research questions: a) whether treatment response to comorbidity is evaluated in transdiagnostic treatments; b) what diagnoses are targeted in transdiagnostic treatments; and c) what the real distribution of the diagnoses is at baseline in these studies. Second, **Chapter 3** presents the study protocol of the RCT conducted in this doctoral thesis. Third, two validation studies were carried out to analyze the psychometric properties of two short scales delivered online for the assessment of the impairment and severity associated with anxiety and depression in Spanish clinical samples, namely, the Overall Anxiety Severity and Impairment Scale (OASIS), and the Overall Depression Severity and Impairment Scale (ODSIS). These scales are included as assessment tools in the RCT presented in the current doctoral thesis and presented in **Chapters 4 and 5**. Fourth, an RCT was conducted to analyze the effectiveness and acceptability of a transdiagnostic Internet-delivered protocol compared to treatment as usual in public specialized mental health care. The results of the RCT are presented in **Chapter 6**. The protocol is based on the treatment components of the UP (i.e. present-focused emotional awareness, cognitive flexibility, emotional avoidance and emotion driven behaviors, and interoceptive and situational exposure). Moreover, a greater emphasis is placed on the component that addresses present-focused emotional awareness by adapting some of the strategies and techniques used in the emotional regulation DBT skills (e.g. “what” and “how” techniques). Unlike most previous transdiagnostic online treatments, it is designed to be broadly applicable to a wide range of anxiety and depressive disorders, including MDD, DD, depression NOS, GAD, PD, AG, SAD, anxiety NOS and OCD. Finally, a pilot study was conducted to explore a transdiagnostic protocol that adds a component for the regulation of positive affectivity to the traditional CBT components for the regulation of negative affectivity. In order to analyze the utility of including treatment modules focused on the regulation of positive affectivity, the feasibility of these two treatment conditions was explored in

terms of preliminary acceptability and differential efficacy, with a particular focus on measures of positive and negative affectivity, depression, and anxiety. This study is presented in **Chapter 7**. The thesis ends with **Chapter 8**, which includes a general discussion of key findings, implications of the current work, strengths and limitations, future directions, and recommendations for research.

References

Aldao, A., & Nolen-Hoeksema, S. (2010). Specificity of cognitive emotion regulation strategies: A transdiagnostic examination. *Behaviour Research and Therapy*, *48*(10), 974–983.

Andersson, G. (2016). Internet-Delivered Psychological Treatments. *Annual Review of Clinical Psychology*, *12*(1), 157–179.

Andersson, G. (2018). Internet interventions: Past, present and future. *Internet Interventions*, *12*, 181–188.

Andersson, G., & Titov, N. (2014). Advantages and limitations of Internet-based interventions for common mental disorders. *World Psychiatry*, *13*(1), 4–11.

Andlin-Sobocki, P., & Wittchen, H.U. (2005). Cost of anxiety disorders in Europe. *European Journal of Neurology*, *12*(s1), 39–44.

Andrews, G. (2001). Should depression be managed as a chronic disease? *BMJ (Clinical Research Ed.)*, *322*(7283), 419–421.

Andrews, G., Basu, A., Cuijpers, P., Craske, M. G., McEvoy, P., English, C. L., & Newby, J. M. (2018). Computer therapy for the anxiety and depression disorders is effective, acceptable and practical health care: An updated meta-analysis. *Journal of Anxiety Disorders*, *55*, 70–78.

Bandura, A. (1977). Self-efficacy: toward a unifying theory of behavioral change. *Psychological Review*, *84*(2), 191–215.

Barlow, D. H. (2000). Unraveling the mysteries of anxiety and its disorders from the perspective of emotion theory. *The American Psychologist*, *55*(11), 1247–1263.

Barlow, D. H., Allen, L. B., & Choate, M. L. (2004). Toward a unified treatment for emotional disorders. *Behavior Therapy*, *35*(2), 205–230.

Barlow, D. H., Craske, M. G., Cerny, J. A., & Klosko, J. S. (1989). Behavioral treatment of panic disorder. *Behavior Therapy*, *20*(2), 261–282.

Barlow, D. H., Ellard, K. K., Sauer-Zavala, S., Bullis, J. R., & Carl, J. R. (2014). The Origins of Neuroticism. *Perspectives on Psychological Science*, *9*(5), 481–496.

Barlow, D. H., Ellard, K. K., Fairholme, C. P., Farchione, T. J., Boisseau, C. L., Allen, L. B., & Ehrenreich-May, J. (2011). *The unified protocol for transdiagnostic treatment of emotional disorders: Client workbook.* New York: Oxford University Press.

Barlow, D., Farchione, T., Bullis, J., Gallagher, M., Murray-Latin, H., Sauer-Zavala, S., … Cassiello-Robbins, C. (2017). The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders Compared With Diagnosis-Specific Protocols for Anxiety Disorders: a Randomized Clinical Trial. *JAMA Psychiatry*, *74*(9), 875–884.

Barlow, D. H., Farchione, T. J., Fairholme, C. P., Ellard, K. K., Boisseau, C. L., Allen, L. B., & Ehrenreich-May, J. (2011). *Treatments that work. Unified protocol for transdiagnostic treatment of emotional disorders: Therapist guide.* New York, NY, US: Oxford University Press.

Barlow, D. H., Farchione, T. J., Fairholme, C. P., Ellard, K. K., Boisseau, C. L., Allen, L. B., & Ehrenreich-May, J. (2016). *Protocolo unificado para el tratamiento transdiagnóstico de los trastornos emocionales* (J. Osma & E. Crespo, Trans.). Madrid: Alianza Editorial.

Barlow, D. H., Sauer-Zavala, S., Carl, J. R., Bullis, J. R., & Ellard, K. K. (2013). The Nature, Diagnosis, and Treatment of Neuroticism: Back to the Future. *Clinical Psychological Science*, *2*(3), 344–365.

Baumeister, H., Reichler, L., Munzinger, M., & Lin, J. (2014). The impact of guidance on Internet-based mental health interventions – A systematic review. *Internet Interventions*, *1*(4), 205–215.

Baxter, A. J., Scott, K. M., Vos, T., & Whiteford, H. A. (2013). Global prevalence of anxiety disorders: a systematic review and meta-regression. *Psychological Medicine*, *43*(05), 897–910.

Baxter, A. J., Vos, T., Scott, K. M., Ferrari, A. J., & Whiteford, H. A. (2014). The global burden of anxiety disorders in 2010. *Psychological Medicine*, *44*(11), 2363–2374.

Berger, T., Urech, A., Krieger, T., Stolz, T., Schulz, A., Vincent, A., … Meyer, B. (2017). Effects of a transdiagnostic unguided Internet intervention ('velibra') for anxiety disorders in primary care: results of a randomized controlled trial. *Psychological Medicine*, *47*(1), 67–80.

Berking, M., Ebert, D., Cuijpers, P., & Hofmann, S. G. (2013). Emotion regulation skills training enhances the efficacy of inpatient cognitive behavioral therapy for major depressive disorder: a randomized controlled trial. *Psychotherapy and Psychosomatics*, *82*(4), 234–245.

Boettcher, J., Åström, V., Påhlsson, D., Schenström, O., Andersson, G., & Carlbring, P. (2014). Internet-based mindfulness treatment for anxiety disorders: A randomized controlled trial. *Behavior Therapy*, *45*(2), 241–253.

Bohus, M., Dyer, A. S., Priebe, K., Krüger, A., Kleindienst, N., Schmahl, C., ... Steil, R. (2013). Dialectical behaviour therapy for post-traumatic stress disorder after childhood sexual abuse in patients with and without borderline personality disorder: a randomised controlled trial. *Psychotherapy and Psychosomatics*, *82*(4), 221–233.

Bolton, P., Lee, C., Haroz, E. E., Murray, L., Dorsey, S., Robinson, C., … Bass., J. (2014). A Transdiagnostic Community-Based Mental Health Treatment for Comorbid Disorders: Development and Outcomes of a Randomized Controlled Trial among Burmese Refugees in Thailand. *PLoS Medicine*, *11*(11), e1001757.

Borkovec, T. D., & Ruscio, A. M. (2001). Psychotherapy for generalized anxiety disorder. *The Journal of Clinical Psychiatry*, *62*(Suppl11), 37–42.

Boswell, J. F., Farchione, T. J., Sauer-Zavala, S., Murray, H. W., Fortune, M. R., & Barlow, D. H. (2013). Anxiety sensitivity and interoceptive exposure: A transdiagnostic construct and change strategy. *Behavior Therapy*, *44*(3), 417–431.

Botella, C., Molinari, G., Fernández-Álvarez, J., Guillén, V., García-Palacios, A., Baños, R. M., & Tomás, J. M. (2018). Development and validation of the openness to the future scale: a prospective protective factor. *Health and Quality of Life Outcomes*, *16*(1), 72.

Brown, T. A., Campbell, L. A., Lehman, C. L., Grisham, J. R., & Mancill, R. B. (2001). Current and lifetime comorbidity of the DSM-IV anxiety and mood disorders in a large clinical sample. *Journal of Abnormal Psychology*, *110*(4), 585–599.

Brown, T. A., Chorpita, B. F., & Barlow, D. H. (1998). Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. *Journal of Abnormal Psychology*, *107*(2), 179–192.

Brown, T. A., & Barlow, D. H. (2009). A proposal for a dimensional classification system based on the shared features of the DSM-IV anxiety and mood disorders: implications for assessment and treatment. *Psychological Assessment*, *21*(3), 256–271.

Brown, T., & Barlow, D. (2009). A proposal for a dimensional classification system based on the shared features of the DSM-IV anxiety and mood disorders: Implications for assessment. *Psychological Assessment*, *21*(3), 256–271.

Bruce, S. E., Machan, J. T., Dyck, I., & Keller, M. B. (2001). Infrequency of

"pure" GAD: Impact of psychiatric comorbidity on clinical course. *Depression and Anxiety*, *14*(4), 219–225.

Bullis, J. R., Fortune, M. R., Farchione, T. J., & Barlow, D. H. (2014). A preliminary investigation of the long-term outcome of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders. *Comprehensive Psychiatry*, *55*(8), 1920–1927.

Bullis, J. R., Sauer-Zavala, S., Bentley, K. H., Thompson-Hollands, J., Carl, J. R., & Barlow, D. H. (2015). The unified protocol for transdiagnostic treatment of emotional disorders: Preliminary exploration of effectiveness for group delivery. *Behavior Modification*, *39*(2), 295–321.

Campbell-Sills, L., & Barlow, D. H. (2007). Incorporating Emotion Regulation into Conceptualizations and Treatments of Anxiety and Mood Disorders. In J.J. Gross (Ed.), *Handbook of emotion regulation* (pp. 542–559). New York, NY, US: Guilford Press.

Campbell-Sills, L., Ellard, K. K., & Barlow, D. H. (2014). Emotion regulation in anxiety disorders (pp. 393-412). In J. J. Gross (Ed.), *Handbook of emotion regulation*. New York, NY, US: Guilford Press.

Campos, D., Bretón-López, J., Botella, C., Mira, A., Castilla, D., Baños, R., & Quero, S. (2016). An Internet-based treatment for flying phobia (NO-FEAR Airlines): study protocol for a randomized controlled trial. *BMC Psychiatry*, *16*(1), 296.

Carl, J. R., Gallagher, M. W., & Barlow, D. H. (2018). Development and Preliminary Evaluation of a Positive Emotion Regulation Augmentation Module for Anxiety and Depression. *Behavior Therapy*, *49*(6), 939–950.

Carl, J. R., Gallagher, M. W., Sauer-Zavala, S. E., Bentley, K. H., & Barlow, D. H. (2014). A preliminary investigation of the effects of the unified protocol on temperament. *Comprehensive Psychiatry*, *55*(6), 1426–1434.

Carl, J. R., Soskin, D. P., Kerns, C., & Barlow, D. H. (2013). Positive emotion regulation in emotional disorders: A theoretical review. *Clinical Psychology Review*, *33*(3), 343–360.

Carlbring, P., Andersson, G., Cuijpers, P., Riper, H., & Hedman-Lagerlöf, E. (2018). Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: an updated systematic review and meta-analysis. *Cognitive Behaviour Therapy*, *47*(1), 1–18.

Cartwright-Hatton, S., Roberts, C., Chitsabesan, P., Fothergill, C., &

Harrington, R. (2004). Systematic review of the efficacy of cognitive behaviour therapies for childhood and adolescent anxiety disorders. *British Journal of Clinical Psychology*, *43*(4), 421–436.

Clark, D. A. (2009). Cognitive Behavioral Therapy for Anxiety and Depression: Possibilities and Limitations of a Transdiagnostic Perspective. *Cognitive Behaviour Therapy*, *38*(sup1), 29–34.

Clark, D. M., Layard, R., Smithies, R., Richards, D. A., Suckling, R., & Wright, B. (2009). Improving access to psychological therapy: Initial evaluation of two UK demonstration sites. *Behaviour Research and Therapy*, 47(11), 910–920.

Clark, L. A., & Watson, D. (1991). Tripartite model of anxiety and depression: psychometric evidence and taxonomic implications. *Journal of Abnormal Psychology*, *100*(3), 316–336.

Cohen, S., & Pressman, S. D. (2006). Positive Affect and Health. *Current Directions in Psychological Science*, *15*(3), 122–125.

Covin, R., Ouimet, A. J., Seeds, P. M., & Dozois, D. J. A. (2008). A meta-analysis of CBT for pathological worry among clients with GAD. *Journal of Anxiety Disorders*, *22*(1), 108–116.

Crawford, J. R., & Henry, J. D. (2004). The Positive and Negative Affect Schedule (PANAS): Construct validity, measurement properties and normative data in a large non-clinical sample. *British Journal of Clinical Psychology*, *43*(3), 245–265.

Cuijpers, P., Beekman, A. T. F., & Reynolds, C. F. (2012). Preventing Depression. *JAMA*, *307*(10), 1033.

Cuijpers, P., Berking, M., Andersson, G., Quigley, L., Kleiboer, A., & Dobson, K. S. (2013). A meta-analysis of cognitive-behavioural therapy for adult depression, alone and in comparison with other treatments. *The Canadian Journal of Psychiatry*, *58*(7), 376–385.

Cuijpers, P., & Smit, F. (2002). Excess mortality in depression: a meta-analysis of community studies. *Journal of Affective Disorders*, *72*(3), 227–236.

Cuijpers, P., van Straten, A., Andersson, G., & van Oppen, P. (2008). Psychotherapy for depression in adults: A meta-analysis of comparative outcome studies. *Journal of Consulting and Clinical Psychology*, *76*(6), 909–922.

Cuijpers, P., van Straten, A., & Warmerdam, L. (2007). Behavioral activation treatments of depression: A meta-analysis. *Clinical Psychology Review*, *27*(3), 318–326.

De Ornelas Maia, A. C. C., Nardi, A. E., & Cardoso, A. (2015). The

utilization of unified protocols in behavioral cognitive therapy in transdiagnostic group subjects: A clinical trial. *Journal of Affective Disorders*, *172*, 179–183.

Dear, B. F., Staples, L. G., Terides, M. D., Karin, E., Zou, J., Johnston, L., … Titov, N. (2015). Transdiagnostic versus disorder-specific and clinician-guided versus self-guided internet-delivered treatment for generalized anxiety disorder and comorbid disorders: A randomized controlled trial. *Journal of Anxiety Disorders*, *36*, 63–77.

Díaz-García, A., González-Robles, A., Fernández-Álvarez, J., García-Palacios, A., Baños, R. M., & Botella, C. (2017). Efficacy of a Transdiagnostic internet-based treatment for emotional disorders with a specific component to address positive affect: Study protocol for a randomized controlled trial. *BMC psychiatry*, *17*, 145.

Donker, T., Blankers, M., Hedman, E., Ljótsson, B., Petrie, K., & Christensen, H. (2015). Economic evaluations of Internet interventions for mental health: a systematic review. *Psychological Medicine*, *45*(16), 3357–3376.

Echeburúa, E., Salaberría, K., de Corral, P., & Cruz-Sáez, S. (2012). Funciones y ámbito de actuación del psicólogo clínico y del psicólogo general sanitario: Una primera reflexión. *Psicología Conductual*, *20*(2), 423–435.

Egan, S. J., Wade, T. D., & Shafran, R. (2011). Perfectionism as a transdiagnostic process: A clinical review. *Clinical Psychology Review*, *31*(2), 203–212.

Ehrenreich-May, J., Rosenfield, D., Queen, A. H., Kennedy, S. M., Remmes, C. S., & Barlow, D. H. (2017). An initial waitlist-controlled trial of the unified protocol for the treatment of emotional disorders in adolescents. *Journal of Anxiety Disorders*, *46*, 46–55.

Ehring, T., & Watkins, E. R. (2008). Repetitive Negative Thinking as a Transdiagnostic Process. *International Journal of Cognitive Therapy*, *1*(3), 192–205.

Eisner, L. R., Johnson, S. L., & Carver, C. S. (2009). Positive affect regulation in anxiety disorders. *Journal of Anxiety Disorders*, *23*(5), 645–649.

Ellard, K. K., Bernstein, E. E., Hearing, C., Baek, J. H., Sylvia, L. G., Nierenberg, A. A., … Deckersbach, T. (2017). Transdiagnostic treatment of bipolar disorder and comorbid anxiety using the Unified Protocol for Emotional Disorders: A pilot feasibility and acceptability trial. *Journal of Affective Disorders*, *219*, 209–221.

Ellard, K. K., Fairholme, C. P., Boisseau, C. L., Farchione, T. J., & Barlow,

D. H. (2010). Unified protocol for the transdiagnostic treatment of emotional disorders: Protocol development and initial outcome data. *Cognitive and Behavioral Practice*, *17*(1), 88–101.

Erickson, D. H., Janeck, A. S., & Tallman, K. (2007). A cognitive-behavioral group for patients with various anxiety disorders. *Psychiatric Services*, *58*(9), 1205–1211.

Fairburn, C. G., & Harrison, P. J. (2003). Eating disorders. *The Lancet*, *361*(9355), 407–416.

Farchione, T. J., Fairholme, C. P., Ellard, K. K., Boisseau, C. L., Thompson-Hollands, J., Carl, J. R., … Barlow, D. H. (2012). Unified protocol for transdiagnostic treatment of emotional disorders: A randomized controlled trial. *Behavior Therapy*, *43*(3), 666–678.

Fernández, A., Haro, J. M., Codony, M., Vilagut, G., Martínez-Alonso, M., Autonell, J., ... Alonso, J. (2006). Treatment adequacy of anxiety and depressive disorders: primary versus specialised care in Spain. *Journal of Affective Disorders*, *96*(1-2), 9–20.

Ferrari, A. J., Charlson, F. J., Norman, R. E., Patten, S. B., Freedman, G., Murray, C. J. L., … Whiteford, H. A. (2013). Burden of Depressive Disorders by Country, Sex, Age, and Year: Findings from the Global Burden of Disease Study 2010. *PLoS Medicine*, *10*(11), e1001547.

Garland, E. L., Fredrickson, B., Kring, A. M., Johnson, D. P., Meyer, P. S., & Penn, D. L. (2010). Upward spirals of positive emotions counter downward spirals of negativity: Insights from the broaden-and-build theory and affective neuroscience on the treatment of emotion dysfunctions and deficits in psychopathology. *Clinical Psychology Review*, *30*(7), 849–864.

González, S., González, M., García, M. C., Ruiz, M., Rojo, M. V., Sandoya, M., ... Caballero, D. P. (2014). Psychological treatments features and outcomes in Spanish public mental health centres. *International Journal of Psychology and Psychological Therapy*, *14*(1), 17–32

Griffiths, F., Lindenmeyer, A., Powell, J., Lowe, P., & Thorogood, M. (2006). Why are health care interventions delivered over the internet? A systematic review of the published literature. *Journal of Medical Internet Research*, *8*(2), e10.

Griffiths, K. M., & Christensen, H. (2007). Internet-based mental health programs: A powerful tool in the rural medical kit. *Australian Journal of Rural Health*, *15*(2), 81–87.

Gross, J. J. (1998). The emerging field of emotion regulation: An integrative review. *Review of General Psychology*, *2*, 271–299.

Gross, J. J., & John, O. P. (2003). Individual differences in two emotion regulation processes: implications for affect, relationships, and well-being. *Journal of Personality and Social Psychology*, *85*(2), 348–62.

Harvey, A. G., Watkins, E., Mansell, W., & Shafran, R. (2004). *Cognitive behavioural processes across psychological disorders : a transdiagnostic approach to research and treatment*. New York, NY, US: Oxford University Press.

Headey, B., Kelley, J., & Wearing, A. (1993). Dimensions of mental health: Life satisfaction, positive affect, anxiety and depression. *Social Indicators Research*, *29*(1), 63–82.

Hendriks, S. M., Spijker, J., Licht, C. M. M., Beekman, A. T. F., Hardeveld, F., de Graaf, R., … Penninx, B. W. J. H. (2014). Disability in anxiety disorders. *Journal of Affective Disorders*, *166*, 227–233.

Hofmann, S. G., & Smits, J. A. J. (2008). Cognitive-behavioral therapy for adult anxiety disorders: a meta-analysis of randomized placebo-controlled trials. *The Journal of Clinical Psychiatry*, *69*(4), 621–632.

Hofmeijer-Sevink, M. K., Batelaan, N. M., van Megen, H. J. G. M., Penninx, B. W., Cath, D. C., van den Hout, M. A., & van Balkom, A. J. L. M. (2012). Clinical relevance of comorbidity in anxiety disorders: A report from the Netherlands Study of Depression and Anxiety (NESDA). *Journal of Affective Disorders*, *137*(1–3), 106–112.

Hollon, S. D., & Ponniah, K. (2010). A review of empirically supported psychological therapies for mood disorders in adults. *Depression and Anxiety*, *27*(10), 891–932.

Ito, M., Horikoshi, M., Kato, N., Oe, Y., Fujisato, H., Nakajima, S., ... Usuki, M. (2016). Transdiagnostic and transcultural: pilot study of unified protocol for depressive and anxiety disorders in Japan. *Behavior Therapy*, *47*(3), 416–430.

Ito, M., Okumura, Y., Horikoshi, M., Kato, N., Oe, Y., Miyamae, M., ... Ono, Y. (2016). Japan Unified Protocol Clinical Trial for Depressive and Anxiety Disorders (JUNP study): study protocol for a randomized controlled trial. *BMC psychiatry*, *16*(1), 71.

Karyotaki, E., Riper, H., Twisk, J., Hoogendoorn, A., Kleiboer, A., Mira, A., … Cuijpers, P. (2017). Efficacy of Self-guided Internet-Based Cognitive Behavioral Therapy in the Treatment of Depressive Symptoms. *JAMA Psychiatry*, *74*(4), 351–359.

Kazdin, A. E., & Blase, S. L. (2011). Rebooting Psychotherapy Research and Practice to Reduce the Burden of Mental Illness. *Perspectives on Psychological Science*, *6*(1), 21–37.

Kazdin, A. E. (2015). Technology-based interventions and reducing the burdens of mental illness: Perspectives and comments on the special series. *Cognitive and Behavioral Practice*, *22*(3), 359–366.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime Prevalence and Age-of-Onset Distributions of. *Archives of General Psychiatry*, *62*, 593–602.

Kessler, R. C., Chiu, W. T., Demler, O., Merikangas, K. R., & Walters, E. E. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, *62*(6), 617–627.

Kobau, R., Seligman, M. E. P., Peterson, C., Diener, E., Zack, M. M., Chapman, D., & Thompson, W. (2011). Mental health promotion in public health: perspectives and strategies from positive psychology. *American Journal of Public Health*, *101*(8), e1–9.

Kohn, R., Saxena, S., Levav, I., & Saraceno, B. (2004). The treatment gap in mental health care. *Bulletin of the World Health Organization*, *82*, 858–866.

Kotov, R., Gamez, W., Schmidt, F., & Watson, D. (2010). Linking "big" personality traits to anxiety, depressive, and substance use disorders: A meta-analysis. *Psychological Bulletin*, *136*(5), 768–821.

Kroenke, K., Spitzer, R. L., Williams, J. B. W., Monahan, P. O., & Löwe, B. (2007). Anxiety Disorders in Primary Care: Prevalence, Impairment, Comorbidity, and Detection. *Annals of Internal Medicine*, *146*(5), 317–325.

Laposa, J. M., Mancuso, E., Abraham, G., & Loli-Dano, L. (2017). Unified protocol transdiagnostic treatment in group format: A preliminary investigation with anxious individuals. *Behavior Modification*, *41*(2), 253–268.

Linehan, M. M. (1993). *Skills training manual for treating borderline personality disorder. Diagnosis and treatment of mental disorders.* New York, NY: Guilford Press.

Livingstone, K. M., & Srivastava, S. (2012). Up-regulating positive emotions in everyday life: Strategies, individual differences, and associations with positive emotion and well-being. *Journal of Research in Personality*, *46*(5), 504–516.

Luthar, S. S., Cicchetti, D., & Becker, B. (2000). The Construct of Resilience: A Critical Evaluation and Guidelines for Future Work. *Child Development*, *71*(3), 543–562.

Lyubomirsky, S., King, L., & Diener, E. (2005). The Benefits of Frequent

Positive Affect: Does Happiness Lead to Success? *Psychological Bulletin*, *131*(6), 803–855.

Mahoney, A. E. J., & McEvoy, P. M. (2012). A transdiagnostic examination of intolerance of uncertainty across anxiety and depressive disorders. *Cognitive Behaviour Therapy*, *41*(3), 212–222.

Mansell, W., Harvey, A., Watkins, E. R., & Shafran, R. (2008). Cognitive Behavioral Processes Across Psychological Disorders: A Review of the Utility and Validity of the Transdiagnostic Approach. *International Journal of Cognitive Therapy*, *1*(3), 181–191.

Mansell, W., Harvey, A., Watkins, E., & Shafran, R. (2009). Conceptual foundations of the transdiagnostic approach to CBT. *Journal of Cognitive Psychotherapy: An International Quarterly*, *231*, 13–27.

Martín-Jurado, A., De La Gándara Martín, J. J., Carbajo, S. C., Hernández, A. M., & Sánchez-Hernández, J. (2012). Análisis de concordancia de las derivaciones de Atención Primaria a Salud Mental. *SEMERGEN-Medicina de Familia*, *38*(6), 354–359.

Mayo-Wilson, E., Dias, S., Mavranezouli, I., Kew, K., Clark, D. M., Ades, A. E., & Pilling, S. (2014). Psychological and pharmacological interventions for social anxiety disorder in adults: a systematic review and network meta-analysis. *The Lancet Psychiatry*, *1*(5), 368–376.

McEvoy, P. M., Nathan, P., & Norton, P. J. (2009). Efficacy of Transdiagnostic Treatments: A Review of Published Outcome Studies and Future Research Directions. *Journal of Cognitive Psychotherapy: An International Quarterly*, *23*(1).

McHugh, R. K., & Barlow, D. H. (2010). The dissemination and implementation of evidence-based psychological treatments: A review of current efforts. *American Psychologist*, *65*(2), 73–84.

McHugh, R. K., Murray, H. W., & Barlow, D. H. (2009). Balancing fidelity and adaptation in the dissemination of empirically-supported treatments: The promise of transdiagnostic interventions. *Behavior Research and Therapy*, *47*(11), 946–953.

McLean, C. P., Asnaani, A., Litz, B. T., & Hofmann, S. G. (2011). Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. *Journal of Psychiatric Research*, *45*(8), 1027–1035.

McManus, F., Shafran, R., & Cooper, Z. (2010). What does a transdiagnostic approach have to offer the treatment of anxiety disorders? *The British Journal of Clinical Psychology*, *49*(4), 491–505.

Meidlinger, P. C., Hope, D. A. (2017). The new transdiagnostic cognitive behavioral treatments: Commentary for clinicians and clinical researchers. *Journal of Anxiety Disorders*, *46*, 101–109.

Mendlowicz, M. V., & Stein, M. D. (2000). Quality of Life in Individuals with Anxiety Disorders. *American Journal of Psychiatry*, *157*(5), 669–682.

Mira, A., Bretón-López, J., García-Palacios, A., Quero, S., Baños, R. M., & Botella, C. (2017). An Internet-based program for depressive symptoms using human and automated support: a randomized controlled trial. *Neuropsychiatric Disease and Treatment*, *13*, 987–1006.

Mitte, K. (2005). A meta-analysis of the efficacy of psycho- and pharmacotherapy in panic disorder with and without agoraphobia. *Journal of Affective Disorders*, *88*(1), 27–45.

Mohsenabadi, H., Zanjani, Z., Shabani, M. J., & Arj, A. (2018). A randomized clinical trial of the Unified Protocol for Transdiagnostic treatment of emotional and gastrointestinal symptoms in patients with irritable bowel syndrome: evaluating efficacy and mechanism of change. *Journal of Psychosomatic Research*, *113*, 8–15.

Montero-Marín, J., Araya, R., Pérez-Yus, M. C., Mayoral, F., Gili, M., Botella, C. ... García-Campayo, J. (2016). An internet-based intervention for depression in primary care in spain: A randomized controlled trial. *Journal of Medical Internet Research, 18*(8), e231.

Montilla, J. F., González, C., Retolaza, A., Dueñas, C., & Alameda, J. (2002). Uso de servicios ambulatorios de salud mental en España. Consumo de recursos en el primer año de asistencia a pacientes nuevos. *Revista de la Asociación Española de Neuropsiquiatría, 84, 25*–47.

Murray, L. K., Dorsey, S., Haroz, E., Lee, C., Alsiary, M. M., Haydary, A., ... Bolton, P. (2014). A common elements treatment approach for adult mental health problems in low-and middle-income countries. *Cognitive and Behavioral Practice*, *21*(2), 111–123.

Musiat, P., & Tarrier, N. (2014). Collateral outcomes in e-mental health: a systematic review of the evidence for added benefits of computerized cognitive behavior therapy interventions for mental health. *Psychological Medicine*, *44*(15), 3137–3150.

Nathan, P. E., & Gorman, J. M. (Eds.). *A guide to treatments that work*. New York, NY, US: Oxford University Press.

Neacsiu, A. D., Bohus, M., & Linehan, M. M. (2014). Dialectical behavior therapy: An intervention for emotion dysregulation (pp. 491-508). In

J. J. Gross (Ed.), *Handbook of emotion regulation*. New York, NY, US: Guilford Press.

Neacsiu, A. D., Eberle, J. W., Kramer, R., Wiesmann, T., & Linehan, M. M. (2014). Dialectical behavior therapy skills for transdiagnostic emotion dysregulation: A pilot randomized controlled trial. *Behaviour Research and Therapy*, *59*, 40–51.

Neacsiu, A. D., Herr, N. R., Fang, C. M., Rodriguez, M. A., & Rosenthal, M. Z. (2015). Identity disturbance and problems with emotion regulation are related constructs across diagnoses. *Journal of Clinical Psychology*, *71*(4), 346–361.

Newby, J. M., McKinnon, A., Kuyken, W., Gilbody, S., & Dalgleish, T. (2015). Systematic review and meta-analysis of transdiagnostic psychological treatments for anxiety and depressive disorders in adulthood. *Clinical Psychology Review*, *40*, 91–110.

Newby, J. M., Twomey, C., Yuan Li, S. S., & Andrews, G. (2016). Transdiagnostic computerised cognitive behavioural therapy for depression and anxiety: A systematic review and meta-analysis. *Journal of Affective Disorders*, *199*, 30–41.

Nordgren, L. B., Hedman, E., Etienne, J., Bodin, J., Kadowaki, Å., Eriksson, S., … Carlbring, P. (2014). Effectiveness and cost-effectiveness of individually tailored Internet-delivered cognitive behavior therapy for anxiety disorders in a primary care population: A randomized controlled trial. *Behaviour Research and Therapy*, *59*, 1–11.

Norton, P. (2017). Transdiagnostic approaches to the understanding and treatment of anxiety and related disorders. *Journal of Anxiety Disorders*, *46*, 1–3.

Norton, P. J., & Hope, D. A. (2005). Preliminary evaluation of a broad-spectrum cognitive-behavioral group therapy for anxiety. *Journal of Behavior Therapy and Experimental Psychiatry*, *36*(2), 79–97.

Olatunji, B. O., Cisler, J. M., & Deacon, B. J. (2010). Efficacy of cognitive behavioral therapy for anxiety disorders: a review of meta-analytic findings. *The Psychiatric Clinics of North America*, *33*(3), 557–577.

Olatunji, B. O., Cisler, J. M., & Tolin, D. F. (2007). Quality of life in the anxiety disorders: A meta-analytic review. *Clinical Psychology Review*, *27*(5), 572–581.

Osma, J., Suso-Ribera, C., García-Palacios, A., Crespo-Delgado, E., Robert-Flor, C., Sánchez-Guerrero, A., ... Torres-Alfosea, M. Á. (2018). Efficacy of the unified protocol for the treatment of emotional disorders in the Spanish public mental health system

using a group format: study protocol for a multicenter, randomized, non-inferiority controlled trial. *Health and Quality of Life Outcomes*, *16*(1), 46.

Öst, L.G., Havnen, A., Hansen, B., & Kvale, G. (2015). Cognitive behavioral treatments of obsessive-compulsive disorder. A systematic review and meta-analysis of studies published 1993–2014. *Clinical Psychology Review*, *40*, 156–169.

Palacios, A. J., Fraga, M., Hoyas, B., Laíz, N., & Rodríguez, N. (2006). Los psicólogos clínicos en el sistema nacional de salud. *Revista de Psicopatología y Psicología Clínica*, *11*(1), 51–61.

Palmqvist, B., Carlbring, P., & Andersson, G. (2007). Internet-delivered treatments with or without therapist input: does the therapist factor have implications for efficacy and cost? *Expert Review of Pharmacoeconomics & Outcomes Research*, *7*(3), 291–297.

Parés-Badell, O., Barbaglia, G., Jerinic, P., Gustavsson, A., Salvador-Carulla, L., & Alonso, J. (2014). Cost of Disorders of the Brain in Spain. *PLoS ONE*, *9*(8), e105471.

Păsărelu, C. R., Andersson, G., Bergman Nordgren, L., & Dobrean, A. (2017). Internet-delivered transdiagnostic and tailored cognitive behavioral therapy for anxiety and depression: a systematic review and meta-analysis of randomized controlled trials. *Cognitive Behaviour Therapy*, *46*(1), 1–28.

Pearl, S. B., & Norton, P. J. (2017). Transdiagnostic versus diagnosis specific cognitive behavioural therapies for anxiety: A meta-analysis. *Journal of Anxiety Disorders*, *46*, 11–24.

Rachyla, I., Pérez-Ara, M., Molés, M., Campos, D., Mira, A., Botella, C., & Quero, S. (2018). An internet-based intervention for adjustment disorder (TAO): study protocol for a randomized controlled trial. *BMC psychiatry*, *18*(1), 161.

Rapaport, M. H., Clary, C., Fayyad, R., & Endicott, J. (2005). Quality-of-Life Impairment in Depressive and Anxiety Disorders. *American Journal of Psychiatry*, *162*(6), 1171–1178.

Reinholt, N., & Krogh, J. (2014). Efficacy of Transdiagnostic Cognitive Behaviour Therapy for Anxiety Disorders: A Systematic Review and Meta-Analysis of Published Outcome Studies. *Cognitive Behaviour Therapy*, *43*(3), 171–184.

Richards, D. (2011). Prevalence and clinical course of depression: A review. *Clinical Psychology Review*, *31*(7), 1117–1125.

Richards, D., & Richardson, T. (2012). Computer-based psychological treatments for depression: a systematic review and meta-analysis.

Clinical Psychology Review, *32*(4), 329–42.

Roca, M., Gili, M., Garcia-Garcia, M., Salva, J., Vives, M., Campayo, J. G., & Comas, A. (2009). Prevalence and comorbidity of common mental disorders in primary care. *Journal of Affective Disorders*, *119*(1-3), 52–58.

Rosellini, A. J., Lawrence, A. E., Meyer, J. F., & Brown, T. A. (2010). The effects of extraverted temperament on agoraphobia in panic disorder. *Journal of Abnormal Psychology*, *119*(2), 420–426.

Rowe, G., Hirsh, J. B., & Anderson, A. K. (2007). Positive affect increases the breadth of attentional selection. *Proceedings of the National Academy of Sciences*, *104*(1), 383–388.

Rutter, M. (1985). Resilience in the face of adversity: Protective factors and resistance to psychiatric disorder. *The British Journal of Psychiatry*, *147*(6), 598–611.

Sandín, B. (2012). Transdiagnóstico y psicología clínica: Introducción al número monográfico. *Revista de Psicopatología y Psicología Clínica,* 17(3), 181–184.

Sandín, B., Chorot, P., Lostao, L., Joiner, T. E., Santed, M. A., & Valiente, R. M. (1999). Escalas PANAS de afecto positivo y negativo: Validacion factorial y convergencia transcultural. *Clínica y Salud*, *16*(2), 121–142.

Sauer-Zavala, S., Gutner, C. A., Farchione, T. J., Boettcher, H. T., Bullis, J. R., & Barlow, D. H. (2017). Current Definitions of "Transdiagnostic" in Treatment Development: A Search for Consensus. *Behavior Therapy*, *48*(1), 128–138.

Seligman, M. E., & Csikszentmihalyi, M. (2000). Positive psychology: An introduction. *American Psychologist, 55*(1), 5–14.

Schmidt, N. B., Buckner, J. D., Pusser, A., Woolaway-Bickel, K., Preston, J. L., & Norr, A. (2012). Randomized Controlled Trial of False Safety Behavior Elimination Therapy: A Unified Cognitive Behavioral Treatment for Anxiety Psychopathology. *Behavior Therapy*, *43*(3), 518–532.

Shankman, S. A., Nelson, B. D., Harrow, M., & Faull, R. (2010). Does physical anhedonia play a role in depression? A 20-year longitudinal study. *Journal of Affective Disorders*, *120*(1–3), 170–176.

Sherbourne, C. D., & Wells, K. B. (1997). Course of depression in patients with comorbid anxiety disorders. *Journal of Affective Disorders*, *43*(3), 245–250.

Sloan, E., Hall, K., Moulding, R., Bryce, S., Mildred, H., & Staiger, P. K. (2017). Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: A systematic review. *Clinical Psychology Review*, *57*, 141–163.

Southwick, S. M., Vythilingam, M., & Charney, D. S. (2005). The Psychobiology of Depression and Resilience to Stress: Implications for Prevention and Treatment. *Annual Review of Clinical Psychology*, *1*(1), 255–291.

Spek, V., Cuijpers, P., Nyklícek, I., Riper, H., Keyzer, J., & Pop, V. (2007). Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis. *Psychological Medicine*, *37*(3), 319–328.

Spurgeon, J. A., & Wright, J. H. (2010). Computer-Assisted Cognitive-Behavioral Therapy. *Current Psychiatry Reports*, *12*(6), 547–552.

Steel, Z., Marnane, C., Iranpour, C., Chey, T., Jackson, J. W., Patel, V., & Silove, D. (2014). The global prevalence of common mental disorders: a systematic review and meta-analysis 1980–2013. *International Journal of Epidemiology*, *43*(2), 476–493.

Steele, S. J., Farchione, T. J., Cassiello-Robbins, C., Ametaj, A., Sbi, S., Sauer-Zavala, S., & Barlow, D. H. (2018). Efficacy of the Unified Protocol for transdiagnostic treatment of comorbid psychopathology accompanying emotional disorders compared to treatments targeting single disorders. *Journal of Psychiatric Research*, *104*, 211–216.

Taylor, S. E., & Brown, J. D. (1988). Illusion and well-being: A social psychological perspective on mental health. *Psychological Bulletin, 103*(2), 193–210.

Titov, N., Dear, B. F., Schwencke, G., Andrews, G., Johnston, L., Craske, M. G., & McEvoy, P. (2011). Transdiagnostic internet treatment for anxiety and depression: A randomised controlled trial. *Behaviour Research and Therapy*, *49*(8), 441–452.

Tugade, M. M., & Fredrickson, B. L. (2007). Regulation of Positive Emotions: Emotion Regulation Strategies that Promote Resilience. *Journal of Happiness Studies*, *8*(3), 311–333.

van Ballegooijen, W., Cuijpers, P., van Straten, A., Karyotaki, E., Andersson, G., Smit, J. H., & Riper, H. (2014). Adherence to Internet-Based and Face-to-Face Cognitive Behavioural Therapy for Depression: A Meta-Analysis. *PLoS ONE*, *9*(7), e100674.

Wang, P. S., Aguilar-Gaxiola, S., Alonso, J., Angermeyer, M. C., Borges, G., Bromet, E. J., … Wells, J. E. (2007). Use of mental health services for anxiety, mood, and substance disorders in 17 countries in the WHO world mental health surveys. *The Lancet*, *370*(9590), 841–850.

Warmerdam, L., Van Straten, A., Twisk, J., Riper, H., & Cuijpers, P. (2008). Internet-based treatment for adults with depressive symptoms: Randomized controlled trial. *Journal of Medical Internet Research*, *10*(4), e44.

Werner-Seidler, A., Banks, R., Dunn, B. D., & Moulds, M. L. (2013). An investigation of the relationship between positive affect regulation and depression. *Behaviour Research and Therapy*, *51*(1), 46–56.

Wetherell, J. L., Ayers, C. R., Sorrell, J. T., Thorp, S. R., Nuevo, R., Belding, W., … Patterson, T. L. (2009). Modular Psychotherapy for Anxiety in Older Primary Care Patients. *The American Journal of Geriatric Psychiatry*, *17*(6), 483–492.

Chapter 2. Comorbidity and diagnosis distribution in transdiagnostic treatments for emotional disorders: A systematic review of randomized controlled trials

This chapter has been published as:

González-Robles, A., Díaz-García, A., Miguel, C., García-Palacios, A., & Botella, C. (2018). Comorbidity and diagnosis distribution in transdiagnostic treatments for emotional disorders: A systematic review of randomized controlled trials. *PLoS ONE*, *13*(11), e0207396.

Comorbidity and diagnosis distribution in transdiagnostic treatments for emotional disorders: A systematic review of randomized controlled trials

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Abstract

The advantages of transdiagnostic protocols for emotional disorders (ED) (anxiety and depression) include the ability to treat multiple psychological disorders using the same treatment protocol, and the capacity to better address comorbidity. Comorbidity in ED has been associated with higher rates of severity, functional impairment, and chronicity. However, no attempts have been made in the literature to systematically review whether these studies include assessments to evaluate the treatment response in comorbid diagnoses, in addition to the principal diagnosis. Moreover, transdiagnostic treatments have been developed for a range of ED, but to date no study has analyzed the real distribution of diagnoses in these studies. The current study aimed to analyze: a) whether treatment response in comorbidity is evaluated in transdiagnostic treatments for ED; b) what diagnoses are targeted in transdiagnostic treatments for ED; and c) the real distribution of the diagnoses at baseline in these studies. A systematic search of the literature was conducted in PsycINFO, PubMed, EMBASE, and the Cochrane Library. Fifty-two randomized controlled trials were identified, with a total of 7007 adult participants. The results showed that, although most of the studies reported data on comorbidity at baseline, only 40% of them examined the effects of the intervention on the comorbid disorders. The most commonly targeted diagnoses in transdiagnostic protocols were panic/agoraphobia, generalized anxiety, social anxiety, and depression. Other disorders, such as obsessive-compulsive disorder, posttraumatic stress disorder, and anxiety/depression not otherwise specified, were marginally included in these studies. Regarding the distribution of diagnoses at baseline, generalized anxiety, panic/agoraphobia, social anxiety, and depression were the most frequently observed, whereas depression not otherwise specified was the least represented. The results highlight the importance

of assessing comorbidity in addition to the principal diagnoses in transdiagnostic treatments, in order to draw conclusions about the true potential of these interventions to improve comorbid symptoms. Implications of the current study and directions for future research are discussed.

Introduction

Emotional disorders (ED) (depression and anxiety disorders) are common mental health conditions and one of the main causes of suffering and impairment worldwide [1, 2]. In the past few decades, a large number of disorder-specific cognitive-behavioral treatments (CBT) have been developed for ED and tested in clinical trials, with evidence found for their efficacy and effectiveness [3-7]. However, although disorder-specific treatment protocols have been shown to work effectively, there are still some barriers related to these protocols. One of them stems from the high comorbidity rates observed in ED, ranging between 40 and 80% for these disorders [8, 9].

Comorbidity in ED has been associated with greater severity and impairment [8], worse quality of life [10], and higher chronicity rates [11]. The literature has proposed different ways to manage comorbidity, such as combinations of treatments or the sequential application of treatments [12]. Another strategy involves applying a protocol to target one of the disorders and expecting an impact on the comorbid disorders. Nevertheless, the effective use of these strategies is not well supported by the existing empirical evidence (for a review of the evidence, see McManus et al., 2010) [12]. A more recent development to deal with comorbidity is the application of treatments based on a transdiagnostic perspective. Although the term transdiagnostic has been employed to refer to different treatment approaches [13], the common denominator of these treatments is that one protocol is applied to address various psychological disorders [14]. Research on transdiagnostic treatments for ED has increased in recent years [15-17], with a noteworthy rise in the number of trials assessing the efficacy and effectiveness of transdiagnostic treatments in the past 15 years [18-27]. Several advantages have been attributed to transdiagnostic treatments. The first and most important is the ability to address multiple ED using the same treatment protocol. Thus, these disorders can be treated in a more cost-effective way because clinicians only have to be trained in one protocol that addresses various psychological disorders [13, 15]. Second, training clinicians in one treatment approach, rather than in a different protocol for each ED, may facilitate the dissemination of evidence-based treatments for these specific problems [15]. This approach could be of particular interest in ecological settings such as public services, where clinicians have to treat patients

with diagnostically heterogeneous presentations, which makes the adequate selection of protocols and techniques difficult [13]. Third, another important advantage is that comorbid mental disorders can be more adequately targeted because these protocols usually focus on what these disorders have in common, rather than on disorder-specific symptom variations [17, 22, 26, 28]. For instance, extensive research shows the key role played by neuroticism in the onset and maintenance of both anxiety and depressive disorders, indicating its relevance in research and clinical practice [15-17, 29, 30]. In this regard, the "shared mechanisms approach", described by Sauer-Zavala et al. [13], is based on the assumption that there are core mechanisms underlying both anxiety and depressive disorders, and that, consequently, in order for the specific symptoms to improve (e.g. symptoms of panic, symptoms of social anxiety, and so on), treatment should focus on addressing these common processes. Based on this approach, some authors have argued that a transdiagnostic treatment may be appropriate for a wide range of disorders, including all the anxiety and unipolar mood disorders, and even somatoform and dissociative disorders [15,22], while facilitating the treatment of patients with comorbidity (12). There are, nevertheless, other transdiagnostic approaches to the treatment of ED (including the treatment of comorbid presentations), such as individually-tailored CBT [20] or "third wave" therapies (e.g. mindfulness and acceptance and commitment therapy) [31-33]. Finally, transdiagnostic treatments also have the potential to address "not otherwise specified" (NOS) diagnoses for which there are no evidence-based treatments in the literature (e.g. anxiety NOS) [13].

There is a growing body of literature on the efficacy and effectiveness of transdiagnostic treatments for ED. To date, various meta-analyses have shown the efficacy of these treatments in adults with ED, compared to control conditions, on measures of overall anxiety [34-38] and disorder-specific anxiety [38], as well as depression [35-38] and quality of life [36-38]. Moreover, a meta-analysis of the efficacy of these protocols, compared to disorder-specific CBT, found no significant differences in the efficacy of these two treatment approaches on anxiety outcomes [39]. Nevertheless, no prior study has examined how comorbidity is reported and assessed in trials analyzing transdiagnostic protocols, despite the importance of comorbidity in aspects such as the clinical severity, the clinical course, and the rate of relapse in patients with comorbid anxiety and depressive disorders [8, 10, 11]. Some studies on transdiagnostic treatments for ED have assessed treatment effects on comorbid symptoms, as well as the symptoms primarily targeted in the study. For instance, some studies include self-reported measures to assess a range of comorbid disorder-specific symptoms [21, 40, 41], and

others assess the impact of the intervention in terms of the number of comorbid disorders, in addition to the number of principal diagnoses [22]. However, this aspect has not yet been systematically analyzed in the literature on transdiagnostic treatments for ED.

Regarding the types of diagnoses targeted by transdiagnostic treatments, the transdiagnostic treatments published to date may range from those targeting only two disorders [42-44] to those addressing a larger number of ED [45-47]. Moreover, transdiagnostic treatments may focus on anxiety disorders alone [48-50], or anxiety disorders along with depressive disorders [51-53]. There is, therefore, great disparity in the types and frequencies of anxiety and depressive disorders targeted in transdiagnostic treatments. However, to our knowledge, the real distribution of specific diagnoses in these interventions, i.e. the classes of disorders and the most frequent and infrequent disorders targeted in transdiagnostic treatments for ED, has not yet been analyzed.

Taking all this into consideration, a systematic review was conducted to answer the following research questions: a) Are comorbid disorders evaluated in transdiagnostic treatments for emotional disorders? b) What diagnoses are targeted in transdiagnostic treatments for emotional disorders? and c) What is the real distribution of the diagnoses at baseline in transdiagnostic treatments for emotional disorders?

Methods

Search strategy, data extraction, and coding

A systematic search of the peer-reviewed literature was conducted through the following databases: PsycINFO, PubMed, EMBASE and the Cochrane Register of Controlled Trials. The following terms were combined to conduct the search: “transdiagnostic”, “unified”, “mixed anxiety and depression”, “mixed depression and anxiety”, “heterogeneous” “depression”, “anxiety”. The deadline for inclusion of studies was February 6th (2018) (with no limits applied for year of publication). The systematic review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO, CRD42018088138). Studies were included based on the following eligibility criteria:

a) The study was a randomized controlled trial (RCT) that was compared to one of the following conditions: a waiting list control condition, placebo, attention control condition, active control condition (i.e. other treatment), and care as usual/treatment as usual control condition.
b) The study was written in English.

c) Participants were adults (18 years old and older).
d) Participants had at least a principal diagnosis of an anxiety disorder or a score above a cutoff point on an anxiety self-report scale, and/or a principal diagnosis of a depressive disorder or a score above a cutoff point on a depression self-report scale.
e) The study evaluated a transdiagnostic treatment for anxiety disorders and/or depression (i.e. unipolar mood disorders, anxiety disorders, posttraumatic stress disorder, and obsessive-compulsive disorder). To be included in the systematic review, the intervention had to target at least two different anxiety disorders or an anxiety disorder in addition to a depressive disorder.

Two assessors (AG-R and AD-G) conducted the review and selection of studies independently. The final selection of the included studies was supervised by a third expert evaluator (CB).

The following variables were included: a) study (authors and year of publication); b) country; c) aims of the study; d) hypotheses (when available); e) setting (e.g. community, primary care) and delivery format (e.g. Internet, face-to-face, individual, group); f) inclusion criteria regarding the types of diagnoses or symptoms targeted ("or" when the participants had to have at least one of the disorders, and "+" when the participants had to have both disorders); g) groups (sample size); percentage of females; and i) the distribution of each type of diagnosis at baseline. In order to evaluate the data on comorbidity, three dichotomous variables (yes/no) were created and added to the table: a) whether a principal diagnostic or symptom complaint was reported (e.g. main complaint of generalized anxiety symptoms); b) whether comorbid disorders and/or symptoms were reported. To belong to this category, the study had to report at least the proportion of patients presenting comorbid disorders or symptoms (e.g. the number of patients with one comorbid disorder, two comorbid disorders, and so on); and c) whether treatment response on comorbid disorders/symptoms was evaluated, i.e. a diagnosis made using a diagnostic interview or the severity of the disorder or symptoms through scales. All the aforementioned variables were extracted and coded independently by AG-R and AD-G, and disagreements were solved by discussion with a third author (CB).

Definition of emotional disorders included in the study

ED were considered for this study following the criteria of the Diagnostic and Statistical Manual of mental disorders, 4th edition (DSM-IV-TR) [54] and the definitions of these disorders adopted by previous authors (15), namely, unipolar mood disorders and anxiety disorders. Unipolar mood disorders included major depressive disorder (MDD),

dysthymic disorder (D), and depression not otherwise specified (Depression NOS), whereas anxiety disorders included generalized anxiety disorder (GAD), panic disorder with or without agoraphobia (PD/AG), social anxiety disorder (SAD), posttraumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), specific phobia (SP), and anxiety disorder not otherwise specified (Anxiety NOS). Although the classification of some of these disorders has changed with the publication of the DSM-5 [55] (i.e. PTSD and OCD are no longer considered anxiety disorders), the DSM-IV-TR was followed because most of the studies analyzed had recruited participants based on this diagnostic manual.

Quality assessment

The quality of the included studies was assessed using four items from the Cochrane Collaboration Risk of bias tool [56], which estimates potential bias in randomized controlled trials, including the following domains: random sequence generation, allocation concealment, blinding of outcome assessment (if applicable), and handling of incomplete outcome data. Each item on the tool was rated as low, high, or, in the case of insufficient information, unclear risk. This process was conducted by two independent researchers (AG-R and AD-G). Disagreements were resolved through discussion and, when necessary, by asking a senior researcher (CB).

Results

Selection and inclusion of studies

The study selection process is presented in the PRISMA flowchart (Figure 1). A total of 1881 studies were identified through database searches (Pubmed = 367; PsycINFO = 327; Embase = 510; Cochrane Library = 677), and 23 additional records were identified through other sources (i.e. meta-analyses about the efficacy of transdiagnostic treatments for anxiety and depression). After removing duplicates, 1103 records were screened based on title and abstract. Of them, 128 full-articles were assessed for eligibility, of which 52 were selected for final inclusion in the systematic review.

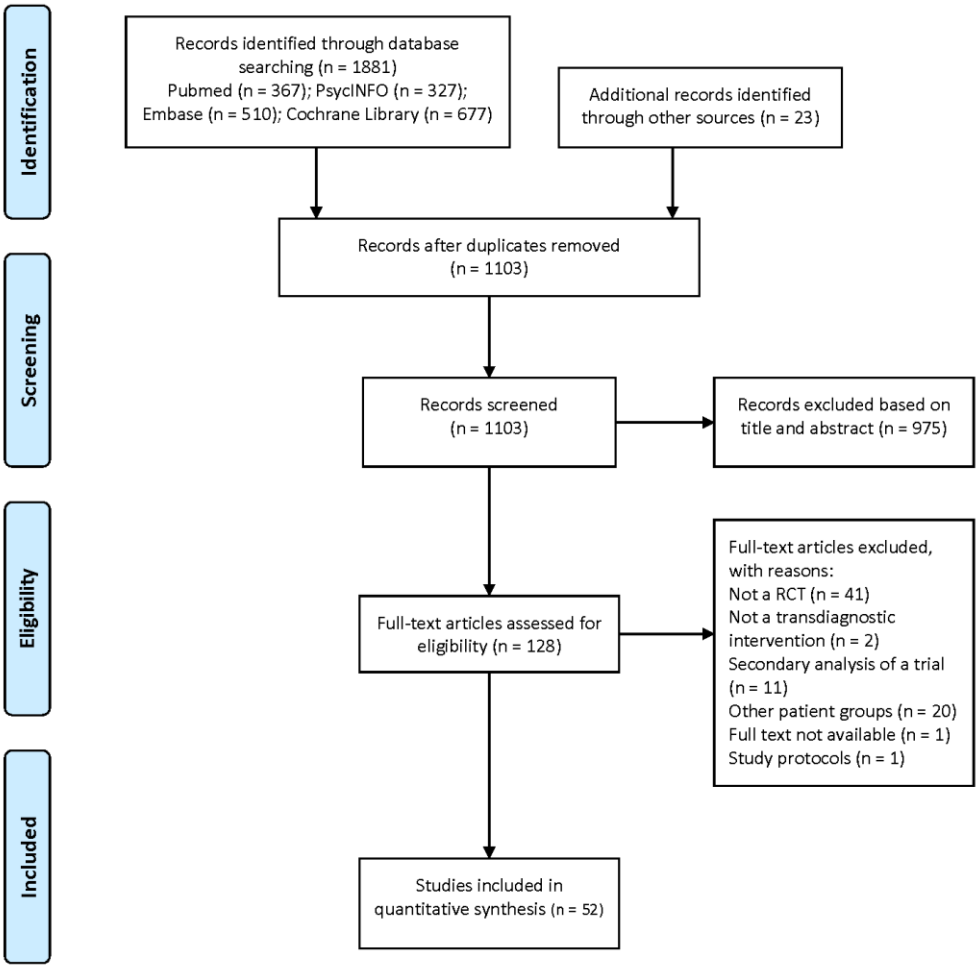

Figure 1. PRISMA flowchart

Characteristics of included studies

Relevant characteristics of the included studies are shown in Table 1. All the studies were randomized controlled trials with a total of 7007 participants. Most of the studies were conducted in the United States (n = 19, 37%), Australia (n = 12, 23%), Sweden (n = 6, 12%), and the United Kingdom (n = 5, 10%). The most common setting was the community (37 studies, 71%), followed by primary care (6 studies, 12%), specialized care (4 studies, 8%), community/primary care (3 studies, 6%) [57-59], and university students (2 studies, 4%) [60, 61]. Regarding the delivery format (i.e. face-to-face vs. web-based/computerized; individual vs. group), 24 treatments were delivered face-to-face (46%), 23 were Internet-based (44%), 4 were computerized (8%) [25, 62-64], and 1 was delivered by telephone (2%) [58]. Of the 52 studies, 38 were delivered in an individual format (73%), whereas 13 were delivered in a group format (25%), and one combined individual and group formats (2%) [65]. Regarding the control conditions, 21 studies used an active control condition (of which 8

were disorder-specific treatments), 19 studies used a waiting list control, 8 employed a care as usual/treatment as usual condition, 4 used an attention control condition [20, 64, 66, 67], and 1 employed a placebo control condition [50]. Finally, only 1 cost-effectiveness study was identified [67].

Table 1. Characteristics of included studies

Study	Ctry	Aims	Hypotheses	Setting & Delivery format	Targeted diagnoses (inclusion criteria)	Groups (n)	Age	% female	Diagnoses (distribution) at baseline	Principal diagnosis reported	Comorb reported	Comorb assessed
Arch et al., 2012 [31]	US	To compare ACT and CBT in a sample with multiple anxiety disorders.	ACT would improve cognitive flexibility and valued living to a greater degree than CBT.	C F2F Indv	D/AG, SAD, SP, OCD, or GAD	1. ACT (57) 2. CBT (71)	37,93 (11,70)	52,3	PD/AG (N = 53) SAD (N = 25) GAD (N = 26) OCD (N = 17) SP (N = 6)	Yes	Yes	Yes
Arch et al., 2013 [32]	US	To compare MBSR and CBT in the treatment of anxiety disorders.	1. CBT would improve anxiety symptoms to a greater degree than MBSR 2. MBSR would improve broader symptoms (depression and co-occurring emotional disorders) to a greater degree than CBT.	SP F2F Group	PD/AG, SAD, SP, OCD, GAD, or PTSD	1. MBSR (45) 2. CBT (60)	45,91 (13,68)	17	PD/AG (N = 31) GAD (N = 38) SAD (N = 16) PTSD (N=15) OCD (N=5)	Yes	Yes	Yes
Barlow et al., 2017 [18]	US	To explore whether the UP is at least as efficacious as single-disorder protocols in the treatment of anxiety disorders.	The UP would be at least as efficacious as single-disorder CBT at post-treatment and at 6-month follow-up.	C F2F Indv	PD/AG, SAD, OCD, or GAD	1. UP (88) 2. SD-CBT (91) 3. WLC (44)	31,10 (11,0)	55,6	OCD (N = 44) GAD (N = 62) PD/AG (N = 59) SAD (N = 58)	Yes	Yes	Yes

Barrowclough et al., 2001 [57]	UK	To compare CBT and SC in older adults with anxiety disorders.	N/A	PC + C F2F Indv	PD/AG, SAD, GAD, or Anx NOS	1. CBT (19) 2. SC (24)	72 (6,2)	77	PD/AG (N = 22) SAD (N = 1) GAD (N = 8) Anx NOS (N = 12)	Yes	Yes	No
Berger et al., 2014 [19]	CH	To compare T-CBT for symptoms of SAD, PD/AG, and GAD to SD-CBT and a WLC.	1. To study whether T-CBT outpferforms SD-CBT. 2. To analyze whether both active treatment conditions outperform the WLC.	C Internet Indv	SAD, PD/AG, or GAD	1. T-CBT (44) 2. SD-CBT (44) 3. WLC (44)	35,1 (11,14)	56	SAD (N = 113) PD/AG (N = 44) GAD (N = 33)	No	Yes	Yes
Berger et al., 2017 [48]	CH	To compare CBT+CAU for anxiety disorders to CAU in PC.	CBT + CAU would reduce anxiety and related symptoms to a greater degree than CAU in patients with SAD, PD/AG and/or GAD.	PC Internet Indv	SAD, PD/AG, or GAD	1. CBT + CAU (70) 2. CAU (69)	42 (12,1)	70,5	SAD (N = 40) PD/AG (N = 63) GAD (N = 36)	Yes	Yes	Yes
Boettcher et al., 2014 [68]	DE	To compare MT to an online DF for SAD, PD, GAD, and/or Anx NOS.	MT would improve anxiety, depression, insomnia, and quality of life to a greater degree than the online DF.	C Internet Indv	SAD, PD/AG, GAD, or Anx NOS	1. MT (45) 2. Online DF (46)	38 (10,3)	71,4	GAD (N = 17) SAD (N = 26) PD (N = 30) Anx NOS (N = 18)	Yes	Yes	No
Bolton et al., 2014[a] [42]	US	To test transdiagnostic CBT for comorbid presentations of depression, anxiety, and trauma symptoms among trauma	N/A	C F2F Indv	Dep or PTSD	1. CBT (182) 2. WLC (165)	1: 36,5 (12,6) 2: 34,3 (11,4)	63	PTSD/Dep (N = 347)	No	No	No

		survivors in a low-resource setting.										
Brenes et al., 2012 [58]	US	To compare CBT-T and IO for the treatment anxiety disorders in older adults.	CBT-T would improve anxiety, worry, depressive symptoms, and quality of life to a greater degree than IO.	PC + CT Indv	GAD, PD, or Anx NOS	1. CBT-T (30) 2. IO (30)	1: 68,8 (7,3) 2: 69.5 (6.9)	83,3	GAD (N = 30) GAD+PD (N = 25) PD (N = 3) Anx NOS (N = 2)	Yes	Yes	Yes
Bressi et al., 2010 [69]	IT	To compare STPP and TAU in the treatment of patients with anxiety or depressive disorders.	1. STPP would produce equal or greater reductions in psychiatric symptoms than TAU. 2. Patients in STPP would show fewer interpersonal problems than patients in TAU at post-treatment.	SC F2F Indv	GAD, PD, SAD, MDD, or DD	1. STPP (30) 2. TAU (30)	1: 35,75 (9,25) 2: 38,67 (9,28)	76,7	Dep (N = 21) PD (N = 15) SAD (N = 8) GAD (N = 16)	Yes	No	No
Carlbring et al., 2011 [20]	SE	To compare T-CBT to an attention control condition (online discussion group) in anxiety disorders.	T-CBT would reduce symptoms of anxiety and mood, and increase quality of life.	C Internet Indv	Any specific anxiety disorder, or Anx NOS	1. T-CBT (27) 2. AC (27)	38,8 (10,7)	76	Dep (N = 23) PD (N = 5) PD+AG (N = 12) OCD (N = 1) PTSD (N = 1) SAD (N = 21) GAD (N = 11) Anx NOS (N = 7)	No	Yes	No
Craske et al., 2007 [65]	US	To compare T-CBT for the treatment of principal PD/AG + CBT for the comorbid	1. CBT would improve symptoms of PD/AG to a greater degree than T-CBT	C F2F Indv /group	PD/AG + 1 anxiety disorder/mood disorder	1. CBT (33) 2. T-CBT	36,8 (9,1)	60	PD/AG (N = 65)	Yes	Yes	Yes

		condition to CBT focused only on PD/AG	2. CBT would improve comorbid symptoms to a greater degree than T-CBT			(32)						
Day et al., 2013[b] [60]	CA	To compare CBT for the treatment of anxiety, depression and/or stress to a WLC in university students.	1. CBT would improve anxiety, depression and stress symptoms to a greater degree than the WLC. 2. The improvements would be maintained at a 6-month follow-up.	Univ stud Internet Indv	Symptoms of depression, anxiety or stress	1. CBT (33) 2. WLC (33)	23,55 (4,98)	89,3	Participants had symptoms of anxiety, stress, and/or depression (information on diagnoses unavailable)	No	No	No
Dear et al., 2015 [21]	AU	To compare transdiagnostic CBT for GAD and comorbid symptoms to SD-CBT, in terms of relative efficacy and acceptability when provided in both clinician-guided and self-guided formats.	1. Transdiagnostic CBT and SD-CBT would improve symptoms of GAD. 2. TD-CBT would improve symptoms of comorbid Dep, SAD and PD at each time point to a greater degree than SD-CBT.	C Internet Indv	Symptoms of GAD	1. CBT (170) 2. SD-CBT (168)	43,78 (11,29)	76	GAD (N = 338)	Yes	Yes	Yes
Dear et al., 2016 [35]	AU	To compare transdiagnostic CBT for SAD and comorbid symptoms to SD-CBT, in terms of efficacy and acceptability when provided in both clinician-guided and self-guided formats.	1. Transdiagnostic CBT and SD-CBT would improve symptoms of SAD similarly. 2. Transdiagnostic CBT would reduce symptoms of comorbid Dep, GAD and PD at each time point to a greater degree than	C Internet Indv	Symptoms of SAD	1. CBT (105) 2. SD-CBT (115)	41,57 (10,89)	58	SAD (N = 220)	Yes	Yes	Yes

			SD-CBT.									
Ejeby et al., 2014 [70]	SE	To compare CBT and MMI to CAU alone for patients with anxiety, depressive, and stress-related disorders.	CBT and MMI would improve quality of life and psychological symptoms to a greater degree than CAU alone.	PC F2F Group	Depression, anxiety, stress, or somatoform disorders	1. CBT + CAU (84) 2. MMI + CAU (80) 3. CAU (81)	1: 43,3 (10,3) 2: 44,3 (9,5) 3: 45,0 (9,5)	80,8	Dep (N = 139) Anx disorders (N = 81) Somatoform disorders (N = 10) Eating disorders (N = 6) AUD (N = 2)	No	No	No
Erickson et al., 2007 [71]	CA	To compare CBT for different anxiety disorders to a WLC.	1. CBT would improve anxiety symptoms to a greater degree than the WLC. 2. CBT would improve within-group symptoms of anxiety at post-treatment and follow-up.	C F2F Group	PD/AG, OCD, SAD, GAD, SP, or PTSD	1. CBT (73) 2. WLC (79)	1: 40,7 (11,8) 2: 41,0 (11,1)	63,8	SAD (N = 46) PD/AG (N = 36) GAD (N = 31) PSTD (N = 16) OCD (N = 16) SP (N = 7)	Yes	Yes	No
Farchione et al., 2012 [22]	US	To compare the UP for anxiety disorder to a WLC.	1. The UP would be efficacious in improving the symptoms of patients with GAD, SAD, PD/AG, and OCD. 2. The UP would reduce the severity of comorbid disorders at both post-treatment and follow-ups.	C F2F Indv	Anxiety disorders	1. CBT (26) 2. WLC (11)	1: 29,38 (9,86) 2: 30,64 (9,15)	59,5	GAD (N = 7) SAD (N = 8) OCD (N = 8) Anx NOS (N = 2) PDA (N = 8) PTSD (N = 1) SAD+Anx NOS (N = 1) GAD+SAD (N = 1) OCD+PD/AG (N = 1)	Yes	Yes	Yes

Fogliati et al., 2016 [23]	AU	To compare transdiagnostic CBT for PD and comorbid symptoms to SD-CBT in terms of efficacy and acceptability when provided in both clinician-guided and self-guided formats.	1. Transdiagnostic CBT and SD-CBT would improve symptoms of PD similarly. 2. Transdiagnostic CBT would reduce symptoms of comorbid Dep, GAD, and SAD at each time point to a greater degree than SD-CBT.	C Internet Indv	Symptoms of PD	1. CBT (72) 2. SD-CBT (73)	41,40 (11,28)	79	PD (N = 145)	Yes	Yes	Yes
Forman et al., 2007 [51]	US	To compare ACT and CBT in the treatment of anxiety and depression.	1. CBT would show stronger mediation effects for the ability to identify and report on internal experiences than ACT. 2. ACT would show stronger mediation effects for experiential acceptance and current-moment awareness than CBT.	C F2F Indv	Symptoms of anxiety and/or depression	1. ACT (55) 2. CBT (44)	27,87 (7,25)	80,2	Dep (N = 34) Anxiety disorder (N = 32) AD (N = 10)	No	No	No
Hadjistavro-poulos et al., 2017 [72]	CA	To compare CBT + standard support to CBT + optional support in the treatment of anxiety and depression.	1. CBT + optional support would not be inferior to CBT + standard support. 2. CBT + optional support and CBT+ standard support would be similar in terms of symptom improvement, completion rates, and	C Internet Indv	Symptoms of anxiety and/or depression	1. CBT + standard support (92) 2. CBT + optional support (88)	38,29 (12,92)	78,7	Dep (N = 97) GAD (N = 100) PD (N = 80) SAD (N = 96)	No	Yes	Yes

			satisfaction with the treatment.									
Johansson et al., 2012 [73]	SE	To compare T-CBT for anxiety and comorbid symptoms to CBT, and to an active control group (Online DF focused on depression).	1. T-CBT and CBT would produce improvements. 2. T-CBT would produce greater improvements than CBT. 3. An effect was expected on the online DF, but smaller than in the CBT treatment groups.	C Internet Indv	MDD	1. T-CBT (39) 2. CBT (40) 3. Online DF (42)	44,7 (12,1)	71,1	Dep (N = 121)	Yes	Yes	No
Johansson et al., 2013 [46]	SE	To compare PP and SC in patients with depression and anxiety disorders.	1. PP would improve measures of depression and anxiety to a greater degree than SC. 2. Larger effects were expected on measures of depression in patients with depression as their principal diagnosis compared to patients who did not have depression as their principal diagnosis. 3. Larger effects were expected on measures of anxiety in patients with anxiety as their principal diagnosis compared to patients	C Internet Indv	MDD, SAD, PD, GAD, Anx NOS, or Dep NOS	1. PP (50) 2. SC (50)	44,9 (13,1)	82	Dep (N = 72) GAD (N = 49) SAD (N = 36) PD (N = 19) Anx/Dep NOS (N = 4)	No	Yes	Yes

			who did not have an anxiety disorder as their principal diagnosis.									
Johnston et al., 2011 [50]	AU	To compare Clinician-guided CBT and Coach-guided CBT to a WLC.	1. The pooled Clinician-guided and Coach-guided groups would improve in general and on disorder-specific measures of anxiety, depression, and disability to a greater degree than the WLC. 2. Participants in the CBT groups would rate the treatment as acceptable. 3. The pooled Clinician-guided and Coach-guided groups would show significant improvement on disorder-specific measures of anxiety over time. 4. Participants in both CBT groups would show similar outcomes on all measures and at all measurement points.	C Internet Indv	GAD, SAD, or PD/AG	1. Clinician guided CBT (46) 2. Coach guided CBT (43) 3. WLC (42)	41,62 (12,83)	58,8	GAD (N = 59) SAD (N = 45) PD/AG (N = 27)	Yes	Yes	Yes
Kim et al., 2009 [43]	KR	To compare MBCT to a Psychoeducation control group in	N/A	SC F2F Group	GAD, or PD/AG	1. MBCT (24) 2.	1: 40,8 (7,3) 2: 38,1	37	GAD (N = 11) PD (N = 35)	Yes	No	No

		patients with PD and GAD.				Psychoeduc (22)	(9,7)					
Lang et al., 2017 [59]	US	To compare ACT and P-CT in veterans with anxiety or depressive disorders, or those with postconcussive symptoms.	N/A	PC + C F2F Indv	Anxiety or depressive disorder	1. ACT (80) 2. P-CT (80)	34,2 (8)	20	Dep (N = 97) PTSD (N = 131) PD/AG (N = 124) SAD (N = 26) OCD (N = 21) GAD (N = 32) Anx NOS (N = 6)	No	No	No
Marks et al., 2004 [62]	UK	To compare Comp SE and face-to-face SE to a placebo group (relaxation) in patients with phobias or panic disorder.	1. Comp-SE would show similar efficacy to face-to-face SE. 2. Both SE groups would be more effective than Comp Self-Relaxation.	SC Comp Indv	PD/AG, SAD, or SP	1. Comp SE (37) 2. Face-to-face SE (39) 3. Comp Self-Relaxation (17)	38 (12)	69	PD+AG (N = 24) AG (N = 3) SAD (N = 24) SP (N = 39)	Yes	Yes	No
Mullin et al., 2015 [61]	AU	To compare CBT for university students with stress, anxiety, low mood, and depression to WLC, in terms of both efficacy and acceptability.	1. CBT would reduce symptoms of anxiety and depression at post-treatment to a greater degree than the WLC. 2. Participants with clinical levels symptoms would show improvements consistent with those found in prior studies on Internet CBT.	Univ stud Internet Indv	Symptoms of anxiety or depression	1. CBT (30) 2. WLC (23)	1: 28,6 (10,05) 2: 26,9 (11,51)	64,2	GAD (N = 40) PD (N = 12) SAD (N = 19) Dep (N = 18)	No	Yes	No

			3. Symptom improvements would be maintained at 3-month follow-up. 4. Participants would be satisfied with the treatment.									
Neacsiu et al., 2014 [66]	US	To compare DBT-ST for emotion dysregulation to an activities-based support group in order to: 1. Explore the effects of DBT-ST on anxiety and depression. 2. Investigate the mediation effects of DBT skills use on differential changes. 3. Explore whether confounding effects accounted for any significant outcomes. 4. Explore the feasibility of DBT-ST in terms of retention rates, treatment credibility and satisfaction, and compliance with the treatment protocol.	1. DBT-ST would reduce emotion dysregulation to a greater degree than the activities-based support group. 2. The use of DBT skills would mediate the differential changes between groups.	C F2F Group	Anxiety or depressive disorder	1. DBT (22) 2. AC (22)	1: 32,37 (10,50) 2: 38,82 (13,55)	65,9	Dep (N = 34) PD (N = 6) AG (N = 3) GAD (N = 29) SAD (N = 16) SP (N = 8) OCD (N = 5) PTSD (N = 4) Anx NOS (N = 4) SUD (N = 3)	No	Yes	No
Newby et al., 2013 [52]	AU	To compare CBT for mixed GAD and MDD to a WLC.	CBT would show greater improvements than the WLC.	C Internet Indv	Symptoms of anxiety + depression	1. CBT (46) 2. WLC	44,3 (12,2)	77,8	GAD/MDD (N = 47) GAD (N = 37)	Yes	Yes	Yes

						(53)			MDD (N= 15)			
Nordgren et al., 2014 [67]	SE	To compare CBT to an AC group in terms of cost-effectiveness on anxiety disorders.	1. CBT would be moderately more effective than the AC group both at post-treatment and at 1-year follow-up. 2. CBT would be cost-effective.	PC Internet Indv	Anxiety disorders	1. CBT (50) 2. AC (50)	1: 35 (13) 2: 36 (12)	63	GAD (N = 10) SAD (N = 32) PD/AG (N = 31) AG (N = 8) Anx NOS (N = 19)	Yes	Yes	No
Norton, 2012 [28]	US	1. To compare CBT to relaxation in terms of overall efficacy. 2. To compare CBT to relaxation on treatment credibility and acceptability. 3. To compare CBT effects across diagnoses to analyze differential efficacy by diagnosis.	1. Participants in both groups would show significant improvements in anxiety over the course of treatment. 2. CBT would show equivalence/non inferiority with relaxation. 3. Participants would not show differences in outcomes by primary or secondary diagnosis.	C F2F Group	Anxiety disorders	1. CBT (65) 2. Relaxation (22)	32,98 (10,73)	62,1	SAD (N = 37) PD/AG (N = 31) GAD (N = 15) Anx NOS (N = 2) OCD (N = 1) SP (N = 1)	Yes	Yes	Yes
Norton & Hope, 2005 [24]	US	1. To compare CBT to a WLC in patients with different anxiety disorders.	1. CBT would produce significant improvements on diagnostic indices. 2. CBT would show significant reductions at post-treatment on measures of anxiety, whereas no improvement would be	C F2F Group	Anxiety disorders	1. CBT (12) 2. WLC (12)	39,58 (11,88)	60,9	SAD (N = 5) PD/AG (N = 4) GAD (N = 10) OCD (N = 3) PD (N = 1) PTSD (N = 1)	Yes	Yes	No

			observed in the WLC on these measures. 3. CBT would improve measures of the common core psychopathology during the second phase of treatment, whereas no improvement would be observed in the WLC on these measures.									
Norton & Barrera, 2012 [49]	US	To compare transdiangostic CBT to SD-CBT for PD, GAD, and SAD.	Both conditions would significantly improve anxiety over the course of treatment, and these results in both conditions would be non-inferior.	C F2F Group	PD, SAD, or GAD	1. CBT (23) 2. SD-CBT (23)	31,46 (8,93)	50	SAD (N = 25) GAD (N = 10) PD (N = 11)	Yes	Yes	No
Proudfoot et al., 2003 [25]	UK	To compare CBT to TAU in patients with anxiety, depression, or mixed anxiety and depression.	CBT would produce greater improvements than TAU.	PC Comp Indv	Depression, mixed anxiety-depression, or anxiety disorders	1. CBT (88) 2. TAU (77)	1: 43,7 (14,7) 2: 45,7 (14,1)	73,7	Mixed anx-dep (N = 80) Dep (N = 61) PD (N = 10) SP (N = 4) AG (N = 5) SP (N=5)	Yes	No	No
Proudfoot et al., 2004 [63]	UK	1. To compare CBT to TAU in patients with anxiety, depression, or mixed anxiety and depression in terms of efficacy. 2. To investigate interactions of CBT	N/A	PC Comp Indv	Depression, mixed anxiety-depression, or anxiety disorders	1. CBT (145) 2. TAU (128)	1: 43,6 (14,3) 2: 43,4 (13,7)	73,7	Mixed anx-dep (N = 142) Dep (N = 92) PD (N = 14) SP (N = 11) AG (N = 8) SP (N = 6)	Yes	No	No

		with clinical, demographic, and setting variables.										
Riccardi et al., 2017 [74]	US	To compare FSBET to a WLC.	1. FSBET would improve overall outcome to a greater degree than the WLC. 2. FSBET would produce clinically significant improvements on principal diagnosis and secondary diagnosis symptoms. 3. Improvements in the FSBET group would be maintained at 1-month follow-up. 4. The relationship between pre- and post-treatment changes would be mediated by the reduction in safety aid use.	C F2F Indv	PD/AG, SAD, or GAD	1. FSBET (16) 2. WLC (12)	28,6 (11,8)	75	GAD (N = 9) PD (N = 8) SAD (N = 11)	Yes	Yes	Yes
Roy-Byrne et al., 2010 [47]	US	To compare CBT to CAU in patients with PD, GAD, SAD, or PTSD.	CBT would reduce symptoms of anxiety, and improve measures of health-related quality of life, functioning, and quality of care delivered to a greater degree than CAU.	PC Internet Indv	PD, GAD, SAD, or PTSD	1. CBT (503) 2. CAU (501)	43,47 (13,4)	71,1	PD (N = 475) GAD (N = 756) SAD (N = 405) PTSD (N = 181) Dep (N = 648)	No	Yes	No

Schmidt et al., 2012 [75]	US	To compare FSBET to a WLC in patients with multiple anxiety disorders.	1. FSBET would improve in overall outcomes to a greater degree than the WLC. 2. FSBET would show efficacy on each of the anxiety disorders evaluated. 3. Improvements in the FSBET group would be maintained at 6-month follow-up.	C F2F Group	PD/AG, SAD, or GAD	1. FSBET (57) 2. WLC (39)	36,3 (10,7)	72	GAD (N = 26) PD (N = 36) SAD (N = 34)	Yes	Yes	No
Schmidt et al., 2017 [64]	US	To compare CAST + CBM to PHET + sham CBM in patients with co-ocurring anxiety and suicidal ideation.	1. CAST + CBM would improve overall anxiety sensitivy and the cognitive dimension of anxiety sensitivity to a greater degree than PHET + sham CBM. 2. Reductions in anxiety sensitivity would be maintained at the 4-month follow-up. 3. Changes in anxiety sensitivity would affect symptoms of suicidal ideation at the follow-up period.	C Comp Indv	Clinical anxiety sensitivity + Suicidal ideation + Anxiety or depressive disorder	1. CAST+ CBM (37) 2. PHET+sham CBM (AC) (37)	30,77 (14,16)	75,6	PD (N= 7) SAD (N = 10) OCD (N= 1) PTSD (N = 11) GAD (N = 2) Anx/Dep NOS (N = 2) Dep (N = 37)	Yes	No	No
Schneider et al., 2005 [76]	UK	To compare CBT to minimal CBT in the treatment of PD/AG, SAD, and SP.	CBT would improve phobia/panic to a greater degree than minimal CBT at post-treatment and follow-	C Internet Indv	PD/AG, SAD, or SP	1. CBT (45) 2. Minimal CBT	39 (11)	74	PD+AG (N = 25) AG (N = 2) SAD (N = 24) SP (N = 17)	Yes	Yes	Yes

			up.			(23)						
Schröder et al., 2017 [77]	DE	1. To compare CBT to CAU in individuals with panic and phobias. 2. To explore differences in treatment effects by diagnosis. 3. To explore treatment moderators.	N/A	C Internet Indv	PD/AG, SAD, or SP	1. CBT (89) 2. CAU (90)	1: 36,5 (9,95) 2: 36,5 (10,26)	72	PD (N = 91) AG (N = 119) PD+AG (N = 73) SAD (N = 98) SP (N = 66)	No	No	No
Silfvernagel et al., 2012 [78]	SE	To compare T-CBT to a WLC in patients with panic symptoms with comorbid anxiety and depressive symptoms, in two age groups (18-30 and 31-45 years old).	1. T-CBT would produce decreases in measures of panic, anxiety, and depression. 2. T-CBT would increase quality of life. 3. The effects of T-CBT would be maintained at 12-month follow-up. 4. No significant differences would be observed between the two age groups.	C Internet Indv	Recurrent panic attacks	1. T-CBT (29) 2. WLC (28)	32,4 (6,9)	65	PD (N = 4) PD+AG (N = 47) GAD (N = 11) SAD (N = 9) Anx NOS (N = 1) Dep (N = 5)	No	Yes	No
Taylor et al., 2017 [79]	US	To compare PAI to a WLC in individuals with anxiety or depression.	N/A	C F2F Indv	Anxiety or depressive symptoms	1. PAI (16) 2. WLC (13)	1: 29,8 (12,2) 2: 29,0 (12,0)	60,7	MDD (N = 16) SAD (N = 16) GAD (N = 11) PTSD (N = 6) PD (N = 2) OCD (N = 1) Eating disorder (N = 3)	No	Yes	No

									AUD (N = 2) SUD (N = 1)			
Titov et al., 2010 [26]	AU	1. To compare CBT to a WLC in individuals with PD/AG, GAD, and/or SAD. 2. To analyze whether additional gains would be shown by the WLC after mofifying the treatment program with the feedback of the patients in the treatment group.	1. CBT would improve measures of overall and disorder-specific anxiety, depression, neuroticism, and disability to a greater degree than the WLC. 2. Participants allocated to CBT would rate the procedure as acceptable.	C Internet Indv	GAD, SAD, or PD	1. CBT (40) 2. WLC (38)	39,5 (13,0)	67,9	GAD (N = 34) PD/AG (N = 21) SAD (N = 23)	Yes	Yes	Yes
Titov et al., 2011 [27]	AU	To compare CBT to a WLC in patients with GAD, SAD, and/or PD/AG.	1. CBT would improve generic measures of depression and anxiety, neuroticism, and disability to a greater degree than the WLC 2. Fewer patients would meet the diagnostic criteria for MDD, GAD, SAD, or PD/AG in the treatment group 3. Participants allocated to CBT would rate the procedure as acceptable.	C Internet Indv	Depression, GAD, SAD, or PD/AG	1. CBT (37) 2. WLC (37)	43,9 (14,6)	73	Dep (N = 38) GAD (N = 21) PD/AG (N = 7) SAD (N = 8)	Yes	Yes	Yes
Titov et al., 2013 [80]	AU	1. To compare CBT + automated emails to	1. CBT + automated emails would produce	C Internet	Depression, GAD, SAD,	1. CBT+ autom	41,30 (9,76)	73,5	Dep (N = 85) GAD (N = 84)	Yes	No	No

		CBT alone for symptoms of anxiety and depression in terms of clinical outcomes and adherence. 2. To provide preliminary data on safety and acceptability.	better completion rates and reductions in clinical outcomes than CBT alone. 2. CBT + automated emails would be more beneficial for more severe patients.	Indv	or PD	emails (100) 2. CBT only (106) 3. WLC (51)			PD (N = 34) SAD (N = 54)			
Titov et al., 2015 [41]	AU	To compare transdiagnostic CBT for depression and comorbid symptoms toSD-CBT in terms of efficacy and acceptability when provided in both clinician-guided and self-guided formats.	1. Transdiagnostic CBT and SD-CBT would improve symptoms of depression similarly. 2. Transdiagnostic CBT would reduce symptoms of comorbid PD, GAD, and SAD at each time point to a greater degree than SD-CBT.	C Internet Indv	Depression symptoms	1. CBT (149) 2. SD-CBT (141)	44,19 (11,75)	72	Dep (N = 290)	Yes	Yes	Yes
Vøllestad et al., 2011 [45]	NO	To compare MBSR to a WLC in patients with PD/AG, SAD, and GAD.	N/A	C F2F Group	PD/AG, SAD,or GAD	1. MBSR (39) 2. WLC (37)	42,5 (11,3)	67,1	PD/AG (N = 38) SAD (N = 25) GAD (N = 13)	Yes	Yes	No
Wetherell et al., 2009 [44]	US	To compare MP to Enhanced community treatment in patients with GAD or Anxiety NOS.	MP would improve anxiety, depression, and quality of life to a greater degree than Enhanced community treatment.	C F2F Indv	GAD or Anx NOS	1. MP (15) 2. Enchanced community treatment (16)	1: 71 (7) 2: 73,3 (6,3)	83,9	GAD (N = 27) Anx NOS (N = 4)	Yes	Yes	No

Wuthrich & Rapee, 2013 [81]	AU	To compare CBT to a WLC in older patients with comorbid anxiety and depression.	CBT would produce significant improvements on all symptom measures at post-treatment. Improvements would be maintained at the 3-month follow-up.	C F2F Group	Anxiety + depression symptoms	1. CBT (27) 2. WLC (35)	67,44 (6,19)	64,5	GAD (N = 21) SAD (N = 6) SP (N = 1) PTSD (N = 3) Dep (N = 29) Anx NOS (N = 2)	Yes	Yes	No
Wuthrich et al. 2016 [53]	AU	To compare CBT to a discussion group in older patients with comorbid anxiety and depression.	Both conditions would improve diagnostic severity and symptom outcomes. CBT would improve anxiety and depression and diagnostic severity to a greater degree than the discussion group Improvements of participants allocated to CBT would be maintained at the 6-month follow-up.	C F2F Group	Anxiety disorder + depressive disorder	1. CBT (76) 2. Discussion group (57)	67,35 (5,44)	55,6	GAD (N = 44) Dep (N = 37)	No	No	No

Note. Ctry: Country; Comorb: Comorbidity; C: Community; F2F: Face-to-face; Indv: Individual; N/A: Not available; SP: Specialized care; PC: Primary care; T: Telephone; Univ stud: University students; Comp: Computerized; PD/AG: Panic disorder/agoraphobia; SAD: Social anxiety disorder; SP: Specific phobia; OCD: Obsessive-compulsive disorder; GAD: Generalized anxiety disorder; PTSD: Posttraumatic stress disorder; Anx NOS: Anxiety disorder not otherwise specified; MDD: Major depressive disorder; Dep NOS: Depressive disorder not otherwise specified; Dep: Depression (major depressive disorder, dysthymic disorder or dep NOS); M anx-dep: Mixed anxiety and depression; ACT: Acceptance and Commitment Therapy; CBT: Cognitive Behavioral Therapy; MBSR: Mindfulness-based Stress Reduction; UP: Unified Protocol; SD-CBT: Single-disorder Cognitive Behavioral Therapy; WLC: Waiting-list Control; SC: Supportive Counseling; T-CBT: Tailored Cognitive Behavioral Therapy; CAU: Care as Usual; MT: Mindfulness Treatment; CBT-T: Cognitive Behavioral Therapy delivered by Telephone; IO: Information-only; STPP: Short-term Psychodynamic Psychotherapy; TAU: Treatment as Usual; AC: Attention Control; MMI: Multimodal Intervention; PP: Psychodynamic Psychotherapy; MBCT: Mindfulness-based Cognitive Therapy; P-CT: Present-centered Therapy; SE: Self-exposure; DBT: Dialectical Behavioral Therapy; FSBET: False Safety Behavior Elimination Therapy; CAST: Cognitive Anxiety Sensitivity Treatment; CBM: Cognitive Bias Modification; PHET: Physical Health Education Training; PAI: Positive Activity Intervention; MP: Modular Psychotherapy; Hp: Hypochondriasis; SD: Somatoform disorder; AUD: Alcohol use disorder; AD: Adjustment disorder; SUD: Substance use disorder

[a]Data on diagnoses from Bolton et al. (2014) were not included in the analysis because patients with PTSD could not be distinguished from those with Dep (i.e. we could not determine whether patients had both PTSD and Dep, or how many patients had PTSD and how many had Dep)

[b]Data from Day et al. (2013) were not included in the analysis because no information on diagnoses was provided in this study

Quality of the included studies

The risk of bias assessment of the included trials is represented in Figure 2. In all, 38 of the 52 studies (73%) used an adequate random sequence generation method, whereas 14 studies did not report information about the randomization method. Allocation concealment was reached in 26 of the assessed trials (50%), but it was not clearly reported in the other half (50%). With regard to blinding the outcome assessment, 23 trials (44%) reported using blinded raters, whereas 12 (23%) used only self-report measures. Almost all of the studies (92%) used an appropriate method for handling incomplete outcome data (i.e. intention-to-treat analyses). Sixteen studies (31%) met all the quality criteria, 30 studies (58%) met two or three criteria, and the six remaining trials met none or only one quality criterion.

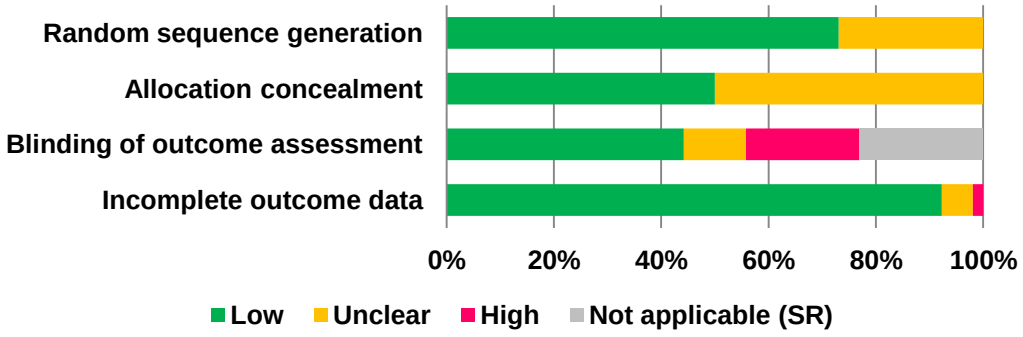

Figure 2. Risk of bias assessment
Note. SR = Self-report

Are comorbid disorders evaluated in transdiagnostic treatments for emotional disorders?

We were also interested in the number of studies that reported and assessed comorbidity in their samples. Of the 52 studies analyzed, 39 (75%) reported the presence of comorbid disorders (i.e. whether the sample presented comorbidity at baseline), and 13 (25%) did not. However, of the total number of studies, only 21 (40%) assessed the effects of the intervention on comorbid disorders (i.e. through scales or diagnostic interviews).

What diagnoses are targeted in transdiagnostic treatments for emotional disorders?

Figure 3 presents the number of studies that target each of the different diagnoses. In this figure, both specific diagnoses and broad diagnosis categories (i.e. anxiety, depression, and mixed anxiety-

depression) are shown because we identified studies that targeted either specific diagnoses or broader categories of anxiety and depression.

Of the 52 studies included in the review, the most commonly targeted diagnoses were PD/AG, (26 studies; 50%), GAD (24 studies; 46%), and SAD (22 studies; 42%). In addition, SP was targeted in 6 studies (12%) [31, 32, 62, 69, 76, 77], Anxiety NOS in 6 studies (12%) [20, 44, 46, 57, 58, 68], PTSD in 4 studies (8%) [32, 42, 47, 71], and OCD in 4 studies (8%) [18, 31, 32, 71]. Moreover, we identified 1 study targeting Depression NOS (2%) [46] and 1 study targeting somatoform disorders (2%) [70]. Finally, 22 studies targeted symptoms or diagnoses of depressive disorders (i.e. MDD or DD) (42%), 19 studies targeted symptoms or diagnoses of anxiety disorders (any type) (36.5%), 15 targeted depression symptoms or diagnoses (any type) (29%), 3 targeted mixed anxiety and depression (6%) [25, 52, 63], and 2 targeted stress (4%) [60, 70].

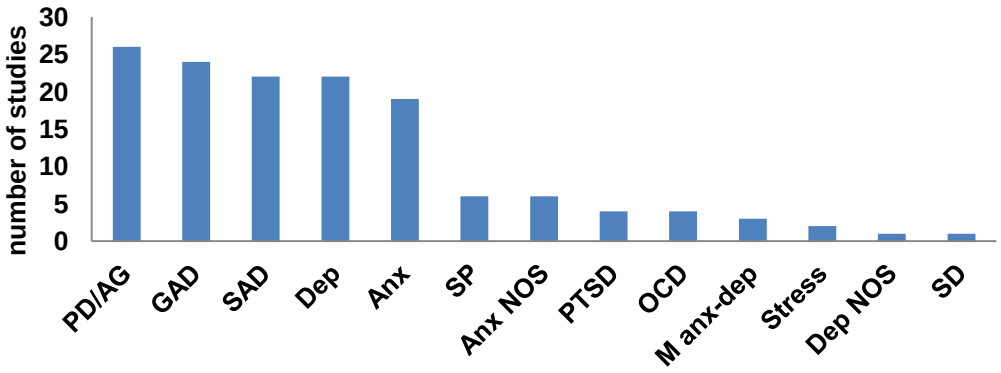

Figure 3. Number of studies that target the different diagnoses
Note. PD/AG: Panic disorder/agoraphobia; GAD: Generalized anxiety disorder; SAD: Social anxiety disorder; Dep: Depression; Anx: Anxiety; SP: Specific phobia; Anx NOS: Anxiety not otherwise specified; PTSD: Posttraumatic stress disorder; OCD: Obsessive-compulsive disorder; M anx-dep: mixed anxiety and depression disorder; Dep NOS: Depression not otherwise specified; SD: somatoform disorder

What is the real distribution of diagnoses at baseline in transdiagnostic treatments for emotional disorders?

In order to obtain the distribution of each of the different diagnoses, we classified the studies into those that reported a principal diagnosis (subsample 1) and those that did not (subsample 2). Of the 52 studies included in the review, 36 established a principal diagnosis, and 4125 patients with a principal diagnosis were identified in this subsample. The proportion of these patients for each of the different principal diagnoses can be seen in Figure 4. The most common diagnoses were GAD (n =

998; 24.1%), PD/AG (n = 935; 22.6%), SAD (n = 826; 20.0%), Dep (i.e. MDD or DD) (n = 789; 19.1%), and mixed anxiety and depression (n = 222; 5.4%). Other much less frequent diagnoses were OCD (n = 95, 2.3.%), SP (n = 86; 2.1%), Anxiety NOS (n = 61; 1.5%), and PTSD (n = 47; 1.1%).

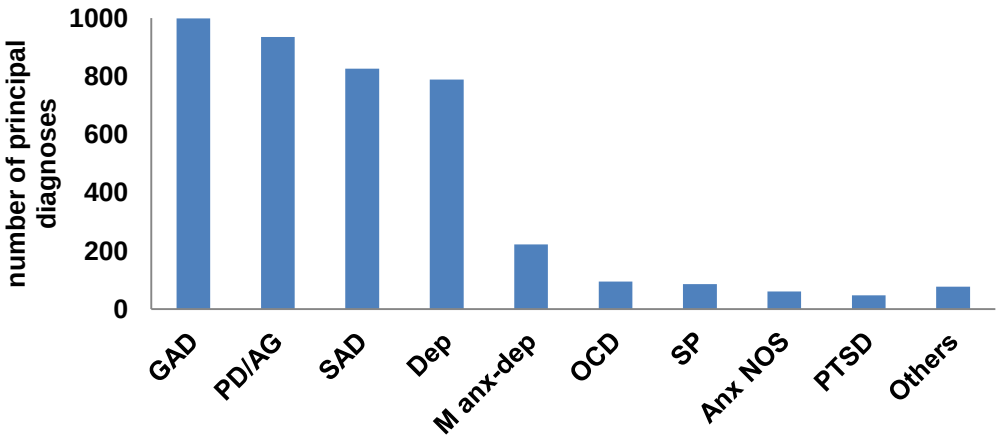

Figure 4. Total number of principal diagnoses in subsample 1

Note. GAD: Generalized anxiety disorder; PD/AG: Panic disorder and/or agoraphobia; SAD: Social anxiety disorder; Dep: Depression; M anx-dep: Mixed anxiety and depression; OCD: Obsessive-compulsive disorder; SP: Specific phobia; Anx NOS: Anxiety not otherwise specified; PTSD: Posttraumatic stress disorder. "Others" included GAD + MDD (n = 47), GAD + PD (n = 25), GAD + SAD (n = 1), SAD + Anxiety NOS (n = 1), OCD + PD/AG (n = 1), and anxiety/depression NOS (n = 2).

The proportion of different diagnoses in the studies that did not include information about a principal diagnosis (subsample 2) is shown in Figure 5. In this subsample, a total of 4926 diagnoses were identified (pertaining to 2882 patients), and the most common diagnoses were Dep (n = 1220; 24.8%), PD/AG (n = 1135; 23%), GAD (n = 1119; 22.7%), SAD (n = 855; 17.4%), and PTSD (n = 323; 6.6%). Other disorders in these studies included SP (n = 74; 1.5%), OCD (n = 28; 0.6%), and Anxiety NOS (n = 18; 0.4%).

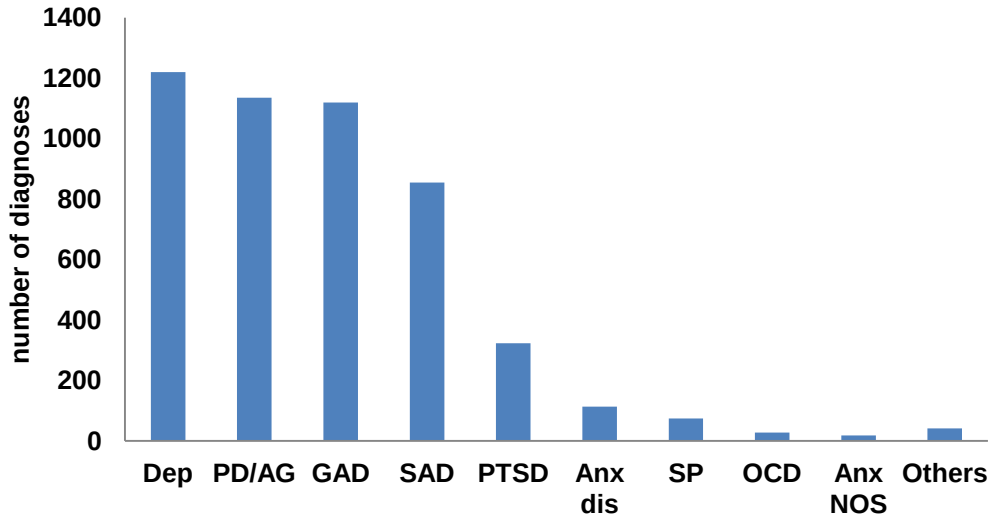

Figure 5. Total number of diagnoses of each type in subsample 2
Note. Dep: Depression; PD/AG: Panic disorder and/or agoraphobia; GAD: Generalized anxiety disorder; SAD: Social anxiety disorder; PTSD: Posttraumatic stress disorder; Anx dis: Anxiety disorders; SP: Specific phobia; OCD: Obsessive-compulsive disorder; Anx NOS: Anxiety not otherwise specified. "Others" included somatoform disorder (n = 10), adjustment disorder (n = 10), eating disorders (n = 9), alcohol use disorder (n = 4), substance use disorder (n = 4), and anxiety/depression NOS (n = 4).

Discussion

The aim of this systematic review was to analyze the following aspects about transdiagnostic treatments for ED: first, whether treatment response in the comorbid disorders is evaluated in transdiagnostic treatments for ED; second, what disorders are targeted in these studies; and third, what the real distribution of these disorders is at baseline in these studies.

The first objective was to analyze how comorbidity is reported and whether the treatment change produced in comorbid disorders is assessed in transdiagnostic trials for ED. The results showed that the number of studies reporting comorbidity was quite high, with 39 out of 52 reporting the presence of comorbid disorders in their samples at baseline. However, the number of studies assessing comorbidity was much lower, with only 21 (40.4%) studies assessing the comorbid conditions as well as the symptoms of the principal diagnosis, using either diagnostic interviews [18, 22] or self-report questionnaires [21, 40, 41]. From a transdiagnostic perspective that addresses the common maintenance vulnerabilities across disorders (e.g. neuroticism), it makes more sense to explore the extent to which these treatments are effective in improving both principal and comorbid disorders. In order to gain insight into how transdiagnostic treatments work in patients with comorbidity, we believe this strategy

should be followed in future research on transdiagnostic treatments for ED. Furthermore, future meta-analyses of transdiagnostic treatments for ED would benefit from this strategy because they could analyze the impact of these treatments on comorbidities, in addition to their effects on broader measures of anxiety and depression. To date, some studies have included measures to assess treatment response in comorbidity in addition to the principal diagnosis [21-23]. However, as the results of this systematic review show, this is not the typical approach in RCTs on transdiagnostic treatments (i.e. only 40.4% of the trials analyzed in this review assessed the impact of the intervention on comorbidity). As an example of this emphasis on comorbid diagnoses, a recent study tested the efficacy of a transdiagnostic treatment (the UP), compared to disorder-specific CBT with a specific focus on comorbid conditions, finding no differences in efficacy between the two treatment approaches [82]. These authors have also acknowledged the low number of treatments that, in general, evaluate treatment effects on comorbid disorders [82], whereas other authors have highlighted that transdiagnostic treatments should improve not only overall anxiety and depression, but also the disorder-specific comorbid psychopathology [38]. In this vein, most of the meta-analyses published to date have only analyzed the effects of transdiagnostic treatments using measures of overall anxiety and depression, except one recent meta-analysis that also explored the impact of these interventions on comorbidities [38]. To do so, the authors compared the effects of transdiagnostic treatments for ED to control conditions on disorder-specific measures of generalized anxiety, panic, and social anxiety. However, only 5 studies were included in this meta-analysis, which suggests the overall lack of attention paid to the evaluation of comorbidity in transdiagnostic treatments.

It is important to note that some of the studies included in this review follow a treatment perspective that does not fall into the “shared mechanisms approach” described by Sauer-Zavala et al. [13]. Some of these approaches include tailoring the treatment to the specific disorders and comorbidities of each individual [19, 20, 73], changing the relationship of the patient with her or his own subjective experience (regardless of the specific disorder involved) through the delivery of “third wave” therapies (e.g. mindfulness, acceptance, and commitment therapy) [31, 32, 43, 51], or helping the patients to resolve their inner psychic conflicts using psychodynamic therapy [46, 69]. Regarding the usefulness of these transdiagnostic treatments for comorbid presentations, whereas tailored treatments aim to tailor the treatment according to the specific symptoms of the patient, third wave and psychodynamic therapies are considered transdiagnostic because they are usually applied indistinctly to treat

different types of disorders. In sum, all of these approaches represent different strategies used to target comorbidity.

Regarding the second objective, (i.e. *what diagnoses are targeted in transdiagnostic treatments for emotional disorders?)* PD/AG was targeted in half of the studies, followed by GAD, SAD, and Dep, which were also targeted in almost half of the studies (46, 42, and 42%, respectively). By contrast, Anxiety NOS and Depression NOS were only targeted in 12 and 2% of the studies, respectively.

Finally, the third question tried to answer *what the real distribution of the diagnoses is at baseline in transdiagnostic treatments for emotional disorders.* Regarding this question, the findings show that, in patients with a principal diagnosis (subsample 1), GAD was the most frequent diagnosis, followed by PD/AG, SAD, and Dep. Taken together, these disorders represented 85.8% of subsample 1, with anxiety disorders being the most common disorders targeted in transdiagnostic treatments for ED. Other ED appeared much less frequently. These disorders included OCD, SP, Anxiety NOS, PTSD, and Depression NOS. In patients with unreported principal diagnoses (subsample 2), Dep was the most common diagnosis, followed by PD/AG, GAD, SAD, and PTSD. These disorders represented 94.5% of the total number of diagnoses, and anxiety disorders were again the most frequent disorders targeted in the transdiagnostic treatments. By contrast, Anxiety NOS and OCD only represented 1% of this subsample. Overall (both subsamples), the most common disorders targeted in transdiagnostic trials were GAD, PD/AG, SAD, and Dep. These results are consistent with the high prevalence rates observed for these disorders [8, 9, 54]. For instance, according to the DSM-IV-TR [54], lifetime prevalence is 5% for GAD, 10-25% (female) and 5-12% (male) for major depression, 6% for dysthymic disorder, 1.5-3.5% for PD/AG, 2.5% for OCD, 3-13% for SAD, and 1-14% for PTSD. However, other ED, such as OCD, PTSD, Anxiety NOS, and SP, have received much less attention in the research on transdiagnostic treatments for ED, and they are usually not targeted in these protocols. On the one hand, it is worth noting that there is a low proportion of patients with OCD as the principal diagnosis included in the transdiagnostic interventions, even though this disorder can be appropriately treated from a transdiagnostic perspective, based on common maintenance vulnerabilities across ED [15, 17, 22]. In the case of PTSD, earlier studies with transdiagnostic protocols like the UP [83], which originally targeted this diagnosis, do not include this category in later studies [18, 22], in spite of the fact that this disorder might be an appropriate treatment target from a mechanistically transdiagnostic approach (i.e. a treatment approach that addresses the common underlying mechanisms across a range of disorders) [18, 84]. On the other hand, transdiagnostic treatments have

the potential to target diagnoses that do not fit any specific category (e.g. Anxiety NOS) [12,15]. Although there are data indicating that there is a high proportion of these presentations [85, 86], the number of diagnoses with Anxiety NOS analyzed in this study represented less than 1% of all the patients. In this regard, one somewhat surprising result is that the overall number of patients with a diagnosis of SP is larger than the number of patients with Depression or Anxiety NOS, even though one of the advantages of the transdiagnostic perspective is the possibility of treating NOS diagnoses, clinical presentations for which there is a lack of evidence-based treatments.

Regarding the control conditions, both the waitlist control and the active control conditions were the most frequent among the analyzed studies. Of the studies that used active control conditions, only 8 were disorder-specific treatments. In order to accumulate evidence about the efficacy of transdiagnostic treatments, more studies should compare these protocols to disorder-specific treatments [21, 23]. Thus, although there is some evidence showing that a transdiagnostic approach may benefit depressive symptomatology more than disorder-specific protocols [36], overall the literature suggests that these two treatment approaches have equivalent effects [18, 39-41]. However, the number of studies comparing these two approaches is still low, and so more research is warranted to more firmly establish their relative efficacy. Likewise, research comparing the cost-effectiveness of transdiagnostic treatments and disorder-specific protocols is of paramount importance, for a number of reasons. First and foremost, by using a transdiagnostic treatment, less training of clinicians is required because a single protocol is used to address multiple disorders, which is likely to facilitate its implementation in real-world settings (e.g. primary care and mental health services). Second, these treatments may be more useful for clinicians that have to address comorbid presentations, either by targeting the underlying common processes, by tailoring the treatment to the symptoms and needs of each patient [20], or by addressing how the patients relate to their own cognitive, behavioral, and emotional experiences [31, 32]. Although the aforementioned reasons are true for most transdiagnostic treatments, there are other reasons specific to the protocols that fall in the category of the “shared mechanisms approach”. For instance, transdiagnostic treatments are designed to address the underlying common vulnerabilities across ED that are hypothesized to account for the onset and maintenance of these disorders [15]. Thus, by focusing on treating these processes rather than disorder-specific variations, larger and more lasting effects on clinical outcomes would be expected [13]. These results would lead to a lower prevalence of ED, and therefore to a decreased need for treatments in the short and long term, resulting in increased cost-effectiveness. For these reasons,

more research on the cost-effectiveness of transdiagnostic treatments is needed, especially in comparison with disorder-specific protocols, as evidenced by the scarcity of studies of this kind found in this review (e.g. the study by Nordgren et al.) [67]. Given the substantial burden of ED and the lack of resources to tackle these disorders, especially in public services, research on how to enhance the cost-effectiveness of psychological interventions should be a research priority. A characteristic example of a treatment strategy to further increase the efficiency of transdiagnostic protocols entails personalizing the treatment to a specific presentation, i.e. by selecting the treatment components that best fit the specific set of symptoms or "weaknesses" shown by each patient [87], thereby lowering the number of sessions required to successfully treat an individual's symptoms.

Regarding the settings, 71% of the studies were conducted in community samples, whereas 20% were carried out in primary or specialized care, and only 4% with university students. Thus, community samples continue to be the setting of choice when conducting transdiagnostic trials for ED. Regarding the way these treatments were delivered, approximately half of the studies were face-to-face, whereas the other half were delivered through Information and Communication Technologies (web-based and computerized), and only one study was delivered by telephone. These results are not surprising because research on Internet interventions has increased enormously in recent years, and these interventions have been applied to different problems using a variety of treatment approaches [88]. As the field of Internet interventions advances, researchers are more likely to select this delivery format to explore new interventions. Finally, transdiagnostic treatments were mostly individual, with 68% of the studies conducted in an individual format and the rest in groups. These results are not surprising because most transdiagnostic treatments were originally developed to be applied individually, with some exceptions [89]. However, the potential of transdiagnostic treatments for improving the dissemination of empirically supported treatments (i.e. only one protocol is needed to address a range of psychological disorders) may be enhanced by modifying the way the treatments are delivered [90]. For example, Internet or group formats can be used to reach a larger number of people in need of psychological help [92 ,93], especially in ecological settings where resources are generally scarcer, such as primary care or public mental health units [91, 93].

Finally, regarding the risk of bias assessment, the overall quality of the trials included was acceptable, especially regarding the handling of incomplete outcome data, with almost all the studies using an appropriate approach. However, it is worth noting that a large percentage of the studies did not properly report specific methodological aspects, such as

the sequence random generation method and whether it was performed by an independent party, which led us to rate it as unclear. In order to improve the methodological quality of trials and reduce the different sources of bias, we encourage authors to follow guidelines for conducting and reporting on clinical trials, such as the CONSORT statement (Consolidated Standards of Reporting Trials) [94, 95] or the SPIRIT guidelines (Standard Protocol Items: Recommendations for Interventional Trials) [96, 97].

Limitations

This systematic review has several limitations that should be mentioned. First, although a comprehensive search was conducted (4 different databases were used), some important studies might have not been identified. Moreover, studies written in languages other than English were excluded, which might have affected the representativity of the findings in this study. Second, the generalizability of the results is also limited by the fact that most of the studies included in this review were conducted in Western countries. Third, although aspects of the methodology were unreported or not clear in some studies, we did not contact the authors of these studies to obtain information that might have clarified these details. Thus, aspects of the study methods that were not clear were rated as unclear. However, based on our experience in conducting prior systematic reviews, we have observed that contacting the authors of these studies is often very difficult and, therefore, impractical. Fourth, as in any systematic review, this study is vulnerable to publication bias, and so some relevant unpublished studies might have been missed.

Conclusions

In conclusion, this systematic review found that, although most of the studies reported the presence of comorbid disorders in their samples at baseline, less than half of them evaluated the effects of the intervention on the comorbid disorders. Patients with comorbid disorders normally exhibit greater rates of severity, disability, and chronicity. One main reason for using a transdiagnostic approach to the treatment of ED is better management of comorbidity. Therefore, efforts should be made to assess the impact of the intervention on the comorbid disorders, in addition to the principal diagnoses targeted in these studies. On the other hand, as the results showed, the most commonly targeted diagnoses in transdiagnostic treatments were PD/AG, GAD, SAD, and Dep. More research is needed with other diagnoses much less targeted in transdiagnostic treatments, such as PTSD, OCD, and anxiety/depression NOS, to further explore the potential of transdiagnostic treatments in treating these disorders.

Abbreviations

ED: Emotional disorders; CBT: Cognitive behavioral therapy; RCT: Randomized controlled trial; DSM-IV-TR: Diagnostic and Statistical Manual of mental disorders, 4th edition-text revision; MDD: Major depressive disorder; DD; Dysthymic disorder; NOS: Not otherwise specified; GAD: Generalized anxiety disorder; PD: Panic disorder; AG: Agoraphobia; SAD: Social anxiety disorder; PTSD: Posttraumatic stress disorder; OCD: Obsessive-compulsive disorder; SP: Specific phobia; DSM-5: Diagnostic and Statistical Manual of mental disorders, 5th edition; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SR: Self-report; Mixed anx-dep: Mixed anxiety and depression disorder; SD: Somatoform disorder; Dep: Depression; CONSORT: Consolidated Standards of Reporting Trials; SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials

Supporting Information

S1 Table. PRISMA 2009 checklist.

DOCX

References

1. Kazdin AE, Blase SL. Rebooting Psychotherapy Research and Practice to Reduce the Burden of Mental Illness. Perspect Psychol Sci. 2011;6(1):21–37. doi: 10.1177/1745691610393527

2. McLean CP, Asnaani A, Litz BT, Hofmann SG. Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. J Psychiat Res. 2011;45(8):1027–35. doi: 10.1016/j.jpsychires.2011.03.006

3. Antony MM, Stein MB. Oxford handbook of anxiety and related disorders. New York: Oxford University Press; 2009.

4. Barlow DH. Anxiety and its disorders: The nature and treatment of anxiety and panic. 2nd ed. New York: Guilford Press; 2002.

5. Cuijpers P, Smit F, Bohlmeijer E, Hollon SD, Andersson G. Efficacy of cognitive–behavioural therapy and other psychological treatments for adult depression: meta-analytic study of publication bias. Brit J Psychiat. 2010;196(3):173–8. doi: 10.1192/bjp.bp.109.066001

6. Hollon SD, Ponniah K. A review of empirically supported psychological therapies for mood disorders in adults. Depress Anxiety. 2010;27(10):891–932. doi: 10.1002/da.20741

7. Nathan PE, Gorman JM. A guide to treatments that work. New York: Oxford University Press; 2015.

8. Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. 2005. Arch Gen Psychiat;62(6):617–27. doi: 10.1001/archpsyc.62.6.617

9. Wittchen HU, Jacobi F, Rehm J, Gustavsson A, Svensson M, Jönsson B, et al. The size and burden of mental disorders and other disorders of the brain in Europe 2010. Eur Neuropsychopharm. 2011;21(9):655–79. doi: 10.1016/j.euroneuro.2011.07.018

10. Rapaport MH, Clary C, Fayyad R, Endicott J. Quality-of-life impairment in depressive and anxiety disorders. Am J Psychiatry. 2005;162(6):1178–8. doi: 10.1176/appi.ajp.162.6.1171

11. Hofmeijer-Sevink MK, Batelaan NM, van Megen HJ, Penninx BW, Cath DC, van den Hout MA, et al. Clinical relevance of comorbidity in anxiety disorders: a report from the Netherlands Study of Depression and Anxiety (NESDA). J Affect Disorders. 2012;137(1-3):106–12. doi: 10.1016/j.jad.2011.12.008

12. McManus F, Shafran R, Cooper Z. What does a transdiagnostic approach have to offer the treatment of anxiety disorders? British J Clin Psychol. 2010;49(4):491–505. doi: 10.1348/014466509X476567

13. Sauer-Zavala S, Gutner CA, Farchione TJ, Boettcher HT, Bullis JR, Barlow DH. Current Definitions of “Transdiagnostic” in Treatment Development: A Search for Consensus. Behav Ther. 2016;48(1):128–38. doi: 10.1016/j.beth.2016.09.004

14. Clark DA, Taylor S. The Transdiagnostic Perspective on Cognitive-Behavioral Therapy for Anxiety and Depression: New Wine for Old Wineskins? J Cogn Psychother. 2009;23(1):60–6. doi: 10.1891/0889-8391.23.1.60

15. Barlow DH, Allen LB, Choate ML. Toward a unified treatment for emotional disorders. Behav Ther. 2004;35(2):205–30. doi: 10.1016/S0005-7894(04)80036-4

16. Brown T, Barlow D. A proposal for a dimensional classification system based on the shared features of the DSM-IV anxiety and mood disorders: Implications for assessment. Psychol Assessment. 2009;21(3):256–71. doi: 10.1037/a0016608

17. Harvey AG, Watkins E, Mansell W, Shafran R. Cognitive behavioural processes across psychological disorders: A transdiagnostic approach to research and treatment. New York, NY: Oxford University Press; 2004.

18. Barlow DH, Farchione TJ, Bullis JR, Gallagher MW, Murray-Latin H, Sauer-Zavala S, et al. The Unified Protocol for transdiagnostic treatment of emotional disorders compared with diagnosis-specific protocols for anxiety disorders: A randomized clinical trial. JAMA Psychiat. 2017;74(9):875–84. doi: 10.1001/jamapsychiatry.2017.2164

19. Berger T, Boettcher J, Caspar F. Internet-based guided self-help for several anxiety disorders: A randomized controlled trial comparing a tailored with a standardized disorder-specific approach. Psychother. 2014;51(2):207–19. doi: 10.1037/a0032527

20. Carlbring P, Maurin L, Törngren C, Linna E, Eriksson T, Sparthan E, et al. Individually-tailored, Web-based treatment for anxiety disorders: A randomized controlled trial. Behav Res Ther. 2011;49(1):18–24. doi: 10.1016/j.brat.2010.10.002

21. Dear BF, Staples LG, Terides MD, Karin E, Zou J, Johnston L, et al. Transdiagnostic versus disorder-specific and clinician-guided versus self-guided internet-delivered treatment for generalized anxiety disorder and comorbid disorders: A randomized controlled trial. J Anxiety Disord. 2015;36:63–77. doi: 10.1016/j.janxdis.2015.09.003

22. Farchione TJ, Fairholme CP, Ellard KK, Boisseau CL, Thompson-Hollands J, Carl JR, et al. Unified Protocol for Transdiagnostic Treatment of Emotional Disorders: A Randomized Controlled Trial. Behav Ther. 2012;43(3): 666–78. doi: 10.1016/j.beth.2012.01.001

23. Fogliati VJ, Dear BF, Staples LG, Terides MD, Sheehan J, Johnston L, et al. Disorder-specific versus transdiagnostic and clinician-guided versus self-guided internet-delivered treatment for panic disorder and comorbid disorders: A randomized controlled trial. J Anxiety Disord. 2016;39:88–102. doi: 10.1016/j.janxdis.2016.03.005

24. Norton PJ, Hope DA. Preliminary evaluation of a broad-spectrum cognitive-behavioral group therapy for anxiety. J Behav Ther Exp Psy. 2005;36(2):79–97. doi: 10.1016/j.jbtep.2004.07.002

25. Proudfoot J, Goldberg D, Mann A. Computerized, interactive, multimedial cognitive behavioural program for anxiety and depression in general practice. Psychol Med. 2003;33(2):217–27. doi: 10.1017/S0033291702007225

26. Titov N, Andrews G, Johnston L, Robinson E, Spence J. Transdiagnostic Internet treatment for anxiety disorders: A randomized controlled trial. Behav Res Ther. 2010;48(9):890–9. doi: 10.1016/j.brat.2010.05.014

27. Titov N, Dear BF, Schwencke G, Andrews G, Johnston L, Craske MG, et al. Transdiagnostic internet treatment for anxiety and depression: A

randomised controlled trial. Behav Res Ther. 2011;49(8):441–52. doi: 10.1016/j.brat.2011.03.007

28. Norton P. A randomized clinical trial of transdiagnostic cognitve-behavioral treatments for anxiety disorder by comparison to relaxation training. Behav Ther. 2012;43(3):506–17. doi: 10.1016/j.beth.2010.08.011

29. Barlow DH, Ellard KK, Sauer-Zavala S, Bullis JR, Carl JR. The origins of neuroticism. Perspect Psychol Sci. 2014;9(5):481–96. doi: 10.1177/1745691614544528

30. Barlow DH, Sauer-Zavala S, Carl JR, Bullis JR, Ellard KK. The nature, diagnosis, and treatment of neuroticism: Back to the future. Clin Psychol Sci. 2014;2(3):344–65. doi: 10.1177/2167702613505532

31. Arch JJ, Eifert GH, Davies C, Plumb Vilardaga JC, Rose RD, Craske MG. Randomized clinical trial of cognitive behavioral therapy (CBT) versus acceptance and commitment therapy (ACT) for mixed anxiety disorders. J Consult Clin Psych. 2012;80(5):750–65. doi: 10.1037/a0028310

32. Arch JJ, Ayers CR, Baker A, Almklov E, Dean DJ, Craske MG. Randomized clinical trial of adapted mindfulness-based stress reduction versus group cognitive behavioral therapy for heterogeneous anxiety disorders. Behav Res Ther. 2013;51(4):185–96. doi: 10.1016/j.brat.2013.01.003

33. Hayes SC, Luoma JB, Bond FW, Masuda A, Lillis J. Acceptance and commitment therapy: Model, processes and outcomes. Behav Res Ther. 2006;44(1):1-25. doi: 10.1016/j.brat.2005.06.006

34. Reinholt N, Krogh J. Efficacy of Transdiagnostic Cognitive Behaviour Therapy for Anxiety Disorders: A Systematic Review and Meta-Analysis of Published Outcome Studies. Cogn Behav Therapy. 2014;43(3):171–84. doi: 10.1080/16506073.2014.897367

35. Andersen P, Toner P, Bland M, McMillan D. Effectiveness of Transdiagnostic Cognitive Behaviour Therapy for Anxiety and Depression in Adults: A Systematic Review and Meta-analysis. Behav Cogn Psychoth. 2016;44(6):673–90. doi: 10.1017/S1352465816000229

36. Newby JM, McKinnon A, Kuyken W, Gilbody S, Dalgleish T. Systematic review and meta-analysis of transdiagnostic psychological treatments for anxiety and depressive disorders in adulthood. Clin Psychol Rev. 2015;40:91–110. doi: 10.1016/j.cpr.2015.06.002

37. Newby JM, Twomey C, Li S, Andrews G. Transdiagnostic computerised cognitive behavioural therapy for depression and anxiety: A systematic review and meta-analysis. J Affect Disorders. 2016;199:30–41. doi: 10.1016/j.jad.2016.03.018

38. Păsărelu CR, Andersson G, Bergman Nordgren L, Dobrean A. Internet-delivered transdiagnostic and tailored cognitive behavioral therapy for anxiety and depression: a systematic review and meta-analysis of randomized controlled trials. Cogn Behav Therapy. 2016;46(1):1–28. doi: 10.1080/16506073.2016.1231219

39. Pearl SB, Norton PJ. Transdiagnostic versus diagnosis specific cognitive behavioural therapies for anxiety: A meta-analysis. J Anxiety Disord. 2016;46:11–24. doi: 10.1016/j.janxdis.2016.07.004

40. Dear BF, Staples LG, Terides MD, Fogliati VJ, Sheehan J, Johnston L, et al. Transdiagnostic versus disorder-specific and clinician-guided versus self-guided internet-delivered treatment for Social Anxiety Disorder and comorbid disorders: A randomized controlled trial. J Anxiety Disord. 2016;42:30–44. doi: 10.1016/j.janxdis.2016.05.004

41. Titov N, Dear BF, Staples LG, Terides, MD, Karin, E, Sheehan J, et al. Disorder-specific versus transdiagnostic and clinician-guided versus self-guided treatment for major depressive disorder and comorbid anxiety disorders: A randomized controlled trial. J Anxiety Disord. 2015;35:88–102. doi: 10.1016/j.janxdis.2015.08.002

42. Bolton P, Lee C, Haroz EE, Murray L, Dorsey S, Robinson C, et al. A Transdiagnostic Community-Based Mental Health Treatment for Comorbid Disorders: Development and Outcomes of a Randomized Controlled Trial among Burmese Refugees in Thailand. PLoS Med. 2014;11(11):e1001757. doi: 0.1371/journal.pmed.1001757

43. Kim YW, Lee SH, Choi TK, Suh SY, Kim B, Kim CM, et al. Effectiveness of mindfulness-based cognitive therapy as an adjuvant to pharmacotherapy in patients with panic disorder or generalized anxiety disorder. Depress Anxiety. 2009;26(7):601–6. doi: 10.1002/da.20552

44. Wetherell JL, Ayers CR, Sorrell JT, et al. Modular psychotherapy for anxiety in older primary care patients. Am J Geriatr Psychiat. 2009;17(6):483–92. doi: 10.1097/JGP.0b013e3181a31fb5

45. Vøllestad J, Sivertsen B, Nielsen GH. Mindfulness-based stress reduction for patients with anxiety disorders: Evaluation in a randomized controlled trial. Behav Res Ther. 2011;49(4):281–88. doi: 10.1016/j.brat.2011.01.007

46. Johansson R, Björklund M, Hornborg C, Karlsson S, Hesser H, Ljótsson B, et al. Affect-focused psychodynamic psychotherapy for depression and anxiety through the Internet: a randomized controlled trial. PeerJ. 2013;1:e102. doi: 10.7717/peerj.102

47. Roy-Byrne P, Craske MG, Sullivan G, et al. Delivery of Evidence-Based Treatment for Multiple Anxiety Disorders in Primary Care. Jama-J Am Med Assoc. 2010;303(19):1921–28. doi: 10.1001/jama.2010.608

48. Berger T, Urech A, Krieger T, Stolz T, Schulz A, Vincent A, et al. Effects of a transdiagnostic unguided Internet intervention ('velibra') for anxiety disorders in primary care: results of a randomized controlled trial. Psychol Med. 2017;47(1):67–80. doi: 10.1017/S0033291716002270

49. Norton PJ, Barrera TL. Transdiagnostic Versus Diagnosis-Specific CBT for Anxiety Disorders: A Preliminary Randomized Controlled Noninferiority Trial. Depress Anxiety. 2012;29(10):874–82. doi: 10.1002/da.21974

50. Johnston L, Titov N, Andrews G, Spence J, Dear BF. A RCT of a Transdiagnostic Internet-Delivered Treatment for Three Anxiety Disorders: Examination of Support Roles and Disorder-Specific Outcomes. PLoS One. 2011;6(11):e28079. doi: 10.1371/journal.pone.0028079

51. Forman EM, Herbert JD, Moitra E, Yeomans PD, Geller PA. A randomized controlled effectiveness trial of acceptance and commitment therapy and cognitive therapy for anxiety and depression. Behav Modif. 2007;31(6):772–99. doi: 10.1177/0145445507302202

52. Newby JM, Mackenzie A, Williams AD, McIntyre K, Watts S, Wong N, et al. Internet cognitive behavioural therapy for mixed anxiety and depression: a randomized controlled trial and evidence of effectiveness in primary care. Psychol Med. 2013;43(12):2635–48. doi: 10.1017/S0033291713000111

53. Wuthrich VM, Rapee RM, Kangas M, Perini S. Randomized controlled trial of group cognitive behavioral therapy compared to a discussion group for co-morbid anxiety and depression in older adults. Psychol Med. 2016;46:785–95. doi: 10.1017/S0033291715002251

54. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed., text rev. Washington, DC: APA; 2000.

55. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.

56. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928. doi: 10.1136/bmj.d5928

57. Barrowclough C, King P, Colville J, Russell E, Burns A, Tarrier N. A randomized trial of the effectiveness of cognitive-behavioral therapy and supportive counseling for anxiety symptoms in older adults. J Consult Clin Psych. 2001;69(5):756–62. doi: 10.1037/0022-006X.69.5.756

58. Brenes GA, Miller ME, Williamson JD, McCall WV, Knudson M, & Stanley MA. A randomized controlled trial of telephone-delivered cognitive-behavioral therapy for late-life anxiety disorders. Am J Geriat Psychiat. 2012;20(8):707–16. doi: 10.1097/JGP.0b013e31822ccd3e

59. Lang AJ, Schnurr PP, Jain S, He F, Walser RD, Bolton E, et al. Randomized controlled trial of acceptance and commitment therapy for distress and impairment in OEF/OIF/OND veterans. Psychol Trauma.2017;9(Suppl 1):74–84. doi: 10.1037/tra0000127

60. Day V, McGrath PJ, Wojtowicz M. Internet-based guided self-help for university students with anxiety, depression and stress: A randomized controlled clinical trial. Behav Res Ther. 2013;51(7):344–51. doi: 10.1016/j.brat.2013.03.003

61. Mullin A, Dear BF, Karin E, et al. The UniWellbeing course: A randomised controlled trial of a transdiagnostic internet-delivered cognitive behavioural therapy (CBT) programme for university students with symptoms of anxiety and depression. Internet Interv. 2015;2(2):128–36. Doi: 10.1016/j.invent.2015.02.002

62. Marks IM, Kenwright M, McDonough M, Whittaker M, Mataix-Cols D. Saving clinicians' time by delegating routine aspects of therapy to a computer: a randomized controlled trial in phobia/panic disorder. Psychol Med. 2004;34(1):9–17. doi: 10.1017/S003329170300878X

63. Proudfoot J, Ryden C, Everitt B, Shapiro DA, Goldberg D, Mann A, et al. Clinical efficacy of computerised cognitive-behavioural therapy for anxiety and depression in primary care : randomised controlled trial. Brit J Psychiat. 2004;185(1):46–54. doi: 10.1192/bjp.185.1.46

64. Schmidt NB, Norr AM, Allan NP, Raines AM, Capron DW. A randomized clinical trial targeting anxiety sensitivity for patients with suicidal ideation. J Consult Clin Psychol. 2017;85(6):596–610. doi: 10.1037/ccp0000195

65. Craske MG, Farchione TJ, Allen LB, Barrios V, Stoyanova M, Rose R. Cognitive behavioral therapy for panic disorder and comorbidity: More of the same or less of more? Behav Res Ther. 2007;45(6),1095–109. doi: 10.1016/j.brat.2006.09.006

66. Neacsiu AD, Eberle JW, Kramer R, Wiesmann T, Linehan MM. Dialectical behavior therapy skills for transdiagnostic emotion dysregulation: a pilot randomized controlled trial. Behav Res Ther. 2014;59:40–51. doi: 10.1016/j.brat.2014.05.005

67. Nordgren LB, Hedman E, Etienne J, Bodin J, Kadowaki A, Eriksson S, et al. Effectiveness and cost-effectiveness of individually tailored Internet-delivered cognitive behavior therapy for anxiety disorders in a

primary care population: A randomized controlled trial. Behav Res Ther. 2014;59:1–11. doi: 10.1016/j.brat.2014.05.007

68. Boettcher J, Aström V, Påhlsson D, Schenström O, Andersson G, Carlbring P. Internet-based mindfulness treatment for anxiety disorders: a randomized controlled trial. Behav Ther. 2014;45(2):241–53. doi: 10.1016/j.beth.2013.11.003

69. Bressi C, Porcellana M, Marinaccio PM, Nocito EP, Magri L. Short-term psychodynamic psychotherapy versus treatment as usual for depressive and anxiety disorders: a randomized clinical trial of efficacy. J Nerv Ment Dis. 2010;198(9):647–52. doi: 10.1097/NMD.0b013e3181ef3ebb

70. Ejeby K, Savitskij R, Ost LG, Ekbom A, Brandt L, Ramnerö J, et al. Randomized controlled trial of transdiagnostic group treatments for primary care patients with common mental disorders. Fam Pract. 2014;31(3):273–80. doi: 10.1093/fampra/cmu006

71. Erickson DH, Janeck AS, Tallman K. A cognitive-behavioral group for patients with various anxiety disorders. Psychiatr Serv. 2007;58(9):1205–11. Doi: 10.1176/ps.2007.58.9.1205

72. Hadjistavropoulos HD, Schneider LH, Edmonds M, Karin E, Nugent MN, Dirkse D, et al. Randomized controlled trial of Internet-delivered cognitive behaviour therapy comparing standard weekly versus optional weekly therapist support. J Anxiety Disord. 2017;52:15–24.

73. Johansson R, Sjöberg E, Sjögren M, Johnsson E, Carlbring P, Andersson T, et al. Tailored vs. Standardized Web-based Cognitive Behavior Therapy for Depression and Comorbid Symptoms: A Randomized Controlled Trial. PLoS One. 2012;7(5):e36905. doi: 10.1371/journal.pone.0036905

74. Riccardi CJ, Korte KJ, Schmidt NB. False safety behavior elimination therapy: A randomized study of a brief individual transdiagnostic treatment for anxiety disorders. J Anxiety Disord. 2017;46:35–45. doi: 10.1016/j.janxdis.2016.06.003

75. Schmidt NB, Buckner JD, Pusser A, Woolaway-Bickel K, Preston JL, Norr A. Randomized Controlled Trial of False Safety Behavior Elimination Therapy: A Unified Cognitive Behavioral Treatment for Anxiety Psychopathology. Behav Res Ther. 2012;43(3):518–32. doi: 10.1016/j.beth.2012.02.004

76. Schneider AJ, Mataix-Cols D, Marks IM, Bachofen M. Internet-guided self-help with or without exposure therapy for phobic and panic disorders: A randomised controlled trial. Psychother Psychosom. 2005;74(3):154–64. Doi: 10.1159/000084000

77. Schröder J, Jelinek L, Moritz S. A randomized controlled trial of a transdiagnostic Internet intervention for individuals with panic and phobias - One size fits all. J Behav Ther Exp Psy. 2017;54:17–24. doi: 10.1016/j.jbtep.2016.05.002

78. Silfvernagel K, Carlbring P, Kabo J, Edströmk S, Eriksson J, M, Månson L. Individually tailored internet-based treatment for young adults and adults with panic attacks: randomized controlled trial. J Med Internet Res. 2012;14(3):e65. doi: 10.2196/jmir.1853

79. Taylor C, Lyubomirsky S, Stein MB. Upregulating the positive affect system in anxiety and depression: Outcomes of a positive activity intervention. Depress Anxiety. 2017;34(3):267–80. doi: 10.1002/da.22593

80. Titov N, Dear BF, Johnston L, Lorian C, Zou J, Wootton B, et al. Improving Adherence and Clinical Outcomes in Self- Guided Internet Treatment for Anxiety and Depression: Randomised Controlled Trial. PLoS One. 2013;8(7):e62873. doi: 10.1371/journal.pone.0062873

81. Wuthrich VM, Rapee RM. Randomised controlled trial of group cognitive behavioural therapy for comorbid anxiety and depression in older adults. Behav Res Ther. 2013;51(12):779–86. doi: 10.1016/j.brat.2013.09.002

82. Steele SJ, Farchione TJ, Cassiello-Robbins C, Ametaj A, Sbi S, Sauer-Zavala S, Barlow DH. Efficacy of the Unified Protocol for transdiagnostic treatment of comorbid psychopathology accompanying emotional disorders compared to treatments targeting single disorders. J Psychiat Res. 2018;104:211–16. doi: 10.1016/j.jpsychires.2018.08.005

83. Ellard KK, Fairholme CP, Boisseau CL, Farchione TJ, Barlow DH. Unified protocol for the transdiagnostic treatment of emotional disorders: Protocol development and initial outcome data. Cogn Behav Pract. 2010;17(1):88–101. doi: 10.1016/j.cbpra.2009.06.002

84. Gutner CA, Galovski T, Bovin MJ, Schnurr PP. Emergence of Transdiagnostic Treatments for PTSD and Posttraumatic Distress. Curr Psychiat Rep. 2016;18(10):95. doi: 10.1007/s11920-016-0734-x

85. Keller MB. The long-term clinical course of generalized anxiety disorder. J Clin Psychiat. 2002;63(Suppl. 8):11–6.

86. McLaughlin T, Geissler EC, Wan GJ. Comorbidities and associated treatment charges in patients with anxiety disorders. Pharmacotherapy. 2003;23:1251–6. doi: 10.1592/phco.23.12.1251.32700

87. Sauer-Zavala S, Cassiello-Robbins C, Ametaj AA, Wilner JG, Pagan D. Transdiagnostic Treatment Personalization: The Feasibility of Ordering Unified Protocol Modules According to Patient Strengths and Weaknesses. Behav Modif. 2018. doi: 10.1177/0145445518774914

88. Andersson G. Internet-delivered psychological treatments. Annu Rev Clini Psycho. 2016;12:157-79. doi: 10.1146/annurev-clinpsy-021815-093006

89. Norton PJ, Hayes SA, Hope DA. Effects of a transdiagnostic group treatment for anxiety on secondary depression. Depress Anxiety. 2004;20(4):198–202. doi: 10.1002/da.20045

90. Kazdin AE, Blase SL. Rebooting Psychotherapy Research and Practice to Reduce the Burden of Mental Illness. Perspect Psychol Sci. 2011;6(1):21–37. doi: 10.1177/1745691610393527

91. Andersson G, Titov N. Advantages and limitations of Internet-based interventions for common mental disorders. World Psychiatry. 2014;13(1):4–11. doi: 10.1002/wps.20083

92. Bennet GG, Glasgow RE. The delivery of public health interventions via the Internet: actualizing their potential. Annu Rev Public Health;30:273–92. doi: 10.1146/annurev.publhealth.031308.100235

93. Saxena S, Thornicroft G, Knapp M, Whiteford H. Resources for mental health: scarcity, inequity, and inefficiency. Lancet. 2007;370(9590):878–89. doi: 10.1016/S0140-6736(07)61239-2

94. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. J Am Podiatr Med Assoc. 2001;91:437–42.

95. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. J Clin Epidemiol. 2010;63(8):e1–37. doi: 10.1016/j.jclinepi.2010.03.004

96. Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-7. doi: 10.7326/0003-4819-158-3-201302050-00583

97. Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ. 2013;346:e7586. doi: 10.1136/bmj.e7586

98. **Section/topic**	#	**Checklist item**	**Reported on page #**
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	21
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Not applicable
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Not applicable
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Not applicable
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9-20
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Not applicable
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Not applicable
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	21-24

Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	21
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not applicable
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	24-28
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	28-29
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	29
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Not applicable

Chapter 3. Effectiveness of a transdiagnostic Internet-based protocol for the treatment of emotional disorders versus treatment as usual in specialized care: Study protocol for a randomized controlled trial

This chapter has been published as:

González-Robles, A., García-Palacios, A., Baños, R., Riera, A., Llorca, G., Traver, F., Haro, G., Palop, V., Lera, G., Romeu, J. E., & Botella, C. Effectiveness of a transdiagnostic internet-based protocol for the treatment of emotional disorders versus treatment as usual in specialized care: study protocol for a randomized controlled trial. *Trials*, *16*, 488.

Effectiveness of a transdiagnostic internet-based protocol for the treatment of emotional disorders versus treatment as usual in specialized care: Study protocol for a randomized controlled trial

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Abstract

Background: Emotional disorders (depression and anxiety disorders) are highly prevalent mental health problems. Although evidence showing the effectiveness of disorder-specific treatments exists, high comorbidity rates among emotional disorders limit the utility of these protocols. This has led some researchers to focus their interest on transdiagnostic interventions, a treatment perspective that might be more widely effective across these disorders. Also, the current way of delivering treatments makes it difficult provide assistance to all of the population in need. The use of the Internet in the delivery of evidence-based treatments may help to disseminate treatments among the population. In this study, we aim to test the effectiveness of EmotionRegulation, a new transdiagnostic Internet-based protocol for unipolar mood disorders, five anxiety disorders (panic disorder, agoraphobia, social anxiety disorder, generalized anxiety disorder and anxiety disorder not otherwise specified), and obsessive-compulsive disorder in comparison to treatment as usual as provided in Spanish public specialized mental health care. We will also study its potential impact on basic temperament dimensions (neuroticism/behavioral inhibition and extraversion/behavioral activation). Expectations and opinions of patients about this protocol will also be studied.

Methods/Design: The study is a randomized controlled trial. 200 participants recruited in specialized care will be allocated to one of two treatment conditions: a) EmotionRegulation or b) treatment as usual.

Primary outcome measures will be the BAI and the BDI-II. Secondary outcomes will include a specific measure of the principal disorder, and measures of neuroticism/behavioral inhibition and extraversion/behavioral activation. Patients will be assessed at baseline, pos post-treatment, and 3- and 12-month follow-ups. Intention to treat and per protocol analyses will be performed.

Discussion: Although the effectiveness of face-to-face transdiagnostic protocols has been investigated in previous studies, the number of published transdiagnostic Internet-based programs is still quite low. To our knowledge, this is the first randomized controlled trial studying the effectiveness of a transdiagnostic Internet-based treatment for several emotional disorders in public specialized care. Combining both a transdiagnostic approach with an Internet-based therapy format may help to decrease the burden of mental disorders, reducing the difficulties associated with disorder-specific treatments and facilitating access to people in need of treatment. Strengths and limitations are discussed.

Trial registration: ClinicalTrials.gov NCT02345668. Registered 27 July 2015.

Keywords: Transdiagnostic, Internet, Randomized controlled trial, Emotional disorders, Depression, Anxiety, Computer-delivered psychotherapy, Neuroticism/behavioral inhibition, Extraversion/behavioral activation

Background

Introduction

Emotional disorders (ED) (anxiety and mood disorders) are among the most prevalent mental disorders, with a life prevalence of 29 % and comorbidity rates ranging between 40 and 80 % [1, 2]. If the person experiencing the disorder is not adequately treated, the course often becomes chronic and can significantly affect important functioning areas such as work and social relationships [3, 4]. Moreover, the medical care costs and production losses associated with these mental health problems in Europe are huge [2]. These data strongly suggest that efficacious and efficient treatments are needed to address this important health problem [5–8]. Nevertheless, despite these alarming data, evidence exists indicating that most people with depression and anxiety disorders (less than 50 %) do not receive treatment. [9]. To reduce the burden of mental illness, some authors have emphasized the need for an approach that goes beyond the dominant face-to-face treatment approach in order to provide help to people in need of evidence-based treatments, and this

approach includes the use of the media, self-help interventions, the use of special settings and information and communication technologies (ICT) [10].

Efficacious psychological treatments for ED currently exist, and a number of evidence-based cognitivebehavioral treatments (CBT) targeting specific disorders have been developed in the past 20 years [11–17]. However, disorder-specific treatment protocols have some problems. First, the high comorbidity rates among ED. Epidemiological studies have shown that at least 55 % of people suffering from depression and an anxiety disorder suffer from another anxiety disorder at the time of the assessment, and this prevalence rate increases to 76 % when different lifespan diagnoses are taken into account [18]. Consequently, clinicians often have to decide on which is the most adequate disorderspecific protocol in these cases, and because these treatments focus on disorder-specific symptomatology, other comorbid diagnoses do not receive sufficient attention [19]. Second, disorder-specific protocols frequently do not target subthreshold symptoms that did not meet diagnostic thresholds for one disorder or another but that may be important to address in the treatment [20]. Third, the high rate in which “not otherwise specified” diagnoses of clinical significance are assigned as current and lifetime conditions for which there are not specific interventions [18]. Finally, the fact that each manualized specific-disorder treatment requires the use of separate handbooks, workbooks and protocols may be an obstacle in the dissemination of evidence-treatments due to its costs and the important amount of training to become adequately familiar with each of the different treatments [20].

Transdiagnostic approach

In recent years, there has been great interest in treatment strategies (referred to as transdiagnostic treatments) that might be more widely effective across these diverse mental health disorders. Unlike disorder-specific treatment protocols, transdiagnostic treatments generally include treatments aimed at addressing different disorders (for example, different anxiety disorders) with a single protocol [21]. A growing body of research showing the efficacy of transdiagnostic treatments for anxiety disorders [22–27], and for comorbid depression and anxiety disorders [28–30] has emerged in the past years. Moreover, the efficacy and effectiveness of transdiagnostic treatment protocols for ED have been shown in two recent meta-analyses [31, 32].

An important line of research within the transdiagnostic approach is that initiated by D. H. Barlow [20, 33–36]. Barlow’s theory of triple vulnerability emphasizes the underlying vulnerabilities that are common to emotional disorders and help to explain the comorbidity among these

diverse conditions [20, 33]. From this theoretical framework, ED are regarded as minor variations in the manifestation of a broader syndrome (that is, “ general neurotic syndrome”) such that the development of treatments directly targeting this underlying syndrome rather than symptom-specific variations would result in a more parsimonious, easier to disseminate treatment approach [20]. It would also result in a more inclusive approach, as it lays on the existence of biological and psychological vulnerabilities that are hypothesized to be common among anxiety disorders, unipolar mood disorders, and other disorders such as somatoform and dissociative disorders [20, 37]. Based on this perspective, Barlow’s team designed the Unified Protocol (UP) [37–41], a transdiagnostic treatment protocol that emphasizes the role of emotion regulation in understanding and treating ED. Due to difficulties in emotion regulation, people with ED often react negatively to their own emotions, and they are more likely to use maladaptive emotion regulation strategies that, in turn, increase the frequency and intensity of negative emotions [37]. To enhance adaptive emotion regulation strategies, the UP focuses on four essential aspects: increasing present-focused emotional awareness, addressing emotional avoidance, promoting cognitive flexibility, and facilitating exposure to avoided situations and sensations. The results obtained using this protocol in a traditional face-to-face format demonstrate its effectiveness and are encouraging [30, 38, 42].

The core of all emotion regulation difficulties has been pointed out to be neuroticism/behavioral inhibition (N/BI) [34, 43, 44]. Previous research supports the role of N/BI in accounting for the onset, overlap, and maintenance of ED [33, 44–46]. Literature has also highlighted the role of extraversion/behavioral activation (E/BA) in ED. For instance, structural models have indicated that low E/BA is associated with unipolar depression [47], social anxiety [48] and agoraphobia [49]. Also, a recent meta-analysis indicated that most individuals with anxiety and mood disorders show low levels of E/BA [50]. The effect of the UP on these two temperament dimensions has been demonstrated recently [51].

Literature about Dialectical Behavior Therapy (DBT) has also highlighted the role of emotion dysregulation in psychological disorders [52, 53]. A primary goal in DBT is training patients in adaptive emotion regulation strategies, as emotion dysregulation is assumed to be a key factor in the development and maintenance of these problems [52]. Emotion regulation difficulties have also been shown to be a transdiagnostic factor across a number of psychological disorders, including anxiety and depression [54–58]. A treatment protocol derived from DBT emotion regulation skills training has been tested in a recent study, suggesting that training patients in emotion regulation strategies (for

example increasing emotional awareness) may help to reduce anxious and depressive symptoms among distinct ED [59].

Internet-based treatment protocols

ICT such as the Internet may facilitate access by people for whom traditional therapy is not available [10]. Internet-based treatments have proven to be a very promising tool for solving several mental health problems and enhancing the dissemination of evidence-based treatments [60–63]. Several advantages regarding the recruitment of patients, assessment, diagnosis and case management in Internet-based treatment protocols have been indicated in a recent article [64]. A number of systematic reviews have shown that Internet-based treatments are efficacious [65–69]. Moreover, meta-analyses reveal that these protocols produce higher effect sizes compared to control groups [60, 65, 70] and that they are as efficacious as face-to-face traditional treatments [66, 70–72]. In sum, there is extensive evidence showing the efficacy of these treatments. However, the evidence available about Internet-based treatments is almost exclusively limited to disorder-specific protocols. Indeed, very few studies combining both a transdiagnostic approach and an Internet-based delivery format have been tested through randomized controlled trials (RCT) [25, 26, 29, 73]. Moreover, studies analyzing the efficacy of transdiagnostic Internet-based treatments, address the treatment of anxiety disorders only [25, 26, 73] or have used open-trial designs [28, 74]. Among those focused on anxiety and depression the existing protocols do not contemplate either the treatment of " not otherwise specified" diagnoses or obsessive-compulsive disorder [29], or target a small range of ED [29]. Moreover, to our knowledge, no RCT have been carried out on the effectiveness of a transdiagnostic Internet-based protocol versus treatment as usual (TAU) in public mental specialized care settings.

Current study

Our research group has developed a traditional transdiagnostic treatment that is partly based on the UP [37]. Taking into account the importance of emotion regulation in the treatment of ED, it also includes components of emotion regulation from DBT [52]. Based on the traditional treatment protocol, we developed EmotionRegulation, an adaptation of this treatment that can be applied online over the Internet.

In this study, we aim to present EmotionRegulation, and test its effectiveness for the treatment of ED in an RCT with a sample made up of participants from specialized care in the Spanish public mental health system, compared to TAU. The ED targeted in this study will be major

depression disorder (MDD), dysthymic disorder (DD), panic disorder (PD), agoraphobia (A), social anxiety disorder (SAD), generalized anxiety disorder (GAD), and obsessive-compulsive disorder (OCD). Anxiety disorder not otherwise specified (ADNOS) and (unipolar) mood disorder not otherwise specified (MDNOS) will also be targeted. Secondary objectives will include the following: a) study of the effects of EmotionRegulation on two dimensions of temperament (that is, N/BI and E/BA) and b) study of the acceptability (expectations and opinions) of the online program by patients. In this article, we present the study design.

Methods/Design

Study design

A two-armed simple-blinded randomized controlled trial will be conducted. Participants will be randomly allocated to one of two conditions: a) EmotionRegulation and b) TAU. Randomization will be stratified by primary diagnosis. Block randomization will be performed within each strata in order to ensure all primary diagnoses are equally represented across conditions. The study will be conducted following the CONSORT statement (Consolidated Standards of Reporting Trials, http://www.consort-statement.org) [75, 76] and CONSORT-EHEALTH guidelines [77]. Participants will be assessed at pre- and post-treatment, and at 3- and 12-month follow-ups. The study flowchart is shown in Figure 6.

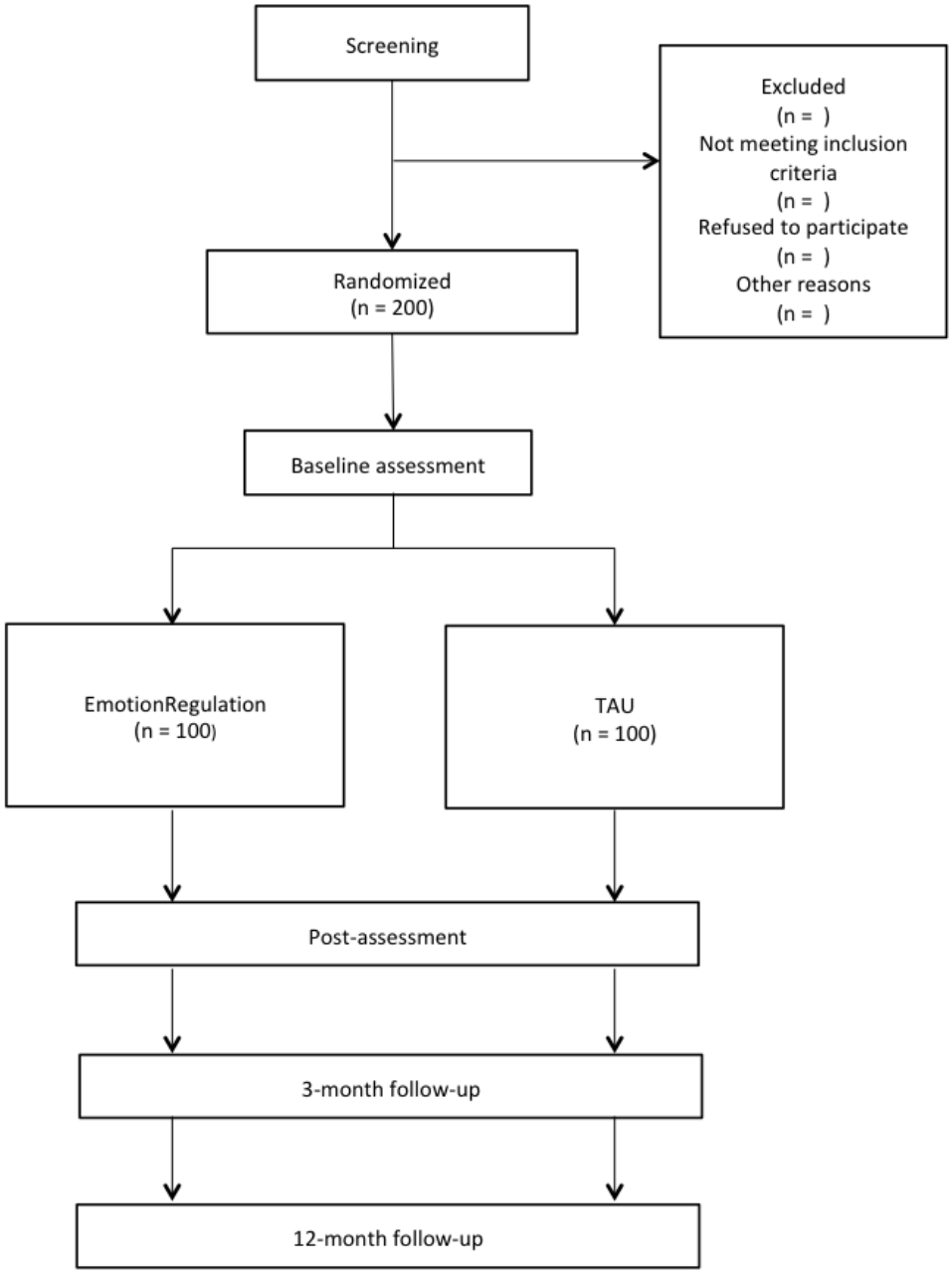

Figure 6. Study flowchart
EmotionRegulation, transdiagnostic Internet-based protocol; TAU, treatment as usual

Study population

The clinical trial will be conducted in the Mental Health Department of the Provincial Consorcio Hospitalario in Castellon and the University Hospital La Ribera in Valencia (Spain). Participants will be adult outpatients from specialized care who attend mental health units to seek psychological and/or psychiatric treatment. Participants will be recruited by clinical psychologists and psychiatrists working in these centers, until the

required sample is complete. In order to facilitate the selection of participants in the study, both clinical psychologists and psychiatrists will be given a sheet containing the eligibility criteria.

Ethics

This trial will be conducted in compliance with the study protocol, the Declaration of Helsinki and good clinical practice. Data security/confidentially will be guaranteed; all relevant EU legislation and international texts on privacy will be observed and respected. Access to the Internet platform is through a unique usernamepassword combination and will be available on a 24/7 basis. All transferred data will be secured via AES-256 encryption.

The study has been approved by the Ethics Committee of University Jaume I (Castellon, Spain) and the Clinical Research Ethics Committee from two hospitals (Consorcio Hospitalario Provincial de Castellon, and Hospital Universitario de la Ribera). The trial was registered at clinicalstrials.gov as NCT02345668. For ethical reasons, patients allocated to TAU will be offered free access to EmotionRegulation after the study has been completed.

Eligibility criteria

Inclusion criteria will include the following: a) be 18 years or older; b) ability to understand and read Spanish; c) access to Internet at home and having an email address; d) meeting the DSM-IV diagnostic criteria [78] for ED (MDD, DD, MDNOS, PD, A, SAD, GAD, ADNOS, OCD); and e) providing written, informed consent. Exclusion criteria include the following: a) suffering from a severe mental disorder (schizophrenia, bipolar disorder, and alcohol and/or substance dependence disorder); b) the presence of a high risk of suicide; c) medical disease/condition that prevents the participant from carrying out the psychological treatment; or d) receiving another psychological treatment during the study in the experimental group. Receiving pharmacological treatment is not an exclusion criterion during the study period, but patients having an increase and/or change in the medication 2 months prior to enrollment will not be considered for the trial. Also, the increase and/or change in the medication during the study period in the experimental group will imply the participant's exclusion from subsequent analyses (a decrease in pharmacological treatment is accepted).

Recruitment

When the psychiatrist or clinical psychologist identifies a potential participant, he or she will describe the study characteristics to him/her. Those candidates interested in participating will sign an informed consent, and the professional will fill out a document describing the participant's

sociodemographic and clinical characteristics, and give him/her a patient information sheet and a handout describing the study. After confirming that the participant has signed the informed consent and understands the study and the treatment options, the researcher will administer assessment instruments related to the inclusion criteria. If the patient fulfills all the study criteria, the researcher will contact an independent researcher to implement randomization. Participants who meet all the inclusion criteria will then be randomized to either EmotionRegulation or TAU and complete the remaining assessment instruments. Participants will be free at any time to withdraw from the treatment or the study without giving any explanation.

Randomization and blinding

Patients will be randomly allocated in a 1:1 ratio to either of the two groups (EmotionRegulation or TAU) using a computer-generated random number sequence. The Epidat 4.1 program will be used to generate this sequence. The allocation will be carried out by an independent researcher who will be unaware of the characteristics of the study. The sequence will be concealed until interventions are assigned. Patients will agree to participate before the random allocation and without knowing to which treatment they will be allocated. Study researchers conducting psychological assessments (that is, diagnostic interviews) throughout the entire study will be masked to the participants' treatment conditions and unaware of the treatment group to which the patient belongs. For ethical and practical reasons, participants will not be blind to the treatment conditions.

Interventions

Transdiagnostic Internet-based protocol (EmotionRegulation)

Our research group developed a transdiagnostic protocol made up of 12 modules designed for the treatment of the following mental disorders: MDD, DD, MDNOS, PD, A, SAD, GAD, ADNOS and OCD. This protocol is partly based on the UP by David H. Barlow [37] and partly on the emotion regulation skills from DBT by Marsha Linehan [52]. The intervention aims to enhance present-focused emotional awareness, facilitate cognitive flexibility, identify and modify behavioral and emotional avoidance patterns, and promote interoceptive and situational exposure. Each module includes several tasks to practice the different techniques and skills.

We have adapted this protocol for its application on the Internet (EmotionRegulation). EmotionRegulation is an internet-delivered, multimedia, interactive, selfadministered program for ED that allows the individuals to learn and practice adaptive ways to regulate their emotions

from a transdiagnostic perspective. EmotionRegulation will be delivered through a web platform (https://www.psicologiaytecnologia.com/) designed by our research group. This web platform has four main sections (shown in Table 2).

EmotionRegulation includes a Welcome module that provides the participant with general information about the protocol and its objectives, as well as recommendations for benefiting from it, and the following 12 treatment modules:

M1. Emotional disorders and emotion regulation. This module provides information about the role of emotion regulation in emotional disorders. A brief description of the program modules is also presented, as well as videos with examples of people suffering from different ED.
M2. Motivation for change. The aims are to analyze the advantages and disadvantages of changing, emphasize the importance of being motivated, and highlight the importance of establishing significant life goals.
M3. Understanding the role of emotions. This module provides information about the adaptive roles and functions of emotions and the three-component model of emotions.
M4. The acceptance of emotional experiences. This module aims to teach the patient the acceptance of emotional experiences and its importance in the treatment.
M5. Practicing acceptance. The objective is to continue to learn about the acceptance of emotional experiences and increase awareness of physical sensations, thoughts, emotions and daily activities.
M6. Learning to be flexible. It focuses on the importance of maladaptive ways of thinking in the maintenance of emotional disorders, and on learning how to identify them.
M7. Practicing cognitive flexibility. This module aims to teach the patients the ways maladaptive ways of thinking can be modified. It also provides information about intrusive thoughts and how to deal with them.
M8. Emotional avoidance. This module aims to teach the patients the emotion avoidance strategies that contribute to the maintenance of emotional disorders.

Table 2. Main sections of the web platform

a) “Home”: This section is the start point from which participants can access the other sections. It also displays a progress bar (0 to 100 %) that shows the progress through the treatment.

b) “Calendar”: This section shows pending tasks as well as the days in which the participant has accessed the program and has done the module tasks.

c) “Review”: This section allows participants to review the treatment modules already done as many times as they want.

d) “How am I?”: This section allows participants to monitor their progress through several graphs as they advance in the program.

M9. Emotion Driven Behaviors (EDBs). The aim is to learn the concept of EDBs, and replace their own maladaptive EDBs with other more adaptive behaviors.
M10. Accepting and facing physical sensations. The objectives are to teach the patients the role of physical sensations in the emotional response and train them in interoceptive exposure, in order to increase tolerance and promote habituation to physical sensations.
M11. Facing emotions in the contexts in which they occur. The purpose is the construction of exposure hierarchies to help the patients to begin to face the avoided situations that contribute to the maintenance of the problem.
M12. Relapse prevention. This module aims to review the strategies learned throughout the program and teach the patient how to identify and cope with future high-risk situations.

These modules are sequential, in order to move through the program step by step. The program duration can vary among the users, and it is estimated that for most participants the duration will be 18 weeks. During the study, EmotionRegulation will be accessible only to participants in the online intervention group. Participants will be allowed to use the program at any time they want during the trial period. See Table 3 for other functionalities in EmotionRegulation.

Participants in the EmotionRegulation condition will be allowed to maintain medication if there are not changes and/or increases but will not be allowed to receive another psychological treatment during the study period. Failure to fulfill these criteria will result in the participant’s data being excluded from data analysis.

Table 3. Other functionalities in EmotionRegulation

a) Assessments: The program allows the pre-, post- and follow-up instruments to be completed online.

b) Module self-assessments: Each module ends with a short list of multiple-choice questions that allow participants to assess their understanding of the module and help them to decide whether they need to review its contents.

c) Automatic e-mails with reminders when participants have not accessed the program in the past 15 days.

d) Suicide risk alarms: Therapists receive warnings of participants with high risk of suicide (when participants answer questionnaires that include items assessing high suicide risk).

e) Post-module questionnaires: Each module includes three brief questionnaires (OASIS, ODSIS and PANAS) to evaluate anxiety, depression and positive/negative affect after each treatment module. Participants are able to monitor these scores in the feedback section through the 'How am I?' button.

f) Printable documents: Each module contains several printable documents (PDF) with summaries and self-monitoring sheets that participants are encouraged to use to practice the skills and strategies.

Treatment as usual

Treatment as usual (TAU) is treatment as delivered in current daily practice by psychiatrists and clinical psychologists in the mental health centers in Spain. TAU may refer to psychiatric treatment, which typically includes prescription and monitoring of antidepressant and/or anxiolytic medication, psychological treatment (this may include case management, group psychotherapy, empathic listening and/or supportive counselling), or a combination of both. Patients in the TAU condition already receiving any of the aforementioned treatments are informed they will continue to receive as usual the services received before enrollment in the study.

Support

Meta-analyses have shown that attrition rates are higher when no support of any kind is provided to patients in self-administered Internet-based programs [60, 68]. Therefore, we will provide human support and ICT support to all participants in EmotionRegulation.

Human support will be provided by trained predoctoral students in our group and will include the following: a) an initial face-to-face session to explain the participant the characteristics of the study and to administer the diagnostic interview to confirm him/her to fulfill the eligibility criteria, b) an initial phone call encouraging participants to start the intervention once baseline assessments have been completed, and c) one weekly brief phone call (maximum of 10 minutes) during the treatment period. The objective of these weekly phone calls will be as follows: 1) to ask the participants about any difficulties or doubts they might have found in the use of the online protocol and help them to solve those problems, 2) to remind them to review the treatment contents as many times as necessary, 3) to emphasize the importance of doing the homework tasks, 4) to encourage participants to keep using the protocol and reinforce them for engaging in the treatment, and 5) to recommend that they complete one module per week. Finally, d) a final phone call will be made after the 18-week treatment period to remind participants that they will be allowed to use the program at any time they want during the trial period and that they will be contacted for follow-up assessments.

ICT support will consist of two weekly mobile phone text messages with reminders about the importance of doing the homework tasks and encouraging participants to review the modules. A commercial platform (www.trendoo.es) will be used to send these messages.

Instruments

Patients will be assessed at baseline, post-treatment (18 weeks after baseline), and at 3- and 12-month follow-ups. Scores on anxiety, depression and negative and positive affect will also be obtained after each module has been completed. The study variables and assessment times are summarized in Table 4.

Diagnosis interview

Mini International Neuropsychiatric Interview Version 5.0.0 (MINI) [79]. It is a short structured diagnostic psychiatric interview that yields key DSM-IV and ICD-10 diagnoses. The MINI can be administered in a short period of time, and clinical interviewers need only brief training. The MINI has been translated into Spanish and validated [80].

Table 4. Study variables and assessment points

Instrument	Assessment area	Time of assessment
MINI Neuropsychiatric Interview	Psychiatric diagnosis	Baseline, Post-T and follow-ups
BAI	Severity of anxiety	Baseline, Post-T and follow-ups
BDI-II	Severity of depression	Baseline, Post-T and follow-ups
Sociodemographic data	Gender, age, marital status, education, occupation, economic level	Baseline
OASIS	Severity of anxiety	Post-module
ODSIS	Severity of depression	Post-module
SIAS	Severity of SAD symptoms	Baseline, Post-T and follow-ups
PDSS-SR	Severity of PD and A symptoms	Baseline, Post-T and follow-ups
PSWQ	Severity of GAD symptoms	Baseline, Post-T and follow-ups
OCI-R	Severity of OCD symptoms	Baseline, Post-T and follow-ups
EQ-5D	Health-related quality of life	Baseline, Post-T and follow-ups
PANAS	Positive and negative affect	Post-module
BIS-BAS	Behavioral inhibition/activation	Baseline, Post-T and follow-ups
ETS	Expectation of treatment	Baseline
OTS	Opinion of treatment	Post-T

Post-T, post-treatment (18 weeks after baseline); follow-ups, 3- and 12-month follow-ups. BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-II; OASIS, Overall Anxiety Severity and Impairment Scale; ODSIS, Overall Depression Severity and

Impairment Scale; SIAS, Social Interaction Anxiety Scale; PDSS-SR, Self-Reported Panic Disorder Severity Scale; PSWQ, Penn State Worry Questionnaire; OCI-R, Obsessive-Compulsive Inventory-Revised; EQ-5D, EuroQoL-5D questionnaire PANAS, Positive and Negative Affect Scale; BIS-BAS, Behavioral Inhibition and Behavioral Activation Scales; ETS, Expectation of Treatment Scale; OTS, Opinion of Treatment Scale

Primary outcomes

Beck Anxiety Inventory (BAI) [81]. The BAI is a 21-item self-report measure designed to assess anxiety, with a maximum of 63 points. Each item has a four-point severity scale (for example, not at all, mildly, moderately, and severely) that addresses symptoms experienced during the past week. The internal consistency of the BAI has been found to range from .85 to .94, and it has shown adequate convergent and divergent validity. The Spanish version of the BAI has shown high internal consistency (α = .93) [82].

Beck Depression Inventory (BDI-II) [83]. It is one of the most widely used questionnaires to evaluate depression severity in pharmacological and psychotherapy trials. It consists of 21 items about the different symptoms characterizing major depression disorder, added together to obtain the total score, which can be a máximum of 63 points. The instrument has good internal consistency (α = 0.76 to 0.95). The Spanish version of this instrument has also shown a high internal consistency (α = 0.87) for both the general and clinical populations (α = .89) [84].

Secondary outcomes

Sociodemographic variables

The following sociodemographic variables will be collected: gender, age, marital status (single, married/relationship, separated/divorced, and widowed), education (years of education), and work status.

Diagnosis-specific measures

In order to evaluate the specific anxiety disorder shown by each participant, four different instruments will be implemented. One of the four following questionnaires will be selected and included at pre, post-treatment, and 3- and 12-month follow-up assessments, depending on the main diagnosis given to each participant.

SAD: Social Interaction Anxiety Scale (SIAS) [85]. This scale is made up of twenty items rated from 0 to 4 that assess the anxiety experienced by the patient in social interaction situations. The scale has good internal consistency (α = .88 to .94), good test-retest and discriminant reliability, and appropriate construct validity. The Spanish

validation showed adequate internal consistency and good construct validity [86].

PD/A: Self-Reported Panic Disorder Severity Scale (PDSS-SR) [87]. The scale evaluates the severity of the PD symptomatology through measures of panic attack frequency, distress during panic attacks, anticipatory anxiety, fear and agoraphobic avoidance, fear and avoidance of physical sensations, and work and social impairment. Scale reliability (α = .917) and test-retest reliability (ICC = .81) were shown to be excellent. The psychometric analysis of the Spanish version showed excellent internal consistency (α = .85), good test-retest reliability, and adequate convergent validity [88].

GAD: Penn State Worry Questionnaire (PSWQ) [89], which evaluates worry as an uncontrollable, generalized and excessive experience. The PSWQ has good psychometric properties, with an internal consistency ranging from .91 to .95, and good validity and test-retest reliability. The Spanish version of the scale showed an internal consistency of .90 and a test-retest reliability of .82, as well as adequate convergent and discriminant validity [90].

OCD: Obsessive-Compulsive Inventory-Revised (OCI-R) [91]. The OCI-R is a scale made up of 18 items rated from 1 to 4 and organized in six dimensions (washing, verification, order, obsession, hoarding and mental neutralization) that assess obsessive-compulsive behaviors. The OCI-R has showed good internal consistency (α = .81 to .93), good to excellent test-retest reliability (α = .57 to .91) and good convergent validity. The internal consistency of the Spanish version of the OCI-R has been found to be good (α = .86) [92].

N/BI and E/BA

Behavioral Inhibition and Behavioral Activation Scales (BIS/BAS) [93]. These scales were designed to assess two temperaments identified in Gray' s biobehavioral theory of emotion [94], namely, behavioral inhibition and behavioral activation. The scale is made up of 20 items rated from 1 to 4, with seven BIS subscale items that evaluate individuals' emotional responses to impending negative events and 13 BAS items that assess individuals' behavioral and emotional responses to potentially positive events. The BIS/BAS have demonstrated good reliability in a large sample of individuals with emotional disorders (α = .73 to .92), and stronger associations with other measures of temperament (that is, neuroticism/negative affect and extraversion/positive affect, respectively) than with measures of anxiety or depressive disorder constructs, suggesting that they have good convergent and discriminant validity as indicators of temperament [95]. The internal consistency of the Spanish version ranges between .65 and .82 [96].

Post-module measures

Overall Anxiety Severity and Impairment Scale (OASIS) [97]. The OASIS consists of a 5-item questionnaire, rated from 0 to 4, that assesses the frequency and severity of the anxiety symptoms. The instrument also provides measures of avoidance, as well as work, academic, social and everyday life impairment related to anxiety symptoms. A psychometric analysis of the OASIS scale found good internal consistency ($\alpha = .80$), test-retest reliability ($k = .82$) and convergent validity for this instrument.

Overall Depression Severity and Impairment Scale (ODSIS) [98]. The ODSIS is a self-report measure with five items that evaluate experiences related to depression. The ODSIS measures the frequency and severity of depression, as well as the level of avoidance, work/ school/home interference, and social interference associated with depression. The internal consistency of the scale has been shown to be excellent, with a Cronbach's alpha between .91 and .94 and good convergent and discriminant validity. The Spanish psychometric properties of both the OASIS and the ODSIS are being studied by members of our research team at the time of the publication of this paper.

Positive and Negative Affect Scale (PANAS) [99]. The PANAS consists of 20 items that evaluate two independent dimensions: positive affect (PA) and negative affect (NA). The range for each scale (10 items on each) is from 10 to 50. The Spanish version has demonstrated high internal consistency ($\alpha = 0.89$ and 0.91 for PA and NA in women, respectively, and $\alpha = 0.87$ and 0.89 for PA and NA in men, respectively) in college students [100].

Quality of life

EuroQoL-5D questionnaire (EQ-5D) [101]. It is a generic instrument that measures healthrelated quality of life and consists of two parts: Part 1 assesses self-reported problems in each of five domains: mobility, self-care, daily activities, pain/discomfort and anxiety/depression. Each domain is divided into three levels of severity corresponding to no problems, some problems, and extreme problems, yielding a population-based preference score or societal index (SI). A total of 243 theoretically possible health states can be obtained, and the SI is calculated on the basis of these health states. Values range from 1 (best health state) to 0 (death). However, this index may also provide negative values that correspond to health states perceived as worse than death. Utility scores for these health states were assigned using readily available Spanish population tariffs [102]. Part 2 records the subject's self-assessed health on a visual analogical scale (VAS), a 10 cm vertical line on which the best and worst imaginable health states score 100 and 0, respectively.

Treatment expectations and treatment opinion

Expectation of Treatment Scale (ETS) and Opinion of Treatment Scale (OTS). These questionnaires are adapted from Borkovec and Nau [103]. The content of the six items, rated on a scale from 0 to 10, cover how logical the treatment seemed, to what extent it could satisfy the patient, whether it could be used to treat other psychological problems, its usefulness for the patient' s specific problem, and to what extent the treatment could be aversive. The expectation scale is applied once the treatment rationale has been explained, at the end of the welcome module. Its aim is to measure subjective patient expectations about this treatment. The opinion scale is administered when the patient has completed the treatment, and its aim is to assess satisfaction with this treatment. Our group has used this questionnaire in several research studies [104, 105].

Sample size

The data from an RCT using the UP yielded betweengroup effect sizes of 0.56 for anxiety and 1.11 for depression, as measured with the BAI and BDI-II, respectively [30]. As we aim to compare the intervention with a TAU group, the results of a meta-analysis comparing CBT transdiagnostic treatments versus TAU have also been considered in the estimation of the expected sample size [106]. This meta-analysis reported a medium post-treatment effect size of 0.44 for depression and of 0.34 for anxiety between transdiagnostic treatment protocols vs. TAU conditions. The type of support we provide in this intervention (contact with researchers before, during and after the treatment period) has also been taking into account when estimating the expected sample size, as defined in a previous meta-analysis focused on Internet-based psychological treatments for depression [107]. Based on a power of .80 in a one-tailed test, an alpha of .05, and an estimated drop-out rate of around 30 % [65, 108] we need a sample size of 100 per condition to detect a post-treatment effect size of 0.40 (Cohen' s d) between both groups. Therefore, the total sample size was determined at 200.

Analysis

Intention-to-treat analyses and per protocol analyses will be performed. Reporting of the results will follow CONSORT recommendations [75, 76]. First, the two groups will be compared in order to verify that there are no significant differences between them at baseline using samples t-tests for continuous distributed variables and chi-squares test of independence for categorical to confirm that they are comparable after randomization.

The intention-to-treat principle will be used when analyzing primary and secondary post-treatment data and data collected at the 3- and 12-month follow-ups using mixed effect models with full information maximum likelihood estimation. This method has been recommended for its flexibility over repeated-measures ANOVAs to handle missing date more appropriately [109].

Within and between-group changes will be computed calculating standardized effect sizes (Cohen's d). Cohen's d is calculated by dividing the differences between means by the pooled standard deviation [110]. An effect size of 0.20 is considered to be small, of 0.50 to be moderate, and 0.80 and above to be large [110].

Per protocol analyses (compliers only analysis) will also be conducted. Despite this procedure suffers from selection bias, it can help to draw conclusions about the maximum treatment efficacy in patients who comply fully with the treatment [111].

As the trial is still in execution, the state of the art regarding analytic methodology for RCT will be reviewed before analyzing the data, thus variations in the selection of the most appropriate analytic procedures may occur.

Discussion

This study has several aims. The first is to provide data from a RCT about the effectiveness of a transdiagnostic Internet-based protocol for the treatment of ED in a sample of participants from specialized care in the Spanish public mental health system, compared to TAU. Second, whether the treatment may temper the psychological vulnerability by analyzing its effect on psychological higher-order dimensions (neuroticism/behavioral inhibition and positive affect/behavioral activation) will be studied. The third aim is to study the acceptability of this online program by patients in an ecological setting (public specialized care in Spain).

The advantages of a transdiagnostic Internet-based protocol are two-fold. First, a wide range of ED can be treated with a single protocol, reducing the costs associated with disorder-specific protocols and contributing to solving the problem of comorbidity and NOS diagnoses, as the protocol focuses more on the common pathological processes than on any specific disorder and/or symptomatology. Second, Internet-based protocols can help to disseminate CBT evidence-based treatments, so that more people can benefit from them. This study will provide additional data about the transdiagnostic perspective proposed by Barlow [20], as well as data on the combination of a transdiagnostic perspective and the use of ICTs.

In addition, this study has various strengths. First, this is the first RCT of transdiagnostic Internet-based psychotherapy in specialized care in our country. Positive results achieved with this protocol may have an important impact, since protocols of this type could help to decrease the saturation of the public mental health system, reducing costs and contributing to a general improvement in the public mental health services in our country (for example, reductions in waiting lists, hours of clinical assistance and hours of face-to-face treatment; a higher number of patients who receive psychological treatment; etcetera). Second, the online protocol combines the transdiagnostic cognitive-behavioral principles (psychoeducation about emotions, enhancement of cognitive flexibility, interoceptive and situation-based emotion exposure) with components of acceptance and emotion regulation for the treatment of ED. The data obtained with this protocol can help us to understand the psychopathology of these mental disorders. And third, even though transdiagnostic Internet-based protocols are thought to treat different ED, most of the existing studies exclusively target anxiety disorders [25, 26, 73], and others have used open-trial designs [28, 74] and do not contemplate either the diagnosis of obsessive-compulsive disorder or NOS diagnoses [29] or they focus on a smaller number of ED [29]. We consider that this study broadens the current literature about transdiagnostic Internet-based protocols as it is designed for a wide range of anxiety and depressive disorders. Combining the advantages of both a more inclusive transdiagnostic intervention and an Internet-based delivery format may broaden the scope of evidence-based treatments among the population in need. Moreover, the population in which the study is being conducted, that is, patients who attend a variety of public specialized care settings across Spain, can help to draw conclusions about the external validity of the intervention.

Finally, a number of potential limitations should be indicated. First, dropout rates are expected to be high (around 30 %) [67, 110]. Efforts to maintain these dropout rates below this percentage will be made by providing human support (before, during, and after the intervention) and ICT-support (for example, emails and mobile phone text messages). Second, negative attitudes towards Internet interventions by both clinicians and patients may affect recruitment as well as dropout rates. To minimize the effect of negative attitudes, the nature and characteristics of the intervention will be explained to clinicians involved in the trial. Moreover, for this purpose they will be given a handbook with relevant information about the study (for example objectives of the study, study design, and characteristics of the intervention). In order to increase participant's credibility, prior to enrollment they will be given a sheet with relevant information concerning the characteristics and objectives of the

study, and other issues related to ethics, voluntary participation and confidentiality of the data. Finally, other difficulties could be problems with recruitment, as many people who attend public mental health units do not have access to the Internet at home.

Trial status

The trial is active and recruiting.

Abbreviations

A: agoraphobia; ADNOS: anxiety disorder not otherwise specified; BAI: Beck anxiety inventory; BDI-II: Beck depression inventory-II; BIS/BAS: Behavioral Inhibition and Behavioral Activation Scales; CBT: Cognitive Behavioral Treatments; DBT: Dialectical Behavior Therapy; DD: dysthymic disorder; DSM-IV-TR: Diagnostic and statistical manual of mental disorders, fourth text-revised edition; E/BA: Extraversion/Behavioral Activation; ED: emotional disorders; EDB: Emotion driven behaviors; EQ-5D: EuroQoL-5D questionnaire; ETS: Expectation of treatment scale; GAD: generalized anxiety disorder; ICD-10: International classification of diseases 10th revision; ICT: Information and communication technologies; MDD: major depression disorder; MDNOS: mood disorder not otherwise specified; MINI: Mini-international Neuropsychiatric Interview; NA: negative affect; N/BI: neuroticism/ behavioral inhibition; NOS: not otherwise specified; OASIS: Overall anxiety and impairment scale; OCD: obsessive-compulsive disorder; OCI-R: obsessivecompulsive inventory-revised; OTS: opinion of treatment scale; ODSIS: Overall Depression and Impairment Scale; PA: positive affect; PANAS: Positive and Negative Affect Schedule; PD: panic disorder; PDSS-SR: Self-reported Panic Disorder Severity Scale; PSWQ: Penn State Worry Questionnaire; RCT: randomized controlled trial; SAD: social anxiety disorder; SI: Societal index; SIAS: Social interaction anxiety inventory; TAU: treatment as usual; UP: unified protocol; VAS: Visual Analog Scale.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

AG-R drafted the manuscript with important contributions from CB and AG-P. AG-R, in collaboration with CB and AG-P, designed the study

and participated in each of its phases. CB and AG-P designed the traditional version of the transdiagnostic protocol and carried out the Internet-based adaptation with important contributions by RB and AR. GH, G-Ll, VP, GL, JER, and FT were in charge of recruiting study participants at several mental health services from both hospitals. All authors participated in the review and revisión of the manuscript and have approved the final manuscript to be published.

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Acknowledgements

Funding for the study was provided by grants P1.1B2014-43 (RCT of a Transdiagnostic Internet-based Treatment for Emotional Disorders); Generalitat Valenciana, Programa PROMETEO/2013/003 Red de Excelencia PSI2014-56303-REDT: PROMOSAM: Research in processes, mechanisms and psychological treatments for mental health promotion, from the Ministerio de Economía y Competitividad (2014); and a PhD grant from the Ministerio de Educación, Cultura y Deporte (FPU13/00576).

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Received: 10 August 2015 Accepted: 21 October 2015

Published online: 31 October 2015

References

1. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005;62:593–602.
2. Wittchen HU, Jacobi F, Rehm J, Gustavsson A, Svensson M, Jönsson B, et al. The size and burden of mental disorders and other disorders of the brain in Europe 2010. Eur Neuropsychopharmacol. 2011;21:655–79.
3. Fehm L, Pelissolo A, Furmark T, Wittchen HU. Size and burden of social phobia in Europe. Eur Neuropsychopharmacol. 2005;15:453–62.
4. Hofmann SG, Heinrichs N, Moscovitch DA. The nature and expression of social phobia: toward a new classification. Clin Psychol Rev. 2004;24:769–97.
5. Craske MG, Roy-Byrne PP, Stein MB, Sullivan G, Sherbourne C, Bystritsky A. Treatment for anxiety disorders: efficacy to effectiveness to implementation. Behav Res Ther. 2009;47:931–7.
6. Emmelkamp PMG, David D, Beckers T, Muris P, Cuijpers P, Lutz W, et al. Advancing psychotherapy and evidence-based psychological interventions. Int J Methods Psychiatr Res. 2014;23:58–91.
7. Stein MB, Roy-Byrne PP, Craske MG, Campbell-Sills L, Lang AJ, Golinelli D, et al. Quality of and patient satisfaction with primary health care for anxiety disorders. J Clin Psychiatry. 2011;72:970–6.
8. Kazdin AE. Evidence-based psychotherapies I: Qualifiers and limitations in what we know. S Afr J Psychol. 2014;44:381–404.
9. Bebbington PE, Meltzer H, Brugha TS, Farrell M, Jenkins R, Ceresa C, et al. Unequal access and unmet need: neurotic disorders and the use of primary care services. Psychol Med. 2000;30:1359–67.
10. Kazdin AE, Blase SL. Rebooting psychoteraphy research and practice to reduce the burden of mental illness. Perspect Psychol Sci. 2011;6:21–37.
11. Antony MM, Stein MB, editors. Oxford handbook of anxiety and related disorders. New York: Oxford University Press; 2009.

12. Barlow DH. Anxiety and its disorders: The nature and treatment of anxiety and panic. 2nd ed. New York: Guilford Press; 2002.
13. Cuijpers P, Smit F, Bohlmeijer E, Hollon ED, Andersson G. Efficacy of cognitive–behavioural therapy and other psychological treatments for adult depression: meta-analytic study of publication bias. Br J Psychiatry. 2010;196:173–8.
14. Hollon SD, Ponniah K. A review of empirically supported psychological therapies for mood disorders in adults. Depress Anxiety. 2010;27:891–932.
15. Nathan PE, Gorman JM. A guide to treatments that work. 3rd ed. New York: Oxford University Press; 2007.
16. Norton PJ, Price EP. A meta-analytic review of cognitive-behavioral treatment outcome across the anxiety disorders. J Nerv Ment Dis. 2007;195:521–31.
17. Olatunji BO, Cisler JM, Deacon BJ. Efficacy of cognitive behavioral therapy for anxiety disorders: a review of meta-analytic findings. Psychiatr Clin North Am. 2010;33:557–77.
18. Brown TA, Campbell LA, Lehman CL, Grisham JR, Mancill RB. Current and lifetime comorbidity of the DSM-IV anxiety and mood disorders in a large clinical sample. J Abnorm Psychol. 2001;110:585–99.
19. McManus F, Shafran R, Cooper Z. What does a transdiagnostic approach have to offer the treatment of anxiety disorders? Br J Clin Psychol. 2010;49:491–505.
20. Barlow DH, Allen LB, Choate ML. Toward a unified treatment for emotional disorders. Behav Therapy. 2004;35:205–30.
21. Clark DA, Taylor S. The transdiagnostic perspective on cognitive-behavioral therapy for anxiety and depression: new wine for old wineskins? J Cogn Psychother. 2009;23:60–6.
22. Norton PJ. An open trial of a transdiagnostic cognitive-behavioral group therapy for anxiety disorder. Behav Therapy. 2008;39:42–250.
23. Norton PJ, Hayes SA, Hope DA. Effects of a transdiagnostic group treatment for anxiety on secondary depression. Depress Anxiety. 2004;20:198–202.
24. Norton PJ, Barrera TL. Transdiagnostic versus diagnosis-specific CBT for anxiety disorders: a preliminary randomized controlled noninferiority trial. Depress Anxiety. 2012;29:874–82.
25. Titov N, Andrews G, Johnston L, Robinson E, Spence J. Transdiagnostic Internet treatment for anxiety disorders: A randomized controlled trial. Behav Res Ther. 2010;48:890–9.
26. Carlbring P, Maurin L, Törngren C, Linna E, Eriksson T, Sparthan E, et al. Individually-tailored, Internet-based treatment for anxiety disorders: A randomized controlled trial. Behav Res Ther. 2011;49:18–24.
27. Roy-Byrne P, Craske MG, Sullivan G, Rose RD, Edlund MJ, Lang AJ, et al. Delivery of evidence-based treatment for multiple anxiety

disorders in primary care: a randomized controlled trial. J Am Med Assoc. 2010;303:1921–8.
28. Dear BF, Titov N, Schwencke G, Andrews G, Johnston L, Craske MG, et al. An open trial of a brief transdiagnostic internet treatment for anxiety and depression. Behav Res Ther. 2011;49:830–7.
29. Titov N, Dear BF, Schwencke G, Andrews G, Johnston L, Craske MG, et al. Transdiagnostic internet treatment for anxiety and depression: a randomised controlled trial. Behav Res Ther. 2011;49:441–52.
30. Farchione TJ, Fairholme CP, Ellard KK, Boisseau CL, Thompson-Hollands J, Carl JR, et al. Unified protocol for transdiagnostic treatment of emotional disorders: a randomized controlled trial. Behav Therapy. 2012;43:666–78.
31. Newby JM, McKinnon A, Kuyken W, Gilbody S, Dalgleish T. Systematic review and meta-analysis of transdiagnostic psychological treatments for anxiety and depressive disorders in adulthood. Clin Psychol Rev. 2015;40:91–110.
32. Reinholt N, Krogh J. Efficacy of transdiagnostic cognitive behaviour therapy for anxiety disorders: a systematic review and meta-analysis of published outcome studies. Cogn Behav Ther. 2014;43:171–84.
33. Brown T, Barlow D. A proposal for a dimensional classification system based on the shared features of the DSM-IV anxiety and mood disorders: Implications for assessment. Psychol Assess. 2009;21:256–71.
34. Barlow DH, Sauer-Zavala S, Carl JR, Bullis JR, Ellard KK. The nature, diagnosis, and treatment of neuroticism: back to the future. Clin Psychol Sci. 2013;2:344–65.
35. Barlow DH, Ellard KK, Sauer-Zavala S, Bullis JR, Carl JR. The origins of neuroticism. Perspect Psychol Sci. 2014;9:481–96.
36. Carl JR, Soskin DP, Kerns C, Barlow DH. Positive emotion regulation in emotional disorders: A theoretical review. Clin Psychol Rev. 2013;33:343–60.
37. Allen LB, McHugh RK, Barlow DH. Emotional disorders: A unified protocol. In: Barlow DH, editor. Clinical handbook of psychological disorders. 4th ed. New York: Guilford Press; 2008. p. 216–49.
38. Ellard KK, Fairholme CP, Boisseau CL, Farchione TJ, Barlow DH. Unified protocol for the transdiagnostic treatment of emotional disorders: Protocol development and initial outcome data. Cogn Behav Pract. 2010;17:88–101.
39. Ehrenreich J, Goldstein C, Wright L, Barlow DH. Development of a unified protocol for the treatment of emotional disorders in youth. Child Family Behav Ther. 2009;31:20–37.
40. Boisseau CL, Farchione TJ, Fairholme CP, Ellard KK, Barlow DH. The development of the Unified protocol for the transdiagnostic treatment of emotional disorders: A case study. Cogn Behav Pract. 2010;17:88–101.

41. Wilamowska ZA, Thompson-Hollands J, Fairholme CP, Ellard KK, Farchione TJ, Barlow DH. Conceptual background, development, and preliminary data from the unified protocol for transdiagnostic treatment of emotional disorders. Depress Anxiety. 2010;27:882–90.
42. Bullis J, Fortune M, Farchione T, Barlow DH. A preliminary investigation of the long-term outcome of the unified protocol for transdiagnostic treatment of emotional disorders. Compr Psychiatry. 2014;55:1920–7.
43. Gray JA, McNaughton N. The neuropsychology of anxiety: An enquiry into the functions of the septohippocampal system. 2nd ed. Oxford: Oxford University Press; 2000.
44. Brown TA. Temporal course and structural relationships among dimensions of temperament and DSM-IV anxiety and mood disorder constructs. J Abnorm Psychol. 2007;116:313–28.
45. Gershuny B, Sher K. The relation between personality and anxiety: Findings from a 3-year prospective study. J Abnorm Psychol. 1998;107:252–62.
46. Kessler RC, Cox BJ, Green JG, Ormel J, McLaughlin KA, Merikangas KR, et al. The effects of latent variables in the development of comorbidity among common mental disorders. Depress Anxiety. 2011;28:29–39.
47. Clark LA, Watson D. Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications. J Abnorm Psychol. 1991;103:103–16.
48. Brown TA, Chorpita BF, Barlow DH. Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. J Abnorm Psychol. 1998;107:179–92.
49. Rosellini AJ, Lawrence AE, Meyer JF, Brown TA. The effects of extraverted temperament on agoraphobia in panic disorder. J Abnorm Psychol. 2010;119:420–6.
50. Kotov R, Gámez W, Schmidt F, Watson D. Linking “big” personality traits to anxiety, depressive, and substance use disorders: A meta-analysis. Psychol Bull. 2010;136:768–821.
51. Carl JR, Gallagher MW, Sauer-Zavala SE, Bentley KH, Barlow DH. A preliminary investigation of the effects of the unified protocol on temperament. Compr Psychiatry. 2014;55:1426–34.
52. Linehan MM. Skills training manual for treating borderline personality disorder. Diagnosis and treatment of mental disorders. New York: Guilford Press; 1993.
53. Neacsiu AD, Bohus M, Linehan MM. Dialectical behavior therapy: An intervention for emotion dysregulation. In: Gross JJ, editor. Handbook of emotion regulation. 2nd ed. New York: Guilford Press; 2014. p. 491–507.

54. Ehring T, Tuschen-Caffier B, Schnülle J, Fischer S, Gross JJ. Emotion regulation and vulnerability to depression: Spontaneous versus instructed use of emotion suppression and reappraisal. Emotion. 2010;10:563–72.
55. Hayes SC, Strosahl K, Wilson KG, Bissett RT, Pistorello J, Toarmino D, et al. Measuring experiential avoidance: A preliminary test of a working model. Psychol Rec. 2004;54:553–78.
56. Campbell-Sills L, Barlow DH, Brown TA, Hofmann SG. Acceptability and suppression of negative emotion in anxiety and mood disorders. Emotion. 2006;6:587–95.
57. Cisler JM, Olatunji BO, Feldner MT, Forsyth JP. Emotion regulation and the anxiety disorders: an integrative review. J Psychopathol Behav Assess. 2010;32:68–82.
58. Kring AM, Bachorowski JA. Emotions and psychopathology. Cogn Emot. 1999;13:575–99.
59. Neacsiu AD, Eberle JW, Kramer R, Wiesmann T, Linehan MM. Dialectical behavior therapy skills for transdiagnostic emotion dysregulation: A pilot randomized controlled trial. Behav Res Ther. 2014;59:40–51.
60. Andersson G, Cuijpers P. Internet-based and other computerized psychological treatments for adult depression: A meta-analysis. Cogn Behav Ther. 2009;38:196–205.
61. Caspar F. Technological developments and applications in clinical psychology and psychotherapy: introduction. J Clin Psychol. 2004;60:221–38.
62. Clark DM, Layard R, Smithies R, Richards DA, Suckling R, Wright B. Improving access to psychological therapy: Initial evaluation of two UK demonstration sites. Behav Res Ther. 2009;47:910–20.
63. Rochlen AB, Zack JS, Speyer C. Online therapy: review of relevant definitions, debates, and current empirical support. J Clin Psychol. 2004;60:269–83.
64. Andersson G, Titov N. Advantages and limitations of Internet-based interventions for common mental disorders. World Psychiatry. 2014;13:4–11.
65. Andrews G, Cuijpers P, Craske MG, McEvoy P, Titov N. Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: a meta-analysis. PLoS One. 2010;5:e13196.
66. Cuijpers P, van Straten A, Andersson G. Internet-administered cognitive behavior therapy for health problems: a systematic review. J Behav Med. 2008;31:169–77.
67. Spek V, Cuijpers P, Nyklicek I, Keyzer J, Pop V. Internet-based cognitive behavior therapy for symptoms of depression and anxiety: A meta-analysis. Psychol Med. 2007;37:319–28.

68. Richards D, Richardson T. Computer-based psychological treatments for depression: a systematic review and meta-analysis. Clin Psychol Rev.
69. 2012;32:329–42.
70. Titov N. Internet-delivered psychotherapy for depression in adults. Curr Opin Psychiatry. 2011;24:18–23.
71. Cuijpers P, Donker T, Johansson R, Mohr DC, van Straten A, Andersson G. Self-guided psychological treatment for depressive symptoms: A metaanalysis. PLoS One. 2011;6:1–7.
72. Bee PE, Bower P, Lovell K, Gilbody S, Richards D, Gask L, et al. Psychotherapy mediated by remote communication technologies: a meta-analytic review. BMC Psychiatry. 2008;8:60.
73. Cuijpers P, van Straten A, Warmerdam L, Andersson G. Psychotherapy versus the combination of psychotherapy and pharmacotherapy in the treatment of depression: a meta-analysis. Depress Anxiety. 2009;26:279–88.
74. Berger T, Boettcher J, Caspar F. Internet-based guided self-help for several anxiety disorders: A randomized controlled trial comparing a tailored with a standardized disorder-specific approach. Psychother. 2014;51:207–19.
75. Andersson G, Estling F, Jakobsson E, Cuijpers P, Carlbring P. Can the patient decide which modules to endorse? An open trial of tailored Internet treatment of anxiety disorders. Cogn Behav Ther. 2011;40:57–64.
76. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. J Am Podiatr Med Assoc. 2001;91:437–42.
77. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. J Clin Epidemiol. 2010;63:e1–37.
78. Eysenbach G, CONSORT-EHEALTH Group. CONSORT-EHEALTH: improving and standardizing evaluation reports of web-based and mobile health interventions. J Med Internet Res. 2011;13:e126.
79. American Psychological Association. Diagnostic and statistical manual of mental disorders (4th ed. Rev.). Washington, DC: American Psychological Association; 2000.
80. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998;59:34–57.
81. Ferrando L, Bobes J, Gibert J, Lecubrier Y. Mini International Neuropsychiatric Interview. In: Bobes J, Bousoño M, González MP,

editors. Manejo de los trastornos mentales y del comportamiento en Atención Primaria. 2nd ed. Oviedo: Gofer; 1997.
82. Beck AT, Steer RA. Beck anxiety inventory manual. San Antonio: Psychological Corporation; 1993.
83. Magán I, Sanz J, García-Vera MP. Psychometric properties of a Spanish version of the Beck Anxiety Inventory (BAI) in general population. Span J Psychol. 2008;11:626–40.
84. Beck AT, Steer RA, Brown GK. Manual for the Beck Depression Inventory-II. San Antonio: Psychological Corporation; 1990.
85. Sanz J, Navarro ME, Vázquez C. Adaptación española del Inventario para la Depresión de Beck-II (BDI-II): 1. Propiedades psicométricas en estudiantes universitarios. Anal Mod Cond. 2003;29:239–88.
86. Mattick RP, Clarke JC. Development and validation of measures of social phobia scrutiny fear and social interaction anxiety. Behav Res Ther. 1998;36:455–70.
87. Zubeidat I, Salinas JM, Sierra JC, Fernández-Parra A. Psychometric properties of the Social Interaction Anxiety Scale and separation criterion between Spanish youths with and without subtypes of social anxiety. J Anxiety Disord. 2007;21:603–24.
88. Houck PR, Spiegel DA, Shear MK, Rucci P. Reliability of the self-report version of the panic disorder severity scale. Depress Anxiety. 2002;15:183–5.
89. Santacana M, Fullana MA, Bonillo A, Morales M, Montoro M, Rosado S, et al. Psychometric properties of the Spanish self-report version of the panic disorder severity scale. Compr Psychiatry. 2014;55:1467–72.
90. Meyer TJ, Miller ML, Metzger RL, Borkovec TD. Development and validation of the Penn State Worry Questionnaire. Behav Res Ther. 1990;28:487–95.
91. Sandín B, Chorot P, Valiente RM, Lostao L. Validación española del cuestionario de preocupación PSWQ: Estructura factorial y propiedades psicométricas. Rev Psicopatol Psicol Clin. 2009;14:107–22.
92. Foa EB, Huppert JD, Leiberg S, Langner R, Kichic R, Hajcak G, et al. The obsessive-compulsive inventory: development and validation of a short version. Psychol Assess. 2002;14:485–96.
93. Fullana MA, Tortella-Feliu M, Caseras X, Andión O, Torrubia R, Mataix-Cols D. Psychometric properties of the Spanish version of the obsessive-compulsive inventory-revised in a non-clinical sample. J Anxiety Disord. 2004;19:893–903.
94. Carver CS, White TL. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/ BAS scales. J Pers Soc Psychol. 1994;67:319–33.

95. Gray JA. The psychology of fear and stress. Cambridge: Cambridge University; 1987.
96. Campbell-Sills L, Liverant GI, Brown TA. Psychometric evaluation of the behavioral inhibition/behavioral activation scales in a large sample of outpatients with anxiety and mood disorders. Psychol Assess. 2004;16:244–54.
97. Caseras X, Àvila C, Torrubia R. The measurement of individual differences in Behavioural Inhibition and Behavioural Activation Systems: a comparison of personality scales. Pers Individ Dif. 2003;34:999–1013.
98. Norman SB, Cissell SH, Means-Christensen AJ, Stein MB. Development and validation of an Overall Anxiety Severity and Impairment Scale (OASIS). Depress Anxiety. 2006;23:245–9.
99. Bentley KH, Gallagher MW, Carl JR, Barlow DH. Development and validation of the Overall Depression Severity and Impairment Scale. Psychol Assess. 2014;26:815–30.
100. Crawford JR, Henry JD. The Positive and Negative Affect Schedule (PANAS): Construct validity, measurement properties and normative data in a large non-clinical sample. Br J Clin Psychol. 2004;43:245–65.
101. Sandín B, Chorot P, Lostao L, Joiner TE, Santed MA, Valiente RM. Escalas Panas de afecto positivo y negativo: Validación factorial y convergencia transcultural. Psicothema. 1999;11:37–51.
102. Badía X. EuroQol; un instrumento para valorar la salud EQ-5D guía del usuario, versión española. Med Clin (Barc). 1999;114:6–14.
103. Badía X, Roset M, Montserrat S, Herdman M, Segura A. The Spanish version of EuroQol: a description and its applications. European Quality of Life scale. Med Clin. 1999;112:79–85.
104. Borkovec TD, Nau SD. Credibility of analogue therapy rationales. J Behav Ther Exp Psychiatry. 1972;3:257–60.
105. Botella C, Gallego MJ, Garcia-Palacios A, Baños RM, Quero S, Alcañiz M. The acceptability of an Internet-based self-help treatment for fear of public speaking. Br J Guid Couns. 2009;37:297–311.
106. Botella C, García-Palacios A, Villa H, Baños RM, Quero S, Alcañiz M, et al. Virtual reality exposure in the treatment of panic disorder and agoraphobia: A controlled study. Clin Psychol Psychother. 2007;14:164–75.
107. Watts SE, Turnell A, Kladnitski N, Newby JM, Andrews G. Treatment-as-usual (TAU) is anything but usual: A meta-analysis of CBT versus TAU for anxiety and depression. J Affect Disord. 2015;175:152–67.
108. Johansson R, Andersson G. Internet-based psychological treatments for depression. Expert Rev Neurother. 2012;12:861–70.
109. Van Ballegooijen W, Cuijpers P, van Straten A, Karyotaki E, Andersson G, Smit JH, et al. Adherence to internet-based and face-to-face cognitive behavioural therapy for depression: a meta-analysis. PLoS One. 2014;9:e100674.

110. Gueorguieva R, Krystal JH. Move over ANOVA: progress in analyzing repeated- measures data and its reflection in papers published in the Archives of General Psychiatry. Arch Gen Psychiatry. 2004;61:310–7.
111. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale: Erlbaum; 1988.

Wright CC, Sim J. Intention-to-treat approach to data from randomized controlled trials: A sensitivity analysis. J Clin Epidemiol. 2003;56:833–42.

Chapter 4. A brief online transdiagnostic measure: Psychometric properties of the Overall Anxiety Severity and Impairment Scale (OASIS) among Spanish patients with emotional disorders

This chapter has been published as:

González-Robles, A., Mira, A., Miguel, C., Molinari, G., Díaz-García, A., García-Palacios, A., Bretón-López, J. M., Quero, S., Baños, R., & Botella, C. (2018). A brief online transdiagnostic measure: Psychometric properties of the Overall Anxiety Severity and Impairment Scale (OASIS) among Spanish patients with emotional disorders. *PLoS One*, *13*(11), e206516.

A brief online transdiagnostic measure: psychometric properties of the Overall Anxiety Severity and Impairment Scale (OASIS) among Spanish patients with emotional disorders

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Abstract

The Overall Anxiety Severity and Impairment Scale (OASIS) is a self-report questionnaire designed to evaluate the severity and functional impairment associated with anxiety. Given its transdiagnostic nature, it can be used indistinctly across anxiety and depressive disorders. In this study, the psychometric properties of the online version of the OASIS were evaluated in a Spanish clinical sample with emotional disorders. Patients (n = 583) with anxiety (n = 250) and depression (n = 333) with a mean age of 37.21 (SD = 12.22), underwent a diagnostic interview and questionnaires assessing anxiety, depression, positive and negative affectivity, and quality of life. Factorial structure, internal consistency, convergent and discriminant validity, cutoff scores, and sensitivity to change were analyzed. Confirmatory Factor Analysis yielded a unidimensional factor structure, consistent with previous validations of the instrument. The analyses showed good internal consistency and adequate convergent and discriminant validity, as well as sensitivity to change. A cutoff score of 7.5 was found to meet the criteria used in this study to select the optimal cutoff point. Overall, in this study, the psychometric properties of the online version of the OASIS were found to be appropriate. The brevity and ease of use of the OASIS support its adequacy as a valid measure of anxiety severity and impairment in Spanish clinical samples with anxiety and depression.

Introduction

Anxiety and depressive disorders, also known as emotional disorders (ED), are prevalent [1, 2] and costly [3, 4] and an important cause of suffering and disability worldwide [5, 6]. Moreover, the literature has shown the high comorbidity rates among anxiety disorders, and between anxiety and depressive disorders [7].

Along with depression, anxiety disorders are one the most prevalent disorders, with a 12-month prevalence of 18.1% [8], and a lifetime prevalence of 28.8% [1]. In Spain, the 12-month prevalence of an anxiety disorder has been estimated at 6.2%, and the lifetime prevalence at 9.3% [9]. Anxiety disorders are associated with important impairments [10], significantly poorer quality of life [11], and high rates of comorbidity with other anxiety disorders and with depression [2, 7]. Therefore, the development of treatments for anxiety is a key aspect in addressing this important health problem. Moreover, the impact of these interventions cannot be ascertained without the use of appropriate assessment instruments. In this vein, despite the importance of evidence-based assessment (i.e. the use of research and theory to guide the selection of the most appropriate instrument for the assessment of a specific construct) [12], the attention paid to assessment is more recent than the importance given to evidence-based treatments, first described in a book published ten years earlier [13]. Therefore, the development and validation of rigorous assessment tools is an important task for researchers and clinicians involved in the assessment and treatment of anxiety disorders. In this vein, the need for digital versions of pen and paper scales has increased exponentially due to the proliferation of web-based interventions [14, 15]. Nevertheless, the literature highlights that paper and online versions of the same instrument show strong correlations but may differ in psychometric properties [14]. Therefore, as research on web-based treatments advances, it becomes crucial to develop and validate assessment instruments that can be applied online [16].

Currently, there are a number of measurement tools to assess overall anxiety, such as the Beck Anxiety Inventory [17] or the State-Trait Anxiety Inventory [18]. These scales have been translated into Spanish and validated in previous research [19–21]. Additionally, several instruments have been developed and validated for the assessment of the symptoms associated with each of the different anxiety disorders (i.e. disorder-specific symptoms), such as the Penn State Worry Questionnaire [22] for generalized anxiety disorder, the Panic Disorder Severity Scale [23] for panic disorder and/or agoraphobia, and the Social Interaction Anxiety Scale [24] for social anxiety disorder. However, all these instruments focus on the assessment of individual anxiety symptoms (i.e. the occurrence of cognitive, emotional, and physiological symptoms), but

they do not provide a measure of the global severity and impairment associated with these problems.

The Overall Anxiety Severity and Impairment Scale (OASIS) is a short scale made up of 5 items developed to assess the severity and impairment associated with anxiety disorders and/or symptoms [25–27]. Two advantages of the OASIS include its brevity and ease of use and its transdiagnostic nature. Regarding brevity, the need for short scales (i.e. less than 10 items) has been highlighted in the literature [25]. Several advantages have been indicated in this regard, such as the fact that it is an easier way to obtain relevant data in clinical settings such as primary care (where resources are normally limited) (Laura Campbell-Sills et al., 2009; Ziegler, Kemper, & Kruyen, 2014) or that symptoms can be more easily monitored throughout a treatment [12]. For instance, this latter aspect might be particularly useful when it is necessary to evaluate anxiety symptoms repeatedly throughout a treatment (i.e. after each treatment module or session). Finally, in a more general way, even though brevity might compromise a scale's validity [29], compared to longer scales, the use of shorter scales provides a more efficient way to collect data and maximize the representativeness of the sample [28]. In addition, from a transdiagnostic perspective, it is logical to develop and validate measures that capture the severity and impairment of anxiety disorders, regardless of the specific anxiety disorder suffered by the patients [25, 30] . Following the DSM-IV-TR guidelines to establish the severity and associated impairment caused by anxiety, the five items on the OASIS were developed in an attempt to capture the most important domains of anxiety that are common to all anxiety disorders, namely, severity (i.e. frequency and intensity), behavioral avoidance, and functional impairment (i.e. work and social interference) [26]. Because the OASIS focuses on the severity and functional consequences of anxiety, rather than the occurrence of specific anxiety symptoms (which might vary depending on the specific presentation of each patient), the scale can be used in a transdiagnostic manner across different anxiety disorders. Given the theoretical and empirical association between anxiety and depression [2] and the high comorbidity rates between these disorders, the scale can also be used to assess the severity and impairment of anxiety in individuals with depression.

Previous versions of the OASIS have been validated in both clinical [25, 31–33] and non-clinical samples [26, 27]. In sum, the OASIS has shown sound psychometric properties in the existing literature. Nevertheless, to our knowledge, the OASIS has not yet been validated in Spanish clinical samples with anxiety and depressive disorders. Furthermore, most of the previous work in clinical populations has focused on patients with principal diagnoses of anxiety disorders, with some

exceptions [31, 32] that also included patients with a principal diagnosis of depression. However, in these studies, the proportion of patients with depression was low, compared to patients with anxiety [31]. Regarding the online validation of the OASIS, to our knowledge, only one study in the literature has used online surveys [32]. However, even though this study showed good psychometric properties, it relied on patients' self-reports to establish a formal diagnosis, rather than well-validated measures such as diagnostic interviews or self-report questionnaires.

Current study

In this study, we aimed to contribute to filling this gap by analyzing the psychometric properties of the OASIS in two clinical subsamples of individuals with emotional disorders: a subsample with a principal diagnosis of anxiety (n = 250) and a subsample with a principal diagnosis of depression (n = 333). Specific objectives were: a) to examine how the scale performs in patients with anxiety disorders vs. depressive disorders; b) to examine the scale's factorial structure, reliability, and validity; c) to obtain cutoff scores; and d) to analyze sensitivity to change. To the best of our knowledge, this is the first study to evaluate the psychometric properties of the online version of the OASIS in a sample of adults with anxiety and depressive disorders in the Spanish population.

Methods

Spanish Translation of the OASIS

First, a native Spanish-speaker who was aware of the purpose of the study translated the OASIS items from English to Spanish. Second, a Spanish-English bilingual speaker who was not familiar with the questionnaire performed a back-translation from Spanish to English. The person involved in the translation process is a native English speaker who has been living in Spain for many years and is fluent in both languages. The two English versions were compared, and the Spanish version of the OASIS was judged to be an accurate translation of the original English version.

Procedure

The sample was recruited from patients attending the Emotional Disorders Clinic at Jaume I University (Castellon, Spain), whose principal focus is the treatment of ED using Information and Communication Technologies such as web-based interventions. Individuals who were waiting to receive an online treatment were invited to participate in the study, and those who agreed to participate provided written, informed

consent. Only participants with a principal diagnosis of an emotional disorder (i.e. anxiety and depressive disorders) were considered for the study. All participants were assessed with a structured diagnostic interview, and a battery of questionnaires. All these measurement tools are described in detail in the Instruments section. The study was approved by the Ethics Committee of Universitat Jaume I.

Participants

A total of 583 individuals with a mean age of 37.21 years (SD = 12.22; range: 18-68 years old) took part in the study. Most participants were female (n= 421; 72.21%), married or living with a partner (n = 273; 46.83%), and had completed higher education studies (n = 371; 56.3%). All of the participants were Caucasian. Regarding their diagnoses, 333 patients had a principal diagnosis of a mood disorder (i.e. major depressive disorder, dysthymic disorder, mood disorder not otherwise specified), and 250 had a principal diagnosis of an anxiety disorder. In all, more than half the sample had at least one comorbid anxiety or depressive disorder (53.5%). Diagnostic assessments were performed by pre-doctoral students who had been previously trained in the use of the diagnostic interview. A full description of the patients' sociodemographic and clinical data is displayed in Table 5.

Table 5. Sociodemographic and clinical characteristics of the sample (n = 583)

Age in years, Mean (SD)	37.21 (12.22)
Sex, n (%)	
Female	421 (72.21)
Male	162 (27.79)
Relationship status, n (%)	
Single	235 (40.31)
Married/de facto	279 (47.86)
Divorced	62 (10.63)
Widowed	7 (1.20)
Education level, n (%)	
Basic	94 (16.12)
Medium	179 (30.70)
Superior	310 (53.17)
Principal diagnosis, n (%)	
Major depressive disorder	318 (34.5)
Generalized anxiety disorder	99 (17)
Social anxiety disorder	57 (9.8)
Panic disorder/agoraphobia	50 (8.6)
Obsessive-compulsive disorder	14 (2.4)
Dysthymic disorder	13 (2.2)

Anxiety disorder NOS	12 (2.1)
Specific phobia	10 (1.7)
Postraumatic stress disorder	4 (0.7)
Mood disorder NOS	2 (0.3)
Intermittent explosive disorder	2 (0.3)
Somatoform disorder	1 (0.2)
Hypochondriasis	1 (0.2)
Number of comorbid disorders, n (%)	
0	271 (46.5)
1	210 (36)
2	80 (13.7)
≥ 3	22 (3.8)
Symptom severity, Mean (SD)	
OASIS	8.69 (4.21)
BAI	20.12 (11.80)
BDI-II	23.39 (11.09)
ODSIS	7.70 (4.91)
PANAS-P	21.31 (7.49)
PANAS-N	26.16 (7.95)
QLI	4.79 (1.68)

OASIS = Overall Anxiety Severity and Impairment Scale; BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory-II; ODSIS = Overall Depression Severity and Impairment Scale; PANAS-P = Positive and Negative Affect Schedule-Positive Affect; PANAS-N = Positive and Negative Affect Schedule-Negative Affect; QLI = Multidimensional Quality of Life Questionnaire

Instruments

Diagnostic Interview

Mini-International Neuropsychiatric Interview [34]. The MINI is a short, structured clinical interview designed to perform diagnoses according to the DSM-IV and ICD-10 criteria. It has shown excellent test-retest and interrater reliability, as well as high predictive validity rates. The Spanish validation was used in this study [35].

Self-reported questionnaires

Overall Anxiety Severity and Impairment Scale (OASIS) [25]. The OASIS is a 5-item self-report scale that evaluates the frequency and severity of anxiety symptoms, the functional impairment related to these symptoms (i.e. school, work, home, or social impairment), and behavioral avoidance. Each item instructs respondents to endorse one of five responses that best describes their experiences over the past week. Response items are coded from 0 to 4, added together to obtain a total score ranging from 0 to 20. Previous studies have shown high internal consistency (α=0.80), test-retest reliability, and convergent and

discriminant validity [25–27]. In the current study, Cronbach's alpha coefficient for the five items on the OASIS was good (0.86).

Beck Anxiety Inventory (BAI) [17]. This is a 21-item self-report questionnaire for the measurement of anxiety symptoms experienced during the past week. Each item is rated from 0 to 3 (i.e. not at all, mildly, moderately, severely), added together to obtain a maximum score of 63. The BAI has demonstrated good to excellent internal consistency in prior validations of the scale (.85-.94), as well as adequate convergent and divergent validity [20]. Cronbach's alpha for the BAI in the present study was excellent (.91).

Beck Depression Inventory (BDI-II) [36]. The BDI-II is a 21-item self-report scale designed to assess depressive symptoms experienced during the past week. Items are rated on a Likert scale rated from 0 to 3, and the total score ranges from 0 to 63. The BDI-II has shown optimal validity and reliability in both clinical and nonclinical samples [36-38]. Cronbach's alpha for the BDI-II in the present study was excellent (0.91).

Overall Depression Severity and Impairment Scale (ODSIS) [39]. The ODSIS consists of five items that measure the severity and impairment related to depression, as well as its interference with school, work, and social life. The measure has shown excellent internal consistency (α=0.94 in an outpatient sample, 0.92 in a community sample, and 0.91 in a student sample) [39] and good convergent and discriminant validity. In the present study, the ODSIS showed excellent internal consistency (0.93).

Positive and Negative Affect Schedule (PANAS) [40]. The PANAS is a self-report measure that evaluates two dimensions on two independent scales: positive (PANAS-P) and negative affect (PANAS-N). Each scale is composed of 10 items coded in a range from 10 to 50 points. The PANAS has shown excellent convergent and divergent validity, as well as high internal consistency [40-42]. In the current study, Cronbach's alpha was excellent for the PANAS-P (0.93) and good for the PANAS-N (0.88).

Multidimensional Quality of Life Questionnaire (QLI) [43]. The QLI is a self-report questionnaire that consists of 10 items aimed at assessing quality of life in ten areas: psychological well-being, physical well-being, emotional and social support, interpersonal functioning, self-care and independent functioning, community and service support, occupational functioning, self-realization, spiritual satisfaction, and an overall assessment of quality of life. The Spanish version of the QLI has shown good internal consistency and test-retest reliability in previous studies [44]. Cronbach's alpha for the QLI in the present study was excellent (0.90).

Data analysis

First, descriptive statistics (mean, standard deviation, skewness, and kurtosis) for the anxiety and depression subsamples were calculated for all the measures. Next, one-way ANOVAs were calculated to analyze whether there were significant differences in the scores on the OASIS based on gender, marital status, studies, and diagnosis. Furthermore, correlations between age and the OASIS score were calculated in order to study whether there were any associations between these variables. In addition, reliability was analyzed by calculating internal consistency indexes (Cronbach's alpha) for the five items on the OASIS.

To analyze the factor structure of the OASIS, we performed Confirmatory Factor Analysis (CFA), a procedure based on Classical Test Theory (CTT) [45]. CFA models were estimated with maximum likelihood and robust corrections (MLR), given the scale's non-normality and five-point response scale. Full Information Maximum Likelihood was employed to handle missing data. Following Norman et al. [27], a single latent factor with correlated error variances between items 1 and 2 was tested as the basis for the CFA model. Model fit was evaluated using several criteria, specifically, the chi-square test ($\chi 2$), comparative fitness index (CFI), Tucker-Lewis index (TLI), standardized root mean residuals (SRMR), and root mean square error of approximation (RMSEA). The following cutoff scores were used to determine good fit: CFI and TLI above .90 (better if above .95) and RMSEA below .08 [46]. Following recommendations by McNeish, An, & Hancock [47], factor loadings with their corresponding p values and the correlations between the error variances of the items were reported to evaluate the validity of the factor model. A correlation between the error variance of items 1 and 2 was expected because a response of 0 to item 1 (frequency of anxiety) would entail a response of 0 to item 2 (intensity of anxiety) [25].

Construct validity was examined through correlations with measures of anxiety (BAI), depression (BDI-II), positive and negative affect (PANAS-P and PANAS-N), and quality of life (QLI). Cohen's [48] benchmarks for the interpretation of the correlation values were used, where effect sizes between .10 and .30 are considered small, those between .30 and .50 are considered medium, and those of .50 or above are considered large.

To assess the sensitivity and specificity of the OASIS scores in detecting anxiety symptoms, cutoff scores of the BAI scores were used to classify participants between those without anxiety (BAI score < 10) and with anxiety (BAI score ≥10) [49]. The cutoff point on the BAI to assess the sensitivity and specificity of the OASIS scores was 10, so that BAI scores ≥10 were considered to reflect anxiety symptoms. To examine the

precision of the OASIS scores in detecting cases with and without anxiety symptoms, the receiver operating characteristic (ROC) curve was calculated, as well as the area under the curve (AUC). The AUC is a quantitative index that combines sensitivity and specificity in order to provide information about the precision of a test score as a proportion, so that the larger the proportion, the greater the precision of the test. The sensitivity of test scores is the proportion of positive cases (i.e., participants with anxiety, assessed with the BAI) that are correctly identified by the OASIS scores. The specificity of test scores is the proportion of negative cases (i.e., participants without anxiety, assessed by the BAI) correctly identified by the OASIS scores as the best result. AUC values under .5 will reflect lack of precision, whereas AUC values above .9 indicate excellent precision, values between .7 and .9 indicate moderate precision, and values between .5 and .7 indicate mild precision. The AUC represents the probability that a participant randomly selected from the group with anxiety will obtain a higher score on the OASIS than another participant, also randomly selected, from the group of people without anxiety. A 95% confidence interval around the AUC and its statistical significance were also calculated [50]. Sensitivity and specificity were calculated for each cutoff point, as well as Positive Predictive Values (PPV), Negative Predictive Values (NPV), and their corresponding 95% confidence intervals. PPV represents the proportion of cases correctly identified by the OASIS as positive with regard to all the positive cases, whereas NPV represents the proportion of cases correctly identified as negative by the OASIS with regard to all the negative cases. In order to identify the optimum cutoff point for the OASIS, four methods were applied to each cutoff score [51]: the Youden index (J), Index of Union (IU), Closest to (0, 1) Criteria (ER), and Concordance Probability Method (CZ). The Youden index is defined as J = max(Sensitivity + Specificity -1), so that the OASIS cutoff point that correspond to the maximum J value is considered the optimal cutoff point. The Index of Union (IU) was calculated as IU = min(|Sensitivity – AUC| + |Specificity - AUC|). The IU is calculated to guarantee that the sensitivity and specificity obtained at this cutoff point is simultaneously close to the AUC value, and the difference between the sensitivity and specificity obtained at this cutoff point should be minimal. The Closest to (0, 1) Criteria is calculated as $\sqrt{\text{ty})}$, and the optimal cutoff point according to this index is defined as the point closest to the point (0, 1) on the ROC curve. Finally, the Concordance Probability Method defines the optimal cutoff point as the point that maximizes the product of sensitivity and specificity. CZ is calculated as CZ = Sensitivity*Specificity. The OASIS score that met the four criteria, or most of them, was selected as the optimal cutoff point.

Finally, in order to analyze sensitivity of OASIS scores to change, means and standard deviations for the pretest and posttest were calculated with the OASIS scores from two studies about the efficacy of Internet CBT in patients with emotional disorders. Part of the total sample completed the OASIS before and immediately after receiving an Internet-based treatment. Thus, 24 patients received Smiling is Fun [52] (hereinafter subsample 1), and 68 patients received Emotion Regulation [53, 54] (hereinafter subsample 2). Smiling is Fun is an 8-module Internet-based treatment for depression that includes components of evidence-based treatments. The protocol stresses the importance and benefits of being active and staying involved in life, values, and goals. It allows the individual to learn and practice adaptive ways to cope with depressive symptoms and confront daily problems. Specifically, some components of Barlow's Unified Protocol (UP) have been adapted, namely, motivation, psychoeducation, cognitive therapy, and relapse prevention [55]. Furthermore, the program incorporates a Behavioral Activation component [56] and a Positive Psychology component, which includes strategies to promote and enhance personal strengths, positive feelings, positive cognitions, and positive behavior [57, 58]. Emotion Regulation is a 12-module transdiagnostic Internet-based treatment for anxiety and depressive disorders. The treatment protocol is delivered through a multimedia web platform https://www.psicologiaytecnologia.com/) (with videos, images, printable documents, etc.), which allows participants easy and optimal use on a PC or tablet. The content of the protocol is adapted from the Unified Protocol [59] and from Marsha Linehan's protocol [60], with four core components: present-focused emotional awareness, cognitive flexibility, behavioral and emotional avoidance patterns, and interoceptive and situational exposure. The protocol also includes traditional therapeutic components of evidence-based treatments, such as psychoeducation, motivation for change, and relapse prevention.

Minimum and maximum OASIS scores were also obtained from the pretest to check potential floor or ceiling effects. Evidence of floor or ceiling effects is present when more than 17% of the participants obtained the lowest or highest possible score on the test, respectively [in our case, 0 and 20). In addition, t-tests were applied to test the statistical significance of the pretest-posttest mean differences. To quantify the OASIS scores' sensitivity to change, the standardized mean change index was used as the effect size, defined as the difference between the pretest and the posttest means divided by the standard deviation of the change scores. The positive bias of the d index for small sample sizes was corrected with the c(m) correction factor [61]:

with and being the pretest and posttest means, and c(m) being:

In addition, 95% confidence intervals for the d indices were calculated by means of d ± 1.96xSE(d), with 1.96 being the 97.5 percentile of the standard normal distribution, and SE(d) being the standard error of the d index [61]:

All of these calculations were applied separately for subsamples 1 and 2. To offer a contextualized interpretation of the d indices obtained in subsamples 1 and 2, we used the results of a systematic review of meta-analyses carried out on the efficacy of psychological treatments that applied the standardized mean change index as the effect size [62]. In this review, percentiles 25, 50, and 75 of the d indices' distribution were 0.64, 0.75, and 1.26. Therefore, a reasonable interpretation of these three values is to consider them as reflecting low, moderate, and large magnitudes of the effect.

CFA was calculated using the EQS program, version 6.1. Sensitivity, specificity, PPV, and NPV were calculated using a web application (http://vassarstats.net/clin1.html). The software SPSS Statistics version 22.0 was used for the remaining analyses.

Results

Preliminary analyses

The mean OASIS score was 8.69 (SD= 4.21) in the total sample (n = 583), 8.92 (SD= 4.28) for females (n= 421), and 8.15 (SD= 3.96) for the male participants (n= 162). Table 6 and Table 7 show descriptive statistics for each item and the total score on the OASIS, and for the remaining instruments, for both the depressive and anxiety disorder samples, respectively.

Table 6. Descriptive statistics for each item and the total score on the OASIS in depressive and anxiety disorder samples

	Anxiety sample (n = 250)				Depression sample (n = 333)			
	M	SD	λ_1	λ_2	M	SD	λ_1	λ_2
Item 1	1.96	1.06	.108	-.466	2.05	1.04	-.145	-.881
Item 2	1.80	.88	-.157	-.911	1.79	.86	-.285	-.124
Item 3	1.56	1.16	.330	-.049	1.65	1.13	.246	-.684
Item 4	1.61	1.08	.229	-.723	1.70	1.05	-.087	-.925
Item 5	1.53	1.11	.371	-.808	1.70	1.06	-.045	-.697
Total score	8.37	4.29	.230	-.624	8.96	4.17	-.190	-.420

M = Mean; SD = Standard deviation; λ_1 = skewness; λ_2 = kurtosis

Table 7. Descriptive statistics for convergent and discriminant validity measures in depressive and anxiety disorder samples

	Anxiety sample				Depression sample			
	M	SD	λ_1	λ_2	M	SD	λ_1	λ_2
BAI	20.41	11.94	.451	-.588	19.13	11.39	-.690	-.008
BDI-II	21.74	11.45	.284	-.339	24.70	10.70	.409	.331
ODSIS	6.41	4.93	.384	-.899	8.64	4.68	-.107	-.778
PANAS-P	23.45	8.13	.695	.073	19.64	6.53	.828	.317
PANAS-N	27.24	7.81	.110	-.574	25.32	7.98	.286	-.282
QLI	4.94	1.66	.041	-.473	4.51	1.71	.275	-.407

M = Mean; SD = Standard deviation; λ_1 = skewness; λ_2 = kurtosis; BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory-II; ODSIS = Overall Depression Severity and Impairment Scale; PANAS-P = Positive and Negative Affect Schedule-Positive Affect; PANAS-N = Positive and Negative Affect Schedule-Negative Affect; QLI = Multidimensional Quality of Life Questionnaire

Significant differences were found in the OASIS scores based on the number of comorbid disorders ($F= 6.91$; $p < .001$), with higher anxiety levels found the participants with a larger number of comorbid disorders. There were no significant differences based on sex, civil status, education level, or principal diagnosis. In addition, no statistical relationships were observed between the participants' age and OASIS scores.

Factor Structure

A single-factor model resulted in an adequate model fit: $\chi 24 = 11.693$, $p > .01$; SRMR= .027; RMSEA= .058, 90% CI [.015, .104]; CFI= .995. Factor loadings showed that all the items were strongly related to this factor, with values ranging from .65 to .82 All these values reached significance at $p < .05$ (see Figure 7).

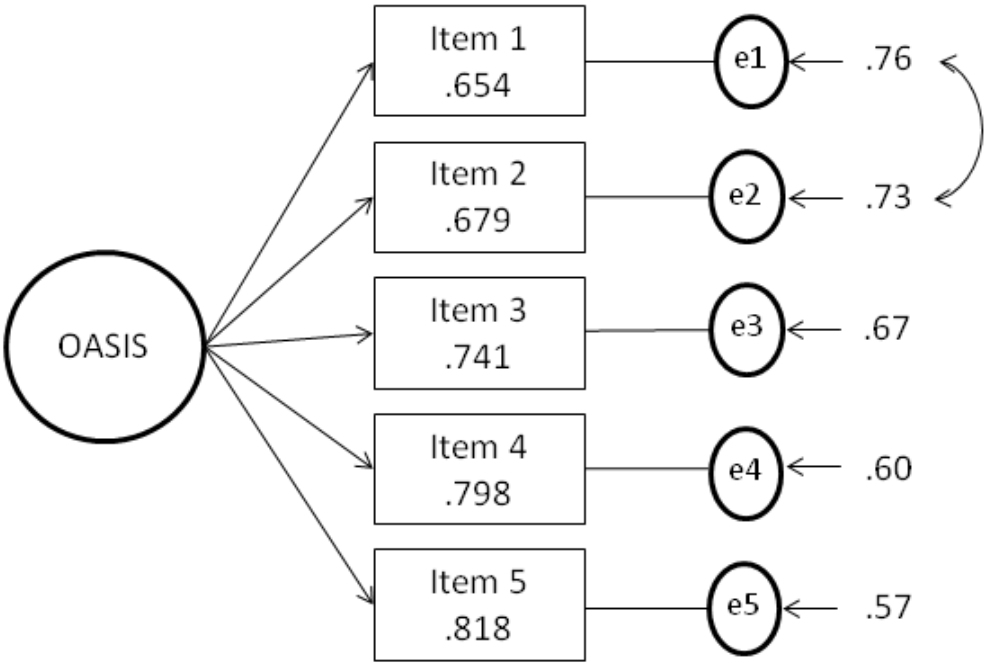

Figure 7. Confirmatory factor analysis (CFA) model
Rectangles are measured variables, the large circle is the latent construct, and small circles are residual variances. Factor loadings are standardized. All values are significant at $p < .05$. The solution specified correlated error variance between items 1 and 2.

Internal Consistency

Cronbach's alpha for the five items on the OASIS was .86. Table 8 shows the results for Cronbach's alpha when omitting items, corrected correlations between each item and the total score, and correlations between the five items of the OASIS. The results obtained indicate good internal consistency of the OASIS that would not be increased by excluding any item.

Table 8. Cronbach's alpha if item is deleted, corrected item-total score correlation, and correlations between items

	Cronbach's Alpha if item deleted	Corrected item-total correlation	Correlations between items				
			I1	I2	I3	I4	I5
I1	.842	.658	1				
I2	.838	.692	.689*	1			
I3	.849	.640	.422*	.464*	1		
I4	.825	.726	.560*	.585*	.587*	1	
I5	.824	.729	.543*	.543*	.643*	.628*	1

*Correlation was significant at $p < .01$ (two-tailed)

Convergent validity

Table 9 shows the correlation between the OASIS and the convergent validity measures. A large positive correlation was expected between the OASIS and the BAI. A positive but medium correlation was expected between the OASIS and the BDI-II. Given the theoretical and empirical associations between the dimensions of positive and negative affect and anxiety [2], we anticipated a positive but medium correlation between the OASIS and the PANAS-N, and a negative and medium correlation with the PANAS-P. Finally, we anticipated a negative and medium correlation between the OASIS and QLI (quality of life). All these results were interpreted as evidence for convergent validity.

The OASIS correlated significantly with all the measures. As predicted, positive and large correlations were found between the OASIS and the BAI (r = .61, p < .01). In addition, large and positive correlations were found between the OASIS and the BDI-II (r = .60, p < .01), and between the OASIS and the ODSIS (r = .65, p < .01). The OASIS correlated largely with the PANAS-N (r = .60, p < .01). Finally, the analyses yielded a negative medium correlation between the OASIS and the PANAS-P (r = -.40, p < .01), and a negative large correlation between the OASIS and the QLI (r = -.58, p < .01).

Table 9. Correlations of the OASIS with convergent validity measures

	OASIS	BAI	ODSIS	BDI-II	PANAS-P	PANAS-N	QLI
OASIS	-	.61*	.65*	.60*	-.40*	.60*	-.58*
BAI		-	.35*	.47*	-.25*	.53*	-.41*
ODSIS			-	.67*	-.57*	.49*	-.69*
BDI-II				-	-.56*	.57*	-.76*
PANAS-P					-	-.32*	.71*
PANAS-N						-	-.48*
QLI							-

*Correlation was statistically significant at p < .01 (2-tailed); OASIS = Overall Anxiety Severity and Impairment Scale, BAI = Beck Anxiety Inventory, ODSIS = Overall Depression Severity and Impairment Scale, BDI-II = Beck Depression Inventory-II, PANAS-P = Positive and Negative Affect Schedule-Positive Affect, PANAS-N = Positive and Negative Affect Schedule-Negative Affect, QLI = Multidimensional Quality of Life Questionnaire

Receiver Operating Characteristic (ROC)

A ROC curve was calculated in the sample when a cutoff point ≥ 10 was applied to the BAI scores. The AUC obtained was .817 (95%CI: .731 and .903) and reached statistical significance (p < .001). This AUC can be interpreted as indicating that there was a .817 probability of randomly selecting a participant from the anxiety group (i.e., with a BAI score ≥ 10) with an OASIS score higher than that of any other participant, also randomly selected, from the group without anxiety (i.e., with BAI score < 10). An AUC = .817 can also be interpreted as reflecting moderate precision from a clinical point of view. Therefore, the precision of the OASIS scores in detecting any type of anxiety (mild, moderate, or severe) can be considered to have a moderate magnitude. Table 10 presents the sensitivity, specificity, PPV, and NPV obtained with the OASIS scores for the cutoff point ≥ 10 on the BAI. The table also shows the results of the four methods used to select the optimal cutoff score for the OASIS (Youden index, J, Index of Union, IU, the Closest to (0, 1) Criteria, ER, and the Concordance Probability Method, CZ). The OASIS score = 7.5 met three of the four criteria (IU, ER, and CZ criteria); regarding the Youden index, this score obtained the second best value (.498), very close to the maximum value obtained with this method (.503). Therefore, 7.5 was selected as the optimal cutoff point to detect anxiety symptoms (i.e., OASIS scores over 7 indicate anxiety symptoms). For this cutoff point, sensitivity was .727 (95% CI: .650; .792), and specificity was .771 (95% CI: .594; .889). PPV was .936 (95% CI: .874; .970), and NPV was .380 (95% CI: .270; .504).

Table 10. Statistics to assess the diagnostic accuracy of the OASIS scores

OASIS score	*Se*	*Sp*	*PPV*	*NPV*	*J*	*IU*	*ER*	*CZ*
0.5	.994	.171	.846	.857	.165	.823	.829	.170
1.5	.994	.200	.851	.875	.194	.794	.800	.199
2.5	.975	.314	.867	.733	.289	.661	.686	.306
3.5	.969	.457	.891	.762	.426	.512	.544	.443
4.5	.932	.571	.909	.645	**.503**	.361	.434	.532
5.5	.876	.600	.910	.512	.476	.276	.419	.526
6.5	.814	.657	.916	.434	.471	.163	.390	.535
7.5	**.727**	**.771**	**.936**	**.380**	**.498**	**.136**	**.356**	**.561**
8.5	.627	.800	.935	.318	.427	.207	.423	.502
9.5	.528	.857	.944	.283	.385	.329	.493	.452
10.5	.435	.914	.959	.260	.349	.479	.572	.398
11.5	.354	.914	.950	.235	.268	.560	.652	.324
12.5	.242	.914	.928	.208	.156	.672	.763	.221
13.5	.161	.971	.963	.201	.132	.810	.840	.156
14.5	.124	1	1	.199	.124	.876	.876	.124

15.5	.093	1	1	.193	.093	.907	.907	.093
16.5	.043	1	1	.185	.043	.957	.957	.043
17.5	.019	1	1	.181	.019	.981	.981	.019
18.5	.006	1	1	.179	.006	.994	.994	.006
20	0	1	NA	NA	0	1	1	0

Se = Sensitivity; *Sp* = Specificity; *PPV* = Positive Predictive Value; *NPV* = Negative Predictive Value; *J* = Youden index; *IU* = Index of Union; *ER* = Closest to (0, 1) Criteria; *CZ* = Concordance Probability Method; NA = Not applicable.

Analysis of sensitivity to change

Two subsamples were used for the analysis of sensitivity to change. Subsample 1 consisted of 24 patients who completed an Internet-based treatment for depression [52], and subsample 2 was made up of 68 patients who underwent a transdiagnostic Internet-based treatment for anxiety and depressive disorders [53, 54]. To examine potential floor and ceiling effects for the OASIS scores, the frequency and percentage of minimum (0) and maximum (20) scores was tabulated for subsamples 1 and 2 on the pretest. The results showed that only 2 patients out of 24 (12%) in subsample 1, and 3 out of 68 in subsample 2 obtained a score of 0 (minimum). In addition, no patient in any of the subsamples obtained a score of 20 (maximum). Therefore, evidence of floor and ceiling effects can be ruled out, as the percentage was lower than 17% in all cases.

To examine the sensitivity to change of the OASIS scores, means and standard deviations were calculated for each subsample, both on the pretest and the posttest. The statistical significance of the pretest-posttest change scores was assessed by applying t-tests, which, as Table 11 reveals, were statistically significant for both studies. The clinical significance was assessed by means of the effect size index 'standardized mean change index' (d). Following Rubio-Aparicio et al. results [62], subsamples 1 and 2 obtained d indices that can be interpreted as reflecting moderate (d = 0.72) and moderate-to-large (d = 0.90) clinical relevance, respectively.

Table 11. Descriptive and inferential results from the two subsamples for the OASIS scores on the pretest and the posttest

		Pretest		**Posttest**			
Subsample	**N**	Mean	SD	Mean	SD	***t***	***d***
1	24	6.42	3.46	3.00	2.62	3.65***	0.72 [0.26, 1.18]
2	68	8.59	4.41	4.50	4.60	7.44***	0.90 [0.61, 1.19]

****p* < .001; N = sample size; SD = standard deviation; *t* = *t* statistic for testing the pretest-posttest mean difference; *d* = standardized mean change index (95% CI in brackets).

Discussion

The aim of this study was to analyze the psychometric properties of the online version of the OASIS in a Spanish sample of patients with emotional disorders. This study evaluated the reliability, construct validity, and latent structure of the OASIS. In addition, cutoff scores were obtained, and sensitivity to change was examined.

First, preliminary analyses showed that patients with more comorbid disorders were significantly more anxious than patients with fewer comorbid disorders, a finding that was somewhat expected given the strong association observed between comorbidity and severity [63]. By contrast, no statistically significant differences were found based on sex, education level, marital status, or principal diagnosis (i.e. anxiety disorder vs. depressive disorder), which, taken together, suggests that the Spanish version of the OASIS can be used indistinctly across patients with different sociodemographic and clinical characteristics. In this vein, it is important to note that a large proportion of patients in this study (53.5%) presented at least with one anxiety or depressive disorder. Second, regarding reliability, the five items on the OASIS demonstrated good internal consistency (alpha = .86). Third, as in previous validations of the instrument [25–27], confirmatory factor analysis revealed a unidimensional factor structure. Moreover, as expected, the model showed correlated error variance between items 1 and 2.

Regarding the ROC analysis, a cutoff point of 7.5 was found to meet three of the four criteria used to select the optimal cutoff point (i.e. Index of Union, Closest to (0, 1) Criteria, and Concordance Probability Method). These findings suggest that this score (i.e. scores above 7 at the OASIS) can be used as a cutoff point to discriminate between patients with anxiety symptoms of clinical consideration vs. anxiety symptoms of no clinical consideration. This information might be useful, for instance, for screening and selecting patients with anxiety symptoms for clinical trials. The results obtained in this study using ROC curves are consistent with prior validations of the instrument in clinical populations, which showed that cutoff scores of around 8 differentiate anxious patients from non-anxious patients [25, 27].

This study also examined sensitivity to change by analyzing the significance of the improvements from pre- to post-treatment on the OASIS scores. The analyses showed moderate to large effect sizes (Cohen’s d between .72 and .90), which suggests that the scale can not only be used for screening purposes (i.e. by using the cut-off point), but also that it is able to detect changes in anxiety and therefore it can be used to examine the impact of an intervention.

Regarding construct validity, positive and large correlations were found between the OASIS and the BAI, as anticipated, which is interpreted in this study as evidence of adequate convergent validity with one of the most widely used questionnaires for the assessment of anxiety. The fact that the OASIS also correlated significantly with measures of positive and negative affectivity, but less than with measures of anxiety (i.e. BAI), was interpreted as evidence for the discriminant validity of the instrument. Finally, although we predicted medium correlations between the OASIS and the depression measures (i.e. ODSIS and BDI-II), the results showed large correlations between these measures. In this regard, it is important to note that a large proportion of the patients (53.5%) had comorbid depressive or anxiety disorders, which might account for the large correlations between anxiety and depression obtained in this study. Overall, the results obtained in this study were interpreted as evidence for construct validity.

Overall, the results of this study are consistent with those obtained in prior validations of the scale [25, 31, 32], and they support the adequacy of the OASIS as a valid measure for the online assessment of the anxiety severity and impairment associated with anxiety symptoms.

This study has several strengths. First, to the best of our knowledge, this is the first study to evaluate the psychometric properties of the OASIS in a Spanish clinical sample of individuals with anxiety and depressive disorders. Brief instruments to assess the severity and impairment related to anxiety are lacking in Spain, and so this study contributes to filling the gap in this particular field. Second, although the OASIS has already been validated in transdiagnostic samples with emotional disorders [31], the sample size of patients with principal diagnoses of a depressive disorder was larger in this study. Unlike the study by Bragdon et al. [31], in which most patients had a principal diagnosis of an anxiety disorder (85.6%), we used a sample with a more balanced number of patients with a principal diagnosis of anxiety (55.2%) versus depression (44.8%). Given the burden and prevalence of depression, as well as its transdiagnostic nature and high comorbidity rates with anxiety disorders [2], the findings obtained in this study contribute to the literature on the OASIS by providing data about how the scale performs in patients with a principal diagnosis of depression. Third, the large sample size used in this study (n = 583), and its high diagnostic heterogeneity (i.e. individuals with a variety of anxiety and depressive disorders), helps to increase the generalizability of the results obtained in the study. Fourth, although various validations of the OASIS have been performed in clinical samples [25, 31, 33, 64], none of them have analyzed how the scale performs as a treatment outcome measure. Following previous recommendations [31, 64], in this study we intended to contribute

to filling this gap by analyzing sensitivity to change in two subsamples of patients who received Internet treatments. Fifth, all the patients in the study completed the OASIS through online surveys. Therefore, the results obtained in this study suggest that the online version of the OASIS is an adequate instrument for the online assessment of anxiety (e.g. in trials examining Internet treatments, where both the assessment and the treatment are delivered through an online platform). Given the proliferation of Internet-based treatments in the past decade, the need for validated online assessment instruments is greater than ever before.

Limitations

This study has some limitations that should be acknowledged. First, test-retest reliability was not evaluated in this study. Because all the participants in this study were derived from clinical samples that were receiving treatment, we were not able to analyze this aspect. Second, we were not able to analyze sensitivity to change with the entire sample because scores from pre- to post-treatment were not available for all participants in this study. Moreover, we were not able to examine the sensitivity to change of the OASIS compared to other scales for the assessment of anxiety, such as the BAI. Third, it might have been useful to include additional measures of anxiety in this study to further evaluate the convergent validity of the OASIS. However, it is important to note that the inclusion of instruments in this study was determined by the fact that all the patients were derived from trials where the selection of instruments was already pre-specified. For this reason, only two measures for the assessment of anxiety were used in this study (OASIS and BAI). Fourth, even though the BAI is a well-established measure and one of the more widely used scales for the assessment of anxiety [65-67], we did not follow the optimum approach for the calculation of the ROC curve because the classification of subjects was based on a cutoff from a scale (BAI) rather than a group of healthy control individuals. Hence, the cutoff score obtained in this study should be considered with caution. Finally, the proportion of females and males in this study was not balanced, which might affect the representativity of the results. However, the proportion of females versus males in this study is likely to have been affected by the higher prevalence rates of anxiety and depressive disorders in females compared to males [68].

Conclusions

In conclusion, the results obtained in this study support the adequacy of the online version of the OASIS in clinical samples of Spanish patients with anxiety and depressive disorders. The brevity and ease of use of the OASIS makes this scale an adequate tool for the quick screening of the severity and impairment associated with anxiety. Future

validations of the OASIS should analyze its sensitivity to change in comparison with other measures of anxiety, in order to draw firmer conclusions about this aspect.

The psychometric properties of the online version of the OASIS were analyzed in this study. Similarly to evidence-based online treatments, the validation of online scales can have a direct impact in the dissemination of evidence-based methods for the assessment of behavioral, cognitive and psychopathological processes.

Supporting Information

S1 Appendix. OASIS (Spanish version).

DOCX

S2 Appendix. OASIS (English version).

DOCX

References

1. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime Prevalence and Age-of-Onset Distributions of DSM-IV Disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005;62(6): 593–602.

2. Brown T, Barlow D. A proposal for a dimensional classification system based on the shared features of the DSM-IV anxiety and mood disorders: Implications for assessment. Psychol Assess. 2009;21(3): 256–71.

3. Parés-Badell O, Barbaglia G, Jerinic P, Gustavsson A, Salvador-Carulla L, Alonso J. Cost of Disorders of the Brain in Spain. Foffani G, editor. PLoS One. 2014;9(8): e105471.

4. Wittchen HU, Jacobi F, Rehm J, Gustavsson A, Svensson M, Jönsson B, et al. The size and burden of mental disorders and other disorders of the brain in Europe 2010. Eur Neuropsychopharmacol. 2011;21(9):655–79.

5. Kazdin AE, Blase SL. Rebooting Psychotherapy Research and Practice to Reduce the Burden of Mental Illness. Perspect Psychol Sci. 2011;6(1):21–37.

6. McLean CP, Asnaani A, Litz BT, Hofmann SG. Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. J Psychiatr Res. 2011;45(8): 1027–35.

7. Brown TA, Campbell LA, Lehman CL, Grisham JR, Mancill RB. Current and lifetime comorbidity of the DSM-IV anxiety and mood disorders in a large clinical sample. J Abnorm Psychol. 2001;110(4): 585–99.

8. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005;62(6): 617–27.

9. Haro J, Palacín C, Vilagut G, Bernal M, Luque I, Codony M, et al. Prevalencia de los trastornos mentales y factores asociados: resultados del estudio ESEMeD-España. Med Clin. 2006;126(12): 445–51.

10. Kroenke K, Spitzer RL, Williams JBW, Monahan PO, Löwe B. Anxiety Disorders in Primary Care: Prevalence, Impairment, Comorbidity, and Detection. Ann Intern Med. 2007;146(5): 317-25.

11. Olatunji BO, Cisler JM, Tolin DF. Quality of life in the anxiety disorders: A meta-analytic review. Clin Psychol Rev. 2007;27(5): 572–81.

12. Hunsley J, Mash EJ. Developing Criteria for Evidence-Based Assessment. In: Hunsley J, Mash EJ. Oxford series in clinical psychology. A guide to assessments that work . New York: Oxford University Press; 2008. pp. 3–14.

13. Nathan PE, Gorman JM. A Guide to Treatments That Work. New York: Oxford University Press; 1998.

14. Alfonsson S, Pernilla M, Timo H. Interformat reliability of digital psychiatric self-report questionnaires: a systematic review." J Med Internet Res. 2014;16(12): e268.

15. Andersson G. Internet-delivered psychological treatments. Annu Rev Clin Psycho. 2016;12: 157–79.

16. Van Ballegooijen W, Riper H, Cuijpers P, van Oppen P, Smit JH. Validation of online psychometric instruments for common mental health disorders: a systematic review. BMC Psychiatry; 2016;16: 45.

17. Beck AT, Steer RA. Manual for the Beck Anxiety Inventory. San Antonio, TX: The Psychological Corporation; 1993.

18. Spielberger CD. Manual for the State-Trait Anxiety Inventory (STAI). Palo Alto, CA: Consulting Psychologists Press; 1983.

19. Guillén-Riquelme A, Buela-Casal G. Actualización psicométrica y funcionamiento diferencial de los items en el State Trait Anxiety Inventory (STAI). Psychometric revision and differential item functioning in the State Trait Anxiety Inventory (STAI). Psicothema. 2011;23(3): 510–15.

20. Magán I, Sanz J, García-Vera MP. Psychometric properties of a Spanish version of the Beck Anxiety Inventory (BAI) in general population. Span J Psychol. 2008; 11(2): 626–40.

21. Spielberger CD, Gorsuch RL, Lushene R. Manual del Cuestionario de Ansiedad Estado/Rasgo (STAI). Madrid: TEA Ediciones; 1982.

22. Meyer TJ, Miller ML, Metzger RL, Borkovec TD. Development and validation of the penn state worry questionnaire. Behav Res Ther. 1990;28(6): 487–95.

23. Houck PR, Spiegel DA, Shear MK, Rucci P. Reliability of the self-report version of the panic disorder severity scale. Depress Anxiety. 2002;15(4): 183–5.

24. Mattick RP, Clarke JC. Development and validation of measures of social phobia scrutiny fear and social interaction anxiety. Behav Res Ther. 1998;36(4): 455–70.

25. Campbell-Sills L, Norman SB, Craske MG, Sullivan G, Lang AJ, Chavira DA, et al. Validation of a brief measure of anxiety-related severity and impairment: the Overall Anxiety Severity and Impairment Scale (OASIS). J Affect Disord. 2009;112(1–3): 92–101.

26. Norman SB, Hami Cissell S, Means-Christensen AJ, Stein MB. Development and validation of an Overall Anxiety Severity And Impairment Scale (OASIS). Depress Anxiety. 2006;23(4): 245–9.

27. Norman SB, Campbell-Sills L, Hitchcock CA, Sullivan S, Rochlin A, Wilkins KC, et al. Psychometrics of a brief measure of anxiety to detect severity and impairment: the Overall Anxiety Severity and Impairment Scale (OASIS). J Psychiatr Res. 2011;45(2): 262–8.

28. Ziegler M, Kemper CJ, Kruyen P. Short Scales – Five Misunderstandings and Ways to Overcome Them. J Individ Differ. 2014;35(4): 185–9.

29. Haynes SN, Richard D, Kubany ES. Content validity in psychological assessment: a functional approach to concepts and methods. Psychol Assess. 1995;7(3): 238–47.

30. Barlow DH, Allen LB, Choate ML. Toward a unified treatment for emotional disorders. Behav Ther. 2004;35(2): 205–30.

31. Bragdon LB, Diefenbach GJ, Hannan S, Tolin DF. Psychometric properties of the Overall Anxiety Severity and Impairment Scale (OASIS) among psychiatric outpatients. J Affect Disord. 2016;201: 112–5.

32. Ito M, Oe Y, Kato N, Nakajima S, Fujisato H, Miyamae M, et al. Validity and clinical interpretability of Overall Anxiety Severity And Impairment Scale (OASIS). J Affect Disord. 2015;170: 217–24.

33. Moore SA, Welch SS, Michonski J, Poquiz J, Osborne TL, Sayrs J, et al. Psychometric evaluation of the Overall Anxiety Severity And Impairment Scale (OASIS) in individuals seeking outpatient specialty treatment for anxiety-related disorders. J Affect Disord. 2015;175: 463–70.

34. Sheehan D V, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998; 59 Suppl 20: 22-33.

35. Ferrando L, Franco-Alfonso L, Soto M, Bobes J, Soto O, Franco L, et al. M.I.N.I. Mini International Neuropsychiatric interview. Spanish version 5.0.0. DSM-IV. Madrid: Instituto IAP; 1998.

36. Beck AT, Steer RA, Brown GK. Beck Depression Inventory. San Antonio: The Psychological Corporation; 1996.

37. Sanz J, García-Vera MP, Espinosa R, Fortún M, Vázquez C. Adaptación española del Inventario para la Depresión de Beck-II (BDI-II): 3. Propiedades psicométricas en pacientes con trastornos psicológicos. Clínica y Salud. 2005;16(2): 121–42.

38. Storch EA, Roberti JW, Roth DA. Factor structure, concurrent validity, and internal consistency of the beck depression inventory? – second edition in a sample of college students. Depress Anxiety. 2004;19(3): 187–9.

39. Bentley KH, Gallagher MW, Carl JR, Barlow DH. Development and validation of the Overall Depression Severity and Impairment Scale. Psychol Assess. 2014;26(3): 815–30.

40. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. J Pers Soc Psychol. 1988;54(6): 1063–70.

41. Crawford JR, Henry JD. The Positive and Negative Affect Schedule (PANAS): Construct validity, measurement properties and normative data in a large non-clinical sample. Br J Clin Psychol. 2004;43(3): 245–65.

42. Sandín B, Chorot P, Lostao L, Joiner TE, Santed MA, Valiente RM. Escalas PANAS de afecto positivo y negativo: Validacion factorial y convergencia transcultural. Psicothema. 1999;11(1): 37–51.

43. Mezzich JE, Cohen NL, Ruiperez MA, Banzato CEM, Zapata-Vega MI. The Multicultural Quality of Life Index: presentation and validation. J Eval Clin Pract. 2011;17(2): 357–64.

44. Mezzich JE, Ruipérez MA, Pérez C, Yoon G, Liu J, Mahmud S. The Spanish version of the quality of life index: presentation and validation. J Nerv Ment Dis. 2000;188(5): 301–5.

45. DeVellis RF. Classical Test Theory. Med Care. 2006;44(Suppl 3): S50–9.

46. Marsh HW, Hau KT, Wen Z. In Search of Golden Rule : Comment on Hypothesis Testing Approaches to Setting Cutoff Value for Fit Indexes and Danger in Overgeneralizing Hu and Bentler's (1999) Findings. Struct Equ Modeling. 2004; 11(3): 320–41.

47. McNeish D, An J, Hancock GR. The thorny relation between measurement quality and fit index cutoffs in latent variable models. J Pers Assess. 2018;100(1): 43–52.

48. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale: Erlbaum; 1988.

49. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety. J Consult Clin Psych. 1988;56(6): 893–97.

50. Argimon JM, Jiménez J. Métodos de investigación clínica epidemiológica (4th ed.). Barcelona: Elsevier España; 2013.

51. Unal I. Defining an optimal cut-point value in ROC analysis: An alternative approach. Comput Math Methods Med. 2017. doi: 10.1155/2017/3762651

52. Mira A, Bretón-López J, García-Palacios A, Quero S, Baños RM, Botella C. An internet-based program for depressive symptoms using human and automated support: A randomized controlled trial. Neuropsychiatr Dis Treat. 2017;13: 987–1006.

53. Gonzalez-Robles A, Garcia-Palacios A, Banos R, Riera A, Llorca G, Traver F, et al. Effectiveness of a transdiagnostic internet-based protocol for the treatment of emotional disorders versus treatment as usual in specialized care: study protocol for a randomized controlled trial. Trials. 2015;16: 488.

54. Díaz-García A, González-Robles A, Fernández-Álvarez J, García-Palacios A, Baños RM, Botella C. Efficacy of a Transdiagnostic internet-based treatment for emotional disorders with a specific component to address positive affect: Study protocol for a randomized controlled trial. BMC Psychiatry. BMC Psychiatry; 2017;17(1): 145.

55. Barlow DH, Ellard KK, Fairholme CP, Farchione TJ, Boisseau CL, Allen LB, Ehrenreich-May J. The unified protocol for transdiagnostic treatment of emotional disorders: Client workbook. New York: Oxford University Press; 2011.

56. Lejuez CW, Hopko DR, Hopko SD. A brief behavioral activation treatment for depression: Treatment manual. Behav Modif. 2001; 25, 225–86.

57. Seligman ME, Steen TA, Park N, Peterson C. Positive psychology progress: Empirical validation of interventions. Am Psychol. 2005; 60: 410–21.

58. Sin NL, Lyubomirsky S. Enhancing well-being and alleviating depressive symptoms with positive psychology interventions: A practice-friendly metaanalysis. J Clin Psychol. 2009;65: 467–87.

59. Barlow DH, Farchione TJ, Fairholme CP, Ellard KK, Boisseau CL, Allen LB, Ehrenreich-May J. The unified protocol for transdiagnostic treatment of emotional disorders: therapist guide. New York: Oxford University Press; 2011.

60. Linehan MM. Skills training manual for treating borderline personality disorder. Diagnosis and treatment of mental disorders. New York: Guilford Press; 1993.

61. Morris SB, DeShon RP. Combining effect size estimates in meta-analysis with repeated measures and independent-groups designs. Psychol Methods. 2002;7(1): 105–25.

62. Rubio-Aparicio M, Marín-Martínez F, Sánchez-Meca J, López-López JA. A methodological review of meta-analyses of the effectiveness of clinical psychology treatments. Behav Res Methods. 2017: 1–17.

63. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005;62(6): 617–27.

64. Hermans M, Korrelboom K, Visser S. A Dutch version of the Overall Anxiety Severity and Impairment Scale (OASIS): Psychometric properties and validation. J Affect Disord. 2015;172: 127–32.

65. Julian LJ. Measures of anxiety: State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory (BAI), and Hospital Anxiety and Depression Scale Anxiety (HADS-A). Arthrit Care Res. 2011;63(S11): S467–S72.

66. Piotrowski C. The status of the Beck inventories (BDI, BAI) in psychology training and practice: A major shift in clinical acceptance. J Appl Biobehav Res. 2017: e12112.

67. Piotrowski C, Gallant N. Research Use of Clinical Measures for Anxiety in the Recent Psychological Literature. J Instruct Psychol. 2009;36(1): 84–6.

68. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.

Overall Anxiety Severity and Impairment Scale (OASIS)

Los siguientes ítems preguntan sobre ansiedad y miedo. Para cada ítem, selecciona el número que mejor describe tu experiencia durante la última semana.

1. Durante la última semana, ¿con qué frecuencia te has sentido ansioso?
0 = No me sentí ansioso durante la última semana.
1 = Ansiedad infrecuente. Me sentí ansioso en algunos momentos.
2 = Ansiedad ocasional. La mitad del tiempo me sentí ansioso y la otra mitad no. Me costó relajarme.
3 = Ansiedad frecuente. Me sentí ansioso la mayor parte del tiempo. Me resultó muy difícil relajarme.
4 = Ansiedad constante. Me sentí ansioso todo el tiempo y nunca llegué a relajarme.

2. Durante la última semana, cuando te sentiste ansioso, ¿en qué medida tu ansiedad fue intensa o severa?
0 = Poco o nada. La ansiedad estuvo ausente o casi no la noté.
1 = Leve. La ansiedad fue de baja intensidad. Pude relajarme cuando lo intenté. Los síntomas físicos fueron sólo un poco molestos.
2 = Moderada. La ansiedad me generó malestar en algunos momentos. Me resultó difícil relajarme o concentrarme, pero pude hacerlo cuando lo intenté. Los síntomas físicos fueron molestos.
3 = Severa. La ansiedad fue intensa la mayor parte del tiempo. Me resultó muy difícil relajarme o concentrarme en cualquier otra cosa. Los síntomas físicos fueron enormemente molestos.
4 = Extrema. La ansiedad me sobrepasó. Me fue totalmente imposible relajarme. Los síntomas físicos fueron insoportables.

3. Durante la última semana, ¿con qué frecuencia evitaste situaciones, lugares, objetos o actividades debido a tu ansiedad o miedo?
0 = Ninguna. No evité lugares, situaciones, actividades o cosas por miedo.
1 = Infrecuente. Evité algunas cosas de vez en cuando, pero por lo general me enfrenté a las situaciones u objetos. Mi estilo de vida no se vio afectado.
2 = Ocasional. Tuve algo de miedo a ciertas situaciones, lugares u objetos, pero todavía pudo manejarlos. Mi estilo de vida sufrió pocos cambios. Siempre o casi siempre evité las cosas que me dan miedo si estaba solo, pero las pude manejar si alguien venía conmigo.
3 = Frecuente. Tuve bastante miedo y realmente intenté evitar las cosas que me asustan. He hecho cambios significativos en mi estilo de vida para evitar objetos, situaciones, actividades o lugares.
4 = Todo el tiempo. Evitar objetos, situaciones, actividades o lugares ha ocupado gran parte de mi vida. Mi estilo de vida se ha visto enormemente afectado y ya no hago cosas con las que solía disfrutar.

4. Durante la última semana, ¿en qué medida ha interferido la ansiedad en tu capacidad para hacer las cosas que tenías que hacer respecto al trabajo, el colegio o tu hogar?

0 = Nada. La ansiedad no interfirió en mi trabajo/hogar/colegio.

1 = Leve. La ansiedad me causó algo de interferencia en mi trabajo/hogar/colegio. Las cosas eran más difíciles, pero pude realizar todo lo que necesitaba hacer.

2 = Moderada. La ansiedad definitivamente interfirió en mis tareas. He podido realizar la mayoría de las cosas, pero sólo algunas las he hecho tan bien como en el pasado.

3 = Severa. La ansiedad verdaderamente ha cambiado mi capacidad para hacer las cosas. Algunas cosas las he podido realizar, pero otras no. Mi rendimiento se ha visto definitivamente afectado.

4 = Extrema. La ansiedad ha llegado a ser incapacitante. He sido incapaz de completar mis tareas y he tenido que irme del colegio, he dejado o me han despedido de mi trabajo o he sido incapaz de completar las tareas del hogar y he sufrido consecuencias como desalojos, cobradores, etc.

5. Durante la última semana, ¿en qué medida ha interferido la ansiedad en tu vida social y en tus relaciones?

0 = Nada. La ansiedad no interfirió en mis relaciones.

1 = Leve. La ansiedad apenas interfirió en mis relaciones. Algunas de mis amistades y otras relaciones se han visto afectadas, pero en conjunto mi vida social sigue siendo satisfactoria.

2 = Moderada. La ansiedad interfirió algo en mi vida social, pero sigo teniendo algunas relaciones cercanas. No paso tanto tiempo con otros como en el pasado, pero sigo teniendo relaciones sociales algunas veces.

3 = Severa. Mis amistades y otras relaciones se han visto muy afectadas a causa de mi ansiedad. No disfruto de las actividades sociales. Tengo muy pocas relaciones sociales.

4 = Extrema. La ansiedad ha alterado completamente mis actividades sociales. Todas mis relaciones se han visto afectadas o han finalizado. Mi vida familiar es extremadamente tensa.

Overall Anxiety Severity and Impairment Scale (OASIS)

The following items ask about anxiety and fear. For each item, select the number for the answer that best describes your experience over the past week.

1. In the past week, how often have you felt anxious?
0 = No anxiety in the past week.
1 = Infrequent anxiety. Felt anxious a few times.
2 = Occasional anxiety. Felt anxious as much of the time as not. It was hard to relax.
3 = Frequent anxiety. Felt anxious most of the time. It was very difficult to relax.
4 = Constant anxiety. Felt anxious all of the time and never really relaxed.

2. In the past week, when you have felt anxious, how intense or severe was your anxiety?
0 = Little or None: Anxiety was absent or barely noticeable.
1 = Mild: Anxiety was at a low level. It was possible to relax when I tried. Physical symptoms were only slightly uncomfortable.
2 = Moderate: Anxiety was distressing at times. It was hard to relax or concentrate, but I could do it if I tried. Physical symptoms were uncomfortable.
3 = Severe: Anxiety was intense much of the time. It was very difficult to relax or focus on anything else. Physical symptoms were extremely uncomfortable.
4 = Extreme: Anxiety was overwhelming. It was impossible to relax at all. Physical symptoms were unbearable.

3. In the past week, how often did you avoid situations, places, objects, or activities because of anxiety or fear?
0 = None: I do not avoid places, situations, activities, or things because of fear.
1 = Infrequent: I avoid something once in a while, but will usually face the situation or confront the object. My lifestyle is not affected.
2 = Occasional: I have some fear of certain situations, places, or objects, but it is still manageable. My lifestyle has only changed in minor ways. I always or almost always avoid the things I fear when I'm alone, but can handle them if someone comes with me.
3 = Frequent: I have considerable fear and really try to avoid the things that frighten me. I have made signifi cant changes in my lifestyle to avoid the object, situation, activity, or place.
4 = All the Time: Avoiding objects, situations, activities, or places has taken over my life. My lifestyle has been extensively affected and I no longer do things that I used to enjoy.

4. In the past week, how much did your anxiety interfere with your ability to do the things you needed to do at work, at school, or at home?
0 = None: No interference at work/home/school from anxiety.

1 = Mild: My anxiety has caused some interference at work/home/school. Things are more difficult, but everything that needs to be done is still getting done.
2 = Moderate: My anxiety definitely interferes with tasks. Most things are still getting done, but few things are being done as well as in the past.
3 = Severe: My anxiety has really changed my ability to get things done. Some tasks are still being done, but many things are not. My performance has definitely suffered.
4 = Extreme: My anxiety has become incapacitating. I am unable to complete tasks and have had to leave school, have quit or been fired from my job, or have been unable to complete tasks at home and have faced consequences like bill collectors, eviction, etc.

5. In the past week, how much has anxiety interfered with your social life and relationships?
0 = None: My anxiety doesn't affect my relationships.
1 = Mild: My anxiety slightly interferes with my relationships. Some of my friendships and other relationships have suffered, but, overall, my social life is still fulfilling.
2 = Moderate: I have experienced some interference with my social life, but I still have a few close relationships. I don't spend as much time with others as in the past, but I still socialize sometimes.
3 = Severe: My friendships and other relationships have suffered a lot because of anxiety. I do not enjoy social activities. I socialize very little.
4 = Extreme: My anxiety has completely disrupted my social activities. All of my relationships have suffered or ended. My family life is extremely strained.

Chapter 5. Capturing the severity and impairment associated with depression: Psychometric properties of the Overall Depression Severity and Impairment Scale (ODSIS) administered online in a Spanish clinical sample with emotional disorders

This chapter has been submitted as:

Mira, A., González-Robles, A., Molinari, G., Miguel, C., Díaz-García, A., Bretón-López, J., García-Palacios, A., & Botella, C. Capturing the severity and impairment associated with depression: Psychometric properties of the Overall Depression Severity and Impairment Scale (ODSIS) administered online in a Spanish Clinical sample with emotional disorders.

Chapter 6. Effectiveness of a transdiagnostic internet-based protocol for emotional disorders versus treatment as usual in specialized care: Results of a randomized controlled trial

This chapter has been submitted as:

González-Robles, A., Díaz-García, A., García-Palacios, A., Roca, P., Ramos-Quiroga, J. A., & Botella, C. Effectiveness of a transdiagnostic Internet-based protocol for emotional disorders versus treatment as usual in specialized care: Results of a randomized controlled trial.

Chapter 7. Up-regulating positive affectivity in the transdiagnostic treatment of emotional disorders: A randomized pilot study

This chapter has been published as:

González-Robles, A., García-Palacios, A., Baños, R., Quero, S., & Botella, C. (2017). Up-regulating Positive Affectivity in the Transdiagnostic Treatment of Emotional Disorders: A Randomized Pilot Study. *Behavior* Modification, *43*(1), 26–55.

Up-regulating Positive Affectivity in the Transdiagnostic Treatment of Emotional Disorders: A Randomized Pilot Study

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Abstract

Transdiagnostic cognitive-behavioral therapy for emotional disorders (ED) has proven to be effective. However, current transdiagnostic treatment protocols address only the regulation of negative affectivity, and they do not include treatment components to more directly target the regulation of positive affectivity. In this study, we propose to evaluate the preliminary efficacy and acceptability of a transdiagnostic treatment protocol for ED that includes, as an innovative feature, a specific treatment component to directly upregulate positive affectivity based on positive psychology interventions. A total of 24 participants were randomized to either a transdiagnostic treatment protocol (n = 12) or a transdiagnostic treatment protocol with an additional component designed to regulate positive affectivity (n = 12). Participants completed measures of anxiety, depression, positive and negative affectivity, and quality of life, as well as treatment acceptability at pre- and posttreatment and at the 3-month follow-up. Both interventions led to improvements in all measures at posttreatment, and these outcomes were maintained at the 3-month follow-up, with large effect sizes for all measures. The effect sizes for positive affect were larger in the condition that included the component to upregulate positive affectivity. Attrition rate was low, and both treatment protocols were well accepted by participants. The results obtained in this study indicate the feasibility of testing the treatment protocol in a larger, randomized, controlled trial, and they suggest the potential of including treatment components for directly upregulating positive affectivity in future research on transdiagnostic treatment protocols for ED.

Keywords: Positive affectivity, transdiagnostic, cognitive-behavioral therapy, emotional disorders, emotion regulation

Introduction

Emotional disorders (ED; depression and anxiety disorders) are highly prevalent mental disorders (Kessler et al., 2005; Wittchen et al., 2010) and one of the main causes of disability worldwide (Kazdin & Blase, 2011; McLean, Asnaani, Litz, & Hofmann, 2011). Currently, there is extensive evidence showing the efficacy and effectiveness of disorder-specific cognitive-behavioral therapy (CBT) for several ED, including major depression disorder (MDD; Cuijpers, Smit, Bohlmeijer, Hollon, & Andersson, 2010; Hollon & Ponniah, 2010), obsessive-compulsive disorder (OCD; McKay et al., 2015), and different anxiety disorders, such as generalized anxiety disorder (GAD), panic disorder (PD), agoraphobia (AG), and social anxiety disorder (SAD; Antony & Stein, 2009; Barlow, 2002; Nathan & Gorman, 2007; Olatunji, Cisler, & Deacon, 2010). However, high comorbidity rates among ED (Kessler et al., 2005) have led some researchers to shift the focus to treatment strategies (referred to as transdiagnostic treatments) that might be more widely effective across these diverse mental health problems (D. A. Clark & Taylor, 2009).

To date, there is evidence showing the efficacy of transdiagnostic treatments for anxiety disorders (Reinholt & Krogh, 2014), and for mixed depression and anxiety disorders (Newby, McKinnon, Kuyken, Gilbody, & Dalgleish, 2015; Păsărelu, Andersson, Nordgren, Dobrean, 2016). An important line of research within the transdiagnostic treatment of ED was initiated by D. H. Barlow (Barlow, Allen, & Choate, 2004). Barlow's theory of triple vulnerability emphasizes the common underlying vulnerabilities in ED and helps to explain the comorbidity among these diverse conditions (Brown & Barlow, 2009). A central aspect within this theoretical perspective is the role of emotion regulation in ED (Barlow et al., 2004). Emotion regulation has been defined as the attempt to influence the types of emotions people experience, when they experience these emotions, and how these emotions are expressed and experienced (Gross, 1998), with regard to either negative or positive emotions. Moreover, people can use emotion regulation to upregulate (increase and/or maintain) or downregulate (decrease) emotions (Gross, 1998). Difficulties in the regulation of both negative and positive emotions have emerged in research as a common feature in depression and anxiety disorders (Carl, Soskin, Kerns, & Barlow, 2013; Hofmann, Sawyer, Fang, & Asnaani, 2012). The core of these emotion regulation difficulties has been identified as neuroticism or negative affect (N/NA; Barlow, Sauer-Zavala, Carl, Bullis, & Ellard, 2013; Brown & Barlow, 2009). However, these déficits have also been associated with low extraversion/positive affect (E/PA). For instance, the association between low PA and several ED, such as unipolar depression (L. A. Clark & Watson, 1991), SAD (Brown, Chorpita, & Barlow, 1998), and AG (Rosellini, Lawrence, Meyer, & Brown, 2010),

has been shown in previous research. In addition, there is evidence indicating that most individuals with anxiety and mood disorders show low levels of PA (Kotov, G.mez, Schmidt, & Watson, 2010). Regarding depression, literatura has suggested that there is a link between the maladaptive strategies used by depressed patients to regulate PA and depression symptoms (Gilbert, 2012; Gilbert, Nolen-Noeksema, & Gruber, 2013; Werner-Seidler, Banks, Dunn, & Moulds, 2013), and that deficits in PA regulation are associated with a worse depression prognosis (Shankman, Nelson, Harrow, & Faull, 2011). Finally, a review focused on PA regulation in ED concluded that there are transdiagnostic disturbances in the strategies used to regulate positive emotions that may account for low levels of PA in depression and several anxiety disorders such as GAD, AG, PD, SAD, and OCD (Carl et al., 2013).

The regulation of negative emotions in transdiagnostic models for ED such as the unified protocol (UP) has received a great deal of attention in research (Barlow, Sauer-Zavala, Carl, Bullis, & Ellard, 2013; Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010). This protocol focuses on four essential aspects that have the general purpose of downregulating NA: increasing present-focused emotional awareness, addressing maladaptive emotional avoidance behavior patterns, promoting cognitive flexibility, and facilitating interoceptive and situational exposure. However, although Barlow highlighted the role of low PA in the onset and maintenance of ED (Barlow et al., 2004; Brown & Barlow, 2009), the main objective of the treatment components in the UP is to train patients in NA regulation, and less attention is paid to the inclusion of treatment components to directly target PA regulation. This is also the case in other empirically evaluated transdiagnostic treatments for anxiety disorders (e.g., Norton, 2012; Titov, Andrews, Johnston, Robinson, & Spence, 2010) and mixed anxiety and depression (e.g., Berger, Boettcher, & Caspar, 2013; Titov et al., 2011).

PA regulation may have important implications in treatment because high PA is associated with better physical and psychological health, healthier lifestyles, and better general functioning (S. Cohen & Pressman, 2006; Fredrickson, 2001; Livingstone & Srivastava, 2012; Pressman & Cohen, 2005; Quoidbach, Berry, Hansenne, & Mikolajczak, 2010; Tugade & Fredrickson, 2007). Moreover, the importance of fostering PA, in addition to reducing NA, to improve treatment outcomes in depression and anxiety disorders has been highlighted in the literature (Carl et al., 2013) because high PA seems to promote general well-being, prevent relapses, and produce resilience (Dunn, 2012; Tugade & Fredrickson, 2007; Wood & Joseph, 2010).

Positive psychology interventions (PPIs) mainly focus on enhancing positive emotional functioning and well-being (Schueller, Kashdan, &

Parks, 2014). Schueller and Parks (2014) distinguished five categories under the umbrella of PPIs: (a) savoring experiences and sensations, (b) cultivating and expressing gratitude, (c) engaging in kind actions, (d) promoting positive relationship processes, and (e) pursuing hope and meaning. Meta-analyses have shown that these interventions are effective for enhancing well-being and reducing depressive symptoms in both the general population and in individuals with a variety of psychosocial problems (Bolier et al., 2013; Schueller & Parks, 2014; Sin & Lyubomirsky, 2009; Weiss, Westerhof, & Bohlmeijer, 2016). The addition of PPIs to existing CBT interventions (e.g., transdiagnostic interventions) could help to strengthen their effect on PA, leading to greater and more lasting effects on positive emotional functioning and wellbeing. Taylor, Lyubomirsky, and Stein (2017) recently studied the efficacy of a transdiagnostic intervention based on PPIs for mixed anxiety and depression, reporting significant gains in PA and secondary gains in NA, depression, and anxiety symptoms. However, this study differs from ours in that it does not include strategies for downregulating NA. In regard to this point, the literature has mainly focused on studying the impact of PPIs on depressive symptoms rather than anxiety (see Bolier et al., 2013; Sin & Lyubomirsky, 2009; Weiss et al., 2016). However, research suggests that anxiety disorders may be also appropriate targets for treatments based on PPIs. For instance, AG or SAD has been shown to be characterized by low levels of PA (Brown et al., 1998; Rosellini et al., 2010). Another reason why anxiety disorders may benefit from PPIs is that anxious individuals often engage in strategies that lead to the avoidance of positive experiences and emotions, as outlined in the review by Carl et al. (2013). Accordingly, well-being may be increased in these patients by training them in strategies to upregulate PA.

Another intervention for depression that can help to promote well-being is behavioral activation (Lejuez, Hopko, & Hopko, 2001; Lewinsohn, 1974). From the approach of behavioral activation, depressive symptoms are deemed as the result of decreased levels of activity that lead to a loss of positive reinforcement (Lewinsohn, 1974). The efficacy of behavioral activation in improving well-being has been shown in previous research in both depressed (Mazzucchelli, Kane, & Rees, 2009) and nondepressed populations (Mazzucchelli, Kane, & Rees, 2010). Thus, the ability to increase well-being and positive emotional functioning may be strengthened by including behavioral activation procedures in interventions, at least for individuals with depression.

Taking all this into consideration, an important treatment goal from a transdiagnostic treatment approach would be to increase PA while decreasing NA.

Aims

We developed a transdiagnostic protocol (TP) for ED based on the UP (Barlow et al., 2011) and another version of this protocol that also includes a specific component mainly based on PPIs to directly address PA regulation (TP + PA).

Both protocols were tested using a two-armed randomized pilot study. The aim was to assess the differential effect of both interventions on measures of depression, anxiety, and quality of life, and on PA and NA. Another goal was to evaluate treatment retention and the acceptability of both interventions by participants. It was hypothesized that (a) both interventions would result in significant improvements on all clinical measures at posttreatment, and these results would be maintained in the short term (3-month follow-up); (b) the TP + PA would significantly outperform the TP group on PA measures; (c) acceptability would be high in both conditions, with no statistical differences between conditions.

Method

Procedure

Participants were recruited from individuals seeking treatment at the Emotional Disorders Clinic (Castellon, Spain). After an initial screening assessment that included the administration of a diagnostic interview, participants who met the inclusion criteria were asked to sign a consent form and then randomly assigned to either the TP group or the TP + PA group. Block randomization in blocks of four was performed using a computer-generated random number sequence. Once participants had been assigned to one of the conditions, they completed pretreatment primary and secondary outcome measures (self-reported questionnaires). In both groups, the interventions started immediately after pretreatment assessment. After each treatment session, participants were given a patient treatment handbook and asked to do homework tasks to review the specific contents and practice the proposed strategies and skills learned in each session. After completing the treatment protocols, a diagnostic interview and primary and secondary outcome measures were administered to obtain posttreatment data. The assessment instruments were also applied at the 3-month follow-up. All assessments (i.e., diagnostic interviews) were conducted by independent assessors who were blind to the participants' allocation.

The study was registered in Clinicaltrials.gov (https://clinicaltrials.gov/) as NCT02790398 and approved by the Ethics Committee of Universitat Jaume I (Castellon, Spain).

Participants

In total, 26 participants met the inclusion criteria. In the TP + PA group, one participant dropped out after 11 treatment sessions, stating that she had no time to dedicate to the therapy. In the TP group, one participant dropped out after Session 5 because she had to move to another city. These participants were excluded from the analyses; therefore, the final sample included 24 participants (see flow of participants in Figure 12).

The baseline characteristics of the sample are described in Table 12. Inclusion criteria were as follows: (a) being 18 years old or older; (b) meeting the Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev.; DSM-IV-TR; American Psychiatric Association [APA], 2000) diagnostic criteria for ED, which included MDD, dysthymic disorder (DD), GAD, SAD, PD, AG, anxiety disorder not otherwise specified (ADNOS), (unipolar) mood disorder not otherwise specified (MDNOS), and OCD; and (c) ability to understand and read Spanish. Exclusion criteria included (a) schizophrenia, bipolar disorder, or alcohol and/or substance dependence disorder; (b) high risk of suicide; (c) receiving another psychological treatment during the study; and (d) in the case of receiving pharmacological treatment, an increase and/or change in this treatment during the study period (a decrease in pharmacological treatment was accepted).

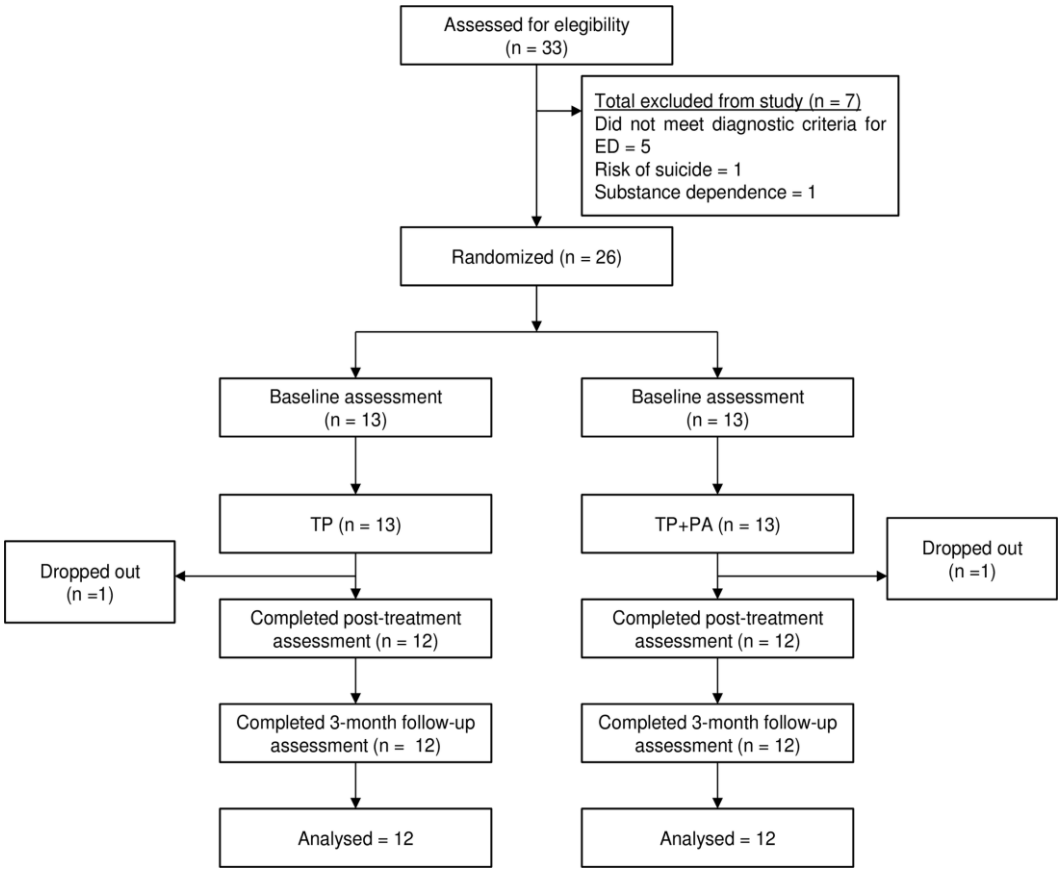

Figure 8. Flowchart of participants

Note. ED = Emotional disorders; TP = Transdiagnostic Protocol; PA = Positive affect

Table 22. Description of participants at baseline

	TP+PA	TP
Gender, n (%)		
Female	8 (67)	11 (92)
Male	4 (33)	1 (8)
Age; M (SD), range	31.33 (12.48), 21-61	27.75 (10.91), 18-57
Education, n (%)		
Basic studies	3 (25)	1 (8)
Medium studies	7 (58)	4 (33)
Superior studies	2 (17)	7 (58)
Marital status, n (%)		
Married/partnered	6 (50)	5 (42)
Single	6 (50)	6 (50)
Divorced/Widowed	0 (0)	1 (8)
Principal diagnostic, n (%)		
Generalized anxiety disorder	5 (42)	6 (50)
Major depressive disorder	2 (17)	2 (17)
Agoraphobia	2 (17)	1 (8)
Panic disorder	2 (17)	1 (8)
Social anxiety disorder	1 (8)	1 (8)
Dysthymic disorder	0 (0)	1 (8)
Number of comorbid diagnoses, n (%)		
0	7 (58)	6 (50)
1	3 (25)	3 (25)
≥ 2	2 (17)	3 (25)

Note. TP + PA = Transdiagnostic protocol + positive affect regulation component; TP = Transdiagnostic protocol

In the TP group, four participants were taking pharmacological treatment at the time of enrollment. All of them were taking benzodiazepines. In the TP + PA group, three participants were receiving pharmacological treatment at the time of enrollment. Two of them were taking benzodiazepines, and one was taking antidepressants in addition to benzodiazepines. All participants in both conditions decreased the dosage or stopped taking medication during the study. At posttreatment and at the 3-month follow-up, none of the participants were receiving pharmacological treatment.

Measures

Diagnostic measure

Mini International Neuropsychiatric Interview, Version 5.0.0 (MINI). This is a short, structured, diagnostic psychiatric interview that yields key Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV;

APA, 1994) and International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) diagnoses (Sheehan et al., 1998). The MINI can be administered in a short period of time, and clinical interviewers only need brief training. The MINI has been translated into Spanish and validated (Ferrando, Bobes, Gibert, & Lecrubier, 1997).

Self-administered questionnaires

Overall Anxiety Severity and Impairment Scale (OASIS). This is a five-item scale, rated from 0 to 4, that evaluates the frequency, severity, and work, social, academic, and everyday life impairment caused by anxiety symptoms in the past week (Norman et al., 2011). The internal consistency of the OASIS has been found to be good (α = .80). The scale has also shown good test–retest reliability (k = .82) and convergent validity. We used the Spanish version of the instrument, which also showed adequate psychometric properties (Mira et al., 2015). In the present study, the Cronbach's alpha for the OASIS was α = .81.

Beck Depression Inventory–II (BDI-II). It is one of the most widely used questionnaires to evaluate depression severity in pharmacological and psychotherapy trials (Beck, Steer, & Brown, 1990). It consists of 21 items about the different symptoms characterizing MDD, added together to obtain the total score, which can yield a maximum of 63 points. The instrument has shown good internal consistency (α = .76-.95). The Spanish version of this instrument has also shown high internal consistency (α = .87) in both general and clinical populations (α = .89) (Sanz, Navarro, & Vázquez, 2003). In the present study, the Cronbach's alpha for the BDI-II was α = .92.

Positive and Negative Affect Schedule (PANAS). The PANAS consists of 20 items that evaluate two independent dimensions: PA and NA (Watson, Clark, & Tellegen, 1988). It contains 10 descriptors evaluating PA (e.g., "enthusiastic," "inspired," "proud") and 10 others assessing NA (e.g., "scared," "irritable," "guilty"). The range for each scale (10 items on each) is from 10 to 50, and the patient has to answer how he or she usually feels regarding each of these emotions. The scale showed excellent internal consistency (α between .84 and .90) and convergent and discriminant validity. The Spanish version has demonstrated high internal consistency (α = .89 and .91 for PA and NA in women, respectively, and α = .87 and .89 for PA and NA in men, respectively) in college students (Sand.n et al., 1999). In the present study, the Cronbach's alpha for the PANAS PA was α = .94, and for the PANAS NA, α = .88.

The Quality of Life Inventory (QLI). This is a brief self-report questionnaire that assesses perceived quality of life in different life-related areas (Mezzich, Cohen, & Ruiperez, 1996). The questionnaire includes 10 items, rated on a scale from one to 10, that assess physical well-being,

psychological well-being, self-care and independent functioning, occupational functioning, interpersonal functioning, social emotional support, community and services support, personal fulfillment, spiritual fulfillment, and overall quality of life. The QLI has shown excellent internal consistency (between .90 and .92), test–retest reliability (.87), and discriminant validity. The Spanish validation of the QLI (Mezzich et al., 2000) has also demonstrated good test–retest reliability (α = .89) and discriminant validity. In the present study, the Cronbach's alpha for the QLI was α = .87.

Acceptability of treatment

Expectations and Opinion of Treatment Scales. These questionnaires are adapted from Borkovec and Nau (1972). Each scale is made up of five items, rated on a scale from 0 (nothing at all) to 10 (completely), that cover how logical the treatment seems to be ("How logical do you think this treatment is?"), to what extent it could satisfy the patient ("How satisfied are you with the treatment?"), whether it could be recommended to a person with the same problem ("To what extent do you feel confident recommending this treatment to a friend who has the same problems?"), whether it could be used to treat other psychological problems ("To what extent do you think this treatment could be useful in treating other psychological problems?"), and its usefulness for the patient's problem ("To what extent do you think this treatment will be/was helpful to you?"). The expectation scale is applied once the treatment rationale has been explained. Its aim is to measure subjective patient expectations about this treatment. The opinion scale is administered when the patient has completed the treatment, and its aim is to assess satisfaction with this treatment. Our group has used this questionnaire in several research studies (Botella et al., 2009, 2007).

Interventions

Transdiagnostic Protocol (TP)

We developed a TP for the treatment of ED, adapted from the UP (Barlow et al., 2011) and some of the strategies for emotion regulation from dialectical behavior therapy (DBT; Linehan, 1993). All the strategies and techniques from the original protocols (UP) have been translated into Spanish, and the contents (e.g., clinical examples) adjusted for cultural differences. The addition of some strategies from DBT (i.e., mindfulness "what" and "how" skills) was considered important because emotion regulation difficulties have been shown to be a key transdiagnostic factor across distinct ED (Campbell-Sills, Barlow, Brown, & Hofmann, 2006; Cisler, Olatunji, Feldner, & Forsyth, 2010) and an important treatment target (Neacsiu, Eberle, Kramer, Wiesmann, & Linehan, 2014). The main

differences between the UP and the protocol developed for the present study (TP) are shown in Table 13.

The TP is a manualized, structured treatment protocol made up of 12 treatment modules with the general aim of regulating NA (Botella, GarcÍa- Palacios, Baños, 2012). These modules are usually administered in 12 to 15 weekly face-to-face sessions (maximum of 18) lasting 60 min. Modules 1 to 11 contain strategies for the regulation of NA with the following main therapeutic components from the UP: (a) present-focused emotional awareness, (b) cognitive flexibility, (c) emotion avoidance and emotion-driven behaviors (EDB), (d) awareness and tolerance of physical sensations, and (e) interoceptive and situation-based emotion exposure. Modules 1 to 11 are preceded by three modules (Module 1 is an introduction to treatment, Module 2 is focused on motivation enhancement, and Module 3 provides psychoeducation about emotions) and followed by a relapse prevention module (Module 12). The treatment protocol includes one patient handbook and one therapist handbook for each treatment session. In this condition, participants completed a mean of 13.25 sessions (SD = 0.75; range = 12-14). Modules 1 to 12 are described below:

Module 1. Introduction to treatment: Provides a framework about the role of emotion regulation in ED. A brief description of the program modules is also presented, as well as videos with examples of people suffering from different ED.

Module 2. Motivation for change and goal-setting: The aims are to analyze the advantages and disadvantages of changing, emphasize the importance of being motivated, and highlight the importance of establishing significant life goals.

Module 3. Understanding the role of emotions: Provides psychoeducation about the adaptive roles and functions of emotions and trains the patient in tracking of emotional experiences using the three-component model of emotions.

Module 4. Nonjudgmental emotional awareness and acceptance of emotional experiences: This module aims to train the patient in nonjudgmental emotional awareness (i.e., mindfulness “what” and “how” skills) and in the acceptance of emotional experiences and its importance in the treatment.

Module 5. Practicing present-focused awareness: The objective is to continue to learn about the acceptance of emotional experiences and increase awareness of physical sensations, thoughts, emotions, and daily activities.

Module 6. Learning to be flexible: It focuses on the importance of maladaptive ways of thinking (i.e., thinking traps) in the maintenance of ED, and on learning how to identify them.

Module 7. Practicing cognitive flexibility: This module aims to teach the patients how maladaptive ways of thinking can be modified (i.e., cognitive reappraisal). It also provides information about intrusive thoughts and how to deal with them.
Module 8. Emotional avoidance: This module aims to teach the patients to identify the emotion avoidance strategies that contribute to the maintenance of ED.
Module 9. EDB: The aim is for patients to learn the concept of EDB and replace their own maladaptive EDB with other more adaptive behaviors.
Module 10. Accepting and facing physical sensations: The objectives are to teach the patients the role of physical sensations in their emotional response and train them in interoceptive exposure, to increase tolerance and promote habituation to physical sensations.
Module 11. Facing emotions in the contexts in which they occur: The purpose is the construction of exposure hierarchies to help the patients begin to face the avoided situations that contribute to the maintenance of the problem.
Module 12. Relapse prevention: This module aims to review the strategies learned throughout the program, schedule the future practice of the learned strategies, and teach the patient how to identify and cope with future high-risk situations.

Table 23. Differences between the TP and the UP

TP	UP (Barlow et al., 2011)
M1. Introduction to treatment	M0. Introduction to treatment
M2. Motivation for change and goal setting	M1. Motivation engagement for treatment enhancement
M3. Understanding the role of emotions (psychoeducation about emotions and goal setting)	M2. Psychoeducation and tracking of emotional experiences
Component 1: Present-focused emotional awareness	**Component 1: Present-focused emotional awareness**
M4. Non-judgmental emotional awareness and acceptance of emotional experiences	M3. Emotion awareness training
M5. Practicing present-focused awareness: physical sensations, thoughts, emotions and daily activities	
Component 2: Cognitive Flexibility	**Component 2: Cognitive Flexibility**
M6. Learning to be flexible (identification of thinking traps)	M4. Cognitive Appraisal and Reappraisal
M7. Practicing cognitive flexibility (cognitive reappraisal and evaluation of intrusive thoughts)	
Component 3: Emotion avoidance and emotion-driven behaviors	**Component 3: Emotion avoidance and emotion-driven behaviors**
M8. Emotional avoidance	M5. Emotion avoidance and emotion-driven behaviors
M9. Emotion-driven behaviors	

Components 4 and 5: **Awareness and tolerance of physical sensations** **Interoceptive and situation-based emotion exposure**	**Components 4 and 5:** **Awareness and tolerance of physical sensations** **Interoceptive and situation-based emotion exposure**
M10. Accepting and facing physical sensations M11. Facing emotions in the contexts in which they occur M12. Relapse prevention	M6. Awareness and tolerance of physical sensations M7. Interoceptive and situation-based emotion exposures M8. Relapse prevention
Number of sessions: 12-18 Session duration: 60 minutes	Number of sessions: maximum of 18 Session duration: 50-60 minutes

Note: A full description of UP modules can be found in Barlow et al. (2011)

Transdiagnostic protocol + positive affectivity regulation component (TP + PA).

This intervention comprises 16 modules generally delivered in 16 to 19 treatment sessions (maximum of 22). As in the TP, this protocol also includes one patient handbook and one therapist handbook for each module. The structure of this protocol is as follows: (a) Modules 1 to 11 are the same modules as in the TP; (b) Modules 12 to 15 constitute a treatment component aimed at the regulation of PA (i.e., enhancement and maintenance of PA); (c) Module 16 is focused on relapse prevention. In this condition, participants completed a mean of 17.42 sessions (SD = 1.08; range = 16-19). Modules 12 to 15 (PA regulation component) are depicted below:

Module 12. Learning to move on. This module is focused on the role of behavioral activation, teaching the patient the importance of "moving on." Behavioral activation is trained using a diary of daily activities. To complete this diary, the patient is provided with monitoring sheets with a scale ranging from 0 to 10 to score both the level of satisfaction with the activities the patient is involved in during the day and to what extent they are linked to his or her personal goals and values. The practice of this exercise is intended to help the patient realize the positive relationship between meaningful activities and mood to promote behavioral activation (Lejuez et al., 2001).

Module 13. Learning to enjoy. This module consists of psychoeducation about the role of positive emotions in life and how to generate and maintain them (e.g., using savoring strategies; Bryant & Veroff, 2007). The strategies included in this module are consistent with Fredrickson's Broaden-and-Build Theory (Fredrickson, 2001), which highlights the effect of positive emotions in broadening intellectual, social, and physical resources. The module contains the following techniques:

- The importance of smiling. The week is divided into days when the patient has to smile as much as possible when interacting with other people and days when the patient has to act normally. The effects of “smiling days”/normal “no-smiling days” are discussed with the therapist in the following session.
- Savoring. The patient is asked to engage in everyday activities that he or she normally does fast and without paying attention in a slower and more mindful manner (e.g., eating, taking a shower, walking, or driving to work). The patient is then asked to think about how the slow, mindful way of doing these activities makes him or her feel compared with engaging in activities fast and unmindfully.
- Daily time of enjoyment. The patient is encouraged to engage in some pleasant activity on a daily basis (e.g., drinking a cup of coffee or tea, doing sports, listening to music, going for a walk, having a conversation). The patient is also asked to think about how he or she felt during the activity and whether he or she would repeat it again, change it, or add something new to it.

Module 14. Learning to live. This module is divided into two sections. The first section is focused on the importance of identifying the individual’s own psychological strengths. The patients are shown the list of strengths proposed by Peterson and Seligman (2004)—for example, curiosity, creativity, kindness, self-control, honesty, enthusiasm, equity, respect, gratitude—and asked to choose some of them and think about the ways to promote these strengths. The second section addresses the dimensions of well-being identified by Ryff (1995, 2014)—for example, purpose in life, autonomy, and personal growth. This section includes an exercise to help the patient select and perform meaningful activities linked to personal values (e.g., for the value “being a thoughtful friend”: “calling my friends once a week”/“catch up with a friend who I have not seen in a while”).

Module 15. Living and learning. One objective is to practice some exercises to promote emotions linked to well-being, such as gratitude (e.g., visit of gratitude, expressing gratitude; Seligman, Steen, Park, & Peterson, 2005), hope (using an exercise based on the best possible self; Sheldon & Lyubomirsky, 2006), and curiosity (encouraging the patient’s interest in different topics or activities). Another aim is to teach the patient to identify episodes of well-being and maintain them, using the strategy proposed by Fava (1999) in Well-Being Therapy, which consists of identifying thoughts and beliefs leading to the premature interruption of well-being. The patient is then asked to think about a more realistic way to interpret the situation to prolong the feelings of well-being as long as possible.

Therapists and Treatment Fidelity

The treatment protocols were administered by five different therapists working at the Emotional Disorders Clinic at Universitat Jaume I. All therapists but one delivered both protocols (TP and TP + PA). All of them were PhDs or PhD students with 3 to 5 years of experience in the diagnosis, psychological assessment, and application of CBT for several ED. To ensure treatment fidelity, both therapists and patients were provided with detailed manualized treatment protocols for each of the modules. In addition, therapists had been previously trained in the application of the treatment manuals, and they were supervised on a weekly basis by expert clinical psychologists, members of our research team who had been involved in the design and development of the treatment protocol.

Statistical Methods

All analyses were performed using the software SPSS Version 22.0. Descriptive statistics (means and standard deviations) were calculated for all measures. Two-way repeated-measures ANOVAs (time, treatment, Treatment x Time) were performed to explore the statistical significance of the differences within and between subjects on all measures. The magnitude of the intervention was expressed as Hedges's g , a variation of Cohen's d (J. Cohen, 1988) that corrects for biases due to small sample sizes (Hedges & Olkin, 1985) and a recommended effect size estimator when sample sizes are lower than 20 (Hunter & Schmidt, 2004). To interpret effect sizes, Cohen's d convention (J. Cohen, 1988) was used, according to which an effect size of 0.20 is considered small, 0.50 is considered moderate, and 0.80 and above is considered large. Confidence intervals were also calculated for each of the effect sizes.

Because the number of participants who dropped out from both groups is low (1 participant in each condition), only completer analyses were performed.

Results

Within- and Between-Group Changes in Primary and Secondary Outcomes

Means and standard deviations for both groups before and after the intervention and at the 3-month follow-up are displayed in Table 14.

Table 24. Descriptive statistics for all measures

	TP+PA			TP		
	Pre-T Mean (*SD*)	Post-T Mean (*SD*)	F/U Mean (*SD*)	Pre-T Mean (*SD*)	Post-T Mean (*SD*)	F/U Mean (*SD*)
OASIS	8.50 (3.99)	1.92 (2.43)	3.83 (5.04)	6.75 (3.79)	1.92 (2.11)	2.25 (1.82)
BDI-II	20.33 (11.13)	3.08 (4.30)	4.92 (6.71)	15.58 (10.14)	2.58 (1.93)	2.75 (2.60)
PANAS +	22.83 (7.72)	32.75 (7.11)	32.83 (7.66)	25.58 (7.51)	31.50 (7.82)	31.17 (5.54)
PANAS -	29.83 (8.10)	14.67 (7.39)	15.92 (7.39)	25.25 (7.28)	14.67 (3.99)	15.67(3.70)
QLI	5.10 (1.46)	7.21 (1.11)	7.40 (1.22)	5.84 (1.27)	7.67 (.94)	7.65 (.80)

Note. Pre-T: Pre-treatment; Post-T: Post-treatment; F/U: 3-month follow-up. TP+PA: Transdiagnostic Protocol + Positive Affect regulation component; TP: Transdiagnostic Protocol; OASIS: Overall Anxiety Severity and Impairment Scale; BDI-II: Beck Depression Inventory; PANAS +: Positive and Negative Affect Schedule – Positive Affect; PANAS -: Positive and Negative Affect Schedule – Negative Affect; QLI: Quality of Life Inventory

Within- and between-group effect sizes (Hedges's g), as well as confidence intervals, are displayed in

Table 15. In general, within-group effect sizes were large to very large for the OASIS, the BDI-II, and the QLI in both treatment groups. Regarding the PANAS-PA, within-group effect sizes were mainly large in both groups, with overall larger effect sizes in the TP + PA group than in the TP group at posttreatment and at the follow-up. However, the effect size for the TP group at posttreatment was in the moderate range ($g = -.77$). For the PANAS-NA, within-group effect sizes were all in the large range, with slightly larger effect sizes found in the TP + PA group than in the TP group at posttreatment and at the follow-up. Regarding comparisons between conditions (between-group effect sizes), a small effect size was observed at posttreatment and at the follow-up on all measures, including the PANAS-PA. To explore the statistical significance of the treatment gains and the differences between conditions, a two-way repeated-measures ANOVA was performed. The ANOVA showed a significant time effect on all measures: PANAS-PA: $F(1.72, 37.88) = 15.47$, $p < .001$, PANAS-NA: $F(1.54, 33.85) = 44.13$, $p < .001$, BDI-II: $F(1.22, 26.82) = 49.84$, $p < .001$, OASIS: $F(1.72, 37.91) = 23.25$, $p < .001$, and QLI: $F(1.57, 34.57) = 36.21$, $p < .001$. The participants significantly improved from pre- to posttreatment on all outcomes, and these improvements were maintained at the 3-month follow-up. Nevertheless, the analysis failed to find a significant interaction effect (Time x Group) on any of the measures ($p > .05$). Thus, no significant differences were found between the two groups.

Table 25. Within- and between-group effect sizes for all measures

	Within-group effect size, *g* [95% CI]				Between-group effect size, *g* [95% CI]	
	Pre-post		Pre-F/U		Post-T	F/U
	TP+PA	TP	TP+PA	TP		
OASIS	1.99	1.57	1.03	1.51	.00	.42
	[.96, 2.89]	[.61, 2.43]	[.14, 1.84]	[.56, 2.36]	[-.80, .80]	[-.41, 1.21]
BDI-II	2.04	1.78	1.66	1.73	.15	.43
	[1.00, 2.95]	[.78, 2.66]	[.68, 2.52]	[.74, 2.60]	[-.66, .95]	[-.40, 1.22]
PANAS +	-1.34	-.77	-1.30	-.85	.17	.25
	[-2.17, -.41]	[-1.57, .08]	[-2.13, -.38]	[-1.65, .02]	[-.64, .96]	[-.56, 1.04]
PANAS -	1.96	1.80	1.79	1.66	.00	.04
	[.93, 2.85]	[.80, 2.68]	[.79, 2.67]	[.93, 2.68]	[-.80, .80]	[-.76, .84]
QLI	-1.63	-1.64	-1.71	-1.71	-.45	-.24
	[-2.49, -.66]	[-2.50, -.66]	[-2.58, -.72]	[-2.57, -.72]	[-1.24, .38]	[-1.04, .57]

Note. Pre: Pre-treatment; Post: Post-treatment; F/U: 3-month follow-up. TP+PA: Transdiagnostic Protocol + Positive Affect regulation component; TP: Transdiagnostic Protocol; OASIS: Overall Anxiety Severity and Impairment Scale; BDI-II: Beck Depression Inventory; PANAS +: Positive and Negative Affect Schedule – Positive Affect; PANAS -: Positive and Negative Affect Schedule – Negative Affect; QLI: Quality of Life Inventory. Positive effect sizes denote a decrease in scores, negative effect sizes denote an increase.

Diagnostic Status

Results assessed by the MINI interview showed that seven participants (58%) in the TP + PA condition and eight participants in the TP condition (67%) no longer met the diagnostic criteria for any disorder at posttreatment. At the 3-month follow-up, eight participants in the TP + PA condition no longer met the diagnostic criteria for any ED (67%), whereas seven participants in the TP condition (58%) no longer met these criteria. A chi-square test did not reveal any statistical difference in the proportion of diagnosis-free participants at posttreatment and at follow-up.

Acceptability of the Treatment

Means and standard deviations for expectations and opinions about treatment are depicted in Table 16. In the TP + PA condition, results indicate that participants reported high scores on all the items measuring treatment expectations (scores between 7.83 and 8.58): logic of the treatment, satisfaction with the treatment, recommendation of the treatment to other people with similar problems, usefulness of the treatment for other psychological problems, and usefulness of the treatment for one's specific problem. After receiving the intervention, scores for treatment opinions improved compared with scores for treatment expectations (scores between 8.08 and 8.83). Overall, the results for expectations and opinions in the TP condition were higher than in the TP + PA condition, ranging between 8.83 and 9.17 for expectations, and between 8.58 and 9.67 for opinions. As indicated by a two-way repeated-measures ANOVA, no significant differences were found between the two groups on any of the items assessing expectations and opinions.

Table 26. Means and standard deviations for expectations and opinion of treatment

	TP+PA		**TP**	
	Expectations M (*SD*)	Opinion M (*SD*)	Expectations M (*SD*)	Opinion M (*SD*)
Treatment is logical	7.83 (1.80)	8.25 (1.82)	9.08 (.90)	9.42 (.67)
Satisfaction with the treatment	8.08 (1.73)	8.08 (2.23)	9.08 (.79)	9.50 (.67)
Recommend to others	8.58 (1.38)	8.83 (1.80)	9.00 (.95)	9.67 (.65)
Usefulness for other psychological problems	7.75 (1.06)	8.17 (1.70)	8.83 (1.03)	8.58 (.67)
Usefulness for one's specific problems	7.83 (1.70)	8.25 (1.66)	9.17 (.94)	9.42 (.79)

Note. Scale ranges from 0 to 10, with higher scores indicating greater satisfaction.

Discussion

The aim of the present study was to evaluate the feasibility, in terms of preliminary efficacy and acceptability, of a new transdiagnostic treatment protocol for ED that includes a specific therapeutic component to directly upregulate PA. To do so, two versions of the same protocol were developed and tested in a randomized pilot study. One treatment protocol includes strategies that focus on the regulation of NA alone (TP), and the other protocol adds these strategies to a treatment component to upregulate PA (TP + PA). To the best of our knowledge, this is the first study to empirically investigate a TP for ED that integrates a specific component to directly upregulate PA.

One aim was to assess the effect of both interventions on a set of clinical measures. Overall, the analyses showed that both interventions resulted in significant improvements in all measures at posttreatment, and that the clinical gains were maintained at the 3-month follow-up. Both interventions were effective in reducing depression and anxiety, and these gains were maintained at the follow-up assessment. In addition, both treatment protocols led to significant improvements in quality of life at posttreatment and at the 3-month follow-up. However, the analyses did not reveal any significant differences between groups on any of the scales.

We were also interested in studying the differential effects of the two interventions on PA. The first hypothesis was that the TP + PA would lead to significantly higher PA outcomes than the TP. The effect sizes for PA were larger in the TP + PA group than in the TP group at posttreatment (g = 1.34 vs. g = 0.77) and at the 3-month follow-up (g = 1.30 vs. g = 0.85). Although not significant, these findings suggest that the inclusion of a treatment component to upregulate positive affectivity might be important in enhancing PA outcomes. This component has already been empirically tested in a randomized controlled trial (RCT) exploring the efficacy of a web-based intervention for depression (Mira et al., 2017). As in the present study, this RCT examined an intervention that combined CBT techniques (i.e., psychoeducation about emotions, cognitive restructuring, behavioral activation) and PPIs, reporting significant improvements in NA and PA compared with a waitlist control group. Although there is a body of literature on PPIs, it is difficult to relate the results of this study to those of previous meta-analyses (e.g., Bolier et al., 2013; Sin & Lyubomirsky, 2009; Weiss et al., 2016) of these types of interventions, mainly because these meta-analyses utilized well-being as the main outcome measure, rather than PA. Furthermore, the samples included in the aforementioned meta-analyses are rather heterogeneous, making the comparisons between this study and previous research on PPIs even more difficult. In any case, the treatment approach followed in the present work is consistent with recommendations about the

importance of well-being and positive emotional functioning (Fava, 2016; Hasler, 2016) and the need for further research on these interventions. Finally, although the main focus of this study was on PA, future research should study whether adding treatment components designed to upregulate PA to transdiagnostic treatments for ED may result in better NA outcomes, compared with treatments where these components are absent. In any case, these results should be interpreted considering the pilot nature of this study.

Regarding diagnostic status, the number of patients who met the diagnostic criteria for a principal disorder decreased at posttreatment, and this proportion was maintained at the 3-month follow-up. There were no significant differences between groups in the number of participants who no longer met the diagnostic criteria for any disorder after the treatment, and these changes were maintained at the follow-up.

Another objective was to explore the participants' acceptability of the intervention. Results showed that participants in both groups had high expectations about the treatment protocol before receiving it. Moreover, after receiving the intervention, scores on their opinions improved compared with scores for treatment expectations. Attrition rate was low in both groups (one patient dropped out in each group), which also suggests the feasibility of this intervention for a sample of patients with ED. Taken together, the results support the acceptability of both interventions. Although the acceptability of the PA regulation component was not specifically assessed in this study, the results for adherence and acceptability are consistent with those found by Mira et al. (2017) for a web-based intervention for depression that also included the same component based on PPIs.

In summary, these results suggest that both interventions were equally effective for the treatment of several ED. Moreover, acceptability did not differ significantly between conditions, suggesting that both interventions were similarly accepted by participants. The main strength of this study is the inclusion of a treatment component that directly addresses PA regulation (i.e., by increasing and maintaining PA). This protocol differs from other transdiagnostic treatments in that it addresses the regulation of PA in a more direct way, whereas other transdiagnostic treatments only integrate treatment strategies essentially aimed to downregulate NA (e.g., Ellard et al., 2010; Norton, 2012; Titov, Andrews, Johnston, Robinson, & Spence, 2010; Titov et al., 2011). Previous research has proposed some directions to address both the assessment and treatment of PA regulation from a transdiagnostic perspective (e.g., Carl, Fairholme, Gallagher, Thompson-Hollands, & Barlow, 2014; Carl et al., 2013), but this field is quite new, and more research is needed on this topic. Questions remain about the specific contribution of treatment components aimed at PA

regulation in TPs: what the most effective strategies are; in what proportion; how and when each treatment component (regulation of PA and regulation of NA) should be present in TPs; who this treatment approach might benefit the most (e.g., depression vs. anxiety disorders); and what the incremental effect of these strategies is on other relevant treatment outcomes such as anxious and depressive symptomatology and quality of life.

This study has limitations that bear mention. First, it is a pilot study with a low number of participants and no waiting list control group. Second, the high effect sizes observed in this study must be interpreted in light of the nonsignificant confidence intervals shown at most measurement points. Third, this study does not allow us to separate the effects of the NA and PA regulation components. Improvements in PA might be partly due to a carryover effect, as participants underwent the PA regulation sessions (Sessions 12-15) after 11 sessions of NA regulation (Sessions 1-11), which makes it difficult to draw conclusions about the specific contribution of each of these treatment components. Fourth, although we assessed the effect of the intervention on both PA and NA, we did not include any measure focused on the underlying emotion regulation mechanisms that are hypothesized to be responsible for these changes. Five, most of the therapists involved in the study delivered both versions of the treatment (TP and TP + PA) and were not blind to the treatment conditions. Finally, the addition of a treatment component to one of the treatments tested in this study (TP + PA) resulted in a treatment with more sessions in one condition than in the other. For these reasons, future research should focus on exploring to what extent each of the different treatment components accounts for the improvement in measures of PA and NA and other clinical measures. One possible strategy to do so is conducting dismantling studies. Our research group is currently conducting a dismantling study to explore the specific contribution of different therapeutic components in the treatment of depression: a protocol that combines different components (i.e., CBT and PPIs), a protocol based on behavioral activation only, and a protocol based on PPIs only (the study protocol is available in https://clinicaltrials.gov/show/NCT03159715).

In conclusion, this study represents an attempt to contribute to the existing gap in transdiagnostic treatments for ED by adding a treatment component that more directly addresses the regulation of PA. Preliminary efficacy and acceptability results indicate that both interventions are feasible to be tested in a larger RCT. Although we were unable to find a significant difference in PA due to the impact of the PA regulation component, the results found in this study suggest the potential impact that including treatment components to directly target PA regulation may have on this temperament dimension.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Funding for the study was provided by a PhD grant from the Spanish Ministerio de Educaci.n, Cultura y Deporte (FPU13/00576) and a grant from the Ministerio de Econom.a y Competitividad (PSI2014-54172-R).

References

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: APA.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: APA.

Antony, M. M., & Stein, M. B. (Eds.). (2009). *Oxford handbook of anxiety and related disorders*. New York, NY: Oxford University Press.

Barlow, D. H. (2002). *Anxiety and its disorders: The nature and treatment of anxiety and panic* (2nd ed.). New York, NY: Guilford Press.

Barlow, D. H., Allen, L. B., & Choate, M. L. (2004). Toward a unified treatment for emotional disorders. *Behavior Therapy*, *35*, 205-230. doi:10.1016/j.beth.2016.11.005

Barlow, D. H., Farchione, T. J., Fairholme, C. P., Ellard, K. K., Boisseau, C. L., Allen, L. B., & Ehrenreich-May, J. (2011). *The unified protocol for transdiagnostic treatment of emotional disorders: Therapist guide.* New York, NY: Oxford University Press.

Barlow, D. H., Sauer-Zavala, S., Carl, J. R., Bullis, J. R., & Ellard, K. K. (2013). The nature, diagnosis, and treatment of neuroticism: Back to the future. *Clinical Psychological Science*, *2*, 344-365.

Beck, A. T., Steer, R. A., & Brown, G. K. (1990). *Manual for the Beck Depression Inventory–II.* San Antonio, TX: Psychological Corporation.

Berger, T., Boettcher, J., & Caspar, F. (2013). Internet-based guided self-help for several anxiety disorders: A randomized controlled trial comparing a tailored with a standardized disorder-specific approach. *Psychotherapy*, *51*, 207-219. doi:10.1037/a0032527

Bolier, L., Haverman, M., Westerhof, G. J., Riper, H., Smit, F., & Bohlmeijer, E. (2013). Positive psychology interventions: A meta-analysis of randomized controlled studies. *BMC Public Health*, *13*(1), Article 119. doi:10.1186/1471-2458-13-119

Borkovec, T. D., & Nau, S. D. (1972). Credibility of analogue therapy rationales. *Journal of Behavior Therapy and Experimental Psychiatry*, *3*, 257-260. doi:10.1016/0005-7916(72)90045-6

Botella, C., Gallego, M. J., García-Palacios, A., Baños, R. M., Quero, S., & Alcañiz, M. (2009). The acceptability of an Internet-based self-help treatment for fear of public speaking. *British Journal of Guidance & Counselling*, *37*, 297-311. doi:10.1080/03069880902957023

Botella, C., García-Palacios, A., Villa, H., Baños, R. M., Quero, S., Alcañiz, M., & Riva, G. (2007). Virtual reality exposure in the treatment of panic disorder and agoraphobia: A controlled study. *Clinical Psychology & Psychotherapy*, *14*, 164-175. doi:10.1002/cpp.524

Botella, C., García-Palacios, A., Quero, S., & Baños, R. (2012). *A Transdiagnostic Treatment for Emotion Disorders: Manualized Treatment Protocol.* Unpublished manuscript.

Brown, T. A., & Barlow, D. (2009). A proposal for a dimensional classification system based on the shared features of the DSM-IV anxiety and mood disorders: Implications for assessment. *Psychological Assessmen*t, *21*, 256-271. doi:10.1037/a0016608

Brown, T. A., Chorpita, B. F., & Barlow, D. H. (1998). Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. *Journal of Abnormal Psychology*, *107*, 179-192. doi:10.1037/0021-843X.107.2.179

Bryant, F. B., & Veroff, J. (2007). *Savoring: A new model of positive experience.* Mahwah, NJ: Erlbaum.

Campbell-Sills, L., Barlow, D. H., Brown, T. A., & Hofmann, S. G. (2006). Acceptability and suppression of negative emotion in anxiety and mood disorders. *Emotion*, *6*, 587-595. doi:10.1037/1528-3542.6.4.587

Carl, J. R., Fairholme, C. P., Gallagher, M. W., Thompson-Hollands, J., & Barlow, D. H. (2014). The effects of anxiety and depressive symptoms on daily positive emotion regulation. *Journal of*

Psychopathology and Behavioral Assessment, *36*, 224-236. doi:10.1007/s10862-013-9387-9

Carl, J. R., Soskin, D. P., Kerns, C., & Barlow, D. H. (2013). Positive emotion regulation in emotional disorders: A theoretical review. *Clinical Psychology Review*, *33*, 343-360. doi:10.1016/j.cpr.2013.01.003

Cisler, J. M., Olatunji, B. O., Feldner, M. T., & Forsyth, J. P. (2010). Emotion regulation and the anxiety disorders: An integrative review. *Journal of Psychopathology and Behavioral Assessment*, *32*, 68-82. doi:10.1007/s10862-009-9161-1

Clark, D. A., & Taylor, S. (2009). The transdiagnostic perspective on cognitive-behavioral therapy for anxiety and depression: New wine for old wineskins? *Journal of Cognitive Psychotherapy*, *23*(1), 60-66. doi:10.1891/0889-8391.23.1.60

Clark, L. A., & Watson, D. (1991). Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications. *Journal of Abnormal Psychology*, *100*, 316-336. doi:10.1037/0021-843X.100.3.316

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale, NJ: Erlbaum.

Cohen, S., & Pressman, S. D. (2006). Positive affect and health. *Current Directions in Psychological Science*, *15*, 122-125.

Cuijpers, P., Smit, F., Bohlmeijer, E., Hollon, E. D., & Andersson, G. (2010). Efficacy of cognitive-behavioural therapy and other psychological treatments for adult depression: Meta-analytic study of publication bias. *British Journal of Psychiatry*, *196*, 173-178. doi:10.1192/bjp.bp.109.066001

Dunn, B. D. (2012). Helping depressed clients reconnect to positive emotion experience: Current insights and future directions. *Clinical Psychology & Psychotherapy*, *19*, 326-340. doi:10.1002/cpp.1799

Ellard, K. K., Fairholme, C. P., Boisseau, C. L., Farchione, T. J., & Barlow, D. H. (2010). Unified protocol for the transdiagnostic treatment of emotional disorders: Protocol development and initial outcome data. *Cognitive and Behavioral Practice*, *17*, 88-101. doi:10.1016/j.cbpra.2009.06.002

Fava, G. A. (1999). Well-being therapy: Conceptual and technical issues. *Psychotherapy and Psychosomatics*, *68*, 171-178. doi:10.1159/000012329

Fava, G. A. (2016). Well-being therapy: Current indications and emerging perspectives. *Psychotherapy and Psychosomatics*, *85*, 136-145. doi:10.1159/000444114

Ferrando, L., Bobes, J., Gibert, J., & Lecrubier, Y. (1997). Mini international neuropsychiatric interview. In J. Bobes, M. Bousoño, & M. P. González (Eds.), *Manejo De Los Trastornos Mentales Y Del Comportamiento En Atención Primaria* (2nd ed.) (p. 9). Oviedo, Spain: Gofer.

Fredrickson, B. L. (2001). The role of positive emotions in positive psychology: The broaden-and-build theory of positive emotions. *American Psychologist Association*, *56*, 218-226. doi:10.1037/0003-066X.56.3.218

Gilbert, K. E. (2012). The neglected role of positive emotion in adolescent psychopathology. *Clinical Psychology Review*, *32*, 467-481. doi:10.1016/j.cpr.2012.05.005

Gilbert, K. E., Nolen-Hoeksema, S., & Gruber, J. (2013). Positive emotion dysregulation across mood disorders: How amplifying versus dampening predicts emotional reactivity and illness course. *Behaviour Research and Therapy*, *51*, 736-741. doi:10.1016/j.brat.2013.08.004

Gross, J. J. (1998). The emerging field of emotion regulation: An integrative review. *Review of General Psychology*, *2*, 271-299. doi:10.1037/1089-2680.2.3.271

Hasler, G. (2016). Well-being: An important concept for psychotherapy and psychiatric neuroscience. *Psychotherapy and Psychosomatics*, *85*, 255-261. doi:10.1159/000447268

Hedges, L. V., & Olkin, I. (1985). *Statistical methods for meta-analysis*. Orlando, FL: Academic Press.

Hofmann, S. G., Sawyer, A. T., Fang, A., & Asnaani, A. (2012). Emotion dysregulation model of mood and anxiety disorders. *Depression and Anxiety*, *29*, 409-416. doi:10.1002/da.21888

Hollon, S. D., & Ponniah, K. (2010). A review of empirically supported psychological therapies for mood disorders in adults. *Depression and Anxiety*, *27*, 891-932. doi:10.1002/da.20741

Hunter, J. E., & Schmidt, F. L. (2004). *Methods of meta-analysis* (2nd ed.). Thousand Oaks, CA: SAGE.

Kazdin, A. E., & Blase, S. L. (2011). Rebooting psychotherapy research and practice to reduce the burden of mental illness. *Perspectives on Psychological Science*, *6*, 21-37. doi:10.1177/1745691610393527

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Archives of General Psychiatry*, *62*, 593-602. doi:10.1001/archpsyc.62.6.593

Kotov, R., G.mez, W., Schmidt, F., & Watson, D. (2010). Linking “big” personality traits to anxiety, depressive, and substance use disorders: A meta-analysis. *Psychological Bulletin*, *136*, 768-821. doi:10.1037/a0020327

Lejuez, C. W., Hopko, D. R., & Hopko, S. D. (2001). A brief behavioral activation treatment for depression: Treatment manual. *Behavior Modification*, *25*, 225-286. doi:10.1177/0145445501252005

Lewinsohn, P. M. (1974). A behavioral approach to depression. In R. J. Friedman & M. M. Katz (Eds.), *Psychology of depression: Contemporary theory and research* (pp. 157-178). Oxford, UK: John Wiley.

Linehan, M. M. (1993). *Skills training manual for treating borderline personality disorder. Diagnosis and treatment of mental disorders.* New York, NY: Guilford Press.

Livingstone, K. M., & Srivastava, S. (2012). Up-regulating positive emotions in everyday life: Strategies, individual differences, and associations with positive emotion and well-being. *Journal of Research in Personality*, *46*, 504-516. doi:10.1016/j.jrp.2012.05.009

Mazzucchelli, T. G., Kane, R. T., & Rees, C. S. (2009). Behavioral activation treatments for depression in adults: A meta-analysis and review. *Clinical Psychology: Science and Practice*, *16*, 383-411. doi:10.1111/j.1468-2850.2009.01178.x

Mazzucchelli, T. G., Kane, R. T., & Rees, C. S. (2010). Behavioral activation interventions for well-being: A meta-analysis. *The Journal of Positive Psychology*, *5*, 105-121. doi:10.1080/17439760903569154

McKay, D., Sookman, D., Neziroglu, F., Wilhelm, S., Stein, D. J., Kyrios, M., . . .Veale, D. (2015). Efficacy of cognitive-behavioral therapy for obsessive- compulsive disorder. *Psychiatry Research*, *225*, 236-246. doi:10.1016/j.psychres.2015.02.004

McLean, C. P., Asnaani, A., Litz, B. T., & Hofmann, S. G. (2011). Gender differences in anxiety disorders: Prevalence, course of illness, comorbidity and burden of illness. *Journal of Psychiatric Research*, *45*, 1027-1035. doi:10.1016/j.jpsychires.2011.03.006

Mezzich, J. E., Cohen, N. L., & Ruiperez, M. A. (1996). *A Quality of Life Index: Brief description and validation.* Paper presented at the International Congress of the International Federation for Psychiatric Epidemiology. Santiago de Compostela, Spain.

Mezzich, J. E., Ruipérez, M. A., Pérez, C., Yoon, G., Liu, J., & Mahmud, S. (2000). The Spanish version of the Quality of Life Index: Presentation and validation. *The Journal of Nervous and Mental Disease*, *188*, 301-305. doi:10.1097/00005053-200005000-00008

Mira, A., Bretón-López, J., García-Palacios, A., Quero, S., Baños, R. M., & Botella, C. (2017). An internet-based program for depressive symptoms using human and automated support: A randomized controlled trial. *Neuropsychiatric Disease and Treatment*, *13*, 987-1006. doi:10.2147/NDT.S130994

Mira, A., González, A., Botella, C., Bretón-López, J., García-Palacios, A., Riera, A., & Baños, R. M. (2015, November). *Psychometric properties of the Overall Anxiety Severity and Impairment Scale in Spanish sample: Clinical and general populations.* Poster Presented at the 49th Annual ABCT Convention, Chicago, IL.

Nathan, P. E., & Gorman, J. M. (2007). *A guide to treatments that work (3rd ed.)*. New York, NY: Oxford University Press.

Neacsiu, A. D., Eberle, J. W., Kramer, R., Wiesmann, T., & Linehan, M. M. (2014). Dialectical behavior therapy skills for transdiagnostic emotion dysregulation: A pilot randomized controlled trial. *Behaviour Research and Therapy*, *5*, 940-951.

Newby, J. M., McKinnon, A., Kuyken, W., Gilbody, S., & Dalgleish, T. (2015). Systematic review and meta-analysis of transdiagnostic psychological treatments for anxiety and depressive disorders in adulthood. *Clinical Psychology Review*, *40*, 91-110. doi:10.1016/j.cpr.2015.06.002

Norman, S. B., Campbell-Sills, L., Hitchcock, C., a Sullivan, S., Rochlin, A., Wilkins, K. C., & Stein, M. B. (2011). Psychometrics of a brief measure of anxiety to detect severity and impairment: The Overall Anxiety Severity and Impairment Scale (OASIS). *Journal of Psychiatric Research*, *45*, 262-268. doi:10.1016/j.jpsychires.2010.06.011

Norton, P. (2012). A randomized clinical trial of transdiagnostic cognitive-behavioral treatments for anxiety disorder by comparison to relaxation training. *Behavior Therapy*, *43*, 506-517. doi:10.1016/j.beth.2010.08.011

Olatunji, B. O., Cisler, J. M., & Deacon, B. J. (2010). Efficacy of cognitive behavioral therapy for anxiety disorders: A review of meta-analytic findings. *Psychiatric Clinics of North America*, *33*, 557-577. doi:10.1016/j.psc.2010.04.002

Păsărelu, C. R., Andersson, G., Nordgren, L. B., & Dobrean, A. (2016). Internetdelivered transdiagnostic and tailored cognitive behavioral therapy for anxiety and depression: A systematic review and meta-analysis of randomized controlled trials. *Cognitive Behaviour Therapy*, *46*, 1-28. doi:10.1080/16506073.2016.1231219

Peterson, C., & Seligman, E. P. (2004). *Character strengths and virtues: A handbook and classification*. Oxford, UK: Oxford University Press.

Pressman, S. D., & Cohen, S. (2005). Does positive affect influence health? *Psychological Bulletin*, *131*, 925-971. doi:10.1037/0033-2909.131.6.925

Quoidbach, J., Berry, E. V., Hansenne, M., & Mikolajczak, M. (2010). Positive emotion regulation and well-being: Comparing the impact of eight savoring and dampening strategies. *Personality and Individual Differences*, *49*, 368-373. doi:10.1016/j.paid.2010.03.048

Reinholt, N., & Krogh, J. (2014). Efficacy of transdiagnostic cognitive behaviour therapy for anxiety disorders: A systematic review and meta-analysis of published outcome studies. *Cognitive Behaviour Therapy*, *43*, 171-184. doi:10.1080/16506073.2014.897367

Rosellini, A. J., Lawrence, A. E., Meyer, J. F., & Brown, T. A. (2010). The effects of extraverted temperament on agoraphobia in panic disorder. *Journal of Abnormal Psychology*, *119*, 420-426. doi:10.1037/a0018614

Ryff, C. D. (1995). The structure of psychological well-being revisited. *Journal of Personality and Social Psychology*, *69*, 719-727. doi:10.1037/0022-3514.69.4.719

Ryff, C. D. (2014). Psychological well-being revisited: Advances in the science and practice of eudaimonia. *Psychotherapy and Psychosomatics*, *83*, 10-28. doi:10.1159/000353263

Sandín, B., Chorot, P., Lostao, L., Joiner, T. E., Santed, M. A., & Valiente, R. M. (1999). Escalas Panas de afecto positivo y negativo: Validación factorial y convergencia transcultural [Positive and Negative Affect Schedule: Factorial Validity and Cross-cultural Convergence]. *Psicothema*, *11*, 37-51.

Sanz, J., Navarro, M. E., & Vázquez, C. (2003). Adaptación española del Inventario para la Depresión de Beck II (BDI-II): 1. Propiedades psicométricas en estudiantes universitarios [Spanish Adaptation of

the Beck Depression Inventory II (BDI-II): Psychometric Properties in University Students]. *Análisis Y Modificación De Conducta*, *29*(124), 239-288.

Schueller, S. M., Kashdan, T. B., & Parks, A. C. (2014). Synthesizing positive psychological interventions: Suggestions for conducting and interpreting meta-analyses. *International Journal of Wellbeing*, *4*(1), 91-98. doi:10.5502/ijw.v4i1.5

Schueller, S. M., & Parks, A. C. (2014). The science of self-help: Translating positive psychology research into increased individual happiness. *European Psychologist*, *19*, 145-155. doi:10.1027/1016-9040/a000181

Seligman, M. E., Steen, T. A., Park, N., & Peterson, C. (2005). Positive psychology progress: Empirical validation of interventions. *American Psychologist*, *60*, 410-421. doi:10.1037/0003-066X.60.5.410

Shankman, S. A., Nelson, B. D., Harrow, M., & Faull, R. (2011). Does physical anhedonia play a role in depression? A 20-year longitudinal study. *Journal of Affective Disorders*, *120*, 170-176. doi:10.1016/j.jad.2009.05.002

Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., . . . Dumbar, G. C. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry*, *59*, 34-57.

Sheldon, K. M., & Lyubomirsky, S. (2006). How to increase and sustain positive emotion: The effects of expressing gratitude and visualizing best possible selves. *The Journal of Positive Psychology*, *1*, 73-82. doi:10.1080/17439760500510676

Sin, N. L., & Lyubomirsky, S. (2009). Enhancing well-being and alleviating depressive symptoms with positive psychology interventions: A practice-friendly metaanalysis. *Journal of Clinical Psychology*, *65*, 467-487. doi:10.1002/jclp.20593

Taylor, C. T., Lyubomirsky, S., & Stein, M. B. (2017). Upregulating the positive affect system in anxiety and depression: Outcomes of a positive activity intervention. *Depression and Anxiety*, *34*, 267-280. doi:10.1002/da.22593

Titov, N., Andrews, G., Johnston, L., Robinson, E., & Spence, J. (2010). Transdiagnostic Internet treatment for anxiety disorders: A randomized controlled trial. *Behaviour Research and Therapy*, *48*, 890-899. doi:10.1016/j.brat.2010.05.014

Titov, N., Dear, B. F., Schwencke, G., Andrews, G., Johnston, L., Craske, M. G., & McEvoy, P. (2011). Transdiagnostic internet treatment for anxiety and depression: A randomised controlled trial. *Behaviour Research and Therapy*, *49*, 441-452. doi:10.1016/j.brat.2011.03.007

Tugade, M. M., & Fredrickson, B. L. (2007). Regulation of positive emotions: Emotion regulation strategies that promote resilience. *Journal of Happiness Studies*, *8*, 311-333. doi:10.1007/s10902-006-9015-4

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology*, *54*, 1063-1070. doi:10.1037/0022-3514.54.6.1063

Weiss, L. A., Westerhof, G. J., & Bohlmeijer, E. T. (2016). Can we increase psychological well-being? The effects of interventions on psychological wellbeing: A meta-analysis of randomized controlled trials. *PLoS ONE*, *11*(6), 1-16. doi:10.1371/journal.pone.0158092

Werner-Seidler, A., Banks, R., Dunn, B. D., & Moulds, M. L. (2013). An investigation of the relationship between positive affect regulation and depression. *Behaviour Research and Therapy*, *51*, 46-56. doi:10.1016/j.brat.2012.11.001

Wittchen, H. U., Jacobi, F., Rehm, J., Gustavsson, A., Svensson, M., J.nsson, B., . . . Steinhausen, H. C. (2010). The size and burden of mental disorders and other disorders of the brain in Europe. *European Neuropsychopharmacology*, *21*, 655-679. doi:10.1016/j.euroneuro.2011.07.018

Wood, A. M., & Joseph, S. (2010). The absence of positive psychological (eudemonic) well-being as a risk factor for depression: A ten year cohort study. *Journal of Affective Disorders*, *122*, 213-217. doi:10.1016/j.jad.2009.06.032

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Chapter 8. General Discussion

General discussion

To date, most transdiagnostic Internet-delivered treatments have been conducted in community and primary care settings, with no studies of this kind carried out in public specialized mental health care (González-Robles et al., 2018). Based on the advantages of both the transdiagnostic approach (e.g. lower costs, better management of comorbidity) and Internet-delivered formats (e.g. increased reach of evidence-based treatments), we decided to conduct a randomized controlled trial (RCT) to test the effectiveness of a transdiagnostic Internet-delivered protocol (EmotionRegulation) designed to address a wide range of anxiety and depressive disorders in this particular setting. Therefore, the principal aim of the current doctoral thesis was to develop a transdiagnostic Internet-based protocol for emotional disorders to be tested in public specialized mental health care, compared to treatment as usual (TAU), using an RCT design. The RCT protocol was first registered at Clinicaltrials.gov (NCT02345668). The details about the study protocol were published, and then the RCT was conducted and the results analyzed. In addition, a number of secondary studies were conducted in relation to the RCT. First, a systematic review was carried out to summarize the state-of-the-art with regard to transdiagnostic treatments for emotional disorders. More specifically, the review sought to answer how the assessment of comorbidity is approached in published transdiagnostic protocols for emotional disorders, and what the most commonly targeted specific diagnoses are in these interventions. Second, the psychometric properties of the online versions of the Overall Anxiety Severity and Impairment Scale (OASIS) and the Overall Depression Severity and Impairment Scale (ODSIS) were analyzed in Spanish clinical samples with anxiety and depressive disorders. The Spanish validation of these scales allowed us to include them in the RCT in order to evaluate the progress (or stagnation) of each patient module by module, throughout the entire treatment process. Finally, given the importance of promoting protective factors such as positive affectivity to improve mental health, a randomized pilot study was conducted to study the utility of adding treatment modules for the regulation of positive affectivity to a transdiagnostic protocol with traditional components for the regulation of negative affectivity.

In the following sections, a general discussion is presented, structured as follows. First, a brief summary of the most important findings and implications of each study are presented. Next, the main strengths and limitations of the studies are discussed. The last section is devoted to discussing future directions and recommendations for research.

Principal findings

1) ***What is the state-of-the-art of transdiagnostic treatments for emotional disorders with regard to the assessment of comorbidity, and what are the most commonly targeted diagnoses in these interventions?***

Research has systematically shown that high rates of comorbidity are the rule rather than the exception in anxiety and depressive disorders (e.g. Brown & Barlow, 2009; Kessler et al., 2005a, 2005b). Furthermore, individuals with comorbidity usually exhibit greater severity, chronicity, and disability than individuals with no comorbid disorders (Hofmeijer-Sevink et al., 2012; Rapaport, Clary, Fayyad, & Endicott, 2005). Unlike disorder-specific protocols, each of which is designed to treat symptom-specific variations of particular disorders, transdiagnostic treatments focus on their commonalities, and so they may be a more optimal solution for the treatment of comorbid presentations. Moreover, because the number of transdiagnostic treatments has grown considerably in the past 15 years, we thought there would be enough studies to synthesize the trends in the research regarding the most commonly targeted diagnoses in these interventions. With these ideas in mind, a systematic review was conducted with the following objectives: a) to analyze whether treatment response in comorbid disorders is evaluated in transdiagnostic treatments for emotional disorders; b) to explore what diagnoses are targeted in transdiagnostic treatments for emotional disorders; and c) to explore what the real distribution of the diagnoses is at baseline in these treatments. Regarding the assessment of comorbidity, the results showed that the assessment of the clinical change in comorbidity was not typically performed in transdiagnostic treatments, with only 40% of the studies conducting assessments of the comorbid disorders. Regarding the distribution of diagnoses, the most significant finding was that the most commonly targeted diagnoses in these treatments were GAD, PD/AG, SAD, and depression, and that other diagnoses such as PTSD, OCD, and Anxiety NOS were marginally included in these studies. On the other hand, this review also analyzed both the settings and delivery formats, and the comparison groups of these studies. We concluded that most transdiagnostic treatments to date have been conducted in the community and in an individual format. Regarding the delivery format, 27 out of 52 studies (52%) were Internet- or computerized-delivered treatments. Finally, only 8 of the 52 studies (15%) used disorder-specific protocols as comparison groups, which highlights the gap in the relative efficacy of transdiagnostic treatments compared to disorder-specific treatments. Although transdiagnostic treatments have been shown to be effective

when compared to control groups, these results led us to conclude that studies comparing these two treatment approaches are particularly necessary, especially because transdiagnostic treatments offer a number of advantages in terms of dissemination and implementation (e.g. lower training costs) that could make them superior to disorder-specific treatments for practical purposes.

2) ***What are the psychometric properties of two brief scales for the assessment of the severity and impairment associated with anxiety and depression?***

The psychometric properties of two brief scales for the assessment of the severity and impairment associated with anxiety and depression were analyzed in Chapters 4 and 5. The first study focused on the OASIS, whereas the second addressed the ODSIS. For these studies, the psychometric properties of the online versions were analyzed. Therefore, contributions to the literature about the online versions of these instruments were made through these studies. As far as we know, only two prior studies have analyzed the psychometrics of both instruments using online surveys (Ito et al., 2015a, 2015b). However, unlike in the studies by Ito et al., which relied on patients' self-reports to establish a formal diagnosis, in our study the diagnoses were performed more rigorously, using a structured diagnostic interview. Overall, both instruments demonstrated adequate psychometric properties in Spanish patients with emotional disorders, with good to excellent reliability and evidence found for both convergent and divergent validity. Moreover, the unidimensional factor structure reported in previous validations of these studies (e.g. Bentley et al., 2014; Campbell-Sills et al., 2009; Norman et al., 2006) was confirmed in both studies using Confirmatory Factor Analysis. In addition, cutoff scores were obtained for both scales, indicating that they may be used as screening instruments. Finally, evidence for sensitivity to change was shown for the OASIS. These characteristics, along with their brevity and transdiagnostic nature, make these scales particularly well-suited instruments for testing psychological or psychiatric interventions or collecting data in large-scale research (e.g. epidemiological studies) across anxiety and depressive disorders.

3) ***What was the effectiveness and acceptability of EmotionRegulation compared to TAU in public specialized mental health care?***

Chapters 3 and 6 presented the study protocol and the results of an RCT comparing a transdiagnostic Internet-based protocol (EmotionRegulation) to TAU in specialized mental health care. The results revealed that EmotionRegulation was more effective than TAU in reducing anxiety and depression, and in improving health-related quality of life. These findings have implications for both research and clinical practice. Regarding research, this study demonstrated that a transdiagnostic Internet-delivered CBT protocol can effectively be deployed in specialized care. With regard to clinical practice, the results showed that a transdiagnostic Internet-delivered protocol was more effective than TAU, which in our country is currently the best treatment alternative that patients can expect from the national public care system. Moreover, high scores on expectations and opinions were observed among participants, which indicated the acceptability of EmotionRegulation for participants. Although some methodological issues arose (e.g. rather than 200, 178 participants were recruited and, therefore, some of the results were underpowered), taken together, the results of this RCT were very promising and encourage us to keep exploring the potential of transdiagnostic Internet-based interventions in this specific setting. On the other hand, because no inferences about the effectiveness of EmotionRegulation on disorder-specific measures (e.g. OCI-R for OCD symptoms, SIAS for social anxiety symptoms, etc.) can be drawn, more research with adequate levels of statistical power is needed to study the effectiveness of this type of therapy, compared to disorder-specific CBT, for each of the anxiety and depressive disorders. Likewise, the lack of research testing transdiagnostic Internet-delivered protocols in public specialized mental health care warrants the study of predictors and moderators of treatment outcomes in this specific population.

4) ***What is the feasibility of including treatment modules for the regulation of positive affectivity in a transdiagnostic protocol for emotional disorders?***

Most research on transdiagnostic treatments to date has focused on alleviating the deficit and psychopathological factors, with little attention paid to the promotion of positive protective factors. For these reasons, in Chapter 7 we addressed a randomized pilot study aimed at analyzing the feasibility, in terms of differential efficacy and acceptability, of a transdiagnostic protocol with a treatment component for the regulation of

positive affectivity (TP+PA). This treatment was compared to a transdiagnostic protocol that only included traditional components targeting the regulation of negative affect (TP). In spite of the pilot nature of the study, in general, greater improvements were shown by the TP+PA group on all measures, in particular with regard to positive affectivity. In addition, low attrition rates were observed for both groups, and acceptability was high across conditions. In sum, the results obtained in this study suggested the feasibility of testing the intervention in a larger, sufficiently powered RCT.

Strengths and limitations

The findings of the studies contained in the current doctoral thesis should be interpreted in light of their strengths and limitations. The first section outlines the strengths, and the second section summarizes the limitations.

Strengths

The systematic review (Chapter 2) presents both methodological and clinical strengths. With regard to the methodological strengths, it was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42018088138). Moreover, the most relevant databases were used (i.e. PsycINFO, PubMed, EMBASE, and the Cochrane Register of Controlled Trials), which allowed us to conduct a comprehensive search of the literature about RCTs focused on transdiagnostic treatments. Finally, the PRISMA guidelines were followed to ensure that the minimum criteria for conducting systematic reviews were met. Regarding the clinical strengths, to our knowledge, this is the first study to systematically approach the topic of the assessment of comorbidity in transdiagnostic treatments for emotional disorders. Furthermore, it also highlights that some emotional disorders (e.g. PTSD, OCD, anxiety NOS) commonly found in clinical practice are underrepresented in trials about transdiagnostic treatments, in spite of the fact that they are theoretically appropriate for transdiagnostic treatment.

Regarding the validation studies (Chapters 3 and 4), the following strengths are worth noting. First, to our knowledge, these are the first studies to analyze the psychometric properties of the OASIS and the ODSIS in Spanish clinical samples with depression and anxiety. Both validation studies showed good to excellent internal consistency, adequate construct validity, and a latent structure consistent with prior validations of the instruments. In addition, cut-off scores were provided for both measures. Thus, because both instruments showed adequate psychometric properties, they may be soundly used in research and

clinical practice with Spanish patients. Second, large samples of patients with anxiety and depressive disorders were used in both studies, with results that are more generalizable to these populations. Finally, the online versions of these instruments were validated. With the continuous increase in research on Internet interventions, assessment instruments that are delivered online are increasingly demanded by researchers in this field. Thus, these studies contribute to the realm of online evidence-based assessment.

With regard to the RCT (Chapters 3 and 6), both clinical and methodological strengths are underscored. First, to the best of our knowledge, this was the first RCT to explore the effectiveness of a transdiagnostic Internet-delivered protocol for emotional disorders in the context of public specialized mental health care. Moreover, promising results were shown for both the effectiveness and the acceptability of this intervention, compared to TAU, opening up avenues for further research, such as the study of predictors and moderators of treatment, or the comparison of transdiagnostic Internet-delivered treatments with disorder-specific protocols in this specific population. With regard to the methodological strengths, the study protocol was registered at Clinicaltrials.gov (NCT02345668) and published in an indexed open-access journal (*Trials*). Furthermore, an RCT design was used, and we adhered to all the relevant guidelines and recommendations about reporting and conducting clinical research and RCTs: the CONSORT statement (Moher et al., 2010; Moher, Schulz, & Altman, 2001), the CONSORT-EHEALTH guidelines (Eysenbach, 2011), the Declaration of Helsinki, and good clinical practice.

Finally, a randomized pilot study was conducted (Chapter 7) to study the utility of adding components for the regulation of positive affect to a transdiagnostic face-to-face protocol, with the following strengths, both clinical and methodological. With regard to the clinical strengths, this was the first study to acknowledge the importance of including treatment components for the regulation of positive affect in existing transdiagnostic treatments for emotional disorders. Thus, a randomized design was selected to compare a *traditional* transdiagnostic protocol (i.e. with components for the regulation of negative affect) to an extended version of this protocol that added intervention modules targeting the regulation of positive affect. The protocols were compared in terms of both relative efficacy and acceptability. Although preliminary, the results suggested more favorable results for the transdiagnostic protocol with components for the regulation of positive affect and equal acceptability across conditions, suggesting the feasibility of testing this study in a larger RCT. On the other hand, regarding the methodological strengths, a randomized

design was selected, and the study protocol was registered in ClinicalTrials.gov (NCT02790398) prior to being conducted and published.

Limitations

In this section, the main limitations of the studies are discussed.

First, although a comprehensive search was conducted, only studies written in English and developed in Western countries were included in the systematic review (Chapter 2). Moreover, although aspects of the methodology were not reported or unclear in some of the included studies, we did not contact the authors of these studies to clarify these details. Therefore, these studies were rated as unclear. However, we have observed from prior systematic reviews conducted by our research team that contacting the authors is often unfruitful and, thus, has little practical value. Finally, publication bias could not be ruled out. Therefore, some relevant studies might not have been included in the review.

Second, although the OASIS showed good psychometric properties, test-retest reliability was not examined in this study (Chapter 3). Moreover, the sample size used to explore the sensitivity to change of the instrument was low, and it was not analyzed in relation to other measures for the assessment of anxiety. However, it is important to note that these limitations are largely due to the fact that participants were derived from trials with assessment instruments and measurement points that were already predetermined. Finally, rather than a sample of non-clinical control individuals, a cutoff from a self-report questionnaire (Beck Anxiety Inventory) was selected to classify the participants in the Receiver Operating Characteristic analysis. However, unlike previous validations of the OASIS, which only rely on parameters such as sensitivity and specificity (e.g. Campbell-Sills et al., 2009; Norman et al., 2006, 2009), a wider array of criteria were used in our study to select the most optimum cutoff score.

Third, regarding the validation of the ODSIS (Chapter 4), the same procedure as in the OASIS validation was employed to determine the cutoff score (i.e. cut points on the Beck Depression Inventory – BDI-II), but the selection of the cutoff point was based on several criteria, as in the OASIS validation. In addition, although the BDI-II is one of the most validated and accepted measures for the assessment of depression, conclusions about the construct validity of the instrument could only be drawn in relation to this measure because no other instruments to evaluate depression were included in the study. Finally, as in the OASIS validation, good psychometric properties were found for the ODSIS.

However, some important properties such as test-retest reliability were not explored.

Fourth, regarding the RCT (Chapters 3 and 6), a sample size of 200 participants was determined in the study protocol in order to reach conclusions that met the minimum levels of statistical power. However, because of time and funding restraints for this study, we were only able to recruit 178 participants. As a consequence, some results were slightly underpowered, limiting the generalizability of the findings. Furthermore, the long-term effects of EmotionRegulation could not be reported because follow-up assessments (3- and 12-month follow-ups) are still being conducted and, thus, were not available. However, because the maintenance of the effects over time is of vital importance, we plan to report the results of follow-up assessments once they are completed. In addition, attrition was high in both conditions (around 35%), consistent with what is commonly observed in the field of Internet Interventions (Andrews, Cuijpers, Craske, McEvoy & Titov; Van Ballegooijen et al., 2014). However, intention-to-treat analyses were performed to handle missing data. On the other hand, the effects of the intervention on disorder-specific measures (e.g. PSWQ for generalized anxiety, PDSS for panic disorder, and so on) were underpowered due to the low sample size of each of the diagnosis subgroups.

Fifth, although the randomized pilot study yielded results that suggested the feasibility of a transdiagnostic protocol with components for the regulation of positive affect (Chapter 7), the sample size in this study was low, which led to underpowered results that kept us from drawing conclusions about the efficacy of the intervention. Moreover, two active treatments were compared in this study, with the absence of a control group (e.g. waiting list control group or attention control). Finally, carryover effects in the group with components for the regulation of positive affect (TP+PA) cannot be ruled out, which makes it difficult to draw conclusions about the specific contribution of each treatment component to the outcomes.

Recommendations and directions for future research

The findings in this doctoral thesis, as well as its strengths and limitations, open up avenues for future research. Several recommendations for research are discussed in the following section.

First, one of the aims of this doctoral thesis was to conduct a systematic review focused on transdiagnostic treatments for anxiety and depressive disorders (Chapter 2). We concluded that the existing RCTs testing transdiagnostic protocols do not typically evaluate the effects of these treatments on the comorbid disorders, in spite of the clear

association between comorbidity and several indicators of morbidity (e.g. clinical severity, greater chronicity, and poorer clinical course) (Hofmeijer-Sevink et al., 2012; Kessler et al., 2005b; Bruce, Machan, Dyck, & Keller, 2001). For this reason, further empirical data are needed to conclusively demonstrate the assumed superiority of these treatments in addressing comorbidity. Therefore, future studies examining transdiagnostic treatments should make efforts to include assessment instruments that analyze the effect of these treatments on the comorbid disorders. In this vein, one important concern when developing protocols to evaluate new interventions is the selection of the most relevant assessment tools. However, because there are many aspects susceptible to evaluation (e.g. broad and specific symptoms, quality and life, work and social functioning, psychopathological processes, and so on), if not chosen carefully, the assessment protocol might end up with an excessive number of scales. In our experience, a common solution for this problem is to evaluate some aspects at the expense of others. In the field of transdiagnostic treatments, the data from the systematic review (Chapter 2) seem to indicate that instruments for anxiety and depression are selected as principal outcomes in most studies, whereas less attention is paid to the inclusion of measures for the assessment of more specific, but also important, measures, such as disorder-specific instruments to assess treatment effects on comorbid disorders. A possible alternative to this problem may be the inclusion of shorter scales in these trials that allow reliable and valid assessment of the comorbid disorders. For instance, in a recent study, Staples et al. (2018) analyzed the GAD-2, a shorter version of the Generalized Anxiety Disorder Scale (GAD-7), for the assessment of generalized anxiety symptoms, showing good psychometric properties such as discriminant validity, internal consistency, and sensitivity to change. Consequently, it might be worthwhile to develop shorter versions of these scales because they may ease the inclusion of measures for the assessment of comorbidity in studies evaluating transdiagnostic treatments. On the other hand, the systematic review showed that some emotional disorders that are theoretical targets for transdiagnostic treatment (e.g. PTSD, OCD, and anxiety/depression not otherwise specified) are underrepresented in RCTs on these treatments, in spite of their high prevalence rates. Thus, more attention should be paid to these disorders in future research on transdiagnostic interventions.

Second, the RCT (Chapters 3 and 6) conducted in the current doctoral thesis represents, to our knowledge, the first attempt to test a transdiagnostic Internet-delivered protocol in the context of public specialized mental health care. Although encouraging results were found, further research should be carried out in this particular setting to extend the findings obtained in this study, especially because the results that can

be reached in this context have more ecological value. In our RCT, an Internet-delivered format was selected to test a transdiagnostic protocol. The advantages of using the Internet to provide treatments have been highlighted throughout this doctoral thesis (e.g. regarding dissemination). However, the literature in general, and our RCT in particular, has shown that dropout rates in Internet-delivered treatments are notably high (Andrews et al., 2010; Richards & Richardson, 2012). Therefore, more research focused on dropout rates should be conducted with patients attending public specialized care. To this end, both quantitative and qualitative methods should be undertaken to address the study of dropout in these treatments. For instance, the study of predictors can help to shed light on the characteristics of the patients (e.g. sociodemographic and clinical) that make them more prone to dropout (Karyotaki et al. 2015), whereas qualitative research can explore the opinions and attitudes of these patients in a more profound way. Some research has been conducted in this regard (Fernández-Álvarez et al., 2017; Johansson, Michel, Andersson, & Paxling, 2015), showing the importance of taking into account the patients' perspectives in identifying both the barriers and facilitators of Internet-delivered treatments. However, the number of qualitative studies analyzing these aspects is still low, and so more research of this kind is needed to achieve a deeper understanding of this phenomenon. On the other hand, the literature has shown that there is still considerable room for improvement in the attitudes and perceptions of users toward Internet interventions (e.g. Apolinário-Hagen, Vehreschild, & Alkoudmani, 2017; Klein & Cook, 2010; Musiat, Goldstone, & Tarrier, 2014). Although we did not explore the relationship between attitudes and attrition in our RCT, this aspect is of vital importance because attitudes can significantly determine the patients' willingness to engage with these interventions (Mohr et al., 2010), as well as their likelihood of dropping out of them (Fernández-Alvarez et al., 2017). Thus, research efforts should be made to educate the population about the true value of these interventions in improving mental health, specifically with regard to anxiety and depressive disorders. Moreover, although we did not assess the attitudes and opinions of the clinicians involved in the RCT (i.e. psychiatrists and clinical psychologists), it is worth mention that many of them refused to participate in the recruitment process, which might be reflecting negative attitudes towards Internet-delivered interventions among these professionals. The reasons for these negative attitudes might include concerns about the efficacy, privacy, and safety of these treatments (Rochlen, Zack, & Speyer, 2005). Moreover, the possibility of establishing a good therapeutic alliance with the patients in digital interventions is also a matter of concern among clinicians (Sucala, Schnur, Brackman, Constantino, & Montgomery, 2013). However, there is research indicating that Internet-delivered CBT leads to therapeutic alliance levels that are

comparable to face-to-face treatments (Berger, 2016). In this scenario, research efforts to educate the population about the benefits of empirically supported Internet-delivered interventions should also be extended to clinicians, especially because they are seen as authority figures and, therefore, their attitudes can have a major impact on patients' perceptions. Likewise, along with the study of patients' attitudes, more research should be conducted with clinicians to examine their opinions and attitudes about Internet-delivered treatments. In this attempt to measure attitudes toward Internet interventions, different scales have been developed and applied to different populations, such as the Attitudes towards Psychological Online Interventions Questionnaire (APOI) (Schröder et al., 2015) for patients, and the Computer-assisted Therapy Attitudes Scale (CATAS) for clinicians (Becker & Jensen-Doss, 2013). In order to identify barriers and improve the quality of Internet-delivered treatments, future studies should strive to collect data about the attitudes of both users and providers towards these interventions, and scales like the aforementioned may help in this endeavor.

Along the same lines, the results of the RCT showed that, overall, patients in the EmotionRegulation condition improved to a greater degree than patients in the TAU condition. However, as expected, differences between participants emerged when we analyzed the significance of the clinical gains using Jacobson and Truax's (1991) method, with a proportion of these patients showing deterioration at post-treatment. In this vein, there is research indicating that most published trials on Internet-delivered treatments for anxiety and depressive disorders fail to report data about potential negative effects, such as harm, side effects, and deterioration rates (Arnberg, Linton, Hultcrantz, Heinzt, & Jonsson, 2014). Therefore, efforts should be made to report these aspects in order to draw more precise conclusions about the safety of these interventions. In this regard, a few recent meta-analyses have examined predictors of deterioration in Internet-delivered treatments (Ebert et al., 2016; Karyotaki et al., 2018; Rozental, Magnusson, Boettcher, Andersson, & Carlbring, 2017), concluding that, in general, deterioration rates are lower in these treatments compared to control conditions. However, studies focused on this aspect are still scarce, and so more research is needed exploring potential predictors and moderators of deterioration in Internet-delivered treatments.

In this regard, although Internet-delivered treatments have been found to be effective across numerous mental health problems (Andersson, 2016), they may not work equally for everyone. Internet-delivered treatments can be either completely self-guided, guided (differing in the types and amount of guidance provided), or combined with face-to-face psychotherapy, as in the so-called *blended treatments*.

Blended treatments represent an innovative treatment modality that combines face-to-face and Internet-delivered psychotherapy (Kooistra et al., 2014). Because blended treatments require a lower number of face-to-face sessions, they fit properly in routine care settings (e.g. public specialized mental health care). Thus, an interesting future line of research may be to explore how transdiagnostic treatments work when they are provided using distinct delivery modalities (e.g. self-guided Internet-delivered treatments, guided Internet-delivered treatments, or blended treatments) in specialized care. Another possibility is to combine the advantages of both transdiagnostic and group approaches to significantly increase the number of people who receive treatment in public specialized mental health care, as in the ongoing study by Osma et al. (2018). Because the combination of these two approaches (transdiagnostic and group) may provide considerable advantages for both patients and clinicians (e.g. reduction of mental health waiting times, lower costs in training clinicians), we hope that this work will encourage other researchers to conduct similar studies in this particular context.

On the other hand, the individualization or personalization of treatment (or the lack of it) has been found to be a relevant aspect of transdiagnostic Internet-delivered treatments. For instance, Fernández-Álvarez et al. (2017) found that one of the main reasons patients gave for dropping out of a transdiagnostic Internet-based protocol was that the treatment was too general, and, as a result, their specific demands and needs were often not met. Consequently, efforts to personalize treatments may contribute to decreasing dropout rates from these treatments. For instance, in order to develop a more personalized treatment, instead of applying a generic, “one-size-fits-all” transdiagnostic treatment, some authors have proposed choosing among a number of treatment modules to address the specific set of “strengths and weaknesses” presented by each individual (Black et al., 2018; Sauer-Zavala, Cassiello-Robbins, Ametaj, Wilner, & Pagan, 2018). Because this approach has potential benefits for both patients (by focusing on “what really matters” for them) and providers (a more cost-effective treatment strategy), and it is closer to what clinicians typically do in routine care settings (i.e. deliver evidence-based psychological treatments in a flexible way) (Black et al., 2018), future studies should be conducted to explore this approach in public specialized care. In this regard, a more personalized treatment could also be achieved by using the information about predictors of treatment outcome in order to provide the therapeutic option that best matches the sociodemographic and clinical profile of each patient (DeRubeis et al., 2014). In sum, more research efforts should be devoted to the personalization and optimization of current evidence-based treatments in order to increase their (cost) effectiveness.

Another implication of the RCT is related to the study of the effects of transdiagnostic treatments on disorder-specific measures. Along with generic measures of anxiety and depression, the study of the efficacy of these treatments on more specific symptoms is necessary in order to shed light on their relative efficacy for each distinct emotional disorder. Although we included measures to assess the effects of the intervention on the different diagnoses (e.g. PSWQ for GAD symptoms, OCI-R for OCD symptoms, and so on), the sample size for each of the diagnostic subgroups was too low, and, therefore, acceptable levels of statistical power could not be met. Therefore, further trials with larger sample sizes are warranted to explore the effects of transdiagnostic Internet-delivered interventions in each of the different emotional disorders. For instance, transdiagnostic treatments may be compared to disorder-specific protocols for each of the different emotional disorders. A number of RCTs using this strategy have already been attempted in community samples, showing equivalent effects between these two treatment approaches for depression (Titov et al., 2015), panic disorder (Fogliati et al., 2016), social anxiety disorder (Dear et al., 2016), and generalized anxiety disorder (Dear et al., 2015). However, the number of studies comparing these two treatment approaches is still very low (González-Robles et al., 2018; Newby et al., 2015, 2016). Additionally, because a) transdiagnostic treatments may be more advantageous than disorder-specific treatments in terms of costs and ease of dissemination, and b) comparing these two treatments approaches can provide data that strengthen the notion of a common transdiagnostic psychopathology underlying anxiety and depressive disorders, further studies comparing these two treatment approaches are warranted, especially in real-world settings (e.g. primary or specialized care), where these aspects are of the highest importance.

Furthermore, in order to ascertain how transdiagnostic treatments modulate the different core processes underlying anxiety and depressive disorders, clinical research should strive to include assessment instruments focused on the evaluation of transdiagnostic cognitive, behavioral, and emotional processes such as neuroticism (Barlow, Allen, & Choate, 2004), rumination (Ehring & Watkins, 2008), anxiety sensitivity (Boswell et al., 2013), and safety behaviors (Schmidt et al., 2012). For instance, in our RCT we included the BISBAS (Carver & White, 1994; Caseras, Ávila, & Torrubia, 2003), a scale to assess the transdiagnostic constructs of behavioral inhibition and behavioral activation. In this vein, the inclusion of measures to assess transdiagnostic mechanisms might be particularly relevant when these treatments are studied in comparison with disorder-specific protocols. Theoretically, because transdiagnostic treatments target deeper and more stable common core processes (e.g. the personality dimension of neuroticism), greater and more durable

effects might be expected compared to disorder-specific treatments (Sauer-Zavala et al., 2017). Therefore, the inclusion of scales to assess transdiagnostic mechanisms is warranted in future clinical research, particularly when these treatments are compared to disorder-specific protocols. On the other hand, transdiagnostic treatments are rarely explored in public specialized care (González-Robles et al., 2018). Because the sociodemographic and clinical characteristics of patients attending public mental health services may differ substantially from that of other settings like the university or community samples (e.g. regarding educational level, Internet usage skills, use of medication, and so on), more studies focused on searching for predictors and moderators of treatment outcome are needed in this particular context.

Third, the online versions of two brief scales for the assessment of anxiety and depression were validated in Spanish clinical samples with heterogeneous anxiety and depressive disorders (Chapters 4 and 5). Taken together, the results showed good internal consistency, construct validity and a factor structure in accordance with previous validations of the scales. However, some important properties such as test-retest reliability were not evaluated. Moreover, although the sensitivity to change of the OASIS was explored, this aspect was not analyzed in the ODSIS. Thus, future validations of both scales should be performed that analyze the test-retest reliability of both scales, as well as the sensitivity to change of the ODSIS. Finally, because we focused on patients with anxiety and depressive disorders, research on the psychometric properties of these questionnaires in other populations, such as nonclinical individuals or patients with more severe psychopathology (e.g. individuals with bipolar or psychotic disorders), is warranted.

Finally, a randomized pilot study was conducted to explore the feasibility of adding treatment modules for the regulation of positive affect in a transdiagnostic protocol with traditional components for the regulation of negative affect (Chapter 7). Although promising results were found, the study presented limitations that warrant further research to more precisely determine the contribution of this component to treatment outcome. The main limitations were the low sample size and the fact that carryover effects could not be ruled out, affecting the understanding of the true contribution of this component to the clinical change. Therefore, future studies are needed with designs that make it possible to draw safer conclusions about the true contribution of these components for the regulation of positive affectivity, such as dismantling studies (Papa & Follette, 2014) or single-case experimental designs (Barlow, Nock, & Hersen, 2009). Another research strategy that may help to ascertain the contribution of each component to outcomes is to collect clinical data conducting assesments at different points throughout the entire

intervention process, and analyze them in relation with the different components integrated in the treatment, such as the post-module measurements included in our RCT to assess anxiety, depression, and positive/negative affectivity. Using this strategy, the results of a recent study by Mira et al. (2018) suggested that positive affectivity only improved after introducing a component based on positive psychology interventions. In summary, further research should be conducted to more accurately determine the extent to which each of these treatment components contributes to clinical outcomes.

Conclusions

The studies in this doctoral thesis contribute to the field of transdiagnostic treatments, showing the effectiveness of a transdiagnostic Internet-delivered protocol for emotional disorders in public specialized mental health care, compared to TAU. To our knowledge, this is the first time that a transdiagnostic Internet-delivered protocol has been tested in this setting, with results that raise the question of whether patients in the Spanish public mental health care system are receiving the most adequate treatment alternatives for anxiety and depressive disorders. Moreover, a systematic review was conducted to synthesize the state-of-the-art of transdiagnostic treatments, highlighting the importance of assessing the comorbid disorders in these interventions. At the same time, contributions to the field of online evidence-based assessment were made through the validation of the OASIS and the ODSIS in clinical samples with emotional disorders. Finally, the importance of promoting protective factors in transdiagnostic treatments was underscored by showing the feasibility of a transdiagnostic treatment that included treatment components for the regulation of positive affect, opening the door to large-scale efficacy and effectiveness studies. Although the results hold promise, we hope that the findings and recommendations discussed in the current doctoral thesis encourage other researchers to continue to explore the possibilities of transdiagnostic Internet-delivered treatments to reduce the burden of emotional disorders. In this endeavor, future research is warranted to improve the effectiveness and acceptability of transdiagnostic Internet-delivered interventions among users, clinicians, and policy makers, in order to increase their dissemination and implementation in current mental health care systems.

References

Andersson, G. (2016). Internet-delivered psychological treatments. *Annual Review of Clinical Psychology*, *12*, 157–179.

Andrews, G., Cuijpers, P., Craske, M. G., McEvoy, P., & Titov, N. (2010). Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: a meta-analysis. *PloS One*, *5*(10), e13196.

Apolinário-Hagen, J., Vehreschild, V., & Alkoudmani, R. M. (2017). Current views and perspectives on e-mental health: an exploratory survey study for understanding public attitudes toward internet-based psychotherapy in Germany. *JMIR Mental Health*, *4*(1), e8.

Arnberg, F. K., Linton, S. J., Hultcrantz, M., Heintz, E., & Jonsson, U. (2014). Internet-delivered psychological treatments for mood and anxiety disorders: a systematic review of their efficacy, safety, and cost-effectiveness. *PLoS One*, *9*(5), e98118.

Barlow, D. H., Allen, L. B., & Choate, M. L. (2004). Toward a unified treatment for emotional disorders. *Behavior Therapy*, *35*(2), 205–230.

Barlow, D. H., Nock, M., & Hersen, M. (2009). *Single-case experimental designs: Strategies for studying behavior for change*. New York, NY, US: Pearson.

Becker, E. M., & Jensen-Doss, A. (2013). Computer-assisted therapies: examination of therapist-level barriers to their use. *Behavior Therapy*, *44*(4), 614–624.

Bentley, K. H., Gallagher, M. W., Carl, J. R., & Barlow, D. H. (2014). Development and validation of the Overall Depression Severity and Impairment Scale. *Psychological Assessment*, *26*(3), 815–830.

Berger, T. (2017). The therapeutic alliance in internet interventions: a narrative review and suggestions for future research. *Psychotherapy Research*, *27*(5), 511–524.

Black, M., Hitchcock, C., Bevan, A., Leary, C. O., Clarke, J., Elliott, R., ... Kuyken, W. (2018). The HARMONIC trial: study protocol for a randomised controlled feasibility trial of Shaping Healthy Minds—a modular transdiagnostic intervention for mood, stressor-related and anxiety disorders in adults. *BMJ open*, *8*(8), e024546.

Boswell, J. F., Farchione, T. J., Sauer-Zavala, S., Murray, H. W., Fortune,

M. R., & Barlow, D. H. (2013). Anxiety sensitivity and interoceptive exposure: A transdiagnostic construct and change strategy. *Behavior Therapy*, *44*(3), 417–431.

Brown, T. A., & Barlow, D. H. (2009). A proposal for a dimensional classification system based on the shared features of the DSM-IV anxiety and mood disorders: implications for assessment and treatment. *Psychological Assessment*, *21*(3), 256–271.

Bruce, S. E., Machan, J. T., Dyck, I., & Keller, M. B. (2001). Infrequency of "pure" GAD: Impact of psychiatric comorbidity on clinical course. *Depression and Anxiety*, *14*(4), 219–225.

Campbell-Sills, L., Norman, S. B., Craske, M. G., Sullivan, G., Lang, A. J., Chavira, D. A., ... Stein, M. B. (2009). Validation of a brief measure of anxiety-related severity and impairment: the Overall Anxiety Severity and Impairment Scale (OASIS). *Journal of Affective Disorders*, *112*(1-3), 92–101.

Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS scales. *Journal of Personality and Social Psychology*, *67*(2), 319–333.

Caseras, X., Avila, C., & Torrubia, R. (2003). The measurement of individual differences in behavioural inhibition and behavioural activation systems: a comparison of personality scales. *Personality and Individual Differences*, *34*(6), 999–1013.

Dear, B. F., Staples, L. G., Terides, M. D., Fogliati, V. J., Sheehan, J., Johnston, L., ... Titov, N. (2016). Transdiagnostic versus disorder-specific and clinician-guided versus self-guided internet-delivered treatment for social anxiety disorder and comorbid disorders: a randomized controlled trial. *Journal of Anxiety Disorders*, *42*, 30–44.

Dear, B. F., Staples, L. G., Terides, M. D., Karin, E., Zou, J., Johnston, L., ... Titov, N. (2015). Transdiagnostic versus disorder-specific and clinician-guided versus self-guided internet-delivered treatment for generalized anxiety disorder and comorbid disorders: a randomized controlled trial. *Journal of Anxiety Disorders*, *36*, 63–77.

DeRubeis, R. J., Cohen, Z. D., Forand, N. R., Fournier, J. C., Gelfand, L. A., & Lorenzo-Luaces, L. (2014). The Personalized Advantage Index: translating research on prediction into individualized treatment recommendations. A demonstration. *PloS One*, *9*(1), e83875.

Ebert, D. D., Donkin, L., Andersson, G., Andrews, G., Berger, T., Carlbring, P., ... Kleiboer, A. (2016). Does Internet-based guided-

self-help for depression cause harm? An individual participant data meta-analysis on deterioration rates and its moderators in randomized controlled trials. *Psychological Medicine*, *46*(13), 2679–2693.

Ehring, T., & Watkins, E. R. (2008). Repetitive Negative Thinking as a Transdiagnostic Process. *International Journal of Cognitive Therapy*, *1*(3), 192–205.

Eysenbach, G. (2011). CONSORT-EHEALTH Group. CONSORT-EHEALTH: improving and standardizing evaluation reports of web-based and mobile health interventions. *Journal of Medical Internet Research*, *13*(4), e126.

Fernández-Álvarez, J., Díaz-García, A., González-Robles, A., Baños, R., García-Palacios, A., & Botella, C. (2017). Dropping out of a transdiagnostic online intervention: A qualitative analysis of client's experiences. *Internet Interventions*, *10*, 29–38.

Fogliati, V. J., Dear, B. F., Staples, L. G., Terides, M. D., Sheehan, J., Johnston, L., ... Titov, N. (2016). Disorder-specific versus transdiagnostic and clinician-guided versus self-guided internet-delivered treatment for panic disorder and comorbid disorders: a randomized controlled trial. Journal of anxiety disorders, 39, 88–102.

González-Robles, A., Díaz-García, A., Miguel, C., García-Palacios, A., & Botella, C. (2018). Comorbidity and diagnosis distribution in transdiagnostic treatments for emotional disorders: A systematic review of randomized controlled trials. *PloS One*, *13*(11), e0207396.

Hofmeijer-Sevink, M. K., Batelaan, N. M., van Megen, H. J. G. M., Penninx, B. W., Cath, D. C., van den Hout, M. A., & van Balkom, A. J. L. M. (2012). Clinical relevance of comorbidity in anxiety disorders: A report from the Netherlands Study of Depression and Anxiety (NESDA). *Journal of Affective Disorders*, *137*(1–3), 106–112.

Ito, M., Bentley, K. H., Oe, Y., Nakajima, S., Fujisato, H., Kato, N., ... Barlow, D. H. (2015). Assessing depression related severity and functional impairment: the overall depression severity and impairment scale (ODSIS). *PloS One*, *10*(4), e0122969.

Ito, M., Oe, Y., Kato, N., Nakajima, S., Fujisato, H., Miyamae, M., ... Norman, S. B. (2015). Validity and clinical interpretability of overall anxiety severity and impairment scale (OASIS). *Journal of Affective Disorders*, *170*, 217–224.

Jacobson, N. S., & Truax, P. (1991). Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. Journal of Consulting and Clinical Psychology, *59*(1), 12–19.

Johansson, O., Michel, T., Andersson, G., & Paxling, B. (2015). Experiences of non-adherence to Internet-delivered cognitive behavior therapy: a qualitative study. *Internet Interventions*, *2*(2), 137–142.

Karyotaki, E., Kemmeren, L., Riper, H., Twisk, J., Hoogendoorn, A., Kleiboer, A., ... Littlewood, E. (2018). Is self-guided internet-based cognitive behavioural therapy (iCBT) harmful? An individual participant data meta-analysis. Psychological Medicine, 48(15), 2456–2466.

Karyotaki, E., Kleiboer, A., Smit, F., Turner, D. T., Mira, A., Andersson, G., ... Christensen, H. (2015). Predictors of treatment dropout in self-guided web-based interventions for depression: an 'individual patient data'meta-analysis. *Psychological Medicine*, *45*(13), 2717–2726.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime Prevalence and Age-of-Onset Distributions of. *Archives of General Psychiatry*, *62*, 593–602.

Kessler, R. C., Chiu, W. T., Demler, O., Merikangas, K. R., & Walters, E. E. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, *62*(6), 617–627.

Klein, B., & Cook, S. (2010). Preferences for e-mental health services amongst an online Australian sample. *Electronic Journal of Applied Psychology*, *6*(1), 27–38.

Kooistra, L. C., Wiersma, J. E., Ruwaard, J., van Oppen, P., Smit, F., Lokkerbol, J., ... Riper, H. (2014). Blended vs. face-to-face cognitive behavioural treatment for major depression in specialized mental health care: study protocol of a randomized controlled cost-effectiveness trial. *BMC psychiatry*, *14*(1), 290.

Mira, A., Bretón-López, J., Enrique, A., Castilla, D., Garcia-Palacios, A., Baños, R. M., & Botella, C. (2018). Exploring the incorporation of a positive psychology component in a cognitive behavioral Internet-based program for depressive symptoms. Results throughout the intervention process. *Frontiers in Psychology*, *9*, 2360.

Mohr, D. C., Siddique, J., Ho, J., Duffecy, J., Jin, L., & Fokuo, J. K. (2010). Interest in behavioral and psychological treatments delivered face-to-face, by telephone, and by Internet. *Annals of Behavioral Medicine*, *40*(1), 89–98.

Musiat, P., Goldstone, P., & Tarrier, N. (2014). Understanding the acceptability of e-mental health-attitudes and expectations towards computerised self-help treatments for mental health problems. *BMC Psychiatry*, *14*(1), 109.

Newby, J. M., McKinnon, A., Kuyken, W., Gilbody, S., & Dalgleish, T. (2015). Systematic review and meta-analysis of transdiagnostic psychological treatments for anxiety and depressive disorders in adulthood. *Clinical Psychology Review*, *40*, 91–110.

Newby, J. M., Twomey, C., Yuan Li, S. S., & Andrews, G. (2016). Transdiagnostic computerised cognitive behavioural therapy for depression and anxiety: A systematic review and meta-analysis. *Journal of Affective Disorders*, *199*, 30–41.

Norman, S. B., Campbell-Sills, L., Hitchcock, C. A., Sullivan, S., Rochlin, A., Wilkins, K. C., & Stein, M. B. (2011). Psychometrics of a brief measure of anxiety to detect severity and impairment: the Overall Anxiety Severity and Impairment Scale (OASIS). *Journal of psychiatric research*, *45*(2), 262–268.

Moher, D., Hopewell, S., Schulz, K. F., Montori, V., Gøtzsche, P. C., Devereaux, P. J., … Altman, D. G. (2010). CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *Journal of Clinical Epidemiology*, *63*, e1–37.

Moher, D., Schulz, K. F., & Altman, D. G. (2001). The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *Journal of the American Podiatric Medical Association*, *91*, 437–442.

Norman, S. B., Hami Cissell, S., Means-Christensen, A. J., & Stein, M. B. (2006). Development and validation of an overall anxiety severity and impairment scale (OASIS). *Depression and Anxiety*, *23*(4), 245–249.

Osma, J., Suso-Ribera, C., García-Palacios, A., Crespo-Delgado, E., Robert-Flor, C., Sánchez-Guerrero, A., ... Torres-Alfosea, M. Á. (2018). Efficacy of the unified protocol for the treatment of emotional disorders in the Spanish public mental health system using a group format: study protocol for a multicenter, randomized, non-inferiority controlled trial. *Health and Quality of Life*

Outcomes, *16*(1), 46.

Papa, A., & Follette, W. C. (2014). Dismantling studies of psychotherapy. *The Encyclopedia of Clinical Psychology*. Guilford Press.

Rapaport, M. H., Clary, C., Fayyad, R., & Endicott, J. (2005). Quality-of-Life Impairment in Depressive and Anxiety Disorders. *American Journal of Psychiatry*, *162*(6), 1171–1178.

Richards, D., & Richardson, T. (2012). Computer-based psychological treatments for depression: a systematic review and meta-analysis. *Clinical Psychology Review*, *32*(4), 329–42.

Rochlen, A. B., Zack, J. S., & Speyer, C. (2004). Online therapy: Review of relevant definitions, debates, and current empirical support. *Journal of Clinical Psychology*, *60*(3), 269–283.

Rozental, A., Magnusson, K., Boettcher, J., Andersson, G., & Carlbring, P. (2017). For better or worse: An individual patient data meta-analysis of deterioration among participants receiving Internet-based cognitive behavior therapy. *Journal of Consulting and Clinical Psychology*, *85*(2), 160–177.

Sauer-Zavala, S., Cassiello-Robbins, C., Ametaj, A. A., Wilner, J. G., & Pagan, D. (2018). Transdiagnostic Treatment Personalization: The Feasibility of Ordering Unified Protocol Modules According to Patient Strengths and Weaknesses. *Behavior Modification*, 0145445518774914.

Sauer-Zavala, S., Gutner, C. A., Farchione, T. J., Boettcher, H. T., Bullis, J. R., & Barlow, D. H. (2017). Current Definitions of "Transdiagnostic" in Treatment Development: A Search for Consensus. *Behavior Therapy*, *48*(1), 128–138.

Schmidt, N. B., Buckner, J. D., Pusser, A., Woolaway-Bickel, K., Preston, J. L., & Norr, A. (2012). Randomized Controlled Trial of False Safety Behavior Elimination Therapy: A Unified Cognitive Behavioral Treatment for Anxiety Psychopathology. *Behavior Therapy*, *43*(3), 518–532.

Schröder, J., Berger, T., Meyer, B., Lutz, W., Späth, C., Michel, P., ... Moritz, S. (2018). Impact and change of attitudes toward Internet interventions within a randomized controlled trial on individuals with depression symptoms. *Depression and Anxiety*, *35*(5), 421–430.

Schröder, J., Sautier, L., Kriston, L., Berger, T., Meyer, B., Späth, C., ... Moritz, S. (2015). Development of a questionnaire measuring Attitudes towards Psychological Online Interventions–the APOI. *Journal of Affective Disorders*, *187*, 136–141.

Staples, L. G., Dear, B. F., Gandy, M., Fogliati, V., Fogliati, R., Karin, E., Nielssen, O., & Titov, N. (2018). Psychometric properties and clinical utility of brief measures of anxiety, depression, and general distress: The PHQ-2, GAD-2, and K-6. *General Hospital Psychiatry*, *56*, 13–18.

Steele, S. J., Farchione, T. J., Cassiello-Robbins, C., Ametaj, A., Sbi, S., Sauer-Zavala, S., & Barlow, D. H. (2018). Efficacy of the Unified Protocol for transdiagnostic treatment of comorbid psychopathology accompanying emotional disorders compared to treatments targeting single disorders. *Journal of Psychiatric Research*, *104*, 211–216.

Sucala, M., Schnur, J. B., Brackman, E. H., Constantino, M. J., & Montgomery, G. H. (2013). Clinicians' attitudes toward therapeutic alliance in E-therapy. *The Journal of General Psychology*, *140*(4), 282–293.

Titov, N., Dear, B. F., Staples, L. G., Terides, M. D., Karin, E., Sheehan, J., ... McEvoy, P. M. (2015). Disorder-specific versus transdiagnostic and clinician-guided versus self-guided treatment for major depressive disorder and comorbid anxiety disorders: a randomized controlled trial. *Journal of Anxiety Disorders*, *35*, 88–102.

Van Ballegooijen, W., Cuijpers, P., van Straten, A., Karyotaki, E., Andersson, G., Smit, J. H., & Riper, H. (2014). Adherence to Internet-Based and Face-to-Face Cognitive Behavioural Therapy for Depression: A Meta-Analysis. *PloS One*, *9*(7), e100674.

Appendix 1. Search strategy

PsycINFO

1. “transdiagnostic” or “unified” or “mixed anxiety and depression” or “mixed depression and anxiety” or “heterogeneous” (38707)

2. “depression” or “anxiety” (433085)

3. 1 AND 2 (6363)

4. Limited to clinical trials, outcome studies (327)

Number of records: **327** (06/02/2018)

Pubmed

("transdiagnostic"[All fields] OR "unified"[All fields] OR "mixed anxiety and depression"[All fields] OR "heterogeneous"[All fields]) AND ("depression"[All fields] OR "anxiety"[All fields]) AND Clinical Trial[ptyp]

Number of records: **367** (06/02/2018)

EMBASE

1. “transdiagnostic” or “unified” or “mixed anxiety and depression” or “mixed depression and anxiety” or “heterogeneous” (213332)

2. “depression” or “anxiety” (734823)

3. 1 AND 2 (9334)

4. Limited to clinical trials, outcome studies (515)

5. Limited to English (510)

Number of records: **510** (06/02/2018)

COCHRANE

1. “transdiagnostic” or “unified” or “mixed anxiety and depression” or “mixed depression and anxiety” or “heterogeneous” (7915)

2. “depression” or “anxiety” (69235)

3. 1 AND 2 (1833)

4. Limited to trials (677)

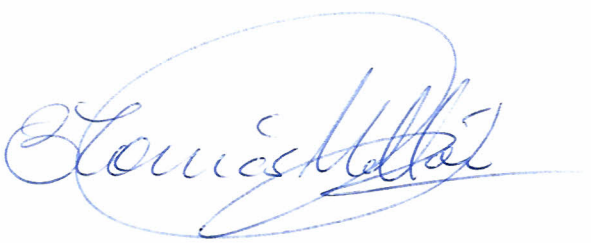
Number of records: **677** (06/02/2018)

Appendix 2. Ethics Committee approval (Universitat Jaume I)

UNIVERSITAT JAUME·I

Beatriz Tomás Mallén, secretaria de la Comisión Deontológica de la Universitat Jaume I de Castelló de la Plana,

CERTIFICA: Que la Comisión Deontológica de la Universitat Jaume I ha emitido informe favorable sobre el procedimiento de investigación titulado: "Diseño, desarrollo y puesta a prueba de un protocolo de tratamiento transdiagnóstico para los trastornos emocionales administrado on-line: Serie de casos", cuya investigadora principal es Cristina Botella Arbona, por considerar que cumple las normas deontológicas exigidas.



Castellón de la Plana, 25 de noviembre de 2013

Appendix 3. Ethics Committee approval (Participating hospitals)

Consorcio Hospitalario
Provincial de Castellón

DICTAMEN DEL COMITÉ ÉTICO DE INVESTIGACIÓN CLINICA

Dª **EVA FELIP VICIANO**, Secretaria del Comité Ético de Investigación Clínica del Consorcio Hospitalario Provincial de Castellón.

CERTIFICA:

Que este Comité ha evaluado en fecha 27 de noviembre de 2013 la propuesta para que se realice el Proyecto de Investigación titulado:

"Puesta a prueba de un protocolo de tratamiento transdiagnóstico para los trastornos emocionales administrado on-line" Investigador Principales: Dr. Francisco Traver Torras; Dr. Gonzalo Haro y Dr. Gines Llorca del área de Salud Mental del Consorcio Hospitalario Provincial de Castellón.

El Comité considera que el proyecto se plantea siguiendo los requisitos necesarios de idoneidad en relación con los objetivos planteados y están justificados los riesgos y molestias previsibles para el sujeto, teniendo en cuenta los beneficios esperados.

El procedimiento para obtener el consentimiento informado, incluyendo la hoja de información para los sujetos y el plan de reclutamiento de sujetos previstos son adecuados, así como las compensaciones previstas para los sujetos por daños que pudieran derivarse de su participación en el proyecto.

La capacidad del investigador y sus colaboradores y las instalaciones y medios disponibles son apropiados para llevar a cabo el proyecto.

Por tanto este Comité acepta que dicho proyecto, sea realizado en el Consorcio Hospitalario Provincial de Castellón por los doctores **Francisco Traver, Gonzalo Haro y Gines Llorca** del área de Salud Mental.

Lo que firmo en Castellón a 27 de noviembre de 2013

Fdo. Eva Felip Viciano

Consorcio Hospitalario Provincial de Castellón - C.E.I.C.

Avda. Dr. Clará 19, 12002 Castellón Tel: 964 359 700 Fax: 964 354 301 www.hospital2000.net NIF: P-6200007-J

HOSPITAL UNIVERSITARIO de LA RIBERA

GENERALITAT VALENCIANA
CONSELLERIA DE SANITAT

INFORME DEL COMITÉ DE ÉTICA DE LA INVESTIGACIÓN- COMISIÓN DE INVESTIGACIÓN

Dra. María Cuenca Torres, Secretaria del Comité de Ética de la Investigación- Comisión de Investigación del Departamento de Salud de La Ribera de la Comunidad Valenciana, Hospital Universitario de La Ribera de Alzira.

CERTIFICA

Que esta Comisión ha evaluado la propuesta del investigador principal Dr. Guillem Lera Calatayud para que se realice el proyecto de investigación titulado: "Puesta a prueba de un protocolo de tratamiento transdiagnóstico para los trastornos emocionales administrado on-lrne (transdtagnosttico)."

Y considera que:

Se cumplen los requisitos necesarios de idoneidad del Proyecto de Investigación en relación con los objetivos.

La capacidad de los investigadores.

La adecuación del proyecto a los medios existentes en este Centro.

La adecuada elaboración y presentación de la Memoria.

La conveniencia e interés de los resultados para el Departamento de Salud y el Sistema Nacional de Salud.

Y que esta Comisión acepta que dicho proyecto sea realizado en el Departamento de Salud de La Ribera/ Hospital Universitario de La Ribera por Dr. Guillem Lera Calatayud como investigadores.

Lo que firmo en Alzira, 3 de Septiembre de 2015

HOSPITAL UNIVERSITARIO de LA RIBERA
Comisión de Investigación

Fdo.: Dra. María Cuenca Torres

Vall d'Hebron
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INFORME DEL COMITÉ ÉTICO DE INVESTIGACIÓN CLÍNICA CON MEDICAMENTOS Y COMISIÓN DE PROYECTOS DE INVESTIGACIÓN DEL HOSPITAL UNIVERSITARI VALL D'HEBRON

Doña Mireia Navarro, Secretaria del COMITÉ ÉTICO DE INVESTIGACIÓN CLÍNICA CON MEDICAMENTOS del Hospital Universitari Vall d'Hebron,

CERTIFICA

Que el Comité Ético de Investigación Clínica del Hospital Universitario Vall d'Hebron, en el cual la Comisión de proyectos de investigación está integrada, se reunió en sesión ordinaria nº 249 el pasado 29/04/2016 y evaluó el proyecto de investigación PR(AG)116/2016 , con fecha 01/04/2016, titulado "*Puesta a prueba de un protocolo de tratamiento transdiagnóstico para los trastornos emocionales administrado on-line"* que tiene como investigador principal al Dr. José Antonio Ramos Quiroga del Servicio de Psiquiatría de nuestro Centro.

El resultado de la evaluación fue el siguiente:

DICTAMEN FAVORABLE

El Comité tanto en su composición como en los PNT cumple con las normas de BPC (CPMP/ICH/135/95) y con el Real Decreto 1090/2015, y su composición actual es la siguiente:

Presidenta: Gallego Melcón, Soledad. Médico
Vicepresidente: Segarra Sarries, Joan. Abogado
Secretaria: Navarro Sebastián, Mireia. Química
Vocales: Armadans Gil, Lluís. Médico
Azpiroz Vidaur, Fernando. Médico
Balasso, Valentina. Médico
Cucurull Folguera, Esther. Médico Farmacóloga
Latorre Arteche, Francisco. Médico
De Torres Ramírez, Inés M. Médico

Fernández Liz, Eladio. Farmacéutico de Atención Primaria
Ferreira González, Ignacio. Médico
Fuentelsaz Gallego, Carmen. Diplomada Enfermería
Fuentes Camps, Inmaculada. Médico Farmacóloga
Guardia Massó, Jaume. Médico
Joshi Jubert, Nayana. Médico
Hortal Ibarra, Juan Carlos. Profesor de Universidad de Derecho
Montoro Ronsano, J. Bruno. Farmacéutico Hospital
Rodríguez Gallego, Alexis. Médico Farmacólogo
Sánchez Raya, Judith. Médico
Solé Orsola, Marta. Diplomada Enfermería
Suñé Martín, Pilar. Farmacéutica Hospital
Vargas Blasco, Víctor, Médico

En dicha reunión del Comité Ético de Investigación Clínica se cumplió el quórum preceptivo legalmente.

En el caso de que se evalúe algún proyecto del que un miembro sea investigador/colaborador, éste se ausentará de la reunión durante la discusión del proyecto.

Lo que firmo en Barcelona a 29 de abril de 2016

Sra. Mireia Navarro

Secretaria CEIm

Appendix 4. Referral document

Cuestionario de recogida de datos
(CRD USM)

PROCEDIMIENTO A SEGUIR:

- Evaluar criterios inclusión/ exclusión al estudio.
- Recabar datos personales.
- Mostrar y comentar hoja de información al paciente (HIP)

Documentos necesarios adicionales a este:

- Hoja de Información al paciente

CRITERIOS DE INCLUSIÓN:

1. Edad: tener 18 años o más.
2. Entender español hablado y escrito.
3. Padecer un Trastorno Emocional (Trastorno Depresivo Mayor, Distimia, Trastorno de Ansiedad Generalizada, Trastorno Obsesivo-Compulsivo, Trastorno de Pánico, Agorafobia, Trastorno de Ansiedad Social, Trastorno de ansiedad no especificado, Trastorno del estado de ánimo no especificado).
4. Acceso a Internet con cuenta de correo electrónico.

CRITERIOS DE EXCLUSIÓN:

1. Padecer un trastorno mental grave. Se excluirán los trastornos siguientes: esquizofrenia, trastorno bipolar.
2. Presencia de riesgo de suicidio.
3. Diagnóstico de dependencia de alcohol y/o sustancias.
4. Enfermedad médica de consideración que impida la realización del tratamiento psicológico.
5. Recibir otro tratamiento psicológico mientras dure el estudio.
6. En el caso de estar recibiendo tratamiento farmacológico, el incremento de dosis y/o cambio del tipo de medicación significará la exclusión del participante del ensayo.

DATOS DEL PACIENTE

NOMBRE: _____APELLIDOS:_____
SEXO: □ Mujer □ Hombre EDAD: _____TELÉFONO:_____
CORREO ELECTRÓNICO (en mayúsculas):_____
ACCESO INTERNET: □ Sí □ No

POSIBLE DIAGNÓSTICO:_____

TRATAMIENTO FARMACOLÓGICO PRESCRITO (Si está recibiendo tratamiento farmacológico indicar tipo, dosis y desde cuándo):

_____
_____
_____

EN CASO DE RECHAZO/ABANDONO DEL ESTUDIO, especificar causa:

- □ No lo necesita
- □ No cree en su utilidad
- □ Falta de tiempo
- □ Falta de habilidad para el manejo del programa
- □ No le gustan los ordenadores
- □ No le gusta el programa / no se siente a gusto con su manejo
- □ Prefiere un trato personal
- □ Falta de confianza en la seguridad de los datos

Otros motivos (especificar):_____
_____
_____

Contacto con Investigadores: Alberto González vrobles@uji.es 964387649

Appendix 5. Patient information document (clinician)

DISEÑO, DESARROLLO Y PUESTA A PRUEBA DE UN PROTOCOLO DE TRATAMIENTO TRANSDIAGNÓSTICO PARA LOS TRASTORNOS EMOCIONALES ADMINISTRADO ONLINE

Hoja de información al paciente (presentada por el centro de salud)

INFORMACIÓN PARA EL PACIENTE

Apreciado Sr./Sra.:

Antes de confirmar su participación en el estudio es importante que entienda en qué consiste. Por favor, lea detenidamente este documento y haga todas las preguntas que le puedan surgir.

Objetivo del estudio:

El objetivo principal de este estudio es desarrollar un programa de psicoterapia aplicado a través de Internet para el tratamiento de los trastornos emocionales (trastorno depresivo mayor, distimia, trastorno de ansiedad generalizada, trastorno de pánico, agorafobia, trastorno de ansiedad social, trastorno obsesivo-compulsivo, trastorno de ansiedad no especificado, trastorno del estado de ánimo no especificado) y evaluar su eficacia.

Desarrollo del estudio:

En una primera fase del estudio se evaluará si los pacientes pueden participar o no en el mismo, aquellos pacientes que puedan participar en el estudio (fase 2) serán adscritos a una de estas dos condiciones:

a) Tratamiento habitual (el tratamiento psiquiátrico y/o psicológico que se administre de forma regular en el centro de salud).

   El tratamiento habitual consistirá en el tratamiento psiquiátrico y/o psicológico de referencia más adecuado a la problemática de cada paciente, y será administrado por un especialista del ámbito clínico (psiquiatra y/o psicólogo clínico) en el centro de salud mental.

b) Protocolo de tratamiento transdiagnóstico aplicado online.

   El tratamiento transdiagnóstico aplicado online consistirá en un programa vía internet e interactivo que el paciente puede realizar desde su casa compuesto por un total de 12 módulos de periodicidad semanal. Estos distintos módulos o componentes terapéuticos tienen como objetivo fundamental: 1) incrementar la conciencia emocional; 2) facilitar la flexibilidad cognitiva; 3) identificar patrones de evitación comportamental y emocional; y; 4) promover la exposición interoceptiva y situacional.

Es posible que, de forma paralela a este estudio, se realicen grupos de discusión formados por los pacientes participantes en el mismo, cuyo contenido será transcrito y analizado, con el objetivo de identificar las barreras y dificultades del uso del programa de psicoterapia. Al ser una posibilidad al margen del estudio, si se diera la oportunidad, se solicitaría la firma de un nuevo consentimiento informado.

Participantes:

Los participantes de este estudio son personas diagnosticadas de trastornos emocionales (trastornos de ansiedad, trastornos depresivos).

Los participantes deben tener una edad mínima de 18 años y disponer de una conexión a Internet.

Participación del paciente en el estudio:

En esta primera fase del estudio se recogerá la siguiente información que nos ayudará a conocer si cumple los criterios para ser incluido en el estudio:

CRITERIOS DE INCLUSIÓN:

1. Tener 18 años o más.
2. Entender español hablado y escrito.
3. Padecer un Trastorno Emocional (Trastorno Depresivo Mayor, Distimia, Trastorno de Ansiedad Generalizada, Trastorno Obsesivo-Compulsivo, Trastorno de Pánico, Agorafobia, Trastorno de Ansiedad Social, Trastorno de ansiedad no especificado, Trastorno del estado de ánimo no especificado).
4. Disponer de acceso a Internet y cuenta de correo electrónico.

CRITERIOS DE EXCLUSIÓN:

1. Padecer esquizofrenia.
2. Padecer trastorno bipolar.
3. Presentar alto riesgo de suicidio.
4. Presentar dependencia de sustancias y/o de alcohol.
5. Padecer enfermedad médica de consideración que impida la realización del tratamiento psicológico.
6. Recibir otro tratamiento psicológico mientras dure el estudio.
7. En el caso de estar recibiendo tratamiento farmacológico, incremento de dosis y/o cambio del tipo de medicación.

El investigador responsable se pondrá en contacto con usted una vez finalizada esta primera fase para indicarle su inclusión en el estudio y las indicaciones para participar en la segunda fase del estudio.

Beneficios/riesgos:

El beneficio para los pacientes será un seguimiento sobre su enfermedad más constante, de forma que cualquier problema será más rápidamente detectado con lo que se remitirá a recibir el tratamiento más adecuado.
No existen riesgos en la realización de estudio.

Participación voluntaria:

Su participación en el estudio es enteramente voluntaria. Usted decide si quiere participar o no. Incluso si decide participar, puede retirarse del estudio en cualquier momento sin tener que dar explicaciones. En ningún caso esto afectará su atención médica posterior.

Confidencialidad:

El estudio se llevará a cabo siguiendo las normas deontológicas reconocidas por la Declaración de Helsinki (52ª Asamblea General Edimburgo, Escocia, Octubre 2000),

las Normas de Buena Práctica Clínica y cumpliendo la legislación vigente y la normativa legal vigente española que regula la investigación clínica en humanos (Real Decreto 1720/2007 que desarrolla la ley orgánica 15/99 y Ley 14/2007 de Investigación Biomédica).
Los datos serán protegidos de usos no permitidos por personas ajenas a la investigación y se respetará la confidencialidad de los mismos de acuerdo a la Ley Orgánica 15/1999, de 13 de diciembre, sobre la Protección de Datos de Carácter Personal y la ley 41/2002, de 14 de noviembre, ley básica reguladora de la autonomía del paciente y de derechos y obligaciones en materia de información y documentación clínica. Por tanto, la información generada en este ensayo será considerada estrictamente confidencial, entre las partes participantes.

Revisión Ética:

Un comité ético independiente ha revisado los objetivos y características del estudio y ha dado su aprobación favorable.

Preguntas/Información:

Si usted o su familia tienen alguna pregunta con respecto al estudio puede contactar con el profesional de su centro de salud o bien con el Investigador Principal.

Si precisa más información, por favor, pregunte en su centro de salud o a:

Dra. Cristina Botella Arbona
Teléfono 964387650

Appendix 6. Patient information document (researcher)

DISEÑO, DESARROLLO Y PUESTA A PRUEBA DE UN PROTOCOLO DE TRATAMIENTO TRANSDIAGNÓSTICO PARA LOS TRASTORNOS EMOCIONALES ADMINISTRADO ONLINE

Hoja de información al paciente (presentada por evaluadores)

INFORMACION PARA EL PACIENTE

Apreciado Sr./Sra.:

Antes de confirmar su participación en el estudio es importante que entienda en qué consiste. Por favor, lea detenidamente este documento y haga todas las preguntas que le puedan surgir:

Objetivo del estudio:

El objetivo principal de este estudio es desarrollar un programa de psicoterapia aplicada a través de Internet para el tratamiento de los trastornos emocionales (Trastorno depresivo mayor, trastorno de ansiedad generalizada, trastorno de pánico, agorafobia, trastorno de ansiedad social y trastorno obsesivo-compulsivo) y evaluar su eficacia.

Desarrollo del estudio:

En una primera fase del estudio se evaluará si los pacientes pueden participar o no en el mismo, aquellos pacientes que puedan participar en el estudio (fase 2) serán adscritos a una de estas dos condiciones:

a) Tratamiento habitual (el tratamiento psiquiátrico y/o psicológico que se administre de forma regular en el centro de salud).

   El tratamiento habitual consistirá en el tratamiento psiquiátrico y/o psicológico de referencia más adecuado a la problemática de cada paciente, y será administrado por un especialista del ámbito clínico (psiquiatra y/o psicólogo clínico) en el centro de salud mental.

b) Protocolo de tratamiento transdiagnóstico aplicado online.

   El tratamiento transdiagnóstico aplicado online consistirá en un programa vía internet e interactivo que el paciente puede realizar desde su casa compuesto por un total de 12 módulos de periodicidad semanal. Estos distintos módulos o componentes terapéuticos tienen como objetivo fundamental: 1) incrementar la conciencia emocional; 2) facilitar la flexibilidad cognitiva; 3) identificar patrones de evitación comportamental y emocional; y; 4) promover la exposición interoceptiva y situacional.

Es posible que, de forma paralela a este estudio, se realicen grupos de discusión formados por los pacientes participantes en el mismo, cuyo contenido será transcrito y analizado, con el objetivo de identificar las barreras y dificultades del uso del programa de psicoterapia. Al ser una posibilidad al margen del estudio, si se diera la oportunidad, se solicitaría la firma de un nuevo consentimiento informado

Participantes:

Los participantes de este estudio serán personas diagnosticadas de trastornos emocionales (trastornos de ansiedad, trastornos depresivos).
Los participantes deben tener una edad mínima de 18 años y disponer de acceso a internet desde su domicilio.

Participación del paciente en el estudio:

En esta segunda fase del estudio se recogerá la siguiente información:

- Variables sociodemográficas, como género, edad, estado civil, nivel educativo, socioeconómico, y ocupación.
- Variables psicológicas:
  a) Entrevista diagnóstica psiquiátrica.
  b) Entrevista de utilización de servicios médicos

Beneficios/riesgos:

El beneficio para los pacientes por su participación en el estudio será un seguimiento sobre su enfermedad más constante, de forma que cualquier problema será más rápidamente detectado con lo que se remitirá a recibir el tratamiento más adecuado.
No existen riesgos en la realización de estudio.

Participación voluntaria:

Su participación en el estudio es enteramente voluntaria. Usted decide si quiere participar o no. Incluso si decide participar, puede retirarse del estudio en cualquier momento sin tener que dar explicaciones. En ningún caso esto afectará su atención médica posterior.

Confidencialidad:

El estudio se llevará a cabo siguiendo las normas deontológicas reconocidas por la Declaración de Helsinki (52ª Asamblea General Edimburgo, Escocia, Octubre 2000), las Normas de Buena Práctica Clínica y cumpliendo la legislación vigente y la normativa legal vigente española que regula la investigación clínica en humanos (Real Decreto 1720/2007 que desarrolla la ley orgánica 15/99 y Ley 14/2007 de Investigación Biomédica).
Los datos serán protegidos de usos no permitidos por personas ajenas a la investigación y se respetará la confidencialidad de los mismos de acuerdo a la Ley Orgánica 15/1999, de 13 de diciembre, sobre la Protección de Datos de Carácter Personal y la ley 41/2002, de 14 de noviembre, ley básica reguladora de la autonomía del paciente y de derechos y obligaciones en materia de información y documentación clínica. Por tanto, la información generada en este ensayo será considerada estrictamente confidencial, entre las partes participantes.

Revisión Ética:

Un Comité Ético Independiente ha revisado los objetivos y características del estudio y ha dado su aprobación favorable.

Preguntas/Información:

Si usted o su familia tienen alguna pregunta con respecto al estudio puede contactar con el profesional de su centro de salud o bien con el Investigador Principal.

Si precisa más información, por favor, pregunte en su centro de salud o a:

Dra. Cristina Botella Arbona
Teléfono 964387650

Appendix 7. Informed consent

CONSENTIMIENTO INFORMADO

Título del PROYECTO: DISEÑO, DESARROLLO Y PUESTA A PRUEBA DE UN PROTOCOLO DE TRATAMIENTO TRANSDIAGNÓSTICO PARA LOS TRASTORNOS EMOCIONALES ADMINISTRADO ON-LINE.

Yo, _____
(Nombre y apellidos del participante)

He leído la hoja de información que se me ha entregado.

He podido hacer preguntas sobre el estudio y he recibido suficiente información sobre el mismo.

He hablado con: _____

(Nombre del investigador/médico)

Comprendo que mi participación es voluntaria.

Comprendo que puedo retirarme del estudio:

1) Cuando quiera.
2) Sin tener que dar explicaciones.
3) Sin que esto repercuta en mis cuidados médicos.

Presto libremente mi conformidad para participar en el estudio.

Deseo ser informado sobre los resultados del estudio: sí no (marque lo que proceda)

Doy mi conformidad para que mis datos clínicos sean revisados por personal ajeno al centro, para los fines del estudio, y soy consciente de que este consentimiento es revocable.

He recibido una copia firmada de este Consentimiento Informado.

Firma del participante: _____

Fecha: _____

He explicado la naturaleza y el propósito del estudio al paciente mencionado

Firma del Investigador: _____

Fecha: _____

Appendix 8. Support protocol

PROTOCOLO DE APOYO POR PARTE DEL TERAPEUTA

A LA CONDICIÓN DE TRATAMIENTO TRANSDIAGNÓSTICO ONLINE

1. **2 SMSs DE APOYO A LA SEMANA**

2. **UNA LLAMADA DE TELÉFONO A LA SEMANA DE UN MÁXIMO DE 10 MINUTOS: EL CONTENIDO DE LA LLAMADA VARIARÁ DEPENDIENDO DE CÓMO VAYAN AVANZANDO EN LOS MÓDULOS.**

    1. Si en una semana **no ha cambiado de módulo** (*ANIMAR*)
    2. Si en una semana **realiza un módulo** (*REFORZAR*)
    3. Si hace **dos módulos en una semana**. (*REFORZAR Y FRENAR*)
    4. Si en una semana **hace más de dos módulos**. (*¡¡¡FRENAR!!!*)

Estructura de las llamadas:

a) Saludar y preguntar si ha tenido algún problema.
b) Resolver dudas concretas sobre el uso del protocolo (p. ej., no entiendo cómo tengo que hacer la tarea "registro de conductas impulsadas por las emociones"), si las hubiera.
b) 1 (animar), 2 (reforzar), 3 (reforzar y frenar) o 4 (¡¡frenar!!):

- 1 (animar): *Te animo a que sigas adelante, recuerda que aunque puedes hacer el programa a tu ritmo, sacarás el máximo beneficio realizando un módulo a la semana.*

- 2 (reforzar): ¡*Muy bien! Estás avanzando a buen ritmo, lo ideal es un módulo a la semana, recuerda que es muy importante realizar las tareas que te propone el programa"*

- 3 (reforzar y frenar): *Bien, has finalizado otro módulo. Vas algo deprisa. No sigas avanzando y repasa las tareas que te ha propuesto el programa. Recuerda que lo mejor es que realices un módulo por semana.*

- 4 (frenar): *Estas avanzando demasiado deprisa, recuerda que para que las estrategias que te propone Sonreír es Divertido se conviertan en habilidades es muy importante que vayas realizando las tareas y practiques mucho por lo recomendable es que realices un módulo semanalmente.*

c) Recordar/animar a que repasen el contenido de los módulos si lo consideran necesario.
d) Recordar la importancia de realizar las tareas.

Esquema orientativo del apoyo recibido a lo largo de la semana:

Lunes	Martes	Miércoles	Jueves	Viernes	Sábado	Domingo
		SMS	Teléfono			SMS

*Importante: todas las llamadas, así como su duración exacta (minutos y segundos) deben registrarse SIEMPRE en el documento Excel correspondiente.