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The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents (UP-A) applied to prevent and/or reduce emotional problems and improve psychological wellbeing in adolescents

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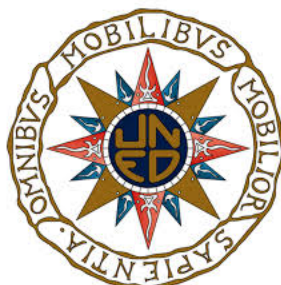
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TESIS DOCTORAL/DOCTORAL THESIS [SHORT VERSION/VERSIÓN CORTA]

Programa de Doctorado en Psicología de la Salud

The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents (UP-A) applied to prevent and/or reduce emotional problems and improve psychological wellbeing in adolescents

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FINANCIÓN DE LA TESIS DOCTORAL

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RESUMEN

APLICACIÓN DEL *UNIFIED PROTOCOL FOR TRANSDIAGNOSTIC TREATMENT OF EMOTIONAL DISORDERS IN ADOLESCENTS (UP-A)* PARA LA PREVENCIÓN Y/O REDUCCIÓN DE PROBLEMAS EMOCIONALES Y LA MEJORA DEL BIENESTAR PSICOLÓGICO EN POBLACIÓN ADOLESCENTE

La ansiedad y la depresión son problemas comunes y altamente comórbidos en adultos, niños y adolescentes que implican un sufrimiento y deterioro significativo en la vida de la persona que los padece, así como altos costes económicos para las familias y la sociedad. Sin embargo, solo un número limitado de personas que sufren trastornos de ansiedad y depresión tienen acceso a servicios de salud mental. La terapia cognitivo-conductual transdiagnóstica (TCC-T), un enfoque que aborda los factores de riesgo y de mantenimiento centrales asociados tanto con la ansiedad como con la depresión, podría reducir la prevalencia y la carga social asociadas con el tratamiento de estos trastornos.

La presente tesis doctoral tuvo dos objetivos principales. En primer lugar, investigar la eficacia de la TCC-T en adultos, niños y adolescentes con trastornos de ansiedad y depresión (Estudio I). En segundo lugar, investigar la eficacia de una intervención preventiva universal basada en la TCC-T en reducir y prevenir los síntomas de ansiedad y depresión en población adolescente (Estudios II y III).

El Estudio I consistió en la realización de un meta-análisis que incluyó tanto ensayos controlados aleatorizados como ensayos no controlados caracterizados por haber aplicado la TCC-T para el tratamiento de la ansiedad y la depresión. A diferencia de las revisiones y meta-análisis previos en este campo, solo aquellos estudios que aplicaron protocolos basados en el marco teórico del transdiagnóstico fueron incluidos. A través de la realización de una búsqueda sistemática en diversas bases de datos se encontraron 48 estudios (21 ensayos controlados aleatorizados y 27 estudios no controlados), que incluían un total de 6291 participantes.

Los resultados incluyendo los estudios realizados con adultos mostraron tamaños del efecto grandes en relación con la reducción de síntomas de ansiedad y depresión. Estos elevados tamaños del efecto se mantuvieron en el seguimiento. Además, los análisis preliminares con muestra de niños y adolescentes mostraron tamaños del efecto medios en relación con los síntomas de ansiedad y depresión. No se encontraron diferencias significativas entre la TCC-T y la terapia cognitivo-conductual (TCC) orientada a trastornos

específicos. Con respecto a los moderadores de la eficacia del tratamiento, encontramos diferencias significativas en la reducción de los síntomas de ansiedad y/o depresión en relación con las siguientes variables: el instrumento de diagnóstico aplicado, la resolución de problemas como un componente de tratamiento, los tratamientos por internet *versus* los tratamientos a cara a cara y, por último, el número de sesiones de tratamiento.

En los Estudios II y III, el Protocolo Unificado para el Tratamiento Transdiagnóstico de los Trastornos Emocionales en Adolescentes (UP-A) fue adaptado por primera vez para ser aplicado como un programa de prevención universal. El programa incluía un total de nueve sesiones de 55 minutos de duración cada una. En ambos estudios, las medidas de resultado primarias evaluaron los síntomas de ansiedad y depresión, mientras que las medidas de resultado secundarias investigaron los cambios en una amplia gama de variables incluyendo el afecto negativo y positivo, la sensibilidad a la ansiedad, la evitación emocional, la autoestima, la satisfacción con la vida y el ajuste escolar.

En el Estudio II, las medidas de resultado primarias y secundarias descritas anteriormente fueron evaluadas en el pretratamiento, en el post-tratamiento y en el seguimiento a los 3 meses. Se encontró una disminución inesperada de los niveles de ansiedad y depresión desde el pretratamiento hasta el post-tratamiento y el seguimiento en ambos grupos, aunque esta disminución fue (no significativamente) más elevada en el grupo que recibió el UP-A. Los análisis de subgrupos se centraron en los adolescentes que presentaban mayores síntomas emocionales y excluyeron a aquellos adolescentes de ambos grupos que recibieron terapia psicológica recientemente. Dichos análisis mostraron una disminución de los síntomas de ansiedad y depresión significativamente mayor en el grupo UP-A en comparación con el grupo control lista de espera.

En el Estudio III, los 28 adolescentes asignados aleatoriamente al grupo control de lista de espera en el Estudio II participaron en un ensayo no controlado. Los resultados revelaron disminuciones en los síntomas de ansiedad, en la interferencia de la ansiedad y la depresión, así como en la severidad media de los problemas principales identificados por los adolescentes. Además, los participantes informaron estar bastante satisfechos con la intervención.

Los tres estudios incluidos en esta tesis doctoral proporcionan una mayor comprensión de la efectividad de la TCC-T en la reducción de los síntomas de ansiedad y depresión en adultos, niños y adolescentes. Se necesitan futuro estudios con muestras más amplias para estimar la efectividad de la versión española del UP-A adaptada como un programa de prevención universal de los trastornos de ansiedad y depresión.

ABSTRACT

Anxiety and depression are common, highly comorbid conditions in adults, children and adolescents that involve significant impairment, individual suffering and high costs to families and society. However, only a limited number of individuals experiencing anxiety and depression disorders receive mental health services. Transdiagnostic cognitive-behavior therapy (T-CBT), an approach that targets core dysfunctions associated with both anxiety and depression, could reduce the prevalence and the burden associated with the treatment of these disorders.

The current thesis had two main aims. First, it investigated the efficacy of T-CBT in adults, children and adolescents with anxiety and depressive disorders (Study I). Second, it investigated the efficacy of a T-CBT universal preventive intervention on anxiety and depression symptoms in adolescents (Studies II and III).

Study I involved a meta-analysis of randomized controlled trials and uncontrolled trials applying T-CBT for the treatment of anxiety and depression. As opposed to previous reviews and meta-analyses, only studies employing transdiagnostic theory-based protocols were included in this study. The systematic search resulted in 48 studies (21 randomized controlled trials and 27 uncontrolled studies), which included 6291 participants.

Results within the adult population showed large overall effect sizes on anxiety and depression that were stable at follow up. Additionally, preliminary analyses with children and adolescents showed medium effect sizes on anxiety and depression. No significant differences between T-CBT and disorder-specific cognitive-behavior therapy (DS-CBT) were found. Regarding moderators of treatment efficacy, we found significant differences for anxiety and/or depression symptoms associated with the following variables: the diagnostic measure applied, using problem solving as treatment component, internet-delivered *vs.* face-to-face treatments, and number of treatment sessions.

In Studies II and III, the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents (UP-A) was adapted to be a universal preventive intervention program for the first time, which included nine 55-minute sessions. In both studies, the primary outcome measures assessed anxiety and depression symptoms, whilst the secondary outcome measures investigated changes in a broad range of variables including negative and positive affect, anxiety sensitivity, emotional avoidance, self-esteem, life satisfaction, and school adjustment.

In Study II, the primary and secondary outcome measures described above were assessed at pre-treatment, post-treatment, and 3- month follow up. An unexpected decline

in anxiety and depression levels from pre- to post-treatment and follow-up was found in both groups, although this decline was (non-significantly) stronger in the UP-A group. The subgroup analyses focused on adolescents with greater emotional symptom severity and excluded those in both groups who recently received psychological therapy. The subgroup analyses revealed a significantly greater decrease in anxiety and depression symptoms in the UP-A group compared to the waitlist control group.

In Study III, 28 adolescents randomized to the waitlist control group in Study II participated in an uncontrolled trial. Results revealed declines in anxiety symptoms, interference of anxiety and depression, and top problems' mean severity. Furthermore, moderate to high participant satisfaction was indicated.

The three studies included in this doctoral thesis provide further understanding of the overall effectiveness of T-CBT in reducing anxiety and depression symptoms in adults, children, and adolescents. Future trials with larger samples are necessary to estimate the effect of the Spanish UP-A adapted as a universal anxiety and depression prevention program.

CHAPTER I. INTRODUCTION

1. Emotional disorders in adults and youth

Emotional disorders are a group of disorders inclusive of all the anxiety and mood (depressive) disorders in the DSM-5 (American Psychiatric Association, 2013), such as generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, specific phobia, major depressive disorder and persistent major disorder as well as other related disorders such as obsessive-compulsive disorder or post-traumatic stress disorder. In the A main characteristic common within emotional disorders is the use of maladaptive emotion regulation strategies that contribute to the maintenance of symptoms (Barlow et al., 2011).

Emotional disorders are highly prevalent conditions in adults, adolescents, and children associated with significant impairment in everyday life. Additionally, these disorders have become a global health problem due to their associated costs. In the next sections we will review the prevalence, comorbidity, and consequences of emotional disorders regarding both adults and youth.

1.1. Prevalence of emotional disorders

The field of psychology has been faced with challenges in building epidemiological knowledge about mental disorders partly because of disagreements about when to consider the presence of a disorder, and partly because of the difficulties in establishing reliable measurements (Eaton et al., 2008).

Additionally, there has been little agreement regarding the time frame to use in reporting data. Some authors report the proportion of participants who meet the criteria for a mental disorder at some point in time within the past six months or 12 months (usually 12 months prevalence), while others report participants who meet the criteria at the time of assessment. Furthermore, others report the proportion of participants who meet the criteria at any time in their life up to the participant's age at the time of the interview (lifetime prevalence) (Kessler, Petukhova, Sampson, Zaslavsky, & Wittchen, 2012). In the next sections we will review prevalence of anxiety and depressive disorders regarding adults, children, and adolescents.

1.1.1. Prevalence of emotional disorders in adults

First, we will review several epidemiological studies that assessed the prevalence of mental disorders in adults and we will pay special attention to the results regarding prevalence of anxiety and depressive disorders. In Table 1, a summary of the reviewed studies' results can be found.

Studies including United States of America (USA), European and worldwide samples

Kessler and colleagues study

Kessler et al. (Kessler et al., 2005a; Kessler, Chiu, Demler, & Walters, 2005; Kessler et al., 2012) conducted a well-known representative face-to-face household survey that was part of the National Comorbidity Survey Replication; a survey of English-speaking household residents aged 18 years and older in the USA.

The survey included face-to-face interviews carried out by professional interviewers who used the fully structured World Mental Health Survey version of the Composite International Diagnostic Interview (WMH-CIDI) (Kessler & Üstün, 2004). The WMH-CIDI is an instrument that assesses the prevalence of mental disorders according to both the Diagnostic and Statistical Manual of Mental Disorders-Forth Edition (DSM-IV; American Psychiatric Association, 2000), and the International Classification of Diseases 10th revision criteria (ICD-10) (World Health Organization, 1993). Kessler et al.' survey was conducted in 2 parts: Part 1[1] included 9,282 participants and Part 2[2] included a total of 5,692 participants (it was administered to all Part 1 respondents who met lifetime criteria for any disorder plus a probability sample of other respondents).

Results indicated the following lifetime prevalence estimates regarding emotional disorders: any anxiety disorder (28.8%), any mood disorder (20.8%), major depressive disorder (16.6%), specific phobia (12.5%), and social phobia (12.1%).

In relation to 12-month prevalence estimates results were the following: any anxiety disorder (18.1%), any mood disorder (9.5%), specific phobia (8.7%), social phobia (6.8%),

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[1] Part 1 included assessment of the following disorders: anxiety disorders (panic disorder, generalized anxiety disorder, agoraphobia without panic disorder, specific phobia, social phobia), mood disorders (major depressive disorder, dysthymia, bipolar disorder I or II), an impulse control disorder (intermittent explosive disorder), and two substance use disorders (alcohol abuse, alcohol dependence)

[2] Part 2 included questions about risk factors and consequences related to mental disorders as well as a diagnostic assessment of the following disorders: posttraumatic stress disorder, obsessive-compulsive disorder, drug abuse, drug dependence and four disorders that require onset of symptoms in childhood (separation anxiety disorder, oppositional-defiant disorder, conduct disorder, and attention-deficit/hyperactivity disorder).

major depressive disorder (6.7%), posttraumatic stress disorder (3.5%), and generalized anxiety disorder (3.1%).

Among participants with a disorder, 22.3% were classified as serious, 37.3% as moderate, and 40.4% as mild. Mood disorders (especially bipolar disorder) had the highest percentage of serious classifications (45%), whereas anxiety disorders demonstrated the lowest serious classifications (22.8%). Consistent with the literature, women had a significantly higher life-time risk than men with respect to anxiety and mood disorders.

Alonso and colleagues 2004 study: Results of the ESEMeD European project

One of the most important papers to date reporting on the prevalence of mental disorders in Europe was published in 2004, entitled "Prevalence of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project" (Alonso et al., 2004). This study included data from six European countries: Belgium, France, Germany, Italy, the Netherlands and Spain.

As in Kessler et al. previously reviewed study, the WMH-CIDI (Alonso et al., 2002) was used to assess the prevalence of mental disorders. Additionally, Alonso et al (2004) calibrated the results of this diagnostic interview by a clinical reappraisal using the Axis 1 Structured Clinical Interview for DSM-IV, known as SCID-I (First, Spitzer, Gibbon, & Williams, 1996).

The sample included 21,425 non-institutionalized adults aged 18 years or older (mean age: 47 years). In relation to the results, one in four of the respondents (25%) reported a lifetime presence of any mental disorder with almost 1 in 10 (9.6%) reporting experiencing a mental disorder in the past 12 months.

Second, the following percentages of participants reported a lifetime history of the following groups of disorders: any mood disorder (14%), any anxiety disorder (13.6%), any alcohol disorder (5.2%). As for specific disorders, percentages were the following regarding emotional disorders: Major depression (12.8%), specific phobia (7.7%), dysthymia (4.1%), generalized anxiety disorder (2.8%), social phobia (2.4%), posttraumatic stress disorder (1.9%), panic disorder (2.1%) and agoraphobia (0.9%),

Third, the following percentages of respondents met the criteria for the following disorders within the 12 months preceding the interview (12-month prevalence): any anxiety disorder (6.4%), any mood disorder (4.2%), and any alcohol disorder (1.0%).

Regarding specific disorders, percentages for anxiety and depressive disorders included: major depression (3.9%), specific phobia (3.5%), social phobia (1.2%), dysthymia (1.1%), generalized anxiety disorder (1%), posttraumatic stress disorder (0.9%), panic disorder (0.8%) and agoraphobia (0.4%).

Together, the findings of this study point out that emotional disorders are common in European citizens: 14% of respondents reported a lifetime history of any mood disorder and a very similar percentage (13.6%) was found regarding any anxiety disorder. As for specific disorders, both for lifetime occurrence and for 12-month occurrence, major depression was the most common psychiatric disorder, followed by specific phobia.

In relation to gender differences, women were almost twice as likely to have had any mental disorder 12 months preceding the interview as well as more likely to have mood and anxiety disorders. By contrast, women were less likely to have alcohol disorders.

Kessler and colleagues 2007 worldwide study

An additional Kessler et al. (2007) paper reports the main results of the World Health Organization World Mental Health Surveys that were conducted in 17 countries in Africa, Asia, the Americas, Europe, and the Middle East.

Surveys included face-to-face interviews carried out by trained interviewers, which included 85,052 adults. Similar to previously reviewed studies, they used the WMH-CIDI (Kessler & Üstün, 2004) to assess the prevalence of mental disorders according to DSM-IV and ICD-10 criteria.

The Part I interview schedule, completed by all respondents, assessed core diagnoses (anxiety disorders, mood disorders, impulse control disorders and substance use disorders). Alternatively, Part ll included respondents who met lifetime criteria for any diagnosis plus a probability sub-sample of other Part I respondents. In part II a range of disorders that require childhood onset and a wide range of correlates were assessed.

Lifetime prevalence estimates regarding a group of disorders were assessed, including: anxiety disorders (4.8-31%), mood disorders (3.3-21.4%), impulse control disorders (0.3-25.0%), substance use disorders (1.3-15.0%), and any disorder (12.0-47.4%). Anxiety disorders were the most prevalent in 10 out of the 17 countries, and mood disorders in all but one country.

Lastly, age-of-onset distributions for mood disorders, generalized anxiety disorder, panic disorder, and post-traumatic disorder followed a similar path; prevalence was consistently low until the early teens, at which time, increases were found through late middle age, with a more gradual increase thereafter.

Studies only including Spanish samples

Haro and colleagues 2006: Results of the ESEMeD study in Spain

Haro et al. (2006) reported their results of the ESEMeD-Spain project, an epidemiological study about mental disorders in Spain. Again, the diagnostic interview used was the WMH-CIDI (Alonso et al., 2002).

The sample included 5,473 non-institutionalized adults aged 18 years or older (mean age: 45.64 years), who were inhabitants from Spain. In relation to the results, 19.46% of respondents reported a lifetime presence of any mental disorder and 8.48% reported having experienced a mental disorder in the past 12 months.

Second, the following percentages of participants reported a lifetime history of the following disorders: any mood disorder (11.47%), any anxiety disorder (9.39%), any alcohol disorder (3.60%). As for specific disorders, percentages were the following for emotional disorders: Major depression (10.55%), specific phobia (4.52%), dysthymia (3.65%), post-traumatic stress disorder (1.95%), generalized anxiety disorder (1.89%), panic disorder (1.70%), social phobia (1.17%), and agoraphobia (0.62%).

Third, as far as 12-month prevalence was concerned, the following percentages of respondents met the criteria for the following disorders within the 12 months preceding the interview: any anxiety disorder (6.2%), any mood disorder (4.37%), and any alcohol disorder (0.69%). Regarding specific disorders percentages were the following for anxiety and depressive disorders: major depression (3.96%), specific phobia (3.60%), dysthymia (1.49%), social phobia (0.60%), generalized anxiety disorder (0.50%), posttraumatic stress disorder (0.50%), panic disorder (0.6%), and agoraphobia (0.3%).

In line with the ESEMeD European study, together the findings of this study point out that emotional disorders are common in Spanish citizens: 11.5% of respondents reported a lifetime history of any mood disorder, and a quite similar percentage (9.39%) was found for any anxiety disorder. Regarding specific disorders, both for lifetime occurrence and for 12-month occurrence, major depression was the most common psychiatric disorder, followed by specific phobia and dysthymia.

Similar to the ESEMeD study including six European countries, women were more than twice as likely to have mood and anxiety disorders compared to men. By contrast, women they were less likely to have alcohol disorders.

Roca and colleagues 2009 prevalence study

Roca et al. (2009) conducted a study to estimate the prevalence and comorbidity of the most common psychiatric disorders in primary care in Spain. The authors selected a

total of 2,000 general practitioners and each of them was asked to recruit four patients that met the inclusion criteria (18 years old or over and consulting their general practitioner for any illness complaint).

The measure used to diagnose psychiatric disorders was the Primary Care Evaluation of Mental Disorders (PRIME-MD), an instrument specifically designed for the evaluation of mental disorders in primary care developed by Spitzer et al. (Spitzer, Kroenke, Williams, & Patient Health Questionnaire Primary Care Study Group, 1999). This instrument was adapted to Spanish by Baca et al. (1999). This instrument assesses the five most prevalent groups of disorders (depressive disorders, anxiety disorders, somatoform disorders, and alcohol- and eating-related disorders) according to DSM-IV criteria but was modified for use in primary care.

The study included a sample of 7,936 adult primary care patients (mean age = 48.6) distributed throughout the country. Results showed that 53.6% of the sample presented with one or more mental disorders, and that the following percentages of participants presented: any mood disorder (35.8%), any somatoform disorders (28.8%), any anxiety disorder (25.6%), and any eating-related disorder (2%).

Regarding specific disorders, emotional disorders had the following prevalence rates: major depression (29%), dysthymia (14.6%), generalized anxiety disorder (11.7%), non-specified anxiety disorder (11.2%) and depressive disorder due to physical disorder, medication, or drugs (7%).

Serrano-Blanco and colleagues 2010 prevalence study

Serrano-Blanco et al. (2010) conducted an epidemiological study to estimate the lifetime and 12-month prevalence of mental disorders in primary care centers of Cataluña (Spain), using structured clinical interviews administered by trained clinical psychologists. The sample was comprised of 3,815 patients (mean age = 54.3) interviewed while attending primary care for a medical visit.

Prevalence of psychiatric disorders was assessed with: 1) the Spanish version of the Structured Clinical Interview for DSM-IV Axis I Disorders, Research Version (SCID-RV)[3] (First et al., 1996) and, 2) the Mini Neuropsychiatric Diagnostic Interview (MINI)[4] (Ferrando et al., 1998; Sheehan et al., 1998).

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[3] The SICID-RV assesses the following disorders: major depression, dysthymia and anxiety disorders (excluding obsessive-compulsive disorder).
[4] The MINI assesses the following disorders: manic/hypomanic episodes, obsessive-compulsive disorder, substance and alcohol use disorders, anorexia nervosa and bulimia nervosa.

Results showed that 45.1% of respondents reported at least one life-time mental disorder and 31.2% reported at least one mental disorder in the previous 12 months. Additionally, 31.8% participants reported a lifetime history of any mood disorder and 20.84% of any anxiety disorder. As for specific disorders, percentages were the following regarding lifetime prevalence: Major depression (29.91%), specific phobia (7.05%), panic disorder (8.81%), social phobia (1.99%), and agoraphobia (3.97%).

Second, as far as 12-month prevalence was concerned, the following percentages of respondents met the criteria for the following disorders: any anxiety disorder (18.49%), any mood disorder (13.41%), any eating disorder (0.64%), and any substance abuse disorder (0.61%). Regarding specific disorders percentages were the following for the most prevalent disorders: major depression (9.60%), panic disorder (7.00%), specific phobia (6.65%), and generalized anxiety disorder (3.80%).

Furthermore, there was a high comorbidity between mood and anxiety disorders, as well as between mental disorders and some chronic physical conditions. Lastly, similarly to previous epidemiological studies, women were more likely to have mood and anxiety disorders, and less likely to have substance use or abuse disorders.

Conclusions on prevalence of emotional disorders in adults

Taking all of the reviewed studies into account, we can conclude that a high proportion of adults in the USA, Europe and Spain meet the criteria for one or more mental disorders at some point in their life. Specifically, according to Kessler et al. 2007, approximately half of the population (47-55%) will eventually have a mental disorder in six of the assessed countries (Colombia, France, New Zealand, South Africa, Ukraine, United States), approximately one-third (30-43%) in six other countries (Belgium, Germany, Israel, Lebanon, Mexico, the Netherlands), and approximately one-fourth (24-29%) in three others (Italy, Japan, Spain).

Taking only the European Union (EU) into account, Wittchen et al. (2011) estimated that each year, 38.2% of the total EU population (approximately, 164.8 million people) suffers from at least one of the 27 mental disorders covered, with the most prevalent disorders being anxiety disorders (69.1 million), unipolar depression (30.3 million) and insomnia (29.1 million). Moreover, one of third of the EU population during any given 12-month period suffers from a mental disorder, most of which are not receiving any treatment, with anxiety disorders being the most common class of mental disorders (Wittchen et al., 2011).

Reviewed studies had several general limitations identified by several of the authors (Kessler et al., 2005a; Kessler et al., 2005b; Kessler et al., 2007). Most of the studies focused on the general population, while several population segments remained underrepresented, including: the homeless, those in institutions, and those who did not speak the official language of the country in which the survey took place. Additionally, prevalence data could have been underreported by respondents of these surveys because of the well-known reluctance to admit mental illness. Furthermore, the studies were almost exclusively based on the DSM-IV criteria and, therefore, only counted people as having mental disorders when all criteria were met, including the mandatory criteria of duration, severity, and dysfunction in psychosocial functioning and disability. However, it is a well-known fact that subthreshold symptoms can be very impairing as well.

Table 1. Prevalence of anxiety disorders and depressive disorders in the context of other mental disorders according to epidemiological studies. Adults sample.

	Study	Procedure	Diagnostic measure	Sample	12-month prevalence	Lifetime prevalence
USA	**Kessler et al., 2005a; Kessler, et al., 2005b; Kessler et al., 2012**	Face-to-face interviews conducted in 2 parts	Structured Interview: WMH-CIDI	Part 1: *n* = 9,282 Part 2: *n* = 5,692	Group of disorders: Any disorder = 26.2%; any ANX disorder = 18.1%; any mood disorder = 9.5%; any impulse control disorder = 8.9%; any substance use disorder = 3.8%. Specific disorders: SP = 8.7%; Soc.P =6.8%; MDD = 6.7%; ADHD = 4.1%; PTSD = 3.5%; GAD = 3.1%; alcohol abuse = 3.1%.	Group of disorders: Any disorder = 46.4%; any ANX disorder = 28.8%; any impulse-control disorder = 24.8%; any mood disorder = 20.8%; any substance use disorder = 14.6%. Specific disorders: MDD = 16.6%; alcohol abuse = 13.2%; SP = 12.5%; Soc.P = 12.1%; conduct disorder = 9.5%; ODD = 8.5%.
Europe	**Alonso et al., 2004**	Face-to-face interviews	Structured Interview: WMH-CIDI	*n* = 21,425 52% women	Group of disorders: any ANX disorder = 6.4%; any mood disorder = 4.2%; and any alcohol disorder = 1.0%. Specific disorders: MDD = 3.9%; SP = 3.5%; Soc.P = 1.2%; DYS = 1.1%; GAD = 1%; PTSD = 0.9%; PD = 0.8%; alcohol abuse = 0.7%; AG = 0.4%; alcohol dependence = 0.3%.	Groups of disorders: Any mood disorder = 14%; any ANX disorder = 13.6%; any alcohol disorder = 5.2%. Specific disorders: MDD = 12.8%; SP = 7.7%; DYS = 4.1%; alcohol abuse = 4.1%; GAD = 2.8%; Soc.P = 2.4%; PTSD = 1.9%; PD =2.1%; alcohol dependence = 1.1%; AG = 0.9%,
Worldwide	**Kessler et al., 2007**	Face-to-face interviews conducted in 2 parts	Structured Interview: WMH-CIDI	*n*= 85,052		ANX disorders = 4.8-31%; mood disorders = 3.3-21.4%; impulse control disorders = 0.3-25.0%; substance use disorders = 1.3-15.0%; any disorder = 12.0-47.4%.
Spain	**Haro et al., 2006**	Face-to-face interviews	Structured Interview: WMH-CIDI	*n*= 5,473 55.76% women	Group of disorders: Any ANX disorder = 6.2%; any mood disorder = 4.37%; any alcohol disorder = 0.69%. Specific disorders: MDD = 3.96%; SP = 3.60%; DYS = 1.49%; Soc.P = 0.60%; GAD = 0.50%; PTSD = 0.50%; PD = 0.6%; AG = 0.3%; alcohol dependence = 0.1%.	Group of disorders: Any mood disorder = 11.47%; any ANX disorder = 9.39%; any alcohol disorder = 3.60%. Specific disorders: MDD = 10.55%; SP = 4.52%; DYS = 3.65%; alcohol abuse = 3.55%; PTSD = 1.95%; GAD = 1.89%; PD = 1.70%; Soc.P = 1.17%; AG = 0.62%; alcohol dependence = 0.57%.
	Roca et al., 2009	General practitioners recruited 4 patients each	PRIME-MD (self-report questionnaire + structured interview)	*n*= 7,936 61.7% women	[Prevalence at the time of assessment] Group of disorders: any mood disorder = 35.8%; any somatoform disorders = 28.8%; any ANX disorder = 25.6%; any eating-related disorder (2%). Specific disorders: non-specific somatoform disorder = 14.8%; DYS = 14.6%; multisomatoform disorder = 14%; GAD = 11.7%; non-specified ANX disorder = 11.2%; probable alcohol abuse or dependence = 9%; depressive	

				dsorder due to physical disorder, medication or drugs = 7%.	
Serrano-Blanco et al., 2010	Trained clinical psychologists did the interviews	Structured interviews: SCID-RV & MINI	*n*= 3,815 63% women	Group of disorders: Any disorder = 31.2%; any ANX disorder = 18.49%; any mood disorder = 13.41%; any eating disorder = 0.64%; any substance abuse disorder = 0.61%. Specific disorders: MDD = 9.60%; PD = 7%; SP = 6.65%; GAD = 3.80%.	Group of disorders: Any disorder = 45.1%; Any mood disorder = 31.80%; Any ANX disorder = 20.84%. Specific disorders: MDD = 29.91%; SP = 7.05%; PD = 8.81%; Soc.P = 1.99%; AG = 3.97%.

Note. ADHD = Attention-deficit/hyperactivity disorder; AG = agoraphobia; ANX = anxiety; DYS = dystimia; GAD = Generalized anxiety disorder; MDD = Major depressive disorder; MINI = The Mini Neuropsychiatric Diagnostic Interview; OCD = Obsessive compulsive disorder; ODD = Oppositional defiant disorder; Panic Disorder = PD; PRIME-MD =Primary Care Evaluation of Mental Disorders; PTSD = Posttraumatic stress disorder; SCID-RV = Structured Clinical Interview for DSM-IV Axis I Disorders, Research Version; Soc.P = Social Phobia; SP = Specific phobia; WMH-CIDI = World Mental Health Survey Version of the Composite Diagnostic Interview

1.1.2. Prevalence of emotional disorders in youth

Studying the prevalence rates of emotional symptoms in children and adolescents provides us with a better understanding of youth psychopathology and makes it possible to improve public health systems at the level of early detection, intervention and prevention (Ortuno-Sierra, Fonseca-Pedrero, Paíno, & Aritio-Solana, 2014). In this section we will review several epidemiological studies and a meta-analysis regarding prevalence of anxiety and depression in children and adolescents. In Table 2 a summary of the reviewed studies' results can be found.

Studies including USA samples

The National Comorbidity Survey Adolescent Supplement is an extension of the National Comorbidity Survey Replication reviewed in the previous section (Kessler et al. 2005 and 2007 studies), which assessed a broad range of DSM-IV disorders in a USA nationally representative sample of 10,123 youth aged 13–18 years (mean age = 15.2 years).

Merikangas et al. (2010) presented estimates of the lifetime prevalence of DSM-IV mental disorders of the National Comorbidity Survey Adolescent Supplement. Face-to-face interviews using the WMH-CIDI (Kessler & Üstün, 2004) took place with the adolescents, while at least one parent completed the self-report questionnaires assessing behavior disorders, depression, and dysthymia.

Life-time prevalence showed that anxiety disorders were the most common condition (31.9%), followed by behavior disorders (19.1%), mood disorders (14.3%), and substance use disorders (11.4%). In relation to specific disorders, the following percentages were obtained regarding emotional disorders: specific phobia (19.3%), major depressive disorder or dysthymia (11.75%), social phobia (9.1%), separation anxiety disorder (7.6%), posttraumatic stress disorder (5%), bipolar disorder (2.9%), agoraphobia (2.4%), panic disorder (2.3%) and generalized anxiety disorder (2.2%) (See Table 2).

Additionally, data from 6,483 pairs of adolescents and parents of in their sample was analyzed and focused on the prevalence and socio-demographic correlates of 12-month serious emotional disturbance within the last 12-months (Kessler et al., 2012). According to the Children's Global Assessment Scale (CGAS) (Shaffer et al., 1983), cases could have been categorized as serious (scores ≤50), moderate (scores 51-60) or mild (scores > 60). Results indicated that 18.8% of respondents with a disorder were serious cases whilst the rest were rated as either mild (58.2%) or moderate (22.9%). Overall, serious emotional disturbance was found among 8% of all adolescents. The highest proportions of those who

were rated serious were associated with oppositional-defiant disorder and conduct disorder followed by depression and panic disorder.

Next, we are going to review one of the most important studies to date on prevalence of mental disorders in children and adolescents, that is, the longitudinal community study conducted by Costello et al. and published in 2003 (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). A representative population sample of 1,420 children aged 9 to 13 years at intake were annually assessed for DSM-IV disorders until age 16 years. Children who were assessed had scored above a predetermined cutoff in the Child Behavior Cheklist (Achenbach & Edelbrock, 1983) completed by a parent as well as for 1 in 10 random sample of the rest of the original sample, who were also included in the assessment.

Parents and children of each family were interviewed separately using The Child and Adolescent Psychiatric Assessment (CAPA) interview (Angold et al., 1995). Regarding three-month prevalence of psychiatric disorder, 13.3% percent had any diagnosis, 2.4% had any anxiety disorder and 2.2% had any depressive disorder. Overall, results indicated that at any time 1 in 6 youth will have a psychiatric disorder and at least 1 in 3 will have 1 or more psychiatric disorders by age 16 years.

Lastly, the overall prevalence of any disorder was highest among 9- to 10-year-olds with very high rates of enuresis, attention-deficit/hyperactivity disorder, tic disorders and separation anxiety disorder. Conversely, the age of 12 was found to be the age at which many of the childhood disorders (e.g., separation anxiety disorder or enuresis) had almost disappeared.

Studies including worldwide and European samples

First of all, we are going to go through the meta-analysis of Polanczyk et al. (Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015) and then we will review the epidemiological study of Bálazs et al. (2013).

Polanczyk et al. (2015) used meta-analytical techniques to estimate the worldwide-pooled prevalence rates of any mental disorder in children and adolescents. They included 41 studies published from 1985 to 2012 which were conducted in 27 countries all over the world. Results showed the following worldwide-pooled prevalence of groups of mental disorders: any disorder (13.4%), any anxiety disorder (6.5%), any depressive disorder (2.6%), and any disruptive disorder (5.7%). As for specific disorders, prevalence rates were estimated as follows: oppositional defiant disorder (3.6%), attention-deficit hyperactivity disorder (3.4%), conduct disorder (2.1%) and major depressive disorder (1.3%).

The sample of Balázs et al. (2013) cross-sectional included 12,395 adolescents (mean age: 14.80) from 11 European countries, including Spain. The following self-report questionnaires were used[5]: Beck Depression Inventory-II (BDI-II) (Beck, Steer, Ball, & Ranieri, 1996), Zung Self-Rating Anxiety Scale (SAS) (Zung, 1971), Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997) and Paykel Suicide Scale (PSS) (Paykel, Myers, Lindenthal, & Tanner, 1974). Based on the BDI-II score, 60.3% adolescents were identified as non-depressed, 29.2% as sub-threshold-depressed, and 10.5% as depressed. Additionally, based on the SAS score, 62.2% were identified as non-anxious, 32.0% as subthreshold-anxious, and 5.8% as anxious. Overall, half of the adolescents in this study had current threshold and/or subthreshold-depression and/or anxiety.

Studies only including Spanish samples

Aláez-Fernández and colleagues 2000 prevalence study

Aláez-Fernández et al.'s study (Aláez-Fernández, Martínez-Arias, & Rodríguez-Sutil, 2000) included a sample of children and adolescents whose parents asked for psychological treatment in a Community Health Center in the city of Madrid (Spain) between years 1990 and 1996.

Their sample included 404 youth aged 0 to 18 years old (mean age = 9.77). Specifically, the following percentages of the sample were between these age ranges: 0-5 years (12.9%), 6-9 years (36.9%), 10-13 years (31.2%) and 14-18 years (19.1%).

According to diagnostic interviews, behavioral disorders were the most prevalent (23.0%), followed by depressive (14.6%), anxiety (13.3%), developmental (12.7%) and elimination (9.7%) disorders.

In children under 6 years of age (n = 52), depressive disorders were common (17.3%) but not anxiety disorders. Between 6 and 9 years (n = 149) percentages of anxiety disorders increased significantly (13.3%) whilst depressive disorders were still highly prevalent (11.5%). In the age group of 10-13 years (n = 126), anxiety disorders (17.4%) increased in prevalence. Lastly, between 14 and 18 years (n = 77), depressive (19.5%) and anxiety disorders (11.7%) were the most prevalent disorders along with behavior disorders (39%).

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[5] BDI-II score: depressed (≥20), subthreshold-depressed (<20 and being positive >0 on items assessing sadness or loss of pleasure) and nondepressed (all other scores); SAS score: anxious (≥ 60), subthreshold-anxious anxious (≥ 45 and < 60) and nonanxious (<45).

Ezpeleta and colleagues 2007 prevalence study

This study (Ezpeleta et al., 2007) assessed a group of children and adolescents over 3 years utilizing structured diagnostic interviews. The children came from two cohorts of children aged 13 (*n* = 79) and 9 (*n* = 72) at intake. The study took place in Badía del Vallés, a city in Cataluña (Spain) with a concentration of those with low socioeconomic levels, social problems and disadvantages.

Psychiatric disorders were identified with the Diagnostic Interview for Children and Adolescents-IV (DICA-IV). This interview covers the most frequent diagnostic categories according to DSM-IV, and was developed by Reich et al. (Reich, Leacock, & Shanfeld, 1997) and adapted and validated for the Spanish population by Ezpeleta et al. (1997). Both adolescents and parents were interviewed in person, separate from each other, and diagnoses from the last year were generated by combining the information from both respondents.

On the one hand, the 12-month prevalence of any anxiety disorder was 36.1% (for 9 years old), 21.4% (for 10 years old), 18.5% (for 11 years old), 27.8% (for 13 years old), 16.7% (for 14 years old) and 13.1% (for 15 years old). On the other hand, the presence of any depressive disorder was 1.4% (9 years old), 0% (10 years old), 1.5% (11 years old), 3.9% (13 years old), 14.1% (14 years old) and 5% (15 years old).

In summary, this study indicated surprisingly high levels of psychopathology: between 3 and 6 of every 10 preadolescents and between 3 and 5 of every 10 adolescents presented some mental disorder. However, these numbers should be interpreted with caution given the small sample and the fact that the assessed children and adolescents were likely to be living in adverse circumstances.

Fonseca and colleagues 2011 prevalence study

The sample of this study (Fonseca-Pedrero, Paino, Lemos-Giráldez, & Muñiz, 2011) was composed of a total of 1,319 students aged 14-17 years old (mean age = 15.70), attending 28 schools in Asturias (Spain).

The Strengths and Difficulties Questionnaire (SDQ) (García et al., 2000; Goodman, 1997) was used for screening behavioral and emotional symptoms, although it was modified to include 5 Likert answer options instead of the 3 included in the original version of the questionnaire.

A high percentage of participants reported some emotional and/or behavioral problems. Specifically, the results showed that the following percentages of adolescents reported the following problematic behaviors (the range depends on the specific item of the

subscale): emotional symptoms (11.6%-34.6%), behavioral problems (4.9%-25.7%), peer problems relationships (2.3%-16.5%) and hyperactivity (16.1%-47.1%).

Ortuño-Sierra and colleagues 2014 prevalence study

This study (Ortuno-Sierra et al., 2014) examined the prevalence of emotional and behavioral symptoms in a sample of 508 adolescents aged 11 to 18 years (mean age= 13.91).

Again, the Strengths and Difficulties Questionnaire (SDQ) (García et al., 2000; Goodman, 1997) was used to screen for behavioral and emotional symptoms[6].

The following percentages of adolescents reported problematic behaviors (range depends on the specific item of the subscale): emotional symptoms (8.7%-22.6%), behavioral problems (2.4%-14.6%), peer problems relationships (2%-9.3%), and hyperactivity (9.8%-32.1%). Regarding age, results revealed that the older group (14-18 years) presented higher mean scores in emotional, behavioral, and hyperactive symptoms and in the total difficulties score compared to the lower-aged group (11-14 years).

Basterra 2016 prevalence study

This study (Basterra, 2016) examined the percentage of psycho-emotional problems in Spanish children and adolescents using data from the Spanish National Health Surveys of 2006 and 2012; a non-institutionalized Spanish population between the ages of 4 and 14 years. The Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997; Rodríguez-Hernández & Herreros, 2005) was again used in this study to assess mental health[7].

Results for year 2006 included 5,894 participants. The percentage of Spanish youths with abnormal scores in the different scales was the following: total difficulties score (6.7%), emotional problems (11.5%), conduct problems (10.2%), hyperactivity (14.7%) and peer-relationship problems (10.1%).

Results for year 2012 included 3,867 participants. The percentage of Spanish youths with abnormal scores in the different scales was the following: total difficulties score (4%), emotional problems (8.5%), conduct problems (6.7%), hyperactivity (10.2%) and peer-relationship problems (7.7%).

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[6] A Total Difficulties score of 0-15 was considered as normal, a score of 16-19 was considered to be on the border-line and a score of 20-40 was considered to be abnormal or pathological.

[7] The participants with abnormal scores were identified according to the following cut-off points: total difficulties ≥20; emotional problems ≥ 5, conduct problems ≥ 5, hyperactivity ≥ 8, peer relationship problems ≥4 and prosocial behavior problems ≤3.

This prospective observational study (Pamias et al., 2016) assessed the prevalence of major depressive disorder in 1,238 adolescents in their final year of secondary education (4ºES0) in Sabadell (Barcelona, Spain). This study is one of the first epidemiological studies on depression performed in Spanish adolescents.

The study was conducted in two phases:

1. An initial screening phase using the Beck Depression Inventory (BDI-II) (Beck et al., 1996) adapted to Spanish (Sanz, Perdigón, & Vázquez, 2003) to identify adolescents with significant depressive symptoms. A total score of 17 points was used as a cut-off. The sample in the first phase including a total of 1,238 adolescents (mean age = 16.06). According to BDI-II scores, 98 participants (7.92%) exhibited significant depressive symptoms (BDI-II ≥ 17).

2. A diagnostic phase to determine whether the adolescents with significant depressive symptoms according to BDI-II scores met the DSM-IV clinical criteria. Specially trained clinical psychologist interviewed the adolescents and their parents using the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) (Kaufman et al., 1997; Ulloa et al., 2006). The sample in the second phase of the study included a total of 68 adolescents. The results of the diagnostic interviews showed a prevalence of 1.29% adolescents with major depressive disorder ($n = 16$).

An important limitation of this study is that the refusal rates in the screening period (45%) and in the second phase (33%) were higher than expected and, thus, the prevalence of depression may have been partially underestimated.

Conclusions on prevalence of emotional disorders in children and adolescents

After reviewing the studies above, it stands to reason that anxiety and depressive disorders affect a significant number of children and adolescents worldwide. Regarding gender differences, female adolescents seem more likely than males to have mood and anxiety disorders, but less likely to have behavioral and substance use disorders.

Taking into account the 2014 estimation by the USA Census Bureau that there are approximately 1.8 billion 5 to 19 years old children and adolescents in the world, approximately 241 million youths around the world are affected by a mental disorder according to Polanczyk and collaborators' meta-analysis (2015). Anxiety disorders would be the most common group of mental disorders (affecting 117 million) followed by disruptive behavior disorder (affecting 113 million), attention-deficit hyperactivity

disorder (affecting 63 million) and depressive disorders (affecting 47 million) (Polanczyk et al., 2015).

It is important to acknowledge that the studies reviewed in this section present a range of important limitations. First, most of the included studies were single-wave, cross-sectional studies (as opposed to longitudinal studies) that probably underestimated the prevalence of mental disorders. For instance, in the Costello et al. (2003) study, although only 13.3% of children, on average, had a diagnosis at any assessment point, almost 3 times this number had 1 or more disorders over the period of the study. This data demonstrates the need for future prevalence studies to take a longitudinal design. Second, most of the studies on prevalence of emotional disorders in children and adolescents did not include youth with subthreshold symptoms; however subthreshold symptoms should be monitored and even treated, indicating the need for more studies on this. Lastly, few empirical studies, especially in Spain, have been carried out that provide information on the prevalence of emotional symptoms in children and adolescents using structured diagnostic interviews. However, the optimal strategy for assessing the prevalence of mental disorders is through the use of structured psychiatric diagnostic interviews, and some even argue that massive screening fails to establish the real prevalence of emotional disorders and merely offers an estimation of its risk (Pamias et al., 2016).

Age of onset of emotional disorders

Alonso and colleagues' paper reviewed in the previous section reported the highest rates of mental illness among the youngest age groups (18-24 years) indicating a possible early age onset for emotional disorders (Alonso et al., 2004). Furthermore, Kessler et al. (2005) reported a median age of onset for anxiety disorders[8] to be at 11 years of age, and for mood disorders at 30 years of age. Similarly, another study by Kessler et al. (2007) reported a very early age of onset for some anxiety disorders (medians in the range 7-14 years old for specific phobias and separation anxiety disorder) and a later age of onsets for other anxiety disorders (such us generalized anxiety disorder, panic disorder, and post-traumatic stress disorder) and mood disorders. Additionally, Merikangas and collaborators' study (2010) reported that the median age of disorder onset was 6 for anxiety disorders, 11 for behavior disorders, 13 for mood disorders, and 15 for substance use disorders. Lastly, Costello and colleagues' study (2003) reported that: 1) the transition to adolescence was

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[8] Separation anxiety disorder and specific phobia had the earliest median ages of onset (age 7 years) whilst social phobia, for instance, had a later median age on onset (age 13 years).

marked by a rise in rates of depression and social phobia in girls (not in boys), 2) in middle adolescence, the increase in substance use disorders was dramatic, and 3) there was also a modest increase in panic and generalized anxiety disorder (for both boys and girls).

Table 2. Prevalence of anxiety, depressive and other mental disorders according to epidemiological studies. Children and adolescents sample.

	Study	Procedure	Diagnostic measure	Sample	Prevalence of disorders	Others
USA	**Merikangas et al., 2010**	Face-to-face diagnostic interviews with adolescents; Self-report questionnaires to one parent	WMH-CIDI adapted to adolescents	*n* = 10,123; age range = 13-18; 48.7% female	[Lifetime prevalence] Group of disorders: Any ANX disorder = 31.9%; any behavior disorder = 19.1%; any mood disorder = 14.3%; any substance use disorder = 11.4%. Specific disorders: SP = 19.3%; ODD = 12.6%; MDD = 11.75%; Soc.P = 9.1%; drug abuse/dependence = 8.9%; ADHD = 8.7%; SAD = 7.6%; alcohol abuse/dependence = 6.4%; PTSD = 5%; bipolar disorder = 2.9%; AG = 2.4%; PD = 2.3%; GAD = 2.2%; any conduct disorder = 2.2%	Mood and ANX disorders were more prevalent among females; males had higher rates of behavior and substance use disorders
	Costello et al., 2013	Longitudinal study until kids were 16; Annually face-to-face interviews with kids and parents	CAPA	*n* = 1,420; age range = 9-13 at intake; 52% female	[3-month prevalence] Group of disorders: Any disorder = 13.3%; any behavioral disorder = 7%; any conduct disorder = 2.7%; any substance use disorder = 2.4%; any ANX disorder = 2.4%; any mood disorder = 2.2% Specific disorders: ODD = 2.7%; ADHD = 0.9%	The overall prevalence of any disorder was highest in 9- to 10-year-olds, falling to its lowest level in 12-year-olds and then rising slowly.
Europe	**Balázs et al., 2013**	Cross-sectional study using self-report questionnaires	BDI-II SAS SDQ PSS	*n* = 12,395; age range = 14-16; 59.3% female	[At the time of assessment] Based on BDI-II score, 29.2% were identified as sub-threshold-depressed and 10.5% as depressed. Based on SAS score, 32.0% were identified as subthreshold-anxious and 5.8% as anxious	Girls were significantly more frequently subthreshold-anxious and anxious as well as subthreshold depressed and depressed.
Spain	**Aláez-Fernández et al., 2000**	Face-to-face diagnostic interviews	Non-reported	*n* = 404; age range = 0-18; 34.3% female	[12-month prevalence] Group of disorders: any behavior disorder = 23%; any depressive disorder = 14.6%; any ANX disorder = 13.3%; any developmental disorder = 12.7%; any elimination disorder = 9.7% The most prevalent disorders in males were behavior disorders (24.2%), development disorders (14.4%), elimination (12.8%), anxiety (11.4%), and depression (10.6%).	The most prevalent disorders in females were mood disorders (22.3 %), behavioral disorders (21.0 %), anxiety (16.5 %), and developmental disorders (9.4 %).
	Ezpeleta et al., 2007	Longitudinal study over 3 years; Face-to-face diagnostic interviews to parents and adolescents	DICA-IV	*n* = 151; age range = 13 or 9 at intake;	[At the time of assessment] Prevalence of any mental disorder was 62.5% at age 9, 40% at age 10, 32.3% at age 11, 48.1% at age 13, 40.3% at age 14 and 30.0% at age 15. Any anxiety disorder: 36.1% at age 9, 21.4% at age 10, 18.5% at age 11, 27.8% at age 13, 16.7% at age 14 years old) and 13.1% at age 15. Any depressive disorder was 1.4% at age 9, 0% at age 10, 1.5% at age 11 years old, 3.9% at age 13, 14.1% at age 14 and 5% at age 15.	The most frequent groups of disorders both in preadolescence and adolescence were behavioral and anxiety disorders.
	Fonseca et al., 2011	Cross-sectional study using self-report questionnaires	SDQ	*n* = 1,319; age range = 14-17;	[At the time of assessment] The following percentages of adolescents reported problematic behaviors (range depends on the specific item of the subscale): emotional symptoms	Females had higher scores in emotional symptoms and prosocial behavior; males had

			52.2% female	= 11.6%-34.6%; behavioral problems = 4.9%-25.7%; peer problems relationships = 2.3%-16.5%; hyperactivity = 16.1%-47.1%	higher scores in behavioral problems and hyperactivity
Ortuño-Sierra et al., 2014	Cross-sectional study using self-report questionnaire	SDQ	*n* = 508; age range = 11-18; 40.9% female	[At the time of assessment] The following percentages of adolescents reported problematic behaviors (range depends on the specific item of the subscale): emotional symptoms (8.7%-22.6%), behavioral problems (2.4%-14.6%), peer problems relationships (2%-9.3%), and hyperactivity (9.8%-32.1%)	Females had higher scores in emotional symptoms and prosocial behavior; males had higher scores in behavioral problems.
Basterra et al., 2016	Cross-sectional study using self-report questionnaire (2006)	SDQ	*n* = 5,894; age range = 4-14; 48.3% female	[At the time of assessment] The percentage of Spanish youths with abnormal scores in the different scales was the following: total difficulties score (6.7%), emotional problems (11.5%), conduct problems (10.2%), hyperactivity (14.7%), and peer-relationship problems (10.1%).	A significant reduction was found for the percentage of children and adolescents with problematic behavior between 2006 and 2012 for all scales (even adjustment for age, sex and social class) except in prosocial behavior problems. Factors such as early intervention and greater social support may have contributed to the improvement.
Basterra et al., 2016	Cross-sectional study using self-report questionnaire (2012)	SDQ	*n* = 3,867; age range = 4-14; 48.9% female	[At the time of assessment] The percentage of Spanish youths with abnormal scores in the different scales was the following: total difficulties score (4%), emotional problems (8.5%), conduct problems (6.7%), hyperactivity (10.2%) and peer-relationship problems (7.7%).	
Pamias et al., 2016	Initial screening phase Cross-sectional study using self-report questionnaire	BDI-II	*n* = 1,238; mean age = 16.06; 58.89% female	[At the time of assessment] According to BDI scores, 98 participants (7.92%) exhibited significant depressive symptoms (BDI-II ≥ 17). The percentage of depressive symptoms was higher in girls (10.28%) than in boys (3.54%).	The percentage of depressive symptoms was higher in girls (10.28%) than in boys (3.54%).
Pamias et al., 2016	Diagnostic phase to adolescents scoring ≥ 17 in the BDI-II Face-to-face diagnostic interviews to adolescents and parents	K-SADS	*n* = 68;	[At the time of assessment] Prevalence of 1.29% adolescents with major depressive disorder (*n* = 16). Prevalence was higher at age 16 or over in both genders, showing a dramatically increase in major depressive disorder from the age of 16 years.	Prevalence was higher in girls (1.92%) than in boys (0.34%).

Note. ADHD = Attention-deficit/hyperactivity disorder; AG = agoraphobia; ANX = anxiety; BDI-II = Beck Depression Inventory – II; CAPA = The Child and Adolescent Psychiatric Assessment interview; DICA-IV = Diagnostic Interview for Children and Adolescents-IV; DYS = dystimia; GAD = Generalized anxiety disorder; K-SADS = Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children; MDD = Major depressive disorder; MINI = The Mini Neuropsychiatric Diagnostic Interview; OCD = Obsessive compulsive disorder; ODD = Oppositional defiant disorder; Panic Disorder = PD; PRIME-MD =Primary Care Evaluation of Mental Disorders; PTSD = Posttraumatic stress disorder; SCID-RV = Structured Clinical Interview for DSM-IV Axis I Disorders, Research Version; PSS = Paykel Suicide Scale; SAD = Separation anxiety disorder; SDQ = Strengths and difficulties questionnaire; Soc.P = Social Phobia; SP = Specific phobia; SAS = Zung Self-Rating Anxiety Scale; SDQ = Strengths and Difficulties Questionnaire; WMH-CIDI = World Mental Health Survey Version of the Composite Diagnostic Interview

1.2.   Comorbidity between emotional disorders

1.2.1.   Studies based on adults' samples

It is a well-known fact that mental disorders are in general associated with high comorbidity. For instance, Kessler et al. reported that, when assessing lifetime prevalence, 27.7% of respondents had two or more lifetime disorders whilst 17.3% had three or more. Similarly, when assessing 12-month prevalence, 22% of respondents carried 2 diagnoses, whilst 23% carried 3 or more diagnoses (Kessler et al., 2005a; Kessler et al., 2005b).

Studies conducted in Spain with primary care patients have also found high rates of comorbidity. As an example, we note that Roca et al. (2009) estimated psychiatric comorbidity in 53.6% of their sample (13.8% had two diagnoses, 8.2% had three diagnoses, 5.6% four, and 2.7% five or more) and that Serrano-Blanco et al. (2010) found that 21.55% of the participants had one 12-month mental disorder, 6.89% patients suffered two comorbid mental disorders, 1.90% patients had three comorbid mental disorders, and 0.91% had four comorbid mental disorders.

On top of that, mental disorders comorbidity has been known to be strongly associated to severity. As an example, in Kessler and collaborators' study 9.6% of respondents with 1 diagnosis, 25.5% with 2 diagnoses, and 49.9% with 3 or more diagnoses were classified as serious (Kessler et al., 2005b).

Particularly frequent comorbidity has been found between anxiety and depressive disorders, disorders that rarely present in isolation of other conditions. Kessler et al. (2005b) reported that: 1) patterns of comorbidity showed the stronger odds ratios within the mood disorders and the anxiety disorders, 2) there were very high odds ratios between anxiety and mood disorders, and 3) the odds ratios between anxiety and mood disorders were generally higher than between pairs of anxiety disorders.

Roca et al. (2009) also found the highest comorbidities in patients with depressive and anxiety disorders (19.1%), followed by depressive disorders and somatoform disorders (18.6%), and anxiety and somatoform disorders (14.8%). Serrano-Blanco et al. (2010) also indicated frequent associations between mood and anxiety disorders, with major depressive episode showing especially frequent comorbidities with social phobia and panic disorder, while dysthymia presented with a high comorbidity with social phobia, specific phobia, agoraphobia, and alcohol dependence.

Moreover, a well-known study on DSM-IV diagnosed anxiety and mood disorders comorbidity (Brown, Campbell, Lehman, Grisham, & Mancill, 2001) found that of the 968 patients with a principal anxiety or depressive disorder, 55% and 76% presented current

and lifetime comorbidity with other anxiety or depressive disorders, respectively. Diagnoses with the highest overall comorbidity included: posttraumatic stress disorder, major depressive disorder, dysthymia and generalized anxiety disorder. Especially strong comorbid patterns were found between social phobia and mood disorders, panic disorder with agoraphobia, and posttraumatic stress disorder and mood disorders.

Additionally, the anxiety disorders associated with the highest depressive disorder comorbidity were posttraumatic stress disorder, generalized anxiety disorder and obsessive-compulsive disorder. Lastly, of the patients who had lifetime major depressive disorder of dysthymia, only 5% never had a current or past anxiety disorder.

1.2.2.   Studies based on children and adolescents' samples

Existing literature also indicates high rates of comorbid emotional disorders in children and adolescents. In the following paragraphs, we will review the results regarding comorbidity of the prevalence studies included in the prevalence section.

Balázs et al. (2013), apart from finding a strong correlation between self-reported depression and anxiety in adolescents, found that only 10% of the respondents with threshold-depression or threshold-anxiety had "pure forms" of the disorders. Interestingly, and in contrast, the percentage of pure forms of subthreshold-depression and subthreshold-anxiety were found to be much higher (up to 40–50%).

Second, Costello et al. (2003) indicated comorbidity between any anxiety disorder and any depressive disorder to be 28.9%. Additionally, they found that depression was comorbid with conduct disorder in girls but not boys. Conversely, depression was comorbid with substance use disorder in boys, but not girls.

Third, Merikangas et al. (2010) reported that only 35% of adolescents with anxiety disorders and 6% of adolescents with mood disorders met criteria for disorders from one class only. These rates were similar than the ones presented by behavior disorders (14%) and substance use disorders (6%). In general, about 25% of adolescents affected had two comorbid disorders from two different classes, 11.0% were affected by three classes of disorders, and 3% were affected by four classes of disorder.

Forth, Pamias et al. (2016) found that 50% of adolescents with major depressive disorder presented comorbidity with other psychiatric pathologies, mainly with eating disorders, followed by anxiety disorders, attention-deficit hyperactivity disorder and tic disorder. Moreover, self-report scores for depressive symptoms were significantly positively associated with scales of trait anxiety and state anxiety, meaning that adolescents with high scores in depressive symptomatology presented high levels of trait and state anxiety.

Lastly, similar to what previously said regarding adults, Kessler et al. (Kessler et al., 2012) found that adolescents who meet criteria for 3 or more 12-month disorders were significantly more likely to be rated serious (43.1%) than those with 2 disorders (12.1%) or 1 disorder (8.5%).

1.3. Consequences or burden of emotional disorders

1.3.1. Studies based on adults' samples

Mental disorders provoke enormous burdens worldwide due to a combination of high prevalence and high disability (Kessler et al., 2007).

The most disabling disorders of the brain and mental disorders in the European Union according to Wittchen et al. (2011) are depression, dementias, and alcohol use disorders, with depression being the most burdensome disorder of all diseases. Another review from Eaton et al. (2008) indicated that schizophrenia and bipolar disorder are the mental disorders with the highest disability ratings, followed by major depressive disorder which was compared roughly with multiple sclerosis or deafness in terms of disability. However, only about one in four of all people with mental disorders receive any professional mental help, and even fewer (around 10%) receive adequate mental health care by drugs or psychotherapy (Wittchen et al., 2011). Additionally, in terms of economic costs, it seems that mental disorders are extremely costly, not necessarily due to high direct treatment costs (i.e., diagnostic measures, treatment, care) but rather, because of very high indirect costs (i.e., sick days, disability, early retirement) (Wittchen et al., 2011).

If we focus specifically on emotional disorders, one of the most striking aspects of the burden of these disorders is that anxiety and depression are associated with mortality. A recent systematic review and meta-analysis included 203 articles that reported a mortality estimate of people with mental disorders compared with a general population or controls from the same study setting without mental disorders (Walker, McGee, & Druss, 2015). Most studies were conducted in Europe (n = 125), followed by North America (n = 51), Asia (n = 16), Australia (n = 8), Africa (n = 2), and South America (n = 1). Diagnostic interviews were conducted in 24.6% of studies and follow-up time ranged from 1 to 52 years (with a median of 10 years). The overall pooled relative risk for mortality showed that approximately 8 million deaths worldwide are attributable to mental disorders each year, since people with mental disorders have a mortality rate (pooled relative risk) that is 2.22 times higher than the general population without mental disorders (95% CI, 2.12–2.33). Moreover, approximately 2.74 million deaths worldwide are attributable to mood disorders (pooled

relative risk: 1.86, 95% CI, 1.73–2.00) and approximately 1.43 million to anxiety disorders (pooled relative risk: 1.43, 95% CI, 1.24 – 1.64) (Walker et al., 2015). Interestingly, although relative risks for unnatural causes of death (i.e., suicide) were higher compared with those of natural causes of death (i.e., cardiovascular disease), natural causes accounted for more than two-thirds of deaths among people with mental disorders; this is not surprising since people with mental health disorders are known to have adverse health behaviors, such us tobacco smoking, poor diet or physical inactivity (Walker et al., 2015)

We are going to now briefly discuss a systematic review that calculated treatment costs and health outcomes of depression and anxiety disorders between 2016 and 2030 in 36 countries (Chisholm et al., 2016). This study estimated that, for all 36 countries, the annual treatment cost of depressive disorders and anxiety problems amounted to $91 billion and $56 billion, respectively. Additionally, this study concluded that the investment needed to substantially scale up effective treatment coverage for emotional disorders between 2016 and 2030 would be substantial ($147 billion); nevertheless, the returns would be also substantial with cost ratios higher than 2 (any cost ratio exceeding 1 provides a rationale for investment).

In Spain, a recent review provided specific estimates of the economic costs of 19 brain disorders for the year 2010 based on 33 published epidemiological studies and on economic evidence (Parés-Badell et al., 2014). In this review, the societal cost of mental disorders (excluding neurological disorders) was estimated in €46 billion (it is worth mentioning that the public healthcare expenditure of Spain was €64 billion in 2010). Regarding emotional disorders, when direct and indirect costs were included, societal costs for mood disorders were estimated to be €10,8 million and €10,4 million for anxiety disorders. These societal costs of emotional disorders were only exceeded by the societal costs of dementia and were higher than the costs attributed to all other brain disorders, including stroke or addiction. Additionally, estimated mean yearly per-patient costs were €3,584 for mood disorders and €1,661 for anxiety disorders (for reference, it is worth noting that dementia was the group with the highest estimated mean yearly per-patient cost: €25,303).

The high direct and indirect costs of mental disorders raise the question of whether the indirect cost burden (i.e., sick days) could be reduced by increasing the direct costs (i.e., psychological treatment) resulting in fewer total costs (Wittchen et al., 2011). Moreover, prevention of mental disorders would be a method to reduce direct and indirect cost burden of mental disorders all together.

1.3.2. Studies based on children and adolescents' samples

It is universally acknowledged that anxiety and depressive disorders are associated with severe impairment, increased risk of future psychiatric problems, and a high economic burden to families and society (Ahlen, Lenhard, & Ghaderi, 2015). In a high proportion of cases, mental disorders, especially anxiety disorders, start in childhood or adolescence and have adverse effects on school and academic achievement, social functioning or social integration; these adverse effects usually persist throughout the lifespan or at least have a lasting impact (Wittchen et al., 2011). Additionally, the costs of supporting children and adolescents with psychiatric disorders can be far higher than for their peers, and these disorders usually lead to continued financial burden into adulthood (i.e., increased use of public sector services, reduced participation in the labor market) (Beecham, 2014).

As for adults, emotional disorders in children and adolescents are also associated with mortality and suicidal ideation. It is estimated that each year around 600,000 adolescents and young adults aged 14 to 28 years commit suicide in the world (with European countries being the most affected) and, according to the World Health Organization, suicide was the second leading cause of death in the age group 15 to 29 years in 2012 (Navarro-Gómez, 2017). Navarro-Gómez (2017) also indicated that according to the National Institute of Statistics [Instituto Nacional de Estadística] (2013), of the total number of suicides that happened in Spain in a year, 7.7% corresponded to people younger than 30 years.

As for suicidal ideation, Balazs et al. (2013) indicated that anxious and subthreshold-anxious adolescents, as well as depressed or subthreshold-depressed adolescents had a greater probability of suicidal thoughts or ideations[9] compared to their non-anxious and non-depressed peers. Both subthreshold and threshold forms of depression showed to increase the risk of having suicidal thoughts/ideations, even more than subthreshold and threshold-anxiety. Additionally, this study showed that both subthreshold and threshold-anxiety and depression were related to functional impairment.

As for the economic costs of emotional disorders in children and adolescents, we are going to review a few important studies in this regard. First, a Dutch cost-of-illness study focusing on 118 anxious 8 to 18-year indicated that mean annual costs per child or

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[9] Anxious and subthreshold-anxious adolescents were predicted to have suicidal thoughts/ideations with 2.8 and 1.8 times, respectively, greater probability that their non-anxious peers. Moreover, depressed or subthreshold-depressed adolescents were predicted to have suicidal thoughts/ideations with a 3.1 and 9.2 times greater probability, respectively, that their non-anxious peers.

adolescent was €2,748, including direct health care and indirect costs (nonmedical care and out of pocket expenses) with societal costs of families with a clinically anxious child being 21 times higher than in families without this problematic (Bodden, Dirksen, & Bögels, 2008).

Second, another study focused on 433 adolescents in the USA (mean age =14.6; *SD* = 1.55; range = 12.17; 54.3% female) who suffered from major depressive disorder (Domino et al., 2009). On average, treatment-related costs for each adolescent were $281 during the 3-month period analyzed, with most of these costs covered by families and private insurers. Interestingly, families with lower income levels had similar costs as their higher income counterparts. It is interesting that less than one third (29.3%) of the sample reported receiving any mental health service, whilst one fourth of the sample (24.7%) reported receiving services from a school guidance counselor, school psychologist, or social worker, and nearly half (43%) of the sample reported use of general health services from an outpatient provider. To our knowledge, no studies have been conducted in Spain that analyzed economic costs of emotional disorders in children and adolescents.

2. What is the rationale for using a transdiagnostic approach?

Disorder-specific cognitive behavior therapy (DS-CBT), based on manualized diagnosis-specific treatments that apply evidence-based components to specific disorders, has proven to be effective in treating anxiety and depressive disorders according to numerous meta-analyses and systematic reviews (Butler, Chapman, Forman, & Beck, 2006). However, there is evidence that treatments aimed at specific pathologies may not adequately address co-morbidity (Van Balkom et al., 2008), do not work for a considerable number of patients, and are difficult to disseminate since it is costly and time consuming to train therapists in a range of different protocols, and it is not possible to treat a group of patients with different disorders at the same time (Craske, 2012; Van Balkom et al., 2008).

In addition, many people with anxiety and depression do not seek treatment (Andrews, Henderson, & Hall, 2001) due to barriers such as the limited number of mental health professionals, large waiting lists (especially in public services), stigma and the direct and indirect costs of treatment (Titov, 2011).

With one of its principal objectives to satisfactorily explain and treat comorbidity, a new approach called *transdiagnostic* has emerged. Its main characteristic is that it hypothesizes the existence of cognitive and/or behavioral processes shared by various psychological disorders that causally contribute to the development and/or maintenance of the symptoms associated with these disorders (Sandín, Chorot, & Valiente, 2012).

It should be noted that the transdiagnostic approach does not only enrich psychopathology from a theoretical point of view, but it also proposes a new therapeutic approach called *transdiagnostic cognitive behavioral therapy* (T-CBT) based on the development of unified treatment protocols that are valid to address a group of disorders simultaneously. Therefore, the final aim of T-CBT is to simultaneously address both principal and comorbid disorders by targeting common and unified factors across the disorders (Mansell, Harvey, Watkins, & Shafran, 2009; Sandín et al., 2012; Wilamowska et al., 2010).

The first T-CBT protocol was developed by Fairburn et al. in relation to eating disorders (Fairburn, Cooper, & Shafran, 2003). Afterwards, other face-to-face T-CBT protocols emerged for anxiety (Norton & Hope, 2005) as well as for anxiety and depression (Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010). Internet-delivered T-CBT for adults (Titov, Andrews, Johnston, Robinson, & Spence, 2010) as well as T-CBT for children and adolescents (Ehrenreich-May, Bilek, Queen, & Hernandez Rodriguez, 2012) have also recently emerged.

In short, a shift to T-CBT could have many advantages over DS-CBT: 1) patients with different disorders could be treated with the same treatment protocol reducing waiting lists for single-disorder treatments, 2) patients with comorbid diagnoses could learn to handle multiple problems at the same time, and 3) therapists would not have to be trained in numerous different protocols (Boisseau, Farchione, Fairholme, Ellard, & Barlow, 2010; Titov, 2011). In addition, T-CBT (and the transdiagnostic approach in general) could attract attention to the disorders severity, have a prominent place in primary care, prevention and mental health promotion and could contribute to reduce the number of diagnostic categories through investigating a set of basic dimensions common to several problems (Sandín et al., 2012).

3. The Unified Protocols for Transdiagnostic Treatment of Emotional Disorders

3.1 Rationale behind the Unified Protocols

The first argument to go for treatments that target different emotional disorders within a single protocol is that commonalities among the emotional disorders are plenty (Barlow et al., 2018; Kennedy & Barlow, 2018). First, and as we have seen in a previous section of this introduction, anxiety and depressive disorders present high rates of current

and lifetime comorbidity, both in adults and youth. Second, emotional disorders share symptoms. For instance, worry takes place in all of the anxiety disorders, with only the focus of this worry varying across disorders (e.g., worry about safety of loved ones in separation anxiety disorder, worry about the future in generalized anxiety disorder). Lastly, a broad treatment response usually happens when targeting one emotional disorder that often generalizes across other comorbid anxiety or mood disorders not specifically targeted during treatment, perhaps because disorder-specific treatments target symptoms from more than one disorder or because they target core underlying features shared by all emotional disorders.

There might be two reasons behind the similarities among emotional disorders. First, research from affective neuroscience has indicated that anxiety and depressive disorders share neurobiological mechanisms, such us hyperexcitability of limbic structures or delimited inhibitory control by cortical structures (Barlow et al., 2011; Kennedy & Barlow, 2018).

Second, and more interesting for psychologists, research suggests that there are three common core vulnerabilities that contribute to the development and maintenance of anxiety and depressive disorders (Barlow et al., 2018; Ehrenreich-May et al., 2018; Kennedy & Barlow, 2018). Firstly, emotional disorders usually affect people with high levels of neuroticism or negative affect, that is, a temperamental propensity to experience frequent, intense unpleasant emotions (e.g., fear, anxiety, sadness, and/or anger) associated with a sense of uncontrollability in response to stress. Secondly, individuals with emotional disorders usually react more negatively to their own emotions (e.g., "I should not be feeling this way"; "I want to stop feeling like this now"), have greater trouble accepting their emotional experiences, and are more intolerant of their unpleasant emotions. Thirdly, in order to relieve this distress, adult, children and youth with emotional disorders typically do things to avoid, suppress, distract from, or control these uncomfortable emotions. Therefore, they usually rely on maladaptive emotion regulation strategies that in the short run are negatively reinforced because the distress goes away but, in the long run, maintain the symptoms since using these maladaptive strategies prevents these individuals from learning more helpful or effective ways to cope with their emotions. Actually, excessive efforts to control our emotions usually (and ironically) provoke an increase in the feelings we are trying to manage. The Unified Protocols target these core vulnerabilities and not the diverse symptoms that are presented within different Emotional disorders.

The Unified Protocols for adults, children and adolescents are based on traditional cognitive-behavioral principles. However, particular emphasis is set on emotion regulation, since the first goal of the treatment is to help patients learn how to experience

uncomfortable emotions and how to respond to these emotions in more adaptive ways, which usually leads to a reduce of the intensity and incidence of maladaptive emotional experiences and to an improvement in functioning (Barlow et al., 2011). Thus, the Unified Protocols are emotion-focused treatment approaches in which the techniques are applied in a flexible manner that permits to tailor the treatment strategies to almost any emotion (Ehrenreich-May et al., 2018).

At this point, it is worth mentioning that the Unified Protocols do not aim to eliminate strong or uncomfortable[10] emotions but, rather, teach individuals to experience emotions with less discomfort and better employment of helpful and non-avoidant strategies to manage their feelings, so that even uncomfortable emotions can be adaptive (Barlow et al., 2011; Barlow et al., 2018; Ehrenreich-May et al., 2018).

3.2 The Unified Protocol for Adults

The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adults (UP) is a treatment for adults that present with anxiety and coocurring emotional disorders. The UP was first published in manual form in 2011 (Barlow et al., 2011) and a second edition has been recently published (Barlow et al., 2018).

The UP consists of the following eight treatment modules. Modules 3, 4, 5, 6 and 7 are considered core modules whereas modules 1, 2 and 8 are considered additional modules. Between brackets we indicate the suggested session lengths according to the authors:

- Module 1: Setting goals and maintaining motivation (1 session)
- Module 2: Understanding emotions (1-2 sessions)
- Module 3: Mindful emotion awareness (1-2 sessions)
- Module 4: Cognitive flexibility (1-2 sessions)
- Module 5: Countering emotional behaviors (1-2 sessions)
- Module 6: Understanding and confronting physical sensations (1 session)
- Module 7: Emotion exposures (4-6 sessions)
- Module 8: Recognizing accomplishments and looking to the future (1 session)

The treatment is intended to last 12-18 individual weekly treatment sessions lasting 50 to 60 minutes each. The therapist is the one to decide the number of sessions per module.

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[10] As done in the Unified Protocols, we purposely use the terms strong or uncomfortable and not the term "negative" to describe emotions since one of the aims of the protocols is to teach that all emotions are useful, normal and necessary under normal circumstances.

The treatment aims that the patient acquires the following skills (Barlow et al., 2011; Barlow et al., 2018):

1. Mindful emotion awareness, that is, practice of present-focused, nonjudgemental attention toward emotions

2. Challenging automatic thoughts (both in relation to external and internal threats) and increasing cognitive flexibility

3. Identifying and changing emotional behaviors (also known as emotion driven behaviors)

4. Increasing awareness and tolerance of physical sensations. The UP does this through exercises design to evoke uncomfortable physical sensations

5. Engaging in exposures (UP authors use the term emotion exercises) both in situational and internal contexts.

The UP has received preliminary support for its efficacy in treating anxiety and depressive disorders from several studies including open trials (Ellard et al., 2010; Ito et al., 2016), randomized controlled trials using wait-list control groups (Farchione et al., 2012), and randomized controlled trials comparing the UP to disorder specific CBT (Barlow et al., 2017; Lotfi, Bakhtiyari, Asgharnezhad-Farid, & Amini, 2014). Additionally, recently the UP has been adapted to a group format with good results (Bullis et al., 2015; De Ornelas Maia, Braga, Nunes, Nardi, & Silva, 2013; Grill, Castañeiras, & Fasciglione, 2017; Osma, Castellano, Crespo, & García-Palacios, 2015).

Lastly, there is preliminary data that indicates that the UP can be successfully applied to patients with emotional disorders and coocurring alcohol abuse or dependence, bipolar disorder, borderline personality disorder and posttraumatic stress disorder (Barlow et al., 2011). Additionally, the UP has recently been adapted and tested as a single-session indicated preventive intervention for young adults (Bentley et al., 2017).

3.3   The Unified Protocols for Children and Adolescents

Drawing from research with the UP in adult samples, Ehrenreich-May's team developed two transdiagnostic unified protocols for treatment of anxiety and depression in children and adolescents: the Unified Protocols for Transdiagnostic Treatment of Emotional Disorders in Children (UP-C) and Adolescents (UP-A) (Ehrenreich-May et al., 2018). These protocols are aimed to treat anxiety and depressive disorders, although the authors state that these protocols can also potentially be used with some trauma and stress-related disorders, obsessive-compulsive disorders, somatic symptom disorders, tic disorders and, in general, with any child or adolescent whose primary area of concern is an emotional

disorder or for whom targeting problematic emotional behaviors is the primary treatment goal (Ehrenreich-May et al., 2018). One of the most striking features of the UP-C and UP-A is that they include sessions with the parents in order to address emotional parenting behaviors (e.g., overcontrol/overprotection, criticism, inconsistency, or criticism), that usually get in the way to adequately treat the child or adolescent presenting with an emotional disorder.

3.3.1. The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Children (UP-C)

The UP-C is a group-based, 15 weeks, 90-minute sessions program for children aged 7 to 13 presenting with emotional disorders. Parents are very involved in this treatment. A child group and a parent group are made, and both meet at the same time for each session with separate clinicians (additionally, parent and child groups meet at the beginning and end of each session for about 30 minutes in total). UP-C authors believe this group format has several advantages, such that the children benefit from the support of their peers (specially while practicing exposures) and parents find the group as a supportive environment in which to practice and discuss new parenting behaviors.

The UP-C sills are presented around the acronym CLUES:

- C – Consider how I feel (sessions 1 to 4)
- L – Look at my thoughts (session 5)
- U – Use detective thinking (sessions 6, 10, 11, 12, 14 and 14) and problem solving (session 7)
- E – Experience my emotions (sessions 8 and 9)
- S – Stay healthy and happy (session 15)

Additionally, the parent group has the following main functions:

1. Introduce parents to the skills their children are learning
2. Introduce parents to inadequate "emotional parenting behaviors" they may be engaging into and teach them how to change these for more helpful "opposite parenting behaviors"
3. Promote support among the parents

Now, we are going to briefly review some important aspects of the UP-C. First, parents are assigned learning assignments or homework between sessions (although UP-C authors suggest avoiding the use of the word "homework" with the parents). This allows them to master the skills their children are learning in the sessions, monitor their child's emotions and their own reactions as a parent, and become aware of their "emotional

parenting behaviors" in order to practice "opposite parenting behaviors" instead. Another key aspect of the UP-C is the importance of positive reinforcement, both delivered by therapists in session and by parents at home. Small rewards are used in the UP-C to maintain the attention of the children and to reinforce appropriate behavior and acquisition of skills.

The UP-C started as a universal anxiety and depression prevention program applied in a summer camp setting (Ehrenreich-May & Bilek, 2011). As a treatment intervention, the UP-C has so far received support for its efficacy treating emotional disorders in an open trial (Ehrenreich-May & Bilek, 2012) and a randomized controlled trial (Kennedy, Bilek, & Ehrenreich-May, 2018).

3.3.2. The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents (UP-A)

The UP-A is a transdiagnostic approach for adolescents (ages 13 to 18) with a principal anxiety or depressive disorder. It consists of the following eight core treatment modules (between brackets we indicate the suggested session lengths) and an additional parent module (Ehrenreich-May et al., 2018):

- Module 1: Building and keeping motivation (1-2 sessions)
- Module 2: Getting to know your emotions and behaviors (2-3 sessions)
- Module 3: Introduction to emotion-focused behavioral experiments (1-2 sessions)
- Module 4: Awareness of physical sensations (1-2 sessions)
- Module 5: Being flexible in your thinking (2-3 sessions)
- Module 6: Awareness of emotional experiences (1-2 sessions)
- Module 7: Situational emotion exposure (more than 2 sessions)
- Module 8: Reviewing accomplishments and looking ahead (1 session)
- Module P: Parenting the emotional adolescent (1-3 sessions)

The UP-A takes a modularized, individual-therapy, flexible approach and, if the recommended session length for each module is followed, the protocol will be applied in 12 to 21 sessions (authors have found an average of 16 sessions in their research trials). Additionally, authors encourage to give the adolescent home learning assignments at the end of each session in order to help him or her generalize the learnt sills to real-life experiences outside of the therapy context.

The UP-A includes several adaptations if we compare it to the UP, including connecting treatment content to topics relevant to adolescents (e.g., peer relationships,

school problems), a greater attention on building treatment motivation, and implicating parents in treatment (Ehrenreich-May, Queen, Bilek, Remmes, & Kristen, 2014).

Regarding the modules' order, the authors encourage therapists applying the UP-A to use all core modules in the order they are provided and to use Module P when needed. Furthermore, they recommend at least one session with the parents to engage support for planning and execution of exposures. Parents can also be included at the end of each session to review learnt content if the therapist and the adolescent agree this is a good idea.

Apart from session 1, most sessions in the UP-A are supposed to have a similar structure (Ehrenreich-May et al., 2018) beginning with something very unique to the UP-A, that is, obtaining a weekly rating of top problems from the adolescent (therapist can obtain top problems from the parent at the beginning or at the end of each session). Then, it is recommended to briefly ask the adolescent of something relevant to her or him (for instance, an activity or event that happened during the week) in order to build rapport. After that, it is time to review the home learning assignments the adolescent has completed making sure to reinforce the adolescent's effort. Next, the therapist can introduce new skills and practice these skills in session, first using a neutral example that does not directly apply to the adolescent and, afterwards, applying the new skill to the adolescent's own emotional experiences. The session finishes with the assignment of home learning forms or worksheets that should be related to session content.

Regarding efficacy of the UP-A, the protocol has been shown to significantly reduce anxiety and depressive symptoms in case studies (Ehrenreich, Goldstein, Wright, & Barlow, 2009; Seager, Rowley, & Ehrenreich-May, 2014; Sherman, Tonarely, & Ehrenreich-May, 2018), an open-trial (Queen, Barlow, & Ehrenreich-May, 2014) and a randomized controlled trial (Ehrenreich-May et al., 2017).

4. Prevention of anxiety and depression using T-CBT

4.1. Prevention of emotional disorders targeting youth samples

One way in which to address the early onset and the costs associated with anxiety and depressive disorders in children and adolescents is via prevention. Prevention is usually defined as any intervention aimed at preventing the onset of new cases of psychological disorders in adults and children who do not yet meet the diagnostic criteria for such a disorder (Mrazek & Haggerty, 1994).

Historically, the most common terminology used for prevention included the terms primary, secondary, and tertiary (Caplan, 1964). *Primary prevention* covered actions to reduce the number of new cases or incidence of a disorder, *secondary prevention* involved early identification and treatment to diminish the prevalence of established cases, and *tertiary prevention* involved treatment to reduce the severity of disability related to an existing disorder.

Three decades later, the Institute of Medicine (IOM) Committee on the Prevention of Mental Disorders' report (Mrazek & Haggerty, 1994) established a new classification for preventive programs: universal, selective, and indicated interventions (Mrazek & Haggerty, 1994).

According to this classification, *universal prevention* programs target the general public or a group of individuals regardless of individual risk of developing the problem. Alternatively, *selective prevention* programs are applied to individuals evidencing higher risk than average for the development of a problem or disorder. These individuals may be identified on the basis of certain risk factors that are known to be associated in the short or long term with the onset of the problem or disorder that is the focus of the program. These risk factors are usually classified into three categories: biological, psychological or social. Lastly, *indicated prevention* programs target individuals who are identified as experiencing minimal but detectable symptoms of a disorder, but who do not meet the DSM diagnostic levels at the present moment.

The IOM report advocated for differentiating prevention from health promotion efforts, as health promotion does not put an emphasis on prevention of illness, but rather an emphasis on the improvement of wellbeing (Mrazek & Haggerty, 1994). However, this approach is not without controversy since some authors consider that there should be a fusion of prevention and promotion approaches in order to combine strategies for reducing risk factors and strategies enhancing protective factors, especially for children and youth (Weissberg, Kumpfer, & Seligman, 2003).

But, where and how should mental health preventive interventions for children and adolescents be applied?

It is well known that children and adolescents spend more time in school than anywhere else apart from home. Additionally, authors point out that school mental health resources are distinctively positioned to identify children at risk for mental health problems and to help intervene when issues emerge (Kase et al., 2017). Several authors agree that the definition of adolescents' psychosocial functioning in the school context ought to include two interconnected aspects: social-emotional functioning and school functioning and that schools should work on both of these aspects (Roeser, Eccles, & Sameroff, 2000; Suldo,

Gormley, DuPaul, & Anderson-Butcher, 2014). To work on the social-emotional functioning of all children in the school, universal preventive interventions should be applied. Benefits associated with universal prevention programs include: avoiding the stigma of singling out individuals for intervention, relatively low dropout rates, and enabling reach children or adolescents who have limited access to treatment services or who may not have been identified as needing services (Ahlen et al., 2015; Fisak, Richard, & Mann, 2011; Horowitz & Garber, 2006).

But, what do we know about the efficacy of universal preventive programs for anxiety and depression? Evidence coming from several meta-analyses suggest that there are small but positive effects regarding anxiety (Ahlen et al.: $g = 0.13$; Corrieri et al.: SMD = 0.14; Werner-Seidler et al.: $g = 0.19$) and depressive symptoms (Ahlen et al. : $g = 0.11$; Werner-Seidler et al.: $g = 0.19$) as measured at immediate post-test (Ahlen et al., 2015; Corrieri et al., 2014; Werner-Seidler, Perry, Calear, Newby, & Christensen, 2017). At short-term follow up, small and not always positive effect sizes have been found regarding anxiety (Ahlen et al.: $g = 0.11$; Werner-Seidler et al.: $g = 0.17$) and depressive symptoms (Ahlen et al. 2015: $g = 0.07$; Corrieri et al. 2014: SMD = -0.06; Werner-Seidler et al. 2017: $g = 0.18$). These effect sizes might seem low but are of importance with respect to the whole population. For instance, a post effect size of .13 for anxiety represents a decline of 18.9% children who score over the cut-off in the experimental group (Ahlen et al., 2015).

Despite the ability of these types of programs in lowering anxiety and depressive symptoms, and the benefits associated with universal preventive programs, a majority of schools, especially in Spain, have yet to implement programs to prevent anxiety and depression. On another note, universal preventive interventions for emotional disorders in youth have either focused on depression or on anxiety as independent constructs (Ahlen et al., 2015; Dozois, Seeds, & Collins, 2009) with FRIENDS for life and Penn Resiliency Program as the most extensively evaluated programs to prevent anxiety and depression, respectively.

4.2. FRIENDS for life and Penn Resiliency Program

FRIENDS for life, the most extensively evaluated program to prevent anxiety (Barrett, 2005), is an Australian cognitive-behavior therapy-based program based on the Coping Cat program (Kendall, 1994) and developed to provide school personnel with a universal approach for preventing the onset of anxiety in children (Maggin & Johnson, 2014). FRIENDS is an acronym that helps children remember the strategies taught in the program: *F* - feeling worried?; *R* - relax and feel good; *I* - inner thoughts; *E* - explore plans; *N* - nice

work so reward yourself; *D*= don't forget to practice; *S* = stay calm, you know how to cope. In the FRIENDS program, children are taught how to: recognize somatic symptoms of anxiety, identify and challenge anxious thoughts, use coping skills (e.g., relaxation, problem solving), and self-reward for trying hard and achieving goals (Essau, Conradt, Sasagawa, & Ollendick, 2012). The FRIENDS program is typically delivered over the course of 10 weekly 60 min-sessions and usually includes two booster sessions (the first and third months after the program is completed) as well as four group sessions offered for parents to increase their awareness about anxiety disorders and learn about program content (Essau et al., 2012; Maggin & Johnson, 2014). A recent meta-analytic review of the FRIENDS program for preventing anxiety in student populations included 17 studies and showed mixed results (Maggin & Johnson, 2014). Low-risk students demonstrated small reductions over controls for immediate posttest measures of anxiety, whereas high-risk students shown no immediate posttest improvements on measures of anxiety compared to controls (Maggin & Johnson, 2014).

Penn Resiliency Program (PRP) (Gillham, Brunwasser, & Freres, 2008), the most extensively evaluated program to prevent depression, is a CBT group program that teaches youth aged 10 to 14 cognitive-behavioral and social problem-solving skills through group discussions and weekly homework assignments (Brunwasser, Gillham, & Kim, 2009; Gillham et al., 2007). It is delivered by teachers, school counselors or psychologists over the course of 12 weekly 90-min sessions. A meta-analytic review published in 2009 including 17 controlled evaluations of PRP concluded that, overall, participants in the included studies reported fewer depressive symptoms at post-intervention and follow-up assessments (compared to youth receiving no intervention) with effect sizes ranging from 0.11 to 0.21 (Brunwasser et al., 2009).

4.3. T-CBT programs to prevent anxiety and depression

Despite the fact that anxiety and depressive disorders frequently co-occur and share a number of risk and maintenance factors, preventive interventions have traditionally been directed to address either anxiety or depression (Dozois et al., 2009; Nehmy & Wade, 2014). Nonetheless, transdiagnostic preventive interventions that target modifiable etiological and vulnerability factors common to emotional disorders might improve the efficacy and cost-effectiveness of preventive interventions and therefore should be explored (Dozois et al., 2009; Nehmy & Wade, 2014).

However, there is only one transdiagnostic, theory-driven CBT protocol to prevent anxiety and depression (Ehrenreich-May & Chu, 2014): EMOTION: "Coping Kids" Managing

Anxiety and Depression (Kendall, Stark, Martinsen, O'Neil, & Arora, 2013). EMOTION (Kendall et al., 2013) is an indicated prevention program that aims to reduce the incidence of anxiety and depressive symptoms in youth showing initial symptoms of these disorders (Martinsen, Kendall, Stark, & Neumer, 2016). It includes techniques such as psychoeducation, problem solving, activation, cognitive restructuring and exposure. The intervention is flexible enough to accommodate these techniques to depressive symptoms (e.g., targeting rumination about past events; reducing withdrawal and encouraging engagement in more activities) as well as to anxiety symptoms (e.g., targeting catastrophic thoughts about the future; facing challenging situations) (Martinsen et al., 2016).

EMOTION is delivered over the course of 20 group sessions that takes place twice a week (each session lasting 45 to 60 minutes) and that are delivered to children aged 8 to 13 years in groups that have two leaders and no more than 6 children (Martinsen et al., 2016). Additionally, the EMOTION program includes two individual sessions between each child and the group leader, as well as eight parent group sessions; the children also attend half of the parenting sessions (Martinsen et al., 2016).

So far, studies applying the EMOTION program have shown promising results (Martinsen, 2017; Martinsen et al., 2016) and the results of a large RCT will likely be published soon (Patras et al., 2016). However, this program was developed and evaluated for children and young adolescents. Universal prevention programs for adolescents are scarce, to say the last.

4.4.   Justification of this doctoral thesis

As we have seen in this introduction section, anxiety and depressive disorders are highly comorbid conditions that affect a significant number of adults, children and adolescents worldwide. Moreover, these disorders are associated with significant mortality, impairment, disability and suffering in everyday life.

On top of that, these conditions (particularly depression) provoke a high burden to society, especially because of their very high indirect costs associated to sick days, medical leaves, early retirement, etc. (Wittchen et al., 2011). In Spain, societal costs have been estimated to be €10,8 million for mood disorders and €10,4 million for anxiety disorders (Parés-Badell et al., 2014).

Taking all these prevalence and burden findings into account, there are grounds for believing that anxiety and depressive disorders must be considered one of the World's foremost health care challenges of the 21st century. However, only a small percentage of people with emotional disorders receive any professional mental help, not to mention

adequate mental health care. For this reason, the research and clinical community believe that these disorders require the widespread dissemination of preventive and treatment interventions as soon as possible.

As we have seen, transdiagnostic cognitive behavior therapy (T-CBT) is a new approach to psychotherapy that enables clinicians to treat patients with different disorders (i.e., the different anxiety and depressive disorders) with the same treatment protocol. This new form of psychotherapy could help disseminate evidence-based treatments improving access to adequate mental health care. However, in order to disseminate T-CBT (especially if we are going to use public health resources) we need to make sure T-CBT works.

Despite the fact that there has been some progress over the years in this regard, much work remains to be done to test the effectiveness of T-CBT. Meta-analyses previously published up until the one included in this doctoral thesis (Study I) have presented several limitations: they focused only on anxiety disorders (Norton & Philipp, 2008; Reinholt & Krogh, 2014), pooled effects of controlled and uncontrolled studies all together (Norton & Philipp, 2008; Reinholt & Krogh, 2014), included studies that were not transdiagnostic theory-based (Newby, McKinnon, Kuyken, Gilbody, & Dalgleish, 2015; Reinholt & Krogh, 2014), only took into account face-to-face interventions (Norton & Philipp, 2008; Reinholt & Krogh, 2014) or did not take into account children and adolescent samples (Newby et al., 2015; Norton & Philipp, 2008; Reinholt & Krogh, 2014).

Therefore, Study I of this doctoral thesis (Efficacy of transdiagnostic cognitive-behavioral therapy for anxiety and depression in adults, children and adolescents) aimed to examine the effectiveness of T-CBT protocols for the treatment of anxiety and/or depression in adults, children and youth addressing and sorting out the limitations of previous meta-analyses.

On the other hand, T-CBT could be interesting if applied in prevention research, since targeting risk factors across several disorders may harvest a larger benefit than addressing risk factors specific to only one category type. However, preventive interventions to date have been traditionally developed to target either anxiety or depressive disorders and the only existing T-CBT protocol for preventing anxiety and depression is EMOTION: "Coping Kids" Managing Anxiety and Depression (Kendall et al., 2013), and this is a protocol that was developed and evaluated for young children.

Since, to our knowledge, there are no T-CBT universal preventive interventions for anxiety and depression in adolescents, Study II (The UP-A adapted as preventive intervention: A cluster randomized controlled trial) and Study III (An open trial applying the UP-A as a preventive intervention) of this doctoral thesis aimed to contribute to transdiagnostic prevention research establishing initial pre- to post and follow-up

outcomes associated with the use of one of the most consolidated T-CBT protocols for anxiety and depression in adolescents, the UP-A (Ehrenreich-May et al., 2018), adapted as a school-based universal preventive intervention in a Spanish context.

CHAPTER II. AIMS AND HYPOTHESES OF THIS DOCTORAL THESIS

1. Main aims

This doctoral thesis had two main aims or objectives. The first one was to increase the knowledge on efficacy and effectiveness of transdiagnostic cognitive behavioral therapy applied to adults, children and adolescents. The second one was to extend transdiagnostic cognitive-behavioral therapy for prevention of anxiety and depressive disorders in adolescents and in a Spanish context.

2. Specific aims and hypotheses

2.1. Study I: Efficacy of transdiagnostic cognitive-behavioral therapy for anxiety and depression in adults, children and adolescents: A meta-analysis

2.1.1. Aims

1. The *first aim* of this study was to test the hypothesis that T-CBT is an effective treatment for reducing symptoms of anxiety and/or depression at post-treatment and follow-up in adults with anxiety and/or depressive disorders or subthreshold anxiety or depressive symptoms. To test this hypothesis, we conducted four different meta-analyses as part of Study I.

2. The *second aim* of this study was to test the hypothesis that T-CBT is an effective treatment for reducing symptoms of anxiety and/or depression at post-treatment and follow-up in children and adolescents with anxiety and/or depressive disorders or subthreshold anxiety or depression symptoms. To test this hypothesis, we conducted two different meta-analyses that are included in Study I.

3. The *third aim* was to conduct an assessment of the studies' methodological quality whilst the *forth aim* was to do an analysis of the publication bias data associated with each of the meta-analysis conducted.

4. The *forth aim* was to explore the impact of the following potential categorical moderators of treatment effect in adults: country in which the study took place in,

diagnostic measure used (interview, telephonic interview or a self-reported measure), inclusion of behavioral activation as a treatment component or not, inclusion of mindfulness or not, inclusion of problem solving or not, inclusion of relaxation training or not, inclusion of response prevention or not, treatment protocol applied (the Unified Protocol, the Wellbeing Protocol, etc.), recruitment method (community or clinical), participants' diagnosis (not reported, clinical or partly subclinical), study design (RCT or uncontrolled), treatment target (anxiety, depression or anxiety and depression) and treatment format (individual, group or internet).

5. The *fifth aim* was to explore the impact of the following potential quantitative moderators of treatment effect in adults: publication date of the study, percentage of women included, number of sessions, percentage of attrition, percentage of participants with comorbid emotional disorders and proportion of categories with high bias assessment.

6. The *sixth aim* was to compare T-CBT efficacy to DS-CBT efficacy. In order to do this, we conducted two different meta-analyses.

2.1.2. Hypotheses

Several hypotheses were made based on previous meta-analyses of T-CBT.

1. We predicted that T-CBT would show to be an effective treatment for reducing symptoms of anxiety and depression in adults, children and adolescents with anxiety and/or depressive disorders or subthreshold anxiety or depression symptoms. We also hypothesized that the therapeutic gains were going to be maintained at follow-up both for anxiety and for depression.

2. Regarding the impact of potential moderators of treatment effect, we predicted that the uncontrolled trials would going to be associated with larger effect sizes, that the addition of behavioral activation would be associated with larger effect sizes for depression and that internet-delivered treatments would have larger effect sizes compared to face-to-face treatments both for anxiety and for depression.

3. We also hypothesized that a high proportion of the included studies would be associated with a high risk of a biased estimate of effect in line with previous meta-analyses.

4. Lastly, we predicted that treatment effect of T-CBT would be at least as strong as DS-CBT.

2.2. Study II: The UP-A adapted as preventive intervention: A cluster randomized controlled trial

2.2.1. Aims

1. The *main aim* of this study was to examine whether the Spanish version of the UP-A, adapted as a 9-sessions school-based preventive intervention was more effective than a waitlist control condition (consisting of the usual academic curriculum) in reducing symptoms of anxiety and depression.

2. The *second aim* was to investigate post-intervention and follow-up changes in a broad range of secondary outcome measures: positive and negative affect, anxiety sensitivity, emotional avoidance, top problems ratings, depression and anxiety-related interference, self-esteem, life satisfaction, quality of life, school adjustment, discipline problems, conduct problems, hyperactivity/inattention symptoms, peer problems and prosocial behavior.

3. The *third aim* was to assess whether any benefits of the intervention were predicted by age, gender, having been born in Spain, and interest in psychology.

4. The *fourth aim* was to conduct exploratory subgroup analyses focused on: a) excluding those in both groups who recently received psychological therapy, b) adolescents with greater emotional symptom severity that had not recently received psychological therapy, and c) adolescents who achieved completer status (attending at least 7 out of the 9 sessions).

5. The *fifth aim* was to examine if the effects at post-intervention were maintained at the 3-month follow-up.

6. The *sixth aim* of this study was to assess the feasibility (i.e., obtaining consent, assessment completion, group attendance) and the acceptability of implementing UP-A in a prevention group format and in a school setting.

7. The *seventh aim* was to calculate the intra-cluster correlation coefficient and measures of variability (i.e. standard deviation) for all primary and secondary outcomes in order to determine sample sizes of future full-scale, cluster randomized controlled trials applying the UP-A adapted as a preventive intervention.

8. The *eighth aim* was to translate and adapt the UP-A to Spanish.

2.2.2. Hypotheses

1. We predicted that the UP-A preventive intervention group would exhibit greater improvement on all primary and secondary outcome measures at post-intervention and follow-up compared to the waitlist control group.

2. Regarding exploratory subgroup analyses, greater improvement in the primary and secondary outcome variables was expected in those with higher levels of anxiety and/or depression symptoms and those who achieved completer status.

3. As for exploratory predictors of efficacy analyses, no hypotheses were formulated in relation to age and gender since earlier studies have shown contradictory results regarding these variables. Regarding possible predictors "have been born in Spain or not" and "interest in psychology", no hypotheses were formulated due to the lack of similar previous studies assessing these variables.

4. We also hypothesized that results would support the feasibility of school-based implementation of UP-A in a prevention group format, as evidenced by number of participants achieving treatment completer status (attending at least 7 out of the 9 sessions), as well as the acceptability of the intervention, as evidenced by participants' self-rated satisfaction at post-intervention.

2.3. Study III: An open trial applying the UP-A as a preventive intervention

2.3.1. Aims

1. The *primary aim* of this study was to examine whether the Spanish version of the UP-A adapted as a 9-sessions school-based preventive intervention was effective in reducing pre- to post-intervention symptoms of anxiety and depression.

2. The *second aim* was to investigate post-intervention changes in a broad range of secondary outcome measures: negative and positive affect, anxiety sensitivity, emotional avoidance, top problems ratings, depression and anxiety-related interference, self-esteem, life satisfaction, quality of life, conduct problems, hyperactivity/inattention symptoms, peer problems, prosocial behavior, school adjustment, and discipline problems.

3. The *third aim* was to assess the feasibility (e.g., assessment completion, group attendance) and the acceptability of implementing UP-A adapted as a preventive intervention.

2.3.2. Hypotheses

1. The first hypothesis was that there was going to be an improvement on all primary and secondary outcome measures at post-intervention compared to pre-intervention

2. The second hypothesis was that results were going to support the feasibility of school-based implementation of UP-A in a prevention group format, as evidenced by a number of participants achieving treatment completer status (attending at least 7 out of the 9 sessions)

3. The third hypothesis was that the acceptability of the intervention was going to be high, as evidenced by participants' self-rated satisfaction at post-intervention.

CHAPTER III. METHODS

1. Method Study I[11]

1.1. Background

There are several reasons why a new meta-analysis is necessary at this point. The first, and perhaps the most significant, is that a number of relevant studies investigating the efficacy of T-CBT protocols for anxiety and depression disorders have been published in the last two years, yet some of them are not included in these meta-analyses. Second, the most recent meta-analysis (Newby et al., 2015) included studies with no CBT-based treatment protocols, such as mindfulness therapy, psychodynamic psychotherapy, and acceptance and commitment therapy. Third, all of these previous reviews incorporated a number of studies that did not use T-CBT protocols (i.e., T-CBT protocols explicitly derived from some transdiagnostic model), such as classical CBT applied to several specific anxiety disorders, hybrid protocols (transdiagnostic/disorder-specific protocols), tailored treatments (i.e., treatments adapted to the patients' specific diagnoses) or modular approaches. Fourth, the previous meta-analyses did not take into account the pre- and post-treatment data when calculating the RCT effect size. Finally, most of the published T-CBT meta-analyses (e.g., Ewing et al., 2015; Reinholt & Krogh, 2014) only focused on anxiety disorders. These problems make it difficult to draw valid conclusions about the efficacy of T-CBT for the treatment of emotional disorders.

The present meta-analysis aimed to test the hypothesis that T-CBT is an effective treatment for reducing symptoms of anxiety and depression in adults and young people with principal or comorbid anxiety and/or depressive disorders, or subthreshold anxiety or depression. Moreover, we aimed to explore the impact of potential moderators of treatment effect, including participants' primary characteristics, diagnostic measures, and delivery format.

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[11] Content of this section was retrieved from **"Efficacy of transdiagnostic cognitive-behavioral therapy for anxiety and depression in adults, children and adolescents: A meta-analysis" by J. García-Escalera, P. Chorot, R.M. Valiente, J.M. Reales, & B. Sandín. 2016,** *Revista de Psicopatología y Psicología Clínica***, 21 (3), pp. 147-175.** Reprinted with permission. Copyright Asociación Española de Psicología Clínica y Psicopatología.

Thus far, this is the first meta-analysis to examine the efficacy of T-CBT protocols explicitly based in the transdiagnostic theory-driven approach, to include studies conducted with both adult and children/adolescent samples, and to use a more complete Hedges' *g* formula to calculate the effect size of RCT, taking into account pre- and post-treatment data.

1.2. Protocol and registration

This review was developed following the procedures outlined in the Cochrane Handbook for systematic reviews (Higgins & Green, 2011) and it is reported following the PRISMA guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009).

1.3. Eligibility criteria

Types of participants. We included patients with a primary diagnosis of an anxiety and/or a depressive disorder, or with subclinical anxiety and/or depression symptoms. In order to encompass studies conducted prior to the development of DSM-5, we decided to include patients with post-traumatic stress disorder, acute stress disorder, and obsessive-compulsive disorder.

Types of interventions. We included studies that applied theory-driven T-CBT protocols (i.e., protocols designed to target common mechanisms or processes that occur across a group of disorders) to treat multiple anxiety and/or depressive disorders, without tailoring the protocol to specific diagnoses (i.e., the same intervention was delivered for all the subjects). Studies that delivered treatment in an individual, group, or internet/computer-based format were included.

Types of comparisons. RCTs were included in which the effects of transdiagnostic treatment were compared with: (a) a waiting list control group (WLCG) condition, (b) an attention control condition (e.g., discussion group), and (c) other therapies (e.g., DS-CBT). We did not exclude uncontrolled studies since a high proportion of the published studies on T-CBT are uncontrolled; we conducted separate analyses for the RCTs and the uncontrolled studies.

Types of outcomes. Studies were included if at least one self-reported measure of anxiety or anxiety and depression was administered at both baseline and post-treatment[12]. We were also interested in examining outcomes at follow up.

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[12] The studies of Norton (2012) and Norton & Barrera (2012) did not report pre-treatment data, but we contacted the first author and were able to obtain all the data needed.

Types of study design. RCTs or uncontrolled studies were used if they (a) had at least five participants in the T-CBT condition at pretreatment, (b) were written in English or in Spanish, (c) were published in a peer-re-viewed journal, and (d) provided the necessary statistical data to calculate the effect size.

1.4.   Exclusion criteria

Studies were *excluded* if they (a) used alternative therapies to CBT, (b) used any form of protocol tailored to the treatment of any specific disorder, (c) included a psychological treatment that was combined with drug therapy, (e) included patients with psychotic disorders, personality disorders, or substance use disorders, or (f) included case studies.

1.5.   Information sources and search and study selection

The studies were traced in several ways. First, comprehensive searches were undertaken in the databases Scopus, PsycINFO, Science Direct, PsycArticles, and Google Scholar using the search string "(transdiagnostic AND anxiety OR depression OR emotional disorder OR depressive disorder OR mood disorder OR anxiety disorder OR internalizing OR negative affectivity)" in keywords, titles and abstracts. Second, the references of the systematic reviews and meta-analysis on T-CBT published to date were reviewed. Third, a search of the reference sections of the retrieved papers was conducted to identify additional studies. The main search for studies was completed in July 2015 and was last updated in March 2016. Those abstracts clearly irrelevant for the current study were discarded, while the remaining full texts were reviewed to assess whether they met the inclusion criteria.

1.6.   Data collection process and data items

A range of *study characteristics* were coded and extracted from each study: study type (RCT/uncontrolled), control condition if existent, sample size, publication date, country, percentage of attrition, risk of bias, diagnostic measure applied, sample recruitment (community/clinical) and follow-up period. With regard to *intervention characteristics*, application format (group/individual/ internet), treatment target (anxiety and/ or depression), and total number of sessions were coded and extracted. *Participant characteristics* studied were as follows: age group (adults/children-adolescents), mean age, gender, inclusion or exclusion of subclinical patients, and primary mental disorder.

1.7. Risk of bias in individual studies

An assessment of the studies' methodological quality was undertaken as previous studies have shown that a high risk of bias tends to overestimate the treatment effect size (Savovic et al., 2012). The Cochrane Collaboration's tool for assessing risk of bias was used (Higgins & Green, 2011), although minor adaptations of the tool were made in order to be able to assess psychotherapy studies. Performance bias was not coded since it is not feasible to blind therapists and clients to a psychotherapeutic intervention. The main domains assessed included selection bias, detection bias, attrition bias, reporting bias and "other biases." In uncontrolled trials, attrition bias, reporting bias, and other biases were the only domains coded. A judgment of low risk, unclear, or high risk of bias was given within each domain.

1.8. Summary measures

An a priori decision was made to calculate an effect size for anxiety in those studies that included patients with principal or comorbid anxiety disorders and another effect size for depression in those studies that included patients with principal or comorbid depressive disorders. Except for 6 studies that only reported the changes in anxiety (Essau et al., 2014; Norton, 2008; Norton, 2012; Norton & Barrera, 2012; Titov et al., 2010), effect sizes for both anxiety and depression outcomes were calculated in all studies. The measures chosen to calculate the effect sizes were the ones present to a greater extent in the majority of included studies (Table 4), and most of the times were the ones defined by the studies' authors as principal outcome measures. The formulas for Hedges' g and its' standard deviation, specifically the formulas (1) and (2) (Botella & Sánchez Meca, 2015), were used. In the case of the RCTs, we chose a complete non-biased estimator of g with a mean weighted standard deviation considering control and experimental groups because these groups are matched at pretest in the majority of original studies. This equation also corrects the effect that other factors could have had on the control group and uses the descriptive statistics usually reported in the assessed literature.

Like Cohen's *d*, Hedges' *g* is based on the standardized mean difference and effect sizes of 0.2, 0.5, and 0.8 are considered small, medium, and large, respectively (Cohen, 1992).

$$k = \left(1 - \frac{3}{4n-5}\right); \; g = k\left[\frac{(\bar{X}_{Pre} - \bar{X}_{Post})}{SD_{Pre}}\right]$$

$$SD_g = \sqrt{\frac{n-1}{n(n-3)}(1+n\cdot g^2) - \frac{g^2}{k^2}}$$

(1) **Standardized mean change index (Hedges'g) used for uncontrolled studies and its standard deviation**. *Note*: k =sample bias correcting factor; *n* = treatment sample size; *g* = Hedges'g; *X* = mean; *Pre* = pre-treatment; *Post* = post-treatment; *SD* = standard deviation; *SDg* = Hedge's *g* standard deviation.

$$k = \left(1 - \frac{3}{4(n_T + n_C) - 9}\right); \; g = k\left[\frac{(\bar{X}_{T\_Pre} - \bar{X}_{T\_Post}) - (\bar{X}_{C\_Pre} - \bar{X}_{C\_Post})}{\sqrt{\frac{(n_T - 1)SD^2_{T\_Pre} + (n_C - 1)SD^2_{C\_Pre}}{n_T + n_C - 2}}}\right]$$

$$SD_g = \sqrt{k^2\left(\frac{n_T + n_C}{n_T \cdot n_C}\right)\left(\frac{n_T + n_C - 2}{n_T + n_C - 4}\right)\left(1 + \frac{(n_T \cdot n_C)g^2}{n_T + n_C}\right) - g^2}$$

(2) **Standardized mean change index (Hedges'g) used for RCTs and its standard deviation.** *Note*: *k* = sample bias correcting factor; *n* = sample size; *C* = control; *T* = treatment; *g* = Hedges'g; *X* = mean; *Pre* = pre-treatment; *Post* = post-treatment; *SD* = standard deviation; SD_g = Hedge's g standard deviation.

1.9.   Synthesis of results, risk of bias and additional analysis

The software program, Comprehensive Meta-analysis (2.2) was employed to conduct all the statistical analysis. Because of the variations in methods and samples of the studies, a random effects model was used. The analyses were based on intent-to-treat data to the extent possible. For each comparison between a psychotherapy group and a comparison group, the effect size indicating the difference between the two groups at pre- and post-treatment was calculated. When possible, the effect sizes for pre-treatment to follow-up changes were also computed. The degree of heterogeneity was examined using the Cochrane´s Q statistic and the I^2 index (Higgins & Thompson, 2002). Heterogeneity refers to substantial differences in effect sizes between studies that are due to between-trial differences rather than to chance. The I^2 statistic is a quantification of this heterogeneity with 25%, 50% and 75% reflecting respectively low, medium, and high heterogeneity (Higgins, Thompson, Deeks, & Altman, 2003).

Publication bias was tested using Duval and Tweedie`s trim-and-fill procedure (2000) within the comprehensive meta-analysis. The Tweedie`s trim-and-fill test provides an adjusted effect size correcting for publication bias.

Finally, subgroup analyses were conducted in order to assess possible variations in the effect sizes. A random effects model was used to combine studies within each subgroup. A fixed effects model was used to combine subgroups and yield the overall effect. The between-study variance (tau-squared) was assumed to be the same for all subgroups.

2. Methods Studies II and III[13]

Studies II and III were granted ethical approval from the Research Ethics Committee of Universidad Nacional de Educación a Distancia, Madrid, Spain. All parents or guardians as well as adolescent participants provided written informed consent. The study is registered in Clinicaltrials.gov (NCT03123991)

2.1. Study design

Study II was implemented as a two-arm, cluster RCT (Campbell, Elbourne, Altman, & CONSORT group, 2004), with an intervention condition, the UP-A group (UP-A adapted as a preventive intervention program) and a 3-month WLCG. Study III was an uncontrolled trial including the participants allocated to the WLCG who received the intervention.

An urban secondary school in the city of Madrid (Spain) that was previously known to the authors expressed interest in being involved in research and agreed to participate. Measurements were taken on three occasions along the 2016-2017 school year: Time 1 (T1; one week before the UP-A group started the intervention), Time 2 (T2; one week after the

[13] Content of this section was retrieved from: **"The Spanish Version of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents (UP-A) Adapted as a School-Based Anxiety and Depression Prevention Program: Study Protocol for a Cluster Randomized Controlled Trial" by J. García-Escalera, R.M. Valiente, P. Chorot, J. Ehrenreich-May, S.M. Kennedy, & B. Sandín. 2017,** *JMIR research protocols***, 6(8), pp. 1-18.** Originally published in JMIR Research Protocols (http://www.researchprotocols.org), 21.08.2017. This is an open-access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited.

UP-A group finished the intervention), Time 3 (T3; three months after the UP-A group finished the intervention and one week before the WLCG started the intervention), and Time 4 (T4; 1 week after the WLCG finished the intervention). On all occasions, both groups completed the outcome measures at about the same time and during school hours. This represents a 3 (time) by 2 (group) repeated measures design.

Inclusion criteria for participants were providing written, informed consent (both the adolescent and at least 1 parent or legal guardian) and being able to understand, write, and read Spanish. Spanish proficiency was determined based on teacher report. Due to the universal prevention goal of this study, there were no other exclusion criteria.

2.2. Intervention

Participants received the Spanish version of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents (UP-A) (Ehrenreich-May et al., 2018), modified for delivery as a 9-session, school-based universal preventive intervention. Core modules of the UP-A include: (1) Building and Keeping Motivation; (2) Getting to Know Your Emotions and Behaviors; (3) Emotion-focused Behavioral Experiments; (4) Awareness of Physical Sensations; (5) Being Flexible in Your Thinking; (6) Awareness of Emotional Experiences; (7) Situational Emotion Exposures, and (8) Keeping it Going-Maintaining Your Gains (Ehrenreich-May et al., 2018).

The preventive intervention applied in Studies II and III consists of 9 weekly lessons, the length of which corresponds to a school's typical class period (55 minutes in the school in our study). It was delivered in a group format to entire classes of adolescents as part of the school curriculum. Specifically, the intervention sessions were carried out during school hours designated for "Tutorías." "Tutorías" are one-hour weekly sessions that, in the Spanish Education System, are meant to serve as a time for students to do several activities with their "tutor" (mentor). "Tutores" typically use this time to target issues occurring within the school context, such as providing professional development, providing academic support, assisting in solving problems between students or between students and teachers, etc. The WLCG received their normal class schedule without any planned socioemotional focus, followed by the intervention after the Time 3 assessment was completed. A detailed description of the content of each UP-A session can be found in Table 3.

Table 3. The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents (UP-A) preventive intervention session descriptions.

Session	Corresponding UP-A[a] Module	Main content
1	Module 1: Building and Keeping Motivation	Introduce confidentiality and group rules; obtain 3 top problems, severity ratings, and a SMART[b] goal for each problem; complete emotion identification skills activity if sufficient time remains.
2	Module 2: Getting to Know Your Emotions and Behaviors	Psychoeducation about emotions and their function; introduce emotional behaviors, the 3 parts of an emotional experience, and the "Before, During and After" form for tracking emotional experiences outside of sessions.
3	Module 3: Emotion-Focused Behavioral Experiments	Psychoeducation about cycle of avoidance, opposite action, and behavioral experiments; reflect on current use of free time and come up with a list of enjoyed activities; introduce weekly activity tracker for on-going behavioral activation.
4	Module 4: Awareness of Physical Sensations	Psychoeducation about body sensations, their relationship to intense emotions and their harmlessness; introduce the concept of "fight or flight response" and review cycle of avoidance; conduct sensational exposures with the group.
5	Module 5: Being Flexible in My Thinking	Introduce the concept of "thinking traps" (i.e., cognitive distortions) and teach common thinking traps; introduce the concept of automatic and alternative thoughts as well as detective thinking skills; re-rate top problems obtained in session 1.
6	Module 5: Being Flexible in Your Thinking	Review thinking traps and detective thinking skills; introduce and ensure understanding of problem solving skills; conduct examples using problems solving skills with group members; review skills learnt so far in the program.
7	Module 6: Awareness of Emotional Experiences	Introduce the rationale for present-moment awareness and practice this skill in session using non-emotional stimuli (e.g., focus on breathing); introduce rationale for non-judgmental awareness; do an individual mini-test assessing skills taught in the program so far.
8	Module 7: Situational Emotion Exposures	Review cycle of avoidance, reinforcement, and maintenance of learned behavior; provide psychoeducation about emotion exposures; create emotional behaviors forms to identify relevant exposures; if time permits, conduct a group exposure activity; assign exposure homework.
9	Module 8: Keeping it Going – Maintaining Your Gains	Review exposure homework and plan future exposures if necessary; re-rate top problems and revisit SMART goals; review skills that have been most useful for each group member and make an individualized post-program plan to practice skills.

[a] UP-A: Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents;
[b] SMART: specific, measurable, attainable, relevant, and time-bound

The students in the preventive intervention group were encouraged to practice skills learned in sessions by completing structured home learning assignments outside of formal session time. Completed home learning assignments were discussed at the beginning of each session, with the exception of the first. All intervention sessions were delivered by JGE, an advanced doctoral student in clinical psychology, and by an advanced masters student in clinical psychology. Session materials included Power Point Slides and handouts.

Researchers attempted to contact students who miss one of the weekly sessions and provided them with the opportunity to make up the content in the following days. During this makeup session, students were given a content summary and any missed home learning assignments to facilitate preparation for the next session.

2.3.   Implementation of the program

Prior to implementing the UP-A program, Julia García-Escalera received training on the UP-A protocol by its developer, Jill Ehrenreich-May at University of Miami (Coral Gables, US). The UP-A was translated into Spanish by Julia García-Escalera, and its translation and

adaptation were supervised by Bonifacio Sandín, Paloma Chorot, and Rosa M. Valiente. The translation process was also supervised by Jill Ehrenreich-May. Adherence to the protocol for the current study was self-monitored by the group leaders, who completed a checklist at the end of each session indicating whether each skill within the session was presented.

2.4.   Sample size

One significant impact of the adoption of a cluster design is the comparatively large sample size requirement since, in contrast to individually randomized trials where inter-individual variation is the only source of variability, cluster studies involve both variation among individuals and variation among clusters. As a result, cluster studies must recruit a larger number of individuals in order to achieve power equivalent to that of an individually randomized trial (Campbell et al., 2004). The magnitude of this within-cluster dependence, which ultimately influences the eventual trial size, is quantified by the intra-cluster correlation coefficient (ICC) (Gao, Earnest, Matchar, Campbell, & Machin, 2015). The ICC accounts for the extent to which responses of adolescents attending the same class (that is, sharing the same classroom, classmates, teacher, etc.) are more likely to be similar compared with adolescents from a different class.

Power analyses were conducted using G*Power Version 3 software (Faul, Erdfelder, Lang, & Buchner, 2007). Sample size required to detect a Cohen's *d* effect of .30 was estimated, based upon effect sizes reported in meta-analyses of school-based anxiety and depression preventive interventions conducted all over the world (Calear & Christensen, 2010; Corrieri et al., 2014), including in Spain (Sánchez-Hernández, Méndez, & Garber, 2014). Calculations showed that with a power level of .80 and a significance level of α = .05, a total sample of $N_{Non\text{-}cluster}$ = 74 was required to detect a significant effect. However, potential loss of power due to data clustering had to be considered in the sample size calculation. The impact of the ICC on the planned trial size depends on the so-called design effect, which can be calculated as $1+(m\text{-}1)$ ICC, with *m* referring to the number of subjects recruited per cluster (Gao et al., 2015). For this study, the ICC is unknown although, on the basis of prior school-based prevention research, the expected ICC for anxiety and depression-related outcomes is approximately 0.02 (Ahlen et al., 2015). The anticipated average class (cluster) size for this study was 27 students meeting inclusion criteria, resulting in a design effect of 1.52. The design effect is then multiplied by the previously calculated $N_{Non\text{-}cluster}$ (Gao et al., 2015), resulting in an estimated sample size for this trial of 112, considering the design effect. In addition, we estimated a dropout rate of 10% based on previous studies (Gallegos, Linan-Thompson, Stark, & Ruvalcaba, 2013; Johnson, Burke,

Brinkman, & Wade, 2016), resulting in an estimated total sample size of 123 (at least 62 students in each group). The total number of clusters required can be calculated dividing the estimated total sample size by the estimated number of subjects recruited per cluster (123/27) resulting in 4.56 clusters (Gao et al., 2015). Therefore, to achieve a sample of this size, a total of 157 students and 5 clusters were recruited.

The final number of participants recruited matches these a priori computations closely: 90 students (10 lost at Time 2) were allocated to the UP-A group and 62 students (4 lost at Time 2) were assigned to the WLCG.

2.5. Randomization

Sequence generation and allocation concealment. Each participating class (cluster) was randomly allocated 1:1 to the UP-A group or WLCG. We used a balanced design, resulting in about the same number of classes in each of the preventive intervention and WLCG. No matching, blocking or stratification took place. Cluster randomization was undertaken for the ecological validity of providing the intervention at the class level. The randomization was conducted by a researcher not involved in the current project by using a computer random number generator. Random assignment occurred before Time 1 measurements took place because the Research Ethics Committee that provided ethical approval for this study requested that the Informed Consent forms signed by parents/guardians and participants state whether the student was going to be in the UP-A group or WLCG.

Implementation and blinding. The adolescents completed all questionnaires using Qualtrics Survey software in a designated classroom, and a research assistant was available to provide assistance if necessary and to ensure independent responding. The research assistant was blind to the allocated treatment group at time of completing questionnaires to reduce risk of bias. Blinding of participants at the cluster or individual level was not possible for ethical reasons explained above. Regardless, blinding participants at the cluster or the individual level after baseline would have been impossible due to the nature of the experimental intervention, which requires active participation from the preventive intervention group compared to no involvement or participation from the WLCG in the first phase of the study. An attention-control intervention would have been ideal but was beyond the scope of this study.

2.6.   Measures

2.6.1. Primary outcome measures

The Revised Child Anxiety and Depression Scale-30 (RCADS-30) (Sandín, Chorot, Valiente, & Chorpita, 2010) is a widely-used questionnaire measuring self-reported anxiety and depressive symptoms in children and adolescents. The scale is comprised of the following subscales derived from the DSM-IV/DSM-5 criteria: (1) social phobia, (2) generalized anxiety disorder, (3) obsessive-compulsive disorder, (4) panic disorder, (5) separation anxiety disorder, and (6) major depressive disorder. The 6 subscales are summed to create a Total Anxiety and Depression score. Each item is scored from 0 ("Never") to 3 ("Always"), with higher scores representing more severe symptoms. The RCADS-30 has demonstrated good psychometric properties with normative and clinical populations (Chorot, Valiente, Magaz, Santed, & Sandin, 2017; Piqueras, Martin-Vivar, Sandín, San Luis, & Pineda, 2017).

Depression Questionnaire for Children (Cuestionario de Depresión para Niños; CDN) (Sandín, Chorot, & Valiente, 2016) is a 16-item, self-report questionnaire designed to assess symptoms of DSM-IV/DSM-5 major depressive disorder and dysthymic disorder in children and adolescents. In this study, the 2 items targeting suicidal ideation were not included as per the request of school personnel. Participants rate each item on a 3-point scale from 0 ("Never"), 1 ("Sometimes"), to 2 ("Very often") to indicate the frequency with which they experience depression symptoms. The sum of all items provides an overall score, with higher scores indicating greater depression symptoms. The CDN has demonstrated adequate psychometric properties (Sandín et al., 2010).

Anxiety Scale for Children (Escala de Ansiedad para Niños; EAN) (Sandín et al., 2016) is a 10-item questionnaire that assesses anxiety symptoms during the past few weeks in children and adolescents. Participants are instructed to indicate how frequently they have experienced general anxiety symptoms on a 4-point, Likert-type scale, ranging from 0 ("Never or almost never") to 3 ("A lot of the times or almost always"). The sum of all items provides an overall score, with higher scores indicating more elevated anxiety symptoms. The EAN has shown good psychometric properties (Chorot, Magaz, Valiente, & Sandín, 2013).

2.6.2. Secondary outcome measures

Top Problems Assessment (TPA) - Adolescent version. The adolescent version of TPA provides a means of collecting information about changes in the severity of problems identified by the adolescent to be of greatest concern. Group leaders first provide instructions and examples about the types of problems that can be targeted within the program and adolescents are then asked to generate 3 top problems of their own. Adolescents also generate a corresponding specific, measurable, attainable, relevant, and time-bound (SMART) goal for each problem. During the first, fifth, and ninth sessions, participants are asked to rate the severity of each problem on a 0 to 8 scale (with higher ratings indicating greater problem severity). Top problems are a central tool for progress monitoring in the UP-A and UP-C protocols. They were adapted by Ehrenreich-May from original work by Weisz et al. (2011). Top problems have been shown to demonstrate good psychometric properties (Weisz et al., 2011).

Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997). The Spanish version by García et al. (2000) was used. The scale provides scores for 5 subscales including emotional symptoms, conduct problems, symptoms of hyperactivity/inattention, peer problems, and prosocial behavior. Each subscale contains 5 items scored on a 3-point, Likert-type scale, ranging from 0 ("Not true") to 2 ("Certainly true"). A Total Difficulties Score is obtained by summing the 5 items on all scales, with the exception of the prosocial behavior scale. The SDQ is widely used and both the original and Spanish versions have good psychometric properties (Gómez-Beneyto et al., 2013; Goodman, 2001).

Depression and Anxiety Interference Scale for Children (Escala de Interferencia de la Depresión y Ansiedad para Niños; EIDAN) (García-Escalera, Sandín, Chorot, & Valiente, 2016). This 11-item questionnaire developed for this investigation assesses the degree to which feeling worried, nervous, or sad interferes with various domains of the adolescent's life (school, peer/family/general functioning), employing a 4-point, Likert-type scale ranging from 0 ("Nothing or almost nothing") to 3 ("A lot"). Higher scores indicate greater levels of interference.

The Positive and Negative Affect Schedule for Children and Adolescents (Escalas PANAS de Afecto Positivo y Negativo para Niños y Adolescentes; PANASN) (Sandín, 2003) questionnaire is an age-downward version of the Positive and Negative Affect Schedule (Watson, Clark, & Tellegen, 1988) for individuals aged 7 to 17 years. The scale provides scores for 2 subscales of 10 items each measuring positive and negative affect. Participants are asked to rate items according to how they usually feel from 1 ("Never or almost never"), 2 ("Sometimes"), to 3 ("A lot of the time"). The PANASN has demonstrated good psychometric properties (Sandín, 2003; Tortella-Feliu, Balle, & Sesé, 2010).

Childhood Anxiety Sensitivity Index (CASI) (Silverman, Fleisig, Rabian, & Peterson, 1991). The Spanish version of the CASI (Sandín, 1997) was used for this study. The CASI is an 18-item self-report questionnaire measuring anxiety sensitivity in children or distress reactions to symptoms of anxiety (e.g., "It scares me when my heart beats fast"). Participants rate the frequency with which they experience each item using a 3-point, Likert-type scale from 1 ("Never"), 2 ("Sometimes"), to 3 ("A lot of the time"). The Spanish adaptation of the CASI used in the present study has demonstrated good psychometric properties and positive correlations with constructs related to anxiety sensitivity (Sandín, Chorot, Santed, & Valiente, 2002).

Emotional Avoidance Strategy Inventory for Adolescents (EASI-A) (Kennedy & Ehrenreich-May, 2016). It is a 17-item self-report questionnaire in which respondents are instructed to indicate the degree to which each statement is true using a 5-point, Likert-type scale ranging from 0 ("Not at all true of me") to 4 ("Extremely true of me"). The EASI-A was translated and adapted to Spanish for this study (García-Escalera et al., 2016). Our Spanish adaptation also uses a 5-point Likert-type scale, but with options indicating frequency rather than degree from 0 ("Never or almost never"), 1 ("Seldom"), 2 ("Sometimes"), 3 ("A lot of times"), to 4 ("Always or almost always"). The EASI-A has demonstrated good psychometric properties and positive correlations with anxiety and depression symptoms (Kennedy & Ehrenreich-May, 2016).

The Satisfaction with Life Scale for Children (SWLS-C) (Sandín, Chorot, & Valiente, 2015). The SWLS-C measure is an age-downward version of the measure of life satisfaction developed by Diener et al. (Diener, Emmons, Larsen, & Griffin, 1985). It is a 5-item, self-report instrument in which respondents are asked to indicate the degree to which each statement is true of their life using a 4-point, Likert-type scale ranging from 1 ("Not at all") to 4 ("A lot or completely").

Kidscreen-10. The official Spanish version developed by the KIDSCREEN Group was used (KIDSCREEN Group, 2006). KIDSCREEN-10 is a widely-used brief questionnaire assessing generic health-related quality of life in children and adolescents that was adapted from the longer KIDSCREEN-27 (KIDSCREEN Group, 2006). The 10 items on the KIDSCREEN-10 index assess affective symptoms of depressed mood, difficulty concentrating, decreased energy, impaired school functioning, and impaired relations with peers and family. It uses a 5-point, Likert-type scale ranging from 1 ("Not at all") to 5 ("Extremely"). KIDSCREEN-10 has been shown to possess good psychometric properties (Erhart et al., 2009).

Self-Esteem Scale (SES) (Rosenberg, 1965). A Spanish adaptation of the SES was used in this study (Sandín, Valiente, & Chorot, 2008). SES is a 10-item self-report instrument

that measures global self-esteem. Respondents are asked to indicate how much they agree with each statement on a 4-point, Likert-type scale from 1 ("Strongly disagree") to 4 ("Strongly agree"). The scale has been shown to possess good psychometric properties in adolescent samples (Molina, Chorot, Valiente, & Sandín, 2014).

School Adjustment Brief Scale (Escala Breve de Ajuste Escolar; EBAE-10) (Moral, Sánchez-Sosa, & Villarreal, 2010). EBAE-10 is a 10-item questionnaire used to measure adaptive functioning in the area of school performance. Respondents are instructed to respond to questions about their grades, their relationships with teachers and peers, and their expectations regarding their educational future. They are asked to indicate how much they agree with each statement on a 6-point, Likert-type scale ranging from 1 ("Completely agree") to 6 ("Completely disagree"). This scale has demonstrated adequate psychometric properties (Sánchez-Sosa, Villarreal-González, Ávila-Guerrero, Vera-Jiménez, & Musitu, 2014).

General Indiscipline Scale (Escala de Indisciplina General; IG), adapted from Martín and collaborators' questionnaire (Martín, Pros, Busquets, & Muntada, 2012), is an 11-item questionnaire that assesses problematic behaviors of students in the classroom. Respondents are asked to indicate the frequency of each behavior stated in the items on a 4-circle bull's-eye, with each circle closer to the bulls-eye's center representing more frequent demonstration of the behavior. For this study, we adapted the scale such that adolescents were asked to rate the frequency with which they demonstrated each behavior on a 4-point, Likert-type scale with options being 0 ("Never or almost never"), 1 ("Only sometimes"), 2 ("Quite a few times"), or 3 ("A lot of the time"). The IG has demonstrated adequate properties (Busquets, Pros, Muntada, & Martín, 2015).

Socio-Demographic Information Questionnaire. All participants were asked to provide demographic information including their age, gender, school grades, socio-economic status, and place of birth.

2.6.3. Other Secondary Outcome Measures

Therapy and Psychology Questions. At Time 2, Time 3, and Time 4 assessments, students are also asked whether they have attended therapy in the last 3 months (and if yes, for how many sessions), as well as a question regarding their interest in psychology, rated on a 4-point, Likert-type scale from 1 ("None") to 4 ("A lot").

2.6.4. Measures Completed at Post-Intervention Only

The following questionnaires were completed by students in the UP-A group at Time 2 and by students in the WLCG at Time 4.

Satisfaction with the Program Questionnaire: We used 6 of the 7 questions from Rapee and colleagues' Satisfaction Questionnaire (2006). The 6 questions assess enjoyment of the program, amount learnt in the program, the effectiveness of the program in improving general life coping skills, likelihood of recommending the program to others, and the ability to cope with emotions before and after the program. We added one other question "Did this program help you to learn more about emotions and how they work?" All items are assessed on a 10-point scale from 1 ("Least or none") to 10 ("A lot"), with the exception of questions related to recommending the program to others and whether this program increased knowledge about emotions and how they work. These latter 2 questions are assessed using a dichotomous, 2-point scale with 1 being "Yes" and 2 being "No." Rapee and colleagues' Satisfaction Questionnaire has showed adequate psychometric properties (Martinsen et al., 2016; Rapee et al., 2006).

Discipline Problems During Sessions Questionnaire: Students were asked 6 questions about how often they demonstrated certain behaviors during the sessions using a 4-point, Likert-type scale from 1 ("In no or almost no sessions of the program"), 2 ("Only in some sessions of the program"), 3 ("In quite a lot of the sessions of the program"), to 4 ("In all or almost all sessions of the program"). Specifically, the items were (1) "I have talked to my classmates when I should not have"; (2) "I have paid attention to what the girls delivering the program were saying"; (3) "I have done things from other subjects during program sessions"; (4) "I have been reprimanded for my behavior"; (5) "I have taken the program seriously"; and (6) "I have tried to do my best when doing the in-class activities of the program."

Other End of Program Questions. Adolescents were also asked the following other questions related to the program: (1) "What did you like best about the program?";(2) "What did you like worst?"; (3) "Being honest with yourself, are you going to make efforts in the future to apply the strategies that you learned in this program in your daily life?"; (4) "When you missed a session, did you read the summary of the session that was given to you?"; and (5) "When you missed a session, did you do the homework that was given to you?". Questions 1 and 2 are open-choice questions and question 3 is to be answered using a dichotomous scale with 1 being "Probably yes" and 2 being "Probably not." Questions 4 and 5 are to be rated on a 3-point scale from 1 ("Most of the time yes"), 2 ("Most of the times no"), to 3 ("I did not miss any sessions").

2.6.5. Measures Completed at Post-Intervention and Follow-Up

The following questionnaires were completed by students in the UP-A group at Time 2 and Time 3, and by students in the WLCG at Time 4.

Curriculum Knowledge Questionnaire. A questionnaire was created on the basis of the program curriculum to assess participants' knowledge of core information presented in the program. Specifically, there were 2 open-choice questions ("What are the three parts of an emotion?" and "What can you do when you are feeling sad or down to feel better?") and one multiple choice question ("What is a thinking trap?") with 3 answer choices ("It is a kind of unpleasant emotion"/"It is what happens when someone tries to trick us into thinking what they want"/"It is a thought that makes us feel unpleasant emotions").

Strategies Practiced Outside of Session Questionnaire. We adapted the questionnaire for our study based on the format used in a previous study by Johnson et al. (2016). Students were asked "During the 9-week course, how often did you practice each of the following techniques outside of the lessons?", were supplied with a list of techniques learned during the course and were asked to rate how much they practiced each technique.

Adolescents rated each item on a 5-point, Likert-type scale from 1 ("Never"), 2 ("Once or twice in total"), 3 ("Greater than twice in total but less than once a week"), 4 ("Once or twice each week"), to 5 ("Three times or more each week"), with higher scores indicating more frequent practice of strategies learned in the program.

Specifically, participants were asked about their use of the following strategies: (1) "Identify the three parts of the emotion you are feeling (what you think, what you feel in your body and what you do)"; (2) "Plan for how long are you going to do school work and what pleasant activities are you going to do"; (3) "When you are sad or worried, do something that you like or value even if you do not feel like it"; (4) "Realize that you are falling into a thinking trap (e.g., thinking the worst, ignoring the positive, etc.) and try to change the thought to an alternative one that makes you feel better"; (5) "When you have a problem, think about all the possible solutions, then think about the good and bad things about each solution and, lastly, choose one of the solutions to try"; (6) "Try to focus in the present moment"; (7) "Meditate, that is, sit and try to focus in your breathing for a few minutes"; and (8) "Expose yourself little by little to those things that scare you or make you nervous because you know it is the only way to overcome your fears." At Time 3, the question was re-worded to: "Since the end of the program at school, how often have you used the following strategies?" In the current sample, this questionnaire demonstrated adequate internal consistency at Time 2 (alpha = .82) and Time 3 (alpha = .85) assessments.

2.7.   Statistical analyses

Analysis of data was in accordance with CONSORT guidelines and, in particular, the extension to cluster randomized trials (Campbell et al., 2004). Statistical significance was considered as a *P* value of less than .05, and statistical analysis was carried out using IBM Statistical Package for the Social Sciences, Version 24.0 (IBM SPSS). Data was analyzed taking the clustering of students within classes into account.

The effectiveness of the intervention was assessed using multi-level (or hierarchical) modeling that includes both fixed (intervention effects) and random (students in classrooms) effects. Experimental and WLCG were compared at 3 points in time: Time 1 (pre-treatment), Time 2 (post-treatment for intervention group), and Time 3 (3-month follow-up for intervention group). In addition, within-participant analyses were conducted only with the WLCG at Time 4. ICCs were calculated for all primary and secondary outcomes to compare the variation due to school class and the total variance.

Secondary analyses included: (1) repeating the primary analysis adjusting for any variables exhibiting significant imbalance at baseline to assess whether this influences the findings; (2) examining intervention changes for adolescents who scored above the clinical cut-off for anxiety and/or depression at Time 1; (3) investigating potential predictors of intervention effects including all participants; (4) comparing observed and expected attrition rates, as well as observed and expected ICCs; and (5) analyzing answers to checklists completed by group leaders.

CHAPTER IV. SUMMARY OF RESULTS

1. Study I[14]

1.1.   Study selection and characteristics

The inclusion of studies process is summarized in Figure 1. The search yielded 1519 hits. A total of 48 studies (included in 41 publications) met our inclusion criteria (21 RCTs, 27 uncontrolled studies; 43 adult samples; 5 child/adolescent samples). The 48 studies investigated 22 different transdiagnostic protocols. Concerning the 21 included RCTs, 20 studied adults whereas only 1 (Chu et al., 2016), which used WLCG, included participants younger than 18 years of age. Out of the 20 RCTs with adults, 13 studies involved WLCG (Bolton et al., 2014; Chu et al., 2016; Farchione et al., 2012; Johnston, Titov, Andrews, Spence, & Dear, 2011; Mullin et al., 2015; Newby et al., 2013; Norton, Hayes, & Hope, 2004; Norton & Hope, 2005; Schmidt et al., 2012; Titov et al., 2013; Titov et al., 2010; Titov et al., 2011; Wuthrich & Rapee, 2013), one study used a discussion group for comparison (Wuthrich, Rapee, Kangas, & Perini, 2016), one used TAU for comparison (Ejeby et al., 2014), one used relaxation training (Norton, 2012), and five studies compared T-CBT with DS-CBT (Dear et al., 2015; Fogliati et al., 2016; Lotfi et al., 2014; Norton & Barrera, 2012; Titov et al., 2015b). The study characteristics can be found in Table 4.

1.2.   Participants

The sample for this meta-analysis totaled 6291 participants. There was a greater representation of females than males across studies, with the overall percentage of females being 61.02 (*SD* = 15.55). Participants were on average 41.14 (*SD* = 12.04) years old in the studies including an adult sample and 11.78 (*SD* = 2.60) years in the ones including children and adolescents. In relation to the recruitment method, patients were recruited from clinical samples in seven studies (all of them including adults), while in the rest of the studies

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[14] Content of this section was retrieved from **"Efficacy of transdiagnostic cognitive-behavioral therapy for anxiety and depression in adults, children and adolescents: A meta-analysis" by J. García-Escalera, P. Chorot, R.M. Valiente, J.M. Reales, & B. Sandín. 2016,** *Revista de Psicopatología y Psicología Clínica***, 21 (3), pp. 147-175.** Reprinted with permission. Copyright Asociación Española de Psicología Clínica y Psicopatología.

patients were recruited, at least partly, through community referrals. A total of 45 studies included data on the percentage of participants who discontinued treatment (attrition). The attrition percentage was on average 23.10 (SD = 15.97).

1519 of records identified through database searching		81 of additional records identified through other sources

1297 of records after duplicates removed

1297 of records screened	→	916 of records excluded

381 of full-text articles assessed for eligibility →

340 of full-text articles excluded, with reasons:
Theoretical articles on transdiagnostic treatment or factors (n=112)
Not CBT transdiagnostic treatment (n=115)
Sample with excluded diagnosis (e.g., eating disorders) (n=35)
Case studies or other excluded study designs (n=36)
Individually tailored treatments (n=34)
Prevention or maintaining therapy studies (n=3)
Secondary analysis of RCTs (n=3)
Not enough data to calculate effect size (n=2)

48 studies (included in 41 articles) included in quantitative synthesis (meta-analysis)

Figure 1. Study flow diagram.

Table 4. Characteristics of included studies evaluating transdiagnostic cognitive behavior therapy treatments for anxiety and/or depression

Study	Mean age (range) %female	Diagnostic measure (Recruit.[a])	Inclussion	Intervention (Protocol)	Design Target	%Primary diagnosis [patients with comorbid emotional disorders][b]	N[c] (attrition)	ANX/DEP outcome measure	Count. Follow up[d]
Bilek & Ehrenreich 2012	9.8 (7-12) 45.5% female	ADIS-IV- C/P (Com)	Principal DSM-IV diagnosis of ANX	T-GCBT: 15 x 90min sessions (UP-C)	Uncontrolled ANX	GAD 40.9; SAD 40.9; SP 9.1; SD 9.1 [NR]	T-GCBT 22 (27%)	SCARED/ ---[e]	USA ---
Bolton et al., 2014	35.6 (18-65) 63% female	HTQ/ HSCL-25 (Com)	Report trauma exposure & meet severity criteria for DEP and/or PTSS	T-CBT: 1h weekly sessions (CETA)	RCT ANX+DEP	NR [NR]	T-CBT 182 (18.7%) WLC 165	HSCL-25/ HTQ	USA ---
Bullis et al., 2015	44.6 (20-69) 63.6% female	ADIS-IV-L (Clin)	Principal DSM-IV diagnosis of ANX or DEP	T-GCBT: 12 x 2h sessions (UP)	Uncontrolled ANX+DEP	SAD 36.4; GAD 9.1; DYS 9.1; OCD 9.1; Pan/Ag 9.1; SP 9.1; ADNOS 9.1; Ag 9.1. [72.7%]	T-GCBT 11 (9.1%)	OASIS/ ODSIS	USA ---
Chu et al., 2009	12.8 (12-14) 60% female	ADIS-IV-C (Com)	DSM-IV diagnosis of ANX or DEP	T-GCBT: 13 x 40min sessions (GBAT)	Uncontrolled ANX+DEP	Soc.P 40; MDD 40; GAD 20 [100%]	T-GCBT 5 (20%)	MAS-CP/ CESD-CP	USA ---
Chu et al., 2016	12.1 (12-14) 71.4% female	ADIS-IV-C/P (Com)	Clinical or subclinical principal diagnosis of DSM-IV-TR unipolar DEP or ANX	T-GCBT: 10 x 1h sessions (GBAT)	RCT ANX+DEP	Soc. P 51.4; GAD 17.1; SD 14.3; MDD 11.4; Minor depression 2.9; DYS 2.9 [NR]	T-GCBT 21 (23.8%) WLC 14	SCARED/ CESD-CP	USA ---
Dear et al., 2011	44.4 (NR) 78% female	MINI-t (Com)	DSM-IV diagnosis of ANX or DEP	T-iCBT: 5 sessions/ 8 weeks (Brief version of The Wellbeing Program)	Uncontrolled ANX+DEP	MDD 56.3; GAD 31.3; Pan/Ag 6.3; Soc.P 6.3 [78.1%]	T-iCBT 32 (19%)	GAD-7/ PHQ-9	Australia 3
Dear et al., 2015	43.8 (19-65) 76% female	MINI-t (Com)	Principal complaint of GAD symptoms	T-iCBT: 5 lessons/ 8 weeks (The Wellbeing Course); DS-iCBT: 5 lessons/ 8 weeks (The Worry Course)	RCT GAD	GAD symptoms 100 Comorbid disorders: MDD, SAD, Pan/Ag [NR]	T-iCBT 170 (37.1%) DS-iCBT 168 (33.3%)	GAD-7/ PHQ-9	Australia 3, 12 & 24
De Ornelas et al., 2013	35.6 (18-58) 87.5% female	MINI (Com)	Principal DSM-IV diagnosis of DEP and at least one ANX disorder	T-GCBT: 12x 2h sessions (UP)	Uncontrolled ANX+DEP	NR [NR]	T-GCBT 16 (NR)	BAI/BDI	Brasil ---
Ejeby et al., 2014	44.2 (18-65) 78.8% female	ADIS-IV (Clin)	Patients referred to the study by their GPs	T-GCBT: 12x 2h sessions(NR); TAU: medication, referrals to the counsellor	RCT ANX+DEP	Mood disorders 57; Anxiety disorders 37.3 [NR]	T-GCBT 84 (12%) TAU 81 (NR)	CPRS-S-A/ CPRS-S-D	Sweden 12
Ellard et al., 2010 (1)	30 (18-54) 58.8% female	ADIS-IV-L (Com)	Primary DSM-IV diagnosis of ANX	T-CBT: 8-15 x 1h sessions (UP)	Uncontrolled ANX+DEP	Pan/Ag 22.2; SAD 22.2; GAD 16.7; OCD 16.7; MDD 11.1; PTSD 5.5; Hypocondriasis 5.5 [NR%] Average nº diagnoses = 1.9	T-CBT 18 (8.3%)	BAI/ BDI	USA ---
Ellard et al., 2010 (2)	29.7 (18-44) 53.3% female	ADIS-IV-L (Com)	Primary DSM-IV diagnosis of ANX	T-CBT: 12-18 x 1h sessions (UP)	Uncontrolled ANX+DEP	SAD 33.3; GAD 20; OCD 20; Pan/Ag 13.3; GAD+SAD 6.7; GAD+Pan/Ag 6.7. [NR] Average nº diagnosis = 2.2	T-CBT 14 (16.7%)	BAI/ BDI	USA 6
Essau et al., 2014	8.8 (8-10) 29.5% female	SCAS (Com)	Referred by teachers for having significant anxiety problems	T-GCBT: 8 x 45min sessions (Super Skills for Life)	Uncontrolled ANX	NR Anxiety scores were in the clinical range as measured using the SCAS [NR]	T-GCBT 51 (16.4%)	SCAS/ ---	UK 6
Espejo et al., 2016	46.4 (24-70) 24.1% female	MINI (Clin)	DSM-IV diagnosis of ANX	T-GCBT: 12 x 2h sessions (Norton and Hope protocol)	Uncontrolled ANX	Pan/Ag 31; GAD 24.1; SAD 19; PTSD 12.1; SP 5.2: ADNOS 5.2; OCD 3.4 [62.9%]	T-GCBT 51 (25%)	Mini-MASQ/ Mini-MASQ	USA ---

Study	Mean age (range) %female	Diagnostic measure (Recruit.[a])	Inclusion	Intervention (Protocol)	Design Target	%Primary diagnosis [patients with comorbid emotional disorders][b]	N[c] (attrition)	ANX/DEP outcome measure	Count. Follow up[d]
Farchione et al., 2012	29.8 (19-52) 59.5% female	ADIS-IV-L (Clin)	Principal DSM-IV diagnosis of ANX	T-CBT: 18 x 1h sessions (UP)	RCT ANX	Pan/Ag 21.6; SAD 21.6; OCD 21.6; GAD 18.9; ADNOS 5.4; PTSD 2.7; 2 principal ANX disorders: 8. [NR] Average nº diagnosis = 2.2	T-CBT 26 (15.4%) WLC 11	BAI/ BDI-II	USA 6
Fogliati et al., 2016	41.4 (18-62) 79% female	MINI-t (Com)	Principal symptoms consistent with Pan/Ag	T-iCBT: 5 lessons/ 8 weeks (The Wellbeing Course);DS-iCBT: 5 lessons/ 8 weeks (The Panic Course)	RCT Pan/Ag	Pan/Ag symptoms 100Comorbid disorders: GAD, SAD, Pan/Ag [NR]	T-iCBT 72 (11.1%) DS-iCBT 73 (20.6%)	GAD-7/ PHQ-9	Australia 3, 12 & 24
Gros, 2014 (1)	50.8 (NR) 7.1% female	MINI (Clin)	Principal DSM-IV affective disorder	T-CBT: 12 x 45-60min sessions (NR)	Uncontrolled ANX+DEP	PTSD 46.7; Pan/Ag 26.6; Soc.P 20; MDD 6.7 [100%]	T-CBT 12 (20%)	DASS-ANX/ DASS- DEP	USA ---
Gros, 2014 (2)	49.5 (NR) 24.1% female	MINI (Clin)	Principal DSM-IV affective disorder	T-CBT: 12-16 x 45-60min sessions (TBT)	Uncontrolled ANX+DEP	PTSD 48.2; Pan/Ag 24.1; MDD 24.1; Soc.P 3.4 [100%]	T-CBT 21 (27.6%)	DASS-ANX/ DASS-DEP	USA ---
Ito et al., 2016	35.2 (22-64) 59% female	MINI (Clin)	DSM-IV diagnosis of an ANX or DEP disorder	T-CBT: 18 x 1h sessions (UP)	Uncontrolled ANX+DEP	MDD 53; SAD 24; Pan/ag 12; PTSD 6; ADNOS 6 [82%]	T-CBT 17 (11.8%)	STAI/BDI-II	Japan 3
Johnston et al., 2011	41.6 (19-79) 58.8% female	MINI-t (Com)	Principal DSM-IV diagnosis of GAD, Soc.P or Pan/Ag	T-iCBT: 8 sessions/ 10 weeks (The Anxiety Program)	RCT ANX	GAD 45; Soc.P 34.4; Pan/ Ag 20.6 [70.2%]	T-iCBT 89 (25%) WLC 42	GAD-7/ PHQ-9	Australia 3
Johnston et al., 2014	20.6 (18-24) 78% female	MINI-t (Com)	At least mild symptoms of ANX or DEP	T-iCBT: 4 lessons/ 5 weeks (Mood Mechanic Course)	Uncontrolled ANX+DEP	MDD 28; GAD 28; Soc.P 22; Pan/Ag 5; 17% subclinical patients [92%]	T-iCBT 18 (39%)	GAD-7/ PHQ-9	Australia 3
Kayrouz et al., 2015	33.6 (24-50) 73% female	MINI-t (Com)	Experience at least mild symptoms of ANX or DEP	T-iCBT: 5 lessons/ 8 weeks (Arab Wellbeing Course)	Uncontrolled ANX+DEP	MDD 36; GAD 27; 36.4% subclinical patients [54.6%]	T-iCBT 11 (9%)	GAD-7/ PHQ-9	Australia 3
Kayrouz et al., 2016	36.2 (19-67) 58% female	Self-reported measures (Com)	Experience at least mild symptoms of ANX or DEP	T-iCBT: 5 lessons/ 8 weeks (Arabic Wellbeing Course)	Uncontrolled ANX+DEP	NR [NR]	T-iCBT 36 (64%)	GAD-7/ PHQ-9	Australia 3
Kirpatrick et al., 2013	NR (25-54) 60% female	Self-reported measures (Com)	Self-identified as experiencing at least mild anxiety symptoms	T-iCBT: 5 lessons/ 8 weeks (The Wellbeing Course)	Uncontrolled ANX+DEP	NR [NR]	T-iCBT 10 (0%)	GAD-7/ PHQ-9	Australia 3
Lotfi et al., 2014	34.2 (NR) 53.6% fem.	NR (Clin)	Principal diagnosis of mood or anxiety disorders	T-CBT: 8 x 45min sessions (UP); DS-GCBT: 8 x 45min sessions (DS-CBT manual)	RCT ANX+DEP	GAD 39.1; MDD 21.7; ADNOS 17.4; SAD 17.4; Pan/Ag 4.4 [NR]	T-CBT 12 (14.3%) DS-GCBT 9 (25%)	BAI/ BDI-II(IRQOL)	Iran ---
McEvoy & Nathan, 2007	35.4 (NR) 59.4% female	MINI (NR)	DSM-IV diagnosis of ANX or DEP	T-GCBT: 10 x 2h sessions (Nathan, Rees, & Smith, 2001)	Uncontrolled ANX+DEP	MDD 56.6; Pan/Ag 12.6; Soc.P 10.5; DYS 9.8; GAD 9.8; SP 0.7 [52.4%]	T-GCBT 143 (34.3%)	BAI/BDI	Australia ---
Mullin et al., 2015	27.8 (19-55) 64.3% female	MINI-t (Com)	Self-identified as experiencing symptoms of ANX or DEP	T-iCBT: 3 lessons/ 6 weeks; 6 lessons/ 6 weeks; 5 lessons/ 5 weeks (UniWellbeing Course)	RCT ANX+DEP	Principal diagnosis NR 15.9% subclinical patients [46.9%]	T-iCBT 30 (57%) WLC 23	GAD-7/ PHQ-9	Australia 3
Newby et al., 2013 (1)	44.4 (21-80) 77.8% female	MINI-t (Com)	DSM-IV diagnosis of GAD and/or MDD	T-iCBT: 6 sessions/ 10 weeks (The Worry and Sadness Program)	RCT ANX+DEP	GAD+MDD 47.1; GAD 37.9; MDD 15.0 [NR]	T-iCBT 46 (11%) WLC 53	GAD-7/ PHQ-9	UK 3

Study	Mean age (range) %female	Diagnostic measure (Recruit.[a])	Inclusion	Intervention (Protocol)	Design Target	%Primary diagnosis [patients with comorbid emotional disorders][b]	N[c] (attrition)	ANX/DEP outcome measure	Count. Follow up[d]
Newby et al., 2013 (2)	39.3 (18-78) 64.7% female	Self-reported measures (Com)	Registered clinicians prescribed the course to their patients	T-iCBT: 6 sessions/ 13 weeks (The Worry and Sadness Program)	Uncontrolled ANX+DEP	NR [NR]	T-iCBT 136 (58.8%)	GAD-7/ PHQ-9	UK ---
Newby et al., 2014	40.2 (18-82) 67.6% female	Self-reported measures (Com)	Registered clinicians prescribed the course to their patients	T-iCBT: 6 lessons/ 12 weeks (The Depression and Anxiety Program)	Uncontrolled ANX+DEP	NR [75%]	T-iCBT 707 (52.7%)	GAD-7/ PHQ-9	Australia ---
Norton et al., 2004	39.6 (NR) 52.6% female	ADIS-IV (Com)	Primary DSM-IV diagnosis of ANX	T-GCBT: 12 x 2.5h sessions (Norton and Hope)	RCT ANX	GAD 36.8; SAD 26.3; OCD 15.8; Pan/Ag 15.8; PTSD 5.3 [79%]	T-GCBT 9 (25%) WLC 10	---/ DASS-DEP	USA ---
Norton & Hope, 2005	39.6 (NR) 52.6% female	ADIS-IV (Com)	Primary DSM-IV diagnosis of ANX	T-GCBT: 12 x 2.5h sessions (Norton and Hope)	RCT ANX	GAD 36.8; SAD 26.3; OCD 15.8; Pan/Ag 15.8; PTSD 5.3 [79%]	T-GCBT 9 (25%) WLC 10	DASS-AN/---	USA ---
Norton, 2008	33.1 (19-71) 56.9% female	ADIS-IV (Com)	Principal DSM-IV diagnosis of ANX	T-GCBT: 12 x 2h sessions (Norton and Hope)	Uncontrolled ANX	SAD 50; Pan/Ag 44; GAD+OCD 4; SP 2. [78%]	T-GCBT 52 (NR)	STAI/---	USA ---
Norton, 2012b	33 (18-62) 62.1% female	ADIS-IV (Com)	Principal DSM-IV diagnosis of ANX	T-GCBT: 12 x 2h sessions (Norton and Hope) RLX: 12 x 2h sessions	RCT ANX	SAD 42.5; Pan/Ag 35.6; GAD 17.2; ADNOS 2.3; SP 1.2; OCD 1.2 [60.7%]	TD- GCBT 65 (29.7%) RLX 22 (57.1%)	BAI/---	USA ---
Norton & Barrera, 2012	31.5 (19-53) 50% female	ADIS-IV (Com)	Principal DSM-IV diagnosis of GAD, SAD or Pan/Ag	T-GCBT: 12 x 2h sessions (Norton and Hope) DS-CBT: 12x 2h sessions	RCT ANX	SAD 54.4; Pan/Ag 23.9; GAD 21.7 [NR]	T-GCBT 23 (21.7%) DS-CBT 23 (39.1%)	STAI/---	USA ---
Queen et al., 2014	15.4 (12-17) 57.6% female	ADIS-IV-C/P (NR)	Principal DSM-IV diagnosis of ANX and/or MDD	T-CBT: 8-21 sessions (UP-A)	Uncontrolled ANX+DEP	GAD 39; Soc.P 32.2; Pan/Ag 8.5; MDD 18.6; ADNOS 8.5; OCD 6.8; SP 5.1; DYS 3.4. [NR] 38.9% had comorbid DEP	T-CBT 59 (18.4%)	RCADS-ANX/ RCADS-MDD	USA 3&6
Schmidt et al., 2012	36.3 (NR) 72.7% female	SCID-IV (Com)	Principal DSM-IV diagnosis of GAD, Pan/Ag or SAD	T-GCBT: 10 x 120 min sessions (F-SET)	RCT ANX	SAD 36.3; Pan/Ag 36.1; GAD 27.7 [NR]	T-GCBT 57 (7%) WLC 39	ASI/ BDI	USA 6
Titov et al., 2010 (1)	39.5 (18-74) 67.9% female	MINI-t (Com)	DSM-IV diagnosis of GAD, Soc.P or Pan/Ag	T-iCBT: 6 sessions/ 10 weeks (The Anxiety Program)	RCT ANX	GAD 43.6; Soc.P 29.5; Pan/Ag 26.9 [75.6%]	T-iCBT 40 (25%) WLC 38	GAD-7/---	Australia 3
Titov et al., 2010 (2)	40.5 (18-73) 63.2% female	MINI-t (Com)	DSM-IV diagnosis of GAD, Soc.P or Pan/Ag	T-iCBT: 6 sessions/ 10 weeks (The Anxiety Program)	Uncontrolled ANX	GAD 42.1; Pan/Ag 28.9; SP 28.9 [73.7%]	T-iCBT 38 (NR)	GAD-7/---	Australia ---
Titov et al., 2011	43.9 (18-79) 73% female	MINI-t (Com)	Principal DSM-IV diagnosis of GAD, Soc.P, Pan/Ag or MDD	T-iCBT: 8 sessions/ 10 weeks (The Wellbeing Program)	RCT ANX+DEP	MDD 51; GAD 28; Soc.P 11; Pan/Ag 10 [81.0%]	T-iCBT 37 (19%) WLC 37	GAD-7/ PHQ-9	Australia 3
Titov et al., 2013	41.5 (18-59) 72.4% female	Self-reported measures (Com)	Self-identified as having a principal complaint of MDD, GAD, Soc.P or Pan/ Ag	T-iCBT: 5 sessions/ 8 weeks (The Wellbeing Course)	RCT ANX+DEP	GAD 31.1; MDD 35.1; Soc.P 21; Pan/Ag 13 [NR]	T-iCBT 103 (49.8%) WLC 51	GAD-7/ PHQ-9	Australia 3

Study	Mean age (range) %female	Diagnostic measure (Recruit.[a])	Inclusion	Intervention (Protocol)	Design Target	%Primary diagnosis [patients with comorbid emotional disorders][b]	N[c] (attrition)	ANX/DEP outcome measure	Count. Follow up[d]
Titov et al., 2015a (1)	NR (18-60) NR% female	Self-reported measures (Com)	Self-identified as experiencing symptoms of ANX and/or DEP	T-iCBT: 5 lessons/ 8 weeks (The Wellbeing Course)	Uncontrolled ANX+DEP	NR [NR]	T-iCBT 1793 (29.1%)	GAD-7/ PHQ-9	Australia 3
Titov et al., 2015a (2)	NR (>60) NR% female	Self-reported measures (Com)	Self-identified as experiencing symptoms of ANX and/ or DEP	T-iCBT: 5 lessons/ 8 weeks (The Wellbeing Plus)	Uncontrolled ANX+DEP	NR [NR]	T-iCBT175 (19.4%)	GAD-7/ PHQ-9	Australia 3
Titov et al., 2015b	44.2 (18-64) 72% female	MINI-t (Com)	Principal complaint of DEP symptoms	T-iCBT: 5 lessons/ 8 weeks (The Wellbeing Course); DS-iCBT: 5 lessons/ 8 weeks; (The Mood Course)	RCT DEP	MDD symptoms 100 Comorbid disorders: GAD, SAD, Pan/Ag [NR]	T-iCBT 149 (53%) DS-CBT 141 (37.6%)	GAD-7/ PHQ-9/	Australia 3, 12 & 24
Titov et al., 2016 (1)	65 (60-78) 65% female	Self-reported measures (Com)	Principal complaint of symptoms of ANX or DEP	T-iCBT: 5 lessons/ 8 weeks (The Wellbeing Plus)	Uncontrolled ANX+DEP	NR [NR]	T-iCBT 153 (2%)	GAD-7/ PHQ-9	Australia 3
Titov et al., 2016 (2)	66 (60-80) 64% female	Self-reported measures (Com)	Principal complaint of symptoms of ANX or DEP	T-iCBT: 5 lessons/ 8 weeks (The Wellbeing Plus)	Uncontrolled ANX+DEP	NR [NR]	T-iCBT 140 (3%)	GAD-7/ PHQ-9	Australia 3
Titov et al., 2016 (3)	67 (60-93) 63% female	Self-reported measures (Com)	Principal complaint of symptoms of ANX or DEP	T-iCBT: 5 lessons/ 8 weeks (The Wellbeing Plus)	Uncontrolled ANX+DEP	NR [NR]	T-iCBT 140 (5%)	GAD-7/ PHQ-9	Australia 3
Wutrich & Rapee, 2013	67.4 (60-84) 64.7% female	ADIS-IV (Com)	DSM-IV clinical or subclinical criteria for an anxiety and mood disorder	T-GCBT: 12 x 2h sessions (The Ageing Wisely)	RCT ANX+DEP	GAD 34.6; MDD 20.6; DYS 14.1; MDNOS 10.3; Soc. P 10.3; PTSD 4.4; SP 3.5; ADNOS 3.3;11.3% subclinical patients [NR]	T-GCBT 27 (12%) WLC 35	GAI/GDS	Australia 3
Wutrich et al., 2016	67.4 (60-88) 55.6% female	ADIS-IV (Com)	DSM-IV diagnosis of ANX and a unipolar mood disorder	T-GCBT: 11 x 2h sessions; (Ageing Wisely) DG: 11 x 2h sessions	RCT ANX+DEP	GAD 33.1; MDD 27.8 [NR] Average nº diagnosis = 2.92	T-GCBT 76 (13.2%) DG 57 (21.1%)	GAI/GDS	Australia 6

Note. ADIS-IV = Anxiety Disorders Interview Schedule for DSM-IV; ADIS-IV-C = Anxiety Disorders Interview Schedule for DSM-IV-Child Interview; ADIS-IV-C/P = Anxiety Disorders Interview Schedule for DSM-IV-Child and Parent Reports; ADIS-IV-L= Anxiety Disorders Interview Schedule for DSM-IV-Lifetime Version; ADNOS = Anxiety disorder not otherwise specified; ANX = anxiety; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; BDI-II = Beck Depression Inventory, second edition; CBT = cognitive behavior therapy; CESD-CP = Center for Epidemiologic Studies Depression Scale for Children-Child and Parent reports; CETA = Common Elements Treatment Approach; Clin = clinical recruitment; Com = at least in part recruitment through the community; CPRS-S-A = Self-Rating Scale for Affective Syndroms (Anxiety); CPRS-S-D = Self-Rating Scale for Affective Syndroms (Depression); DASS = Depression Anxiety Stress Scales 21-Item Version; DEP = depression; DG = discussion group; DS-GCBT = group-delivered disorder specific cognitive behavior therapy; DS-iCBT = internet-delivered disorder specific cognitive behavior therapy; DYS = dystimia; F-SET = False Safety Behavior Elimination Therapy; GAD = generalized anxiety disorder; GAD-7 = Generalized Anxiety Disorder-7 item Scale; GAI = Geriatric Anxiety Inventory; GBAT = Group Behavioral Activation Therapy; GDS = Geriatric Depression Scale; GPs = general practitioners; HSCL-25 = Hopkins Symptom Checklist 25; HTQ = Harvard Trauma Questionnaire; iCBT = internet-delivered cognitive behavioral therapy; MASC-CP = Multidimensional Anxiety Scale for Children-Child and Parent reports; MDD = major depressive disorder; MDNOS = Mood Disorder Not Otherwise Specified; MINI = Mini International Neuropsychiatric Interview version 5.0.0; Mini-MASQ = The Mini Mood and Anxiety Symptom Questionnaire; MINI-SPIN = MINI Social Phobia Inventory; MINI-t = Mini International Neuropsychiatric Interview version 5.0.0 conducted through telephone; NR = not reported; PTSS = post-traumatic stress symptoms; OASIS = Overall Anxiety Severity and Impairment Scale; OCD = obsessive compulsive disorder; ODSIS = Overall Depression Severity and Impairment Scale; Pan/Ag = panic disorder with or without agoraphobia; PDSS = Panic Disorder Severity Scale; PHQ-9 = Patient Health Questionnaire- 9 item; PTSD = posttraumatic stress disorder; RCADS = Revised Children's Anxiety and Depression Scale; RCT = randomized controlled trial; RLX = relaxation training program; SAD = social anxiety disorder; SCARED = Screen for Child anxiety Related Emotional Disorders–Child and Parent Reports; SCAS = Spence Children's anxiety Scale; SCID-IV = Structured Clinical Interview for Axis I DSM-IV Disorders; SD = Separation Disorder; Soc.P = social phobia; SP = specific phobia; STAI = State-Trait Anxiety Inventory; TAU = Treatment As Usual; T-CBT = Transdiagnostic Behavior Therapy; T-GCBT = group- delivered transdiagnostic cognitive behavior therapy; T-iCBT = internet-delivered transdiagnostic cognitive behavior therapy; UK = United Kingdom; UP = Unified Protocol; UP-A = Unified Protocol for the Treatment of Emotional Disorders in Adolescence; UP-C = Unified Protocol for the Treatment of Emotional Disorders in Children; USA = United States of America; WLC = waiting list control.

[a] Recruitment method; [b] Taking into account the overall sample; [c] Number of participants included in the final analysis of the study and used in our meta-analysis; [d] Follow up is in months; [e] Not included in the study (---)

1.3.   Treatments

Of the 48 included studies, 13 evaluated protocols designed to treat mainly anxiety disorders while 33 were intended to treat both anxiety and depressive disorders (Table 4). However, as stated in the methods section, all studies that included patients with depressive symptoms and reported pre- to posttreatment depression outcomes were included in the depression outcomes' analyses. The duration of the treatment in the included studies ranged from 4 to 18 sessions, with an average of 9.14 sessions (SD = 3.99). In 22 studies the treatment was delivered over the Internet; in the remaining 26 it was delivered face to face (in 17 studies in a group format, whereas in 9 in an individual format). The bulk of the studies (23) were conducted in Australia, followed by 18 in the US, 3 in England, 1 in Iran, 1 in Brazil, 1 in Japan, and 1 in Sweden. The studies tested 22 different transdiagnostic protocols. The most common ones were the Unified Protocol (present in 6 studies), the Wellbeing Course (present in 9 studies), with their different variations, and the Transdiagnostic-Group CBT (present in 5 studies) (see Table 4).

Lastly, in relation to the treatment components, we found the following:

o   All studies included psychoeducation and relapse prevention.

o   Exposure was included in all studies except for the one by Essau et al. (2014)

o   Cognitive restructuring was present in all studies except for those by Chu et al. (Chu, Colognori, Weissman, & Bannon, 2009; Chu et al., 2016).

o   Additionally, behavioral activation was included in 33 studies. It was not included in the following studies: (Bullis et al., 2015; De Ornelas Maia et al., 2013; Ellard et al., 2010; Espejo et al., 2016; Farchione et al., 2012; Lotfi et al., 2014; Norton et al., 2004; Norton & Hope, 2005; Norton, 2008; Norton, 2012; Norton & Barrera, 2012; Schmidt et al., 2012; Titov et al., 2010).

o   Problem solving was included in 25 studies: (Bilek & Ehrenreich-May, 2012; Chu et al., 2016; De Ornelas Maia et al., 2013; Dear et al., 2015; Dear et al., 2011; Essau et al., 2014; Fogliati et al., 2016; Kayrouz et al., 2015; Kayrouz et al., 2016; Kirkpatrick, Manoukian, Dear, Johnston, & Titov, 2013; Mullin et al., 2015; Newby et al., 2013; Newby, Mewton, Williams, & Andrews, 2014; Queen et al., 2014; Titov et al., 2013; Titov et al., 2015a; Titov et al., 2016; Titov et al., 2015b; Wuthrich et al., 2016; Wuthrich & Rapee, 2013).

o   Relaxation strategies were included in 29 studies whilst it was not included in the following studies: (Bilek & Ehrenreich-May, 2012; Bullis et al., 2015; Chu et al., 2009; Chu et al., 2016; Ejeby et al., 2014; Ellard et al., 2010; Espejo et al., 2016; Farchione et al., 2012; Gros, 2014; Lotfi et al., 2014; McEvoy & Nathan, 2007; Newby et al., 2014;

Norton, 2008; Norton & Barrera, 2012; Norton, 2012; Schmidt et al., 2012; Wuthrich et al., 2016; Wuthrich & Rapee, 2013).

o Response prevention was included in 15 studies: (Bilek & Ehrenreich-May, 2012; Bullis et al., 2015; De Ornelas Maia et al., 2013; Ellard et al., 2010; Espejo et al., 2016; Farchione et al., 2012; Gros, 2014; Ito et al., 2016; Lotfi et al., 2014; Norton et al., 2004; Norton & Hope, 2005; Norton, 2008; Queen et al., 2014; Schmidt et al., 2012).

o Mindfulness was included in 7 studies: (Bullis et al., 2015; De Ornelas Maia et al., 2013; Ellard et al., 2010; Farchione et al., 2012; Ito et al., 2016; Queen et al., 2014).

1.4.   Risk of bias within studies

Table 5 provides an overview of the potential biases of the studies. The RCTs (21 studies) were assessed in 6 categories whereas the uncontrolled studies (27 studies) were only assessed in 3 categories. Taking into account only the RCTs, 11 studies (52.38%) reported low risk of bias on random sequence generation, 6 studies (28.57%) were assessed with low risk of bias on allocation concealment, and all RCTs reported high risk of bias on blinding of outcome assessment, since in all cases self-report outcome measures were used for the analyses. Taking into account all 48 studies, both RCTs and uncontrolled studies, 27 (56.25%) reported low risk of bias on handling incomplete outcome data, whereas all studies were assessed as having unclear bias on selective reporting. Finally, all studies reported low risk of bias in the other sources of bias categories.

Table 5. Risk of bias in the included studies.

Study	Selection bias		Detection bias	Attrition bias	Reporting bias	Other bias
	Random sequence generation	Allocation concealment	Blinded of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
T-CBT vs. Controls						
Bolton et al., 2014	Low	Low	High	Low	Unclear	Low
Farchione et al., 2012	High	High	High	Low	Unclear	Low
Johnston et al., 2011	Low	Unclear	High	High	Unclear	Low
Mullin et al., 2015	Unclear	Unclear	High	Low	Unclear	Low
Newby et al., 2013 (1)	Low	Low	High	Low	Unclear	Low
Norton et al., 2004	Unclear	Unclear	High	High	Unclear	Low
Norton & Hope, 2005	Unclear	Unclear	High	High	Unclear	Low
Schmidt et al., 2012	Low	Low	High	Low	Unclear	Low
Titov et al., 2010 (1)	Low	Unclear	High	High	Unclear	Low
Titov et al., 2011	Low	Unclear	High	High	Unclear	Low
Titov et al., 2013	Low	Unclear	High	Low	Unclear	Low
Wutrich & Rapee, 2013	Low	Low	High	Low	Unclear	Low
Wutrich et al., 2016	Low	Unclear	High	Low	Unclear	Low
Uncontrolled T-CBT						
Bullis et al., 2015	---	---	---	Unclear	Unclear	Low
Dear et al., 2011	---	---	---	Low	Unclear	Low
De Ornelas et al., 2013	---	---	---	Unclear	Unclear	Low
Ellard et al., 2010 (1)	---	---	---	Unclear	Unclear	Low
Ellard et al., 2010 (2)	---	---	---	High	Unclear	Low
Espejo et al., 2016	---	---	---	High	Unclear	Low
Gros 2014 (1)	---	---	---	High	Unclear	Low
Gros 2014 (2)	---	---	---	High	Unclear	Low
Ito et al., 2016	---	---	---	Low	Unclear	Low
Johnston et al., 2014	---	---	---	Low	Unclear	Low
Kayrouz et al., 2015	---	---	---	Low	Unclear	Low
Kayrouz et al., 2016	---	---	---	Low	Unclear	Low
Kirpatrick et al., 2013	---	---	---	Low	Unclear	Low
McEvoy & Nathan, 2007	---	---	---	High	Unclear	Low
Newby et al., 2013 (2)	---	---	---	Low	Unclear	Low
Newby et al., 2014	---	---	---	Low	Unclear	Low
Norton, 2008	---	---	---	Low	Unclear	Low
Titov et al., 2010 (2)	---	---	---	High	Unclear	Low
Titov et al., 2015a (1)	---	---	---	Unclear	Unclear	Low
Titov et al., 2015a (2)	---	---	---	Unclear	Unclear	Low
Titov et al., 2016 (1)	---	---	---	Low	Unclear	Low
Titov et al., 2016 (2)	---	---	---	Low	Unclear	Low
Titov et al., 2016 (3)	---	---	---	Low	Unclear	Low
T-CBT vs other therapies						
Dear et al., 2015	Low	Low	High	Low	Unclear	Low
Ejeby et al., 2014	Unclear	Low	High	Low	Unclear	Low
Fogliati et al., 2016	Unclear	Unclear	High	Low	Unclear	Low
Lotfi et al., 2014	Unclear	Unclear	High	High	Unclear	Low
Norton, 2012	Unclear	Unclear	High	High	Unclear	Low
Norton & Barrera, 2012	Unclear	Unclear	High	Low	Unclear	Low
Titov et al., 2015b	Unclear	Unclear	High	Low	Unclear	Low
Children and adolescents						
Bilek & Ehrenreich, 2012	---	---	---	High	Unclear	Low
Chu et al., 2009	---	---	---	Low	Unclear	Low
Chu et al., 2016	Low	Unclear	High	Low	Unclear	Low
Essau et al., 2014	---	---	---	High	Unclear	Low
Queen et al., 2014	---	---	---	Unclear	Unclear	Low

1.5.   Results of individual studies

Figures 2 to 9 show the effect size (Hedge's *g*), with its standard error, variance, confidence interval, *z*-value and *p*-value for each study on the considered outcomes (anxiety and depression).

Below, we report the results of the 10 meta-analyses conducted after grouping the studies according to the age sample (adults vs. youth), the existence of a control group (RCTs vs. uncontrolled), the type of control group (WLCG or other therapies), and the outcome (anxiety vs. depression).

a) **Pre- to post- meta-analytic anxiety outcomes in adult – RCTs** (Fig. 2)**.** Of the 12 studies included, 10 reported a significant reduction in self-reported anxiety ($p < .05$), whereas 2 studies did not (Farchione et al., 2012; Wuthrich et al., 2016). Using the random-effects model, the pooled effect size was large, and the heterogeneity was significant ($g = .80$; Q (11) = 39.91; $I^2 = 72.44$; $p < .001$).

b) **Pre- to post- meta-analytic anxiety outcomes in adult – uncontrolled studies** (Fig. 2). Of the 23 studies included, 21 reported a significant reduction in self-reported anxiety ($p < .02$), whereas one did not (Ellard et al., 2010). Pooling the uncontrolled studies, the pooled effect size and the heterogeneity were large and significant ($g = 1.02$; Q (22) = 388.01; $I^2 = 94.33$; $p < .001$).

Finally, pooling together all the studies, the effect size was large, and the heterogeneity was significant ($g = 0.91$; Q (34) = 535.22; $I^2 = 93.65$; $p < .001$). Moreover, the differences between RCTs and uncontrolled studies on pre- and post-anxiety measures were not significant (Q (1) = 1.57; $p = .21$).

c) **Pre- to post- meta-analytic depression outcomes in adults - RCTs** (Fig. 3). All of the 12 studies included reported a significant reduction in self-reported depression ($p < 0.05$). Using the random effects model and combining the RCTs, the pooled effect size was large, and the heterogeneity was not significant ($g = .72$; Q (11) = 14.64; $I^2 = 24.87$; $p = .20$).

d) **Pre- to post- meta-analytic depression outcomes in adults – uncontrolled studies** (Fig. 3). Of the 22 studies included, 19 reported a significant reduction in self-reported depression ($p < .05$), whereas 3 did not (Bullis et al., 2015; Ellard et al., 2010). Combing the uncontrolled studies, the effect size was high, and the heterogeneity was significant ($g = 1.08$; Q (21) = 301.15; $I^2 = 93.03$; $p < .001$).

Pooling together all the studies, the effect size was large, and the heterogeneity was significant ($g = 0.82$; Q (33) = 441.33; $I^2 = 92.52$; $p < .001$). Moreover, the differences

Group by Study type	Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
RCT	Bolton et al., 2014	0,407	0,109	0,012	0,194	0,620	3,740	0,000	Anxiety
RCT	Farchione et al., 2012	0,652	0,371	0,138	-0,076	1,380	1,756	0,079	Anxiety
RCT	Johnston et al., 2011	1,069	0,199	0,040	0,679	1,460	5,366	0,000	Anxiety
RCT	Mullin et al., 2015	2,492	0,513	0,263	1,488	3,497	4,863	0,000	Anxiety
RCT	Newby et al., 2013 (1)	0,874	0,212	0,045	0,459	1,289	4,128	0,000	Anxiety
RCT	Norton & Hope, 2005	1,388	0,533	0,284	0,344	2,433	2,605	0,009	Anxiety
RCT	Schmidt et al., 2012	0,928	0,223	0,050	0,491	1,365	4,163	0,000	Anxiety
RCT	Titov et al., 2010 (1)	0,754	0,236	0,056	0,292	1,215	3,198	0,001	Anxiety
RCT	Titov et al., 2011	0,780	0,243	0,059	0,304	1,255	3,215	0,001	Anxiety
RCT	Titov et al., 2013	0,799	0,178	0,032	0,450	1,147	4,487	0,000	Anxiety
RCT	Wutrich & Rapee, 2013	0,815	0,268	0,072	0,290	1,341	3,040	0,002	Anxiety
RCT	Wutrich et al., 2016	0,057	0,176	0,031	-0,287	0,401	0,323	0,746	Anxiety
RCT		0,800	0,125	0,016	0,555	1,045	6,400	0,000	
Uncontrolled	Bullis et al., 2015	1,031	0,441	0,195	0,166	1,896	2,336	0,019	Anxiety
Uncontrolled	Dear et al., 2011	0,891	0,219	0,048	0,462	1,320	4,068	0,000	Anxiety
Uncontrolled	De Ornelas et al., 2013	0,686	0,305	0,093	0,089	1,283	2,252	0,024	Anxiety
Uncontrolled	Ellard et al., 2010 (1)	0,588	0,276	0,076	0,048	1,128	2,135	0,033	Anxiety
Uncontrolled	Ellard et al., 2010 (2)	0,587	0,320	0,103	-0,041	1,215	1,832	0,067	Anxiety
Uncontrolled	Espejo et al., 2016	0,585	0,155	0,024	0,280	0,889	3,765	0,000	Anxiety
Uncontrolled	Gros 2014 (1)	1,165	0,438	0,192	0,306	2,024	2,657	0,008	Anxiety
Uncontrolled	Gros 2014 (2)	1,071	0,297	0,088	0,489	1,652	3,610	0,000	Anxiety
Uncontrolled	Ito et al., 2016	0,672	0,292	0,085	0,099	1,245	2,298	0,022	Anxiety
Uncontrolled	Johnston et al., 2014	1,210	0,343	0,118	0,537	1,882	3,526	0,000	Anxiety
Uncontrolled	Kayrouz et al., 2015	0,830	0,408	0,166	0,031	1,629	2,035	0,042	Anxiety
Uncontrolled	Kayrouz et al., 2016	1,178	0,167	0,028	0,851	1,505	7,057	0,000	Anxiety
Uncontrolled	Kirpatrick et al., 2013	0,949	0,457	0,209	0,053	1,846	2,076	0,038	Anxiety
Uncontrolled	McEvoy & Nathan, 2007	0,372	0,087	0,008	0,201	0,543	4,269	0,000	Anxiety
Uncontrolled	Newby et al., 2013 (2)	0,958	0,105	0,011	0,752	1,164	9,114	0,000	Anxiety
Uncontrolled	Newby et al., 2014	0,987	0,067	0,004	0,855	1,118	14,744	0,000	Anxiety
Uncontrolled	Norton, 2008	1,050	0,178	0,032	0,701	1,399	5,899	0,000	Anxiety
Uncontrolled	Titov et al., 2010 (2)	0,940	0,203	0,041	0,543	1,338	4,637	0,000	Anxiety
Uncontrolled	Titov et al., 2015a (1)	1,811	0,038	0,001	1,736	1,886	47,150	0,000	Anxiety
Uncontrolled	Titov et al., 2015a (2)	1,715	0,120	0,014	1,480	1,950	14,280	0,000	Anxiety
Uncontrolled	Titov et al., 2016 (1)	1,236	0,109	0,012	1,023	1,449	11,390	0,000	Anxiety
Uncontrolled	Titov et al., 2016 (2)	1,297	0,116	0,013	1,069	1,524	11,173	0,000	Anxiety
Uncontrolled	Titov et al., 2016 (3)	1,261	0,115	0,013	1,037	1,486	11,006	0,000	Anxiety
Uncontrolled		1,017	0,120	0,014	0,782	1,253	8,460	0,000	

Figure 2. Forest plot of the efficacy of T-CBT on self-reported anxiety (pre-post effect sizes in adults). The filled squares represent the overall effect sizes. All RCTs used waiting list control except for Wutrich et al., (2016) that used a discussion group. The decimals are separated with a coma

e) **Uncontrolled pre- to follow-up meta-analytic anxiety outcomes in adults** (Fig. 4)**.** A total of 22 studies (taking into account uncontrolled studies and T-CBT vs. Controls studies) included follow up, 21 of which reported a significant reduction in self-reported anxiety (*p* <.05), whereas 1 study did not (Ellard et al., 2010). Using the random-effects model, the pooled effect size was large and the heterogeneity significant (*g* = 1.24; *Q* (21) = 251.39; I^2 = 91.65; *p* < .001).

f) **Uncontrolled pre- to follow up meta-analytic depression outcomes in adults** (Fig. 5)**.** A total of 22 studies (taking into account uncontrolled studies and T-CBT vs Controls studies) included follow up, 21 of which reported a significant reduction in self-reported depression (*p* < .05), whereas 1 study did not (Ellard et al., 2010). Using the random-

effects model, the pooled effect size was in the high range and the heterogeneity was significant ($g = 1.19$; $Q (21) = 279.32$; $I^2 = 92.48$; $p < .001$).

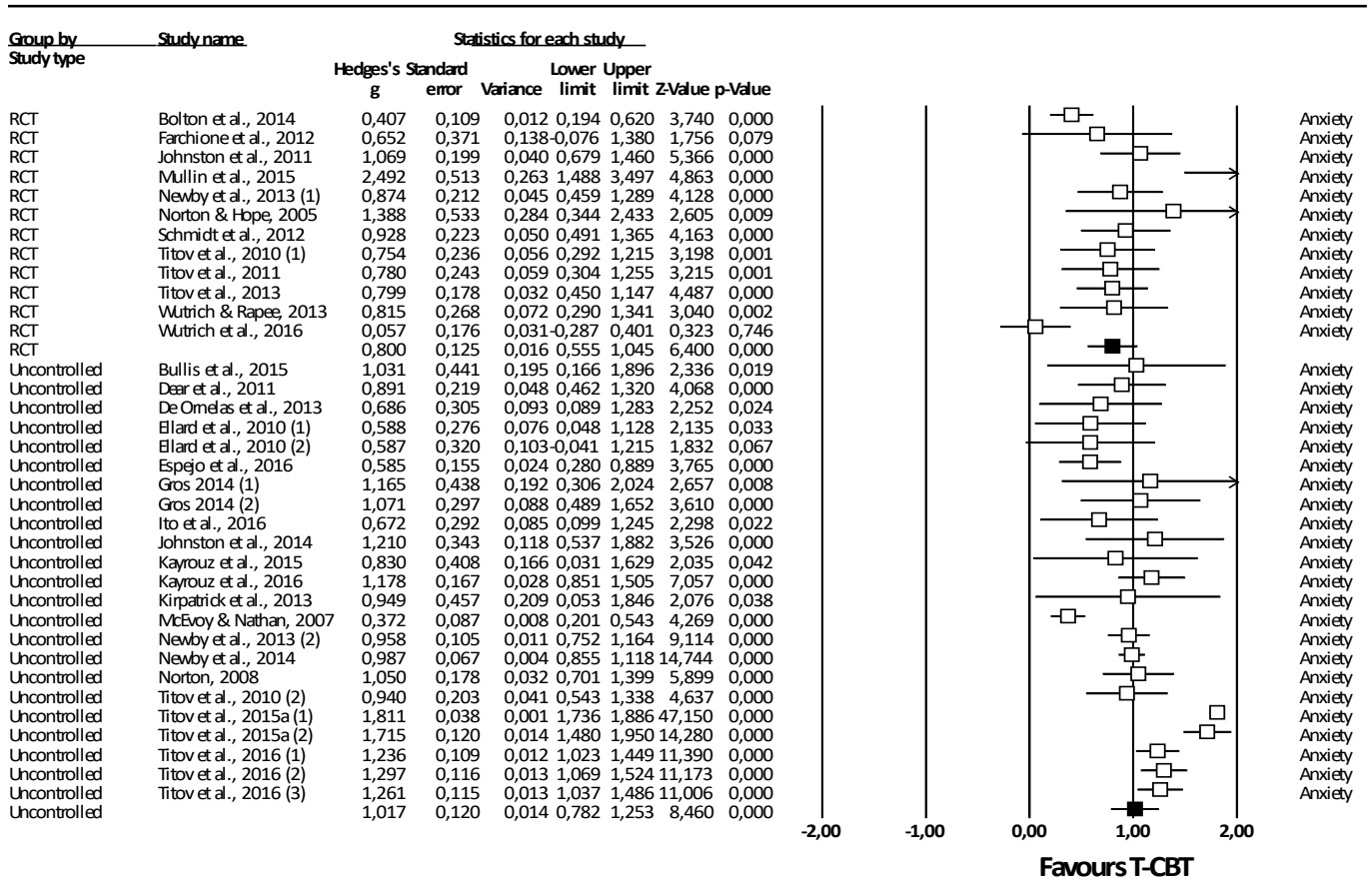| Group by Study type	Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value		
RCT	Bolton et al., 2014	0,694	0,111	0,012	0,477	0,911	6,266	0,000		Depression
RCT	Farchione et al., 2012	0,882	0,379	0,143	0,140	1,624	2,331	0,020		Depression
RCT	Johnston et al., 2011	0,711	0,193	0,037	0,333	1,089	3,688	0,000		Depression
RCT	Mullin et al., 2015	1,133	0,409	0,168	0,331	1,936	2,768	0,006		Depression
RCT	Newby et al., 2013 (1)	0,770	0,210	0,044	0,359	1,181	3,674	0,000		Depression
RCT	Norton et al., 2004	1,992	0,595	0,354	0,826	3,157	3,349	0,001		Depression
RCT	Schmidt et al., 2012	0,635	0,217	0,047	0,209	1,060	2,925	0,003		Depression
RCT	Titov et al., 2010 (1)	0,538	0,232	0,054	0,084	0,992	2,324	0,020		Depression
RCT	Titov et al., 2011	0,728	0,241	0,058	0,255	1,201	3,015	0,003		Depression
RCT	Titov et al., 2013	0,829	0,178	0,032	0,479	1,178	4,647	0,000		Depression
RCT	Wutrich & Rapee, 2013	1,064	0,276	0,076	0,523	1,604	3,858	0,000		Depression
RCT	Wutrich et al., 2016	0,282	0,176	0,031	-0,063	0,628	1,601	0,109		Depression
RCT		0,716	0,073	0,005	0,572	0,860	9,738	0,000		
Uncontrolled	Bullis et al., 2015	0,586	0,374	0,140	-0,147	1,320	1,568	0,117		Depression
Uncontrolled	Dear et al., 2011	0,987	0,226	0,051	0,543	1,431	4,359	0,000		Depression
Uncontrolled	De Ornelas et al., 2013	1,035	0,345	0,119	0,359	1,711	2,999	0,003		Depression
Uncontrolled	Ellard et al., 2010 (1)	0,445	0,265	0,070	-0,075	0,965	1,678	0,093		Depression
Uncontrolled	Ellard et al., 2010 (2)	0,490	0,312	0,097	-0,121	1,101	1,572	0,116		Depression
Uncontrolled	Espejo et al., 2016	0,585	0,155	0,024	0,280	0,889	3,765	0,000		Depression
Uncontrolled	Gros 2014 (1)	1,370	0,476	0,227	0,436	2,303	2,876	0,004		Depression
Uncontrolled	Gros 2014 (2)	1,151	0,306	0,093	0,552	1,751	3,766	0,000		Depression
Uncontrolled	Ito et al., 2016	0,978	0,325	0,106	0,340	1,615	3,006	0,003		Depression
Uncontrolled	Johnston et al., 2014	0,952	0,311	0,097	0,342	1,562	3,059	0,002		Depression
Uncontrolled	Kayrouz et al., 2015	1,225	0,478	0,228	0,288	2,161	2,564	0,010		Depression
Uncontrolled	Kayrouz et al., 2016	1,151	0,165	0,027	0,827	1,475	6,961	0,000		Depression
Uncontrolled	Kirpatrick et al., 2013	1,203	0,508	0,258	0,207	2,199	2,368	0,018		Depression
Uncontrolled	McEvoy & Nathan, 2007	1,012	0,104	0,011	0,808	1,216	9,737	0,000		Depression
Uncontrolled	Newby et al., 2013 (2)	0,878	0,102	0,010	0,677	1,078	8,575	0,000		Depression
Uncontrolled	Newby et al., 2014	1,127	0,070	0,005	0,990	1,265	16,058	0,000		Depression
Uncontrolled	Titov et al., 2010 (2)	0,638	0,184	0,034	0,277	1,000	3,465	0,001		Depression
Uncontrolled	Titov et al., 2015a (1)	1,868	0,039	0,002	1,792	1,945	47,697	0,000		Depression
Uncontrolled	Titov et al., 2015a (2)	1,928	0,129	0,017	1,674	2,181	14,916	0,000		Depression
Uncontrolled	Titov et al., 2016 (1)	1,295	0,111	0,012	1,078	1,512	11,684	0,000		Depression
Uncontrolled	Titov et al., 2016 (2)	1,292	0,116	0,013	1,065	1,519	11,153	0,000		Depression
Uncontrolled	Titov et al., 2016 (3)	1,188	0,112	0,012	0,969	1,407	10,640	0,000		Depression
Uncontrolled		1,077	0,115	0,013	0,852	1,302	9,393	0,000		

Figure 3. Forest plot of the efficacy of T-CBT on self-reported depression (pre-post effect sizes in adults). The filled squares represent the overall effect sizes. All RCTs used waiting list control except for Wutrich et al., (2016), that used a discussion group. The decimals are separated with a coma.

g) **Pre- to post meta-analytic anxiety outcomes of T-CBT vs. other therapies** (Fig. 6).

Of the 7 studies included, only one (Fogliati et al., 2016) reported a significant reduction of anxiety with T-CBT in comparison with another treatment (in this case, DS-CBT). Using the random-effects model, the pooled effect size of the studies that compared T-CBT and DS-CBT was low and the heterogeneity was not significant ($g = .12$; $Q (4) = 6.52$; $I^2 = 38.68$; $p = .163$). Additionally, considering the two studies that compared T-CBT with TAU and relaxation training (Ejeby et al., 2014; Norton, 2012), the pooled effect size was low, and the heterogeneity was not significant ($g = .24$; $Q (1) = .09$; $I^2 = 0$; $p = .763$).

Lastly, pooling together all the studies that compared T-CBT with other therapies, the effect size in anxiety was low and the heterogeneity was not significant ($g = .14$; $Q (6) = 8.01$; $I^2 = 25.07$; $p = .238$).
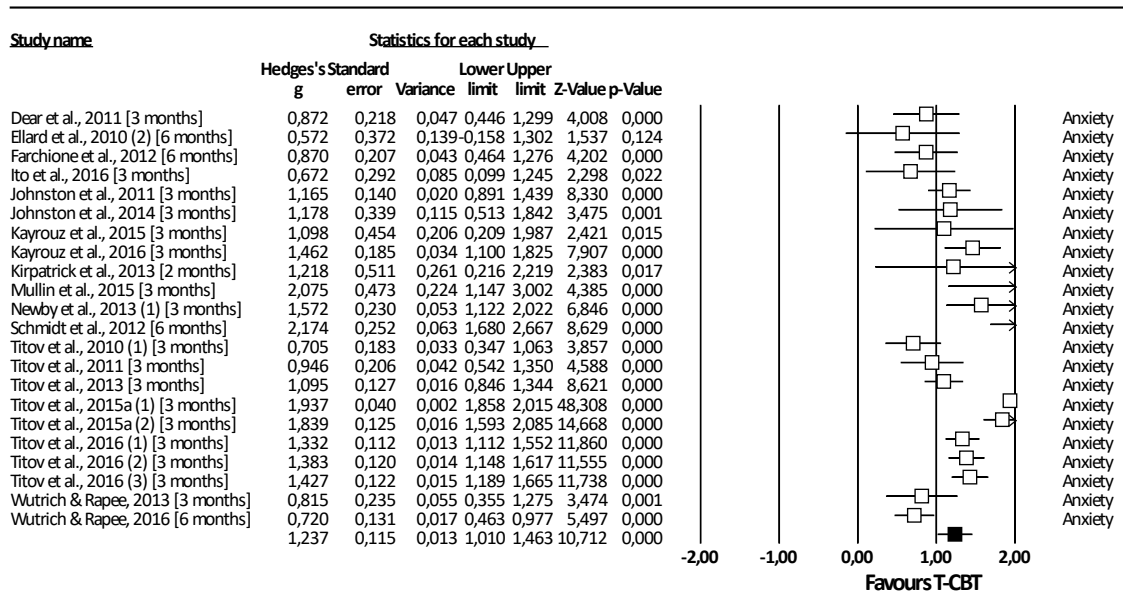
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value		
Dear et al., 2011 [3 months]	0,872	0,218	0,047	0,446	1,299	4,008	0,000		Anxiety
Ellard et al., 2010 (2) [6 months]	0,572	0,372	0,139	-0,158	1,302	1,537	0,124		Anxiety
Farchione et al., 2012 [6 months]	0,870	0,207	0,043	0,464	1,276	4,202	0,000		Anxiety
Ito et al., 2016 [3 months]	0,672	0,292	0,085	0,099	1,245	2,298	0,022		Anxiety
Johnston et al., 2011 [3 months]	1,165	0,140	0,020	0,891	1,439	8,330	0,000		Anxiety
Johnston et al., 2014 [3 months]	1,178	0,339	0,115	0,513	1,842	3,475	0,001		Anxiety
Kayrouz et al., 2015 [3 months]	1,098	0,454	0,206	0,209	1,987	2,421	0,015		Anxiety
Kayrouz et al., 2016 [3 months]	1,462	0,185	0,034	1,100	1,825	7,907	0,000		Anxiety
Kirpatrick et al., 2013 [2 months]	1,218	0,511	0,261	0,216	2,219	2,383	0,017		Anxiety
Mullin et al., 2015 [3 months]	2,075	0,473	0,224	1,147	3,002	4,385	0,000		Anxiety
Newby et al., 2013 (1) [3 months]	1,572	0,230	0,053	1,122	2,022	6,846	0,000		Anxiety
Schmidt et al., 2012 [6 months]	2,174	0,252	0,063	1,680	2,667	8,629	0,000		Anxiety
Titov et al., 2010 (1) [3 months]	0,705	0,183	0,033	0,347	1,063	3,857	0,000		Anxiety
Titov et al., 2011 [3 months]	0,946	0,206	0,042	0,542	1,350	4,588	0,000		Anxiety
Titov et al., 2013 [3 months]	1,095	0,127	0,016	0,846	1,344	8,621	0,000		Anxiety
Titov et al., 2015a (1) [3 months]	1,937	0,040	0,002	1,858	2,015	48,308	0,000		Anxiety
Titov et al., 2015a (2) [3 months]	1,839	0,125	0,016	1,593	2,085	14,668	0,000		Anxiety
Titov et al., 2016 (1) [3 months]	1,332	0,112	0,013	1,112	1,552	11,860	0,000		Anxiety
Titov et al., 2016 (2) [3 months]	1,383	0,120	0,014	1,148	1,617	11,555	0,000		Anxiety
Titov et al., 2016 (3) [3 months]	1,427	0,122	0,015	1,189	1,665	11,738	0,000		Anxiety
Wutrich & Rapee, 2013 [3 months]	0,815	0,235	0,055	0,355	1,275	3,474	0,001		Anxiety
Wutrich & Rapee, 2016 [6 months]	0,720	0,131	0,017	0,463	0,977	5,497	0,000		Anxiety
	1,237	0,115	0,013	1,010	1,463	10,712	0,000		

Figure 4. Forest plot of the efficacy of T-CBT on self-reported anxiety (uncontrolled pre-follow up effect sizes in adults).

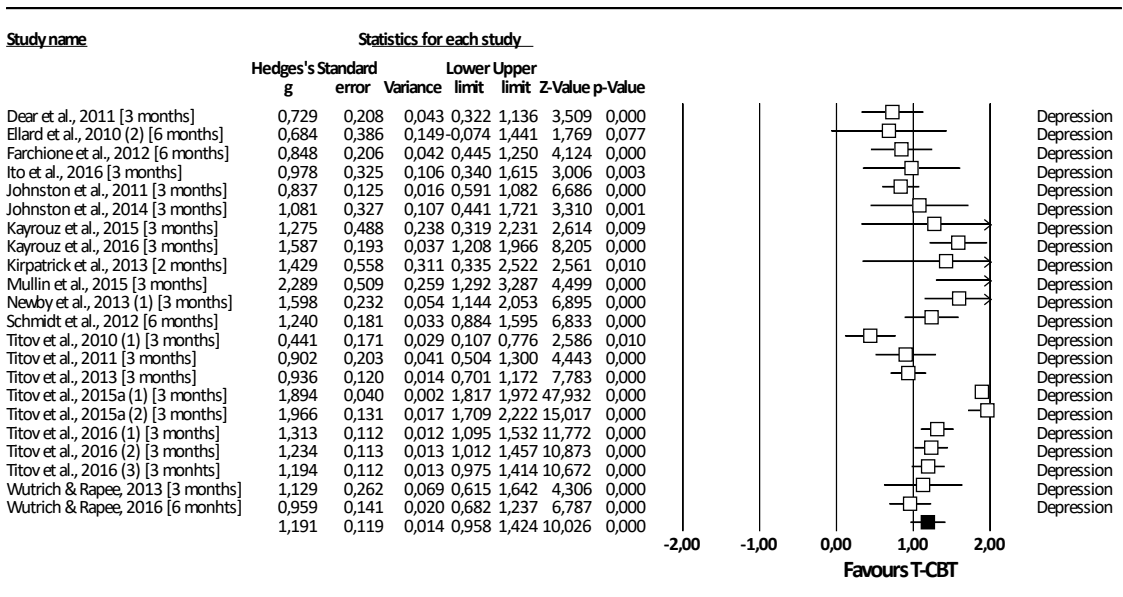| Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value		
Dear et al., 2011 [3 months]	0,729	0,208	0,043	0,322	1,136	3,509	0,000		Depression
Ellard et al., 2010 (2) [6 months]	0,684	0,386	0,149	-0,074	1,441	1,769	0,077		Depression
Farchione et al., 2012 [6 months]	0,848	0,206	0,042	0,445	1,250	4,124	0,000		Depression
Ito et al., 2016 [3 months]	0,978	0,325	0,106	0,340	1,615	3,006	0,003		Depression
Johnston et al., 2011 [3 months]	0,837	0,125	0,016	0,591	1,082	6,686	0,000		Depression
Johnston et al., 2014 [3 months]	1,081	0,327	0,107	0,441	1,721	3,310	0,001		Depression
Kayrouz et al., 2015 [3 months]	1,275	0,488	0,238	0,319	2,231	2,614	0,009		Depression
Kayrouz et al., 2016 [3 months]	1,587	0,193	0,037	1,208	1,966	8,205	0,000		Depression
Kirpatrick et al., 2013 [2 months]	1,429	0,558	0,311	0,335	2,522	2,561	0,010		Depression
Mullin et al., 2015 [3 months]	2,289	0,509	0,259	1,292	3,287	4,499	0,000		Depression
Newby et al., 2013 (1) [3 months]	1,598	0,232	0,054	1,144	2,053	6,895	0,000		Depression
Schmidt et al., 2012 [6 months]	1,240	0,181	0,033	0,884	1,595	6,833	0,000		Depression
Titov et al., 2010 (1) [3 months]	0,441	0,171	0,029	0,107	0,776	2,586	0,010		Depression
Titov et al., 2011 [3 months]	0,902	0,203	0,041	0,504	1,300	4,443	0,000		Depression
Titov et al., 2013 [3 months]	0,936	0,120	0,014	0,701	1,172	7,783	0,000		Depression
Titov et al., 2015a (1) [3 months]	1,894	0,040	0,002	1,817	1,972	47,932	0,000		Depression
Titov et al., 2015a (2) [3 months]	1,966	0,131	0,017	1,709	2,222	15,017	0,000		Depression
Titov et al., 2016 (1) [3 months]	1,313	0,112	0,012	1,095	1,532	11,772	0,000		Depression
Titov et al., 2016 (2) [3 months]	1,234	0,113	0,013	1,012	1,457	10,873	0,000		Depression
Titov et al., 2016 (3) [3 monhts]	1,194	0,112	0,013	0,975	1,414	10,672	0,000		Depression
Wutrich & Rapee, 2013 [3 months]	1,129	0,262	0,069	0,615	1,642	4,306	0,000		Depression
Wutrich & Rapee, 2016 [6 monhts]	0,959	0,141	0,020	0,682	1,237	6,787	0,000		Depression
	1,191	0,119	0,014	0,958	1,424	10,026	0,000		

Figure 5. Forest plot of the efficacy of T-CBT on self-reported depression (uncontrolled pre-follow up effect sizes in adults).

h) **Pre- to post meta-analytic depression outcomes in T-CBT vs. other therapies** (Fig. 7). None of the 6 studies included reported a significant reduction of depression with T-CBT in comparison with other treatments. Using the random-effects model, the pooled effect size of the studies that compared T-CBT and DS-CBT was low and the heterogeneity was not significant ($g = .05$; $Q(4) = 5.80$; $I^2 < 30.97$; $p = .215$). Additionally,

only one study compared T-CBT with other treatment that was not DS-CBT, specifically, with TAU (Ejeby et al., 2014): g = .12; *p* = .445.

Lastly, pooling together all the studies that compared T-CBT with other therapies, the effect size in depression was low and the heterogeneity was not significant (*g* = .06; Q (5) = 6.08; *I²*= 17.75; *p* = .299).
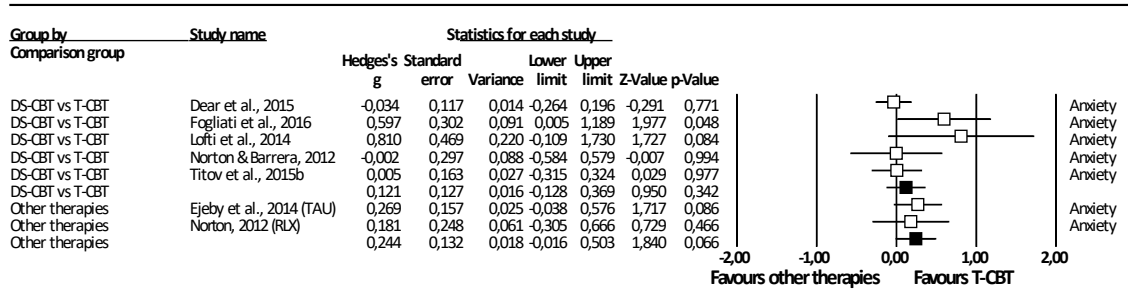
Group by Comparison group	Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value		
DS-CBT vs T-CBT	Dear et al., 2015	-0,034	0,117	0,014	-0,264	0,196	-0,291	0,771		Anxiety
DS-CBT vs T-CBT	Fogliati et al., 2016	0,597	0,302	0,091	0,005	1,189	1,977	0,048		Anxiety
DS-CBT vs T-CBT	Lofti et al., 2014	0,810	0,469	0,220	-0,109	1,730	1,727	0,084		Anxiety
DS-CBT vs T-CBT	Norton & Barrera, 2012	-0,002	0,297	0,088	-0,584	0,579	-0,007	0,994		Anxiety
DS-CBT vs T-CBT	Titov et al., 2015b	0,005	0,163	0,027	-0,315	0,324	0,029	0,977		Anxiety
DS-CBT vs T-CBT		0,121	0,127	0,016	-0,128	0,369	0,950	0,342		
Other therapies	Ejeby et al., 2014 (TAU)	0,269	0,157	0,025	-0,038	0,576	1,717	0,086		Anxiety
Other therapies	Norton, 2012 (RLX)	0,181	0,248	0,061	-0,305	0,666	0,729	0,466		Anxiety
Other therapies		0,244	0,132	0,018	-0,016	0,503	1,840	0,066		

Figure 6. Forest plot of the efficacy of T-CBT vs. DS-CBT/other therapies on self-reported anxiety (pre-post effect sizes in adults). The filled squares represent the overall effect sizes. DS-CBT = Disorder Specific Cognitive-Behavioral Therapy; RLX = Relaxation Training; TAU = Treatment as Usual. The decimals are separated with a coma.

Group by Comparison group	Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value		
DS-CBT vs T-CBT	Dear et al., 2015	0,295	0,162	0,026	-0,022	0,612	1,821	0,069		Depression
DS-CBT vs T-CBT	Fogliati et al., 2016	0,122	0,339	0,115	-0,542	0,787	0,361	0,718		Depression
DS-CBT vs T-CBT	Lofti et al., 2014	-0,057	0,448	0,200	-0,935	0,820	-0,128	0,898		Depression
DS-CBT vs T-CBT	Norton & Barrera, 2012	0,131	0,297	0,088	-0,451	0,713	0,440	0,660		Depression
DS-CBT vs T-CBT	Titov et al., 2015b	-0,202	0,136	0,019	-0,469	0,065	-1,482	0,138		Depression
DS-CBT vs T-CBT		0,045	0,124	0,015	-0,198	0,288	0,364	0,716		
Other therapies	Ejeby et al., 2014 (TAU)	0,119	0,156	0,024	-0,187	0,425	0,764	0,445		Depression
Other therapies		0,119	0,156	0,024	-0,187	0,425	0,764	0,445		

Figure 7. Forest plot of the efficacy of T-CBT vs. DS-CBT/other therapies on self-reported depression (pre-post effect sizes in adults). The filled squares represent the overall effect sizes. DS-CBT = Disorder Specific Cognitive-Behavioral Therapy; RLX = Relaxation Training; TAU = Treatment as Usual. The decimals are separated with a coma.

i) **Pre- to post meta-analytic anxiety outcomes in children/adolescents** (Fig. 8). Of the 5 studies included, 2 (Bilek & Ehrenreich-May, 2012; Queen et al., 2014) reported a significant reduction in self-reported anxiety (*p* < .05), while 3 studies did not (Chu et al., 2009; Chu et al., 2016; Essau et al., 2014). Using the random-effects model, the pooled effect size was moderate, and the heterogeneity was not significant (*g* = .45; *Q* (4) = 2.73; *I²* < .001; *p* = .604].
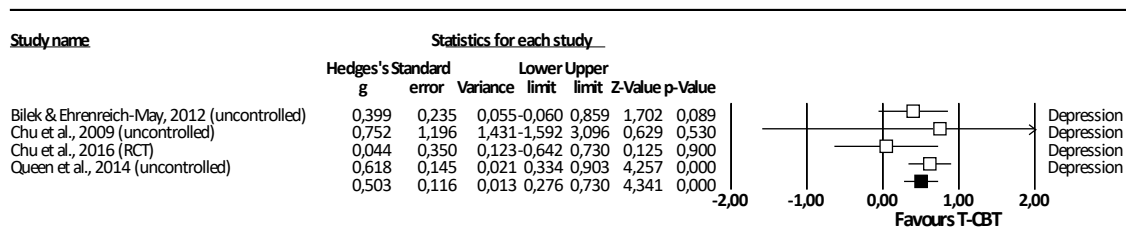
Study name	Statistics for each study							
	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
Bilek & Ehrenreich-May, 2012 (uncontrolled)	0,493	0,239	0,057	0,024	0,962	2,059	0,039	Anxiety
Chu et al., 2009 (uncontrolled)	0,355	0,988	0,976	-1,581	2,291	0,359	0,720	Anxiety
Chu et al., 2016 (RCT)	0,502	0,354	0,125	-0,192	1,196	1,417	0,157	Anxiety
Essau et al., 2014 (uncontrolled)	0,276	0,146	0,021	-0,010	0,561	1,890	0,059	Anxiety
Queen et al., 2014 (uncontrolled)	0,611	0,145	0,021	0,327	0,896	4,207	0,000	Anxiety
	0,454	0,091	0,008	0,276	0,632	4,992	0,000	

Figure 8. Forest plot of the efficacy of T-CBT on self-reported anxiety (pre-post effect sizes in children and adolescents). The filled square represents the overall effect size. RCT = Randomized Controlled Trial. The decimals are separated with a coma.

j) **Pre- to post meta-analytic depression outcomes in children/adolescents** (Fig. 9). Of the 4 studies included, 1 (Queen et al., 2014) reported a significant reduction in self-reported depression ($p < 0.05$), while 3 studies did not (Bilek & Ehrenreich-May, 2012; Chu et al., 2009; Chu et al., 2016). Using the random-effects model, the pooled effect size was moderate, and the heterogeneity was not significant ($g = .50$; Q (3) = 2.59; $I^2 < .001$; $p = .460$).

Study name	Statistics for each study							
	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
Bilek & Ehrenreich-May, 2012 (uncontrolled)	0,399	0,235	0,055	-0,060	0,859	1,702	0,089	Depression
Chu et al., 2009 (uncontrolled)	0,752	1,196	1,431	-1,592	3,096	0,629	0,530	Depression
Chu et al., 2016 (RCT)	0,044	0,350	0,123	-0,642	0,730	0,125	0,900	Depression
Queen et al., 2014 (uncontrolled)	0,618	0,145	0,021	0,334	0,903	4,257	0,000	Depression
	0,503	0,116	0,013	0,276	0,730	4,341	0,000	

Figure 9. Forest plot of the efficacy of T-CBT on self-reported depression (pre-post effect sizes in children and adolescents). The filled square represents the overall effect size. RCT = Randomized Controlled Trial. The decimals are separated with a coma.

1.6.   Risk of bias across studies

Publication bias was tested using Duval and Tweedie's random effects model trim and fill procedure (2000). In relation to the effect sizes, the trim-and-fill method suggested that 3 out of 10 of the conducted meta-analyses studies should be trimmed, reducing the effect sizes in the following meta-analysis: pre-post adult anxiety in the RCTs (from $g = .80$ to $g = .62$), pre-post adult depression in the RCTs (from g = .72 to $g = .65$), and pre-post adult anxiety in T-CBT vs. DS-CBT (from $g = .12$ to .08).

1.7.   Subgroup analyses

Because we found some heterogeneity among the pre-post anxiety and depression outcomes in the uncontrolled studies and in the RCTs that compared T-CBT with a control

group (adult population), we decided to conduct a series of subgroup analyses. For the categorical moderator variable analyses, a random effects ANOVA model was used.

We found that using a self-reported diagnostic measure resulted in a higher effect size in comparison to using a face-to-face interview or a telephonic interview for both anxiety symptoms (Q (2) = 10.46; p = .005) and depression symptoms (Q (2) = 8.88; p = .012). In relation to the treatment components, the inclusion of problem solving strategies was associated with a higher effect size for depression (Q (1) = 4.44; p = .035). There were also significant group differences in relation to the participants' diagnosis (Q (2) = 7.13; p = .028) for depression symptoms. Specifically, those studies that did not report the participants' diagnosis resulted in higher effect sizes than those studies that only included participants with a clinical diagnosis and those that also included participants with a subclinical diagnosis. Finally, the variable treatment format (individual, group or internet) influenced outcomes for anxiety (Q (2) = 7.82; p = .020). The studies that applied an internet treatment had higher effect sizes than the group treatments and the individual treatments.

No indication was found that the effect sizes differed according to the country in which the study was conducted (taking into account USA and Australia, since most studies were conducted in those countries), other treatment components apart from problem solving (behavioral activation, mindfulness, relaxation training and response prevention), the applied protocol (considering the most used protocols: Unified Protocol, The Wellbeing Program/Course, the Norton Protocol), the recruitment method (community or clinical), the study design (RCT or uncontrolled) or the treatment target (anxiety or depression).

Meta-regression was used for the quantitative moderator variable analysis, finding that a higher number of treatment sessions was associated with lower effect sizes in anxiety (Z = -2.21; p = .027). No indication was found that the effect sizes differed according to the studies' publication date, the percentage of women in the sample, the percentage of participants with comorbid emotional disorders, the percentage of attrition, or the proportion of categories assessed as having a high or low risk of bias.

In relation to the pre-test to follow-up outcomes in adults, no indication was found that the effect sizes differed according to the follow-up period (3 or 6 months) for anxiety (Q (1) = .41; p = .524) or depression (Q (1) = .90; p = .343).

2. Study II[15]

2.1. Participants and baseline equivalence

The sample consisted of 151 adolescents, 90 in the UP-A group and 61 in the WLCG, in grades 9 and 10 (3º ESO and 4º ESO in the Spanish educational system), from an urban secondary school in the city of Madrid, Spain. The mean age of the total sample was 15.05 (SD = 1.14), and the sample was comprised of 82 girls (54.3%) and 69 boys (45.7%).

The Chi-squared test for categorical variables revealed no significant differences between groups at T1 in terms of the demographic variables. Liner Mixed Model Analyses (LMMs) taking into account the clustered nature of the data showed no significant differences for the primary outcome measures between the groups at T1 either ($p > 0.21$). Regarding secondary outcome measures, there were no differences between groups at T1 except for Satisfaction with Life Scale (SWLS) where the UP-A group had significantly higher satisfaction with life than the WLCG at baseline.

A participant in the UP-A group was found to be a consistent outlier at T2 in all outcome measures (he had always answered the first available answer choice in all questions) and therefore his data at T2 were excluded from the analyses.

2.2. Intervention effects on primary outcomes

At a descriptive level, between T1 and T3, the reported anxiety and depression levels declined for both the UP-A group and the WLCG, although this positive trend was stronger for the UP-A group. Intra-cluster correlation coefficients (ICCs) for all outcome measures ranged from 0.01 to 0.18. Repeated LMMS measurements found a significant main effect of time for the RCADS total score. There were no significant time*group interactions regarding

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[15] Content of this section (except for "Intervention effects for secondary outcomes" section that will be included in a future manuscript) was retrieved from the following submitted mansucript: **"The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents (UP-A) adapted as a school-based anxiety and depression prevention program: An initial cluster randomized controlled trial"** by J. García-Escalera, R.M. Valiente, B. Sandín, J. Ehrenreich-May, A. Prieto, & P. Chorot. [Under review in journal Behavior Therapy - July 2018]

the RCADS total score, CDN or EAN. Likewise, there were no significant time*group interactions regarding any RCADS total anxiety score or subscales.

2.3. Intervention effects on secondary outcomes

At a descriptive level, ICCs for all outcome measures ranged from 0.01 to 0.13. Repeated LMMS measurements found a significant main effect of time for the anxiety sensitivity score (CASI), the self-esteem score (SES), and the satisfaction with life score (SWLS). Therefore, self-reported anxiety sensitivity significantly decreased in both groups whilst self-esteem and satisfaction with life significantly increased in both groups.

Additionally, there was a significant time*group interaction regarding satisfaction with life (SWLS) favoring the WLCG. Pairwise comparisons adjusted for Bonferroni indicated that the WLCG's scores marginally significantly increased for satisfaction with life from T2 to T3 whilst there were no significant changes in the UP-A group's scores over time for this variable. Specifically, at T1 WLCG's scores were lower than the UP-A group's scores while at T2 the WLCG's scores were significantly marginally lower than the UP-A group scores and at T3 the scores for both groups were not significantly different.

Regarding top problems, severity of top problems was reported at least one time by 86 participants in the UP-A group (WLCG participants did not complete top problems). The following ICCS were obtained at each assessment point: 0.03 (first session), 0.01 (second session), 0.03 (ninth session) and 0.01 (at 3-month follow-up). Additionally, 70% of the students reported severity of 3 top problems, 21.1% of 2 top problems, 4.4% of 1 top problems and 4.4% of 0 top problems. At a descriptive level, severity of top problems decreased over time. LMMs showed that there was a significant effect of time regarding the mean severity of top problems (taking into account the four assessment points).

2.4. Exploratory subgroup analyses

2.4.1. Students currently in therapy *vs.* those not currently receiving additional therapy

At T2, 80 students in the UP-A group (72 at T3) and 57 (48 at T3) in the WLCG completed the questions regarding concurrent interventions.

A subgroup analysis of the adolescents who reported they had received therapy in prior three months ($n = 16$) showed no time*group interactions. However, excluding those 16 adolescents ($n = 135$), there was a marginally significant time*group interaction

regarding the RCADS Obsessive Compulsive Disorder (OCD) subscale, as well as a marginally significant time*group interaction regarding the RCADS Separation Anxiety Disorder (SAD) subscale, which implies that excluding the adolescents who received therapy, there were non-significant greater decreases in OCD symptoms and SAD symptoms in the UP-A group compared to the WLCG.

2.4.2. Low vs high emotional symptoms

As in previous research (Stallard et al., 2014), subgroup analyses were undertaken regarding the 10% of participants with the highest baseline anxiety and depression and the remaining 90% with the lowest anxiety and depression. A total RCADS score of ≥ 51 identified 10.6% of the participants and was used as a cut-off to categorize them as having either high emotional symptoms ($n = 16$) or low emotional symptoms (RCADS score of < 51, $n = 132$). Of the 16 adolescents with high emotional symptoms, 3 in the UP-A group and 1 in the WLCG reported receiving therapy and therefore were excluded from the analyses.

Subgroup analyses of the low-risk group ($n = 135$) using repeated measures LMMs showed no time*group interactions. However, in the high-risk group ($n = 12$) there were significant time*group differences regarding RCADS $_{total\ score}$, CDN and EAN, which implies that in the high-risk group, there was a significantly greater decrease in anxiety symptoms in the UP-A group (compared to the WLCG).

2.4.3. Completer status analyses

Completer analyses excluding the 11 youth who completed fewer than 7 sessions of the UP-A showed no significant patterns of difference from the findings described above in the intent-to-treat sample.

2.5. Exploratory predictors of efficacy analyses

A series of LMMs showed no gender*group, age*group, have been born in Spain or not*group, or interest in psychology*group interaction short-, or long-term effects on any primary outcome measure (changes in the total scores of the RCADS, CDN, or EAN).

2.6.   Results for measures completed at post-intervention only

The Satisfaction with the Program Questionnaire and the Discipline Problems during Sessions Questionnaire were completed at post-treatment by 80 adolescents (88.89% of those in the UP-A group).

Regarding "What did you like best about the program?", the adolescents most often answered "learned to control my emotions," "learned things about my emotions," and "the activities that we did in class." Regarding the question "What did you like the least?", most of the adolescents answered: "having homework," "other classmates interrupting and being loud when they should not have been," and "sometimes the information was repetitive."

Regarding discipline problems during sessions, the results showed that 68.3% of the students reported paying attention to most or almost all the sessions. Furthermore, 54.5% and 43.0% of the adolescents reported, respectively, to have taken the program seriously and to have tried their best when doing the in-class activities in many or almost all the sessions. Regarding undesirable behaviors, 29.1%, 13.9%, and 3.8% of students reported, respectively, to have talked to their classmates when they should not have, to have been reprimanded for their behavior, and to have worked on other assignments during sessions in many or almost all of the sessions.

3. Study III[16]

3.1.   Participants

The sample consisted of 28 adolescents in the ninth grade (3º ESO in the Spanish educational system) from an urban secondary school in Madrid (Spain). The mean age of the total sample was 14.67 (SD = 0.87; range = 13-17) and the sample was comprised of 16 girls (57.1%) and 12 boys (42.9%). Nine students (32.1%) were born in Spain while the rest (n = 17; 60.7%) were born outside of Spain, specifically (specifically, 17 were born in Central/South American countries, 1 was born in China and 1 in Romania).

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[16] Content of this section was retrieved from the following submitted manuscript: "**An open trial applying the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents (UP-A) adapted as a school-based prevention program**" by J. García-Escalera, P. Chorot, B. Sandín, J. Ehrenreich-May, A. Prieto, & R.M. Valiente. [Under review in journal Child and Youth Care Forum - July 2018]

3.2.   Intervention effects on primary outcomes

At a descriptive level, the participants showed positive trends for all of the primary outcome measures at post-intervention in comparison to pre-intervention except for the results associated with the CDN questionnaire. Repeated measures LMMs found a significant decrease for the RCADS Social Phobia Subscale and the RCADS Generalized Anxiety Disorder Subscale. Additionally, a marginally significant decrease was found for the RCADS total score, and the RCADS anxiety total score.

3.3.   Intervention effects on secondary outcomes

Repeated measures LMMs found a significant main decrease for anxiety and depression related interference (questionnaire EIDAN).

In relation to the top problems, their severity was reported at least once by 25 participants (89.29% of those who participated in the program). At the descriptive level, the severity of the top problems decreased from the first session to the fifth session and increased from the fifth session to the ninth session. Repeated measures LMMs showed that there was a significant decrease in the top problems' mean severity taking into account the three assessment points. Pairwise comparisons adjusted for Bonferroni's correction indicated that the top problem severity scores significantly decreased from the first session to the fifth session, whereas there were no significant changes from the fifth session to the ninth session, or from the first session to the ninth session.

3.4.   Feasibility

The parents' consent forms were returned for all of the students, although one parent actively requested that their child not take part in the questionnaire assessments but could participate in the sessions. A total of 21 and 27 participants completed the pre- and post-intervention, respectively, with a total of 20 participants (71.43%) completing both the pre- and post-intervention assessments.

3.5.   Acceptability

The Satisfaction with the Program Questionnaire was completed by 27 adolescents (96.43% of those who participated in the program). Most of the students answered that the program had helped them learn more about emotions and how they work, that they would recommend the program to other adolescents their age, and that they would try in the

future to apply the strategies that they learned in the program to their daily lives. In relation to the question "What did you like best about the program?", the most popular answers were "learned to control my emotions", "learned to face my fears", and "working in teams". In relation to the question "What did you like the least?", the most common answers were "nothing", "sometimes it was boring", and "sometimes the information was repetitive".

CHAPTER V. CONCLUSIONS

1. Main results

As mentioned in Chapter II, this doctoral thesis had two main objectives. First, increasing the knowledge on efficacy of T-CBT applied to adults, children and adolescents through meta-analytic techniques (Study I). Second, assessing the effectiveness of the Unified Protocol for the Transdiagnostic Treatment of Emotional Disorders in Adolescents (Ehrenreich-May et al., 2018) when adapted as a universal anxiety and depression preventive intervention through both a RCT (Study II) and an Open Trial (Study III).

1.1. Study I

Study I assessed the effectiveness of T-CBT for emotional disorders in adults, children and adolescents through meta-analytic techniques including 48 studies (21 RCTs and 27 uncontrolled studies) and a total of 6291 participants. In adults, overall effect sizes of T-CBT were large for anxiety and depression outcomes, as well as stable at follow up. Preliminary studies with children and adolescents, including 5 studies, showed pre- to posttreatment medium effect sizes both or anxiety and for depression outcomes.

Therefore, the results of Study I provide further support for the hypothesis that T-CBT is an effective treatment for reducing symptoms of anxiety and depression in adults, children and adolescents with anxiety and/or depressive disorders, or subthreshold anxiety or depression symptoms. In adults, results also provided further support for the hypothesis that the therapeutic gains of T-CBT are maintained at follow-up whereas in the case of children and adolescents this hypothesis could not be tested since only two of the included studies (Essau et al., 2014; Queen et al., 2014) provided follow-up data.

Based on previous meta-analyses on T-CBT, we had several hypotheses regarding potential moderators of treatment effect. First, we hypothesized that uncontrolled trials would be associated with larger effect sizes. Our results were in line with this hypothesis, since a significant difference was found between the effect size of RCTs (g = .072) and the effect size of uncontrolled studies (g = 1.08) on pre- and post- depression outcomes in adults. By contrast, non-significant larger effects regarding pre- and post- anxiety outcomes in adults were found for the uncontrolled studies (g = 1.02) compared to the RCTs (g =0.80).

Second, we predicted that the inclusion of behavioral activation as a treatment component would be associated with larger effect sizes for depression. Results showed a statistical trend (p = .08) suggesting that studies including behavioral activation (n = 23)

were (non-significantly) associated with larger effect sizes (g = 1.08) than studies not including this component for depression (g = 0.73).

Third, we predicted that internet-delivered treatments would have larger effect sizes compared to face-to-face treatments for anxiety and depression outcomes. Our results only supported this hypothesis in the case of anxiety outcomes in which the 19 studies reporting internet-delivered treatments were associated with larger effect sizes (g = 1.15) than the 9 studies reporting group treatments (g = 0.70) and that the 7 studies reporting individual treatments (g = 0.70) for anxiety outcomes.

Additionally, and in line with our hypothesis, a high proportion of the included studies showed an unclear or high risk of a biased estimate of effect according to the Cochrane Collaboration's tool for assessing risk of bias (Higgins & Green, 2011). This was consistent with previous meta-analyses on T-CBT for anxiety and depression (Newby et al., 2015; Reinholt & Krogh, 2014).

Lastly, we hypothesized that treatment effect of T-CBT would be at least as strong as DS-CBT. Analyses comparing these two therapies only included 5 studies and therefore are very preliminary. Nonetheless, the pooled effect size of the studies that compared both therapies was low, and the heterogeneity was not significant (both for anxiety and for depression), suggesting similar effectiveness of T-CBT and DS-CBT on emotional disorders although a lot more studies are needed to draw firm conclusions.

1.2. Studies II and III

Study II was an RCT conducted in Madrid (Spain) that included a total of 152 adolescents randomized to the intervention condition (the UP-A adapted as a universal preventive intervention program) or to the WLCG. The results of Study II were somewhat mixed, and we are not able to affirm that the data supported our hypothesis that the UP-A group would exhibit greater improvement on all primary and secondary outcome measures.

On the one hand, regarding primary outcome measures, results did not find significant effects of the intervention for anxiety and depression symptoms. As a matter of fact, an unexpected decline in anxiety and depression levels from pre- to post-treatment and follow-up was found both for the UP-A group and the WLCG. However, this decline was (non-significantly) stronger in the UP-A group for all primary outcome measures.

On the other hand, results also failed to find significant effects of the intervention for secondary outcome measures. Conversely, an unexpected decline in anxiety sensitivity was found in both groups as well as unexpected increases in self-esteem and satisfaction with life. Additionally, top problems severity (only assessed in the UP-A group) significantly

decreased along the four assessment points (first session, fifth session, ninth session and 3-month follow-up).

Regarding exploratory subgroup analyses, in line with our hypothesis, adolescents with greater emotional symptom severity that had not recently received additional therapy apart from the UP-A showed greater decrease in anxiety and depression symptoms in the UP-A group (compared to the WLCG). However, this result should be interpreted with caution since this subgroup only included 12 participants. Conversely, contrary to our hypothesis, completer subgroup analyses excluding the 11 adolescents in the UP-A group that assisted to fewer than 7 sessions showed no time*group interactions.

Regarding potential predictors of efficacy, age, gender, having been born in Spain or not, and interest in psychology did not appear as predictors of efficacy (no hypotheses had been made at this regard).

Additionally, in line with our hypothesis, results supported the feasibility of school-based implementation of the UP-A in a universal prevention group format with 87.8% of the participants achieving completion status. Lastly, results regarding satisfaction with the program partially supported our hypothesis regarding acceptability of the intervention. On the one hand, a high proportion of participants positively evaluated the program in terms of recommending the program to others or learning things, but on the other hand, participants showed only medium satisfaction when asked about the effectiveness of the program in helping them cope with life or about their enjoyment participating the program.

Study III involved an uncontrolled study including 28 adolescents randomized to the WLCG in Study II. The study did not include a follow-up period. In line with our hypothesis, intent-to-treat analyses showed significant declines in anxiety symptoms, specifically for social phobia and generalized anxiety disorder. Conversely, results did not support our hypothesis that there was going to be an improvement on depression symptoms. Regarding secondary outcomes, intent-to-treat analyses showed significant declines in top problems' mean severity and interference of anxiety and depression whereas results failed to find significant effects of the intervention on the other secondary outcome measures assessed.

Furthermore, and in line with our hypothesis, results supported the feasibility of school-based implementation of UP-A in a school-based universal prevention group format with 78.57% of the participants achieving completion status. Regarding acceptability of the intervention, participants reported overall moderate to high participant satisfaction when we were expecting high participant satisfaction.

The small effect sizes regarding reduction of anxiety and depressive symptoms in Studies II and III might be due to limits in statistical power to detect effects and not because the UP-A does not work when adapted as a preventive program. Nonetheless, in universal

prevention studies, small effect sizes usually involve larger effects for adolescents showing high levels of symptomatology and this should be of importance for adolescents, families and schools (Ahlen et al., 2015).

This doctoral thesis has hopefully served to increase awareness among the educative community on the importance of schools not only focusing on academic learning, but also on student mental health, especially because research points out that there is a bidirectional connection between mental health and academic outcomes. Specifically, externalizing problems have been shown to specially affect academic outcomes and poor academic achievement has been shown to specially affect internalizing problems (Suldo et al., 2014).

Overall, the findings from Studies II and III suggest that there is merit in continuing to deliver and evaluate the UP-A adapted as a universal preventive program or anxiety and depression.

2. Limitations and strengths of this doctoral thesis

2.1. Study I

The Study I presents several limitations that should be acknowledged, some of which were also presented in the Discussion Section of Study I.

First, in order to assess the effectiveness of T-CBT through meta-analytic techniques, only anxiety and depression outcome measures were taken into account, mostly because of the lack of other outcome measures present in many of the studies. However, including other outcome measures that evaluate symptoms of specific disorders, transdiagnostic variables or level of functioning would have been ideal to have a more complete and holistic vision of the effectiveness of T-CBT.

Second, only self-report measures were used to evaluate the effectiveness of T-CBT, and these measures are known to possibly be affected by situational factors and social desirability bias. Additionally, some generic measures of anxiety and depression may be more sensible to assess some disorders than others, which could influence the ability of these measures to assess sensitivity to change (McEvoy, Nathan, & Norton, 2009). Third, since a high proportion of the included studies were associated with a high risk of a bias estimate of effect, an exaggeration of the true effect of T-CBT could have been taken place in relation to the pooled estimates of this meta-analysis.

Fourth, we were not able to calculate controlled pre- to follow-up meta-analytic outcomes for anxiety and depression in adults since most of the included studies used

waitlist-controlled groups that were receiving treatment at the time the follow-up assessment took place. Therefore, what we know about the effectiveness of T-CBT at follow-up is limited. Fifth, this meta-analysis included 7 studies that did not report whether the diagnoses of the participants were in the clinical or in the subclinical range. It is crucial that we know whether T-CBT is efficacious both with clinical and with subclinical patients. Sixth, only preliminary conclusions can be made for the efficacy of T-CBT applied to children and adolescents as well as for the efficacy of T-CBT compared to DS-CBT since also only 5 studies with youth population as well as only 5 studies comparing these two types of CBT therapy were included in the meta-analysis.

Despite of the acknowledged limitations of this work, we reckon that this meta-analysis makes an important contribution to the field for the following reasons: 1) It included T-CBT studies that had not been previously examined; 2) Contrary to previous meta-analyses on T-CBT for anxiety and depression, it used a rigorous set of inclusion criteria, especially in terms of taking into account whether the examined studies had applied truly transdiagnostic interventions or not; 3) It applied a more rigorous formula to calculate the effect sizes that previous meta-analyses; 4) It did a comprehensive analysis of potential categorical and quantitative moderator variables; 5) It was the first meta-analysis truly reviewing and assessing the effects of studies applying T-CBT on children and adolescents' samples; 6) It offered a preliminary analysis of the efficacy of T-CBT compared to DS-CBT.

2.2. Studies II and III

Studies II and III present several limitations that should be acknowledged, some of which were also presented on the Discussion Section of each of these studies.

First, both studies included a small sample size: 151 adolescents (Study II) and 28 adolescents (Study III). Study III was underpowered prior to the study's start, whereas Study I ended up being underpowered because of higher than expected attrition rates and ICCs. Second, Study II included a waitlist control group when an active control group would have been better, whereas Study III lack the existence of a control group. Third, Study II included a short follow-up period of only three months and Study III did not include a follow-up period. Fourth, regarding recruitment, in both studies the adolescents were recruited from only one school, which could limit generalizability of the findings. Fifth, participants in both studies were not blinded to allocation when answers to outcome measure were obtained due to constraints established by the Ethical Research Committee.

Sixth, only self-report measures were used when using information from multiple sources would have been better and, on top of that, intervention adherence was only

measured by group leader self-report and this could have contributed to biased reporting. Seventh, using the same group leaders to administer the intervention for all classes may have limited the generalizability of findings. Eight, the intervention was not precisely designed to target the needs of ethnic minorities and economically disadvantaged youth who turned out to be present in a quite high proportion in Studies II and III.

Last, since the program was not embedded in the formal curriculum of the school and the classroom teachers were not directly involved in its delivery, it has not been able to continue once the study was over. However, since most of the teachers were in the classrooms whilst the program was delivered they might have been integrated the competencies taught by the program into the daily classroom activities.

Despite of all the reviewed limitations, we believe that Studies II and III made an important contribution to the field for the following reasons. First, these are the first studies worldwide examining the efficacy of the UP-A adapted as a universal preventive intervention and these studies propitiated the translation and the adaptation of the UP-A to Spanish for the first time worldwide.

Additionally, highly reliable assessment measures were used and, contrary similar studies, Studies II and III it assessed the efficacy of the intervention not only in reducing anxiety and depressive symptoms, but also on other variables including positive outcomes (e.g., quality of life), transdiagnostic constructs (e.g., anxiety sensitivity), and educational outcomes (e.g., school adjustment). From our point of view, the inclusion of educational outcomes was especially important since, historically, most of the studies on school-based mental health services have not included these kind of outcomes (Becker, Brandt, Stephan, & Chorpita, 2014; Hoagwood et al., 2007), even despite the fact that school administrators and teachers are mostly interested in educational outcomes. As result, the impact of school-based preventive interventions on educationally relevant behaviors is poorly understood (Hoagwood et al., 2007). Hopefully, this doctoral thesis helps shed some light on this subject.

We also believe it is valuable that Study II included subgroup analyses as well as preliminary predictors of treatment efficacy analysis. Furthermore, both studies assessed and reflected on the quality of adapted UP-A implementation, which has not been common in previous research.

Another strength of this doctoral thesis is the fact that the study protocol for Studies II and III were published (García-Escalera et al., 2017). Publishing study protocols is known to diminish the risk of selective reporting when publishing the results (Werner-Seidler et al., 2017).

Lastly, it is also worth pointing out that Studies II and III were conducted in Spain, therefore expanding knowledge of evidence-based preventive programs applied in South

European countries, given that most of the current evidence comes from the USA and other higher-income countries (Guerra & Duryea, 2017).

3. Future directions

3.1.   Efficacy of Transdiagnostic Cognitive Behavior Therapy

Future research could investigate the impact of T-CBT on higher-order and common factors (e.g., negative affectivity, anxiety sensitivity), on diagnosis-specific symptoms of emotional disorders as well as on primary and secondary comorbidities. We also encourage future studies applying T-CBT for emotional disorders to include not only self-report outcome measures but also clinician-rated outcome measures since most of the meta-analyses and systematic reviews on T-CBT to date have relied on self-report outcome measures.

Furthermore, future research on T-CBT should extend the knowledge of what is the best way to measure improvement for a patient diagnosed with more than one disorder: Should we consider that the intervention was effective once the patient does not present the primary disorder anymore regardless of what happened with the secondary disorder/s?, or should we only consider that the intervention was effective if the patient does not meet the full diagnostic criteria for any primary or secondary disorders?, or should we better rely on a functioning index as better evidence of the efficacy of the intervention? (Păsărelu, Andersson, Bergman Nordgren, & Dobrean, 2017).

Another question that remains unanswered is if T-CBT for emotional disorders is more suitable to patients with several primary and/or comorbid disorders or if it also makes sense to use with patients that present with specific symptom profiles (i.e., patients with one specific disorder). Additionally, future investigations are necessary to study the potential effects of T-CBT on nonspecific factors (e.g., therapeutic alliance, group cohesion, satisfaction with treatment) and attrition since potential disadvantages of this therapy could be related to heterogeneous groups of patients provoking group's content seen less relevant for some patients and diminishing group cohesiveness as a result (McEvoy et al., 2009).

Future research should also further compare T-CBT to DS-CBT and confirm initial findings from meta-analyses to date indicating that both forms of treatment are similarly efficacious. In future work, investigating whether patient preferences affect the degree of benefit experienced across T-CBT versus DS-CBT interventions might prove important (Newby, Twomey, Yuan Li, & Andrews, 2016). Furthermore, comparing the treatment cost-

effectiveness evidence of T-CBT *vs.* DS-CBT is also advisable for future research (Andersen, Toner, Bland, & McMillan, 2016), as well as assessing the efficacy of T-CBT compared to pharmacological treatments for emotional disorders (Newby et al., 2015).

Lastly, future studies of T-CBT should: 1) Make sure that they meet high standards for good methodological quality according to the Crochane Collaboration (Higgins & Green, 2011); 2) Calculate controlled pre- to follow-up outcomes using active control groups instead of waitlist control groups; 3) Clearly report the primary and comorbid diagnoses of the included participants; 4) Include children and adolescent samples; 5) Compare T-CBT to DS-CBT as well as to tailored CBT.

3.2.   Applying the UP-A as a universal preventive intervention

First of all, future research should be devoted to improving reach and availability of anxiety and depression prevention programs in schools, especially in Spain where these kind of preventive interventions (and preventive interventions in general) are lacking.

Regarding study design, several suggestions for future research could be made. First, randomization at the school-level is advised for future studies applying the UP-A adapted as a preventive intervention, since this kind of randomization protects against contamination (Werner-Seidler et al., 2017), a bias that may have reduced outcomes in Study II. Second, the use of active control groups (i.e., applying a structured program that does not include active elements of the prevention program) instead of waitlist control groups is strongly advised. Third, measuring program implementation fidelity should be a priority for future studies and the use of program leader self-report checklists to do so should be avoided (Werner-Seidler et al., 2017).

Regarding choosing appropriate outcome measures, future studies assessing the effectiveness of school-based preventive interventions should keep assessing the impact of the programs on academic outcomes since sustainability of these interventions partially depends on its ability to show their impact on academic achievement (Hoagwood et al., 2007). Future studies applying universal preventive programs should consider implementing the recommended practices for skill training (Durlak & DuPre, 2008), that is, sticking to sequenced or coordinated instructional steps, active learning methods, a focus on skill instruction, and explicit teaching of specific skills, since reviews have shown that programs that apply these practices for teaching skills are more effective than programs that do not (Payton et al., 2008).

Future studies should also assess whether applying several preventive programs in the same school (e.g., Universal *plus* Indicated, or Universal plus Selective) is more effective

that applying only one kind of preventive program (Payton et al., 2008). For instance, a stepped care approach could be adopted in which a universal program is delivered first, and it is then followed up with a selective or indicated preventive program for at risk or symptomatic children or adolescents who do not respond to the universal intervention (Werner-Seidler et al., 2017). Additionally, future research should also consider the potential of delivering booster sessions (face-to-face or computerized) in order to increase the prevention effects in the medium and long-term follow up (Werner-Seidler et al., 2017).

Furthermore, we need to keep investigating the effects of school-based anxiety and depression preventive interventions when used with low-income, urban samples since some reviews have found that school interventions are less effecting at improving mental health and educational outcomes on this population (Becker et al., 2014) and we also need to assess the importance and impact of parental involvement in universal anxiety and depression programs for adolescents.

3.3. Schools as contexts for the promotion and prevention of children's mental health

Probably, the majority of people would agree that schools should aim to "prepare academically, socially and emotionally literate young people who have the skills and emotional resilience necessary to navigate the uncertain of modern life" (pg. 233) (Cefai & Cavioni, 2015). However, in Spain, school-based prevention of mental health problems has a lot improve. We agree with Arauxo et al. that it seems that in Spain, universal or primary prevention of depression (and prevention of mental health problems in general) can wait (Arauxo, Cornes, & Fernández-Ríos, 2008). There are several issues that might be affecting the implementation and dissemination of universal mental health programs in Spain and we believe that policy makers, politicians and professionals should work on them: 1) Lack of professionals specialized on universal prevention programs; 2) Deficiencies in the university curriculum on this specific issue; 3) Deficient economic budget; 4) Political disinterest and apathy of the population; and 5) Lack of clarity about where these programs should be implemented (e.g., schools, hospitals, associations...) and who should implement them (e.g., teachers, mental health professionals, school counselors, etc.) (Arauxo et al., 2008). Additionally, we believe that it is a priority in Spain to work on ways to link the school system with the local mental health system as we have observed that school counselors sometimes struggle to connect children and adolescents to mental health services, especially in the case of families with low or low to medium socio-economic status.

We believe that schools need to go for a *whole school nonmedical approach* to mental health. That is, a framework that puts the school personnel at the center of mental health support and that includes: 1) mental health promotion and universal prevention for all students, 2) early recognition and intervention for students considered at risk in their social and/or emotional development (selective prevention), and, 3) indicated prevention, treatment or adequate derivation for those already experiencing mental health difficulties (Adelman & Taylor, 2009; Cefai & Cavioni, 2015). In order to achieve this, schools need to explicitly address social and emotional issues in the curriculum, as well as promote a whole school context that supports and reinforces the skills being learnt in the classroom as well as a school organization that enables the collaboration of all parties involved (school board, teachers, students, parents, the local community, and external support services) (Cefai & Cavioni, 2015).

But not only schools and policy makers have a lot of work to do regarding school-based mental health promotion. Us researchers need to set a new school mental health research agenda that prioritizes: a) the use of naturalistic resources within schools (e.g., teachers, school counselors) to implement and maintain mental health programs, b) the empowerment of the parents to take responsibility or the promotion of their children mental health as well as on their own wellbeing, and c) the development of effective and efficient models that integrate school-based universal, selective and indicated prevention of mental health problems (Atkins, Hoagwood, Kutash, & Seidman, 2010; Cefai & Cavioni, 2015). Additionally, mental health researchers and policy makers need to find ways to train teachers to have competence in "building healthy relationships with students, developing students' social and emotional learning, recognizing and responding to early signs of mental health difficulties, working collaboratively with colleagues, professionals, and parents in supporting students with mental health difficulties, as well as issues related to program implementation" (pg. 236) (Cefai & Cavioni, 2015). Lastly, researchers should become more active in public policy advocacy in order to increase funding for prevention research (Weissberg et al., 2003).

With the prevalence of mental health disorders increasing and the public mental health services not receiving enough economical support, it is critical that schools address the promotion of mental health and prevention of psychological disorders since schools are the place that has most access to children and young people.

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